UC San Diego School of Medicine

Rady Children's Hospital San Diego

Department of Pediatrics

12TH ANNUAL PEDIATRIC RESEARCH SYMPOSIUM

FRIDAY

APRIL 14, 2023

8:00 AM - 5:00 PM

POSTER SESSIONS

12:45 - 2:15 PM
4:45 - 5:30 PM
located in 1900

KEYNOTE SPEAKERS

Brookie Best, PharmD, MAS

Dean
Professor of Clinical Pharmacy and Pediatrics
Skaggs School of Pharmacy and Pharmaceutical Sciences
University of California, San Diego

Atul Butte, MD, PhD

Priscilla Chan and Mark Zuckerberg Distinguished Professor
Director, Bakar Computational Health Sciences Institute
University of California, San Francisco
Chief Data Scientist, University of California Health

PRESENTERS

SESSION ONE

NOVEL THERAPIES, ASOs & GENE THERAPY

Mark Kay, MD, PhD
Jennifer Puck, MD
Mark Walters, MD
Fyodor Urnov, PhD

SESSION TWO

ENVIRONMENTAL SCIENCE, CLIMATE CHANGE & HEALTHCARE

Manish Arora, BDS, MPH, PhD
Jack Gilbert, PhD
Julia Gohlke, PhD

SESSION THREE

ORGANOIDS & DEVELOPMENTAL DISEASES

Jack Parent, MD
In-Hyun Park, PhD
Bennett Novitch, PhD

UC San Diego School of Medicine
Department of Pediatrics

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Rady Children's Hospital San Diego

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12th Annual Pediatric Research Symposium

Program Schedule

Friday, April 14, 2023

8:00 – 8:10 **Welcome** (10)

Gabriel Haddad, MD
Distinguished Professor of Pediatrics and Neurosciences
Chairman of Pediatrics & Vice Dean, Children's Academic Programs
University of California, San Diego
Physician-In-Chief & Chief Scientific Officer
Rady Children's Hospital – San Diego

8:10 – 8:40 **Keynote Address: "Vision and Potential Collaborations with the Skaggs School of Pharmacy and Pharmaceutical Sciences"** (30)
(Introduction by Gabriel Haddad, MD)

Brookie Best, PharmD, MAS
Dean
UC San Diego | Skaggs School of Pharmacy and Pharmaceutical Sciences

NOVEL THERAPIES, ASOs & GENE THERAPY

Moderator Welcome: Tariq Rana
(8:40-8:45 – Clinical Relevance)

8:45 – 9:15 **"Unraveling the Biological Properties of Adeno-Associated Viruses for Enhanced Gene-Based Therapeutics"** (30)

Mark Kay, MD, PhD
Dennis Farrey Family Professor
Departments of Pediatrics and Genetics
Head, Division of Human Gene Therapy
Stanford University

9:15 – 9:45 **"Development of Gene Therapy for Artemis Deficient Severe Combined Immunodeficiency"** (30)

Jennifer Puck, MD
Professor of Pediatrics
Division of Allergy/Immunology and Blood and Marrow Transplantation
University of California San Francisco School of Medicine
and UCSF Benioff Children's Hospital San Francisco, CA

Program Schedule

continued

Friday, April 14, 2023

9:45 – 10:15 **"Novel Therapies, ASOs & Gene Therapy: Hemoglobinopathies"** (30)

Mark Walters, MD
Professor & Chief, Hematology Division
Dept. of Pediatrics, UCSF School of Medicine
Jordan Family Director, Blood & Marrow Transplant Program
UCSF Benioff Children's Hospital, Oakland

10:15 – 10:45 **"Scaling CRISPR to the Challenge of N=1 Genetic Disease in an Academic/Nonprofit Setting"** (30)

Fyodor Urnov, PhD
Professor of Molecular Therapeutics, MCB Department, UC Berkeley
Scientific Director, Innovative Genomics Institute

10:45 – 11:00 **B R E A K** (15)

ENVIRONMENTAL SCIENCE, CLIMATE CHANGE & HEALTHCARE

Moderator Welcome: Tina Chambers
(11:00-11:05 – Clinical Relevance)

11:05 – 11:35 **"Health Outcomes Across the Lifespan Following Extreme Weather Events: Mitigating and Adapting to Climate Change"** (30)

Julia Gohlke, PhD
Associate Professor, Department of Population Health Sciences Virginia Tech

11:35 – 12:05 **"Environmental Biodynamics: a Novel Exploration of the Time Dimension in Environmental Health Research"** (30)

Manish Arora, BDS, MPH, PhD, FICD
Professor and Vice Chair
Division Director, Environmental Health
Department of Environmental Medicine and Public Health
Icahn School of Medicine at Mount Sinai

12:05 – 12:35 **"Oceans and Human Health: A New Frontier"** (30)

Jack Gilbert, PhD
Associate Vice Chancellor for Marine Science
Professor, Department of Pediatrics and Scripps Institute of Oceanography
University of California, San Diego

12:35 – 1:50 **L U N C H & Poster Session** (75)

Poster Session – Room 1900
Please see booklet for abstracts

Program Schedule

continued

Friday, April 14, 2023

1:50 – 2:30	Closing Keynote: "Translating a Trillion Points of Data into Therapies, Diagnostics, and New Insights into Disease" (Introduction by Gabriel Haddad, MD) Atul Butte, MD, PhD Priscilla Chan and Mark Zuckerberg Distinguished Professor Director, Bakar Computational Health Sciences Institute University of California, San Francisco Chief Data Scientist, University of California Health	(40)

ORGANOIDS & DEVELOPMENTAL DISEASES

Moderator Welcome: Alysson Muotri
(2:30-2:35 – Clinical Relevance)

2:35 – 3:05	"Brain Organoid Models of Genetic Developmental and Epileptic Encephalopathies" Jack Parent, MD William J Herdman Professor of Neurology and Research Professor Michigan Neuroscience Institute, University of Michigan	(30)
3:05 – 3:35	"Generation and Utility of Regionalized Human Brain Organoids" In-Hyun Park, PhD Associate Professor of Genetics Yale Stem Cell Center, Yale University	(30)
3:35 – 4:05	"Distinct Neural Oscillation Activities and Deficits in Cortex and Hippocampus Assembloid Models of Genetic Epilepsy" Bennett Novitch, PhD Professor, Department of Neurobiology David Geffen School of Medicine at University of California, Los Angeles	(30)
4:05 – 4:20	Closing Remarks and Award Winners Announced	(15)
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UC San Diego School of Medicine

Rady Children's Hospital San Diego

KEYNOTE SPEAKER BIO

Brookie Best, PharmD, MAS

Dean
UC San Diego | Skaggs School of Pharmacy and Pharmaceutical Sciences

Brookie M. Best, PharmD, MAS is a Professor of Clinical Pharmacy and Pediatrics and the Dean of UC San Diego's Skaggs School of Pharmacy and Pharmaceutical Sciences (SSPPS), and the Department of Pediatrics, School of Medicine (SOM)-Rady Children's Hospital San Diego. She completed a Bachelor of Science degree at UC San Diego in Chemistry with an Emphasis in Chemical Education. She received her PharmD degree from UC San Francisco, and completed residency training in Pharmacy Practice at the UC San Diego Medical Center. Dr. Best was an NICHD/NIH Fellowship recipient in Pediatric Clinical Pharmacology Research, and completed a Master of Advanced Studies (MAS) in Clinical Research at UC San Diego.

Dr. Best specializes in pharmacokinetics – the processes by which a drug is absorbed, distributed, metabolized and eliminated by the body – and maternal/fetal and pediatric clinical pharmacology research. Her research efforts have focused on studying anti-HIV drugs in pregnant women, children and non-pregnant adults. She also studies drugs used to treat Kawasaki disease, the leading cause of acquired heart disease in children. She has specific interests and expertise in maternal-fetal clinical pharmacology, therapeutic drug monitoring of antiretrovirals, and penetration of antiretrovirals into the central nervous system. Dr. Best's research program encompasses projects with key state-wide, national and international HIV/AIDS and pediatric pharmacology collaborative research networks.

KEYNOTE SPEAKER BIO

Atul Butte, MD, PhD

Priscilla Chan and Mark Zuckerberg Distinguished Professor
Director, Bakar Computational Health Sciences Institute
University of California, San Francisco
Chief Data Scientist, University of California Health

Atul Butte, MD, PhD is the Priscilla Chan and Mark Zuckerberg Distinguished Professor and inaugural Director of the Bakar Computational Health Sciences Institute (bchsi.ucsf.edu) at the University of California, San Francisco (UCSF). Dr. Butte is also the Chief Data Scientist for the entire University of California Health System (health.universityofcalifornia.edu), the tenth largest by revenue in the United States, with 20 health professional schools, 6 medical schools, 6 academic health centers, 10 hospitals, and over 1000 care delivery sites. Dr. Butte has been continually funded by NIH for 20 years, is an inventor on 24 patents, and has authored nearly 300 publications, with research repeatedly featured in the New York Times, Wall Street Journal, and Wired Magazine. Dr. Butte was elected into the National Academy of Medicine in 2015, and in 2013, he was recognized by the Obama Administration as a White House Champion of Change in Open Science for promoting science through publicly available data. Dr. Butte is also a co-founder of three investor-backed data-driven companies: Personalis (IPO, 2019), providing medical genome sequencing services, Carmenta (acquired by Progenity, 2015), discovering diagnostics for pregnancy complications, and NuMedii, finding new uses for drugs through open molecular data. Dr. Butte trained in Computer Science at Brown University, worked as a software engineer at Apple and Microsoft, received his MD at Brown University, trained in Pediatrics and Pediatric Endocrinology at Children's Hospital Boston, then received his PhD from Harvard Medical School and MIT.

SPEAKER ABSTRACT

Environmental Biodynamics: A Novel Exploration of the Time Dimension in Environmental Health Research

Manish Arora BDS, MPH, PhD, FICD
Professor and Vice Chair
Division Director, Environmental Health
Department of Environmental Medicine and Public Health
Icahn School of Medicine at Mount Sinai

In his talk, Arora will discuss the importance of considering temporal dynamics of both the environment and human physiology when studying environmental influences on human health. He will share work on neurodevelopmental outcomes, such as autism spectrum disorder, where a gene-centric approach has produced limited advances and how a focus on environmental exposures provides a new path for discovery of biomarkers and treatments. He will also discuss technologies developed at his laboratory at the Mount Sinai School of Medicine and his journey as an immigrant scientist in the United States.

SPEAKER ABSTRACT

Oceans and Human Health: A New Frontier

Jack Gilbert, PhD
Associate Vice Chancellor for Marine Science
Professor, Department of Pediatrics and Scripps Institute of Oceanography
University of California, San Diego

The Human Microbiome in Precision Medicine
The human microbiome is a dynamic part of our physiology that plays a key role in managing health and individualized responses to diet and medicine. The immune system controls our interaction with the microbial world, and yet the microbial communities in our bodies are central to modulating the immune response. Changes in the human microbiome have substantial influence on atopy, neurological disorders, metabolic disorders, and a range of complex conditions and disease states. Microbiome-Wide Association Studies (MWAS) combined with novel quantitative multi-omic approaches are enabling us to use AI techniques to determine personalized responses to nutrition that drive diseases states and treatment efficacy. Through these innovations we are finally realizing the paradigm of precision medicine for facilitating patient care.

SPEAKER ABSTRACT

Health Outcomes Across the Lifespan Following Extreme Weather Events: Mitigating and Adapting to Climate Change

Julia Gohlke, PhD
Associate Professor, Department of Population Health Sciences
Virginia Tech

This talk will present epidemiological analyses of birth outcomes during and following extreme heat events and flooding events in the United States. These studies utilize a suite of remotely sensed observations to characterize weather extremes and floodwater extents for subsequent analysis of health risks at a fine spatio-temporal scale. The influence of urban and rural landscapes on neighborhood-level health risks and results of community-engaged research on the socioeconomic and cultural contexts for developing climate change adaptation strategies will be presented. Finally, characterization of birth outcomes associated with living in close proximity to surface mine sites contributes to evidence in the design of climate change mitigation strategies, including changes in resource extraction measures for energy production.

SPEAKER ABSTRACT

Unraveling the Biological Properties of Adeno-Associated Viruses for Enhanced Gene-Based Therapeutics

Mark A. Kay MD PhD
Dennis Farrey Family Professor
Departments of Pediatrics and Genetics
Stanford University

The AAV capsid can influence the epigenetic marking of rAAV delivered episomal genomes in a species dependent manner: Implications for human gene therapy

One of the limitations in rAAV vector development is the difficulty in predicting which AAV capsid will provide the most robust expression in human subjects due to the observed discordance in vector-mediated transduction between species. Novel approaches for screening chimeric AAV-capsid libraries provides an approach to select for AAVs with optimized properties. To date, our AAV-LK03 chimeric capsid selected in a humanized mouse liver model was the first used in clinical trials. For the IND enabling pre-clinical studies to support these trials, a surrogate capsid was required for rodent studies because this capsid does not express well in rodents or rodent cells. We have also isolated additional capsids with similar properties. We used AAV-LK03 to explore the mechanism that limits transduction in rodents. To our surprise, AAV-LK03 entered mouse and primate derived cells at similar concentrations. Nuclear uptake and conversion from single to double-strand episomes were also similar between species yet trangene expression and mRNA levels were about 100x lower in mouse vs human cells. We found the difference in gene expression was related to depleted histone H3 chemical modifications related to active transcription, namely H3K4me3 and H3K27ac, on the vector DNA in mouse compared to human cells. A single-amino acid insertion into the AAV-LK03 capsid (AAV-AM) enabled efficient transduction and the accumulation of active-related epigenetic marks on the vector chromatin in mouse without compromising transduction efficiency in human cells. Our study suggests that the capsid protein itself is involved in driving the epigenetic status of the vector genome, most likely during the process of uncoating. Programming viral chromatin states by capsid design may enable facile DNA transduction between vector and host species and ultimately led to rationale selection of AAV capsids for use in humans.

SPEAKER ABSTRACT

Distinct Neural Oscillation Activities and Deficits in Cortex and Hippocampus Assembloid Models of Genetic Epilepsy

Bennett Novitch, PhD
Professor, Department of Neurobiology
David Geffen School of Medicine at University of California, Los Angeles

Many neurodevelopmental disorders are associated with impairments in multiple cognitive domains. For example, while epilepsy is defined by recurrent spontaneous seizures resulting from hyperexcitable neural circuits, it is also highly associated with memory impairment and depression. Though widespread neural circuit dysfunction is apparent, it remains unclear whether a single upstream pathological driver has shared or unique effects on circuit function in distinct brain regions. We developed a pipeline for creating and comparing cortical-ganglionic eminence (GE) and hippocampus-GE assembloids. This approach allows for the intermixing of excitatory and inhibitory neurons and establishment of neural networks that exhibit distinct oscillatory activities. Like cortex, hippocampal assembloids display multifrequency neural oscillations, but additionally generated sharp wave ripple (SWR) complexes and stereotyped patterns of theta-gamma phase amplitude coupling (PAC), patterns of circuit activity that are associated with hippocampal learning and memory in vivo and not seen in cortical-GE preparations. Using assembloids generated from a patient afflicted with developmental epileptic encephalopathy-13 (DEE-13) due to a gain of function mutation in the SCN8A sodium channel, we found substantial hyperexcitability as well as a loss of sustained oscillatory activity in the cortex-GE fusions compared to isogenic controls. By contrast, DEE-13 hippocampus-GE assembloids did not show overt hyperexcitability, yet exhibited distinct activity changes associated with impaired function of hippocampal learning and memory circuits including reduced SWR frequency and disordered patterns of theta-gamma PAC. These changes were associated with a loss of certain groups of interneurons that were not seen in cortex-GE samples and were partially rescued by optogenetic activation of the residual interneurons. Together, these data suggest that: (1) hippocampus-GE and cortex-GE assembloids generate complex and distinct circuit activities and (2) analysis of both structures can provide insights into brain-region specific circuit changes arising from an identical pathogenic gene mutation.

SPEAKER ABSTRACT

Brain Organoid Models of Genetic Developmental and Epileptic Encephalopathies

Jack Parent, MD
William J Herdman Professor of Neurology and Research Professor
Michigan Neuroscience Institute, University of Michigan

Brain Organoid Models of Genetic Developmental and Epileptic Encephalopathies

Reprogramming somatic cells to a pluripotent state via the induced pluripotent stem cell (iPSC) method offers an increasingly utilized approach for neurological disease modeling with patient-derived cells. Many groups, including ours, have applied the iPSC approach to model severe genetic developmental and epileptic encephalopathies (DEEs) with patient-derived cells. These disorders are characterized by developmental delay, intellectual disability and typically severe epilepsy. Although most studies to date involve 2-D cultures of patient-derived neurons, brain organoids are increasingly being employed to explore genetic DEE mechanisms. We are applying this approach to understand PMSE (Polyhydramnios, Megalencephaly and Symptomatic Epilepsy) syndrome caused by STRADA loss of function, and Protocadherin-19 Clustering Epilepsy (PCE). I will discuss challenges and recent advances in the brain organoid field, and then describe our findings of robust structural phenotypes in PMSE related to hyperactivation of mechanistic target of rapamycin (mTOR) signaling. I will then present a new single rosette brain organoid model that we have developed and its application for studying neural tube defects and modeling PCE, an X-linked disorder that arises from brain mosaicism. Complementary work describing findings in a mouse model of PCE will also be presented. The brain organoid field is rapidly advancing, and our findings suggest that brain organoid approaches offer great promise for modeling malformations of neural development and genetic neurodevelopmental epilepsies.

SPEAKER ABSTRACT

Generation and Utility of Regionalized Human Brain Organoids

In-Hyun Park, PhD
Associate Professor of Genetics
Yale Stem Cell Center, Yale University

Brain organoids represent the 3D tissues that recapitulate the structure and function of the developing human brain. Much efforts have been made to advance the regionalization and to utilize the brain organoids to study human diseases. We developed region-specific cortical organoids and used them to study neurodevelopmental disorders, including autism spectrum disorders. However, current brain organoid systems mostly lack the resolution to recapitulate the development of finer brain structures with subregional identity, including functionally distinct nuclei in cortical or subcortical brain regions. We attemped to advance methods to converting human embryonic stem cells (hESCs) into thalamic organoids (ThOs) with transcriptionally diverse nuclei identities. Specifically, adding SHH ventralized the ThOs (vThOs) with a thalamic reticular nucleus (TRN) signature, a GABAergic nucleus located in the ventral thalamus. We further investigated the function of TRN-specific disease-associated genes PTCHD1 and ERBB4 during human thalamic development. Overall, the regionally defined vThOs present an excellent model system for understanding nuclei-specific development and pathology in the thalamus of the human brain.

SPEAKER ABSTRACT

Development of Gene Therapy for Artemis Deficient Severe Combined Immunodeficiency

Jennifer Puck, MD
Professor of Pediatrics
Division of Allergy/Immunology and Blood and Marrow Transplantation
University of California San Francisco School of Medicine
and UCSF Benioff Children's Hospital San Francisco, CA

Defects in the DNA repair enzyme Artemis/DCLRE1C result in Artemis deficient severe combined immunodeficiency (ART-SCID) by preventing normal T- and B-cell receptor rearrangement and also causing radiation-sensitivity in all tissues. Allogeneic transplantation for ART-SCID has been unsatisfactory due to graft resistance, toxicity from standard alkylating conditioning therapy, frequent graft versus host disease and incomplete immune reconstitution, prompting a trial at UCSF starting in June, 2018, of lentiviral gene addition therapy to autologous bone marrow stem cells. Our self-inactivating vector APro-ART contains the human DCLRE1C cDNA driven by its own 700 bp minimal promoter to achieve physiologic expression. Prior to re-infusion of ex vivo transduced autologous CD34+ cells, patients received precisely targeted, low dose busulfan at 25% of the standard ablative tissue exposure (20 mg*hr/L) to make space in the marrow for engraftment of gene-corrected cells. Twelve newly diagnosed ART-SCID infants have been treated, all of them presently healthy and 10 of them now followed for 15-54 months (median 36 months). All of these 10 have developed functional, gene-corrected T cells, with 7 to date also demonstrating B cell reconstitution. One infant with disseminated CMV infection prior to treatment required a second infusion of gene-corrected cells; and autoimmune hemolytic anemia has occurred in 5 patients, responsive to transient immunosuppression if clinically significant. Vector insertion sites have been diverse without clonal expansion, and the same vector insertions have been detected in mature cells of myeloid and lymphoid lineages, indicating gene correction of multipotent progenitors. Thus, lentiviral gene therapy, preceded by low-exposure, targeted busulfan, appears to be safe and effective. Next steps include expansion of the trial to multiple sites and treatment of older individuals with ART-SCID who have insufficient immunity despite prior allogeneic transplantation.

SPEAKER ABSTRACT

Scaling CRISPR to the Challenge of N=1 Genetic Disease in an Academic/Nonprofit Setting

Fyodor Urnov, PhD
Professor of Molecular Therapeutics, MCB Department, UC Berkeley
Scientific Director, Innovative Genomics Institute

A three-decade effort in viral gene therapy has definitively established its curative potential and, in specific cases, proven its commercial potential as well. Genome editing, which largely does not rely on viruses, represents the next wave of genomic therapies entering the clinic. In the 4 years since its CRISPR-Cas-based isoform began clinical development, > 200 subjects have been dosed on genome editing clinical trials for indications in oncology, non-malignant hematology (sickle cell disease and beta-thalassemia), infectious disease (HIV), a sensory system genetic disorder (LCA), a genetic disorder of lipid metabolism (HFH), and degenerative disease (TTR amyloidosis). The clinical track record has shown consistent promise, with the leading program – SCD/TDT – on-track for US approval in 2023. Current trends in manufacture and pricing, however, place in sharp focus the realistic possibility that the vast majority of Mendelian disease will never become targets for genome editing in the clinic: these are individually rare, yet at the present time the path to IND is near-congruent (time- and expense-wise) for an N=1 as for an N=10,000 indication. Here, a solution would be to leverage the inherently platform nature of CRISPR-Cas technology: for a given disease type (eg inborn errors of immunity or triplet expansion diseases), the entirety of the preclinical path can be kept invariant, with solely the target-specifying guide RNA changing between specific diseases. In principle, this could dramatically shorten the timeline and cost to clinic. Implementing this in practice will require formidable end-to-end innovation in how CRISPR therapies are designed, developed, and delivered to patients, with a key role for the academic/nonprofit sector. The Innovative Genomics Institute, in close collaboration with leading clinicians at UCSF and UCLA, is building one such vertically integrated solution to the “N=1” problem that focuses on Mendelian diseases in nonmalignant hematology and in neurology.

SPEAKER ABSTRACT

Novel Therapies, ASOs & Gene Therapy: Hemoglobinopathies

Mark Walters, MD
Professor & Chief, Hematology Division
Dept. of Pediatrics, UCSF School of Medicine
Jordan Family Director, Blood & Marrow Transplant Program
UCSF Benioff Children's Hospital, Oakland

Clinically significant hemoglobinopathies account for the most common hereditary disorders world-wide, for which a curative option and access to cure have been very limited. Several new methods that might expand these options by manipulating autologous hematopoietic stem cells are under development. These methods include: targeting hemoglobinopathy mutations for correction, creating alterations that re-induce fetal hemoglobin and augmenting the genome with a corrected globin gene, all of which show promise. In addition, some of these approaches are nearing or have achieved FDA approval. Because these therapies modify autologous hematopoietic stem cells and bypass the need for a well-matched allogeneic donor, the potential impact of these therapies is significant. This presentation will summarize each strategy and accompanying clinical trial development and outcomes, and include discussion about emerging toxicities after genomic manipulations that will require careful scrutiny in the short- and long-term.

Academic General Pediatrics, Developmental/Behavioral Pediatrics & Newborn Nursery

Poster 91

REDUCTION IN RATES OF REFUSAL OF INTRAMUSCULAR VITAMIN K IN NEWBORNS, A QUALITY IMPROVEMENT PROJECT

Sofia Aedo, Zohar McMurtry, CPNP-PC, Alison Wolf, CPNP, IBCLC, Christopher Longhurst, MD, MS, Julia Cormano, MD, FACOG, Denise Suttner, MD, Michelle Leff, MD, IBCLC, FAAP

Background: UC San Diego Health (UCSDH) has seen an increase in refusal of prophylactic vitamin K injections for newborns. In line with the most recent American Academy of Pediatrics policy statement, UCSDH sought to identify the possible factors driving this change and implement interventions with the goal to decrease refusal by 10% over a 6-month period.

Methods: Typical QI methodology was utilized. Baseline and post-intervention rates of vitamin K acceptance were obtained from EPIC's SlicerDicer. Rates of refusal were calculated from the rates of acceptance. The population as a whole and refusal rates by unit were evaluated.

Results: Root-cause analysis identified inconsistent prenatal education and inaccurate online information as major factors contributing to the increase in refusal. Interventions implemented by the time of reassessment included (1) a script to standardize vitamin K deficiency bleeding (VKDB) education during CenteringPregnancy meetings, (2) a meeting with the OB/GYN resident physicians to raise awareness of the increase of rates of refusals and emphasize the importance of prenatal education on VKDB, and (3) an educational session on VKDB for midwives. During the study period the rate of refusal for all newborns decreased from 5.9% to 5.5%, representing a 7% decrease in the rate of refusal. When separated by unit, the rate of refusal decreased by 7% in the postpartum units and by 15% in the birth center (Run Chart).

Conclusion: The overall, postpartum, and birth center population rates of refusal decreased, with the population who received the most interventions showing the most improvement. Future efforts will focus on all maternity clinics. More time is needed for proper evaluation of our current and planned interventions; we expect that targeting the root causes identified in this project will yield a further and sustained decrease in the rates of refusal of vitamin K injections for newborns at UCSDH.

Poster 1

A RETROSPECTIVE ANALYSIS ON WEIGHT GAIN AND SYMPTOMOLOGY IN ADOLESCENTS WITH ANOREXIA NERVOSA TREATED WITH ARIPIPRAZOLE AND OLANZAPINE AND ADOLESCENTS WITH AVOIDANT/RESTRICTIVE FOOD INTAKE DISORDER TREATED WITH MIRTAZAPINE

Millie Kirchberg, BS; Leo Meller, BS; Yueling Li, MD; Megan Shott, BS; Tamara Maginot, PhD; Walter Kaye, MD; Guido Frank, MD

Background: Anorexia nervosa (AN) is a severe psychiatric disorder characterized by extreme malnourishment and distorted body image. Avoidant/Restrictive Food Intake Disorder (ARFID) involves an inability to meet nutritional needs, however without fear of weight gain or body image struggles. There are currently no FDA approved medications for AN or ARFID. However, we have clinical evidence that the atypical antipsychotics aripiprazole and olanzapine are beneficial for AN, while the tetracyclic antidepressant mirtazapine improves treatment outcomes of ARFID.

Methods: This retrospective cohort study tests the efficacy of aripiprazole and olanzapine in AN (n=855) and mirtazapine in ARFID (n=177) at the medical behavioral unit at Rady Children's Hospital San Diego from Jan 2017- Dec 2022. Age, gender, duration of treatment, comorbid diagnoses, medications, height, weight, and weekly calorie consumption will be reviewed. The primary outcome measure will be weight gain and reduced core illness behaviors in relation to pharmacological treatment.

Results: In a smaller cohort of adolescents with AN (n=106), we found aripiprazole treatment led to greater increases in BMI compared to patients not on the medication ($F=4.578$, $p=0.035$). Presently, by incorporating a more robust sample size, we hope to further elucidate the potential beneficial effects of aripiprazole and olanzapine in AN and mirtazapine in ARFID. Our data analysis is on-going and we aim to showcase the preliminary findings at the time of presentation.

Conclusions: Given the limited treatment effectiveness for AN and ARFID, our work on aripiprazole, olanzapine and mirtazapine will inform clinicians and stakeholders the best medication management of these conditions.

Allergy, Immunology & Rheumatology

Poster 6

AGE AND LOCATION DIFFERENCES IN KAWASAKI DISEASE OCCURRENCE

Laurel DeHaan, Jennifer Burney, Dan Cayan, Chisato Shimizu, Charles Copeland, Jane Burns

Background: The etiology of Kawasaki disease (KD) has been elusive with immunologic and epidemiologic data suggesting different triggers in genetically susceptible hosts. Prof. Nakamura at Jichi Medical Center provided a data set of Japanese KD patients that includes information on over 400,00 patients from 1970 thru 2020, with detailed information on age and location.

Methods: The KD patient data were separated into age brackets and separated by region in order to assess descriptive statistics of each age group and each region individually. The analysis included time series, annual cycle, temporal correlations, and spatial correlations.

Results: The last 30 years witnessed a large increase in the number of older children with KD, with some prominent interannual fluctuations including a temporary dip in 2016-2017. In contrast, the number of infants that were afflicted with KD remained roughly constant over this period. Another important distinction across age groups is the annual cycle in KD occurrence, with that of infants being remarkably different from older children, and another clear distinction between that of toddlers and school-aged children. Over the 30-year period, there were some major changes in the annual cycles of different age groups. Most notable was a large shift in the peak month of occurrence for the 6 to 24-month-old age group starting in 2016. Differences were also seen between prefectures, but they were smaller than the differences between age groups.

Conclusions: The large differences in KD patterns between infants and older children suggest different triggers for KD may be operating. We suspect that infants respond to a trigger within the home while older children have a broader exposure outside the home. The changes in 2016 coincided with a government program wherein subsidies were provided daycare and nursery school. Further analysis may lead to new insights into the etiology of KD.

Poster 4

SARS-COV-2 SPIKE-SPECIFIC REGULATORY T CELLS (TREG) EXPAND IN MRNA BASED-VACCINATED HEALTHY DONORS SUGGESTING A ROLE FOR T CELL-MEDIATED IMMUNE REGULATION IN PREVENTING SEVERE SYMPTOMS IN COVID-19

Alessandra Franco*, Jaeyoon Song*, Alba Grifoni#, Alessandro Sette#
**University of California San Diego, Department of Pediatrics, Division of Allergy, Immunology and Rheumatology, La Jolla, CA*
#La Jolla Institute for Immunology, Center for Autoimmunity and Inflammation, Center for Infectious Disease and Vaccine Research, La Jolla, CA

Background: In healthy subjects that received mRNA-based vaccination, we found very numerous SARS-CoV-2 spike-specific regulatory T cell (Treg) that we believe protect from symptoms vaccinated subjects that contract COVID-19. The immunodominance of different SARS-CoV-2 peptides, measured by epitope-specific T cell responses revealed coordinated CD4+ and CD8+ T cell responses and a T cell memory phenotype comparable to COVID-19 pediatric and adult convalescent subjects that we previously studied.

Methods: Peripheral blood mononuclear cells (PBMC) derived from 16 healthy donors that received the three-vaccine administration within 8 months from blood drawing were stimulated in vitro 24 hours with a pool of SARS-CoV-2 spike peptides prior to study T cell activation by flow cytometry with the Activation Immune Markers (AIM) assay. Treg were further phenotypically and functionally characterized.

Results: CD4+ Th1 cells from all the 16 subjects responded to the spike proteins. Thirteen out of sixteen subjects showed a good CD8+ cytotoxic T cell (CTL) response, three subjects had a detectable but lesser CTL response. CD4+ CD25high Treg were numerous in circulation in all the 16 subjects and expressed the chemokine receptor CCR6 in a considerable percentage, suggesting T cell homing to the vascular endothelium, lungs and gut epithelial cells and brain. Treg developed memory being effector (TEM) and central (TCM) memory T cells. Their phenotype is comparable to natural Treg (nTreg). When we co-cultured spike-specific Treg with spike-specific CD4+ Th1, we found a strong inhibition of IFNg production by CD4+ Th1.

Conclusions: Treg were numerous in vaccine recipients, developed T cell memory and expressed CCR6 suggesting homing to tissues affected by inflammation in COVID-19. In co-culture experiments, Treg regulated pro-inflammatory Tcells. Phenotypically different from peripheral Treg (pTreg), SARS-CoV-2-specific Treg maybe primed from naïve T cells in tissues that synthetize the spike proteins.

Allergy, Immunology & Rheumatology (continued)

Poster 3

ENHANCED TYPE-1 RESPONSES IN PEDIATRIC TYPE-2 DISORDERS FOLLOWING DUPILUMAB

Jamie Casey Lee, Isaac Shamie, Yanfang Peipei Zhu, Lauren Loop, Lawrence Eichenfield, Bob Geng, Seema S. Aceves, Nathan E. Lewis, Ben A. Croker

Background: Dupilumab acts as a neutralizing antibody that targets the IL-4/IL-13 signaling pathway and has shown efficacy in the treatments of various Type 2 disorders including atopic dermatitis and asthma. Improved clinical outcomes necessitate a more comprehensive characterization of the biochemical mechanism underlying the efficacy of dupilumab on the human immune response.

Methods: In this study, we used mass cytometry (CyTOF) and lineage tracing of single-cells using mitochondrial single-cell ATAC-seq (mt-scATAC-seq) to perform longitudinal phenotyping of PBMCs and purified T cells in the blood collected from pediatric patients with moderate- to-severe asthma or atopic dermatitis prior to receiving dupilumab therapy, and again six months post-treatment.

Results: CyTOF immunophenotyping showed increased Th1 and Th17 cells following dupilumab treatment, consistent with mt-scATACseq analysis that revealed upregulation of IL-6, TNF, IFNa, and IFNg pathways accompanied by upregulation of Myc, E2F, MTORC1, PI3K-AKT, and p53 signaling intermediates, and was associated with upregulation of genes controlling apoptosis, the unfolded protein response, and oxidative phosphorylation. Changes in the frequency of T-cell clonal lineages in vivo were detected following dupilumab.

Conclusions: This study utilizes powerful genomics and immunophenotyping tools to characterize the therapeutic action of an IL-4/IL-13 antagonist on the human immune system. The data supports clone-specific effects of dupilumab in pediatric asthma and atopic dermatitis. This approach enables analysis of changes in gene networks in T-cell clones and populations following treatment. Upregulation of Type-1 signaling and changes at the clonal level suggest dupilumab restores the balance of Type-1 and Type-2 cytokine signaling in clonal populations of immune cells.

Poster 2

INFLIXIMAB FOR INTENSIFICATION OF PRIMARY THERAPY FOR PATIENTS WITH KAWASAKI DISEASE AND CORONARY ARTERY ANEURYSMS AT DIAGNOSIS

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Background: Kawasaki disease (KD) is an acute systemic vasculitis of unknown etiology that predominantly affects children <5 years of age. KD is the most common cause of acquired heart disease in children in developed countries with increasing incidence. Children with an initial echocardiogram that demonstrates coronary artery aneurysms (CAA, Z score ≥2.5) are at high risk for severe cardiovascular complications and should receive adjunctive anti-inflammatory therapy. We sought to determine if primary adjunctive infliximab treatment at a dose of either 5 or 10 mg/kg, compared with intravenous immunoglobulin (IVIG) alone, is associated with a greater likelihood of CAA regression in KD patients with CAA at the time of diagnosis.

Methods: This single-center observational study included children with acute KD and a Z score ≥2.5 at baseline. The primary outcome was the incidence of CAA regression to a Zmax < 2 on the last echocardiogram within two months of disease onset.

Results: Of the 168 KD patients, 111 received IVIG alone and 57 received primary adjunctive infliximab therapy: 39 received low-dose 5mg/kg and 18 received high-dose 10mg/kg infliximab within 48 hours of initiating IVIG. Incidence of CAA regression to a Zmax <2 within two months was statistically significant at 52%, 62% and 83% in the IVIG alone, IVIG + infliximab 5mg/kg, and IVIG + infliximab 10mg/kg respectively. The multivariable logistic regression model adjusting for age, sex, baseline Z max, and bilateral CAA at baseline, showed that IVIG plus 10mg/kg infliximab was significantly associated with a greater likelihood of CAA regression (adjusted OR: 4.45, 95% CI1.17-16.89, p=0.028) compared to IVIG alone. The difference between IVIG plus 5mg/kg infliximab and IVIG alone was not significant.

Conclusions: Primary adjunctive high-dose 10mg/kg infliximab treatment was associated with a greater likelihood of CAA regression in patients with CAA at the time of diagnosis.

Allergy, Immunology & Rheumatology (continued)

Poster 11

CHARACTERIZING THE IMMUNOPATHOGENESIS OF PATHOGEN TRIGGERED SEVERE CUTANEOUS ADVERSE REACTIONS

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Background: Severe cutaneous adverse reactions (SCAR) are a group of life-threatening idiosyncratic diseases that affect the skin and mucous membranes. SCAR are often triggered by medications, however, a subset of SCAR occur after bacterial or viral infection. Recently, the term Reactive Infectious Mucocutaneous Eruption (RIME) was created to describe severely painful mucocutaneous eruptions that typically occur in children. The immunopathogenesis is unknown. Our goal is to characterize the immunopathogenesis of RIME and to characterize response to prescribed immunosuppressive therapies.

Methods: Blood samples are obtained from patients with severe cutaneous adverse reactions prior to immunosuppressive therapy, after immunosuppressive therapy and upon recovery. Samples are analyzed using multiplex cytokine analysis and mass cytometry.

Results: In blood and blister fluid obtained from a patient with pathogen-triggered SCAR, we observed an upregulation in cytokines associated with cytotoxic T cells (ie IFNg, CXCL10) and monocyte/neutrophil activation (ie IL-6, IL-8). Using CyTOF, we have identified early infiltration of blister fluid with inflammatory monocytes.

Conclusion: In a single patient with pathogen-triggered SCAR, we have found early recruitment of inflammatory monocytes and a profile indicative of cytotoxic T cell activation. These results reflect similarities with published data in Drug-Induced SCAR, however, more high patients will need to be recruited to confirm these early observations. Better understanding of the underlying etiopathogenesis of RIME and other pathogen triggered SCAR will require early identification and recruitment of additional patients. Immunophenotypic and clinical profiling before immunosuppressive therapy, after immunosuppressive therapy and upon recovery will help build rationale for future clinical trials.

Poster 10

MURINE MODELS OF HUMAN DISEASE DELINEATE THE MECHANISMS OF NLRP3 INFLAMMASOME DRIVEN INFLAMMATION

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Background. The NLRP3 inflammasome is an intracellular, multiprotein complex that regulates the release of proinflammatory cytokines interleukin-(IL)-1β and IL-18, as well as cell death, in response to exogenous pathogens and endogenous danger signals. While first described in patients with a spectrum of rare autoinflammatory disorders known as the cryopyrin associated periodic syndrome (CAPS) and gain-of-function mutations in NLRP3, it is now clear that NLRP3 mediates inflammation in multiple common disorders. How the NLRP3 inflammasome can tailor an immune response to such diverse stimuli and drive a broad range of phenotypes remains unknown. Using novel murine models, we aimed to characterize the key stages of NLRP3 inflammasome assembly, activation and inflammatory effects.

Methods. We generated heterozygous Nlrp3 knockin mice carrying mutations reflecting the three different disorders across the CAPS spectrum: familial cold autoinflammatory syndrome, Muckle Wells syndrome, and neonatal-onset multisystem inflammatory disorder. Mice were bred to knockouts encoding genes required for inflammasome assembly, including ASC, caspase-1, caspase-11, and downstream mediators of inflammation such as gasdermin D, interleukins and related cytokine receptors. Resulting offspring were evaluated for growth/survival, effects on inflammatory cell populations and serum cytokines. In vitro evaluations were used to assess inflammasome activation in response to stimuli.

Results. Nlrp3 knockin mice generate an innate immune inflammatory phenotype, mimicking human CAPS disease, but uniquely in the reverse severity. Knockout of inflammasome assembly proteins showed greater survival, compared to knockouts of downstream mediators, though all had significant downregulation of serum cytokines. In vitro, bone marrow derived macrophages from Nlrp3 knockin mice demonstrated enhanced cytokine secretion and bypassed the requirement for a second activating signal.

Conclusions. Our murine models highlight the critical aspects of NLRP3 inflammasome driven inflammation, and the role of upstream and downstream mediators. The mechanisms uncovered in our knockin and knockout models may offer new therapeutic strategies for NLRP3-mediated disease.

Allergy, Immunology & Rheumatology (continued)

Poster 8

SUDDEN, UNEXPECTED DEATH IN YOUNG ADULTS DUE TO MISSED KAWASAKI DISEASE IN CHILDHOOD

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Background: In California, unexpected deaths outside a medical setting require an autopsy. We collaborated with the San Diego County Medical Examiner's Office (SDCMEO) to determine if young adults with missed Kawasaki disease (KD) were among those with sudden, unexpected death from cardiovascular causes.

Methods: From 2013 to 2022, there were 188 cases age 0-35 yrs with a cardiovascular (CV) cause of death who were autopsied at the SDCMEO. We excluded the following diagnoses: suicide, homicide, cancer, drug/alcohol abuse, congenital heart disease, morbid obesity, spontaneous coronary artery dissection, collagen vascular disease, and diabetes. The remaining causes of CV death were: arrhythmia, atherosclerosis, cardiomyopathy, hypertensive CV disease, myocardial infarction, and myocarditis. We further excluded 30 cases attributed to arrhythmia who had no pathologic findings in the heart. Autopsy reports will be screened for gross and histologic findings suggestive of post-KD vascular damage including calcification, recanalized thrombus, and thrombosed aneurysms.

Results: We identified 92 cases who met the inclusion and exclusion criteria. Review of autopsy reports is in progress. Although the case was outside the age range for our study but met inclusion criteria, the SDCMEO contacted us regarding a 42 yr old woman whose cause of death was myocardial infarction. We reviewed the autopsy report and histology that revealed thrombosed giant coronary artery aneurysms that are pathognomonic of KD. We interviewed the decedent's mother who described a prolonged febrile illness requiring hospitalization at age 19 yrs. for which there was no final diagnosis. The clinical description met criteria for KD.

Conclusions: The diagnosis of KD continues to be missed and individuals suffering from the complications of coronary artery aneurysm and myocardial fibrosis may only be diagnosed at autopsy.

Poster 9

LONG-TERM IMMUNOSUPPRESSION ASSOCIATED WITH DISRUPTION OF B-CELL POPULATIONS AND INCREASED INFECTION RISK

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Solid-organ transplant recipients receive long-term immunosuppression to prevent graft rejection, thereby leading to increased risk of infection. We sought to identify biomarkers of infection risk in pediatric solid-organ transplant recipients to better predict risk of infection in this population.

75 kidney and 20 liver pediatric transplant patients were analyzed in a single-center registry study. Immunologic labs, including lymphocyte subsets, immunoglobulins, and vaccine titers, were collected at 6-month intervals as a part of standard-of-care. Number of infections and immunosuppressive regimens were recorded in corresponding intervals. The association between immune parameters and number of infections was determined via linear mixed-effects regression model. Association between medications and immune parameters was analyzed via 2-sample t-test.

A higher ratio of naïve:memory B-cells was associated with increased risk of infection ($\beta=0.03$, $p<0.001$) with independent contributions from both the naïve B-cell percentage ($\beta=0.03$, $p=0.02$) and decreased memory B-cell percentage ($\beta=-0.02$, $p=0.005$), the latter driven by class-switched memory B-cells ($\beta=-0.03$, $p=0.006$). The β value indicates the increase in the absolute number of infections per 6-month time period for every unit increase in the immune variable by 1. No significant associations were found between number of infections and immunoglobulin levels or vaccine titers.

Mycophenolate mofetil (MMF) was associated with increased naïve:memory B-cell ratio ($\Delta=3.1$, $p=0.008$) driven by decreased memory B-cell percent ($\Delta=10.3\%$, $p<0.0001$), predominantly from the class-switched memory B cell component ($\Delta=6.81\%$, $p<0.0001$). In contrast, azathioprine was associated with decreased naïve:memory B-cell ratio ($\Delta=-5.1\%$, $p<0.0001$) driven by increased memory B-cell percent ($\Delta=15.0\%$, $p<0.0001$) from increased class-switched memory B-cells ($\Delta=10.6\%$ $p<0.0001$). MMF was associated with 0.63 more total infections/year ($\Delta=2.2$, $p=0.03$). Azathioprine and tacrolimus had no association with total infections/year.

An increase in the naïve:memory B-cell ratio may indicate increased infection risk, with MMF as the culprit. The ratio of naïve:memory B-cells has potential as a biomarker to predict infection risk in solid-organ transplant recipients.

Allergy, Immunology & Rheumatology (continued)

Poster 5

ENDOTHELIAL RESPONSE IN KAWASAKI DISEASE AND MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN

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Background: Although Kawasaki disease (KD) and Multisystem inflammatory syndrome in children (MIS-C) have similar signs and symptoms, the cardiovascular outcomes are very different and this may be reflected at the level of the endothelial cell (EC).

Methods: Echocardiographic data (coronary artery (CA) Z-scores= internal dimension of the CA normalized for body surface area and expressed as SD units from the mean, left ventricular ejection fraction (LVEF)) were compared between KD (n=207) and MIS-C (n=101) at Rady Children's Hospital San Diego. To understand the EC response, we performed RNAseq on cultured human umbilical vein ECs incubated with pre-treatment sera from KD (n=5), MIS-C (n=7), and healthy controls (n=3).

Results: CA Z-score ≥2 on the admission echo was detected in 61 (30%) of KD and 11(11%) of MIS-C. Although CA Z-scores in MIS-C patients normalized by 2 wks post-discharge, 22 (11%) and 8 (4%) of KD patients had Z-scores ≥2 at 2wks and ~3years, respectively. LV dysfunction (LVEF<55%) was observed in 8 (4%) of KD and 32 (32%) of MIS-C, which resolved within two weeks. In the EC RNAseq experiment, 41 differentially expressed genes (DEGs) were detected between KD and MIS-C (adjusted $p<0.05$, 2 fold-change). The majority (33 of 41, 80%) of DEGs between MIS-C and KD belonged to NFκB pathway including nine pro-survival genes that were increased in MIS-C. Comparing MIS-C to KD, differential expression analysis also found increased transcripts influencing autophagy (UBD, EBI3 and SQSTM1), and decreased transcripts influencing EndoMT (SNAI1, SNAI2 and ZEB1) and abnormal EC function (CYP26B1, TREH and NOS3).

Conclusion: Compared to KD, ECs in MIS-C had a pro-survival but abnormal function phenotype. These differences in EC response may influence the different cardiovascular outcomes in MIS-C and KD.

Poster 12

SUBGROUPS OF KAWASAKI DISEASE PATIENTS: A DATA-DRIVEN CLUSTER ANALYSIS

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Background: Kawasaki disease (KD) is an acute pediatric vasculitis. Although it is commonly referred to as a single disease, marked variability in its clinical manifestation and disease outcome has been observed. This study aims to identify clinical subgroups using a data-driven approach.

Methods: We analyzed phenotypic data from 1,016 KD patients diagnosed at Rady Children's Hospital-San Diego between 2002 and 2022. Patients were grouped by hierarchical clustering on principal components with k-means parcellation, based on 14 variables including age at onset, ten laboratory results, day of illness at the first intravenous immunoglobulin (IVIG) infusion and echocardiographic measures of coronary artery diameters at diagnosis. To explore the biological underpinnings of KD subtypes, we performed differential abundance (DA) analysis using proteomic data of 6,481 proteins from 32 KD patients with linear regression models that controlled for age and sex effects.

Results: Four clusters were identified with distinct clinical features: (1) liver involvement with elevated liver enzyme and total bilirubin levels, lowest coronary artery aneurysm (CAA) but highest IVIG-resistance rates; (2) highest band neutrophil count and KD shock rate; (3) cervical lymphadenopathy with high markers of inflammation (ESR, CRP, white blood cell and platelet counts, low age-adjusted hemoglobin Z-scores); and (4) young age at KD onset with highest CAA but lowest IVIG-resistance rates. Compared to healthy controls, 211 KD-associated DA proteins (FDR < 0.05) were shared among the subgroups, and many (135, 264, 613 and 46) were unique to a subgroup. Comparing the subgroups, 40 identified DA proteins showed signatures of hepatocyte injury and blockade of IL-18 signaling.

Conclusions: Our data-driven analysis provided insights into the heterogeneity of KD, and characterized four distinct clinical subgroups of KD patients. Further research is needed to confirm the validity and generalizability of these findings, which may influence the search for different triggers of the discrete KD subgroups.

Keywords: Kawasaki disease, clinical subtype, cluster analysis, hierarchical clustering on principal components, proteomics, liver involvement.

Biomedical Informatics (Department of Medicine)

Poster 76

PATIENT RECORD INTEROPERABILITY IN NEWBORNS: EXAMINING POST-DISCHARGE RECORD ACCESS

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Background: In recent years, increased emphasis has been placed on electronic health record (EHR) interoperability, which allows for the exchange of patients' health information between different EHR instances with minimal effort. The extent of interoperability in many settings remains unknown, including post-discharge follow-up for newborns. The implementation of interoperability in newborns presents unique challenges, including the use of temporary names assigned at birth, which can affect accurate matching. We investigated rates of post-discharge record access for newborns via an EHR interoperability tool before and after implementation of multiple quality improvement measures aimed at increasing the use of this tool among outpatient pediatricians.

Methods: Data were collected on the time interval between discharge after birth and first record access via
an EHR interoperability tool between September 2017 and March 2022. Rates of record access within three, seven, and 14 days of discharge were calculated, as well the fraction of first record access requests within three days of discharge originating from pediatricians affiliated with the largest regional pediatrics consortium. Notable events during this period include deployment of several quality improvement initiatives and the COVID–19 pandemic.

Results: Rates of access within three, seven, and 14 days of discharge increased from nadirs of 62.5%, 75.5%, and 81.7% to maxima of 81.1%, 88.1%, and 91.3%, respectively during the study period. A subset of patients with pediatricians affiliated with the largest local pediatrics consortium had rates of access within three days of discharge increase from 65.6% to a maximum of 84.5%. These gains were realized despite increasing numbers of births and the presence of COVID-19.

Conclusions: After implementation of several quality improvement initiatives, increased rates of post–discharge record access for newborns via an EHR interoperability tool were observed. Pediatricians who seek greater availability of newborn records post-discharge may wish to consider implementing similar initiatives.

Cardiology

Poster 17

NEONATAL ATRIAL FLUTTER IN THE MODERN ERA: UNEXPECTED INSIGHTS ON NATURAL HISTORY AND MANAGEMENT

Alejandro Borquez MD, Matthew Williams MD, James Perry MD

Background: Atrial flutter (AFL) is a common arrhythmia in the neonatal period, both in critically ill and otherwise healthy neonates, with and without congenital heart disease. Classically it is considered an idiopathic entity related to neonatal transitions in physiology, and without long term sequalae. Nevertheless, a variable duration of post-conversion anti-arrhythmic therapy is common.

Methods: Single center retrospective review from 2009-2022. Neonates (<30 days of age) treated for AFL reviewed. Intraoperative and postoperative AFL excluded.

Results: 63 neonates with AFL treated. Median gestational age 36 weeks. Median presentation age 1 day. 11% (7/63) diagnosed with fetal tachycardia, 3/7 had fetal treatment. Mean atrial cycle length 150 ms, 84% (53/63) with 2:1 conduction. Ventricular dysfunction (EF <55%) in 27% (17/63). 52% (33/63) had AFL onset immediately after or within hours of placement of a central line with high position. 89% (8/9) of CHD patients with AFL had central lines. 19% (12/63) had spontaneous conversion to sinus rhythm (SR). Of 51% (32/63) with attempted initial chemical cardioversion, successful conversion to SR in 65% (21/32). 48% (30/63) required electrical cardioversion. No correlation between cycle length, conduction pattern, fetal treatment, or ventricular dysfunction with conversion characteristics. 3% (2/63) had recurrence of AFL; one with coexisting AET and one with coexisting SVT. AFL recurrence within 1 day in both. Overall, 13% (8/63) had documented SVT in addition to AFL. 56% (35/63) had outpatient follow-up for a mean of 3.8 months. 33% (21/63) were treated as outpatient, mean duration 3.5 months. 62% (13/21) treated did not have concurrent SVT, average treatment course 2.8 months.

Conclusions: These data represent the largest reported cohort of neonatal AFL. AFL incident to central line placement was significantly higher than expected. Changes in practice guidelines for placement of central lines in neonates may be considered. Rates of spontaneous conversion were higher than expected. Recurrent AFL was found only in 2 patients with a coexisting SVT substrate. We recommend that post-conversion anti-arrhythmics and follow up are not indicated for newborn AFL unless there is concurrent SVT.

Poster 22

FREE BREATHING, MULTI-SHOT REAL-TIME IMAGING USING ADAPTIVE K-SPACE SAMPLING (ARKS) FOR ICMR

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Background: iCMR imaging relies on real-time, low latency, single-shot acquisitions for guidance of catheterization. As a result, image quality is limited. Adaptive radial k-space sampling (ARKS) could improve real-time image quality1 and thus benefit iCMR. However, ARKS was developed for imaging adults with arrhythmias performing breathholds and therefore has not been tested in sedated pediatric patients. Here, we evaluate the extent to which ARKS can improve image quality in imaging of sedated pediatric patients.

Methods: With IRB approval, ECG and respiratory data were recorded from 10 sedated children during 4D flow imaging (median age: 1.9 years old, age IQR: 0.5-8 years, 60% female). The median heart rate was 106.8 bpm (IQR: 85.1 to 126.3 bpm).
A 2D radial bSSFP acquisition was simulated with a TR= 2.6ms for 200 seconds for each patient.
In this work, we added analysis of the respiratory signal via cross-correlation of the respiratory waveform to the previously-described ECG analysis. Periods of similar cardiac and respiratory periods were automatically identified.
We evaluated the impact of two ARKS parameters (the similarity of respiratory position and the search window) on the improvement in data sampling.

Results: The respiratory correlation cutoff (RCC) was strongly, inversely correlated to the number of beats (Nbeats) and acceptance rate (AR) of the multi-shot approach. A lower respiratory cutoff value accepts more beats but enforces less stringent respiratory similarity. Nbeats varied as a function of the overall time window. Narrowing or extending the overall search window did not significantly affect the acceptance rate.

Conclusion: ARKS can be adapted to analyze cardio- and respiratory phase information in children to generate free breathing, multi-shot imaging data and is compatible with real-time imaging.

Cardiology (continued)

Poster 14

DIRECT ORAL ANTICOAGULANTS FOR PATIENTS WITH GIANT CORONARY ARTERY ANEURYSMS AFTER KAWASAKI DISEASE

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Background: There are no randomized clinical trials to inform the management of patients who have suffered giant coronary artery aneurysms (CAA) following Kawasaki disease (KD) in childhood. There is, however, consensus that systemic anticoagulation in conjunction with anti-platelet therapy is reasonable for this patient population based on observational data from Japan that documented a 30% increased incidence of major adverse cardiovascular events (MACE) in patients treated with aspirin alone. Warfarin and low-molecular weight heparin are commonly used for systemic anti-coagulation. However, there are many challenges including narrow therapeutic range and frequent blood draws with standard therapy. Given the excellent safety profile and expanding use of direct oral anti-coagulants (DOACs) for a variety of conditions associated with increased risk of thrombosis, we offered patients the option for chronic therapy with a DOAC rather than standard of care systemic anticoagulation with warfarin or enoxaparin.

Methods: Patients or their parents gave written consent for use of their data from the medical record.

Results: Twenty-four patients with giant aneurysms following KD in childhood were treated with a DOAC and an anti-platelet agent. Twelve patients received immune modulating therapy and two patients received aspirin only in the acute phase. Ten patients presented with acute MI (Myocardial Infarction) in adulthood and imaging consistent with probable KD in childhood. Six patients had initiation of DOAC at age less than 18 years and the remainder were adults at the time of DOAC initiation. The median observation period on DOAC was 4.15 years, for 121 treatment-years observed. Four MACE occurred. There were no major bleeding events.

Conclusions: DOAC therapy was safe and well-tolerated in this patient series. Larger observational studies will be needed to establish the long-term safety of this treatment to prevent thrombosis in KD patients with giant aneurysms.

Poster 19

MR LYMPHATIC IMAGE GUIDANCE OF PERCUTANEOUS LYMPHATIC INTERVENTION FOR PLASTIC BRONCHITIS IN A FONTAN PATIENT WITH PACEMAKER

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Background: A 7-year-old male with hypoplastic left heart syndrome underwent fenestrated extracardiac conduit Fontan and epicardial pacemaker placement. Post-operatively, he had pulmonary hypertension requiring treatment, and recurrent pleural and pericardial effusions. He subsequently developed severe hypoxemia and was diagnosed with plastic bronchitis and failing Fontan physiology. A cardiac catheterization demonstrated elevated Fontan pressures Due to concern for possible lymphatic abnormality, he underwent lymphatic magnetic resonance imaging (MRI).

Methods: He underwent lymphatic MRI imaging as follows: he was intubated, inguinal lymph nodes were accessed with 25G needles, and his pacemaker was programmed to AAO 70. Diluted Gadavist contrast was injected into the inguinal lymph nodes. He underwent T2 weighted 3D turbo spin echo sequence (T2 prep), dynamic contrast-enhanced magnetic resonance lymphangiography (DCMRL) with TWIST sequence and conventional contrast enhanced MR angiogram (MRA).

Results: The T2prep sequence showed increased signal intensity in the supraclavicular region, mediastinum, and along the right lung hilum. On DCMRL, the thoracic duct course was clearly delineated and a prominent lymphatic collateral coursing to the right lung hilum was noted at the level of T6. On contrast enhanced MRA, the thoracic duct and right hilar collateral channel were delineated. The MRA images were utilized as overlay on the fluoroscopic image for guidance during lymphatic intervention. The abnormal lymphatic collateral branch was occluded with liquid embolic material (Onyx, Micro Therapeutics, Inc., Irvine, CA). The patient tolerated the procedure well without adverse events. No further bronchial casts were expelled, and the patient was discharged home.

Conclusion: Understanding the link between failing Fontan physiology and the effect on lymphatic drainage is still unclear, with further studies needed. This case demonstrates utility of MRI evaluation for lymphatic abnormalities in a patient with complex anatomy, pacemaker dependence, and plastic bronchitis in the setting of failing Fontan physiology.

Cardiology (continued)

Poster 16

COMPARISONS BETWEEN GLOBAL AND REGIONAL STRAINS DERIVED BY FEATURE TRACKING ALGORITHMS AND MYOCARDIAL TAGGING IN CHILDHOOD CANCER SURVIVORS

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Background: Myocardial strain is an important measure derived during cardiovascular magnetic resonance (CMR) imaging evaluation of cardio-oncology patients. Our objective was to compare different strain algorithms to assess reproducibility and accuracy.

Methods: Childhood cancer survivors with history of anthracycline therapy were prospectively enrolled. Steady-state free precession (SSFP) cine imaging was obtained in left ventricular (LV) long and short axis. Myocardial tagged cine images were acquired in short axis orientation at mid-LV level. Endocardial and epicardial borders were manually contoured on tagged images and analyzed using Segment (Medviso, Sweden). On SSFP cine imaging, automated endocardial and epicardial contours were generated, manually adjusted, and analyzed using four feature tracking (FT) methods: 2D and 3D algorithms from CVI42 (Circle Cardiovascular Imaging, Canada) and first-generation strain "Image Registration" and new generation "Medical Image Tracking Toolbox" (MITT) on Segment. Interobserver reproducibility was assessed via coefficients of variation (CVs). Analysis for accuracy by comparing with tag and by cardiac dysfunction was performed using Pearson's correlation and describing the m**ean difference.**

Results: There was high reproducibility on GCS (CVs 2.5% - 6.3%) and GLS (CVs 1.2% - 11.9%). The segmental analysis had more variability (average segmental CVs 8.2% - 16.1%). There were moderate CS correlations between FT and tagged strains across the whole mid-LV (Pearson's r=0.35-0.54). Global strain measures were highly correlated across 2D FT algorithms (Pearson's r=0.63 -0.93). Global strain values were worse in participants with cardiac dysfunction across all algorithms with the largest and most significant differences in GCS.

Conclusion: Current algorithms for SSFP cine images demonstrate adequate reproducibility and accuracy to perform GLS and GCS measurements; reliability of regional strain is still suboptimal. GCS is the optimal measure to distinguish patients with cardiac dysfunction from those without and may serve as a helpful adjunct tool to corroborate LVEF measurements. Further study is needed to determine prognostic utility of MRI-based strain measurements in cardio-oncology population.

Poster 20

PORTAL VEIN RECANALIZATION FOR NATIVE PORTAL VEIN THROMBOSIS IN CHILDREN

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Purpose: Portal vein thrombosis (PVT) is the most common cause of pre-hepatic portal hypertension and the leading cause of major gastrointestinal bleeding in children. Affected patients may require medical, endoscopic, or surgical treatments that are not always effective and do not necessarily normalize portal circulatory physiology. Invasive surgical treatments exist, such as a meso-rex bypass or surgical portosystemic shunts, however, they are not equivalent, as meso-rex bypass normalizes portal circulation with hepatopetal flow, whereas surgical portosystemic shunts do not. Transcatheter portal vein (PV) recanalization offers another option in the treatment of PVT that corrects symptoms and restores physiological hepatopetal flow, similar to meso-rex bypass, yet in a minimally-invasive fashion.

Methods: Retrospective review of patients with native PVT who underwent transcatheter PV recanalization in the cardiac or interventional radiology catheterization laboratories at Texas Children's Hospital. Symptoms, liver Doppler ultrasound, and complete blood counts were used to monitor treatment outcomes.

Results: 34 native PVT patients (age range, 7 months-18 years) underwent transcatheter PV recanalization from 02/2013-11/2022. They received a total 66 procedures over a follow-up ranging 1-80 months. Technical success in reopening the occluded PV was achieved in 17/34 children with the following approaches: 14/17 trans-splenic, 2/17 trans-hepatic, and 1/17 requiring both. 15 of 17 initially successful cases have not required invasive surgical treatment. At the most recent follow-up ultrasound (median, 34 months from first intervention), 15/17 patients with initial technical success demonstrated persistent patency of PV. 11/17 successful cases reported gastrointestinal bleeding pre-procedure, and 7 had no further bleeding episodes post-intervention. 12/17 successful cases pre-procedural thrombocytopenia, and 7 normalized post-procedure. 12/66 procedures had complications, with 8 fitting major Society of Interventional Radiology classification, including one death.

Conclusion: PV recanalization in experienced centers offers a safe, minimally invasive, effective, and possibly definitive option to treat native PVT.

Cardiology (continued)

Poster 23

POSTERIOR SPINAL FUSION ON PATIENT WITH SEVERE PULMONARY ARTERIAL HYPERTENSION PERFORMED ON VENOUS- ARTERIAL EXTRACORPOREAL MEMBRANE OXYGENATION

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Background: Pulmonary arterial hypertension (PAH) is a complex disease with poor prognosis despite advances in medical therapies. Anesthesia and surgery for patients with PAH poses risk of life-threatening complications including right ventricular failure, respiratory failure and death. Patients with severe kyphoscoliosis develop restrictive lung disease, altered cardiopulmonary interactions and PAH that can be difficult to manage. There are very few reports of patients with PAH who have undergone repair of kyphoscoliosis. We describe a patient who had successful posterior spinal fusion while on VA-ECMO.

Case Presentation: A 14 year-old female with history of left congenital diaphragmatic hernia, severe PAH, pulmonary vein stenosis, patent ductus arteriosus developed progressive severe kyphoscoliosis with restrictive lung disease. She was on three-drug therapy for PAH with trepostinil, tadalafil, ambrisentan with suprasystemic right ventricular pressures. After extensive consultation with cardiac anesthesiology, the pulmonary hypertension team and Orthopedics, she was taken to the operating room (OR) for posterior spinal fusion (PSF). Intraoperatively, she had worsening RV failure and increased PAH and was emergently cannulated onto Veno-arterial Extra Corporeal Membrane Oxygenation (VA-ECMO). She had a deep and superficial drains and wound VAC placed and was transferred to the Cardiothoracic intensive care unit.

The next day, she returned to the OR for completion of posterior spinal fusion while on VA-ECMO support. Bronchoscopy showed tracheobronchomalacia which was not amenable to stenting. She underwent tracheostomy placement and was eventually decannulated from VA-ECMO. She underwent pulmonary rehabilitation and was discharged home with nighttime ventilator support. Preoperatively, she was deemed not a lung transplant candidate. She is now considered a potential lung transplant candidate for which she is undergoing evaluation.

Discussion and Conclusion: ECMO intraoperatively and post operatively should be considered for pediatric patients with severe PAH undergoing posterior spinal fusion. PSF can be successfully performed in patients with severe kyphoscoliosis and severe pulmonary hypertension with multidisciplinary planning.

Keywords: *pulmonary hypertension, posterior spinal fusion, Extracorporeal membrane oxygenation*

Poster 18

AUTONOMOUS 5D-FLOW WITH RADIAL K-SPACE SAMPLING

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Background: Pre-defined k-space acquisition schemes suffer from suboptimal distribution of samples in k- space and are time-consuming. In 2D, an adaptive radial k-space sampling approach (ARKS) can improve multi-shot sampling uniformity by continuously monitoring and optimizing the acquisition of k-space data in a closed-loop.
Here, we extended ARKS to 3D-flow imaging with cardiac and respiratory binning (5D flow) by simulating the k-space trajectory using physiologic signals from pediatric patients.

Methods: With IRB approval, cardiac and respiratory signals from 18 pediatric patients (11.1±5.1 years-old, 9 females) were extracted from 4D-flow scans. Physiologic data were used to simulate two 5D-flow free-breathing schemes: 3D predetermined golden-angle (GA) spiral phyllotaxis, and 3D ARKS. Data were sorted into 10 cardiac and 3 respiratory phases.
In ARKS, the orientation of each spoke was calculated dynamically. At each repetition time, ARKS identified the current cardio-respiratory bin and from the samples previously acquired within the bin, the ten largest gaps in k-space were determined and collected.
We compared maximum Voronoi area and scan efficiency, which indicates how quickly the largest gap area approaches that obtained by uniform sampling. These were compared using two-way repeated measures ANOVA and post-hoc tests.

Results: At all time-points, the maximum area from ARKS was smaller ($p<0.05$) than that from GA, while scan efficiency was higher ($p<0.05$). The maximum scan efficiency achieved by ARKS and GA was 82.8% and 79.6%, respectively. ARKS reached the scan efficiency of GA 2.5 mins earlier. In ARKS, k-space coverage is more uniform because it incorporates physiologic bin information.

Conclusions: Adaptive k-space sampling may be beneficial in 5D imaging approaches for pediatric patients who have higher physiologic rates with more variation. Here, we showed that 5D ARKS improved the distribution of k-space data and may shorten scan duration. Future work will focus on implementing 5D-flow ARKS in vivo.

Cardiology (continued)

Poster 13

ISOLATED ABSENT AORTIC VALVE: CHARACTERIZATION OF A UNIQUE FETAL CASE AND IDENTIFICATION OF A NOVEL GENETIC ETIOLOGY

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Background: Congenital aortic valve (AoV) defects are common and range from bicuspid to absent aortic valve (AAV). Genetic mechanisms in AoV disease are incompletely understood. AAV is exceedingly rare.

Methods: We performed a clinical, histopathologic analysis as well as whole genome sequencing on a 23-week fetus found to have an isolated absent aortic valve.

Results: Fetal imaging revealed what is the second reported case of isolated AAV in a fetus with continuous aortic insufficiency, profound LV dilation and dysfunction, and inverse circular shunt. Pathology confirmed fibrotic replacement of AoV tissue. Whole genome sequencing demonstrated a novel loss-of-function mutation in the Adenomatous Polyposis Coli (APC) gene. APC suppresses B-catenin-mediated apoptosis of cardiac neural crest cells. These results implicate a critical role for the regulation of apoptosis in cardiac neural crest cells in heart development.

Summary: This case provides hemodynamic and pathologic characterization as well as the identification of a novel genetic mechanism for this rare AoV disease, and illustrates the power of a collaborative approach to patient care and gene discovery through state- of-the-art imaging, histopathologic analysis and whole genome sequencing.

Poster 15

LARGE INFILTRATIVE CARDIAC LIPOMA IN AN ADOLESCENT

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Background: A 15-year-old female presented to the emergency room with severe abdominal pain, vomiting, and diarrhea. She was diagnosed with pelvic inflammatory disease due to positive screening for gonorrhea and chlamydia, and an abdominal Computed Tomography (CT) was performed to evaluate for tubo-ovarian abscess or acute appendicitis. She had a normal abdominal evaluation, but imaging incidentally found a mass within the cardiac apex.

Methods/Results: Cardiac MRI demonstrated a large cardiac mass 3cmx2cm in the mid and apical portions of the left ventricle that extended anterolaterally towards the apex of the right ventricle and into the pericardial space. Tissue imaging demonstrated hyperintensity on T1 without fat saturation on hypointense on T1 with fat saturation, hypointense on SSFP images, hypointense on T2, hypointense on first pass perfusion and hypointense on late enhancement imaging. These findings and the location of the mass were consistent with a lipoma (likely infiltrative type). Cardiac CT further characterized the infiltrative lipoma, demonstrating epicardial/pericardial components encasing the distal segment of the left anterior descending coronary artery with no extension to the anterior chest wall.

Conclusions: Cardiac lipomas are rare benign tumors of the heart composed of mature fat cells. They are rare findings in adults, and extremely uncommon findings in children with only few reported cases. They are typically incidentally found but can cause mass effect resulting in arrhythmias, outflow tract obstruction, or coronary artery compression. Surgical resection of the mass in symptomatic patients is the primary treatment strategy. Cardiac magnetic resonance imaging provides useful information for characterizing cardiac masses in children, and often leads to an accurate diagnosis. In this case, cardiac MRI played a crucial role in identifying a cardiac mass potentially requiring surgical intervention. Tissue imaging by MRI was strongly suggestive of a lipoma, negating need for invasive cardiac biopsy, and guiding further management.

Child Abuse Pediatrics

Poster 25

PRESENTATION, MANAGEMENT, AND REPORTING OF YOUNG CHILDREN WHO TEST POSITIVE FOR CANNABIS

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Background: Rates of cannabis ingestions in young children are increasing. Small studies have evaluated symptomatology of these children, however the literature lacks research regarding circumstances surrounding their presentation and factors influencing medical management. We studied young children who tested positive for cannabis to 1) understand factors leading to ingestion and 2) how parental report influences emergency room management.

Design/Methods: We performed a retrospective cross-sectional study on children under 10 years with cannabis positive urine drug screens from January 2014-June 2022. We excluded children born positive, prescribed cannabis, or who lacked confirmatory testing. Single-factor Anova and Fisher Exact tests were used to assess for trends. Two-tailed T tests and Fisher Exact tests were used to compare management of children with chief complaint "ingestion" versus those without.

Results: Of the 179 children (mean age 3.7 years, 48% male), 50% identified as Hispanic/Latino/Latinx, 30% as non-Hispanic white, and 16% as African American. We observed a significant increase over time in cannabis positive children relative to hospital census ($P < 0.001$). Edible ingestions were most frequently reported. The most common location of exposure was the primary residence (54%) with parents as the most frequent users (46%). In the Emergency Department, the most common chief complaint was ingestion (49%) followed by altered mental status (33%), fatigue (11%), and seizure (6%). Children with an "ingestion" chief complaint were managed with less testing than those with other chief complaints. They received fewer needlesticks (43% vs 91%), less imaging (5% vs 56% CT heads), and fewer procedures (0% vs 8% lumbar punctures). Regarding CPS reporting, those with "ingestion" chief complaint were less likely to be reported to child protective services.

Conclusion(s): Pediatric cannabis exposures are increasing and have a wide array of clinical presentations. Parental report of cannabis ingestion appears to influence and reduce unnecessary testing.

Poster 24

PREVALENCE OF FENTANYL POSITIVE URINE DRUG SCREENS IN AN ASYMPTOMATIC COHORT OF YOUNG DRUG ENDANGERED CHILDREN

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Background: Illicit fentanyl abuse is an increasing problem. Fentanyl is now the leading cause of overdose deaths in adults. Fentanyl intoxication has been described in the pediatric population; however, little is known about asymptomatic children exposed to fentanyl. We hypothesize that children in homes where illicit fentanyl is present will test positive for fentanyl, even if asymptomatic.

Methods: This is a retrospective cross-sectional study of children less than 10 years of age who had confirmed positive urine drug screens for fentanyl between 2020-2022. Children were excluded if they were born positive or given fentanyl in the medical setting. Demographics and reason for visit were analyzed using descriptive statistics. Chi- squared, fisher exact, and unpaired t-tests were used to assess for differences in characteristics between years and between our asymptomatic and symptomatic cohorts.

Results: During the study period, 65 children who met inclusion criteria tested positive for fentanyl. The average age was 30 months and 63% were male. There has been a statistically significant increase in children testing positive for fentanyl since 2020 (p- value <0.001). Of these children, 33% had symptoms related to an opioid ingestion. Children < 24 months who had symptoms of opioid intoxication were less likely to receive Narcan (p-value < 0.001). In our secondary analysis, 21 children were identified as index children testing positive for fentanyl. There were 25 asymptomatic household contacts that were linked to the index children and had urine drug testing completed. Of these, 60% tested positive for fentanyl.

Conclusion: Children residing in homes in which fentanyl is present are at risk of ingestion. Our study shows that these children have a high likelihood of testing positive even when they are asymptomatic. This highlights the importance of timely evaluation for all drug endangered children with consideration of urine drug testing even when children are asymptomatic.

Community Health

Poster 26

RELATIVE ENERGY DEFICIENCY IN SPORT: RAISING AWARENESS AND EDUCATION

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Background: Athletes who participate in sports associated with leanness are at higher risk for Relative Energy Deficiency in Sport (RED-S). This condition can lead to serious medical consequences and often goes unrecognized. Athletes, trainers, and coaches have low knowledge regarding RED-S. The goal of the project was to develop an educational tool for athletes, trainers, and coaches, and evaluate its impact on knowledge and attitudes.

Methods: Using a pre-post study design, we assessed changes in knowledge and attitudes around recognizing and managing RED-S. We recruited 53 collegiate/post-collegiate athletes and athletic trainers/coaches to participate. Participants completed the online consent process and baseline survey via REDCap prior to being directed to educational videos and post-education survey. Videos were created that reviewed signs/symptoms of RED-S, how to talk with athletes about these subjects, and when/how to refer at-risk athletes for assessment. Surveys assessed basic knowledge of RED-S symptoms, how to address RED-S, and resources for referral.

Response choices included 5-point Likert scales, multiple choice, and true-false options. Chi-square and T-tests were used to examine changes in pre-post results

Results: A total of 53 participants completed the baseline survey, and 28 completed both surveys. Participants included 88.7% women, 84.9% athletes/former athletes, 15.1% coaches/trainers. Athlete participants played 16 different sports. There was a significant increase in knowledge of RED-S criteria and comfort with addressing RED-S. Compared to other training materials, many participants found the videos more informative than prior information they had received on RED-S (90.9%) and rated them highly (1.68, range 1-5, S.D. 0.646).

Conclusions: Participants increased knowledge of signs/symptoms of RED-S, how to create healthy environments for athletes, and when to refer for medical evaluation. Satisfaction scores were high when comparing video content to prior information received regarding RED-S. Overall, the data shows that educational videos are beneficial tools for providing RED-S education.

Critical Care

Poster 27

A MULTI-CENTER COHORT ANALYSIS OF RAPID GENOME SEQUENCING IN THE PICU

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INTRODUCTION: Genetic disorders contribute significantly to morbidity and mortality in pediatric critical care. Diagnostic rapid whole genome sequencing (rWGS) has dramatically impacted care in neonatal intensive care units (ICU). There remains a population of undiagnosed patients with rare genetic diseases who present critically ill to the pediatric ICU (PICU) and the application of rWGS in this setting is not yet fully described. This study evaluated the clinical utility of rWGS in the PICU.

METHODS: This was an ambidirectional cohort study conducted at 3 tertiary children's hospitals from 3/2019–7/2022. Data collection was retrospective prior to 5/2021 followed by prospective enrollment. Children were nominated for rWGS by the care team when the etiology of illness was unclear. A priori suspicion of a genetic disorder was not required. Children who received rWGS in the PICU age 1 month–18 years were eligible for inclusion. rWGS interpretation was phenotype-driven. Clinical utility was assessed via provider surveys of PICU physicians and electronic health record review. In the prospective arm, patient families were surveyed to assess impact of rWGS in perception of care.

RESULTS: 80 cases met the inclusion criteria, 58 retrospective and 22 prospective. The diagnostic sensitivity of rWGS was 62%. 55% of rWGS diagnoses were considered to completely describe the phenotypic presentation. 38% of rWGS diagnoses led to changes in management. Of these, 52% occurred in the ICU setting. Average rWGS turnaround time was 10 days. PICU provider surveys indicated that performing rWGS led to changes in management 33% of the time, even when genomes were non-diagnostic. Providers felt that 30% of the time rWGS positively impacted their relationship with the family.

CONCLUSIONS: The potential for improved outcomes when rWGS is implemented within an integrated, multidisciplinary precision medicine delivery system has only recently begun to be explored. Molecular diagnosis of genetic disorders in the PICU population frequently resulted in changes in care during hospitalization, making early case identification and rWGS imperative. Increasing availability of rWGS has significant potential to impact patient care and assist families in making difficult decisions during critical illness.

Emergency Medicine

Poster 36

PILOT STUDY: PERIPARTUM DEPRESSION SCREENING IN THE PEDIATRIC EMERGENCY DEPARTMENT

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Background: Parental peripartum depression (PPD) is under-diagnosed and associated with increased acute healthcare utilization for children. Screening parents, both mothers and fathers, for PPD in the pediatric Emergency Department (ED) may improve PPD detection. We describe the proportion and factors associated with positive PPD screen among parents who bring their infants to the Pediatric ED.

Methods: We piloted a prospective survey in a convenience sample of parents who brought infants <12months for care to our tertiary, standalone pediatric hospital ED. Parents of either English or Spanish language fluency were included. Parents of children requiring medical stabilization were excluded. Participants completed an electronic survey including a demographics questionnaire and a validated PPD screening tool, the Edinburgh Postnatal Depression Scale (EPDS). A score of ≥10 was considered positive. Parents were offered resources, assessment, and referrals as appropriate. We performed descriptive statistics and multiple regression analysis to identify factors associated with a positive screen.

Results: Of 450 parents enrolled from September to December 2022, 387(88%) reported female gender. 125(28%) had a positive EPDS. 14(27%) of fathers screened positive, and female gender was not associated with increased positive screen. While those who reported American Indian/Alaskan Native and Hawaiian/Pacific Islander heritage had higher proportion of positive screens, about one in four parents from all other racial and ethnic backgrounds also screened positive. 160(35%) reported never completing a previous PPD screen.

Conclusions: To date, this is the largest PPD screen conducted in the pediatric ED. Our results demonstrate more than one in four parents had positive EPDS, and one in three parents reported never being screened for PPD. Our study was unique in including fathers alongside mothers, who had similar proportion of positive PPD screen. This study highlights the importance of universal PPD screening and potential role of pediatric EDs in improved detection of PPD.

Poster 35

A REVIEW OF PEDIATRIC CARDIAC ARREST & TERMINATION OF RESUSCITATION PROTOCOLS ACROSS CALIFORNIA

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Background: Pediatric out-of hospital cardiac arrests (OHCA) are low frequency, high severity events and often associated with poor outcomes. In recent years, multiple studies have identified best practic es for pediatric OHCA. However, emergency medical services (EMS) protocols vary significantly across j urisdictions in the United States. This review seeks to compare existing pediatric cardiac arrest and fiel d termination of resuscitation protocols among the 33 local EMS agencies (LEMSAs) in the State of California.

Methods: Pediatric cardiac arrest protocols of each of the 33 LEMSAs in California were compared for consistency with published national guidelines and recent prehospital literature. The specific protocol elements analyzed included: protocol guidance concerning rapid transport versus “stay and play” on-scene resuscitation and termination of resuscitation protocols.

Results: Online protocols were available for all 33 LEMSAs. Five (15.2%) LEMSA protocols called for rapid transport while 10 (30.3%) called for some version of “stay and play” resuscitation. The majority of LEMSA protocols (54.5%) did not explicitly address the question of prioritizing rapid transport or on-scene resuscitation measures, and airway interventions varied widely. Termination of resuscitation was allowed with base contact in 16 (48.5%) and allowed independently in 6 (18.2%) LEMSA’s. Four (12.1%) local agencies require transport in all cases of pediatric cardiac arrest. Seven (21.2%) LEMSA protocols did not address pediatric termination of resuscitation.

Conclusions: Recent prehospital studies and guidelines have been published and taught regarding best practices in pediatric OHCA. California’s EMS jurisdictions demonstrate a wide range of protocols. Guidance for on-scene resuscitation varied significantly, specifically surrounding time on scene, and necessity of advanced airways. Termination of resuscitation was found to be generally acceptable, however further development of these concepts and propagation of these findings are critical for continued advancement in the outcomes of pediatric prehospital cardiac arrest management .

Emergency Medicine (continued)

Poster 38

FOOD INSECURITY AND SOCIAL DETERMINANTS OF HEALTH IN A PEDIATRIC EMERGENCY DEPARTMENT

Andrew Kramer MD, Margaret Nguyen MD, Kathryn Hollenbach PhD, and Michael Gardiner MD

Background: Food insecurity (FI) in childhood has been shown to result in poor health outcomes and increased risk of chronic disease. FI also frequently occurs with other negative social determinants of health (SDH). The California Health Information Survey (CHIS) estimated that 18.8% of San Diego County (SD) children experienced FI in 2017. Our pediatric emergency department (PED) serves the communities of SD, Riverside, and Imperial Counties and represents a unique location to identify a FI population. We aim to estimate the prevalence of FI in families presenting to the PED.

Methods: We conducted a survey of caregivers presenting to the PED. The survey consisted of six previously validated food-insecurity screening questions, and 26 questions regarding demographics and SDH. Caregivers were approached via convenience sampling and were permitted to omit any items. FI was determined according to prior methods from CHIS. Food- secure and FI groups were compared using chi-square for categorical variables and student t- test for continuous variables.

Results: Between 06/2022 and 02/2023, 1000 caregivers were approached for participation with 526 completing the food-insecurity screening questions. Food insecurity was reported by 50.0% of caregivers (95% CI 45.7% - 54.3%). Characteristics of food-secure and food-insecure families are noted in Table 1. Compared with food-secure caregivers, those reporting FI were more frequently hispanic or black, reported lower household income, and higher rates of caregiver disability, difficulty paying rent/mortgage, and homelessness. Despite FI families more frequently receiving local or government food services, greater than 50% of FI families reported not receiving services.

Conclusions: Half of caregivers presenting to the PED screened positive for FI. Families experiencing food insecurity were more likely to have lower income and experience housing and employment insecurity. More than half of FI families reported not receiving food services.

Poster 29

PRE-HOSPITAL ASSESSMENT AND TREATMENT OF INFANTS AND TODDLERS IN RESPIRATORY DISTRESS

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Background: Assessments and treatments for infants and toddlers with respiratory distress vary for upper (stridor - nebulized epinephrine) versus lower (wheezing - albuterol) airway etiologies; however, few studies have explored EMS differentiation between upper and lower airway conditions in children. We sought to describe EMS assessment, identification, and treatment of children with upper and lower airway pathologies.

Methods: Retrospective analysis using linked prehospital and hospital records from the 2018 and 2019 ESO Data Collaborative, including 9-1-1 transports of patients ages 1 day to 3 years with ICD-10 diagnosis codes indicating upper (croup) or lower (bronchiolitis, asthma) airway disease. Patient demographics, documentation of respiratory rate and pulse oximetry, EMS primary impressions, and treatments were reported using descriptive statistics.

Results: Patients with upper airway diagnoses tended to be older compared to those with lower airway diagnoses, were more commonly male (71.0% vs 57.2%), and were more likely to be discharged home from the ED (87.8% vs 59.5%). SpO2 and RR were not documented for 8.2% (n=111) and 2.7% (n=36) of patients, respectively. For upper airway diagnoses, the top three EMS primary impressions were "acute respiratory distress" (60.4%), "laryngitis/croup" (13.9%), and "cough" (5.5%); these conditions were most commonly treated with oxygen (33.2%), albuterol (28.9%), and nebulized epinephrine (25.5%). For lower airway diagnoses, the top three EMS primary impressions were "acute respiratory distress" (50.0%), "fever" (9.2%), and "common cold" (4.4%); these were most commonly treated with oxygen (39.6%), albuterol (31.5%), and ipratropium (10.7%).

Conclusions: EMS impressions most commonly reflected general acute respiratory distress, rather than differentiating between upper and lower airway disease. Generally not indicated in upper airway disease, albuterol was given to nearly 1-in-3 of these patients, suggesting opportunity to improve evidence-based prehospital care.

Emergency Medicine (continued)

Poster 28

A REVIEW OF PEDIATRIC HEAD TRAUMA PROTOCOLS ACROSS THE STATE OF CALIFORNIA

Michelle Safferman, Marianne Gauche-Hill, Karl Sporer, Jordan Cornwell, Shane Wo, Angela Lumba-Brown, Amy Alayari, Joelle Donofrio

Background: Recent prehospital pediatric Traumatic Brain Injury (TBI) guidelines emphasize prevention and treatment of hypotension, hypoxia and hyperventilation to improve morbidity and mortality. The state of California has 33 Local Emergency Medical Service Agencies (LEMSA)s that maintain prehospital protocols and vary widely in organization and mandate descriptors. This study sought to evaluate LEMSA pediatric head injury protocols as compared with current evidence-based best practices.

Methods: Publicly available pediatric protocols from all CA LEMSAs were reviewed in 2020 by 4 trained personnel. Protocols were reviewed for indicators relevant to prehospital care including assessment (GCS scores, blood pressure, fluid resuscitation, oxygenation and ventilation including end-tidal CO2 monitoring recommendations) and management (supplemental oxygenation, elevation of head of bed, avoidance of hyperthermia, avoidance of or indication for hyperventilation) of head injuries with suspected TBI.

Results: Online protocols were reviewed for all 33 LEMSAs. General Features: Pediatric-specific protocols were identified for 97% of LEMSAs and 30% had specific pediatric head trauma guidelines. Assessment: GCS scores documented as critical cutoff points included: 3% GCS ≤ 14, 73% GCS ≤ 13, 12% GCS ≤ 12, 6% GCS ≤ 10, and 6% did not specify. BP for fluid resuscitation was <100(3%), < 90(48%), <80(9%), <70(3%), age specific(31%), and not specified(6%). End-tidal-CO2 monitoring was recommended in 42% of protocols reviewed. Treatment: Supplemental oxygen regardless of respiratory status was documented by 9% of agencies, avoidance of hypothermia was documented in 36%, 33% advised elevating the head-of-bed during transport, 18% specifically advised avoidance of hyperventilation, and 27% recommended hyperventilation in the presence of herniation signs.

Conclusion: Protocols for pediatric head trauma vary widely across California and are not always consistent with current pediatric TBI recommendations. Updates to current protocols are needed to ensure best practices in the care of children with TBI.

Poster 33

SPATIAL PATTERNS OF PEDIATRIC SUICIDE IN SAN DIEGO COUNTY

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Background: Suicide is a leading cause of death among adolescents. Geospatial techniques have demonstrated variable distribution of health indicators within geographic areas, including mental health. Few studies describe geographic patterns in pediatric suicide. The San Diego County Department of the Medical Examiner gathers information regarding pediatric suicide deaths in the county. We hypothesized that pediatric suicide deaths exist in clusters and are not randomly distributed over space.

Methods: We performed a spatial analysis on all suicide events for persons under the age of 18 years reported to the Office of the Medical Examiner in San Diego County from January 1, 2000 through December 31st, 2020. We obtained ZIP code level demographic data from United States 2010 Decennial survey and calculated crude mortality rates per 10,000 children under 18 years per ZIP code. We employed two spatial approaches to identify geographic clustering: scan statistic, and LISA with EB rates. A ZIP code identified in both approaches were considered to be statistically significant clusters.

Results: There were 153 pediatric suicides in San Diego County for the study period. Of these, 146 returned a valid San Diego County ZIP code. The median age of decedents was 15.2 years. Males comprised 69.9% of decedents. The most common manner of death was hanging (n=72, 49.3%) followed by firearms (n=4, 28.1%). The highest rate of pediatric suicides was for ZIP 91963 in Potrero (32.6 per 10,000). The ZIP code identified as cluster in both detection methods was in Alpine ($p<0.001$, RR 2.6).

Conclusion: Our data demonstrate discrete clusters of pediatric suicides within San Diego County. These results can guide advocacy and public health efforts in suicide prevention.

Emergency Medicine (continued)

Poster 34

THE COMBINATION OF CEPHALEXIN AND LL-37 IN EXTENDED SPECTRUM BETA LACTAMASE (ESBL) URINARY TRACT INFECTIONS

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Background: ESBL organisms are increasing in prevalence and can account for nearly 5% of all pediatric urinary tract infections (UTIs). Cephalexin is considered a first line antibiotic for the treatment of pediatric UTIs. ESBL uropathogens have developed resistance to all cephalosporins. Children who have been diagnosed with an ESBL UTI have demonstrated both clinical and microbiologic responses to discordant antibiotics including cephalexin. This suggests that other factors such as the innate immune system may underlie the clearance of the pathogen. Antimicrobial peptides, namely LL-37, protect the urinary tract from infection by two proposed mechanisms: inhibition of bacterial biofilm formation, and at higher concentrations, direct bactericidal effect. This study investigated the role of LL37 in combination with cephalexin using ESBL strains isolated from children diagnosed with UTIs in media and utilizing a murine model.

Methods: 8 ESBL isolates were obtained and identified using CLSI. ESBL defined as: an elevated mean inhibitory concentration (MIC), and an increase of ≥ 5 mm in the zone of diameter in the presence of ceftazidime disk with clavulanic acid. The isolates were inoculated in Mueller-Hinton broth (MHB) bacteriological media and Roswell Park Memorial Institute (RPMI) physiological cell culture media supplemented with 5% Luria-Bertani (LB) broth. MICs were obtained for all isolates in conventional Mueller-Hinton broth (MHB) and in Roswell Park Memorial Institute (RPMI) with 5% Luria-Bertani (LB) broth using cephalexin. Checkerboard assays were completed in RPMI with 5% LB with cephalexin and LL-37.For the murine model, 2 ESBL Isolates and one wild type uropathogenic E. coli were utilized. 10 mice per strain were utilized. The mice were inoculated transurethrally with 1x10CFU E. coli in 50 L sterile D-PBS, 24 hours post infection, mice were treated with 200 mg/kg cephalexin every 12 hours via oral gavage or water (control). 96 hours post infection, mice were euthanized and bladders homogenized, serially diluted, and plated on Luria agar to determine bacterial burden.

Results: MIC of cephalexin for all strains was > 256 in both media. The MIC of LL 37 ranged from 4-16. The addition of LL-37 demonstrated indifference on checkerboard analysis .The recoverable colony forming units (CFUs) in the wild-type (WT) strain was much higher compared to the ESBL E. coli strains, irrespective of treatment condition (H2O vs cephalexin), in a murine bladder infection model. Moreover, there was no significant difference in the bacterial burden recovered from mice treated with H2O (control) versus cephalexin across the WT positive control strain or ESBL strains.

Conclusion: The addition of LL-37 did not demonstrate synergy with cephalexin to all strains and the murine model was not able to capture clearance of the pathogen previously noted among children. The murine bladder infection model did not recapitulate the observed clinical efficacy of cephalexin against pediatric ESBL E. coli UTIs. Compared to wild type, the ESBL strains demonstrated fewer bacterial colonies, possibly suggesting less adhesion to bladder epithelium.

Poster 31

COVID-19 VACCINE HESITANCY AMONG CAREGIVERS OF CHILDREN UNDER FIVE YEARS OLD IN A PEDIATRIC EMERGENCY DEPARTMENT

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Background: Children under five years old have a high rate of SARS-CoV-2 (COVID-19) infection, yet rates of vaccination are relatively low. This study aimed to identify reasons why caregivers of children ages six months to four years old may be hesitant to vaccinate their children against COVID-19.

Methods: This was a qualitative study of a convenience sample of caregivers of patients aged six months up to four years of age who presented for care at a pediatric Emergency Department. We conducted face-to-face semi-structured interviews with caregivers in the emergency department to probe for themes regarding any hesitations they may have regarding vaccinating their children against COVID-19. Interviews were recorded, transcribed, translated if necessary, and coded. When thematic saturation was achieved, we applied grounded theory methodology to assess for themes and adapted the World Health Organization Strategic Advisory Group of Experts model of vaccine hesitancy determinants matrix to provide a framework for the identified themes.

Results: We conducted 20 interviews, two of which were done in Spanish. We required 17 interviews to reach thematic saturation. We categorized themes surrounding vaccine hesitancies into external, patient-centric, and vaccine-centric factors. External factors included sources of information and family/ community influence. Patient-centric factors included the perceived risk versus benefit ratio, caregiver beliefs, and caregiver knowledge and awareness. Vaccine-centric factors included vaccine safety, vaccine efficacy, vaccine information, and barriers to vaccination.

Conclusions: Using qualitative methodology, we gained important insights into caregiver thoughts regarding the COVID-19 vaccine in children under five years old. We identified themes not previously published in the vaccine hesitancy literature that may be specific to the COVID-19 vaccine in the young pediatric population. Moving forward, these concepts can provide insights into educational strategies aimed at increasing COVID-19 vaccination rates and preventing morbidity and mortality in pediatrics.

Emergency Medicine (continued)

Poster 32

THE IMPACT OF UTILIZING PATIENT CARE COORDINATORS (PCCS) TO CLOSE HEDIS CARE GAPS AMONG MEDI-CAL INSURED CHILDREN

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Background: Rady Children's Health Network (RCHN) received funding from three Medi-Cal health plans to support care coordination efforts and close Healthcare Effectiveness Data and Information Set (HEDIS) care gaps among their members. These health plans included Blue Shield Promise, United Healthcare, and Health Net. HEDIS Care Gaps of focus include overdue well child visits, childhood immunizations, lead screenings, and chlamydia screenings. Coordination of care efforts provides an extra level of support needed for children and families to successfully access care, thereby improving RCHN's HEDIS measures.

Methods: A Patient Care Coordinator (PCC) model was utilized to conduct telephonic outreach with the goal of closing HEDIS care gaps. A team of three PCCs conducted telephone outreach to Medi-Cal members and assisted in scheduling preventative health appointments, providing education on the importance of well-childcare and vaccines, and reconciling health records to provide documentation to the health plan of completion of visits, vaccinations, and preventative screenings. All encounters were captured in Epic and Cozeva and served as the basis for this analysis. Additionally, PCCs conducted Social Determinants of Health Screenings (SDoH) and connected families to resources with the most common need to address food insecurity.

Results: Across the three Medi-Cal plans, compliance for 17 HEDIS measures was improved from 2021 to 2022. In 2022, 10 of those HEDIS measures met or surpassed the National Committee for Quality Assurance (NCQA) 50th percentile mark. The measure with the greatest improvement for all health plans was the Well-Child Visit in the First 15 Months measure, increasing from 8.86% to 46.33% for Blue Shield Promise members, 10% to 42.63% for Health Net Medi-Cal members, and 9.09% to 46.3% for United Healthcare Medi-Cal members. This is an overall 40% from 2021 to 2022 across all health plans due to reconciliation and appointment efforts (Blue Shield Promise: p-value < .001, 95% CI [-0.4413, -0.3117]; Health Net Medi-Cal: p-value < .001, 95% CI [-0.4085, -0.2441]; United Healthcare Medi-Cal: p-value < .001, 95% CI [-0.5373, -0.2069]).

Conclusion: Utilizing a PCC model to close pediatric care gaps and improve HEDIS measures had a significant impact on our RCHN Medi-Cal population with respect to compliance with well child visits, vaccinations, and preventative screening. Additionally, we provided an added benefit of providing SDoH screening and connections to community resources when indicated. This model could be expanded to have a greater impact on additional Medi-Cal members.

Endocrinology

Poster 45

¡MÁS FRESCO! MORE FRESH: IMPACT OF A FRUIT AND VEGETABLE PRESCRIPTION PROGRAM IN A PEDIATRIC TYPE 2 DIABETES CLINIC

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Background: Fruit and vegetable prescription (FVRx) programs have improved fruit and vegetable (F&V) intake and glycemic control in adults with diabetes; however, pediatric data is lacking. The aim of this study was to assess if a FVRx program improved fresh F&V intake and health outcomes of children with type 2 diabetes mellitus (T2D).

Methods: Families with a child with T2D and enrolled in Medi-Cal were recruited from our pediatric diabetes clinic. Families were randomized to either receive vouchers immediately (intervention group) or after a 6-month waiting period (delayed-control group). Monthly vouchers were given for 1 year to purchase fresh F&V. Families completed surveys including the Dietary Screening Questionnaire and U.S. Household Food Security Survey every 6 months. Physiologic data and standardized laboratory tests were also collected.

Results: Of the 57 families with baseline surveys, the majority identified as Latino/Hispanic (84%) with a mean age for children of 14.3 years; 46.9% reported low household food security and 16.3% reported very low food security. There were 29 families who completed our baseline and 6-month surveys. For the intervention group (n=14), there was an increase in parent-reported F&V intake from baseline to 6-months for parents (2.4 vs 3.6 cups per day, p=0.003) and children (2.6 vs 4.4 cups per day, p=0.026). There was no significant difference in these measures for the delayed-control group (n=15). There was no significant change in BMI Z-score or hemoglobin A1c for the two groups after 6 months. However, there was an increase in metformin use in the delayed-control group and no change in metformin use for the intervention group.

Conclusion: FVRx programs are a viable intervention to improve F&V intake for families with a child with T2DM. Further research is needed to assess its impact on BMI and glycemic control.

Poster 42

CONTINUED INCREASE IN CASES OF NEW-ONSET TYPE 1 DIABETES IN CHILDREN FOLLOWING THE COVID-19 PANDEMIC

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Background: We previously reported an increased incidence of type 1 diabetes (T1D) in children in the first year following the COVID-19 outbreak in the US. In this study, we investigated whether this trend was transient or persistent beyond that first year. We performed a 7-year review to determine the pattern of cases 5 years before and 2 years after pandemic onset. We assessed serum bicarbonate and insulin infusion use as measures of disease severity as well as rates of detectable COVID infection.

Methods: For this study, we used the electronic medical record system at Rady Children's Hospital. Subjects included children younger than 19 years with newly diagnosed diabetes using standard ADA criteria and at least 1 positive T1D antibody titer. Data included age, sex, BMI percentile, hemoglobin A1c, serum bicarbonate and pH.

Results: For the COVID-19 years in consideration, the first COVID year was defined as March 19, 2020 to March 18, 2021, and the second from March 19, 2021 to March 18, 2022. 187 and 172 children were admitted for new-onset T1D in the first and second years respectively, compared to 123 children in the prior year.
We used a poisson regression model to capture the effect of COVID and found that the rate of T1D cases multiplied by 1.42 following pandemic onset with p-value 0.0017, indicating a significant increase in T1D cases. We also employed a quasi-poisson regression model that allowed us to adjust for seasonality of T1D cases. In this second model, the effect of COVID on T1D cases was 1.51, again showing an increase.
Serum bicarbonate levels were lower (p-value 0.0014) and insulin infusion use was higher (41% pre vs. 53% post) suggesting greater disease severity in the post-COVID period. Only 2.2% of children with newly diagnosed T1D had COVID infection detected at admission.

Conclusions: The increased incidence of T1D at our center continued into the second year of the COVID-19 pandemic. Furthermore, we observed greater disease severity at diagnosis. The rate of COVID infection at T1D onset was low.

Endocrinology (continued)

Poster 43

INCORRECT AGE CAUSING "FALSELY SHORT STATURE" IN AN AFGHAN IMMIGRANT

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Background: Evaluation for short stature routinely includes screening for hormone deficiencies, gastroenterologic disease, and inflammatory processes. "Incorrect age" resulting in falsely short stature, is not often considered in the differential diagnosis.

Clinical Case: A young girl, recently immigrated to the United States from Afghanistan, was referred for endocrine evaluation for short stature. At the time of her initial visit, she was listed in the electronic medical record at 10 years old. Her measured height was 117.8 cm (0.06th percentile, Z = -3.24) and body mass index was 14.7kg/m2 (12th percentile, Z = -1.18). Medical history was significant for bowel injuries sustained three years prior in a bombing incident that required surgery. Available growth charts from the preceding 6 months showed height and weight consistently less than the 1st percentile for her age but normal height velocity. Laboratory work-up obtained by the pediatrician showed normal insulin growth factor 1, insulin growth factor binding protein 3, thyroid stimulating hormone, free and total thyroxine, tissue transglutaminase IgA, sedimentation rate, urinalysis, complete blood panel and complete metabolic panel. Her bone age was markedly delayed at 5 years 6 months. Upon further questioning, her father revealed there was an error in the processing of her immigration documents, resulting in her being listed as three years older than her actual age which was 7 years old. When corrected for this, her height improved to the 23rd percentile (Z = -0.73), and body mass index to 31st percentile (Z = -0.5).

Conclusion: This case demonstrates how children, through the immigration process, may inadvertently have an incorrectly documented age, and thereby are at risk for unnecessary and costly medical evaluation. Therefore it is important to verify their true age, as parents may not think to provide this information voluntarily.

Poster 44

ROLE OF THE GLP1-R IN THE COLLECTIVE BETA CELL NETWORKS IN LIVING PANCREATIC SLICES

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Background: Calcium (Ca2+) uptake drives glucose-stimulated insulin secretion from the pancreatic β-cells.

The "1st-responder" subpopulation of β-cells disproportionally control the Ca2+ uptake during the first phase, which is disrupted with ageing and in diabetes. Here we determine whether alpha cells play a formative role in the order in which beta cells in the islet respond to glucose.

Methods: We used B6 mouse model to produce living pancreatic slices of 150 um thickness. We performed recording of Ca2+ dynamics individual islets in the slice using confocal microscopy. We stimulated islets with glucose, and with the GLP1-R antagonist, exendin 9-39 (Ex9). Based on the first-phase Ca2+ dynamics we defined the "1st responder" and the "last responder" cells. We tested their consistency under repeated glucose stimulation with and without the Ex9. We next post-stained them for insulin, glucagon, and somatostatin and measured distances in 3D from all beta cells to alpha and delta cells.

Results: The Ex9 disrupted the 1st responder consistency (only half of the original 1st responder beta cells remained such under repeated glucose stimulation), compared to the control experiment. Ex9 increased the islet's first-to-last cell response time by 150 +/- 74 seconds making islet's response to glucose two times more heterogeneous compared to control (p=0.0517).

On average 1st responders were located closer to the alpha cells, and last responders – further from them (p=0.0039).

Conclusions: 1st responder beta cells have more alpha cell neighbors than last responders. The role of the alpha cell in the formation of the 1st responder cell state is likely realized via GLP1 receptor paracrine interaction.

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Endocrinology (continued)

Poster 41

EXTREME ESTRADIOL ELEVATION WITH RAPID NORMALIZATION IN A 6-YEAR-OLD GIRL WITH PERIPHERAL PRECOCIOUS PUBERTY

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Background: Peripheral precocious puberty (PPP) in girls is associated with ovarian or adrenal tumors, ovarian cysts, McCune-Albright syndrome (MAS), or exogenous hormone exposure. We present an unusual case of PPP with extreme estradiol elevation and rapid normalization.

Methods: Retrospective Chart Review

Results: A 6.5-year-old girl presented with two-month long bilateral breast growth and tenderness, associated with daily cramping. Subsequently, she developed clear, odorless vaginal discharge. Two days prior to visit she started light vaginal bleeding. Parents denied medication intake or use of lavender or essential oils. She had no family history of early puberty. On exam, she was tall for her age (95%) with recent growth spurt. She had breast buds (Tanner 2) and vaginal bleeding without pubic hair (Tanner 1) or signs of hyperandrogenemia. There were no skin lesions and bone survey showed no fibrous dysplasia. Bone age was normal. She had extreme elevation of estradiol [156pg/mL and 170pg/mL (reference range<=16pg/mL)] measured two weeks apart with prepubertal LH/FSH. Thyroid tests were normal. Pelvic ultrasound and abdomen/pelvis CT showed no abnormalities of ovaries and adrenal glands. Nine days after onset, vaginal bleeding and cramping spontaneously resolved. Estradiol levels measured two days after cessation of vaginal bleeding normalized (7pg/mL) while LH/FSH remained prepubertal. Two weeks after the bleeding stopped her pelvic ultrasound showed significantly enlarged ovaries (R 4.1mL, L 4.3mL), while her estradiol remained normal (5pg/mL). However, her pelvic ultrasound three months later indicated normal ovarian size (R 1.9ml, L 1.5ml).

Conclusions: We suspect PPP secondary to ruptured ovarian cyst not captured by imaging. Differential diagnoses include MAS, exogenous hormone exposure, adrenal or ovarian tumors. These were unlikely due to no abnormal skin or bone findings, environmental hormone exposure and normal imaging. This case emphasizes the importance of prompt assessment of children with PPP and discusses its differential diagnosis.

Environmental Health

Poster 50

ASSOCIATION OF PRENATAL ALCOHOL EXPOSURE AND NEUROTOXIC AND NUTRITIVE METALS CAPTURED IN PRENATAL AND POSTNATAL STRATA OF DECIDUOUS TEETH

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We have identified novel biomarkers of prenatal alcohol exposure (PAE) in deciduous (baby) teeth and are exploring interactions among PAE and metals. Identifying the timing of exposures to both alcohol and metals may help identify mechanisms and vulnerable periods leading to neurodevelopmental impairment.

Caregivers of children diagnosed with an FASD or no FASD (cases and controls), were recruited through CIFASD cohorts (PIs Mattson and Wozniak), consented, and asked to provide deciduous teeth. Samples were analyzed using laser ablation-inductively coupled plasma-mass spectrometry to measure metals at weekly resolution from the second trimester to one-year after birth. We applied reverse distributed lag models to identify critical time windows when metals were associated with diagnosis of FASD, while adjusting for past exposure values.

To date we have measured temporal metal exposure profiles of zinc, magnesium, lead, chromium, arsenic, copper, lithium, manganese, strontium, barium, and cadmium from the teeth of 5 controls and 15 cases. In pooled data from the entire prenatal period, differences in mean Cr and Sr were observed among case and control samples. Both are elevated among case samples. Sr differences persisted into the postnatal period. When viewed in weekly increments, sensitive windows of Mg deficiency in the early second trimester and increased Sr in the postnatal period were observed in case samples.

Our findings mirror those of animal models showing that maternal alcohol ingestion alters maternal-fetal transfer and metabolism of metals, which may contribute to manifestations of FASD in offspring. Lower Mg has also been measured in fetal rats after maternal exposure to ethanol. Maternal nutritional status may exacerbate or ameliorate PAE effects. Identifying critical windows of metal deficiency may contribute to understanding the mechanisms of damage caused by alcohol. Additionally, it may inform targeted interventions to improve outcomes for offspring of mothers who may consume alcohol during pregnancy.

Funding: UH2AA029062 CIFASD grant funded by the NIAAA

Poster 49

RISK OF BIRTH DEFECTS AMONG OFFSPRING OF FIREFIGHTERS IN CALIFORNIA

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Background: Firefighters are exposed to hazards that could affect birth outcomes. Few studies examined: birth defects among offspring of male firefighters and yielded mixed findings. No studies have examined birth defects among offspring of female firefighters. We examined the incidence of birth defects among the offspring of male and female firefighters in a population-based cohort.

Methods: Data from 2007-2019 California birth certificates were probabilistically linked to offspring hospitalization records. Maternal and paternal occupations were reported on birth certificates. We included individuals that had occupational exposure within 90 days of the last menstrual period and created a 4-level independent variable (no parent firefighter, maternal firefighter only, paternal firefighter only, both parents firefighters). Major birth defects, grouped in general by organ system, were measured by ICD codes (oral clefts, circulatory, digestive, musculoskeletal, eye, ear/face/neck, genital, central nervous system, renal, and respiratory). We estimated risk ratios (ref ='no parent firefighter' group) adjusting for maternal age, race/ethnicity, education, payer, and year.

Results: Compared to the reference (n=3,181,485), there was no increased risk of birth defects among offspring of paternal firefighters (n=19,645). However, offspring of paternal firefighters had lower risk of oral clefts (0.4, 95%CI 0.3, 0.7) and respiratory defects (0.7, 95%CI 0.5, 0.9) than the reference. The risk of birth defects among offspring among maternal firefighters (n=281) and among both parents firefighters (n=222) did not differ significantly from the reference.

Conclusions: These results do not incite concern about higher risk of birth defects among firefighter offspring in California. Findings may differ in other regions and birth years. The study is limited because although individuals were firefighters during pregnancy, their specific duties were unmeasured. Future research should investigate whether the protective associations reported above could be due to healthy worker bias or unmeasured confounding. Comparisons to other reference occupations could be useful.

Environmental Health (continued)

Poster 48

ASSOCIATIONS BETWEEN CANNABIS USE DISORDER AND GASTROSCHISIS IN A POPULATION-BASED COHORT

Erin Delker, Ann Kelley, Christina Chambers, Gretchen Bandoli

Background: Gastroschisis is an abdominal wall birth defect with unknown etiology. Researchers have cited concomitant trends of increasing prevalence of cannabis use and gastroschisis as evidence that cannabis use may be a causal factor. However, inferences from etiologic studies are limited. We used individual-level data to estimate the association between cannabis use disorder in pregnancy and gastroschisis.

Methods: Data were from the Study of Outcomes in Mothers and Infants, a cohort compiled from all 2005 to 2019 California birth records probabilistically linked to maternal and baby hospitalization records (n = 6966944). Cannabis use disorder during pregnancy was identified by diagnosis codes in maternal records. Gastroschisis was identified with diagnosis and procedure (gastroschisis repair) codes in offspring records. Covariates included maternal age, race/ethnicity, education, county urbanicity, delivery payer, alcohol use disorder, smoking in pregnancy, non-cannabis drug use, body mass index, and bipolar disorder. We estimated sequentially adjusted risk ratios for the association between cannabis use disorder and gastroschisis. We also stratified by maternal age to evaluate effect modification.

Results: About 1% (n = 56,879) of births had cannabis use disorder. The incidences of gastroschisis in the exposed and unexposed group were 0.14% and 0.06%. In the fully adjusted model, cannabis use disorder was associated with higher risk of gastroschisis (aRR = 1.4, 95%CI 1.1, 1.8). The association varied by maternal age. It was null among people < 18 years (aRR = 1.1, 95%CI 0.4, 3.0), small among people 18 – 34 years (aRR = 1.4, 95% CI 1.1, 1.8), and larger among people > 34 years (aRR = 2.3, 95%CI 1.0, 5.6).

Conclusions: Our findings are consistent with prior literature showing higher incidence of gastroschisis among individuals prenatally exposed to cannabis. Effect modification by maternal age raises the question of whether there are different etiologic factors in young vs older individuals.

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PRENATAL EXPOSURE TO CANNABIS AND RISK OF MAJOR STRUCTURAL BIRTH DEFECTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Our objective was to review and meta-analyze observational studies that examined associations between prenatal cannabis exposure and major structural birth defects.

Methods: We included observational studies that examined the risk of major structural birth defects in people who used cannabis during pregnancy compared to a no cannabis control group. We excluded case reports, ecologic studies, conference abstracts, manuscript preprints, studies designed to examine effects of cannabis concurrent with other drugs, and studies that included synthetic cannabinoids. Information sources included: Google Scholar, BIOSIS, PubMed/MEDLINE, EMBASE CINAHL. We clustered and meta-analyzed measures of association for birth defect outcomes by anatomic group.

Results: Our review included 23 studies that analyzed data from birth years 1968 to 2021. Eleven articles reported an association between cannabis use and the risk of a non-specific outcome (e.g., congenital anomaly). We estimated a pooled RR of 1.3 (95% CI 1.1, 1.6) and a pooled aRR of 1.2 (95% CI 1.0, 1.5). Other anatomic groups examined were cardiac (9 studies), oral cleft (3 studies). digestive (4 studies), genitourinary (3 studies), musculoskeletal (6 studies), and nervous system (5 studies). Across most outcomes, we reported positive pooled unadjusted associations which were usually attenuated after including only adjusted estimates. There were two outcomes where effect estimates did not attenuate to the null after adjustment: Ebstein's anomaly (2 studies, aRR = 2.2 (95% CI 1.3, 3.8)) and gastroschisis (5 studies, aRR = 2.5 (95% CI 1.1, 5.7)).

Discussion: Studies examining associations between prenatal exposure to cannabis and major structural birth defects were heterogeneous. Most published effect estimates were unadjusted and cannot be overinterpreted. Following adjustment of confounding factors, it is plausible to conclude that findings related to gastroschisis and Ebstein's anomaly should be considered for inclusion in further research studies.

Environmental Health (continued)

Poster 51

ADDRESSING FETAL ALCOHOL SPECTRUM DISORDERS (FASD) AND OTHER DEVELOPMENTAL DISABILITIES IN AN INDIGENOUS COMMUNITY

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Background: Over the past 14 years, we have collaborated with a Southern California reservation-based Indigenous community to address Fetal Alcohol Spectrum Disorders (FASD) and other developmental disabilities. In a series of grant funded studies, we investigated community risk factors and awareness, determined the needs and priorities of families living with FASD, obtained an FASD prevalence estimate, established the first Tribal FASD United affiliate, and developed culturally congruent support for families. Our current project has provided detailed health assessments for 25 families, designed and presented individualized family plans informed by all associated studies, and are compiling a corresponding community plan.

Methods: Under the guidance of our Community Advisory Board, using structured interviews (n=101 caregivers, n=>10 key informants), focus groups (n=11), and a community survey (n=305), we determined overall needs, resources, and priorities. Detailed health assessments for 25 families, a subset of the 101 participating caregivers, included medical, dysmorphological, and neurobehavioral assessments for the child, caregiver surveys including CBCL, child Adverse Childhood Experiences, child prenatal exposures, current substance use, Perceived Stress, and Perceived Wellness.

Results: We will present results regarding family and community resources, challenges and barriers, protective factors, and prioritized support; child and caregiver health as it relates to service and treatment capacity; feedback from family plans and implementation of support to date; and critical cultural components.

Conclusions: FASDs present difficulties for individuals affected, their families, and their communities. Reservation-based Indigenous communities often experience different challenges and strengths compared to the general population. Culture, tradition, and Indigenous knowledge are strong protective factors and opportunities for treatment and support. A culturally congruent approach to support and treatment is warranted.

Poster 47

MATERNAL EXPOSURE TO DRY CLEANING AND RISK OF MAJOR STRUCTURAL BIRTH DEFECTS

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Background: Perchloroethylene (PERC), a solvent used in industrial laundry and dry cleaning, has faced regulatory actions in California. Risk evaluations cite studies linking PERC exposure to adverse birth outcomes. Few studies, with small samples, examined effects of PERC on birth defects and yielded mixed results. We estimated associations between occupational exposure to laundry and dry cleaning and birth defects.

Methods: Data were from the Study of Outcomes of Mothers and Infants, a cohort derived from California birth records, 2007-2019. Maternal industry and occupation were recorded on birth certificates. Major structural birth defects were measured using International Classification of Diseases codes. We estimated unadjusted and adjusted risk ratios (RRs) for the incidence of birth defects. Adjusted models included maternal age, county urbanicity, maternal education, race/ethnicity, and payer for delivery. We stratified analyses by time period (2007-2010, 2011-2019), coinciding with regulations requiring removal of old PERC machines.

Results: Laundry and dry cleaning workers (n = 4878) had a higher incidence of oral clefts compared to other occupations (n = 3671612) (RR = 1.7, 95%CI 1.1, 2.7), but no other birth defects. After adjustment, the association with oral clefts was attenuated (1.5 , 95%CI 0.9, 2.4). This association also varied by time. Between 2007 to 2010, the RR was 2.3 (95%CI 1.2, 4.3) and between 2011 to 2019, the RR was 1.2 (95%CI 0.6, 2.5).

Conclusions: Study results showed an association between laundry and dry cleaning and oral cleft defects, which could be due to PERC exposure. Results did not demonstrate relationships with other defects, which have been linked to PERC exposure in prior studies. Future research must use more sensitive measurements of the exposure of interest. Meta-analysis to summarize findings across studies and to identify factors contributing to varied outcomes is needed.

Gastroenterology

Poster 55

THE INDEX OF SEVERITY FOR EOSINOPHILIC ESOPHAGITIS (I-SEE) REFLECTS CLINCOPATHOLOGIC CHANGES OVER TIME IN A PEDIATRIC COHORT

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Background: The Index of Severity for Eosinophilic Esophagitis (I-SEE) has been recently proposed as a metric to capture disease severity in EoE. It has yet to be assessed in a pediatric population.

Methods: We performed a retrospective cohort study of pediatric EoE patients prospectively enrolled into a UCSD/Rady longitudinal database. Patients had a diagnosis of EoE, were enrolled between 2011-2018, maintained follow-up for at least 2 years, and had at least 3 EGDs. Features of symptom frequency, complications (i.e. impactions, malnutrition, EoE-related hospitalization, and treatment refractory disease), and inflammatory/fibrostenotic features from both endoscopic and histologic findings were obtained via chart review. I-SEE was calculated at three time-points: initial, second, and last endoscopy. Patients were classified as mild (1-6 points), moderate (7-14), severe (≥15), or inactive (0). We analyzed clinical, endoscopic, and histologic features at each instance/endoscopy by disease severity. We analyzed change in severity between 1st and 2nd and 1st and last EGDs.

Results: Of 67 patients evaluated (mean age 5.2yrs, 22% female, 78% white), mean I-SEE was 9.7 at baseline with 43% classified as mild, 36% moderate, and 21% severe. Baseline severity was associated with younger age, lower BMI, and difficulty feeding. At the second EGD, most had inactive (9%) or mild (66%) disease compared to baseline, with accompanying decreased symptom frequency and endoscopic inflammatory features. By the last EGD (mean 6.6±2.2 yrs from the first), mean I-SEE score decreased to 3.9 with 88% of patients with inactive or mild disease. Malnutrition significantly decreased over this time, as did symptom frequency, endoscopic inflammatory features, eosinophil counts, and histologic lamina propria fibrosis.

Conclusions: I-SEE reflected longitudinal EoE disease severity features in children. At baseline, severe patients were younger with lower BMI, and difficulty feeding. EoE severity improved over time in this cohort. I-SEE is responsive to therapy and has clinical utility in children.

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GLOBAL, CONTINENTAL, AND NATIONAL PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE IN ADOLESCENTS: AN ANALYSIS OF THE GLOBAL BURDEN OF DISEASE STUDY 2019

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Background: Nonalcoholic fatty liver disease (NAFLD) in adolescents is an increasing health crisis worldwide but its exact global, continental, and national prevalence, and its relationship with the human development index (HDI) globally are not known. Methods: We analyzed data from the Global Burden of Disease Study 2019 to compare global, continental, and national prevalence rates of adolescent NAFLD, and associations with the HDI. We assigned each country their respective 2019 HDI value and HDI group, which we obtained from the "United Nations Development Programme". Results: The global NAFLD prevalence in adolescents increased from 3.73% in 1990 to 4.71% in 2019 (relative increase of 26.27%). The prevalence for males and females was 5.84% and 3.52% in 2019, respectively. Egypt (18.44%), Qatar (17.04%), and Kuwait (15.67%) had the highest NAFLD prevalence rates in adolescents worldwide. The Oceanian and North American continents had the highest adolescent NAFLD prevalence (median 6.54% and 5.64%, respectively), whereas Europe had the lowest prevalence (median 3.98%). South and North America had the highest relative increase in adolescent NAFLD prevalence from 1990-2019 (median 39.25% and 36.87%, respectively). Countries with higher HDIs had larger increases in adolescent NAFLD prevalence from 1990-2019, although countries with the highest HDIs (HDI>0.9) had the lowest NAFLD prevalence in 2019.

Conclusions: NAFLD in adolescents is an increasing health problem on all continents. Improving environmental factors, including lifestyle but also healthcare policies, can help to prevent NAFLD from developing in children and adolescents and help to improve outcomes in children and adolescents with NAFLD.

Gastroenterology (continued)

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SHARING INPATIENT MEDICAL NOTES WITH HOSPITALIZED ADOLESCENTS AND CAREGIVERS: PRELIMINARY RESULTS FROM A MIXED METHODS STUDY

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Background: Rady Children's Hospital (RCH) releases medical notes to adolescent and young adult (AYA) patients (≥ 12 years old) unless withheld by their provider for sensitivity concerns. While research demonstrates notable adult patient benefit from reading medical notes, existing research evaluating AYA patients' reactions to medical notes is extremely limited. Two previous studies in the ambulatory and inpatient psychiatry settings suggest AYA patients adequately comprehend their medical notes and are highly satisfied with reading them1,2. Our mixed-methods study aims to be the first to characterize AYA and their caregivers' experiences in regard to medical note access in the inpatient setting.

Methods: We have begun recruiting English-speaking cognitively-intact patients aged >15y and their caregivers admitted to the RCH inpatient service with access to their medical notes. After informed consent, participants 1) complete a comprehension survey, including rating their understanding of test results and medical treatment plans on a scale of 1(no understanding) to 10 (full understanding), 2) read their most recent medical note, and 3) repeat their comprehension survey and perform a semi-structured interview, which was recorded and transcribed for thematic analysis.

Results: 7 AYA and 4 caregivers have been recruited to date. Preliminary results show that AYA and caregivers had different group responses in their comprehension of test results and treatment plans with reading of the medical note. Transcribed excerpts from semi-structured interviews demonstrate initial themes that AYA and caregivers expressed related to understanding physician's clinical reasoning and the information provided in the medical note. Medical jargon was universally cited as the main barrier to medical note comprehension and usefulness.

Conclusions: We have demonstrated initial feasibility in recruiting AYA and caregivers for our study. Preliminary responses demonstrate overall positive sentiments about medical note access. Next steps include continued subject recruitment to reach target sample size.

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PREVALENCE OF ELEVATED ALANINE AMINOTRANSFERASE IN ADOLESCENTS IN THE UNITED STATES 2011-2018

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Background: Nonalcoholic fatty liver disease (NAFLD) is the most common pediatric liver disease in the U.S. Screening for NAFLD is recommend via measurement of alanine aminotransferase (ALT). In the US information on prevalence of NAFLD in Asian American children are extremely limited. The study aim was to determine prevalence of suspected NAFLD, as measured by elevated ALT, in adolescents, with a specific focus on Asian American adolescents.

Methods: We analyzed data from the National Health and Nutrition Examination Survey from 2011 to 2018 for adolescents aged 12 to 19 years. Participants with causes for elevated ALT other than NAFLD were excluded. Race, ethnicity, sex, body mass index (BMI), and ALT were examined. Elevated ALT was defined as above the biological upper normal limit (ULN) : >22 U/L (females) and >26 U/L (males). Multivariable logistic regression evaluated the association of race/ethnicity and elevated ALT, adjusting for age, sex, and BMI.

Results: The prevalence of elevated ALT in adolescents was 16.5% overall and 39.5% among those with obesity. Prevalence was highest in Hispanic adolescents (21.8%), followed by Asian (16.5%) and White (15.8%) adolescents, and lowest in Black adolescents (10.7%). Among those with obesity prevalence with was higher in Asian (43.1%), Hispanic (43.5%), and White (43.0%) adolescents than in Black adolescents (20.7%). Among participants with overweight, prevalence of elevated ALT was highest in Asian adolescents (27.0%). Independent risk factors for elevated ALT were older age, male sex, Hispanic ethnicity, and higher BMI.

Conclusions: This study found that the national general population prevalence of suspected NAFLD among adolescents in the U.S has increased over the last decade. For 2011-2018, 1 in 6 adolescents had elevated ALT. Hispanic adolescents had the highest risk of elevated ALT. Asian adolescents with elevated BMI may represent an emerging risk group for elevated ALT.

Genetics

Poster 58

HEMATOPOIETIC STEM CELL GENE THERAPY FOR MUCOPOLYSACCHARIDOSIS TYPE IIIC

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Mucopolysaccharidosis type IIIC (MPSIIIC) is a severe progressive childhood neurodegenerative disease caused by loss-of-function of the transmembrane lysosomal protein Heparan-α- glucosamine N-acetyltransferase (HGSNAT). MPS IIIC is part of the lysosomal storage disease (LSD) family and is characterised by the accumulation of glycosaminoglycans (GAGs). This disease has no available treatment and presents early in life with symptoms like missing developmental milestones, neuronal cell loss and loss of motor function, eventually leading to death around the second or third decade of life. Our lab has previously shown that transplantation of hematopoietic stem and progenitor cells (HSPCs) rescue cystinosis, another LSD due to mutations in a transmembrane lysosomal protein. The mechanism of rescue involved lysosomal cross-correction from HSPC-derived macrophages to the disease cells via tunneling nanotubes within tissues. We
believe that the same principles could be used to treat MPSIIIC.

We generated a new MPSIIIC mouse model by knocking-out exon 2 in Hgsnat. We have confirmed the presence of MPSIIIC disease phenotypes such as GAG accumulation, enlarged liver, distended bladder, urine retention, lysosomal expansion, neurological defects, increased inflammation, and the presence of disease specific non-reducing end carbohydrates biomarkers in our mouse model. As the first proof of concept, we transplanted Hgsnat-/- mice with HSPCs isolated from WT GFP-transgenic mice. Even though we see engraftment of HSPC-derived cells, tissue expression of Hgsnat was low and no reduction in GAG storage was observed in the transplanted mice. These data demonstrate that endogenous Hgsnat is not well expressed in HSPC-derived macrophages/microglia explaining the limited impact of WT-HSPC transplant on GAGs. Nonetheless, WT-HSPC transplant did show improvement in hepatomegaly, urine retention, neurological defects, and gait defects, which correlates with decreased inflammatory markers in the treated Hgsnat-/- mice.

Limited efficacy of WT-HPSCs has also been reported in MPSIIIA, which was overcome by using gene-modified HSPCs to overexpress SGSH gene. Therefore, we are developing an autologous transplantation of ex-vivo gene modified HSPCs. We have generated self-inactivated (SIN)-lentivirus vector containing human HGSNAT cDNA (NM_152419 & XM_005273411.2) and performed in vitro testing. Following transduction of mice fibroblasts, human patient fibroblasts and human patient B-lymphoblast, we observed increased human HGSNAT mRNA expression, lysosomal localisation of HGSNAT, recovery of HGSNAT enzyme activity, decreased GAG storage, and decreased lysosomal accumulation.

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CORTICAL BRAIN ORGANOIDS IN A ZERO GLUCOSE ENVIRONMENT, A STEP FURTHER INTO USING ORGANOIDS AS MODELS FOR NEONATAL HYPOGLYCEMIA

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Background and aims: Cortical organoids are self-organizing 3-dimensional structures derived from pluripotent stem cells. They have the advantage of allowing direct measurement of different metabolites, such as glucose. This study aims to determine if exposing cortical brain organoids to zero glucose environment will change the pattern of neuronal differentiation, cell death markers and/or intracellular ATP.

Methods: Three-month-old brain organoids were exposed to zero glucose media for increasing amounts of time: 0 (controls), 1, 3, 6, 24, and 48 hours. Half of the organoids were frozen for biochemical analysis, and half were fixed for Immunohistochemistry. Stains performed included:

- DAPI (for estimating the total number of cells).
- TUNEL (a marker for cell death).
- NeuN (a marker for mature cell neurons).

Pictures of the different stains were obtained for randomly selected organoids. Fiji software was used to analyze the images for intensity quantification.

Results: There was a statistically significant increase in the mean relative intensity of TUNEL from controls to 48 h, consistent with an increase in cell death (Welch test 3.22, p=0.049). There was a statistically significant decrease in the mean relative intensity of NeuN from controls to 1h, 3h, and 6 h conditions, consistent with a reduction of mature neurons. (ANOVA 3.07, p=0.034). Intracellular biochemical data revealed a marked decrease in ATP from 0.75 to 0.36 nanomoles/mg of tissue in the first hour, followed by a significant decline in ADP and AMP.

Conclusions: Using cortical brain organoids, we have created a model to study the effects of hypoglycemia on neurons. Preliminary data suggests clear biochemical and functional changes in organoid cell cycle after one hour of exposure to zero glucose environment. Our data support the use of organoids as models for studying the cellular effects of hypoglycemia.

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SLEEP IN ANGELMAN SYNDROME- DATA ANALYSIS FROM THE NATURAL HISTORY STUDY

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Background: Angelman Syndrome (AS) is a severe neurogenetic disorder characterized by intellectual disability, absent speech, seizures, behavior problems and sleep disturbance.(1) AS is caused by the lack of expression of maternally inherited UBE3A in the central nervous system. Currently, treatment consists of supportive measures. Caregivers of children with AS report high levels of stress, relationship strain, fatigue and irritability, which are exacerbated by sleep deprivation.(2)
We analyzed data from the AS Natural History Study (NHS), to describe the characteristics of sleep disturbance in Angelman syndrome, including any association with molecular diagnosis, age and types of medications used.

Methods and data analysis: Data were obtained from the NHS, a longitudinal observation study which has been enrolling individuals of any age with a molecular diagnosis of AS since 2006. There are two detailed sleep questionnaires administered in the NHS (one a validated instrument [SNAKE] and the other developed by the investigators to determine the extent of sleep difficulties). The statistical analysis was performed using the built-in functions in RStudio.

Results: Sleep data were available on 452 individuals with AS. Overall, 85.9% reported sleep difficulties (80% of individuals between one and 13 years, and in 90% of those older than 13). At least 60% of children with AS reported night awakenings more than 2 nights per week. There were no significant differences in sleep patterns among the different molecular etiologies. Melatonin was the most common sleep pharmacologic treatment used in about 45% of the cohort, while Benadryl and Clonidine were used in approximately 15% of the children.

Conclusion: Sleep difficulties are reported in at least 80% is individuals with AS, while the use of sleep medication is reported in about 45%. These findings indicate a significant unmet clinical need of this population. Future studies are needed to elucidate the effectiveness of pharmacological agents.

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ROLE OF SOCIAL DETERMINANTS OF HEALTH ON CANCER KNOWLEDGE AMONG PARENTS OF CHILDREN WITH NEWLY-DIAGNOSED CANCER AT RADY CHILDREN'S HOSPITAL SAN DIEGO

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Background: It is critical for parents of children with cancer to be knowledgeable regarding their child's diagnosis to effectively navigate their child's cancer care. Research investigating the role of Social Determinants of Health (SDoH) on cancer knowledge is scarce.

Methods: We prospectively assessed levels of disease knowledge among parents of children with newly-diagnosed cancer (past 3 months) and associations with SDoH. Our outcome measure was level of parental cancer knowledge on cancer type, stage/risk stratification, if enrolled in a therapeutic clinical trial or receiving standard of care treatment, and name of protocol if applicable (score 0-100% correct answers). Socio-demographics included parental age, sex, race/ethnicity, English proficiency, marital status, education attainment, insurance type, and employment status. Health literacy (HL) was measured using the Newest Vital Sign (NVS).

Results: 182 English or Spanish-speaking parents completed surveys. 67% of participants were female (n=112) and 47% Hispanic (n=96). On average, parents answered 40% of questions correctly on the cancer knowledge survey (SD+/-19). In univariate analysis, lower cancer knowledge was associated with limited HL (p=0.003), unmarried status (p=0.015), lower education attainment [high-school or less] (p=0.048), and public insurance (p=0.006). In adjusted multivariate analysis, limited HL remained significantly associated with lower knowledge (p=0.036). Moreover, parents with limited HL were 77% less likely to know if their child was receiving treatment enrolled in a clinical trial or standard of care treatment (OR=0.13, p<0.001, 95%CI=0.065-0.403).

Conclusion: Parents of children with newly-diagnosed cancer scored overall low on the baseline knowledge test. Limited HL was significantly associated with lower cancer baseline knowledge after adjusting for SDoH. Our findings underscore the importance of identifying parents with limited HL to effectively increase their cancer knowledge by providing targeted education and support. Future research should assess how parental cancer knowledge affects clinical outcomes and include interventions, particularly tailored to individuals with limited HL.

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A MIXED METHODS PILOT STUDY OF A VIRTUAL THERAPEUTIC WRITING INTERVENTION FOR AYAS WITH CANCER

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Learning Objectives: The participant shall be able to analyze the mixed methods findings of a completed pilot study of a virtual therapeutic writing intervention for AYAs with cancer.

The participant shall be able to determine the next steps for an efficacy trial and workbook development for a virtual therapeutic writing intervention for AYAs with cancer.

Approximately 89,000 adolescents and young adults (AYAs) are diagnosed with cancer each year. AYAs with cancer report elevated levels of distress and unmet needs. AYAs are understudied in cancer, and the few studies of writing interventions in this population have reported beneficial effects on well-being (e.g., distress). This mixed methods pilot study examined the effects of a novel, individualized, virtually delivered therapeutic writing intervention on AYAs' perceptions of their cancer experience, cancer-related distress, and cancer-related growth.

Eleven AYAs with cancer (ages 13-26) were enrolled in a virtual therapeutic writing intervention delivered by a non-clinical creative writing coach. Baseline and post-intervention surveys assessed cancer-related distress, psychosocial illness impact, self-efficacy, health status, depression, anxiety, and cancer-related growth. Pre- and post-intervention semi-structured interviews explored participants' experiences with cancer, writing, and the intervention. The 6-session intervention was conducted over 2-3 months and focused on writing exercises, brainstorming, goal setting, feedback, and formatting, culminating in works that reflected on participants' experiences with cancer. Each session included a brief acceptability survey. Feasibility and acceptability were assessed through descriptive statistics and qualitative findings.

Participants (M age = 16.09, SD = 2.47; 54.5% male) rated sessions as highly enjoyable, helpful, useful, and satisfactory (M's > 4.4), and affirmed these findings in qualitative post-intervention interviews, demonstrating acceptability. Patients especially enjoyed the flexible options for their creative works, working with a non-clinical interventionist, and having the opportunity to process their cancer-related experiences in a creative way. 8 of 11 consented patients completed all study sessions, demonstrating feasibility.

Findings indicated that this writing intervention is feasible and acceptable to AYAs with cancer. Our multidisciplinary team will design a randomized controlled trial and is developing a manual and workbook to aid dissemination of this novel intervention. This future study will incorporate exploratory outcomes such as cancer-related distress, self-efficacy, and cancer-related growth.

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PILOT STUDY OF TELEMEDICINE WELLNESS PROGRAM FOR CHILDREN AND ADOLESCENTS WITH INHERITED BLEEDING DISORDERS

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Background: The World Federation of Hemophilia recognizes physical activity as an essential component of health maintenance. Telemedicine has been suggested for physical therapy and wellness interventions, but data are lacking regarding feasibility, adherence, and outcomes.

Aim: The aim of this study was to determine the feasibility of a six-week virtual wellness program for children and adolescents with inherited bleeding disorders.

Methods: The program included six weekly 45-minute video visits with a physical therapist who specializes in bleeding disorders and included tailored physical activity focused on conditioning and strength, flexibility, stress management, tips for healthy living, and assessment of wellness goals. Data on visit adherence were collected, and baseline and study exit surveys were done to assess current physical activity, physical fitness, and wellness goals.

Results: Thirty eligible persons were invited to participated and 20 (67%) enrolled in the study including 15 (75%) males. Participants were primarily White, Hispanic with mean age of 15 ± 5 years (range 8-18y). Thirteen have hemophilia (including 9 on prophylaxis), 5 VWD, and 2 platelet disorders. At study baseline, reported activity included 4 (20%) none, 4 (20%) cardio, 4 (20%) strength/conditioning, 7 (35%) sports/hobbies, and 1 (5%) unknown. None reported participation on a sports team. Fifteen of 20 (75%) completed all study visits. The range of completed study visits was 0-6 (median 6). The median length of participation was 6 weeks (range 0-15 weeks). One did not complete any visits due to school conflict and one did not complete the program due to moving out of state only 6 (30%) returned written surveys after completion of the program.

Conclusion: A virtual wellness program was feasible with high interest in the program with most participants completing all visits. Additional research in a larger population is indicated to evaluate the program outcomes and include different survey methodology to ensure complete data capture.

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LIMITED HEALTH LITERACY IN HISPANIC CAREGIVERS OF CHILDREN WITH CANCER AND CHILDHOOD CANCER SURVIVORS AT RADY CHILDREN'S HOSPITAL SAN DIEGO

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Background: Health literacy (HL) is the individual's ability to find and use information and services to make health decisions. Limited HL is associated with poorer outcomes. HL is vastly understudied in childhood cancer. Thus, we investigated HL and associations with Social Determinants of Health in caregivers of children with newly-diagnosed cancer and of childhood cancer survivors.

Methods: We conducted a prospective cross-sectional study in caregivers of children with newly-diagnosed
cancer and caregivers of childhood cancer survivors at Rady Children's Hospital (2016-2019). Caregivers completed questionnaires in-person to assess sociodemographics, acculturation and HL with the Test of Functional Health Literacy (S- TOFHLA) and the Newest Vital Sign (NVS).

Results: 459 caregivers were enrolled (199 caregivers of children with newly-diagnosed cancer and 260 caregivers of childhood cancer survivors). 56% (n=256) were Hispanic and of those, 38% were Spanish-speaking, and 53% had low acculturation. Hispanics, compared to non-Hispanic Whites, had lower S-TOFHLA and NVS scores ($p<0.001$). Moreover, Hispanics had lower income ($p<0.001$) and lower education attainment ($p<0.001$), and were more likely to have public insurance ($p<0.001$), and unmarried marital status ($p<0.001$). Adjusted multivariable regression showed a higher odds ratio (OR) of limited HL in caregivers with education level of high school or less (OR=3.040, 95%CI:1.308,7.087), unmarried marital status (OR=2.573, 95%CI:1.065, 6.424), and Spanish as preferred language (OR=5.072, 95%CI:1.960,14.018).

Conclusions: We found that Hispanic and Spanish-speaking caregivers of children with newly-diagnosed cancer and caregivers of childhood cancer survivors were at higher risk for limited HL. Hispanics were also more likely to have public insurance, unmarried marital status, and lower education level. In underserved groups such as these, HL is an especially critical component of navigating cancer care and making informed health decisions. It is, therefore, essential to direct future research efforts towards developing interventions to improve HL in underserved populations to improve cancer clinical outcomes.

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EVALUATION OF A HEMOPHILIA A GENE THERAPY SHARED DECISION-MAKING TOOL FOR CLINICIANS

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Background: As gene therapies are incorporated into clinical practice, shared decision-making (SDM) is recommended for implementation. The aim of this study was to understand gene therapy attributes to include in a clinician SDM tool for valoctocogene roxaparvovec, an adeno-associated virus-based gene therapy for men with severe hemophilia A.

Methods: Clinicians at US Hemophilia Treatment Centers completed semi-structured interviews about their experience with SDM and provided feedback on a clinician SDM tool prototype. The interviews were transcribed for quantitative and qualitative analysis.

Results: Ten participants enrolled, eight physicians and two hemophilia nurses. All participants care for adults with hemophilia (1-27 years of experience) and have gene therapy trials open at their institutions. All participants reported familiarity with SDM and use in clinical practice. Confidence in discussing gene therapy included none (N=1), slight (N=3), moderate (N=5), and high (N=1). Identified attributes to include in the tool were safety (N=10), efficacy (N=7), process of gene therapy including short and long-term follow-up (N=7), insurance coverage (N=7), and durability of response (N=3). Other attributes included mechanism of action, eligibility, comparison to current treatment, generalizability of results, and immunosuppression for transaminitis. All participants agreed the toolwould be useful for their clinical practice. Participants highlighted the importance of providing non-biased information and tailoring discussion to individual patients. They also identified the importance of having a companion tool in lay language for patients.

Conclusion: These data highlight the need for SDM tools for clinicians as well as companion tools for patients. Key information to include are safety, efficacy, cost, and what patients should expect from pre-infusion through long-term follow-up. Data should be provided in a non-biased format and allow comparison to other treatment options. The tool is now ready for dissemination, implementation, and evaluation. It will be further refined as clinical trial data and real-world experience mature.

Poster 65

VITAMIN D DEFICIENCY AND SUPPLEMENTATION IN CHILDHOOD CANCER SURVIVORS AT RADY CHILDREN'S HOSPITAL SAN DIEGO (RCHSD)

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Background: Vitamin D deficiency can exacerbate treatment-related skeletal complications in childhood cancer survivors. Data regarding vitamin D deficiency (VDD) and vitamin D insufficiency (VDI), and Vitamin D supplementation in childhood cancer survivors are scarce. This study aimed to identify baseline VDD and VDI in childhood cancer survivors and determine whether supplementation increased vitamin D levels.

Methods: Childhood cancer survivors [n=188] at RCHSD between 2012-2015 were examined using serum concentration of 25-hydroxy vitamin D for VDD and VDI (≤ 20 ng/mL and 21-29 ng/mL, respectively). Supplementation cycles lasted at least 8 weeks, and increased vitamin D levels were calculated across three groups (non-supplemented, 1 supplement cycle, and 2+ supplement cycles) using general linear modeling (unadjusted and adjusted[a] for age, sex, and ethnicity). Stratified analyses included sex (male vs. female), age (<10 years vs. ≥10 years), ethnicity (non-Hispanic vs. Hispanic), cancer type (solid vs. hematological) and insurance type (private vs. public).

Results: 55.9% of patients were Hispanic, and the mean age was 11.9 ± 5.3. Of the participants, 23.4% were VDD, 39.4% were VDI, and 37.2% were vitamin D sufficient. Vitamin D levels increased by 38% ± 74% after 1 supplementation cycle (P=0.04, Pa=0.1) and 35% ± 57% after 2+ cycles (P=0.06, Pa=0.14). Following 1 supplementation cycle, vitamin D levels increased in boys (percent change 49% ± 89%, P=0.02, Pa=0.04) and non-Hispanics (36% ± 75%, P=0.05, Pa=0.04). Following 2+ supplementation cycles, vitamin D levels increased in older children (39% ± 48% change, P=0.04, Pa=0.09).

Conclusions: VDD and VDI were prevalent in 63% of childhood cancer survivors, and supplementation was effective at improving vitamin D levels in these patients. Boys, non-Hispanics, and older children had a significant response to vitamin D supplementation. Further research is indicated to evaluate disparate responses to Vitamin D supplementation and impact on bone health in childhood cancer survivors.

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IDENTIFYING RISK OF HOUSEHOLD MATERIAL HARDSHIP AND FOOD INSECURITY AMONG CHILDREN WITH CANCER AT RADY CHILDREN'S HOSPITAL SAN DIEGO: ASSOCIATIONS WITH SOCIAL DETERMINANTS OF HEALTH

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Background: Among Latinx children with cancer, socioeconomic barriers such as household material hardship (HMH) and food insecurity (FI) increase risk for poorer outcomes. We investigated prevalence of HMH and FI over time in families of children with cancer and associations with Social Determinants of Health (SDoH).

Methods: Parents/guardians of children (0-17yo) with newly diagnosed cancer and receiving treatment at Rady Children's Hospital San Diego were prospectively enrolled July 2019-November 2021. HMH and FI were assessed via surveys (English or Spanish) at baseline and at 3-, 6-, 12- and 24-months post-enrollment. Adjusted generalized estimating equation (GEEadj) models assessed longitudinal associations with SDoH.

Results: Participants (n=107) included 61 Latinx (57%) and 46 NHW (43%) parents/guardians. The majority were married (74%), <45 years old (80%), and had public insurance (55%). In 46% of Latinx, Spanish was the preferred language. At baseline, 63% Latinx vs. 38% NHW (p=0.25) reported HMH, and 56% Latinx vs. 44% NHW (p=0.65) reported FI. In GEEadj models, risk of HMH (ORadj=0.85, 95%CI:0.39-1.87) and FI (ORadj=0.58, 95%CI:0.22-1.55) over time was not different between Latinx and NHW participants. Public insurance was associated with significantly increased risk of HMH (ORadj=2.71, 95%CI:1.23-5.96) and FI (ORadj=4.09, 95%CI:1.39-12.05) over time, compared to private insurance.

Conclusions: HMH and FI were highly prevalent in Latinx and NHW families at baseline and 24-month follow- up, though there were no significant differences by ethnicity. Public insurance was associated with excess risk of both HMH and FI over time and could potentially be used as a surrogate to assess HMH and FI. It is imperative to address HMH and FI in underserved populations, as these adverse SDoH are associated with poorer clinical outcomes. Further studies with larger samples should investigate the long-term patterns of socioeconomic barriers in Latinx children and their impact on health outcomes.

Poster 63

PARENT-CHILD DIFFERENCES IN PERSPECTIVES ON CANCER PREDISPOSITION SYNDROME GENETIC TESTING IN PATIENTS WITH PEDIATRIC CANCER

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Cancer predisposition syndromes (CPS) impact 6-8% of patients with pediatric cancer. Genetic testing for CPS (CPS-GT) has multiple benefits. Despite the unique ethical considerations needed for CPS-GT in patients with pediatric cancer, such as patient autonomy concerns, literature on parent vs. viewpoints on CPS-GT decision-making is minimal. This study aimed to describe and assess patient and parent differences in CPS-GT-related perspectives.

Patients with pediatric cancer and/or their parents were recruited at RCHSD. Eligible patients were over the age of 15 and within 12-months of diagnosis or relapse. Eligible parents had children (<18 years of age) within 12-months of diagnosis or relapse. 20 parent-patient dyads, 74 parents, and 8 adult patients consented to genetic counseling (GC) and subsequent CPS-GT. Patients and parents completed surveys at baseline, post-GC, and post-CPS-GT in English or Spanish. This study examined baseline CPS-GT-related perspectives across 27 questions on a scale of 1-5 (Strongly Disagree-Strongly Agree). Descriptive statistics and one-way ANOVAs described and compared parent and patient perspectives.

Parents (77% female, 43.6% Latino/Hispanic) and patients (Mage = 16.6, 35.7% female, 42.9% Latino/Hispanic) both agreed with CPS-GT for patients with pediatric cancer (Mparents = 4.50, Mpatients = 4.14), but parents had higher means than patients ($F(1,118) = 4.87$, $p = .02$). They both agreed that parents should decide whether patients under 18 should receive CPS-GT (Mparents = 4.40, Mpatients = 3.71), but parents had higher means than patients ($F(1,119) = 13.30$, $p < .001$). Parents and patients neither agreed nor disagreed that CPS-GT results may cause personal distress (Mparents = 3.03, Mpatients = 2.96).

Parents and patients with pediatric cancer demonstrated certain differences in viewpoints on CPS-GT, but also overlapped on factors such as resultant distress. Future studies should investigate the mechanisms behind these differences and develop interventions to increase patient and parent knowledge and comfort regarding CPS-GT.

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EFFICACY AND TOXICITY OF INOTUZUMAB OZOGAMICIN FOR TREATMENT OF RELAPSED/REFRACTORY B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA IN PEDIATRIC AND YOUNG ADULT PATIENTS AFTER CD19-CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL THERAPY

Deborah Schiff, Nicholas Gloude, Catherine King, Cydele Cortez, Dennis Kuo, Eric Anderson

Background: Inotuzumab ozogamicin (InO), a CD22-directed humanized monoclonal antibody conjugated to cytotoxin calicheamicin, is FDA-approved for the treatment of adults with relapsed or refractory (R/R) B-cell precursor acute lymphoblastic leukemia (BCP-ALL). Data is scarce regarding use of InO for R/R BCP-ALL in pediatric and young adult patients who have previously undergone CD19-CAR T-cell therapy (CD19-CART).

Methods: We performed a retrospective analysis of the efficacy and toxicity of InO for treatment of children and young adults with R/R BCP-ALL after previous treatment with CD19-CART.

Results: Seven patients (ages 13-20 years) were treated with InO between 6/1/2020 and 3/1/2023 for CD22+ R/R BCP-ALL following CD19-CART. The mean InO dose/cycle was 1.5 mg/m2/cycle (range 1.1-1.8). This cohort was heavily pretreated. All had undergone CD19-CART therapy, 3 had received CD19-CART reinfusion (2 for post-CART relapsed leukemia, 1 for loss of B-cell aplasia), 3 had undergone hematopoietic stem-cell transplantation (HSCT)—including 2 who had received 2 previous HSCT, and 1 had received Blinatumomab. Five patients received InO for 2nd relapse, 1 for 3rd relapse, and 1 for 4th relapse. Seven patients were evaluable for response and 6 for toxicity. Estimated ORR was 85.7%. Best response for 3 of 6 responders was complete response (CR); 3 of 6 had complete response with incomplete count recovery (CRi). Five of 6 responders (83.3%) were flow MRD negative. Three of 6 responders underwent HSCT post-InO. One of 3 developed grade 2 sinusoidal obstruction syndrome (SOS) following HSCT. Three of 6 evaluable patients (50%) had delayed count recovery. One of 6 (17%) had > grade 3 ALT elevation. Estimated 1-year EFS and OS post-InO were 40% and 60%, respectively.

Conclusions: InO is effective therapy for heavily pretreated children and young adults with high-risk R/R BCP-ALL who have previously received CD19-CART therapy. Significant adverse effects include post-HSCT SOS and prolonged cytopenias.

Poster 70

SINGLE-CELL TRANSCRIPTOMICS AND TCR CLONALITY REVEAL ROLE FOR IMMUNOTHERAPY IN PEDIATRIC BRAIN TUMORS 11

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Brain tumors in children are a devastating disease in a high proportion of patients despite aggressive multimodal therapy. Because of inconsistent results in early-phase clinical trials in unstratified patient cohorts, the role of immunotherapy in pediatric brain tumors remains unclear. To address this question, we performed an in-depth survey of the single-cell transcriptomes and clonal relationship of intra-tumoral T cells from 24 children with brain tumors. Our results demonstrate that a large fraction of T cells in the tumor tissue are clonally expanded with potential to recognize multiple tumor antigens. Such clonally-expanded T cells display states linked to robust anti-tumor immunity, express higher levels of transcripts encoding for molecules linked to T cell activation, effector functions, immune cell recruitment, tissue-residency, immune checkpoints, and importantly, show significant enrichment of signatures linked to neoantigenspecific T cells. Notably, we identify several neoantigens in pediatric brain tumors, and show that neoantigen-specific T cell gene signatures are linked to better survival outcomes in high grade glioma. We further show that PD1-expressing CD8+ T cells in pediatric brain tumors are indeed functional as evidenced by their capacity for cytotoxicity, cytokine production and proliferation.
Among the patients in our cohort, we observe substantial heterogeneity in the degree of clonal expansion and expression of transcripts encoding immune checkpoints in tumor-infiltrating T cells. We propose that accurate molecular characterization of intra-tumoral T cell responses coupled with TCR repertoire analysis may guide the selection of patients where immunotherapy such as neoantigen-directed vaccines and checkpoint blockers are likely to be beneficial.

Hospital Medicine

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TRAINING RESIDENTS TO RESPOND TO RACIST MICROAGGRESSIONS THROUGH SIMULATION

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Background: Racist Microaggression (MA) trainings frequently present Microresistance Communication Tools (MCTs) as frameworks for MA responses. Studies often measure confidence to evaluate MCT trainings, but their impact on behavior change is unclear. Our goal was to use Standardized Patient Simulation (SPS) in teaching bystander skill acquisition, assessing application of skills in a simulated racist event.

Methods: Two resident groups participated in separate MA trainings (Table 1). Group A (n=17) received didactic lectures on MAs and MCTs. Group B (n=23) reviewed MCTs and discussed emotional self-regulation strategies for responding to racism. Residents practiced responding to racist MAs in SPS scenarios before and after each session; these were recorded for evaluation. We developed an observational assessment tool to measure use of six MCT skills, with a score of the number of skills used by each trainee. Within groups, we compared the proportion of trainees who used MCT skills pre- and post-session with McNemar's test. We compared between-group differences in change in skill use with Fisher's exact test, and used paired t-tests used for composite score means. We calculated effect size for each skill with Cohen's d.

Results: Group A showed improvement in use of several skills and total number of skills used (2.65 [SD 1.0] to 4.18 [SD 1.29], p<0.01). Group B similarly improved in total number of skills used (2.62 [SD 1.06] to 4.27 [SD 1.25], p<0.01). There was a significantly greater change in the proportion of trainees using "Attempt a Resolution" in Group B (Δ=42%, p <0.01, Cohen's d = 0.92) compared to Group A (Δ=6%).

Conclusions: SPS can be used to measure skill acquisition in racist MA trainings. Emotional self-regulation training led to greater use of conflict resolution in SPS scenarios. MA trainings may benefit from emphasis of both cognitive and emotional aspects of communication.

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A QUALITY IMPROVEMENT INITIATIVE TO IMPROVE FAMILY CENTERED ROUNDS THROUGH USE OF BEST-PRACTICE CHECKLISTS

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Background: RCHSD implemented family centered rounds (FCR) 10 years ago, shortly after the AAP identified FCR as the standard for inpatient pediatric care to have the family, physician(s), and nurse rounding at bedside. However, no reliable data exists on the quality of FCR at RCHSD, especially pertaining to FCR best-practice checklists which are shown to improve satisfaction, communication, and patient safety1,2. We aimed to achieve a 50% increase in completion rates of best-practice FCR checklist items over 5 months.

Methods: An interdisciplinary team used quality improvement (QI) methodology to collect baseline data, identify key drivers, and implement PDSA cycles. We chose 8 best-practice checklist items to target. Data was collected by direct observation of FCR on the pediatric hospital medicine service using a structured assessment tool developed by the QI team reflecting evidence-based FCR best practices. Continuous weekly data review is displayed by run chart to evaluate trends or outliers needing immediate intervention. Our primary balancing measure was rounding length.

Results: We observed 126 FCR. Baseline data showed a median checklist completion rate of 50% for all components. The lowest completion rates were seen in C1 (18%), C2 (25%), C6 (18%), C8 (0%). Highest rates were seen in completion of C3 (87.5%), C4 (100%), C5 (100%), and C7 (75%). After focused interventions, we saw increases in completion rates of C1, C2, and C6. Our primary outcome demonstrated a positive shift per IHI run chart rules. Median round length during baseline and last 3 weeks of data were 9 m 8 seconds and 9 m 29 s, respectively.

Conclusions: We increased completion rates of best-practice FCR checklist items, particularly in prompting family for updates/questions at the start of the discussion, prompting nurses for updates/questions at bedside, and discussing contingency planning without increasing length of rounding.

Hospital Medicine (continued)

Poster 71

GLOBAL HEALTH EDUCATION IN PEDIATRIC HOSPITAL MEDICINE FELLOWSHIPS IN THE U.S.

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Background: Interest in global health (GH) among pediatric residents and fellows is growing. While GH curricula and experiences are gaining acceptance in pediatric hospital medicine (PHM), the extent to which it is incorporated into fellowships is unknown.

Objective: To describe the current state of GH education in PHM fellowships.

Methods: In 2022, we conducted a cross-sectional survey of PHM fellowship directors [FDs] and current fellows. Surveys included questions on demographics, GH-specific programming in PHM fellowships, and barriers to GH training. We distributed electronic surveys via PHM listservs and email, using a database of all 69 national PHM FDs with a request to forward to current fellows. Descriptive statistics and Chi-squared tests were performed with Stata and Excel.

Results: 34 FDs responded (49% response rate, Table 1) with 18 programs (53%) offering GH experiences. Older PHM fellowships were more likely to offer GH experiences (p=0.04).. Of 16 programs without GH experiences, 13 (81%) expressed interest in offering GH experiences to PHM fellows. Barriers included lack of global health curricula, insufficient funding and competing educational demands (77%, 69% and 69%, respectively).

Of 102 current fellows (57% response rate), 73% expressed interest in participating in a GH experience, including international or local-global clinical electives and rotations with governmental organizations. Sixty-three percent of current fellows wanted GH content in their fellowship curriculum 76% of FDs and 56% of fellows believe GH experiences would improve recruitment to the program. 82% of FDs and 64% of fellows agree that integrating GH education during fellowship improves overall fellow education.

Conclusion: GH experiences are desired by most PHM fellows. However, only some fellowships currently offer them, leaving many interested PHM fellows without this educational opportunity. Studies about ways to close this mismatch are needed, and there is a demand for GH curriculum development for PHM fellowship.

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TRAINEES' INTERESTS AND ATTITUDES TOWARDS INFORMATICS TRAINING

Tiranun Rungvivatjarus MD, Christopher Cannavino MD, Cynthia Kuelbs MD

Background: While Electronic Medical Records (EMR) have been universally adopted in healthcare settings promising workflow efficiencies and easier acquisition of data, physician training has lagged in both efficient use and application of the EHR. Outside of clinical informatics fellowships, informatics training for pediatric fellows, residents, and medical students (MS) are limited. Providing earlier informatics training to trainees will allow them to better prepare to work more efficiently, be catalysts for needed workflow and EMR improvements.

Objective: This study surveys clinical and surgical fellows and MS on their experience, attitude, and interest regarding clinical informatics education.

Methods: This cross-sectional study surveyed pediatric fellows at a large tertiary pediatric health care system and 1st and 4th year UCSD MS. The survey was distributed between July and March 2023 electronically to trainees. The survey measured self-rated prior informatics training received, interest, and attitude towards clinical informatics education. Descriptive statistics were generated regarding demographics, proficiency level with various EHR-related tasks.

Results: In total, 33/57 fellows and 32/110 MS (39% response rate) completed the survey. Approximately 29% of fellows rated their ability outstanding or excellent in performing basic EMR tasks but only 13% in performing advanced EMR tasks (use clinical decision support, data visualization and extraction). Fifty-three percent of fellows and 23% of MS were interested in incorporating informatics into their career/training. Most participants expressed informatics important in direct clinical care, healthcare management, research, and continuing education. Seventy percent of 4th year MS did not find informatics training during medical school adequate in preparing them for residency.

Conclusions: Many fellows and medical students reported interest in informatics training and found its role to be important in patient care, research, and continuing education. However, EMR training opportunities were limited. Additional informatics training should be offered to trainees to prepare them for a future career in the quickly evolving health care environment.

Host Microbe Systems and Therapeutics

Poster 78

NANOPARTICLE VACCINE PROTECTS AGAINST A. BAUMANNII SEPSIS AND PNEUMONIA

Elisabet Bjanes, Jiarong Zhou, Nishta Krishnan, Liangfang Zhang, Victor Nizet

Background: Multidrug-resistant (MDR) bacterial infections kill 1.3 million people globally each year. The Gram-negative opportunistic pathogen Acinetobacter baumannii is the top priority by the WHO and CDC for new therapeutics development. MDR prevalence in A. baumannii strains is as high as 80%, contributing to hospital-acquired infections including ventilator associated pneumonia and sepsis. Immunosuppression, prolonged antimicrobial therapy, COVID19 infection, and mechanical ventilation increase susceptibility to A. baumannii infection. Vaccines are an alternative strategy to provide immunity while limiting opportunities for antimicrobial resistance.

Methods: Our strategy utilizes outer membranes vesicles (OMVs) as highly immunogenic vaccine antigens; however, OMV heterogeneity renders them undesirable for large-scale clinical development. Studies have employed nanoparticles as vaccine delivery platforms, providing improved stability, delivery efficiency, and immune cell activation. Combining nanotechnology with OMVs may overcome the limitations of OMV-only vaccines. I developed a candidate vaccine platform where gold nanoparticles are coated with OMVs from the hypervirulent clinical isolate A. baumannii Lac-4.

Results: My Ab-NP vaccine completely protects mice from disseminated sepsis and pneumonia. Vaccination generates robust A. baumannii-specific IgG antibody responses and induces increased antigen presenting cells recruitment to draining lymph nodes. Ab-NP vaccination enables rapid control of inflammation, bacterial dissemination, and hypothermia in systemic infection models. Additional analysis shows that Ab-NP vaccination is protective by inducing synergy between the innate and adaptive immune systems, as immune serum significantly enhances the recruitment and killing capacity of neutrophils, and passive vaccination with immune serum completely protects naive mice against lethal sepsis.

Conclusion: My work has generated a protective vaccine candidate against A. baumannii. My ongoing studies seek to ensure the NP vaccine platform is broadly cross-protective against the most common clinical A. baumanii isolates, protects in the context of host immunosuppression such as neutropenia or corticosteroid therapy, and may be extended to other high-priority MDR pathogens.

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REWIRING CAPSULE PRODUCTION BY CRISPRI-BASED GENETIC OSCILLATORS DEMONSTRATES A FUNCTIONAL ROLE OF PHENOTYPIC VARIATION IN PNEUMOCOCCAL VIRULENCE

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Background: The opportunistic human pathogen Streptococcus pneumoniae (the pneumococcus) is responsible for 11% of all deaths in children aged 1-59 months. How the pneumococcus switches its phenotype from a benign colonizer to pathogen is poorly understood. Phenotypic variation is the phenomenon in which clonal cells display different traits even under identical environmental conditions. This variation is thought to be important for processes including bacterial virulence, but direct evidence for its relevance is often lacking. For instance, variation in capsule production in S. pneumoniae has been linked to different clinical outcomes, but the exact relationship between variation and virulence is not well understood due to complex natural regulation.

Methods: In this study, we used synthetic gene regulatory networks (GNRs) based on CRISPR interference (CRISPRi) to engineer controlled phenotypic variation in the pneumococcus. Automated fluorescence time-lapse microscopy of pneumococci within microfluidics devices was used to analyze the constructed synthetic GRNs. Several virulence traits of the constructed strains with various levels of heterogeneity in capsule production, including biofilm formation and mouse colonization, were assessed.

Results: We show that phenotypic variation in pneumococcal capsule production is beneficial for bacterial fitness in traits associated with virulence.

Conclusions: Our results demonstrate that engineered GNRs can be used to mimic and test the biological functions of natural phenotypic variable systems and unequivocally show that heterogeneity in capsule production is advantageous for the pneumococcal lifestyle.

Infectious Diseases

Poster 79

CUTIBACTERIUM-SECRETED HYALURONIDASES ARE MAJOR DETERMINANTS OF HEALTHY OR ACNEIC SKIN

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Acne is a dermatologic disease with strong pathologic association with human commensal Cutibacterium acnes. Conspicuously, certain C. acnes phylotypes are associated with acne, whereas others are associated with healthy skin. Here we investigate if and how evolution of a C. acnes enzyme contributes to health or acne. Two hyaluronidase variants exclusively expressed by C. acnes strains, HylA and HylB, demonstrate remarkable clinical correlation with acne or health. We show that HylA is strongly pro-inflammatory, and HylB is modestly anti- inflammatory in a murine acne model. Structural and phylogenic studies suggest that the enzymes evolved from a common hyaluronidase that acquired distinct enzymatic activity. Health-associated HylB degrades hyaluronic acid (HA) exclusively to HA disaccharides leading to reduced inflammation, whereas HylA generates large-sized HA fragments that drive robust TLR2-dependent pathology. Replacement of an amino acid Serine to Glycine near the HylA catalytic site enhanced the enzymatic activity of HylA and produced an HA degradation pattern intermediate to HylA and HylB. Selective targeting of HylA using peptide vaccine or inhibitors alleviated acne pathology. We suggest that the functional divergence of HylA and HylB is a major driving force behind C. acnes health-and acne-phenotype and propose targeting of HylA as an approach for acne therapy.

Neonatology

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ANTI-AGING FACTOR, ALPHA KLOTHO, IS DECREASED IN CORD BLOOD OF INFANTS WITH PLACENTAL LESIONS OF ACCELERATED VILLOUS MATURATION

Lillian Blank, Erika Lin, Sandra Leibel, Karen Mestan

Background: Alpha klotho (AK) is a protein produced by the placenta found in umbilical cord blood that acts as an "anti-aging" compound implicated in counteracting stress to the intrauterine environment. A known placental stressor is accelerated villous maturation (AVM) that has been specifically linked to the development of bronchopulmonary dysplasia-associated pulmonary hypertension (BPD-PH) in preterm infants. In this exploratory study, we wanted to evaluate the relationship between AK expression, AVM, and other pregnancy factors in hopes of better predicting and treating BPD-PH with biomarkers of accelerated aging.

Methods: Archived cord blood plasma of 38 infants were included in this study—27 infants had AVM placentas. Plasma samples were analyzed via enzyme-linked immunoassays on AK concentration. Placentas were considered to have AVM if the placental pathology report indicated "accelerated villous maturation" and/or "increased syncytial knots". Placentas were considered to have no AVM in the absence of both lesions. Raw AK concentration outliers were removed and duplicates were averaged. Means were compared via t-test, medians were compared via Wilcoxon Rank Sum test, and categorical variables were analyzed via chi-squared tests in R.

Results: There was a non-significant trend of lower AK concentration with AVM, consistent with our lab's previous findings. This has prompted us to test a novel hypothesis: placental aging drives lung aging.

Conclusion: Our studies on the link between placental aging and BPD-PH have prompted further investigation of the mechanisms driving lung aging in a lung organoid model of cell senescence. In fact, in subsequent cord blood studies, we have identified senescence-associated secretory phenotype (SASP) factors—MCP-1, IL-8, MIP-1—are increased with BPD. As such, we plan on interrogating a 3D human lung organoid model in which doxorubicin treatment leads to increased SASP, perhaps similar to hyperoxia-induced injury seen in BPD-PH.

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RACIAL DISPARITIES IN THERAPEUTIC HYPOTHERMIA AND ADVERSE OUTCOMES OF HYPOXIC ISCHEMIC ENCEPHALOPATHY IN A LARGE CALIFORNIA NEONATAL COHORT

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Background: Racial disparities have previously been documented in the neonatal intensive care unit. This is the first study to investigate racial disparities in the use of therapeutic hypothermia (TH) and outcomes in infants with hypoxic ischemic encephalopathy (HIE).

Methods: We queried an administrative birth cohort of mother-baby pairs in California from 2010-2019 using ICD codes to evaluate the association between race/ethnicity and TH and adverse outcomes in infants with HIE. We identified 4,779 term and late preterm infants with HIE. Risk ratios (RR) for TH were calculated using log linear regression adjusting for hospital transfer, rural location, late preterm birth, and HIE severity. Risk of adverse infant outcome was calculated by race/ethnicity and stratified by TH.

Results: From our identified cohort, 1338 (28.0%) neonates underwent TH. White infants were used as the reference population and 410 (28.4%) were treated with TH. Black infants were significantly less likely to receive TH with 74 (20.0%) undergoing cooling with an adjusted risk ratio (aRR) of 0.7 (95% confidence interval 0.5 to 0.9). Hispanic babies were also less likely to undergo TH, but this did not reach statistical significance (aRR 0.9, 95% CI 0.8 to 1.1). Black and Hispanic infants with HIE who did not receive TH were significantly more likely to receive a tracheostomy (aRR 3.1, aRR 2.2 respectively). Hispanic infants were also significantly more likely to have a gastrostomy tube (aRR 2.2, 95% CI 1.4 to 3.3).

Conclusions: TH is currently the only standard treatment for HIE. We found that Black infants with HIE were significantly less likely to receive TH treatment. Black and Hispanic infants had a significantly increased risk of some adverse outcomes of HIE. In future, a larger sample size and longer follow up time may demonstrate further increased risk of adverse events in this population.

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UTILIZING NATURAL GENETIC VARIATION IN MICE TO IDENTIFY THE GENETIC BASIS FOR RESILIENCE IN HYPEROXIA-INDUCED NEONATAL LUNG INJURY

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Background: Bronchopulmonary dysplasia (BPD), a chronic lung disease, is a common complication of preterm birth. However, not every premature infant develops BPD. The molecular mechanisms explaining this variability in disease susceptibility are unknown.

Objectives: Investigate the impact of natural genetic variation on BPD severity by assessing the extent and nature of gene expression variability and gene regulation between two strains of mice differing in susceptibility to oxidant stress.

Method: C57BL/6J (B6) sensitive and DBA/2J (DBA) mice resistant to hyperoxia were exposed to 75% oxygen for 14 days after birth to mimic BPD. Severity of injury was assessed by histology. Transcriptomic differences were analyzed by RNA-seq. P53 expression was measured with Western blot. Regulatory mechanisms by which p53 directs the hyperoxia response was analyzed by ChIP-seq. Data were analyzed with HOMER.

Results: Hyperoxia resulted in less alveolar simplification in resistant DBA mice. Transcriptomic changes were qualitatively different between the strains with only a small fraction of genes commonly up or down regulated. B6 mice showed significant upregulation of genes associated with cell death and p53 pathway (Nupr1, Cdkn1a), whereas DBA mice upregulated cell division related genes. In line with the RNA-seq data, p53 protein expression was higher in the lungs of B6 than DBA mice. Genome wide assessment on p53 binding by ChIP-seq revealed that in hyperoxia-exposed B6 mice p53 collaborates with transcriptional repressors such as Gfi1. In DBA mice p53 binds to Tead and Nkx2.1 involved in progenitor cell renewal and lung development.

Conclusion: Using hyperoxia sensitive and resistant mice we show that the degree of p53 activation has a substantial impact on phenotypic outcomes. An excessive activation of the p53 axis in the sensitive strain is part of an injury-promoting response that derails lung development. The magnitude of interstrain variability in gene expression after hyperoxia exposure could form the basis for understanding human interindividual variability in BPD.

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FLOW AND GROW: A WEANING STRATEGY FOR EXTREMELY PRETERM BABIES ON CPAP

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Background: Non-invasive ventilation in neonates is a life-saving technology, however, most weaning strategies result in clinical instability and/or weaning failure. Many centers with the lowest rates of bronchopulmonary dysplasia don't wean preterm infants off of CPAP until they're 32-34 CGA. This may allow the positive air pressure to facilitate lung growth in a developing preterm infant. The objective of this project is to compare the ideal timing of weaning from non-invasive continuous positive pressure ventilation in infants born at < 30 weeks gestational age.

Methods: To determine the sample size for a prospective randomized clinical trial, we performed a retrospective chart review in babies less than 30 weeks GA from 4 level III NICUs in San Diego. We identified babies over a 6-month period that fit the GA criteria, were intubated for less than 4 weeks prior to extubation, were on any form of non-invasive positive pressure ventilation (CPAP, NIPPV) and did not have congenital anomalies or require surgical interventions. Babies were placed into 2 groups: those that remained on CPAP until 34 weeks GA and those that were weaned from CPAP prior to 34 weeks GA. Weaning failure was defined as having to go back to a higher level of respiratory support (low flow to high flow or CPAP; room air to any type of support). Clinical instability was defined as 50% more stimulation events (apnea, bradycardia, and/or desaturations) 72 hours after weaning from CPAP.

Results: At the NICUs in Jacobs Medical Center, Rady Children's Hospital, Scripps La Jolla and Rancho Springs Medical Center, 55 babies were identified. Twenty babies were on CPAP until 34 weeks CGA while 35 babies were weaned prior to that CGA. Weaning failure including clinical instability after weaning occurred in 19% of babies in the remain on CPAP group while weaning failure occurred in 70% of babies that were weaned prior to 34 weeks CGA.

Conclusions: Weaning preterm babies from CPAP prior to 34 weeks CGA results in significantly higher rates of weaning failure. We aim to verify this data with a prospective, randomized clinical trial.

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OXIDANT STRESS ADDUCTS CORRELATE WITH CUMULATIVE SUPPLEMENTAL OXYGEN EXPOSURE AND BRONCHOPULMONARY DYSPLASIA

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Background: Adductomics is an exposure science approach capturing endogenous electrophilic addition products (adducts) of oxidative reactions. Adducts in blood are bound to the nucleophilic cysteine loci of human serum albumin, which has a 3-week half-life, allowing for reliable capture, quantification, and characterization of oxidative stress, an important pathogenic process in bronchopulmonary dysplasia (BPD).

Methods: 205 extremely preterm and 51 healthy term infants were included. Cord blood was collected at birth in 211 infants. Serial postnatal blood was collected in a separate group at 1 week, 1 month, and 36 weeks postmenstrual age (PMA). 102 extremely preterm infants had BPD. Plasma samples were analyzed using a tandem mass spectrometer. Adduct concentrations were log-transformed and normalized. Cumulative supplemental oxygen (CSO) was calculated as sum of average daily supplemental oxygen (FiO2 – 0.21) over time interval leading up to blood collection. Linear modeling was conducted in R (adj. $P<0.05$).

Results: Among BPD vs. non-BPD infants, gestational age was 26.1±1.6w vs. 27.7±1.2w; birth weight was 854±202g vs. 1110±201g, respectively ($P<0.001$). In targeted analysis, 49 unknown and 56 annotated known adducts were detected. In cord blood, there were significant increased levels of adducts associated with prematurity + BPD (Cys34 → Oxoalanine; $P<0.001$) and BPD + placental dysfunction (Cys34 sulfinic acid; $P<0.001$). In peripheral blood, there were peak levels of oxidative stress adducts at 1 month of life and decreased levels of oxidative stress adducts at 36 weeks PMA with high CSO exposure. Cys34 → Oxoalanine – the same adduct increased in cord blood of BPD infants – had peak levels at 1 month of life.

Conclusion: Serial adductomics identified adducts that vary with placental dysfunction and CSO — important exposures in BPD pathogenesis. Our findings suggest that differences in antioxidant capacities of preterm infants may be influenced by intrauterine and extrauterine environmental exposures to the mother, fetus, or neonate.

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NOVEL ROLE OF BPIFA1 IN THE DEVELOPING HUMAN AIRWAY & REGULATION DURING POSTNATAL INJURY 11

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The human airway epithelium protects the lung from environmental insults, however, premature infants have immature lungs and thus the defensive mechanisms of airway fail to function. At birth, the transition from in-utero hypoxia to postnatal normoxia (or relative hyperoxia) initiates the production of homeostatic proteins that coat the airway to protect the lung; yet, this response may be blunted in an immature lung. Preterm infants are also at risk of developing severe bronchiolitis from respiratory syncytial virus (RSV) infections which may in part be due to airway immaturity and reduced defense.

The airway surface layer (ASL) lines the surface of the lung epithelium and is critical in maintaining airway homeostasis. BPIFA1 is the airway surfactant that maintains ASL balance. However, while BPIFA1 is known to support lung homeostasis in mice and human adults, no research has investigated the role of BPIFA1 in an immature, human airway. We hypothesize that BPIFA1 is gestationally regulated, is impacted by oxygen tension, and reduced BPIFA1 in an immature airway increases the risk of severe RSV infection.

First, gestational expression of BPIFA1 was assessed by analyzing fetal human lung tissue and an in vitro human stem cell derived airway epithelium cultured in air-liquid interface (iALI). We found that BPIFA1 was expressed in the second trimester of development and was present in mucous producing cells and myoepithelial cells. The influence of oxygen tension on BPIFA1 expression was investigated by culturing airway epithelial cells in 5% or 21% oxygen. BPIFA1 protein expression was higher in 21% oxygen. Finally, the iALI lung cells were infected with RSV which resulted in an increase in BPIFA1 expression.

This project investigated the short and long term impact of BPIFA1 in an immature airway. Further investigations will explore the therapeutic potential of BPIFA1 in the preterm infant.

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THE ROLE OF GATA4 IN LUNG HYPOPLASIA AND PULMONARY HYPERTENSION ASSOCIATED WITH CONGENITAL DIAPHRAGMATIC HERNIA

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Background: Congenital diaphragmatic hernia (CDH) is a common and severe malformation affecting 1/2,000 births with a high mortality rate (10-50%) due to lung hypoplasia (LH) and pulmonary hypertension (PHN). Variants causing GATA4 loss-of-function (LOF) are among the most common in CDH patients in the Diaphragmatic Hernia and Research and Exploration; Advancing Molecular Science (DHREAMS) study. GATA4 is required for diaphragm development but its role in lung and pulmonary vascular (PV) development is unclear. Patients with GATA4 LOF variants in the DHREAMS study had a mortality rate of 67%; survivors required oxygen and pulmonary vasodilating medications at discharge. We hypothesize that GATA4 directs lung and PV development and that GATA4 LOF causes LH and PHN independent of its role in diaphragm development.

Methods: We inactivated Gata4 expression in the developing lung mesenchyme of mice using an inducible and tissue-specific gene deletion approach. Gata4 conditional deletion (Gata4 CKO) and control mice were analyzed at embryonic and postnatal stages. We performed histology, immunofluorescence staining, gene expression analysis, and physiology testing (echocardiography and pulmonary function testing) for phenotype analysis.

Results: In contrast to prior related work, Gata4 deletion did not impact embryonic lung branching morphogenesis, postnatal alveologenesis, or epithelial cell development. PV and smooth muscle cell development were normal in Gata4 CKO mice. Physiological testing showed no PHN and no change in pulmonary function.

Conclusions: Despite the high mortality rate, lung hypoplasia, and PHN phenotype in CDH patients with GATA4 LOF variants, conditional deletion of Gata4 in the developing lung did not impact lung or PV development. These data are important because they suggest that lung and PV defects in these patients are due to mechanical compression during development. CDH patients with GATA4 LOF variants may be ideal candidates for fetal procedures, like tracheal occlusion, to improve lung development and increase survival.

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PARTICIPATION IN A STATEWIDE QUALITY IMPROVEMENT COLLABORATIVE AND ADOPTION OF NEW TREATMENT PROTOCOLS IS ASSOCIATED WITH A SIGNIFICANT DECREASE IN UCSD NICU LENGTH OF STAY FOR INFANTS TREATED FOR NEONATAL ABSTINENCE SYNDROME

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Background: Maternal substance use disorder during pregnancy can result in infants born with drug dependency and the potential for complications which may require NICU admission and treatment. In 2019, UCSD Health joined the California Maternal Quality Care Collaborative/California Perinatal Quality Care Collaborative, entitled "CMQCC & CPQCC: Mother and Baby Substance Exposure Quality Improvement Collaborative." UCSD Health implemented a new treatment protocol for its NICU's in La Jolla and Hillcrest on March 11, 2019. This treatment protocol used the Eat, Sleep, Console tool to determine medication treatment and wean.

Methods: This is a retrospective medical record review of infants admitted to the La Jolla or Hillcrest UCSD NICUs. Inclusion criteria includes infants with a diagnosis of neonatal withdrawal symptoms from maternal use of drugs of addiction (ICD-10 code P96.1) and who were either treated with morphine or methadone. All infants admitted after the change in treatment protocol on March 11,2019 were included along with a similar number of infants that were admitted prior to March 11, 2019. An unpaired t-test was used to compare the mean length of
stay between the 2 groups.

Results: In total 184 infants met the inclusion criteria. (92 infants in the intervention group: 3/11/2019 to 3/14/23 and 92 infants in the control group: 9/25/2013 to 3/10/2019.) The intervention group average length of stay was 30 days, (SD 24, Max 170, Min 3, Median 23) and the control group average length of stay of was 42 days (SD 42, Max 288, Min 4, Median 26). An unpaired t-test showed this decrease to be statistically significant. P=0.0184

Conclusions: Participation in the QI collaborative and adoption of the new treatment protocol for NAS is associated with a statistically significant lower NICU length of stay from 42 days to 30 days. (P=0.01840) Further prospective studies are indicated.

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THE EFFECTS OF ORAL FEEDING ON THE PRETERM INFANTS' MICROBIOME, METABOLOME

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Background: Breast milk is beneficial for preterm infants. The route of feeding (tube, bottle, breast) may impact the infants microbiome and/or metabolome which may have long-term impacts on health. The purpose of this study is to determine how the mode of feeding breastmilk impacts the maternal breastmilk and the infants' oral and gut microbiome and metabolome.

Methods: Samples of maternal milk and infant's stool and saliva were collected from a cohort of 11 maternal-infant dyads from: "The Association Between Milk Feedings, the Microbiome and Risk of Atopic Disease in the Preterm Population (MAP) Study" (NCT04835935). Infants < 34 weeks gestational age were recruited. For each subject, 4 longitudinal samples (two prior to oral feeds and two after starting oral feeds) were collected.

Results: Analysis of the milk samples showed that sample collection time had a significant impact on microbial community composition (R2 = 0.06, p=0.002) and that microbial diversity decreased temporarily after the first feed (p=0.04). The infants' saliva samples showed increased microbial diversity over time (p=0.009) and a significant time impact on community composition (R2 = 0.12, p=0.001). Stool microbial diversity did not change over time but was highly associated with participant (R2 = 0.39, p=0.001). Metabolomic analysis is in process.

Conclusions: Our preliminary analysis thus far has demonstrated that the maternal milk and preterm infant's microbiome changes after the initiation of oral feeds. The changes in the genus level community within the saliva sample may reflect changes seen in the milk samples as well as increased exposure to skin. While no significant changes were seen in the diversity of the stool samples, this is likely be driven by participant microbiomes being too different from each other. Given the importance of the infant's microbiome and metabolome on their outcomes, further research is needed to help identify the impact of enteral feeding tubes.

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STATEWIDE QUALITY IMPROVEMENT COLLABORATIVE PARTICIPATION HAS LED TO IMPROVEMENTS IN POSITIVE PARENTAL TOUCH AND TIME TO FIRST SKIN-TO-SKIN ENCOUNTER FOR PRETERM INFANTS IN THE UCSD LA JOLLA NICU

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Background: Family-focused involvement in NICU care and increasing positive environmental interactions have been shown to improve outcomes for preterm infants. UCSD Health joined the California Perinatal Quality Care Collaborative, "NICUs Enabling Optimal Brain Health (NEOBrain)" with the aim to increase neuroprotective care for infants < 32 weeks.

Methods:
This is a retrospective medical record review of infants born < 32 weeks at UCSD NICU after the 6/3/22 NEOBrain start. Positive parental touch occurrences in the 1st 72 hours and time to 1st parental skin-to-skin encounter data were collected. Subgroup analysis was performed for infants <29 weeks. To assess improvement over time, infants enrolled in the first 31 days were compared to the rest of the group. Also, the 1st 50% of infants were compared to the rest of the group. Data analysis used paired t-tests and odds ratios.

Results: 40 infants met the inclusion criteria. A trend towards increased 1st 72 hour positive parental touch was found for the 2nd 50% of the group vs the 1st 50% (12/20, 60% vs 9/20, 45%), but this was not statistically significant. (OR .5455, 95%CI 0.1554-1.9144, p =0.3440) However, this was statistically significant for <29 week infants. (5/9 56% vs 0/9, 0%) (OR 0.043, 95%CI 0.0019-0.9605 P=0.0471) Time to 1st skin to skin encounter was decreased for infants enrolled after the 1st 31 days but was not statistically significant (Mean 197 hours vs 273 hours) P=0.131. However, this was statistically significant for <29 week infants. (Mean 235 hours vs 626 hours) P=0.027

Conclusions: Participation in the NeoBrain Collaborative is associated with a trend towards increased parental positive touch over time and decreased time to 1st skin-to-skin encounter. These findings were statistically significant for infants born less than 29 weeks. Prospective studies are indicated to confirm this association.

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SIN3A DIRECTS LUNG AND PULMONARY VASCULAR DEVELOPMENT BY CONTROLLING THE BALANCE OF HISTONE ACETYLATION

Authors: Nicole Talaba, Zhuowei Li, Giangela Stokes, Rebecca Hernan, Wendy Chung, David McCulley.

Background: A major barrier to the impact of genomic diagnosis in patients with congenital diaphragmatic hernia (CDH) is the lack of clarity regarding the genotype-phenotype relationship of identified variants and how this information could help generate novel treatment approaches. We hypothesize that a core group of genes is required for diaphragm, lung, and pulmonary vascular development and that pathogenic variants here are responsible for failure of diaphragm formation and defects in lung and pulmonary vascular development. To better understand the genetic and developmental mechanisms responsible for CDH, we identified loss-of-function variants in the SIN3A gene. SIN3A regulates gene expression during development by directing the activity of histone deacetylase enzymes—HDAC 1 and 2. The role of SIN3A during lung development, lung hypoplasia, and pulmonary hypertension is unclear. Our objective
is to determine the role of SIN3A during lung and pulmonary vascular development in a mouse model of CDH.

Methods: We conducted tissue-specific deletion of SIN3A in the developing diaphragm and lungs and investigated the mechanisms responsible for abnormal lung development and function using histology, gene expression analysis, and pulmonary vascular physiology experiments.

Results: Deletion of SIN3A in the diaphragm skeletal muscle and mesothelium resulted in left- sided CDH. Deletion of SIN3A in the lungs resulted in failure of mesenchymal cell differentiation, lung simplification, and pulmonary hypertension. We demonstrated that these defects were due to a loss of HDAC function resulting in failure of epigenetic regulation. Defects were rescued by embryonic and early-postnatal inhibition of histone deacetylase.

Conclusion: Our results demonstrate the importance of genetic analysis in complex congenital malformations such as CDH. In this SIN3A loss-of-function model, impaired epigenetic regulation and lung development can be rescued by restoring histone acetylation balance.

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OXIDIZED PHOSPHOLIPID NEUTRALIZING ANTIBODY AMELIORATES BLEOMYCIN-INDUCED PULMONARY FIBROSIS

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Purpose of Study: Increased production of OxPL has been shown to have deleterious effects in acute lung injury, but it's role in lung fibrosis is not known. OxPL are recognized by the IgM natural antibody (Ab) E06 and binding neutralizes their pro-inflammatory effect. We have investigated the role of OxPL in bleomycin (BLM)-induced pulmonary fibrosis (PF) and whether neutralizing OxPL would ameliorate BLM-induced PF.

Methods Used: C57BL/6J(WT) and E06-scFv transgenic (E06-Tg) mice that overexpress the single-chain fragment of E06 were intratracheally instilled with BLM to induce lung fibrosis. We recorded weight change and survival rate after BLM instillation at serial time points. We measured OxPL content in the lungs by immunochemistry and measured hydroxyproline levels by ELISA. We measured gene expression in whole lung by RNA-seq. Data were analyzed with ImageJ, Prism and HOMER.

Summary of Results: E06-Tg mice lost less weight after BLM instillation, and had significantly higher survival rate compared to WT mice. We observed an increased accumulation of OxPL in the lungs of WT mice compared to E06-Tg mice. In addition, we measured higher collagen content in the lung hydrolysates of WT compared to E06-Tg, suggesting more fibrosis in WT mice. To further explore the fibrotic process, we performed RNA-seq of whole lung tissue. After BLM instillation, transcripts that most up-regulated were pro-inflammatory genes and macrophage-related genes.

Conclusions: BLM instillation resulted in a significant accumulation of OxPL in the lungs of WT mice. Elevated OxPL levels were associated with upregulation of pro-inflammatory pathways, and lung macrophage activation. Neutralizing OxPL with E06 Ab resulted in marked improvement in the survival and significantly less lung fibrosis. These data together suggest that OxPL could be a potential target to ameliorate PF by reducing inflammatory responses and collagen deposition.

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PLACENTAL PATHOLOGY, FETAL GROWTH, AND PRETERM NEONATAL OUTCOMES IN HEALTHY PREGNANCIES COMPLICATED BY OBESITY

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INTRODUCTION: Prior studies have shown that placental changes in gene expression, structure, and function occur in placentas of pregnancies complicated by obesity, but little research has been done to investigate the impacts of these placental changes on fetal outcomes. This study used maternal data from the UCSD obstetric database with corresponding placental histopathology and correlated these data with neonatal outcomes in a subset of patients. We hope by better understanding the relationship between placental structure and function, and neonatal outcomes in maternal obesity, we could impact clinical decisions and patient care in the NICU.

METHODS: A cohort of 100 women with singleton pregnancies delivered prematurely (<37 weeks) from 2011-2020 was identified. Data was extracted from an obstetric registry, with available placental pathology data, as well as demographic, obstetric, and neonatal variables. To focus on healthy pregnancies, cases with comorbidities such as diabetic diagnoses and hypertensive disorders, including preeclampsia related diseases, were excluded. Maternal weight categories were defined as: Non-overweight/Obese (BMI <25), overweight (BMI 25-29.9), and obese (BMI ≥30) based on earliest weight recorded during gestation. Associations between obesity, placental pathology, fetal growth, and neonatal outcomes were assessed with Chi-square and ANOVA tests.

RESULTS: Pregnancies from 46 non-overweight/obese (Non-ow/ob), 33 overweight (Ow), and 21 obese (Ob) women were included. In the placenta, maternal obesity was associated with increased normoblastemia (Non-ow/ob 30% vs Ow 36% vs Ob 62%; p=0.05) and increased chronic inflammation, indicated by the presence of chronic villitis and high grade chronic villitis (Non-ow/ob 17% vs Ow 0% vs Ob 19%; p=0.03 and Non-ow/ob 9% vs Ow 0% vs Ob 19%; p=0.04). Placental disc size and placental efficiency was not different between groups. Accelerated villous maturation, interestingly, showed a negative relationship with obesity, with numbers being higher in the lower BMI categories (Non-ow/ob 54% vs Ow 49% vs Ob 19%; p=0.02). Fetal growth did not appear to be affected by obesity, with no significant difference shown in birthweight percentiles between groups. Similarly, post-natal growth patterns were also not different between groups. There were no available neonatal outcomes that significantly differed between groups. Mortality in this cohort was very low, with only 1 death recorded.

CONCLUSION: Our cohort was specific to healthy pregnancies not complicated by medical comorbidities that delivered before 37 weeks gestation. In this group, obesity was shown to be associated with fetal hypoxic stress and chronic inflammation, as evidenced by the presence of increased normoblastemia and chronic villitis of all types in the placenta. Interestingly, obesity seemed to be inversely related to the presence of accelerated villous maturation, something that is commonly found in placentas of neonates delivered prematurely. While infants born to obese women are frequently noted to be large for gestational age, in this premature cohort without comorbidities, that pattern was not seen. Additionally, being born prematurely to an overweight or obese woman did not appear to have any significant postnatal effects. This study was limited by a small sample size, and it is possible that it is not powered to see differences in the neonatal outcomes. Future directions could include multivariate regression analyses to evaluate for effects of specific placental pathologies on fetal growth and neonatal outcomes.

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HIGH-RESOLUTION HLA GENOTYPING INFORMS ASSESSMENT OF HLA T CELL EPITOPE MISMATCHES ASSOCIATED WITH DSA AND REJECTION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Background: The Predicted Indirectly ReCognizable HLA Epitopes (PIRCHE) algorithm predicts mismatched donor HLA-derived epitopes presented to recipient T-cells. Higher PIRCHE has been associated with de novo donor specific antibody (dnDSA) and acute rejection (AR) in kidney transplant recipients (KTR). Prior work relied on imputation from low-resolution HLA in adult cohorts. We hypothesized PIRCHE based on high-resolution HLA genotyping would be associated with dnDSA and AR in pediatric KTR.

Methods: Forty-three pediatric KTR from 2017 to 2022 with high-resolution HLA typing were identified. T-cell epitope mismatches were determined using PIRCHE, and associated with incidence of dnDSA and biopsy-proven AR.

Results:
Of 43 pediatric KTR (median age 13 years old, 51% male, 51% deceased donor), dnDSA were detected in 14% and AR in 33% during the median 27 months follow-up. Of 14 AR cases, 71% were T-cell mediated rejection (TCMR) and 29% mixed TCMR/AMR.

The mean PIRCHE for HLA class II was higher for patients with dnDSA (441 vs 228, p=0.4), most notable at DQB1 loci (78 vs 54, p=0.16). There was a trend toward higher PIRCHE in those with AR, strongest at DQA1 loci (90 vs 55, p = 0.11). PIRCHE was higher in deceased versus living donors, (p<0.01) and was significantly greater at DQA1 in those with AR in this subgroup (118 vs 58, p=0.02).

Conclusions: In our pediatric cohort, we found a trend of higher of T-cell epitope mismatches in those with dnDSA and AR. This was significant at the DQA1 loci in deceased donor recipients, who are at higher risk for adverse immunologic outcomes. These associations were stronger in our adult cohort, suggesting power is limited by fewer pediatric events. Nonetheless, knowledge of T cell epitope mismatch load can be an adjunct for risk stratification of pediatric KTR and informs future study of T cell interactions in the setting of disparate donor/recipient DQA1.

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NPAS4L/CLOCHE AND HAND2 ACT IN PARALLEL TO INHIBIT KIDNEY SPECIFICATION

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Proper organ formation depends on precise organ territories containing defined numbers of progenitor cells. Kidney progenitors reside in the intermediate mesoderm (IM), two bilateral stripes of cells in the posterior mesoderm. Previously we showed that the transcription factors Hand2 and Osr1 are essential for defining the dimensions of the IM by balancing the specification of IM and laterally adjacent vessel progenitors. Recently the transcription factor Npas4l/Cloche – well characterized as an early, essential regulator of vessel and blood progenitor formation – was shown to inhibit kidney development. Here we determine how kidney and IM specification is coordinated among hand2, osr1, and npas4l. First, hand2 and osr1 regulate the development of npas4l-expressing lateral vessel progenitors (LVPs). Interestingly, like hand2 loss-of-function, npas4l loss-of-function rescues osr1 mutant kidney developmental defects. However, unlike in hand2; osr1 double mutants in which LVP specification is restored, vessel progenitor formation is not rescued in npas4l; osr1 mutants, suggesting that hand2 and npas4l may implement different mechanisms to regulate kidney and vessel progenitor fates. Additionally, npas4l and hand2 overexpression can inhibit kidney formation independent of one another's function suggesting the two factors can function in parallel to inhibit kidney specification. Importantly, like hand2 mutants, npas4l mutants have expanded IM, but in npas4l mutants the increased IM is found outside hand2-expressing cells suggesting alternative sources of increased IM within the two mutants. Finally, consistent with parallel functions for hand2 and npas4l in IM inhibition, hand2; npas4l double mutants have increased IM beyond that seen in either single mutant. Together our findings reveal that proper kidney specification depends on parallel genetic pathways that inhibit IM specification while promoting vessel progenitor formation.

Neurosciences

Poster 115

A SURVIVAL ANALYSIS OF IMMUNOTHERAPY EFFECTS ON RELAPSE RATE IN PEDIATRIC AUTOIMMUNE ENCEPHALITIS

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Background: Prior observational studies for autoimmune encephalitis (AE) have mostly focused on outcomes following acute immunotherapies with better outcomes associated with earlier immunotherapy use. However, the impact of long-term immunotherapy on relapsing disease is not well known particularly in the pediatric population.

Methods: We conducted a retrospective study of consecutive patients meeting published clinical criteria for pediatric and adult AE evaluated at Rady Children's Hospital and UC San Diego from January 2007 to November 2021. Survival analysis and Cox multivariable regression models were employed to evaluate relapse risk using rituximab exposure as a time-dependent variable. Pooled and age-stratified analyses were performed.

Results: A total of 204 pediatric participants were screened of which 30 met clinical criteria for seropositive (n=29) and seronegative (n=1) AE. Mean age of presentation was 12.2 ± 4.4 years with 63% female. The most common antibody subtype was anti-NMDAR (76%), and rituximab was the most common chronic immunotherapy used (59%). Relapses occurred in 31% of pediatric seropositive cases but not in the seronegative case. Time to first relapse (TTFR) was 10.6 ± 7.4 months. Rituximab use was associated with a 70% lower hazard for TTFR (HR 0.30, 95% CI 0.05 – 1.69) after adjusting for age, sex, and presence of tumor, and 63% lower hazard for recurring relapses (HR 0.37, 95% CI 0.09– 1.50) after adjusting for IV steroid use, time to immunotherapy and presence of tumor. In a pooled cohort of pediatric and adult participants, the HR for TTFR with rituximab use was 0.42 (95% CI 0.07 – 2.67) for anti-NMDARE and 0.32 (95% CI 0.07 – 1.39) in non-NMDA antibody-positive encephalitis.

Conclusion: Relapses are common in pediatric AE, although less frequently in anti-NMDARE. Employing a rigorous survival model, we demonstrate that rituximab can substantially reduce relapse rates, though larger studies are needed to validate these results.

Orthopedic Surgery

Poster 98

VALIDATION OF IN-CLINIC FUNCTIONAL UPPER EXTREMITY REACH IN CHILDREN WITH CEREBRAL PALSY WITH MICROSOFT KINECT

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Background: Children with cerebral palsy (CP) may experience upper extremity (UE) weakness or spasticity which affects their functional daily activities. Assessment of UE function is challenging due to the complexity of arm motion. Three-dimensional (3D) motion analysis allows for high-quality evaluation, but low accessibility limits its routine use. The Microsoft Kinect system has emerged as a low-cost system to measure UE motion in a clinic setting. This study seeks to validate the Kinect system in the measurement of UE functional reach space (FRS) against a conventional 3D system in pediatric patients with CP.

Methods: Patients ages 3-18 presenting to RCHSD rehab clinic were enrolled prospectively. Participants underwent UE reach exam with data simultaneously captured by a marker-based Qualisys system and the Microsoft Kinect. A model was created in Visual3D and the FRS of the extremity was determined by calculating the volume of reach of the hand node relative to the shoulder node of the modeled skeleton using custom MATLAB software. Reach volumes were normalized by subject height for comparison.

Results: Twenty participants (age 13.7±4.1 years; 10 female) were enrolled; ten underwent validation testing. Fifteen participants with CP (7 hemiplegia; 4 diplegia; 4 quadriplegia) were included. The normalized FRS was similar between the Kinect and Qualisys systems (0.37±0.14 m3/m vs 0.35±0.16 m3/m; p=0.78). For patients with UE involvement, the normalized FRS was significantly decreased in the affected (0.28±0.11m3/m) compared to unaffected extremity (0.43±0.16 m3/m; p=0.002.). There was reduced FRS in the affected arm as GMFCS level increased (I: 0.29±0.07 m3/m; II: 0.25±0.09 m3/m; III 0.18±0.09 m3/m).

Conclusion: The Microsoft Kinect is a valid tool for measurement of UE functional reach in children with CP. FRS was significantly reduced in affected extremities and correlated with GMFCS level. This study represents the preliminary application of this in-clinic technology to quantify UE reach in patients with CP.

Pathology

Poster 116

GASTRIC FOVEOLAR METAPLASIA OF DUODENAL MUCOSA IN THE PEDIATRIC POPULATION

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Objectives: To investigate mucosal changes accompanying duodenal gastric foveolar metaplasia (GFM) in a pediatric population when H. pylori eradicative therapy has significantly reduced the incidence of peptic ulcer disease.

Methods: Chart review of patient characteristics and pathologic findings in patients with a diagnosis of GFM between 2020-2022.

Results: A total of 70 (1.5%) cases from 65 patients (34 M and 31 F) with GFM were identified in 4,778 consecutive duodenal biopsies. The ages ranged from 3 to 19 years (median: 14.2 years). The majority (92.9%) of GFM was in the bulb. 17 cases (24.3%) had coexisting chronic duodenitis, and 52 cases (74.3%) had GFM as the only duodenal histologic finding. 48 (68.6%) cases had pathologic findings in other parts of the gastrointestinal tract, including 20 (28.6%) inflammatory bowel disease (IBD) and 4 (5.7%) H. pylori gastritis. Of all 4,778 biopsies, 136 (2.8%) and 92 (1.9%) were diagnosed as IBD and H. pylori gastritis, which had odds ratio for GFM at 15.8 and 3.2, respectively ($p<0.05$).

Conclusion: GFM is often the only histologic finding in the bulb without corresponding endoscopic abnormalities. H. pylori gastritis still plays a role in GFM while in less percentages than IBD.

Key Words: *gastric foveolar metaplasia, inflammatory bowel disease, peptic ulcer disease, helicobacter pylori*

Pharmacy

Poster 62

EFFECT OF HIGH-DOSE ANTHRACYCLINES ON SERUM CARNITINE LEVELS AND CARDIAC FUNCTION IN PEDIATRIC ONCOLOGY PATIENTS

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Background/Rationale: *Anthracycline chemotherapy agents have significant dose-dependent cardiotoxic effects. Anthracyclines cause cardiac myocyte injury via the generation of free radicals. Carnitine deficiency can result in cardiomyopathy and cardiac arrhythmias. Carnitine supplementation is a potential strategy to prevent cardiotoxicity.*

Objective: *The objective of this study was to characterize changes in serum carnitine levels and cardiac function during and after high-dose anthracycline therapy.*

Methods: *This was a prospective pilot cohort study at RCHSD in patients between 1 and 25 years old with a new diagnosis of acute myeloid leukemia, osteosarcoma, or Ewing sarcoma, treated with high-dose anthracycline chemotherapy, defined as >250 mg/m of cumulative doxorubicin equivalents. Patients had serial serum carnitine levels measured and echocardiography performed at diagnosis, after initiation of anthracycline chemotherapy, at end of therapy, and approximately one year after therapy completion. Univariable linear regression evaluated the associations between changes in carnitine levels and left ventricular ejection fraction (LVEF).*

Results: *Among 21 participants, with a median age at diagnosis of 13 years, the mean cumulative anthracycline exposure was 410 mg/m doxorubicin equivalents. On average, the lowest carnitine level for each participant was 30.5 mmol/L (range 14.7-51.4), and the largest intra-participant change in carnitine throughout therapy was -4.11 mmol/L (range -50.4-28.6). The mean lowest LVEF for each participant was 59.5% (range 49.2-66), and the mean largest change in LVEF throughout therapy was -3.29% (range -16-18). Cardiac dysfunction, defined as a drop in LVEF by at least 5% from baseline to a value <55%, was observed in two participants (9.5%). Further analysis of the associations between carnitine levels, anthracycline therapy, and cardiac function is in process.*

Conclusions/Discussion: *As a pilot study, findings will be used to determine feasibility and utility of a larger primary prevention study of carnitine supplementation to decrease the risk of anthracycline-induced cardiotoxicity.*

Pulmonary

Poster 99

CFTR MODULATOR-ASSOCIATED LIVER INFLAMMATION IN PEDIATRIC CYSTIC FIBROSIS

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Background: *Cystic fibrosis (CF) is an autosomal recessive disease that impairs the CFTR protein, leading to abnormal ion transport and consequential multiorgan dysfunction. CFTR modulators target the root cause of CF by altering the protein function.*

There are four CFTR modulators: Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), Symdeko (tezacaftor/ivacaftor), and Trikafta (elexacaftor/tezacaftor/ivacaftor). Due to reports of liver enzyme elevation in clinical trials, regular monitoring liver function tests (LFTs) is recommended.
This study evaluates effects of the CFTR modulators on liver inflammation in pediatric CF patients.

Methods: *This study was a single-center, retrospective chart review of patients aged 4 months to 21 years diagnosed with cystic fibrosis and initiated on CFTR modulator therapy for at least 1 month between January 2012 and October 2021.*

Results: *Of 99 modulator trials, 65 initial trials were included to avoid the potential confounding effects of previous modulator therapy on each patient. There were 14 patients started on Kalydeco, 33 on Orkambi, 5 on Symdeko, and 13 on Trikafta.*

In comparing the LFTs at baseline and at maximum within 12 months after modulator initiation, there were significant differences identified in ALT and AST within the Orkambi group (p 0.019, p 0.038) and in total bilirubin within the Kalydeco and Trikafta groups (p 0.011, p 0.002).

When analyzing the measured difference between baseline and maximum LFT values across all four modulator groups, significance was only achieved in total bilirubin, in contrast with ALT, AST, and GGT. Within the total bilirubin analysis, significant differences were identified between Kalydeco and Orkambi (p 0.028), Kalydeco and Trikafta (p 0.003), and Trikafta and Orkambi (p <0.001).

Conclusions: *Liver inflammation was observed via LFT elevations in all modulator groups except Symdeko. Across all four CFTR modulators, the most notable marker of altered liver function was total bilirubin, with significant differences between the Kalydeco, Orkambi, and Trikafta groups. Further research with more robust sample sizes may bolster understanding of the association between certain modulators and increased liver inflammation, which can inform clinical decisions when CF patients are eligible for multiple therapies.*

Residents

Poster 83

CLINICAL UTILITY OF RAPID WHOLE GENOME SEQUENCING IN NICU PATIENTS RECEIVING EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

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Background: There is mounting evidence describing the benefits of rapid whole genome sequencing (rWGS) in the neonatal intensive care unit (NICU). rWGS can give higher diagnostic yield at a reduced time compared to
conventional genetic testing, provide actionable information influencing the clinical course of patients, and reduce inpatient health care costs. Neonates who require extracorporeal membrane oxygenation (ECMO) have a high rate of morbidity and mortality. rWGS and early genetic diagnosis in this population could lead to targeted therapies, avoidance of invasive studies, and facilitate clinical decision-making.
Methods: This is a retrospective cohort study at a single-center NICU in a tertiary children's hospital. The study population includes 32 NICU patients who received ECMO, evaluating whether they underwent rWGS or ultra-rapid WGS (urWGS). Outcomes included diagnostic rate, defined as WGS detection of a pathogenic variant, and clinical utility, defined as a change in management based on test results.

Results: Of the 32 neonates who required ECMO during the study period, 23 (72%) had either rWGS or urWGS. The mean gestational age was 39 weeks; mean age of ECMO start was 11.4 days. rWGS was sent in 17 patients (73.9%) with median turnaround time to preliminary report (pTAT) of 7 days (range 2-23 days). urWGS was sent in 6 patients (26.1%) with median pTAT of 4 days (range 2-14 days). For positive WGS, median pTAT was 4 days (range 2-14 days). Fifteen (65.2%) WGS were sent while on ECMO, 7 (30.4%) WGS were sent before ECMO was initiated, and 1 WGS (4.3%) was sent after decannulation. A diagnosis associated with the patient's phenotype was made by WGS in 9 of 23 infants (39.1%); incidental diagnosis was made in 1 of 23 infants (4.4%). A change in clinical management was made due to WGS results in 8 patients (34.8%) including avoidance of imaging studies, palliative care decisions, and new screening studies.

Conclusion: This study demonstrates a high diagnostic rate and clinical utility of rapid WGS for neonates requiring ECMO. Further studies are needed to identify which ECMO patients would benefit most from rapid WGS.

Poster 118

RACE-RELATED PRENATAL STRESS ASSOCIATED WITH DIFFERENTIAL COMPOSITION OF THE 2-WEEK INFANT GUT MICROBIOME

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Background: In utero exposure to maternal stress is associated with differences in brain structure and increased risk of neuropsychiatric disorders. The mechanism is not well understood, but highlights an adverse role for prenatal stress in fetal programming. One suggested mechanism is through the microbiome-gut-brain axis—a bidirectional signaling pathway with demonstrated effects on neurodevelopment. Animal models of prenatal stress demonstrate changes to the microbiome, brain structure, fear and social behavior. Prenatal stress disproportionally impacts women of racial minorities and lower socioeconomic status. It is unknown how the infant gut microbiota are impacted in this population and whether this has a mediating impact on developmental outcomes.

Methods: Pregnant women were recruited from central North Carolina as part of a longitudinal cohort study. Sociodemographic information, inventories of stress, and biosamples were collected in the participant's 3rd trimester (n = 181). Infants returned for fecal collection and brain MRI at approximately 2 weeks of age (n = 111). Fecal samples were prepared with a spike-in control and sequenced via Illumina whole genome shotgun sequencing.

Results: Principle components analysis of prenatal stress inventories separated subjects into components defined by 1) pregnancy related anxiety and BSI-anxiety; 2) perceived stress; 3) race-related stressful events and economic strain. Maternal microbiome diversity measures were not significantly different in stress group 3. Infants born to mothers with increased racist events and economic strain-related stress had significantly increased alpha diversity at 2-weeks. Covariate analysis revealed significant association with formula feeding. Sensitivity analyses including formula as a covariate retained a significant relationship.

Conclusions: This study identifies novel associations between prenatal socioeconomic stress and racism-related stress with differences in 2-week infant gut microbiome diversity. Next steps include further delineation of metagenomic and taxonomic differences in the microbiome as well as the relationship with behavioral and neurodevelopmental outcomes.

Residents (continued)

Poster 75

ASSESSING PEDIATRIC RESIDENT MORAL DISTRESS AND IMPACT OF PEER DEBRIEFING TRAINING

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Background: Resident burnout is widely prevalent and multifactorial, with moral distress increasingly recognized as a contributing factor. Limited supports exist to help residents address and alleviate moral distress. This project evaluated factors contributing to moral distress in pediatric residents as well as efficacy of training residents to lead "hot" debriefs to alleviate moral distress.

Methods: A one-hour training session demonstrating a framework for leading debriefs was embedded into an existing education session for senior pediatric residents at a single residency program in October 2022. Pre- and post-session surveys evaluated prior experiences with debriefs and efficacy of the session. Factors contributing to moral distress were additionally evaluated using the Measure for Moral Distress for Healthcare Professionals (MMD-HP).

Results: 12 residents participated in the session; 9 completed both pre- and post-session surveys. All respondents reported experiencing moral distress in residency, most often around providing futile care, patient codes and deaths, and difficult interactions with families and staff. Other impactful sources of moral distress included "being required to care for more patients than I can safely care for" and "experiencing compromised patient care due to lack of resources/equipment/bed capacity". Seventy-eight percent of respondents agreed that debriefing after distressing events is important. After the session, residents who felt competent leading a peer debrief increased from 21% to 89%.

Conclusions: Pediatric residents widely experience moral distress, due to a variety of factors at both individual and systems levels. Understanding these factors can guide targeted future interventions to alleviate moral distress. While targeting contributing factors, building resident resilience in facing distress is also beneficial. Debriefing is recognized as a useful support after difficult events that can cause moral distress; training senior residents to lead debriefs may help increase access to this tool.

Poster 88

NEONATAL GRAVES DISEASE WITH TRANSIENT HYPERINSULINISM

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Neonatal Graves disease is the most common cause of hyperthyroidism during the newborn period. Neonatal Graves disease has been associated with insulin resistance and glucose intolerance; however, associated transient hyperinsulinism with severe hypoglycemia has not been described. Hypoglycemia is the most common endocrinological disorder during the newborn period but most hypoglycemic episodes resolve within 24-48 hours after birth. We present the case of a female patient born at 34 weeks and 3 days at 1.6 kg (5th percentile) to a mother with recent diagnosis of Graves disease. The infant had persistent hypoglycemia secondary to transient stress-induced hyperinsulinism. This is the first documented case of neonatal Graves disease with severe persistent hypoglycemia due to stress-induced hyperinsulinism. It is important to diagnose neonatal Graves early so that life threatening symptoms, such as tachycardia, heart failure, and in this case, hypoglycemia, can be immediately treated and managed long term.

Residents (continued)

Poster 37

REDUCING TIME TO OPIOID ADMINISTRATION FOR VASO-OCCLUSIVE CRISIS IN PATIENTS WITH SICKLE CELL DISEASE

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Background: The National Heart, Lung, and Blood Institute recommends early opioid administration within 1 hour of arrival for treatment of severe pain in sickle cell VOC crisis. Previous studies have shown that intranasal (IN) fentanyl provides effective analgesia in pediatric sickle cell VOC. The baseline of arrival to time to opioid administration in our pediatric ED was 95 minutes.

Methods: A multidisciplinary team including physicians and nurses reviewed baseline data and identified barriers to achieving this national benchmark. Given this project was initiated during an unprecedented volume surge in our institution and in pediatric EDs nationwide, metric utilized was room to first opioid. The primary aims were to decrease time from rooming to first opioid administration from a baseline of 81 to 45 minutes and to increase the proportion receiving IN fentanyl from a baseline of 12% to 50% both in patients in VOC with a pain score of ³4 by June 2023. Our secondary aim was to decrease time to RN pain reassessment from a baseline of 35 to 20 minutes by June 2023. We conducted monthly PDSA cycles. Interventions included nursing and physician education, reintroduction of a pre-existing ED Sickle Cell Pain order set, and the addition of best practice alerts (BPA) to utilize IN fentanyl.

Results: From June 2021-December 2022, time from rooming to first opioid administration decreased from 81 (UCL 216, LCL -54) to 38.5 minutes (UCL 84, LCL -7) (Figure 1). The proportion of patients who received IN fentanyl increased from 12% (UCL 69, LCL 0) to 43% (UCL 1, LCL 0) but has not sustained a shift (Figure 2). No significant changes have been noted in RN time to pain reassessment.

Conclusion: Time to first opioid delivery to treat moderate-severe pain in sickle cell VOC can be reduced by the implementation of BPAs which promote IN fentanyl utilization.

Poster 59

THE PEDIATRICS DIVERSITY COLLABORATIVE JOURNAL CLUB: A RESIDENT-LED INITIATIVE TO RAISE AWARENESS AND EDUCATE ON RACIAL, SOCIAL, AND ECONOMIC HEALTH DISPARITIES AT THE UC SAN DIEGO DEPARTMENT OF PEDIATRICS

Heriberto Martinez MD(1,2), Natalie Rodriguez MD(1,2), Melissa Campbell DO(1,2), Anne Kaufman MD(1,2), Brennan Ninesling MD, MPH(1,2,3), Gina Allyn MD(1,2), Mandeep Bajwa MD(1,2), Jedidiah Bell MD(1,2,3), Paula Aristizabal MD, MAS (1,2,4,5,6), Atim Ekpenyong MD(1,2,7) on behalf of the Pediatrics Diversity Collaborative

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Acknowledgements: *Gabriel Haddad MD, Caitlin Carter MD, Nancy Graff MD, Richard Silva MD, Rady Children's Hospital, San Diego, Department of Pediatrics, University of California San Diego*

Background: The Center for Disease Control and Prevention (CDC) called systemic racism a public health crisis in 2020. This crisis underscored the already-documented racial/ethnic and socioeconomic disparities in child health. The Pediatrics Diversity Collaborative is a resident-led group at the UC San Diego Department of Pediatrics and Rady Children's Hospital established in 2019. Its mission is to educate future leaders to address child health inequity and structural racism through venues including journal clubs and health equity rounds.

Methods: The Collaborative established a quarterly health equity Journal Club to raise awareness and create discussions on racial/ethnic and socio-economic child health disparities. We conducted a 7-item cross-sectional anonymous survey with Likert-scale and free-text responses to assess impact of our Journal Club, including satisfaction, feedback, and topics of interest.

Results: Four Journal clubs have taken place since 2020. Topics included environmental factors affecting child health, health in vulnerable children populations (gender diverse, migrant), and hospital safety for families with limited English-proficiency. Meetings were conducted in the homes of Pediatric faculty. Attendance per meeting ranged from 15 to 20 participants (65% residents, 35% faculty). 47% participants completed the survey with 100% reporting "high/very high" satisfaction. 100% of respondents "agreed/strongly agreed" that they would recommend attendance to trainees/colleagues. The journal club has led to requests to hospital administration for resources for vulnerable patients (in-person Spanish interpreters and increase hospital signage regarding rights to an interpreter) and involvement in quality improvement projects (improving discharge processes for Spanish-speaking families).

Conclusion: We successfully established a resident-driven health equity-focused journal club. Acceptability and satisfaction are high. The journal club provides a safe environment to engage in sensitive discussions with support from topic-expert faculty. Ensuring pediatrics residents awareness of health inequities can help address structural racism and child health disparities. Next steps include evaluation of impact in knowledge and practice.

Respiratory

Poster 110

ETHNICITY DISPARITIES AMONG PATIENTS WITH LONG-COVID SYMPTOMS: A PRELIMINARY ANALYSIS

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Background: *The RECOVER study, A Multi-Center Observational Study: The RECOVER Post-Acute Sequelae of SARS-CoV-2 (PASC) Pediatric Cohort Study, aims to characterize the incidence of sequelae from COVID. In this preliminary analysis, our goal is to examine if ethnic disparities exist in the prevalence of PASC.*

Methods: *Retrospective cross-sectional analysis of RECOVER data to examine the prevalence of PASC symptoms across ethnicities and vulnerable or special populations, from July 2022 to March 2023. PASC was determined if participants selected any symptoms that lasted ≥ 4 weeks since their COVID infection. Respiratory PASC was defined as having any of the following: runny nose, sore throat, lost voice, pain swallowing, dry cough, wet cough, barking cough, difficulty breathing, pain breathing, or pain in chest. Participants or their caretakers self-identified their ethnicity. Vulnerable population was defined as non-English speakers, rural dwellers or lived in medical underserved areas. Fisher exact tests were used for pairwise comparisons.*

Results: *157 participants were included: 42.7% Hispanic, 29.9% Non-Hispanic (NH) White, 6.3% NH-African American, 5% NH-Asian and 9.5% NH-multi-race. We identified a non-significant higher percentage respiratory PASC in the non-vulnerable populations (57.6% and 45.3%, p=0.17), compared to their counterparts. In subgroup analysis, within both the non-special population and non-vulnerable population groups we found Hispanics had significantly higher Respiratory PASC symptoms compared to Non-Hispanics. We identified a higher percentage of PASC, but this difference was not statistically significant.*

Conclusion: *Hispanic children may be at high risk for PASC and respiratory PASC, although this appears to be particularly enriched in non-vulnerable populations. Larger sample sizes may better elucidate these specific associations.*

Poster 100

CRITICAL ROLE OF LNCRNAS IN EXCESSIVE ERYTHROPOETIC (EE) RESPONSE IN MONGE'S DISEASE: HIKER A MAJOR PLAYER!!

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Background: *Excessive erythrocytosis (EE) is a major hallmark of patients suffering from chronic mountain sickness (CMS, Monge's disease) and is responsible for major morbidity and even mortality in early adulthood. Interestingly children and women (before menopause) do not suffer from this disease. We took advantage of unique populations, one living at high altitude (Peru) showing EE, while another population, at the same altitude and region, shows no evidence of EE (non-CMS). We have built an in-vitro human iPS-derived model system to study the genetic and epigenetic mechanisms related to pathology of excessive erythropoietic response in these Monge's disease patients.*

Methods: *Through RNA-seq, we identified and validated the function of a group of long non-coding RNA (lncRNAs) that regulate erythropoiesis in Monge's disease.*

Results: *Among the lncRNAs, we found that LINC02228 specifically played a critical role in erythropoiesis the CMS cells and non-CMS based on our functional assays in our in-vitro model systems. We observed that LINC02228 has a huge impact on erythroid colony production (>50% reduction in colonies p<0.001 with the control vs LINC02228-KD). Furthermore, we have also assessed the downstream target genes for these lncRNA (Eg. CSNK2B) and mechanism(s) of erythropoietic regulation by these lncRNAs and found an important role and mediation of erythropoietic transcriptional factor GATA1.*

Conclusion: *We conclude that LINC02228 mediates erythropoiesis in Monge's diseases through critical downstream effectors (CSNK2B and GATA1).*

Respiratory (continued)

Poster 111

ASSESSING ADHERENCE TO POSITIVE AIRWAY PRESSURE THERAPY IN PATIENTS WITH DOWN SYNDROME USING CLOUD-BASED DATA

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Background: *Obstructive sleep apnea (OSA) is highly prevalent in Down syndrome (DS). Pediatric OSA is typically treated by adenotonsillectomy, however in DS, OSA is often refractory to surgery, leading to prescriptions of positive airway pressure therapy (PAP). The overall efficacy of PAP in DS is poorly understood.*

Methods: *Retrospective review of objective cloud-based PAP from device monitoring. DS patients using PAP identified from Rady Children's Hospital Sleep Clinic. Cloud-based data, from Airview™ or Care Orchestrator™ onlne databases were extracted 30 and 90 nights following the most recent clinic visit prior to June 2021 (related to the Philips® device recall). Study outcomes were compliance (percentage of nights with device usage ≥4h), and usage (percentage of nights of device usage (any hours)). Impact of demographics and cloud-based parameters (device pressures, residual AHI, and median device leak) on study outcomes was evaluated.*

Results: *73 DS patients using PAP identified however only 47 children (64%) with available cloud-based data were included. Mean age was 17.7±4.6y; females: 23(44%); Hispanic ethnicity: 34(65%); and BMI: 24.63 kg/m2(IQR:20.9,31.7)). Devices consisted of CPAP: 27(57%), APAP: 15(32%) and Bilevel PAP: 5(11%). Compliance was 56.7%(IQR:0,90.8%) following 30 nights and significantly reduced to 34.4% (IQR:0,86.7%) following 90 nights from clinic visit ($p<0.05$). Usage was 58.2% (IQR:13,93.9) and 62% (IQR13,94.4) following 30 and 90 nights from clinic visit and was not different. Comparing compliant patients (usage≥4h for 65% of nights) to non-compliant patients (usage≤4h for 65% of nights), demographics did not impact compliance, whereas from cloud-based data, only EPAP was associated ($p=0.046$) on PAP compliance following 30 nights from clinic visit.*

Conclusion: *In DS patients, PAP adherence is modest 30 nights but significantly reduced 90 nights from clinic visit. The findings imply that supportive care including regular monitoring of PAP device downloads and close clinical follow up is warranted for this unique population.*

Poster 109

METHADONE ALTERS MECHANISMS OF STRUCTURAL SYNAPSE FORMATION IN HUMAN CORTICAL ORGANOIDS

Ila Dwivedi, Gabriel Haddad

Methadone is the most common pharmacological treatment for Opioid Use Disorder (OUD) during pregnancy. Prenatal exposure to this drug has been linked to long term neurocognitive and behavioral sequelae. However, the underlying etiology of these deficits is not well understood, primarily due to limited access to human fetal tissues. To address these limitations, we utilized human iPSC-derived 3D models of cortical development called cortical organoids (hCOs) that contain multiple, spatially organized, and functional cortical cell types, providing access to key aspects of cortico-genesis. We initially found that 2-months of chronic exposure to 1 M methadone in these hCOs led to transcriptional changes associated with both pre- and post-synaptic biology, including signal release via vesicular trafficking/docking, intra- and extra-cellular scaffolding, and signal reception (Synaptic Genes = 166, |Confect| Log2(1.5), FDR < 0.05). These results were consistent with prior patch clamp experiments, which demonstrated significant dose-dependent reductions in the frequency and amplitude of spontaneous excitatory post-synaptic currents following 1-week of treatment with 1 or 10 M methadone, indicating both pre- and post-synaptic functional effects. To further dissect methadone's impact on synaptogenesis in our hCOs, we have conducted preliminary immunofluorescence (IF) and transmission electron tomography experiments to identify, characterize, and quantify changes in structural synapses following methadone treatment. Preliminary IF of 2-3-month-old hCOs revealed that chronic methadone treatment markedly decreased pre- and post-synaptic labeling (SYN1 and PSD-95), congruent with our transcriptional study. Electron tomography studies of control and methadone-treated hCOs have also enabled us to observe alterations in the morphology of synaptic vesicles following shorter-term (2-weeks) exposure in 3-month-old organoids. We believe these findings will help elucidate the mechanisms underlying cognitive and behavioral deficits caused by prenatal methadone exposure and help improve methods of chemical intervention for maternal OUD.

Respiratory (continued)

Poster 106

DISPARITIES IN OBSTRUCTIVE SLEEP APNEA AND EXCESSIVE DAYTIME SLEEPINESS IN LATINO ADOLESCENTS

Landeo-Gutierrez J., Ryu J., Tantisira K., Bhattacharjee R.

Background: *Obstructive sleep apnea (OSA) occurs in ~3-5% of children in the United States. Prevalence rates are disproportionally higher in African American children, while there is limited information on its impact among Latinos. Untreated OSA is linked to excessive daytime sleepiness (EDS); there is insufficient data evaluating this association in children. We hypothesize that Latino adolescents suffer from OSA and EDS at higher rates than their non-Latino peers.*

Methods: *Retrospective review of adolescents 11 to 18 years old who underwent a polysomnogram (PSG) at RCHSD between October 2017 and December 2021. Demographic characteristics, obesity (BMI >95th percentile, past medical history, EDS (Epworth Sleepiness Scale [ESS]>10), home sleep duration report and PSG parameters (obstructive apnea hypopnea index, OAHI; severe OSA [OAHI>10]; central apnea index, CAI), were retrieved. Children with developmental disorders and syndromes were excluded. Statistical analyses included chi-square tests and two sample t tests. Logistic regression was used for analysis of EDS and severe OSA and predictor variables.*

Results: *1787 subjects were included, 58.6% Latino, 24.2% Non-Hispanic (NH) white, 4.4% NH-Asian, 4.2% NH-African American (Table 1-A). Latino and NH-African American adolescents had higher obesity, EDS and severe OSA than their NH-white peers, while only NH-African Americans had lower reported home sleep hours than NH-whites. Logistic regression identified higher odds of EDS in Latinos (OR: 1.41, 95% CI: 1.04-1.93) and NH-African American (OR: 1.85, 95% CI: 1.00-3.42) compared to NH-White (Table 1-B), after adjustment for relevant covariates. Female sex was also associated to increase odds of EDS. Latino ethnicity was associated to 1.53 times higher odds of severe OSA (CI: 1.10-2.15) after adjusting for obesity, age, and sex, compared to NH-whites.*

Conclusions: *Latino and African American adolescents undergoing PSG evaluation are disproportionately affected by EDS compared to their NH-white peers. Moreover, Latino adolescents are at increased risk for severe OSA even after accounting for obesity.*

Poster 108

COORDINATION OF PICKPOCKET ION CHANNEL DELIVERY AND DENDRITE GROWTH IN DROSOPHILA SENSORY NEURONS

Josephine W. Mitchell, Ipek Midillioglu, Ethan Schauer, Bei Wang, Chun Han, Jill Wildonger

Background: *Sensory neurons enable an organism to perceive external stimuli, which is essential for survival. The sensory capacity of a neuron depends on the elaboration of its dendritic arbor and the distribution and density of sensory ion channels in the dendritic membrane. However, it is not well understood how ion channels are trafficked to sensory dendrites*

Methods: *To address this question, we investigated the trafficking of the DEG/ENaC/ASIC ion channel Pickpocket (Ppk) in peripheral sensory neurons in fruit fly larvae. We used CRISPR-Cas9 genome engineering to tag endogenous Ppk1 and visualize it live, including monitoring Ppk1 membrane localization via a novel secreted split-GFP approach*

Results: *Strikingly, Ppk1 is present throughout the membrane of actively growing dendrites, indicating that Ppk1 is integral to the membrane that expands the dendritic arbor. This suggests that the distribution and density of ion channels in dendrites is achieved by coordinating the delivery of membrane and ion channel. Endosomes participate in membrane and ion channel trafficking, and our data implicate the recycling endosome GTPase Rab11 in the forward trafficking of Ppk1 to dendrites*

Conclusions: *Together, our results suggest that Ppk channel transport is coordinated with dendrite morphogenesis, thus ensuring proper ion channel density and distribution in sensory dendrites.*

Respiratory (continued)

Poster 112

ENHANCING ASTHMA PHARMACOGENETICS THROUGH ENDOTYPE SPECIFIC ASSOCIATIONS

Shraddha Piparia, Kelan Tantisira

Background: *Asthma is increasingly recognized as a complex disease with numerous subtypes, or endotypes, each with its own set of underlying pathophysiological mechanisms. One of the mainstays of asthma treatment is inhaled corticosteroids (ICS), but response to this drug varies significantly. Genetic variations in CRHR1, GLCCI1, and T-genes, have been associated with differences in ICS response, but are insufficient as predictive biomarkers. The goal of this study is to assess if endotypic-based pharmacogenetics can enhance the potential for asthma precision medicine.*

Method: *We used hierarchical clustering of key demographic and asthma features, including age, sex, asthma onset age, race, BMI, atopic status, baseline symptoms, and baseline lung function, to stratify two asthma cohorts into smaller samples and performed genetic association analysis of six relevant SNPs in the three candidate genes with ICS-mediated lung function response within each cluster. We initially analyzed the CAMP cohort (n=201) then replicated our findings in the CARE cohort (n=324).*

Results: *Very similar phenotypic composition was noted for three of the five clusters in CAMP and CARE. Five out of the total six variants were found to be similar in directionality and magnitude of association in two out of the five clusters. Two SNPs showed opposite directionality in two clusters. Overall, change in lung function ascribed to a given SNP within clusters exceeded that for each cohort as a whole. These findings suggest that these variants may play a role in the response to changes in lung function in pediatric patients treated with ICS.*

Conclusion: *Our study suggests that pharmacogenetic prediction in asthma may be more specific when in endotypes.*

Poster 103

TROPOMODULIN 3, AS A CRITICAL GENE IN HIGH ALTITUDE PULMONARY HYPERTENSION

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The molecular mechanisms leading to high altitude pulmonary hypertension (HAPH) remains poorly understood. We previously analyzed the whole genome sequence of Kyrgyz highland population and identified eight genomic intervals having a potential role in HAPH. Tropomodulin 3 gene (TMOD3) which encodes a protein that binds and caps the pointed ends of actin filaments and inhibits cell migration, was one of the top candidates. Here we systematically sought additional evidence to validate the functional role of TMOD3. In-silico analysis reveals that some of the SNPs in HAPH associated genomic intervals were positioned in a regulatory region that could result in alternative splicing of TMOD3. In order to functionally validate the role of TMOD3 in HAPH, we exposed HUVECs of different genotypes for the SNPs from the selected interval (identified as sQTL for TMOD3 in lung) to 1% O2. The level of TMOD3 was lower in the A/G (heterozygous) cells compared to the homozygous ancestral allele A/A. We then exposed Tmod3-/+ mice to 4 weeks of constant hypoxia, i.e., 10% O2 and analyzed both functional (hemodynamic measurements) and structural (angiography) parameters related to HAPH. The hemodynamic measurements, such as right ventricular systolic pressure, a surrogate measure for pulmonary arterial systolic pressure, and right ventricular contractility (RV-±dP/dt), increases with hypoxia did not separate between Tmod3-/+ and control mice. Remarkably, there was a significant increase in the number of lung vascular branches and total length of pulmonary vascular branches ($p<0.001$) in Tmod3-/+ after 4 weeks of constant hypoxia as compared to controls. Notably, the Tmod3-/+ endothelial cells migration was also significantly higher than that from the wild-type littermates. Our results indicate that, under chronic hypoxia, lower levels of Tmod3 play an important role in the maintenance or neo-vascularization of pulmonary arteries.

Respiratory (continued)

Poster 113

ENHANCING RECRUITMENT IN UNDERSERVED AREAS AND MINORITY POPULATIONS

Megan R. Warner, Jeremy Landeo-Gutierrez, Almary Akerlundh, Rakesh Bhattacharjee, Cinthia Sanchez, Manaswitha Khare, Julie Ryu, Natacha Akshoomoff, Kelan Tantisira, Kyung Rhee

Background: *Traditionally, research studies do not include a diverse sample, particularly underrepresented minorities. A variety of targeted recruitment strategies may be required to successfully increase the enrollment of diverse populations into research studies. The goal of this analysis was to identify which recruitment strategies would be effective at recruiting traditionally underrepresented populations into a large national research study.*

Methods: *Using data from A Multi-Center Observational Study: The RECOVER Post Acute Sequelae of SARS-CoV-2 (PASC) Pediatric Cohort Study, we performed a retrospective cross-sectional analysis examining which recruitment method resulted in enhanced enrollment of diverse populations. Recruitment data from July 2022 to March 2023 were analyzed. The primary outcome was the proportion of participants from each racial/ethnic category Recruitment methods included: 1) Community Outreach (e.g., community health fairs and text messaging campaigns), 2) Outreach through Rady Children's Hospital San Diego (RCHSD) (e.g., targeting patients who presented for testing/vaccines, sending MyChart messages), 3) Traditional methods (websites, flyers, press releases) and 4) Other. Chi-square tests were used for bivariate analyses.*

Results: *A total of 274 participants were recruited during this time period; 28.1% were non-Hispanic White (NHW), 46.4%Hispanic, 11.6% NH-multi-race and 13.8% reported Other ethnicity; 52.6% were from underserved areas. Community Outreach and outreach through RCHSD avenues were associated with greater recruitment of Hispanic families compared to NHW. Community outreach and outreach through RCHSD methods were also associated with greater recruitment from medically underserved areas.*

Conclusion: *Targeted recruitment methods were successful in recruiting Hispanic and medically underserved families into the RECOVER study. Utilizing a variety of recruitment strategies can aid in the recruitment of diverse families who often do not participate in research studies.*

Poster 107

MICRORNAS AND SHORT-ACTING BETA-2 AGONIST USAGE IN ASTHMA

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Background: *MicroRNAs (miRNAs) are small non-coding segments that can target and influence the pathogenesis of phenotypes in diseases like asthma. GINA guidelines stratify asthma diagnosis and control by several clinical phenotypes. We hypothesized that miRNA expression can worsen asthma symptom control, leading to increased short acting beta agonist (SABA) use. We tested this hypothesis in two independent cohorts of children with asthma, the Childhood Asthma Management Program (CAMP) and the Genetics of Asthma in Costa Rica Study (GACRS).*

Methods: *Banked serum miRNAs sequences were utilized from 491 CAMP and 1159 GACRS participants. Differential gene expression using DESeq in R was conducted on 255 miRNAs in CAMP and 304 miRNAs in GACRS. Cross-cohort analysis focused on differential gene expression by SABA use frequency. Questionnaire answers obtained at the time of sampling were categorized by frequency of SABA use. In both CAMP and GACRS, the frequency of SABA use was dichotomized as "little to no use" (defined as less than once per week) versus "increased use" (defined as greater than or equal to once per week). Statistical significance was defined as a p-value <0.05.*

Results: *We identified 14 miRNAs in CAMP and 28 miRNAs in GACRS that were differentially expressed by increased SABA use at P <0.05. Three miRNAs were differentially expressed in both cohorts: hsa-miR-1246, hsa-miR-3679-5p, and hsa-miR-181c-5p. Increased miRNA expression in hsa-miR-3679-5p was associated with increased SABA use in both cohorts. Regarding increased SABA use, hsa-miR-1246 and hsa-miR-181c-5p had opposing degrees of expression across CAMP and GACRS cohorts.*

Respiratory (continued)

Poster 105

CONTEXT-DEPENDENT FUNCTIONS OF MITOCHONDRIA PROTEIN QUALITY CONTROL IN LUNG

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Background: *Congenital diaphragmatic hernia (CDH) is one of the most common major congenital anomalies affecting lung development, occurring in 1 of every 2,500 live births. It occurs when abdomen organs migrate into the chest through the pathological hole in the diaphragm. The accompanied defects in the heart and lung were normally thought to be the consequence of limited growing space left by the herniation. It is poorly understood if the genetic mutations in CDH babies play any intrinsic roles in lung development. This study sought to identify and characterize the function of CDH gene, Lonp1, in lung development, homeostasis and injury repair.*

Methods: *Genetic mutants were generated by conditionally knockout of Lonp1 in lung epithelium, mesenchyme and diaphragm. Biochemical, physiological and single cell sequencing approaches were used to further dissect the mechanisms.*

Results: *Here, we found that a previously identified CDH gene Lonp1, which encodes a protease for degradation of junk proteins in mitochondria, plays intrinsic roles in lung development, homeostasis and injury repair. Inactivation of Lonp1 in the early lung development led to defects in branching morphogenesis, loss of club/ciliated cells and basal cell hyperplasia. Similar airway phenotypes were recapitulated in the adult mutants. Mechanistically, integrated stress response (ISR) was found specifically activated in the epithelial progenitors and differentiated ciliated cells, which led to cell senescence and apoptosis, respectively. Single cell study revealed that a BCL-2 family member, BOK, is uniquely expressed in the ciliated cells and is required for the ISR activation. Additionally, LONP1 kept airway progenitors from cell cycle arrest upon influenza infection by preventing ISR activation.*

Conclusions: *Taken together, our data suggest that mitochondria proteostasis controls airway cell fate decision in a context-dependent manner. Lonp1-ISR axis is required for airway epithelial cell differentiation during lung development, and is reutilized to promote airway progenitor migration following severe injury.*

This research was funded by R01HL160019 from NIH (Xin Sun and Le Xu) and #827787 from AHA Postdoc fellowship (Le Xu)

Respiratory (continued)

Poster 101

CHOLESTEROL, NOT FAT, IS CRITICAL IN ATHEROGENESIS INDUCED BY INTERMITTENT HYPOXIA AND HYPERCAPNIA

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Obstructive sleep apnea (OSA) is a prevalent sleep disorder characterized by intermittent hypoxia and hypercapnia (IHC) and is known to increase risk for atherosclerosis. Most of OSA patients are obese. However, the particular role of high fat and high cholesterol in inducing or promoting atherosclerosis under IHC remains obscure. To dissect the mechanisms involved, we examined atherosclerotic formation in the Aorta, Aortic arch and Pulmonary artery (PA) in pro-atherogenesis mouse model, the apolipoprotein E (ApoE) deficient mice, after IHC exposure on either high fat diet (HF, 60% fat by Kcal and 0.003% cholesterol by weight) or high fat high cholesterol diet (HFHC, 42% fat by Kcal and 1.3% cholesterol by weight), and compared them to room air (RA) control groups fed with HF, HFHC or regular chow (RC, 10% fat by Kcal and 0.003% cholesterol by weight). Our data revealed that HFHC-treated mice had significantly more atherosclerotic lesions than those fed with RC in room air (e.g. Aorta, RA- HFHC 8.1±0.76% vs RA-RC 1.0±0.27%, $p<0.01$). 10-week IHC treatment further accelerated atherogenesis in Aorta, Aortic arch and PA as compared to RA controls in the presence of HFHC (Aorta, IHC-HFHC 13.8±0.96% vs RA-HFHC 8.1±0.76%, $p<0.01$; Aortic arch, IHC-HFHC 28.5±1.88% vs RA-HFHC 16.6±2.00%, $p<0.01$; PA, IHC-HFHC 28.9±2.81% vs RA-HFHC 12.2±1.51%, $p<0.01$). Intriguingly, HF diet alone didn't cause significant difference in terms of atherosclerotic lesions among RA-RC, Air-HF and IHC-HF groups (Aorta, IHC-HF 0.6±0.20% vs RA- HF 0.1±0.06% vs RA-RC 0.4±0.08%, $p>0.01$; Aortic arch, IHC-HF 2.0±0.73% vs RA-HF 0.4±0.20% vs RA-RC 1.0±0.26%, $p>0.01$; and PA, IHC-HF 1.4±0.33% vs RA-HF 0.2±0.20% vs RA-RC 0.0±0.04%, $p>0.01$), indicating that high fat alone is insufficient to induce atherosclerosis under both RA and IHC conditions. In conclusion, our data demonstrated that (1) high cholesterol, but not high fat, plays a critical role in the development of atherosclerosis; (2) impact of IHC on atherosclerosis depends on the presence of HFHC.

This study is supported by the National Institutes of Health grant 1R01HL157445-01A1

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BUPRENORPHINE AND METHADONE DIFFERENTIALLY ALTER EARLY BRAIN DEVELOPMENT IN HUMAN CORTICAL ORGANOIDS

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Buprenorphine (BUP) and methadone (MTD) are used for medication-assisted treatment (MAT) in opioid use disorder. Although both medications show improved maternal and neonatal outcomes compared with illicit opioid use during pregnancy without either medication, BUP has exhibited more favorable outcomes to newborns than MTD. The underlying cellular and molecular mechanisms for the difference between BUP and MTD are, however, largely unknown. In this work, we examined the growth and neuronal activity in human cortical organoids (hCOs) exposed to BUP or MTD. We found that after neural induction, the growth of hCOs was significantly restricted in the MTD-treated but not in the BUP-treated hCOs and BUP, itself, attenuated the growth-restriction effect of MTD in hCOs. Furthermore, a κ-receptor agonist restricted while an antagonist alleviated the growth-restriction effect of MTD in hCOs. These results suggested that κ-receptor activation can mediate the growth-restriction process induced by MTD and, since BUP is not only a μ-agonist but a k-antagonist, the prevention of this growth-restriction by BUP is due to its κ-receptor-antagonism. In addition, using multielectrode array (MEA) technique, we discovered that both BUP and MTD inhibited neuronal activity in hCOs but BUP showed suppressive effects only at higher concentrations. Furthermore, κ- receptor antagonist nBNI did not prevent the MTD-induced suppression of neuronal activity in hCOs but the NMDA-antagonism of MTD (that BUP lacks) plays a role in the inhibition of neuronal activity. We conclude that BUP κ-receptor antagonism mitigates the MTD-induced growth restriction during neurodevelopment and shows much less suppressive effect on neural network communications due to its lack of NMDA-antagonistic mechanism.

Respiratory (continued)

Poster 114

ABNORMAL FETAL BRAIN DEVELOPMENT IN DOWN SYNDROME USING CORTICAL ORGANOIDS

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Down syndrome (DS) is a genetic disorder with an extra copy of chromosome 21 and DS remains one of the most common causes of intellectual disabilities in humans. All DS patients have Alzheimer's disease (AD)-like neuropathological changes including accumulation of plaques and tangles by their 40's, much earlier than the onset of such neuropathological changes in AD patients. Due to the lack of human samples and appropriate techniques, our understanding of DS neuropathology during brain development or before clinical onset of the disease remains largely unexplored at the cellular and molecular level. With the advancement of induced pluripotent stem cell (iPSC) technology, iPSC-derived 3D cortical organoids allow us not only to model neurodevelopmental disorders such as in Down syndrome, but also explore the earliest cellular and molecular changes during DS fetal brain development. Here, we report that DS iPSCs have a decreased growth rate than control iPSCs due to a decreased cell proliferation. DS iPSC-derived cortical organoids have a much higher immunoreactivity of amyloid beta (Aß) antibodies and a significantly higher amount of amyloid plaques than control organoids. Although Elisa results did not detect a difference of Aß40 and Aß42 level between the two groups, the ratio of Aß42/Aß40 in the detergent-insoluble fraction of DS organoids was significantly higher than control organoids. Furthermore, an increased Tau phosphorylation (pTau S396) in DS organoids was confirmed by immunostaining and western blot. Elisa data demonstrated that the ratio of insoluble Tau/total Tau in DS organoids was significantly higher than control organoids. In conclusion, a) DS iPSC-derived cortical organoids mimic AD-like pathophysiologyical phenotype in vitro, including abnormal Aß and insoluble Tau accumulation, and b) the molecular neuropathologic signature of AD is present in DS much earlier than predicted, even in early fetal brain development, illustrating the notion that brain organoids maybe a good model to study early neurodegenerative conditions.

Poster 102

EVOLUTIONARILY CONSERVED MECHANISMS REGULATING DROSOPHILA HYPOXIA TOLERANCE IN MELANOGASTER

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Hypoxia is one of the critical pathological elements in many human diseases, including ischemic stroke, myocardial infarction and solid tumors. Understanding the mechanisms regulating hypoxia tolerance or susceptibility is essential for developing effective strategies for medical therapy. In this regard, we generated hypoxia-tolerant Drosophila melanogaster populations through experimental hypoxia-directed evolution in the laboratory, sequenced and analyzed their genomes. In parallel, we took advantage of the natural evolution of humans at high-altitude regions and analyzed the whole genomes of Ethiopian and Andean highlanders. Through a comparative genomic approach, we obtained a group of evolutionarily conserved genes (28 human/23 Drosophila genes) that are potentially involved in regulating hypoxia tolerance in both human highlanders and the hypoxia-tolerant flies. We confirmed that ubiquitous knocking down of the conserved genes, such as grn/GATA3, inv/EN1, Mkk4/MAP2K4, Pxt/DUOX1/DUOX2, pyd/TJP1, RapGAP1/RAP1GAP2, Shal/KCN and shep/RBMS3 dramatically enhanced hypoxia tolerance in vivo in Drosophila melanogaster. In addition, we found that glial-specific knocking down of Egfr, grn, pyd and Shal rescued hypoxia- induced lethality. Furthermore, we found that some of these conserved genes (i.e., bnl, croc, Mkk4 and shep) are required by Notch activation-conferred survival in hypoxic environment, whereas Egfr, grn, pyd and Shal regulating hypoxia tolerance through Notch-independent mechanisms. We believe that these evolutionarily conserved mechanisms are novel targets that have a strong potential to be translated into therapeutic strategies to treat or prevent hypoxia-related diseases.

Grant: This project is supported by NIH grant 1R21NS120023-01A1.

Transforming Mental Health Initiative

Poster 40

INITIAL APPOINTMENT DIFFERENCES BETWEEN CAT VS HAND-OFFS

Devin P. Adams, MPH; Jasmine R. Holt, PsyD; Alissa Lazio-Kim, BA; Vanessa Sarabia, BS; and Kathryn A. Hollenbach PhD, MPH

Background: *An integrated primary care behavioral health (BH) model was implemented at 7 pediatric primary care offices. The Integrated Health Therapists (IHT) located in the pediatric office provide short term therapy and conduct warm hand-offs (WHO) for referrals. Previous research has shown that WHOs can be beneficial in improving patient appointment scheduling and adherence (Mitchell et al., 2022; Young et al., 2020). Our model has a Centralized Access Team (CAT) whose function is to contact patients who didn't receive a WHO and offer them telemedicine intakes. We are evaluating potential difference between the patients who received a WHO and those who received a CAT intake to determine if there were any differences in appointment scheduling or adherence.*

Methods: *A patient list was obtained through an EPIC Workbench report. Search criteria were all patient who had been discharged from the program since July 1, 2022. Variables including referral date, patient age, gender, no show rate, and discharge status were pulled automatically. Manual chart abstraction was completed to collect more information around each patient's specific first contact.*

Results: *A total of 535 patients who received a referral since July 1, 2022 and had a visit were abstracted. 429 patients were expected to schedule an initial assessment. Of those, 339 were non-CAT intakes. There was no significant relationship between type of intake and whether patients rescheduled their initial appointments, $X2 (1, N = 409) = 0.85$, $p = 0.356$. A Fisher's exact test was used to determine there was not a statistically significant association between intake type and if initial assessments were completed ($p = 0.595$).*

Discussion: *Our results show that whether patients had a warm hand off or a CAT scheduling first contact was not significantly associated with differences in appointment completion or scheduling.*

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BEHAVIORAL HEALTH DIAGNOSES TREATED WITHIN AN INTEGRATED PRIMARY CARE PROGRAM VS TREATMENT AS USUAL

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Background: *Many families approach their pediatrician when concerned about their child's mental health (Collins et al., 2010). As a result, pediatricians frequently see patients with behavioral, mood, and developmental concerns (Talmi et al., 2016). However, little is known about differences in behavioral health diagnoses of patients referred for services in an integrated primary care (IPC) program compared to treatment as usual (TAU). We will describe the demographic characteristics of pediatric patients receiving referrals for behavioral health concerns in both an IPC program and in TAU and compare the number and type of behavioral health diagnoses in these groups.*

Methods: *Data were collected as part of a larger prospective study comparing the scheduling of behavioral health initial evaluations within an IPC program compared to TAU. Electronic health record (EHR) reports identified patients who received either a referral to the IPC program or TAU. Further data about behavioral health diagnoses are being abstracted from the EHR.*

Results: *Data are being abstracted for 568 behavioral health referrals made between 1/17/2022 and 6/10/2022 for patients with behavioral health concerns at 6 pediatric primary care offices. There were 471 referrals to the IPC program and 97 referrals to TAU. For this cohort study, additional patient behavioral health diagnoses are being collected to compare the number and type of behavioral health diagnoses of patients in each group. We will analyze group proportions using chi square or Fisher's exact tests dependent on data distribution requirements. Data will be analyzed using STATA, 16 (College Station, TX, USA).*

Discussion: *Data analysis is ongoing. Previous literature has shown that mental health concerns are frequently addressed in the pediatrician's office. In our IPC program, we hope to better understand what behavioral health diagnoses we commonly treat and if they differ from the concerns that are referred to services in the community.*

Transforming Mental Health Initiative (continued)

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THE COMPARISON OF A PRIMARY CARE BEHAVIORAL HEALTH INTEGRATION PROGRAM WITH TREATMENT AS USUAL IN SCHEDULING INITIAL EVALUATION VISITS

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Background: *Despite the current mental health crisis , patients and families continue to struggle with obtaining behavioral health (BH) services. Our primary care behavioral health integration (PCBHI) hub and spoke model refers BH concerns to integrated health therapists (IHTs). Treatment as usual (TAU) pediatric primary care clinics without embedded IHTs refer patients to external BH services within the community. We compared the two referral systems.*

Methods: *Data were collected 14 days post BH referrals. Patients without scheduled initial BH appointments from PCBHI and all TAU referrals were contacted. Parents were asked about dates of scheduled appointments, waitlist placement, or reasons for unscheduled appointments for referrals made from 1/17/2022 to 6/10/2022.*

Results: *471 PCBHI and 97 TAU referrals did not differ on demographic characteristics. In the PCBHI Group, 253 (53.7%) referrals received first contact with IHT and were either discharged/referred to PCBHI Hub clinics or care coordination within 14 days of referral. 172 (36.5%) referrals had a scheduled initial evaluation appointment and 29 (6.2%) had no initial appointment scheduled within 2 weeks of referral. We contacted 76 (78.4%) of the 97 BH referrals in the TAU Group. 44 (57.9%) parents did not call external resources to schedule. Of the 32 (42.1%) parents who had attempted to schedule initial BH appointment, only 7 (21.9%) scheduled an initial BH appointment, 5 (15.6%) were waitlisted, and 19 (59.4%) were unable to schedule appointments or waitlist their child within 2 weeks of referral. The PCBHI Group was 5.1 times more likely to schedule initial BH appointments (95% CI=2.5-10.4) compared to TAU. There was no difference in median days to initial appointment (PCBHI (21 (IQR: 15, 27.5)) and TAU (23 (13, 35) (p = 0.71)).*

Conclusion: *Integrated behavioral health care demonstrates significantly higher success rates of patients accessing behavioral health services compared to current care standards.*

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NEW DIRECTIONS IN INTEGRATED CARE: DESCRIBING A HIGHLY COLLABORATIVE, INNOVATIVE PARTNERSHIP WITH RADY CHILDREN'S TRANSFORMING MENTAL HEALTH INITIATIVE AND PRIMARY CARE PEDIATRICS

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Introduction: *Children and adolescents often do not receive mental health care when they need it. By 2021, the complex impact of the coronavirus pandemic, structural racism, inequality in healthcare and lack of available mental health providers led to a national emergency in child and adolescent mental health. The need for effective, accessible treatment for youth is more pressing than ever. Inter-disciplinary team-based integrated care has been shown to be effective, accessible, and cost saving.*

Methods: *In 2020, the Rady Children's Hospital-San Diego Transforming Mental Health Initiative designed an integrated care program drawing elements from Primary Care Behavioral Health (PCBH) and Collaborative Care (CC) models. Model design and implementation, qualitative experiences, primary care satisfaction, measurement-based care trends and barriers to success for our program will be discussed.*

Results: *By 2023, our program established integrated care teams in seven primary care clinics in two large California counties. Provider and patient satisfaction has been high. Measurement based care has been implemented, and data are being analyzed. Currently we are working on sustainability of our program.*

Discussion: *Preliminary results suggest that elements of PCBH and CC can be blended to form an effective, highly collaborative integrated care model serving children and adolescents in primary care settings. Future study targets include sustainability, implementation challenges, funding strategies, and measurement-based care workflow.*