Pediatric Research Day

Wednesday, March 28, 2018
7:45 am – 4:00 pm
Children’s Foundation Research Center • Memphis, TN
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Welcome to the 10th Annual Pediatric Research Day, hosted by the Department of Pediatrics at the University of Tennessee Health Science Center and the Children’s Foundation Research Institute within Le Bonheur Children’s Hospital.

Our research portfolio has continued to strengthen year over year. We are excited about the work presented at Pediatric Research Day, as it highlights the diversity and depth of basic and clinical research being performed at Le Bonheur Children’s Hospital, UTHSC and our academic and clinical partner institutions, including St. Jude Children’s Research Hospital and the University of Memphis. It also demonstrates the exciting progress and significant advances that our researchers are making towards uncovering molecular mechanisms underlying pediatric diseases, preventing childhood illness and improving the quality of pediatric healthcare.

The theme for this year is Neurosciences. This forum is intended to both showcase the work of our researchers and trainees, and allow us to learn from our distinguished guests, all of whom are leaders in their field. Dr. Gregory Holmes, the Pediatric Research Day keynote speaker and recipient of the James Hunt Distinguished Visiting Professorship, will speak about possible links between autism and epilepsy. Dr. William Evans, the former CEO of St. Jude Children’s Research Hospital, will update us on the latest research on pharmacogenomics of anti-cancer agents. Dr. Robert Rooney will describe the development of our exciting Biorepository and Integrative Genomics program. Rounding out the neurosciences theme, Dr. Jim Wheless, the Chief of Neurology and Le Bonheur Endowed Chair, will discuss the latest research in treatment of epilepsy, and Dr. Shalini Narayana will discuss the use of advanced neuroimaging and neuro-diagnostics in understanding degenerative neurologic diseases.

This year too, we had a large number of Pediatric Research Day participants, reflecting a strong and enthusiastic commitment to research, collaboration and innovation. I hope that you will enjoy this opportunity to interact and discuss your work with fellow researchers.

Enjoy the Day!

Jon McCullers, M.D.
Chair, Department of Pediatrics, UTHSC
Pediatrician-in-Chief, Le Bonheur Children’s Hospital
Welcome to the tenth annual Pediatric Research Day! Le Bonheur Children’s Hospital, along with its major partners, the University of Tennessee Health Science Center, the Children’s Foundation Research Institute of Memphis and St. Jude Children’s Research Hospital, has supported cutting edge basic, clinical and translational research for many years, leading to several major breakthroughs impacting on the health and well-being of children. Activities surrounding Pediatric Research Day are designed to showcase our pediatric researchers and their work. We are extremely proud of the high-quality, state-of-the-art research produced by these talented individuals.

This year, Pediatric Research Day spotlights accomplishments in the area of Neuroscience. The keynote speaker, Dr. Gregory Holmes, Chair of Neurological Sciences at the University of Vermont and recipient of the UTHSC James Hunt Distinguished Visiting Professorship Award, will speak on “Epilepsy and Autism: Coincidence or Consequence?” The other Invited Speakers and Short Talk presentations, as well as the Poster presentations, will highlight the breadth and depth of the ongoing research activities here at Le Bonheur, St. Jude and the University of Tennessee Health Science Center. A record number of abstracts were submitted this year, reflecting the continued growth of our research programs.

We are excited by the advances in pediatric research at Le Bonheur Children’s Hospital and think you will be, too. Again, welcome and enjoy!

Dennis D. Black, MD
J. D. Buckman Professor of Pediatrics
Professor of Physiology, UTHSC
Vice Chair for Research, Department of Pediatrics
Director, Children’s Foundation Research Institute of Memphis
Vice President for Research, Le Bonheur Children’s Hospital
Scientific Program

Pediatric Research Day 2018
Wednesday, March 28, 7:45 a.m. – 4:00 p.m.
Chesney Auditorium, Children’s Foundation Research Institute

7:45 - 8:00 am  Breakfast

8:00 - 8:10 am  Welcome
Jonathan McCullers, M.D.
Dunavant Professor and Chair, Department of Pediatrics, UTHSC;
Pediatrician-in-Chief, Le Bonheur Children’s Hospital
Meri Armour, President and CEO, Le Bonheur Children’s Hospital

8:10 - 8:15 am  Opening Remarks from the Organizer
Amali Samarasinghe, Ph.D., Assistant Professor, Division of Pulmonology

8:15 – 9:15 am  Keynote Address: James C. Hunt Visiting Distinguished Professorship
Epilepsy and Autism: Coincidence or Consequence
Gregory Holmes, M.D.
Chair, Department of Neurological Sciences, University of Vermont,
Burlington.

9:15 – 9:30 am  Coffee served in the atrium of the Faculty Office Building

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Auditorium, Faculty Office Building

Session One:

Session Chairs: Joan Chesney, MD [Director, Office of Pediatric Clinical Fellows]
               Elisha McCoy, MD [Director, Pediatric QI]

9:30 – 9:40 am  Introduction by Session Chairs

9:40 – 10:10 am  Early Onset Childhood Epilepsy: Utilizing Modern Genetics to Improve
                 Diagnosis and Treatment Outcome
James Wheless, M.D.
Professor and Chief, Pediatric Neurology. Le Bonheur Children’s Hospital and
UTHSC

10:10 – 10:20 am  Progressive Reduction in Right Ventricular Contractility in an Aging
                   Mouse Model of Arrhythmogenic Cardiomyopathy
Emmanuel Camors, Ph.D.
Department of Pediatrics, Outstanding Abstract Award: Junior Faculty

10:20 – 10:30 am  Improving Documentation of Menstrual History in Patients at risk for
                   PCOS, with QI in an Academic Pediatric Continuity Clinic
Sarah Carey Robinson, M.D.
Department of Pediatrics, Outstanding Abstract Award: Clinical Resident

10:30 – 10:45 am  Coffee Break
10:45 – 11:15 am  **The Biorepository and Integrative Genomics (BIG) Initiative**  
Robert Rooney, Ph.D.  
Director of Integrative Genomics Biorepository,  
Assistant Professor, Department of Pediatrics, UTHSC

11:15 – 11:25 am  **Systems Genetics Analysis of Arrhythmogenic Cardiomyopathy Induced by p.S368L Mutation in Transmembrane Protein 43**  
Undral Munkhsaikhan, Ph.D.  
Department of Pediatrics, Outstanding Abstract Award: Postdoctoral Fellow

11:25 – 1:20 pm  **POSTER SESSION** and Lunch  
CFRI Ground and Lobby Levels  
Presenters must be available at posters from 12:00 - 1:00 pm

**Session Two:**  
Session Chairs: Jon McCullers, MD [Chair of Pediatrics]  
James Wheless, MD [Chief of Neurology]

1:20 – 1:30 pm  Introduction by Session Chairs

1:30 – 2:00 pm  **Pharmacogenomics of Glucocorticoid Resistance in Acute Leukemia and Chronic Kidney Disease**  
William Evans, Pharm. D.  
Chair of Pharmacogenomics, Department of Pharmaceutical Sciences,  
St. Jude Children’s Research Hospital

2:00 – 2:10 pm  **MicroRNAs as Novel Biomarkers in Pediatric Severe Sepsis**  
Madhura Hallman, M.D.  
Department of Pediatrics, Outstanding Abstract Award: Clinical Fellow

2:10 – 2:20 pm  **TMS Localization of Eloquent Cortices in Patient with Rasmussen Encephalitis. A Case Report.**  
Luke Embury  
Department of Pediatrics, Outstanding Abstract Award: Research Staff

2:20 – 2:30 pm  **BioLegend and You: A Neuroscience Story**  
John Rutigliano, PhD. Technical Application Scientist II  
Team Leader, BioLegend, Inc.

2:30 – 2:45 pm  Coffee Break (Kindly Sponsored by BioLegend. Inc.)

2:45 – 3:15 pm  **Diagnostic and Neuromodulatory Applications of Transcranial Magnetic Stimulation: Coming of “Age” of a Non-invasive Brain Stimulation Modality**  
Shalini Narayana, Ph.D.  
Associate Professor, Division of Pediatric Neurology,  
Department of Anatomy and Neurobiology, UTHSC
Scientific Program

3:15 – 3:25 pm 17,20S(OH)2pD Suppresses Total Collagen Synthesis in the Bleomycin Model of Fibrosis

Imara-Safi Olu Scott
BioLegend – Graduate Student Research Award

Session Three:

3:25 – 4:00 pm Award Ceremony and Closing Remarks

Dennis Black, MD. Scientific Director, CFRI
Ajay Talati, MD. Division Chief, Neonatology

• Outstanding Abstract Awards from the Department of Pediatrics:
  o Junior Faculty: Emmanuel Camors
  o Clinical Fellow: Madhura Hallman
  o Postdoctoral Fellow: Undral Munkhsaikhan
  o Clinical Resident: Sarah Carey Robinson
  o Research Staff: Luke Embury

• BioLegend, Graduate Student Research Award: Imara-Safi Olu Scott

• Outstanding Poster Awards from the Department of Pediatrics:
  o Faculty
  o Clinical Fellow
  o Postdoctoral Fellow
  o Clinical Resident
  o Research Staff
  o Graduate Student

• Outstanding Poster Awards from the College of Medicine:
  o Three Medical Students

SAVE THE DATE

11th Pediatric Research Day: 29th March, 2019
Le Bonheur Children's Hospital

Le Bonheur Children's Hospital is recognized as a top children's hospital by *U.S. News & World Report* and the Leapfrog Group. The hospital is Magnet certified and has the only ACS Level 1 Pediatric Trauma Program in the region. Le Bonheur is a comprehensive, not-for-profit hospital that serves more than 250,000 children in the hospital, clinics and through outreach programs each year. While primarily serving the Mid-South, children come from all 50 states for treatment at Le Bonheur. Families that travel long-distances for care can stay free of charge at the FedExFamilyHouse. Le Bonheur serves as the primary pediatric teaching hospital for the University of Tennessee Health Sciences Center.

**The Children’s Foundation Research Institute at Le Bonheur Children's Hospital**

Founded in 1995, the Children’s Foundation Research Institute (CFRI) represents the culmination of a unique partnership between the Children’s Foundation of Memphis, the University of Tennessee Health Science Center (UTHSC) and Le Bonheur Children’s Hospital to support the expansion of pediatric research. The CFRI provides comprehensive basic and clinical research infrastructure to support all research activities at Le Bonheur, including clinical trial support, provision of lab space, safety assistance, grant submission, budgeting services, scientific editing, and statistical assistance. This centralized and coordinated support accelerates discovery and innovation and forges collaboration, allowing our physicians and scientists to concentrate on what they do best: cutting-edge research aimed at improving the health of children.

**The Children’s Foundation of Memphis**

The Children’s Foundation of Memphis is a private foundation established in 1982 with the sale of The Crippled Children's Hospital. The organization’s mission is to serve the health and well-being of children in the Memphis area. The Foundation has given more than $17 million to support pediatric medical research at the Children’s Foundation Research Institute (CFRI). This sustained and significant support makes the CFRI’s groundbreaking research possible and is vital to improving the health of children in Memphis.
The goals of the Department have been to establish a strong partnership with Le Bonheur Children’s Hospital, to recruit outstanding faculty and house-staff, and to promote excellence in pediatric clinical care, research, education, and service to our community. Resources have been acquired from a number of sites, including Le Bonheur, St. Jude Children's Research Hospital, the Regional Medical Center, the Boling Center, the Children's Foundation of Memphis, and national funding agencies to fulfill these goals. We are particularly proud of our outstanding pediatric and medicine-pediatric residency training programs. Dr. Jon McCullers is Chair of the Department and Pediatrician-in-Chief of Le Bonheur.

The Department has strong clinical and research programs in Allergy-Immunology & Pulmonology, Cardiology, Critical Care, Developmental Pediatrics, Endocrinology, Gastroenterology, General Pediatrics, Genetics, Infectious Diseases, Neonatology, Nephrology, Neurology, and Rheumatology. Two outstanding integrated clinical and translational programs are housed in the Heart Institute and the Neuroscience Institute. The Department also has strong ties in both clinical and research areas to the Department of Surgery and Maternal Fetal Medicine in OB-GYN.

The Departmental Philosophy is to develop new models of care for the most pressing problems in our community including broad, cross-disciplinary challenges such as pediatric obesity, asthma, and developmental disabilities. We strive to meet changing environments head-on; our facilities, leaders, and faculty focus on innovative methods in patient care and target research to meet new demands.

The UTHSC Department of Pediatrics continues to play a very important role at Le Bonheur Children’s Hospital, and its goal remains to fulfill its education, research, patient care, and advocacy missions.
The James Hunt Visiting Professorship

The James C. Hunt Visiting Professorship in Pediatrics was established through a generous endowment from the Greater Memphis Community Foundation. The Professorship was established to honor Chancellor Emeritus of the University of Tennessee Health Science Center, Dr. James C. Hunt. Dr. Hunt was born in Lexington, N.C. He received his undergraduate degree from Catawba College in 1949. His M.D. degree was conferred from Bowman Gray School of Medicine. He completed his residency and fellowship at Mayo Clinic. He worked his way through the hierarchy at Mayo from instructor to professor, then nephrology Division Chief, then Chairman of the Department of Medicine, and finally Associate Dean of Clinical Programs. Dr. Hunt came to UTHSC in 1978 as Dean of the College of Medicine. He became Chancellor of UTHSC in 1981 and served until 1993. He then served as a Distinguished Professor and Director of the Clinical Scholars Program until 2001. He is currently Chancellor Emeritus and Vice-President of Health Affairs. His list of awards and honors is long. He has served as President of the National Kidney Foundation and received the Gift of Life Award from that organization in 1991. He has been honored by both of his undergraduate and medical schools with distinguished alumnus awards. He has served on the Board of Directors for numerous organizations. Dr. Hunt served as a Trustee of Le Bonheur Children’s Medical Center from 1981 to 1993. His long-standing commitment to the health and well-being of children led to the establishment of a visiting professorship in his name in pediatrics.
Keynote address

Biography

Gregory L. Holmes, MD

Gregory L. Holmes, MD, is Professor of Neurological Sciences and Pediatrics and Chairman of the Department of Neurological Sciences at the Larner College of Medicine at the University of Vermont. He graduated from the University of Virginia, School of Medicine in 1974 and did residencies in pediatrics at Yale University School of Medicine and pediatric neurology at the University of Virginia, School of Medicine. Prior to moving to Burlington, Vermont he was the inaugural Chair of the Department of Neurology at Dartmouth Medical School. He spent 16 years at Harvard Medical School where he was Professor of Neurology serving as Director of the Division of Clinical Neurophysiology and Epilepsy, Children’s Hospital. He did a sabbatical from 1996-1997 under the tutelage of Professor Y. Ben-Ari at INSERM Unit 29, Unite de Neurobiologie et Physiopathologie du Developpement, Paris.

Dr. Holmes does translational research with a focus on pediatric epilepsy. In particular, his laboratory is interested in the long-term consequences of seizures on the developing brain. His laboratory uses single cell and field recording techniques in freely moving rats, hippocampal slice electrophysiology, behavioral studies and immunohistochemistry. Dr. Holmes has received continuous funding by NIH since 1979. Dr. Holmes has a long history of training undergraduate, graduate and medical school students, residents, postdoctoral fellows and junior faculty, having trained over 100 people since 1979.

Dr. Holmes has served on numerous professional society boards, including the American Epilepsy Society, American EEG Society, and Child Neurology Society and has been on multiple study sections. He is the former President (2005-2006) of the American Epilepsy Society. Dr. Holmes has served on the United States Food and Drug Administration Peripheral and Central Nervous System Drugs Advisory Committee from 2007. He has been on numerous NIH study sections. He has been on the editorial board of multiple medical journals including Epilepsy Research, Brain & Development, Epilepsy & Behavior, Pediatric Drugs and Annals of Neurology.

His contributions have been recognized for numerous awards including the Sidney Farber Research Award from the United Cerebral Palsy Association, the John Horsley Memory Prize from the University of Virginia School of Medicine, the American Epilepsy Society Research Award, Basic Science Award, Ambassador for Epilepsy Award from the International League Against Epilepsy, the Pierre Gloor Research Award from the American Clinical Neurophysiology Society and the Sachs Award from the Child Neurology Society. In 2008 he gave the NINDS sponsored Judith Hoyer Lecture at the American Epilepsy Society in Seattle, Washington. From 2010-2012 he was a member of the National Academy of Science sponsored Committee on the Public Health Dimensions of the Epilepsies culminating in the book Epilepsy Across the Spectrum.
Epilepsy and Autism: Coincidence or Consequence?

Autism spectrum disorder (ASD) refers to a group of complex neurodevelopmental disorders, characterized by deficits in social communication and interaction and demonstrating restricted, repetitive and stereotyped patterns of behavior. Since the earliest writings about ASD, there has been a known association with epilepsy and a recognition that both conditions exist in the same child at a much higher rate than expected by chance alone. Because of the myriad of genetic and nongenetic causes resulting in both epilepsy and ASD, a singular pathophysiological mechanism responsible for the seizures and autistic phenotype is unlikely. However, the high rate of co-occurrence of epilepsy and ASD has led many to search for common pathological links between the two conditions that could provide a final pathway to either seizures or ASD.

There is increasing evidence that the common final pathway of ASD and epilepsy is through altered function brain connectivity, defined as the “temporal correlations between remote neurophysiological events.” Genetic and acquired models of epilepsy which have autistic-like behavior suggest that excitatory/Inhibitory (E/I) balance has a role in both the epilepsy and the aberrant behavior.\(^1\) In a rat model of early-life seizures, field recordings from dorsal and ventral hippocampus and prefrontal cortex demonstrated marked increase in coherence as well as a decrease in voltage correlation at all bandwidths compared to controls.\(^2\) Rats with early-life seizures had resulting impairment in the sociability and social novelty tests. In addition, rats with early-life seizures had lower seizure thresholds than controls, indicating long-standing alterations in the E/I balance. Bumetanide, a pharmacological agent that blocks the activity of NKCC1 and induces a significant shift of the equilibrium potential of chloride toward more hyperpolarized values, administration at the time of the seizures precluded the subsequent abnormalities in coherence and resulted in normal sociability and seizure threshold. In parallel, EEG spectral power, coherence, phase lag, Pearson and partial correlations, and epileptiform activity were assessed during the awake, slow wave sleep, and REM sleep states in 137 children aged 2 to 6 years with autism (n = 87), developmental delay without autism (n = 21), or typical development (n = 29).\(^3\) Brain connectivity, as measured by coherence, phase lag, and Pearson and partial correlations distinguished children with autism from both neurotypical and developmentally delayed children. In addition, in this cohort of young children with autism, sleep spindle density was reduced when compared to groups of age matched children with developmental delay or typically developing children.\(^4\)

Thus, functional connectivity is distinctly altered in both an animal models of early-life seizures with autistic-like behaviors and children with ASD. The altered communication between brain regions in epilepsy and ASD could reflect the physiological underpinnings underlying social cognitive deficits seen in ASD.

References

**Keynote address**

James W. Wheless, M.D., FAAP, FACP, FAAN, FAES

Professor and Chief of Pediatric Neurology  
Le Bonheur Chair in Pediatric Neurology  
University of Tennessee Health Science Center  
Director, Neuroscience Institute & LeBonheur Comprehensive Epilepsy Program  
LeBonheur Children’s Hospital

Dr. Wheless is Professor and Chief of Pediatric Neurology and the Le Bonheur Chair in Pediatric Neurology at the University of Tennessee Health Science Center in Memphis. He also serves as Director of the Neuroscience Institute and the Le Bonheur Comprehensive Epilepsy Program for the Le Bonheur Children’s Hospital.

Dr. Wheless is a Diplomat of the American Board of Pediatrics, and the American Board of Psychiatry and Neurology with special qualifications in Child Neurology, Clinical Neurophysiology, and Epilepsy. He is a fellow of the American Academy of Pediatrics, the American College of Pediatrics, the American Academy of Neurology & the American Epilepsy Society. Dr. Wheless is a member of the Editorial Board of Journal of Child Neurology, Formulary, and Epilepsy.com and serves as reviewer of a number of journals including Neurology, Epilepsia, Pediatrics, and Epilepsy and Behavior. Dr. Wheless’s primary interests include childhood convulsive disorders. His research is focused on pediatric anti-epileptic drug development, the ketogenic diet, epilepsy surgery, device therapy, and non-invasive functional brain mapping. Dr. Wheless is the author of more than 560 chapters, articles and abstracts on these subjects. He is the editor of three textbooks on Epilepsy. He has lectured widely on pediatric epilepsy. He received his medical degree from the University of Oklahoma and completed residency training in pediatrics at the University of Oklahoma and then pediatric neurology at Northwestern University in Chicago at Children’s Memorial Hospital. His EEG/clinical epilepsy training was at the Medical College of Georgia in Augusta.

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**Early Onset Childhood Epilepsy: Utilizing Modern Genetics to Improve Diagnosis & Treatment Outcome**

Severe epilepsies of infancy and childhood are a group of devastating disorders characterized by frequent epileptic seizures and developmental delay or regression. Standard diagnostic approaches include biochemical and enzyme analysis for neurometabolic disorders, brain MRI imaging, and EEG. Increasingly the contribution of genetic factors is being recognized when previously no etiology was determined by standard testing. This has allowed clinicians to target the unique genetic abnormality to treat the epilepsy with non-traditional medicines and use a precision medicine approach to targeting novel therapies for these children. In this presentation I will review the role of genetic testing for infants and young children when evaluating their epilepsy, illustrating key points with case examples. I will then discuss the role of precision medicine in these epilepsies, and how this has already led to novel therapies. Finally, I will present the Children’s Foundation of Memphis (CFOM) research protocol we will be starting this fall. This will allow us to perform whole genome sequencing on all children with epilepsy in the first three years of life. Our goal is to use this testing to define the etiology for these children, discover new genetic causes in this age group, and evaluate the benefit of performing this testing. We plan to couple this with evaluating the abnormality to respond to medical therapy by using high through-put medicine libraries to evaluate each child for an unique treatment for their epilepsy.
Invited Speakers

Robert J. Rooney, Ph.D.

Assistant Professor, Department of Pediatrics
Adjunct Assistant Professor, Department of Genetics, Genomics and Informatics
University of Tennessee Health Science Center
Director, Integrative Genomics Biorepository
Le Bonheur Children’s Hospital

Dr. Robert Rooney graduated with a PhD in Biological Sciences from Columbia University in 1986 and received his post-doctoral training at Rockefeller University and Duke University, first under an NIH fellowship (1987-1989) and then as a Howard Hughes Medical Institute Research Associate (1990-1992).

Dr. Rooney joined the faculty in the Department of Biochemistry at St. Jude Children’s Research Hospital in 1992 and moved to the Department of Molecular Genetics and Microbiology at Duke University Medical Center in 1998. In 2004, he became the Chief Scientific Officer and Scientific Director of Genome Explorations Inc., a CLIA-approved commercial genomic analysis service provider. In March of 2015, Dr. Rooney joined the Department of Pediatrics at UTHSC in his current capacity as the Director of the Integrative Genomics Biorepository.

Dr. Rooney’s academic research interests have focused on the mechanisms of transcriptional regulation by viral oncogenes, their influence on cellular growth and survival, and more recently have moved toward genomics, epigenetics and transcriptomics. He is an author on 40 published scientific articles, book chapters and books.

The Biorepository and Integrative Genomics (BIG) Initiative

Precision Medicine leverages genomic research and personalized testing to advance more precise and cost-effective clinical care and preventative health planning, but few pediatric hospitals have the appropriate infrastructure to do so. The BIG Initiative was launched in 2015 to help develop precision medicine platforms at Le Bonheur (LBCH) and facilitate genomics research at UTHSC. BIG has thus far developed: 1) an enrollment process to approach the majority of LBCH pediatric patients for consent to isolate, store and analyze their genomic DNA; 2) informatics systems for HIPAA-compliant participant sample and data management, linkage to de-identified clinical information, and on-line sample and data requests; and 3) a governance structure, including advisory boards for operations, ethics, and community outreach, that guides and reviews BIG planning and activities. Approximately 150 participants per week are currently enrolled into BIG from the hospital's in-patient and out-patient center populations. Through 2017, BIG enrolled >7,000 participants and archived >3,800 individual DNA samples. Creation of facilities for genomic analysis and clinical interpretation is currently under way. However, thus far, NO requests for DNA samples have been received from UTHSC faculty. The BIG Initiative has begun to develop institutional infrastructure for precision medicine that can serve as the basis for clinical platforms at LBCH. Genomic research by UTHSC faculty can benefit from the use of this resource.
William E. Evans, Pharm.D.
Endowed Chair in Pharmacogenomics
Department of Pharmaceutical Sciences
St. Jude Children's Research Hospital
Professor of Pediatrics and Clinical Pharmacy
University of Tennessee Health Science Center

Dr. Evans joined St. Jude Children's Research Hospital (SJCRH) as a student in 1972, chaired the Pharmaceutical Sciences Department from 1986-2002, served as Scientific Director & EVP from 2002-2004, and as CEO of SJCRH from 2004-2014. He currently holds an Endowed Chair of Pharmacogenomics at SJCRH and is a Professor at the University of Tennessee.

During his decade as CEO, St. Jude was ranked the #1 Children's Cancer Hospital by USNWR and by Parents Magazine, #1 in the Best Places to Work in Academia by Scientist Magazine, among the Top 100 Best Places to Work by Fortune Magazine, received a perfect score by The Joint Commission and received an “Exceptional” ranking as an NCI Comprehensive Cancer Center. Evans received his BSc and Pharm.D. degrees from the University of Tennessee HSC (1973, 1974) and spent a sabbatical year (1987-88) at the University of Basel. He has received honorary doctoral degrees from Rhodes College, the Ohio State University and the University of Florida.

For the past 40 years his research has focused on the pharmacodynamics and pharmacogenomics of anticancer agents in children with acute lymphoblastic leukemia, for which he has received three consecutive NIH MERIT Awards from NCI. Evans has authored over 400 scientific publications and has received several national awards for his research, including the 2009 Pediatric Oncology Award from ASCO (with Mary V. Relling of SJCRH), the 2009 Team Science Prize from AACR (shared with SJCRH colleagues), the 2012 Remington Medal from APhA, and the 2013 Oscar B. Hunter Award from ASCPT.

He was elected to the Institute of Medicine of the US National Academy of Sciences in 2002, the US National Academy of Medicine in 2015 and the German National Academy of Sciences in 2016. Evans currently serves on the Board of Trustees of the University of Tennessee (2014-2020), chairs the Scientific Advisory Board of the Princess Maxima Children's Cancer Center in The Netherlands (2014-present), and served on the Board of Trustees of Rhodes College (2005-2014).

Pharmacogenomics of glucocorticoid resistance in acute leukemia and chronic kidney disease

Glucocorticoids (GC) are widely used in the treatment of many malignant (e.g., acute lymphoblastic leukemia) and non-malignant diseases (e.g., asthma, allergies, chronic kidney disease, auto-immune disorders). Although there are multiple mechanisms by which cells can develop resistance to glucocorticoids, this is poorly understood in many diseases, and the extent to which this involves genetic and epigenetic mechanisms remains to be fully elucidated. We recently identified a new epigenetic mechanism by which leukemia cells develop resistance to GC, involving the hypomethylation of caspase 1 (CASP1) and its activator NLRP3, leading to their over-expression and the hyper-activation of caspase 1 (Paugh et al Nature Gen. 2015). We showed that caspase 1 cleaves the glucocorticoid receptor, thereby causing cells to become resistant to GC, and that this can be mitigated by inhibition of caspase 1. We subsequently showed that this mechanism is also evident in patients with chronic kidney disease that are resistant to GC treatment (Zaza et al, unpublished data). We have more recently expanded our agnostic genome-wide assessment of genetic and epigenetic mechanisms influencing GC sensitivity of ALL cells, and identified ~35 of 39 genes previously linked to GC resistance, while revealing multiple additional genes not previously associated with GC resistance. Our aim is to identify genetic and epigenetic mechanisms that cause GC resistance to provide a foundation for developing novel strategies to overcome GC resistance in the clinic.
Shalini Narayana, MBBS, MS, Ph.D.

Associate Professor
Department of Pediatrics, Division of Pediatric Neurology
Department of Anatomy and Neurobiology
UTHSC College of Medicine, Memphis TN, USA.
Director, Transcranial Magnetic Stimulation Laboratory
Neuroscience Institute, Le Bonheur Children's Hospital, Memphis
TN, USA.

Shalini Narayana studies the human motor, somatosensory, and
language systems in both clinical and neurotypical populations
utilizing non-invasive imaging tools including transcranial magnetic
stimulation (TMS), functional magnetic resonance imaging,
magetoencephalography, and positron emission tomography.

Dr. Narayana has more than 20 years of experience in the field of
imaging and brain stimulation and has published extensively on the interaction of TMS with the
cortex and its effects on behavior in both humans and in non-human primates. Dr. Narayana performs
motor and language mapping using TMS patients with epilepsy and brain tumor as part of
presurgical evaluation and is working to optimize and validate clinical applications of TMS. Her research
emphasis is on understanding the neuroplasticity resulting from behavioral treatments and brain
stimulation. Specifically she examines practice and treatment induced alterations in the limb and
speech motor systems. Dr. Narayana is also investigating the neurophysiological underpinnings of
TMS adjuvancy in enhancing skill learning. Dr. Narayana is an associate professor in the department
of Pediatrics, division of pediatric neurology, and the department of Anatomy and Neurobiology at
University of Tennessee Health Science Center in Memphis, TN. She received her bachelor of medicine
and surgery from Bangalore University, India and doctorate degree in Radiation Biology from the
University of Iowa. Shalini came to UTHSC from the University of Texas Health Science Center at San
Antonio where she was assistant professor in the Department of Radiology.

Diagnostic and Neuromodulatory Applications of Transcranial Magnetic Stimulation: Coming
of “Age” of a Non-invasive Brain Stimulation Modality

Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation method that was
initially developed as a non-invasive alternative to direct cortical stimulation for the purposes of
functional brain mapping. However, its neuromodulatory properties have led to several therapeutic
applications. Further, its non-invasive nature, ease of use, and excellent safety profile have especially
facilitated its application in children. This presentation will describe the basic principles of TMS and
provide examples of its novel clinical applications in evaluating motor and language functions in
children. Next, ongoing research studies examining the neurophysiology in healthy children and
pediatric stroke will be described. The behavioral and neurophysiological correlates of therapeutic
effects of TMS in epilepsy and Parkinson's Disease will be presented. Finally, the utility of TMS in
treating other neuropsychiatric disorders and future potential applications will be discussed.
Oral Presentations
Progressive Reduction in Right Ventricular Contractility in an Aging Mouse Model of Arrhythmogenic Cardiomyopathy

Emmanuel M. Camors¹, Joseph R. Alef¹, Ryan D. Sullivan², Enkhsaikhan Purevjav¹, Jeffrey A. Towbin¹
Heart Institute, Department of Pediatrics, University of Tennessee Health Science Center¹; Department of Comparative Medicine, University of Tennessee Health Science Center²
Email Address: ecamors@uthsc.edu

Background: Arrhythmogenic cardiomyopathies (ACM) are inherited disorders that originate from desmosomal gene mutations. By promoting the loss of cell-cell adhesion, the replacement of cardiomyocytes by fat and fibrosis infiltration, and the mistargeting of key action potential (AP) ion channels, ACM mutations cause a reduction in right ventricular (RV) contractility and enhance the risks of life-threatening arrhythmias. Hypothesis: ACM mutations impair myocyte contractility via altered intracellular Ca²⁺ (Ca²⁺i) response to AP.

Methods: We studied our new knock-in mouse model of ACM created after a reported familial case of truncated plakophilin-2 protein (PKP2-L404fsX5).

Results: Echocardiography and electrocardiogram recordings of PKP2 heterozygous mice (PKP2+/-) revealed, respectively, a reduction in RV contractility that progressed with aging, and an increased susceptibility to ventricular arrhythmias. Isolated RV myocytes from PKP2+/- hearts responded to external pacing by an age-dependent decreased in contractility, while their Ca²⁺i transients remained constant, suggesting the uncoupling of Ca²⁺i and contractile sarcomeres. In contrast, aging LV myocytes exhibited normal Ca²⁺i transients and contractile properties.

Conclusions: These data show that mice expressing the human PKP2 mutation L404fsX5 reproduce the hallmarks of ACM revealing that progressive RV dysfunction proceeds from reduction in myocyte contractility, which is likely due to impaired sarcomere function.

Funding/Grant Support: Le Bonheur Junior Faculty Grant 2016-2017, and 2016 Annual Bea Gerber Award

Improving documentation of menstrual history in patients at risk for PCOS, with QI in an academic pediatric continuity clinic

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Hypothesis: Implementing QI methods will improve menstrual history documentation

Background: PCOS presents in 6-10% of women. Identifying these patients improves treatment of obesity, acne, hirsutism, and pre-diabetes. To diagnose these patients, one must identify irregular menses persisting >2 years past-menarche. Our aim was to improve documentation in order to better identify patients at risk for PCOS.

Methods: We reviewed 30 charts for baseline data and found poor documentation of menstrual history. The Model for Improvement guided our PDSA cycles. Over 4 months we added a Menstrual History section to the clinic note templates; presented the project at noon conference; gave a noon conference on PCOS; and created and distributed an algorithm in clinic detailing how to approach patients with PCOS. We collected data showing how the documentation changed following these interventions.

Results: Documentation of whether patient was post-menarche improved by 50%; documentation of age of menarche, LMP, regularity of menses, pads used, and length of menses improved by 650%, 382%, 234%, 1167%, and 283%, respectively. Documentation of PCOS in the differential improved by 400%, and documentation of presence or absence of hirsutism and acne improved by 757% and 650%, respectively.

Conclusions: These results demonstrate that the most dramatic improvement in menstrual history documentation occurred after modifying the clinic note templates, and this improvement has largely been sustained
MicroRNAs as Novel Biomarkers in Pediatric Severe Sepsis

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Background: There are currently no definitive molecular predictors of pediatric severe sepsis (SS). MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression and molecular pathways, including inflammation. MiRNAs are attractive biomarkers due to their stable expression in body fluids, and we have only limited knowledge about their role in pediatric SS. We hypothesized in this IRB-approved prospective study that miRNAs are aberrantly expressed in SS-positive pediatric patients.

Methods: Eight miRNAs (miR-15a, miR-16, miR-25a, miR-133a, miR-122, miR-146a, miR-150, miR-223) were identified as potential biomarkers based on literature review. Through our electronic medical record-integrated SS screening algorithm, eASSIST, we recruited patients ages 6-17 at risk for SS who did not meet exclusion criteria. Plasma (3 mL) was obtained from these patients within 24 hours of the alert. MiRNA was extracted and quantified by real-time PCR was performed. Results: Among 29 patient samples thus far, SS-positive patients (n=20) had large increases in mean expression of miR-146a, miR-223, miR-150, miR-133a and miR-16, compared to SS-negative patients (n=9).

Conclusions: Selected miRNAs are increased in SS-positive pediatric patients. Further studies are necessary to validate these miRNAs as novel biomarkers and to assess their correlation with clinical outcomes. Additionally, mechanistic studies of these miRNAs are essential to understand their role in the pathogenesis of SS.

Funding/Grant Support: LeBonheur Department of Pediatrics Fellow Grant

Systems Genetics Analysis of Arrhythmogenic Cardiomyopathy Induced by p.S368L Mutation in Transmembrane Protein 43

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Hypothesis: We hypothesized that p.S368L-TMEM43 mutation causes AVC5 via disturbed Ppar, major regulators of adipogenesis. We studied AVC5 gene networks using systems genetics.

Method: Knock-in Tmem43S358L mice were created. BXD mice derived from C57BL/6J and DBA/2J crosses were used as genetic reference population (GRP). Cardiac transcriptomics analysis using Affymetrix Mouse Gene 2.0ST arrays were performed in Tmem43S358L and 40 BXD strains. Genetic correlation, functional enrichment, and co-expression network were performed using GeneNetwork and Webgestalt online tools.

Results: We found highly significant broad variability expression levels of Tmem43 hearts among the BXD strains. A co-expression Tmem43-gene network consisting of 25 highly associated genes was created. In this network, Ppargc1a and Jup are highly significantly connected with Tmem43 and each other (r>0.5, p<0.00075). A significant negative correlation (p<0.01) between Tmem43 expression and heart mass and heart rate was noted. Significant downregulation of Ppargc1a and Pparg (p<0.0001) that significantly related with decreased Tmem43 expression in RV was found in Tmem43S358L mice hearts compared to WT.

Conclusion: We conclude that Tmem43 is essential for normal cardiac function. Tmem43-S358L mutation disrupts Ppargc1a and Pparg expression, leading to AVC5.

Funding/Grant Support: Enkhsaikhan Purevjav
Selected Short Talk Abstracts

TMS Localization of Eloquent Cortices in Patient with Rasmussen Encephalitis? A Case Report

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Introduction: Preoperative functional mapping with magnetoencephalography (MEG) and functional MRI (fMRI) in pediatric patients requires sedation, which precludes localization of expressive language areas. Recently, transcranial magnetic stimulation (TMS) has been demonstrated to be both an effective and safe modality for preoperative localization of eloquent cortices.

Hypothesis: Since TMS does not require the patient to remain still during the study we propose that language mapping can be successfully completed with TMS in young children. Here we report one such case where TMS was effectively used to localize eloquent cortices.

Methods: A 4 year 11 month-old female patient presented with a history of epilepsy partialis continua of the right arm and face and right-sided weakness. MEG, fMRI and TMS were attempted for localizing and lateralizing language function.

Results: MRI and clinical exam confirmed the diagnosis of Rasmussen’s encephalitis involving left frontal lobe and insula. Language mapping with MRI and MEG were unsuccessful. TMS identified bilateral representation of expressive language. Postoperatively, the patient was seizure free at discharge and her speech remained intact, reinforcing TMS findings.

Conclusion: This patient serves as an example of the importance and effectiveness of utilizing TMS for mapping language function in pediatric patients.

Funding/Grant Support: Le Bonheur neuroscience Institute

17,20S(OH)2pD Suppresses Total Collagen Synthesis in the Bleomycin Model of Fibrosis

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Objectives: This study was designed to determine whether 17,20S(OH)2pD: (i) suppresses total collagen synthesis; (ii) modulates mediators of the TGF-β1 pathway; and (iii) alters inflammatory cytokines using the BLM model of fibrosis.

Methods: Fibrosis was induced into the skin of female C57BL/6 mice subcutaneously with BLM. Simultaneously, mice received daily oral gavage with either vehicle (propylene glycol) or 17,20S(OH)2pD at either 5μg/kg, 15μg/kg, or 30μg/kg for 21 days, after which the injected skin was biopsied and analyzed for total collagen, mRNA expression of MMP-13, BMP-7, MCP-1, and dermal thickness. Serum was analyzed for cytokines using the BIO-Plex Pro Mouse Cytokine 23-Plex panel.

Results: 17,20S(OH)2pD [similar to 1,25(OH)2D3] suppressed total collagen production in the BLM fibrosis model. Biopsies of skin after injection with BLM showed a significant decrease in dermal thickness after treatment with all three doses of 17,20S(OH)2pD. 17,20S(OH)2pD [similar to 1,25(OH)2D3] also decreased MMP-1, BMP-7, MCP-1 in-vivo. 17,20S(OH)2pD suppressed production of: IL-12p70, IL-13, IL-17, IL-1β, IL-2, IL-6, and TNF-α. 17,20S(OH)2pD increased production of IL-12p40.

Conclusion: 17,20S(OH)2pD modulates mediators of fibrosis in-vivo, suppresses total collagen production and dermal thickness, wherein a balance will favor reduction of fibrosis and may offer a new therapeutic approach for treating SSC and other disorders of fibrosis.

Funding: The National Scleroderma Foundation, Arthritis Foundation, Department of Veterans Affairs Merit Review Grant, and Department of Veterans Affairs Program Project Grant, and R21AR066505 grant for National Institute of Health, NIAMS
Poster Presentations:

Faculty

[Image of a faculty member standing in front of a poster presentation]

Localizing Severe Behavior in Tuberous Sclerosis Complex using DTI: A Potential Therapeutic Opportunity

- **Background**
  - Developmental abnormalities in Tuberous Sclerosis Complex (TSC)
  - Diffusion Tensor Imaging (DTI) for structural connectivity
  
- **Objective**
  - To explore the use of DTI to correlate behavioral changes
  - Correlation between structural connectivity and behavioral changes

- **Methods**
  - DTI analysis of subjects with TSC
  - Correlation between DTI and behavioral changes

- **Results**
  - Increased DTI in areas associated with behavioral changes
  - Correlation between DTI and behavioral scores

- **Conclusions**
  - Potential therapeutic targets for behavioral intervention
  - Addressing the underlying structural connectivity issues

- **References**
  - Literature on TSC and DTI applications
**Amplitude-Integrated Electroencephalogram (aEEG) in Newborns Exposed to Prenatal Marijuana (THC)**

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**Background:** Marijuana (THC) is the most common illicit substance of abuse among pregnant women. Based on recent reports, infants with in-utero THC exposure may be at risk for cognitive impairments or behavioral problems. At this time no neonatal screening is available to distinguish at risk infants. Amplitude-Integrated EEG that measures background activity, sleep-wake cycle and seizure activity has been used as a predictor of neurodevelopmental outcome in many neonatal disorders.

**Objective:** We hypothesize that aEEG can be used as a tool to distinguish neonates with in-utero marijuana exposure who might be at risk for poor neurodevelopmental outcome.

**Design/Methods:** This is a retrospective (January 2013 through December 2016) study. Prenatal exposure to drugs was based on maternal admission to drug use, positive urine or umbilical drug screening in neonates. Data from 11 newborns with exposure to prenatal THC and 11 gestational age matched control (negative drug screen) neonates who had aEEG monitoring during the first 24 h of life were collected. These neonates had bedside single-channel aEEG monitoring as part of EEG for neonates prenatally exposed to drugs study using Olympic CFM 6000 monitor (Natus Medical Inc., San Carlos, CA).

**Results:** During study period the overall rate of MSA was 40.2/1000 live births with THC use being the most common (27/1000 live births). Among all MSA (n=623), 59% (n=366) had evidence of THC use during pregnancy. Among THC users, 41% (n=257) were positive for only THC, 5% (n=30) THC with opioids and 13% (n=79) THC with other illicit substances. The mean gestational age and birth weight in these 22 infants were 36.4±3 weeks and 2622±741 gm, respectively. In THC groups, an abnormal aEEG was observed in 55% (6/11) with either broad variability or absent sleep/wake cycle, compared to 18% (2/11) in control group.

**Conclusions:** Marijuana (THC) has become a common substance of abuse among pregnant women. Our findings in this small group of THC-exposed infants are concerning. It warrants the initiation of study with larger number of THC-exposed neonates with neurodevelopmental follow up. We speculate aEEG may be used as an adjunct measure of assessment for at risk infants exposed to THC.

**Funding/Grant Support:** Division of Neonatology

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**Evaluation of the impact of antimicrobial stewardship guidelines on necrotizing enterocolitis outcomes**

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Necrotizing enterocolitis (NEC) is a commonly encountered gastrointestinal condition in neonates, with a high mortality rate of 20-30%. 25% of survivors develop long-term sequelae with a substantial portion needing surgical intervention and medical management. The optimal antimicrobial management of NEC is unclear and challenging. The aim of this study was to evaluate the impact of the antimicrobial stewardship guidelines implemented promoting the use of shorter duration, more narrow spectrum therapy, vancomycin and gentamicin, compared to vancomycin and meropenem, on clinical outcomes associated with NEC. We hypothesize that use of antimicrobial agents with a more narrow-spectrum of activity and defined duration of use has resulted in similar clinical outcomes. After implementation of guidelines for NEC, a lower incidence of fungal sepsis, late onset bacterial sepsis and stricture development was observed. There was a reduction in mean antibiotic duration observed in NEC stage 3 indicating the implementation of guidelines recommending a defined duration of therapy may have resulted in a reduction in overall antibiotic days. Although no difference was noted in mortality, sample size and overall low mortality rates may have limited ability to detect a difference. Use of more narrow spectrum antimicrobial therapy and defined duration of therapy appears to have generated outcomes that are no worse when compared to previous standard of care.
Case profiles of noninvasive functional brain imaging as an alternatives to cortical stimulation mapping

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Cortical stimulation mapping (CSM) has long been considered the gold-standard for localizing the eloquent cortex in the presurgical evaluation of patients with epilepsy and brain tumors. In recent years, however, the introduction of non-invasive brain mapping techniques—namely functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG) and transcranial magnetic stimulation (TMS)—has presented an alternative to CSM for identifying the central sulcus and specifying the motor cortex, as well as approximating expressive and receptive language cortices, particularly in cases where invasive monitoring may not be practical. Moreover, the efficacy of the non-invasive methods as a viable substitute for CSM has been attested to in a number of comparison studies in clinical cohorts. We present two case studies which demonstrate the utility of the non-invasive functional mapping techniques during presurgical evaluation. First, we report an instance of preserved sensorimotor function within an area frontal polymicrogyria coincident with the ictal onset zone in a female with intractable symptomatic partial epilepsy; second, we present findings of from a female patient where language-specific foci localized to the boundary of a left temporal lobe ganglioglioma. In both cases, the outcome of the non-invasive techniques was deemed to be of sufficient utility to defer surgery and seek alternative treatment measures, in order to preserve function and reduce morbidity.

Utilizing Magnetoencephalography in Infantile Spasms to Assess Outcome

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Adrenocorticotropic hormone (ACTH) is the standard of care for treatment of Infantile Spasms (IS), with its efficacy assessed by both the resolution of epileptic spasms (ES) and of hypsarrhythmia (HYP) on electroencephalogram (EEG). However, little is known about how the treatment responses of IS to ACTH may improve the neurophysiological profile of IS compared to nonresponders. Our goal is to evaluate resting background brain activity using magnetoencephalography (MEG) both before and after treatment with ACTH in order to use MEG as a marker for ACTH response and as a predictor for the development of other seizure types after IS. Simultaneous MEG/EEG data was obtained for three subjects at the time of diagnosis of IS and after 2 weeks of. While visual inspection of the MEG spectral profiles in each individual patient revealed some variability in patterns of background activity, consistent differences across patients were present most notably in the delta and theta bands, pre- and post- treatment. Though preliminary, the present findings provide some insights into short-term effects of ACTH on resting cortical rhythms in children with IS. Applying this approach to a larger sample of patients may further highlight the utility of MEG as a marker for ACTH response, with implications for neurodevelopment, in particular as it relates to integration of sensorimotor processes and higher cognitive functions, which may be adversely effected in IS.

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The Biorepository and Integrative Genomics (BIG) Initiative

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Background: Precision Medicine leverages personalized genomic testing and genomic research results to advance more precise cost-effective clinical care and preventative health planning. Most pediatric hospitals do not have the appropriate infrastructure for effective precision medicine. The BIG Initiative was launched in 2015 to help develop precision medicine platforms at Le Bonheur (LBCH) to facilitate genomics research at UTHSC.

Methods: We developed institutional infrastructure to seek informed participation from all LBCH pediatric patients for isolation, storage and analysis of their genomic DNA for UTHSC research. Informatics systems were established for HIPAA-compliant participant sample and data management, linkage to de-identified clinical information, and on-line sample and data requests. A governance structure that includes advisory boards for operations, ethics, and community outreach guides and reviews BIG planning and activities.

Results: Approximately 150 participants per week are currently enrolled into BIG from the hospital’s in-patient and out-patient center populations. Through 2017, BIG enrolled >7,000 participants and archived >3,800 individual DNA samples. Creation of a genomics facility is currently under way. No requests for DNA samples have been received thus far from UTHSC faculty.

Conclusions: The BIG Initiative has begun to develop institutional infrastructure for precision medicine that can serve as the basis for clinical platforms at LBCH.

Funding/Grant Support: Assisi Foundation of Memphis Children’s Foundation Research Institute Le Bonheur Children’s Hospital Memphis Research Consortium Urban Child Institute UT Institute for Research, Innovation, Synergy and Health Equity UT Department of Pediatrics UT Research Foundation

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Predicting seizure outcome of vagus nerve stimulation using magnetoencephalography (MEG)

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Background: Vagus nerve stimulation (VNS) is a low-risk surgical option for patients with epilepsy. However, VNS is effective in reducing seizure in 50% of patients (responder), and it is still impossible to predict which patients respond to VNS treatment. We, for the first time, used pre-VNS magnetoencephalography (MEG) and predicted VNS seizure outcome.

Methods: 89 controls (including 62 twins) and 23 patients with epilepsy (14 responders and 9 non-responders) were included. MEG data from patients were collected before implantation of VNS. The phase-locking value between MEG sensors was used to calculate three graph measures, i.e., modularity, transitivity, and characteristic path length. We investigated whether the graph measures have a biological basis by establishing them as heritable traits. The values of graph measures were statistically compared in three groups (controls, responders, and non-responders). Finally, the graph measures were used as input features of a machine learning approach to classify three groups.

Results: Our results revealed that: 1) the graph measures were significantly heritable (h2 > 0.57, P < 0.006); 2) the modularity and transitivity were significantly different in three groups (P < 0.05); 3) we achieved an accuracy > 80% in classifying non-responders from responders and controls.

Conclusions: MEG-based graph measures are reliable biomarkers and can be used to accurately predict the outcome of VNS treatment.

Funding/Grant Support: Children’s Foundation Research Institute
**F07**

**A Mouse Model of Tsc Renal Cystic Disease**

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**BACKGROUND**

Tuberous sclerosis complex (TSC) renal cystic disease affects over 500,000 patients worldwide. There are five patterns of TSC-associated renal cystic disease, and they are the macrocystic diseases including polycystic, cortical cystic, multicystic, focal cystic diseases, and microcystic disease. The cysts can have a simple single cellular layer, have a multiply layer or even papillary histology. Although the basic histology has been described, the cystogenic mechanism in TSC is poorly understood.

**METHODS**

To begin to better understand this cystic disease process, we created a mouse model of TSC renal cystic disease by targeting principle cells by using aquaporin 2-driven Cre recombinase expression to delete the floxed Tsc2 gene. Double immunofluorescence labeling was performed to determine the identity of cyst epithelium.

**RESULTS**

In this cell specific model, we identify the similar histological characteristics of the renal cystic epithelium as occurs in the human. Interestingly, the cyst epithelium was predominantly comprised of intercalated cells as determined by intense and uniform apical expression of H+-ATPase in both mouse and human. There was no expression of AQP-2, NHE-3, NBC-e1, NCC or Na-K-ATPase, indicating the absence of principal, proximal tubule, distal convoluted and thick ascending limb epithelial cells in the cyst wall. The cysts in human and mouse also exhibited a significant decrease in cilia expression.

**CONCLUSION**

We have developed a mouse model that resembles human TSC-associated renal cystic disease. This TSC renal cystic disease in both the mouse model and human exhibits significant histopathological differences compared to other renal cystic diseases. These differences raise the possibility that therapies like V2 receptor antagonism may not have similar efficacy.

**Funding/Grant Support:** Department of Defense

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**F08**

**The incidence of delayed splenic bleeding in pediatric blunt trauma**

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**BACKGROUND:** One of the concerns associated with nonoperative management of splenic injury in children has been delayed splenic bleed (DSB) after a period of hemostasis. This study evaluates the incidence of DSB from a multicenter 3-year prospective study of blunt splenic injuries (BSI).

**METHODS:** A 3-year prospective study was done to evaluate nonoperative management of pediatric (≤18 years) BSI presenting to one of 10 pediatric trauma centers. Patients were tracked at 14 and 60 days. Descriptive statistics were used to summarize patient and injury characteristics.

**RESULTS:** During the study period, 508 children presented with BSI. Median age was 11.6 [IQR: 7.0, 14.8]; median splenic injury grade was 3 [IQR: 2, 4]. Nonoperative management was successful in 466 (92%) with 18 (3.5%) patients undergoing splenectomy at the index admission, all within 3h of injury. No patient developed a delayed splenic bleed. At least one follow-up visit was available for 372 (73%) patients.

**CONCLUSION:** A prior single institution study suggested that the incidence of DSB was 0.33%. Based on our results, we believe that the rate may be less than 0.2%.
F09  Early fortification of feeds to optimize nutritional outcomes in VLBW infants

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Background: Enhancing nutrition and growth of our Very Low Birth Weight (VLBW) babies will help improve postnatal growth and outcomes.

Rationale: We identified from previous years data review, that we had a high rate of growth failure in our VLBW babies.

Aim: Decrease our postnatal growth failure at discharge by 25% by December 2017, as measured by change in Z-score (Δ Z) from birth to discharge.

Interventions: 1. Start early Total Parenteral Nutrition (TPN) and improve adherence to our revised standardized feeding guidelines 2. Stop checking feed residuals; 3. Audit and collect anthropometric data on regular basis; 4. Increase human milk use.

Measurements: Performance measures included time to starting TPN, initiation of enteral feeds, days to achieve full target calorie, protein goals. Z-scores at birth and discharge were compared to see effects of our interventions. Growth parameters and anthropometric measurements for our VLBW infants were collected from Jan 2016 – Dec. 2017 as performance measures.

Results: We saw an improvement in our Δ Z scores for weight from -1.46 in Jan. 2016 to -0.82 in Sept 2017. The head circumference Δ Z scores also improved from -1.04 to -0.18. Our babies also showed improved linear growth. Our growth failure at 36 weeks is now 40%, compared to previous at 55%.

Discussion: As a multidisciplinary team, we have been successful in improving growth of our VLBW infants. Our future goals are to monitor long term developmental follow.

F10  Siglec-E protects mice against E coli-induced sepsis by enhancing bacterial clearance

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Siglec-E protects mice against E coli-induced sepsis by enhancing bacterial clearance Guo-Yun Chen, Yin Wu
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Background: Sepsis is one of the leading causes of death worldwide. Despite the availability of the treatment for sepsis with antibiotic therapy, the case-fatality rate is still higher (more than 30%). Therefore, there is a critical need for targeted and effective sepsis therapy to reduce mortality from this disease. Siglec-E is a member of immunoglobulin superfamily and binds to sialic acid. Previously, we found that Siglec-E deficient mice decreases resistance to E. coli challenge (Wu et al, J Immunol, 2016) Methods We take genetic, cellular and molecular approaches to examine the role of Siglec-E during infection Results: We found that Siglec-E-deficient mice were more susceptible to E. coli-induced sepsis than their wild-type littermates. Bacterial clearance was markedly impaired in Siglec-E-deficient mice following E. coli infection. Consistently, Siglec-E-deficient mice displayed a defect in bactericidal activity in response to bacterial challenges with severely impaired reactive oxygen species (ROS) production Conclusion: Siglec-E plays an important role in the development of E. coli-induced sepsis and targeted manipulation of Siglec-E could lead to a new therapeutic opportunity for patients with sepsis.

Funding/Grant Support: This study is supported by grants from National Institutes of Health (AI105727) and UTHSC startup funding.
Concordance between TMS and fMRI derived lateralization and localization of language in clinical pediatric cohorts

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Neuroradiated TMS (nTMS) has emerged as a robust mapping tool that is safe and well-tolerated, but has yet to be validated in children. This study examined the concordance between TMS and validated fMRI derived hemispheric dominance (HD) and localization of language specific cortices (LSC) in a clinical pediatric cohort. Due to inherent difference between TMS and fMRI, we hypothesized that a gross measure such as HD would be more concordant and the specific LSC mapped by the two methods would be less so.

Children (n=86) underwent language mapping with fMRI using covert object naming (ONM) and verb generation (VGM) and then with 5 Hz nTMS using overt object naming (ONT). A laterality index (LI) calculated for both modalities was used to determine HD and activations in LSC were determined individually, and sensitivity and specificity were determined. HD found by VGM (82% left [L], 12% right [R], 6% bi [B]) was consistent with previous reports, but ONM overestimated the incidence of R-HD (23%). ONT results were less consistent (62% L, 15% R, 23% B) with higher incidence of B-HD. Compared to ONM, ONT had 75% sensitivity and 67% specificity. In LSC, ONM identified more LSC in right hemisphere than VGM. Accuracy of ONT across LSC was 73%, with high specificity and greater left hemisphere reliability. This study is the first to demonstrate good concordance of TMS and fMRI derived HD. However, that LSC showed only moderate concordance indicating a need for further TMS optimization.

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Waitlist Management in a Pediatric Obesity Treatment Program: Implementation of an Orientation Session

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Primary care providers (PCPs) are encouraged to refer severe cases of pediatric obesity for multidisciplinary weight management; the volume of referrals results in waitlists. Unmanaged pediatric obesity predicts greater morbidity and longer waits lead to decreased motivation and nonattendance. This study evaluates adding an orientation session to address a waitlist >2000 patients at the Healthy Lifestyle Clinic (HLC), a pediatric weight management program in the Mid-South. In November 2016, a group-based orientation (50 families/session) providing information about the structure and expectations of the clinic as well as education on healthy lifestyle recommendations. Since October 2014, PCPs have referred 2874 patients to the HLC with ~30 new referrals per month. Since November 2016, 1674 patients from the waitlist have been contacted with 580 scheduling an orientation session. Of the 532 scheduled for an orientation that has occurred, 188 (35%) attended and demonstrated improved knowledge of recommendations (p<0.001). Of the 188 orientation participants, 174 (93%) scheduled an HLC appointment. For the 117 with appointments have occurred, 93 (79.5%) completed the visit. Currently, only 444 patients (15% of the waitlist) still need first contact, and 588 patients have not reached. Orientation has been an effective and efficient way to triage patient referrals while maximizing attendance in the limited clinic slots for patients and families demonstrating interest and motivation.

Funding/Grant Support: Urban Child Institute; Children’s Foundation Research Institute
**F13**  
**Association of FADS1 genotype with metabolic health, body composition, and dietary intake in children with obesity**  
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Modern Western Diets (MWD) are obesogenic and inflammation-promoting, which may be particularly harmful in those with a FADS1 variant (SNP rs174537, higher prevalence of homozygosity for the risk allele in African Americans [AA]), which encodes a fatty acid desaturase that favors metabolism of polyunsaturated fatty acids into arachidonic acid, a known contributor to chronic inflammation. Both diet and genetic risk may be important factors in the obesity-related health complications that disproportionately affect AA. The purpose of this study was to evaluate FADS1 variants and associations with metabolic health, body composition, and dietary intake in children with severe obesity. Genotyping of FADS1 was performed on 91 children with obesity (12.0±3.7 yr; 58% female; 53% AA, 38% Caucasian; BMI z-score 2.54±0.45). Genotype frequencies were 70% GG, 23% GT, and 7% TT, with higher percentage GG in AA vs. Caucasian (81% vs. 62%, p<0.05). There were no significant differences in clinical components of metabolic syndrome, body composition or fat distribution by FADS1 genotype (p's>0.2). GG was associated with trend for higher kcal/kg (p=0.13) and saturated fat/kg (p=0.10) intake (adjusted for age, sex, race). FADS1 GG genotype may predispose to consumption of and unfavorable metabolism of MWD. Our pilot cohort may have been underpowered to observe differences by genotype in metabolic health parameters warranting further studies in a larger sample.  
**Funding/Grant Support:** UTHSC Office of Research Support (CORNETT Award); UCI; CFRI

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**F14**  
**G-protein-Coupled Bile Acid Receptor Attenuates Liver Injury in a Murine Model of Acute Parenteral Nutrition**  
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Parenteral Nutrition (PN) provides essential caloric support in patients unable to feed but is associated with hepatic injury. PN disrupts host-microbial interactions, including bile acid enterohepatic circulation. We hypothesized that G-protein coupled bile acid receptor deficiency (TGR5/-/-) would influence hepatic injury in a murine model of acute PN. TGR5/-/- and wild type (WT) received PN for 96 hours. PN elevated serum triglycerides, resistin, PAI-1 and fatty acid synthesis genes in both genotypes. However, compared with WT, PN-treated TGR5/-/- had significantly larger liver weights with histologically enlarged hepatocytes, but without altered triglycerides or water %. Accordingly, TGR5/-/- displayed elevated hepatic IL-6 expression and serum AST and ALT levels compared with WT. TGR5/-/- with PN also displayed lower bile acid synthesis genes, including Cyp7A1, Cyp8B1, Cyp7B1, and BAT, compared to WT. We then examined serum bile acid composition, discovering PN elevated total conjugated primary bile acid levels (TCA, TCDCA, TmMCA, and TaMCA) compared with chow. However, compared with WT on PN, TGR5/-/- on PN displayed higher levels of unconjugated primary bile acids (CDCA, aMCA) and secondary bile acids (oMCA and DCA). Predictive 16S metagenomics suggested altered microbial enzymes including BSH and 7alpha hydroxylase. We conclude TGR5 is protective during PN, potentially through the regulation of bile metabolism and roles in microbiota-bile acid interactions.  
**Funding/Grant Support:** CFRI; UTHSC Ped recruitment fund
F15 Colonization of Minimal Altered Schaedler Flora Induces Specific Bile Acid Changes and Rapid Adipose Gain on High Fat Diet

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Germ-free (GF) animals are resistant to obesity, supporting a microbial role in metabolism. Host-microbial interactions are complex, and elucidating precise mechanisms remains challenging. Defined microbial communities allow focused investigation of host-microbial interactions. Here we colonized GF animals with 4 species, including 2 Lactobacillus, 1 Parabacteriodetes, and 1 Mucisperillium species, herein called mASF, for 7 weeks on chow or high fat diet (HFD) compared with GF controls. GF animals remained lean on HFD. In contrast, mASF animals on HFD rapidly gained weight characterized by larger white adipose tissue depots despite equal caloric intake and lower or unchanged enterohormones. Total serum bile acids (BA) were unchanged, but BA composition showed mASF reduced TbMCA, while elevating TCA and bMCA. Ileum expression of FXR and bile acid transporters, OST, ABST, and iBABP, were decreased by mASF and HFD. Concurrently, ileal FGF15 expression, which stimulates peripheral energy expenditure and insulin sensitivity, was significantly elevated in GF following HFD, but attenuated in mASF. Consistently, adipose tissue PPAR, a target of FGF15, was lower in mASF on HFD, while fatty acid transporters, CD36, FABP6, and ATGL, were unaltered. In conclusion, we demonstrate a mASF can promote obesity under HFD, which may involve microbial augmentation of bile acids that alter gut signals of adipose tissue energy regulation.

Funding/Grant Support: CFRI; UTHSC Pediatric recruitment fund

F16 Detection of clinically-relevant severe sepsis in children using a real-time EMR algorithm

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Healthcare providers continue to face challenges in recognition of pediatric severe sepsis. We previously modified current pediatric severe sepsis criteria in a real-time EMR-integrated algorithm to screen inpatient adolescents (ages 13-17) and found that patients with severe sepsis could be identified with high accuracy (sensitivity – 90.4%, specificity – 96.2%). We have termed these modifications “clinically-relevant severe sepsis”. Here, we utilize clinically-relevant severe sepsis criteria to screen pediatric inpatients ages 6-12. We hypothesize that the accuracy of this screening mechanism would be high in children ages 6-12.

We conducted a single-center, prospective diagnostics study, which was IRB-approved prior to initiation of study procedures. All children between ages 6-12 admitted to Le Bonheur Children's Hospital from July 2016 - July 2017 were screened using a real-time EMR algorithm for severe sepsis designed according to current pediatric severe sepsis guidelines and modified by 48-hour exclusion of the following patients: trauma/polytrauma, status asthmaticus, status epilepticus, and post-operative patients. Patients identified as positive for severe sepsis using the algorithm were verified by a trained critical care nurse and a critical care-trained physician.

Of 3299 patients screened for 136 unique admissions, 291 alerts identified potential severe sepsis cases. Of these, 131 alerts were identified as true positive and 160 alerts as false positive. Multiple alerts for unique admissions were included in this analysis. No false negatives were reported, leading to a sensitivity of 100% and a specificity of 94.9%. Positive predictive value was decreased (0.45), however, the negative predictive value was 1.

Clinically-relevant severe sepsis in children ages 6-12 (modified severe sepsis criteria) can be detected using an EMR-based algorithm with a high sensitivity. Yet, larger more robust prospective studies are warranted to clearly define clinically-relevant severe sepsis in all age groups and to apply this definition in our EMR-based, real-time screening algorithm.

Funding/Grant Support: Le Bonheur Foundation
F17  Text data in EMRs has a lot to say about surgery outcome

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Background: Surgical risk prediction models are mainly based on structured data in EMRs. Unstructured text data such as nursing, physician, and social work notes are underutilized because they are complex and require manual review.

Hypothesis: Automated analysis of preoperative text notes in EMR can be used in predicting surgical outcomes.

Data: We studied 6552 inpatient surgeries from 1/2014 to 5/2017 at LeBonheur Children’s Hospital. There were 71 deaths (cases) within 30 days of surgery; the remaining 6481 patients served as controls.

Methods: Risk of death within 30 days of surgery was derived using the Quire Predictive Modeling (QPM) approach on preoperative text notes. QPM uses a proprietary algorithm based on vector-space modeling of text to identify similarities between cases and controls. Text-based risk scores were then used in logistic regression to identify children at high risk of postsurgical death.

Results: Over 770,000 text notes from 6552 surgeries were analyzed to obtain risk scores. Model training was done on 4860 controls and 49 cases (death) and tested on 1621 controls and 22 cases. The risk scores obtained in test data were significantly (p<0.001) higher for cases (0.86; 0.83-0.89) compared to controls (0.45; 0.43-0.47). The logistic regression model predicted death after surgery in the test data with specificity of 76% and sensitivity of 77%.

Conclusions: Machine learning of text data in EMR may improve prediction of surgical outcomes.

F18  Does Obesity Affect the Diagnosis and Treatment of Appendicitis in Children? Analysis of 1973 Patients

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Purpose: Previous studies have reported increased complexity in diagnosis and treatment of obese children with appendicitis. Our aim was to assess differences in work up and outcomes in obese (O) patients as compared to non-obese (NO) patients.

Methods: After IRB approval, suspected appendicitis patients over 4 years were reviewed. Patient characteristics, symptoms, ED work up, length of stay and outcomes were recorded. CDC definition of obesity (BMI > 95%ile) was used. O patients were compared to NO patients using Chi-Square test and Wilcoxon Rank Sum Test.

Results: 2645 patients were identified - 661 excluded for missing height, 11 for implausible BMI %iles. 1611 NO and 362 O patients were analyzed. There was a higher proportion of Latino patients (16.9% vs 11%, p<0.01) and more frequent CT use (19.9% vs 12.9%, p<0.01) in the O group. The groups were similar in gender breakdown, age, symptom length, frequency of ultrasound use, frequency of false negatives and false positives, time in ED, and proportion of final diagnoses. For patients admitted for appendicitis, O patients had slightly longer hospitalizations (median hours=67.7 vs 49.5, p<0.01) but similar frequency of postoperative complications.

Conclusion: Obese patients with suspected appendicitis may require more frequent CT use for diagnosis and longer hospital stays for treatment of appendicitis, but otherwise have similar ED course, likelihood of accurate diagnosis and similar outcomes as non-obese patients.
Novel Myeloid Slc2a1-deficient Murine Model Revealed Macrophage Activation and Metabolic Phenotype is Fueled by GLUT1

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Macrophages (MΦs) are metabolically flexible; a classic response to proinflammatory activation is increased flux through glycolysis with a downregulation of oxidative metabolism, while alternative activation is primarily oxidative. Is targeting glucose metabolism is a viable approach to limit proinflammatory MΦ activation? We created a novel murine model of myeloid-specific glucose transporter GLUT1 (Slc2a1) deletion ("M-/-"). MΦs from Slc2a1M-/- mice failed to uptake glucose and demonstrated reduced glycolysis and PPP and oxidative metabolism. Slc2a1M-/- BMDM displayed an inflammatory phenotype demonstrated by a reduction of the classically-activated proinflammatory markers, metabolites, and measures of oxidative stress. Whereas metabolites indicative of alternative activation such as ornithine and polyamines were greatly in the absence of GLUT1. Obese Slc2a1M-/- mice exhibited only minor protection from hyperglycemia with no significant GLUT1-mediated differences in other physiologic measures. Despite expression of CD206 (M2-like) in adipose tissue MΦs of lean Slc2a1M-/- mice, the results herein demonstrate that myeloid-specific GLUT1 is not a critical mediator in the development of obesity-associated metabolic dysregulation. Ldlr-/- mice lacking myeloid GLUT1 developed unstable lesions compared to control Ldlr-/- mice. Defective phagocytic capacity in Slc2a1M-/- MΦs may have contributed to unstable atheroma formation. MΦs in obesity or atherosclerosis are less dependent on glucose.
Weight loss normalizes obesity-associated claudin-low breast cancer: role of Mammary fat pad immune cell infiltrates

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Obesity contributes to triple negative breast cancer (TNBC). TNBC, which is comprised of the basal-like (BBC) and claudin-low (CLBC) intrinsic subtypes, currently has no targeted therapies. We previously reported that obesity-induced elevation of hepatocyte growth factor (HGF)/cMET pathway and accelerated tumor development in the C3(1)-Tag mouse model of spontaneous BBC- which was reversed by weight loss. To differentiate tumor-intrinsic from microenvironmental mechanisms, we injected a C3(1)-Tag-derived TNBC cell line into lean, obese, and formerly obese (FOb) mice. Tumor growth in FOb mice paralleled that in lean mice, with tumors in obese mice progressing at the fastest rate. Tumor volume at sacrifice was significantly greater in obese animals compared to lean and FOb animals. Diets did not alter tumor leukocyte infiltration as measured by flow cytometry. However, the mammary fat pad (MFP) demonstrated a significant obesity-associated influx of arginase-1+ macrophages compared to lean and FOb. Obesity also significantly increased MFP HGF, CCL2, IL1beta, EMR1, and IL6. Mast cells are increased in obesity and associated with advanced tumors; mast cell activation was also increased by 2-fold in obese compared to lean and FOb mice. Critically, using human samples from the Normal Breast Study, we demonstrated an overweight- and obesity-associated increase in a mast cell gene signature that was depressed in normal weight subjects (N=249).
Hemoglobin Levels in First Postnatal Week are Associated with Neonatal Acute Kidney Injury: Results from AWAKEN Study

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Background: The co-existence of anemia and acute kidney injury (AKI) is very common. In addition to being one of the main complications of AKI, anemia has been shown to be independently associated with AKI in adults. There is no published data on the association of hemoglobin (Hb) levels and AKI in neonates.

Objective: To address the association between the minimum and maximum Hb levels in the first week of life and the development of AKI

Methods: The Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates (AWAKEN) study included 2162 neonates admitted to the NICU at 24 institutions (4 countries) from 01/14-03/14. Inclusion criteria: intravenous fluids for 48 hrs. Exclusion criteria: congenital heart disease repair at <7 days of life, lethal anomaly or death at 48 hrs. For this analysis, we excluded 159 infants who had no Hb levels documented during the first week of life and 140 infants who did not have at least 2 serum creatinines or at least one day of urine output quantification during the first week of life. We defined AKI as an increase in serum creatinine of 0.3 mg/dL or more or 50% or more from the previous lowest value, or a urinary output of less than 1 mL/kg/hr on postnatal days 2-7. Analysis was done for the entire cohort and for 3 stratified groups (<29 weeks, 29-36 weeks and > 36 weeks gestational age (GA)

Results: Of the 1891 newborns, 551 (29%) had at least one episode of AKI. The mean minimum Hb was significantly lower in AKI group versus the no-AKI group (P < 0.0001) for the entire cohort, as well as for each of the 3 stratified groups. Mean maximum Hb was significantly higher in the no-AKI group versus the AKI group (P < 0.0001) for the entire cohort and for the <29 GA group, but not for the 29-36 weeks, or the >36 weeks group

Conclusion(s): The AWAKEN study shows for the first time that Hb levels in the first week of life are associated with AKI and could be a modifiable risk factor for AKI in neonates. It is possible that this association is due to illness severity or other factors in these newborns. It is also possible that higher Hb levels, blood transfusion, the use of erythropoietin, delayed cord clamping may have a protective effect against AKI in this group. This data opens the possibility that efforts to improve higher Hb levels in at-risk neonates may be protective against AKI. Further analysis of this and other observational cohorts are underway.

Abstract withdrawn
Poster Presentations:
Clinical Fellows
Early Observations of Combined Use of Arginine Vasopressin and Calcium Chloride in Pediatric Heart Failure

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Background: Low cardiac output (CO) states necessitate use of inotropes and vasopressors. Along with catecholamines, Arginine vasopressin (AVP) and Calcium Chloride (CaCl) are being used as adjunctive pharmacologic drugs. We report the observed hemodynamic effects of combined use of AVP and CaCl infusions in low CO states in pediatric heart failure.

Hypothesis: Combined use of AVP and CaCl may augment CO, improve end-organ perfusion and decrease the need for catecholamines in pediatric heart failure.

Results: 89 patients (0-18 yrs.) admitted with low CO states received combined AVP and CaCl infusions. Median age (yrs.) and weight (kg) were 0.88 (0-3.75) & 6.62 (3.5-13.7) respectively. Congenital heart disease was present in 65% (58/89) patients. Median duration (days) of AVP and CaCl was 2 (1-3) & 3 (2-6) respectively. Using Wilcoxon signed rank test and Bonferroni correction, post hoc comparison showed that at 8 hours post infusion, all SBP and DBP results and urine output (UO) were greater than those 1 hour prior to infusion. HR decreased between 1 hour prior to infusion and 8 hours post. Within first 8 hours, median UO increased from 6ml/hour to 20 ml/hr. Median pediatric logarithmic organ dysfunction scores on days 4-7 post infusion were lowered compared to day 1 and median inotropic scores on days 2-7 post infusion were lower compared to day 1.

Conclusion: Combined use of AVP and CaCl may improve surrogates of CO and prevent organ dysfunction in pediatric heart failure.

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Tick Paralysis: A Treatable Disease Not To Be Missed

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Tick paralysis is a rare condition which can be treated easily but if undiagnosed can lead to significant morbidity and mortality. It is prevalent in certain areas especially in North America and Australia. It is characterized by acute onset symmetric lower extremity weakness and if not diagnosed early the weakness involves the upper extremities, cranial nerves, respiratory musculature leading to respiratory failure requiring mechanical ventilation. The clinical picture is often confused with other causes of acute onset paralysis eg., Guillain-Barre syndrome, the Miller Fisher variant, leading to unnecessary investigations and interventions complicating the clinical picture. The condition can be easily diagnosed by careful history and physical examination. Tick removal will lead to early and complete recovery of the condition. It is very important for the clinicians to be aware of this condition so that it can be recognized early to avoid unnecessary and expensive investigations, interventions, morbidity and mortality. We report a severe case of Tick paralysis admitted in our academic center who had complete recovery after the identification of tick.
**CF03** Reducing Time to Insulin in Management of Diabetes Ketoacidosis- A QI Project

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**Background:** Diabetic ketoacidosis (DKA) is defined as a blood pH level of less than 7.30, a bicarbonate level of less than 16 meq/dL, the presence of hyperglycemia and the presence of ketonuria. Delays in the care of the acidic patient with diabetes in the emergency department (ED) can lead to longer time to acidosis resolution, increased length of stay (LOS) and associated costs.

**Objective:** Our team developed a quality improvement project aimed at decreasing the time to insulin (time from patient registration to administration of insulin) to less than 120 minutes in the pediatric ED by June 2018.

**Methods:** Our hospital has a standardized protocol for all children presenting in DKA, including a computerized order set (power plan) to streamline orders. Our team mapped the current path of care through the ED for a patient in DKA. We identified key drivers causing delays to insulin administration and chose to focus our first plan-do-study-act cycle on decreasing the time it takes to obtain insulin from central pharmacy.

**Results:** In the ED, time to insulin was collected monthly. Mean time to insulin during the baseline period (January 2017 to August 2017) was 144.6 minutes. During this same timeframe, mean ED LOS was 204.6 minutes. Current times from September to November are similar.

**Conclusions:** We hypothesize that conversion from centralized insulin bag assembly to local assembly in ED will improve our time to insulin and help to reduce ED LOS.

**CF04** Recurrent Candidal Esophagitis Associated with Dexamethasone Use in a Cardiac Transplant Patient

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Perioperative use of dexamethasone has been shown to decrease pain, nausea, and vomiting without increasing infections in immunocompetent patients. There are no guidelines for its use in cardiac transplant patients who are at risk for fungal esophagitis given the immunosuppression required to prevent allograft rejection. The antifungal treatment can alter the metabolism of calcineurin inhibitors leading to significant morbidity. We present a case of Candida esophagitis following routine surveillance cardiac catheterization in a cardiac transplant patient. A 15-year-old female one year status post cardiac transplantation presented with dysphagia, weight loss, and chest pain beginning two days after routine surveillance cardiac catheterization. She underwent esophagogastroduodenoscopy (EGD) and was diagnosed with Candida esophagitis. She developed acute kidney injury necessitating continuous renal replacement after starting therapy with fluconazole, which has a known interaction with tacrolimus metabolism. She was successfully treated with complete resolution of symptoms. She presented similarly two years post-transplant, again after surveillance cardiac catheterization where she received dexamethasone. EGD confirmed Candida esophagitis. With both episodes, she had had no recent antibiotic use, inhaled corticosteroid use, or oral candidiasis. Studies should be done to assess the safety of perioperative dexamethasone in post cardiac transplant patients.
Maternal antibiotic exposure enhances weight gain in offspring

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**Background:** Early life antibiotic exposure may be associated with increased risk of obesity later in life. We tested if antibiotic exposure of pregnant mice is associated with weight gain in newborn mice.

**Design/Methods:** We randomized pregnant mice to one of three dosing regimens of penicillin or water on gestational day 18. Neonatal mice were exposed to 10 or 15 days duration of continued maternal antibiotics. We performed 16S rRNA gene sequencing on fecal contents. Differentially abundant microbial taxa will be used to predict differential metabolic pathways. Serum triglycerides and ileal metabolic genes will also be measured. Results: 16 pregnant mice gave birth to 39 mice, 10 were control mice and 29 were exposed to maternal antibiotic treatment. At 15 days, mice exposed to antibiotics gained 10.8%, 20.0%, and 39.8% more weight than controls (total body weight (mean ± SEM): 6.65 ± 0.59 g, 7.37 ± 0.07 g, 7.98 ± 0.23 g, 9.30 ± 0.52 g, respectively, ANOVA, P = 0.004). Antibiotic exposure and duration were associated with increased weight (ANOVA, P = 0.04), as was each factor independently (ANOVA, duration P > 0.001, exposure P = 0.03).

**Conclusions:** Maternal antibiotic exposure promotes excessive weight gain in neonatal mice.

**Funding/Grant Support:** Department of Pediatrics, UTHSC

A randomized trial of IV Acetaminophen versus for treatment of PDA in VLBW infants

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**Background:** Indomethacin (IND) has been the drug of choice for treatment of hemodynamically significant patent ductus arteriosus (hsPDA). Recent evidence suggests acetaminophen (APAP) may be as effective as indomethacin in closing hsPDA in VLBWs with potentially fewer side effects.

**Objective:** To compare the rate of successful treatment of hsPDA by echocardiogram (ECHO) after use of IV APAP or IV IND in VLBW infants.

**Design/Methods:** The study was a multi-center, randomized control trial. Cardiologist interpreting ECHO was blinded to randomization of treatment. Infants were included if PDA treatment was indicated within the first 21 days after birth with birth weight ≤1500g, gestational age of <32 weeks, and hsPDA on echocardiogram. hsPDA was defined as left to right ductal flow across PDA and 2 of the 3 following findings: ductal size ≥1.5mm, left atrium to aortic root ratio ≥1.5, or reversal of diastolic flow in the abdominal aorta. Eligible infants were randomized to treatment with either IV APAP or IV IND. A repeat ECHO was done within 7 days of initiation of PDA treatment to assess for successful treatment as defined by predetermined criteria. Other demographic and outcome data was collected and compared.

**Results:** Of 65 eligible infants, 30 were enrolled. Fourteen infants were randomized to APAP and 16 to IND. One (7%) PDA in the APAP group closed compared to 9 (56%) in the IND group closed (p=0.008). Six infants (43%) in the APAP and 1 infant (6%) in IND group required transcatheter closure of PDA (p=0.026). Table 1 shows baseline characteristic of enrolled patients. Table 2 shows comparison of ECHO findings. All other outcomes were comparable between the two groups except post-treatment serum creatinine (APAP 0.7±0.3, IND 0.9±0.2 mg/dl, p 0.01).

**Conclusions:** IND was more effective than APAP for treatment of hsPDAs by ECHO criteria without increased side effects. More infants in the APAP group needed transcatheter closure. The small sample size may be a limiting factor in this randomized trial.
Assessing for pulmonary hypertension and viral load patterns in mechanically ventilated infants with RSV

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Introduction: Infants with RSV bronchiolitis can develop pulmonary hypertension (PHTN). Higher viral loads (VL) have been associated with mechanical ventilation (MV) and ICU admission, however, it is unknown whether high VL is associated with the development of PTHN. Methods: This prospective observational study of pediatric patients aged < 2 years, with RSV bronchiolitis, who required MV, was conducted at the PICU at Le Bonheur from 2015. Serial VL measurements were obtained from tracheal aspirates (TA) and nasal washings (NW) and compared to echocardiogram results obtained within the first 72hrs. Results: Patients (n= 33 patients, 106 ± 117.8 days old; gestational age 35.5 ± 3.1 weeks at birth) were recruited. Ten subjects had evidence of mild-moderate PHTN which was associated with lower birth weight (2090.3 g vs 2877.5 g, p = 0.005). No significant differences were found in viral load patterns between those with PHTN on day 1 through day 5. Conclusion: In mechanically ventilated infants with severe RSV bronchiolitis, mild-moderate PHTN was identified in 30% of the subjects, and was associated with lower birthweight. Higher viral loads were not associated with the development of PTHN in this study.

Funding/Grant Support: Division and Departmental Grant Award

Pilot study using telemedicine in the PICU with a hand held device during the transfer of critically ill pediatric patients

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Introduction: Telemedicine medicine in the ICU (tele-ICU) provides a modality to improve communication between providers and improve assessments of critically ill children in challenging situations who present to small rural hospitals with limited resources. We report a pilot-effort trialing video telemedicine using hand held devices to assist critically ill pediatric transfers from these types of facilities to our PICU.

Purpose: To assess the practicality of using a tele-ICU communication tool during the transfer process for critically ill pediatric patients. Methods: A HIPPA compliant video-communication platform, Vidyo was trialed during several transfer encounters. Practicality and barriers to usage were based on feedback by providers involved in patient care. Results: 7 successful transfer were completed with Vidyo, 1 using FaceTime in a patient who had cardiac arrest, 3 encounters were not successful due to technical issues. Barriers to usage included legal concerns, additional time to set up, and connectivity issues.

Conclusion: We found the Vidyo to be a practical modality for improving pediatric transfers to the PICU. This benefit will likely show the most impact in real-time for rural facilities awaiting the arrival of the pediatric transfer team as experience with critically ill children is limited. Further investigations are needed to better understand its utilization.
**CF09**

**Excess Serum Uric Acid Is Associated With Metabolic Syndrome In Obese Adolescent Patients**

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**Background/Aims:** Obesity is a significant cause of morbidity in adolescents. Excess serum uric acid (SUA) has been strongly associated with metabolic syndrome (MS) and some of its components among adults. This association has not yet been proven in obese adolescent patients. We evaluated the relationship among SUA and markers of insulin resistance (IR) and inflammation in obese adolescents with and without MS.

**Methods:** Body mass index standard deviation score (BMI SDS), blood pressure (BP), body composition, fasting lipids, glucose, high sensitivity CRP (hs-CRP), SUA, HbA1c, insulin and the homeostatic model assessment for insulin resistance (HOMA-IR) were evaluated in 67 obese adolescents (55.2% female). Results: Hyperuricemia (SUA >357 umol/L) was present in 41.8% of the cohort without ethnic/gender differences except for higher fat mass (FM) in females. Patients with hyperuricemia had higher waist circumference, FM, systolic blood pressure (SBP), A1C, insulin and HOMA-IR (p<0.05). SUA was positively correlated with FM, SBP, HOMA-IR and HbA1c (p<0.05). Patients with MS (32.8% of cohort) showed significantly higher FM, BP, SUA, insulin, HOMA-IR, and TG:HDL-c ratio than non-MS subgroup (p<0.05). FM was correlated with HOMA-IR and hsCRP (p<0.01).

**Conclusions:** Hyperuricemia is strongly associated with FM and indices of MS. SUA correlates with MS comorbidities such as higher BP and IR. Future studies are needed to investigate the mechanism leading to MS and its sequela.

**CF10**

**Frequency of organic pathology in patients with premature adrenarche**

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**Background:** Premature adrenarche (PA) is secretion of adrenal androgens before the age of 8 years in girls and 9 years in boys, manifesting as body odor, axillary and pubic hair growth. PA is a benign variant in most patients. However, a small number have organic pathology, such as non-classical congenital adrenal hyperplasia (NC-CAH) and adrenal tumors. We hypothesize the prevalence of organic pathologies in our population is lower than reported in other studies.

**Methods:** One hundred charts were reviewed of patients with signs of PA seen in an endocrine clinic between 11/2014 and 11/2017. BMI SD score (BMI SDS), Tanner stage for pubic hair, and androgen levels were obtained. Statistical significance using T-tests was defined as a p-value <0.05. Results: Of the 100 patients, one patient was found to have NC-CAH: a Caucasian female with premature adrenarche at age 6. This patient had a higher 17-OH-progesterone level for Tanner stage. Males with PA have increased BMI SDS (p-value of 0.008 and 0.01 respectively) compared to females. Females presented at a younger age with signs of PA (p=0.002). Conclusions: Our PA cohort is unique in its composition with the majority being AA and 1/3rd being males. Prevalence of NC-CAH in our cohort of PA is 1% with no adrenal tumors. Our patient with NC-CAH had no history/exam finding differentiating her from other patients. Lower incidence of pathology in our patients suggests a need to develop cost effective algorithms based on clinical grounds.
**CF11**

**Lowe Syndrome and Marfanoid Habitus from Novel Xq25q26.1 Deletion**

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This case highlights a patient who was found at birth to be macrocephalic with significant hypotonia with bilateral congenital cataracts, long-tapered fingers and low set ears. A microarray showed a large 1.93 MB copy loss of Xq25q26.1 including ORCL with several other genes, which are described to cause other pathology including ACTRT1, SMARCA1, OCRL, APLN, XPNPEP2, SASH3 and ZDHHC9. Lowe syndrome is an X-linked condition which involves ocular defects such as infantile glaucoma, intellectual disability, hypotonia and renal disease. Here, we present a case of a patient with Lowe syndrome, which was secondary to a significant gene deletion. The proband presented with hypotonia and poor feeding at birth. He was profoundly macrocephalic with congenital cataracts, low set ears and severe hypotonia. He also had long hands with tapered fingers, which are not classically seen in Lowe syndrome. Maternal testing indicated this deletion is likely de novo. His severe presentation is likely secondary to other genes deletions. The ZDHHC9 gene has been shown in another case report to present with a marfanoid habitus and mental retardation. Consequently, we believe that his presentation will likely be compounded by the combined effect of the two gene deletions. We recommend considering a similar deletion in patients who are seen with a marfanoid habitus. This case was unique given that it is Lowe syndrome secondary to a gene deletion that also involved other genes which may alter his course.

**CF12**

**A Randomized Trial on the Impact of Continuous vs Bolus Feeding on Anthropometric Measurements in ≤1250g Birth Weight Infants**

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Continuous and bolus feeding methods are equally acceptable ways to feed premature infants. Animal data shows higher tissue protein synthesis in bolus feeds. We hypothesized that in infant ≤1250g birth weight, bolus feeds would be associated with improved growth over continuous feeds. Methods: Infants were randomized to either feeding method. Anthropometric measurements were collected weekly. Results: 70 infants were enrolled. There were no differences in baseline characteristics. There were no differences in days to reach full feeds, age at discharge, or incidence of various morbidities. All measurements showed a drop in z-score at 1500g weight followed by a substantial growth catch up from that point onwards. Both groups behaved similarly in weight and length. However, continuously fed infants had a head circumference growth rate of 0.75±0.21 cm/week compared to 0.62±0.21 cm/week in the bolus group, p=0.02. By discharge, this difference abated. Conclusions: In infants born ≤ 1250g, the continuous feeding method was associated with less head growth delay than bolus feeding in the period from birth to 1500g weight; however, by discharge there were no differences in anthropometric measurements between the two groups.
Impact and utility of bacterial colonization and surveillance cultures in pediatric hematopoietic transplant patients

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Background: Evidence has highlighted the impact of colonization with multidrug resistant (MDR) bacteria in hematopoietic transplant (HCT) patients. In adults, MDR colonization prior to transplant has been associated with blood stream infections (BSI), graft versus host disease (GVHD) and increased mortality. We describe complications associated with MDR colonization identified by rectal surveillance cultures (RSC) in pediatric HCT patients.

Methods: Data were retrospectively analyzed from patients undergoing allogeneic and autologous HCT at our institution who had RSC obtained between 2014-2017. RSC and blood culture results were reviewed at the time of transplant and throughout the transplant course. Results: 165 patients (with 1095 RSC) were included. 48 patients (29%) were colonized with MDR bacteria. Of those, 21 were colonized prior to transplant, and 27 developed colonization in the course of transplant. 20 patients (12%) developed a MDR BSI (28 episodes). 20 of the episodes occurred in patients colonized with MDR bacteria (OR: 7.618 [2.7, 21.3]). The positive and negative predictive values of RSC for this purpose were determined to be 51.3 and 87.9%, respectively.

Conclusion: These data demonstrate an increased risk of MDR BSI in colonized HCT patients. While low prevalence of MDR infections in this cohort limits the positive predictive value of RSC, knowledge of colonization status of HCT patients may impact decisions regarding empiric antibiotics during transplant.

Teenager with a noisy breathing in sleep - A rare case of Catathrenia

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Introduction: Catathrenia is a sleep-disordered breathing pattern characterized as expiratory groaning or moaning during sleep. It is a rare disorder which is often confused with stridor, sleep related laryngospasm and sleep talking. Current literature, includes reports primarily in adults with onset in young adulthood. We report a case of polysomnography (PSG) video documented catathrenia in a 13-year-old male.

Report of case: 13-year-old male with ADHD presented to our sleep clinic with complaints of loud breathing and nightly snoring. He had a consistent sleep/wake schedule and average sleep duration of 8-9 hrs. His mother reported restless sleep and moaning associated with long pauses. He denied excessive daytime sleepiness. His review of symptoms was unremarkable. Physical examination was notable for BMI-24, 2+ tonsillar size and Mallampati score of II. Epworth sleepiness score was 4/24. Video PSG was performed which resulted in mild overall disruption of the sleep architecture with 91.0% sleep efficiency. Sleep onset latency and REM sleep latency were normal at 11.5 and 95.5 minutes respectively. The total arousal index was elevated at 12.5/hour. N1, N2 and N3 sleep were 11.9%, 54.4%, 14.4% respectively and REM sleep was 19.4%. The total Apnea-Hypopnea Index (AHI) was 8.3 with obstructive AHI of 2.7 and central apnea index of 5.58. Frequent expiratory moaning was associated with central apneas, ranging from 13-17 sec in duration, without desaturations. It occurred equally in both NREM and REM sleep. Furthermore, the prolonged expiration was preceded by arousals. Brain MRI showed no significant abnormality. Hence, he was diagnosed with catathrenia.

Conclusion: Catathrenia, although classified in ICSD-3 under sleep related breathing disorder, still remains underrecognized in a pediatric age group. Without the video the diagnosis can easily be missed or mistakenly recognized as central sleep apnea. PSG video monitoring therefore remains essential for establishing a diagnosis and guiding treatment.
CF15  Resolution of Late Gadolinium Enhancement in a Series of Pediatric Patients with Clinical Myocarditis

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Background: Pediatric patients with acute myocarditis may present with nonspecific signs and symptoms including chest pain and troponin elevation. Cardiac magnetic resonance imaging (CMR) can show areas of myocardial necrosis or fibrosis by late gadolinium enhancement (LGE) in a significant portion of these patients. The evolution or progression of LGE in clinically resolved myocarditis in children is not well studied.

Methods: This was a retrospective case series at a tertiary care children’s hospital of 10 patients with clinical diagnosis of myocarditis based on history and laboratory data with LGE positive CMR who underwent repeat CMR for reevaluation following convalescence from hospitalization for myocarditis. The presence of LGE, interval LGE changes, left ventricle (LV) volumes, LV mass, and left atrial volumes were recorded. Results: 7 patients with LGE positive CMR (85% male, median age 15 year old, interquartile range 8-17) underwent repeat studies to reevaluate LGE burden. Median time to follow-up CMR was 11 months (IQR 3.5-15). 4 patients (57%) demonstrated either interval improvement or complete resolution of LGE (Table). During the median follow-up period of 25 months (IQR 23-26), no adverse clinical events of mortality, significant arrhythmia, or cardiac transplantation were reported.

Conclusions: CMR is useful in surveillance for changes in LGE burden in pediatric patients with history of myocarditis who have clinical resolution of illness. Clinical outcome in a small series of patients with LGE positive myocarditis appears favorable following hospital discharge.

CF16  Late Gadolinium Enhancement Pattern in a Child with Arrhythmogenic Right Ventricular Cardiomyopathy and Myocarditis: Role of Serial CMR

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A 10-year-old male with a family history of sudden cardiac death was diagnosed with arrhythmogenic right ventricular cardiomyopathy (ARVC). Cardiovascular magnetic resonance (CMR) fulfilled minor criteria for ARVC with RV free wall dyskinesia, and showed full thickness late gadolinium enhancement (LGE) in the left ventricular (LV) inferolateral mid-ventricular wall. Workup was positive for a frameshift mutation in DSG2 (desmoglein-2). One year after diagnosis, he presented with severe substernal chest pain. Troponin level was elevated with a peak troponin of 33 ng/mL during hospitalization. He had vomiting the previous week after exposure to a sick family member, but no syncope or palpitations. Physical exam was unremarkable, and a respiratory viral serologic panel was negative. Transthoracic echocardiogram was essentially normal. Due to concern for myocarditis in a patient with known ARVC a CMR was obtained. Contrast-enhanced CMR showed mild LV dilation and mildly reduced biventricular systolic function. T2 weighted imaging showed myocardial edema in the LV septum and continued full thickness LGE in the inferolateral mid-ventricular wall. However, he also demonstrated new findings of subepicardial LGE of the anterolateral LV wall. CMR was repeated at 1 month and showed low normal LV systolic function and no significant change in the LGE pattern. However, CMR 6 months later showed improvement in the subepicardial LGE within the anterolateral LV wall. Clinical presentation was consistent with an episode of acute myocarditis in a patient with ARVC. Serial CMR proved useful as the new epicardial LGE, T2 abnormality, and improvement in LGE pattern supported a second acquired process rather than worsening of his cardiomyopathy.
**CF17**

**Delirium Screening and Unplanned Extubations**

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Pediatric delirium has been under recognized and undertreated due to a lack of screening tools and limited clinician familiarity with the disease. Unplanned extubations (UE) are a significant patient harm event in the Pediatric Intensive Care Unit (PICU) that should be minimized. We hypothesize that there was a correlation between delirium and UE. From 8/1/16 to 7/30/17 we screened and followed all patients admitted to the Le Bonheur PICU who are between 6 months and 18 years of age, require invasive mechanical ventilation, can see, and who are developmentally over 6 months to assess for signs of delirium. In addition, we have been collecting data on drug usage, adverse events, and other patient-care factors. All data was recorded and tracked in REDCap for further analysis. There were 20 UEs in the group which met criteria for delirium screening. 19 of these patients had signs of agitated delirium in the 24 hours preceding extubation (p=0.0001). 9 patients (45%) required reintubation within 24 hours, all of whom had signs of delirium. All of the patients with delirium had recently received benzodiazepines or were on a benzodiazepine infusion. The incidence of UE in delirious patients highlights the importance of recognition and management of this condition. The presence of delirium provides an early warning sign for possible unplanned extubation, and through further work to reduce delirium in pediatric ventilated patients one could hope to reduce unplanned extubations.

**Funding/Grant Support:** Le Bonheur Fellow’s Research Grant

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**CF18**

**Nasal cytokines in pediatric allogeneic hematopoietic cell transplant recipients with respiratory viral infections**

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Respiratory viruses may lead to prolonged viral shedding and lower respiratory tract infection (LRTI) in HCT recipients. Nasal cytokine expression as it relates to symptoms in pediatric HCT recipients has not been studied. We hypothesize that lower pro-inflammatory cytokine expression heralds lower respiratory tract involvement and prolonged viral shedding in HCT recipients. We identified patients with banked nasal wash samples who had a respiratory viral infection after HCT at St. Jude. Allogeneic recipients were included for cytokine measurement if they had nasal wash(es) with a positive viral test and at least one nasal wash with a negative viral test. A Milliplex 41-plex panel was used to obtain cytokine concentrations. From 19 patients with 24 infections that met the above criteria, 97 samples were tested on the cytokine panel. 11 (46%) infections developed within 100 days following HCT, 6 (25%) infections occurred between 100 and 365 days after HCT, 5 (21%) occurred more than 365 days after HCT, and 2 (8%) developed immediately prior to HCT. 12 (50%) infections were associated with prolonged viral shedding and 8 (33%) were associated with LRTI. Statistical analyses on nasal cytokine concentrations currently in progress include longitudinal cytokine expression analyses in patients with prolonged shedding, a comparison between URTI and LRTI, and analysis by time after transplant.

**Funding/Grant Support:** ALSAC/St. Jude
**CF19**  
Sleeping in sitting position in patients with Down Syndrome: Parasomnia or Adaptive response to Obstructive Sleep Apnea?

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**Background:** Parental report of odd sleeping postures in Down’s syndrome is common. Often, parents report children with Down’s syndrome are "sleeping sitting and leaning forward". The prevalence of ‘sleeping while sitting and leaning forward’ posture is not unknown in Down’s syndrome. In spite of parental concern and report of this behavior there is very little literature to support this association and its role in the sleep patterns of patients with Down’s syndrome.

**Case report:** A 4 year old child with Down’s syndrome presented with excessive snoring and gasping at night to the clinic. On examination, tonsils were not noted as patient had a previous adenotonsillectomy. The snoring and night time behaviors had persisted in spite of the attempted surgical treatment for OSA with adenotonsillectomy. Due to persistent night time behaviors and snoring patient was referred for a polysomnogram. An overnight polysomnogram study was done with various EEG channels, video monitoring, nasal pressure transducer and thermistor. Patient was noted to have persistent severe OSA with an Apnea Hypopnea Index of 10.7 events/hour with a nadir desaturation of 87 percent. At multiple times during the sleep study patient was noted to sitting while the EEG leads indicated patient to be asleep. This overnight study confirmed the presence of severe OSA and presence of a possibly compensatory behavior of ‘sitting and sleeping’

**Conclusion:** Obstructive Sleep Apnea (OSA) is more common in patients with Down’s syndrome. It is not known if sleeping sitting leaning forward is a compensatory response to the high prevalence of OSA in Down’s syndrome or a parasomnia. Also, there is no explanation to the occurrence of this sleep related behavior in this patient population. We report this case to describe the occurrence of this phenomenon during sleep of patients with Down syndrome and its possible association with OSA. Further, epidemiological studies studying sleep related behaviors in patients with Down syndrome are required to delineate if this a parasomnia or a compensatory response to OSA.

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**CF20**  
Respiratory Syncytial Virus Bronchiolitis Complicated by Necrotizing Enterocolitis

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**Background:** Respiratory Syncytial Virus (RSV) bronchiolitis is generally a self-limited disease; however, hospitalized infants may develop significant complications, including gastrointestinal comorbidities. An association of necrotizing enterocolitis (NEC) with RSV illness has not been reported.

**Objective:** We report two infants with PCR(+) RSV bronchiolitis complicated with stage III NEC in this RSV season. Case Review: Two previously healthy 1-month old infants diagnosed with RSV bronchiolitis and respiratory failure developed septic ileus within 3-5 days of admission. Case 1 was a full-term infant who developed complex ascites and free air on day 14. His NEC stage IIIB was treated with partial colectomy and diverting ileostomy. Case 2 was a 34-week preterm infant who developed portal venous air on day 2, followed by complex ascites and sepsis/ARDS that required VA-ECMO for 4 days. Her NEC stage IIIA was treated non-operatively.

**Discussion:** NEC involves an interplay between inflammation, bacterial translocation, and ischemia that leads to bowel necrosis. Our cases suggest that in rare instances, NEC may develop in patients with RSV(+) bronchiolitis. We theorize that an inadequate or exaggerated inflammatory response to RSV may lead to mediator imbalance and altered intestinal blood flow. Septic ileus and/or complex ascites may represent important clinical harbingers. At-risk infants should be identified for initiation of early management.
Poster Presentations:
Residents
**R01** Inaccurate diagnosis of urinary tract infection in children leads to unnecessary antibiotic use

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**BACKGROUND:** Urinary tract infection (UTI) is a common infection in children. Optimal diagnosis is paramount to appropriate antibiotic use. We hypothesized that UTI in children is over diagnosed and sought to determine factors related to over diagnosis.

**METHODS** Children 0-18 years of age, admitted with a diagnosis of uncomplicated, community-acquired UTI from 2013 to 2015 were included. Urine was collected by catheter or clean catch. We collected urinalysis, urine culture results, and antibiotic use data. We defined a UTI as >10,000 colony forming units (CFU)/mL of a pathogenic organism in a urine culture. Proportional comparisons were done using the chi-square test.

**RESULTS** 573 patients were diagnosed with a UTI and treated with at least 5 days of antibiotics; 103 (18%) did not meet the definition for UTI (<10,000 CFU/mL). 8.4% of children diagnosed with UTI had a urine culture with no bacterial growth (negative). Negative cultures occurred more frequently in patient’s > 2 years compared to those younger than 2 (16.2% vs 4.1%, p<0.001). Fever and leukocyte esterase occurred more frequently there were >10,000 CFU/mL on culture (81.1% vs 61.2% and 84.5% vs 58.2%, respectively, both p<0.001), but they also frequently present in patients with an incorrect UTI diagnosis.

**CONCLUSION** Fever at presentation or LE on urinalysis were not specific for a correct diagnosis of UTI in our patient population. Children older than 2 are more likely to be treated despite a negative urine culture.

**R02** Assessing Consenters Attitudes and Opinions of Genetic Biorepository Research in Children

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**Background:** Maximum participation in genetic biorepositories ensures broad applicability of study findings. We aimed to understand attitudes and opinions influencing participation in the Biorepository and Integrative Genomics (BIG) Initiative at Le Bonheur Children’s Hospital.

**Methods:** After families of inpatients watched a brief informational video and agreed or declined participation in the biorepository, we surveyed them about their backgrounds, prior research experience, and motivations for or against participation in BIG.

**Results:** Consenters characteristics associated with participation were: race (80% white vs 61% black, p<0.01), education level (81% with some college or more vs 64% with only high school education, p<0.01) and prior participation in research (98% with prior participation vs 68% with no participation, p=0.01). The most common reason for participation was helping the hospital (82%). The most common reasons for declining to participate were: no personal benefit to participation (57%), being unsure of the use of the sample (31%), and concern about government or law enforcement obtaining information (30%). Most (96%) survey participants reported being satisfied with the white, male physician presenting the study in the consent video.

**Conclusions:** Our results show decision-making about consent for genetic research may be socially contextualized and more often based on preconception rather than the content of the information presented.

**Funding/Grant Support:** LeBonheur Biorepository and Integrated Genomics Initiative
**R03**

**Pediatric Obesity: Clinic Follow Up Rates and Impact on BMI**

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**PURPOSE:** Pediatric obesity is a growing epidemic, with 37% of children ages 10-17 in Tennessee being overweight or obese. The purpose of our study was to track trends in BMI and clinic follow-up rates for overweight and obese children in our pediatric resident clinic.

**METHOD:** We performed a retrospective chart review assessing overweight and obese patients under 18 years of age within our pediatrics clinic. We recorded BMI percentile at initial well child checks, as well as at any additional clinic visits the patients had in the following 12 months, whether for acute visits or dedicated weight visits.

**RESULTS:** Data for 125 qualifying patients has been reviewed to date. The average initial BMI percentile was 94.73. 32% of patients had dedicated weight visits scheduled, with a show rate of 42.5%. Of the patients who showed, the average change in BMI percentile over a 12-month period was +0.33. Of the patients who scheduled a weight visit but did not show, the average change in BMI percentile was +0.27. Patients who never scheduled a dedicated weight visit but were seen in clinic for an acute visit had an average change in BMI percentile of -0.73.

**CONCLUSIONS:** Our results indicate that the majority of overweight and obese patients who attended well child checks were not scheduled for dedicated weight visits. There is not a significant difference in BMI percentile change between those who attended dedicated weight management visits compared to those who did not, and overall BMI percentile trended up despite these visits. These results indicate a need to reevaluate the general pediatrician’s approach to weight management.

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**R04**

**The Modified Epworth Sleepiness Scale Predicts Hypersomnia but not Obstructive Sleep Apnea in a Pediatric Population**

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**INTRODUCTION:** The Epworth Sleepiness Scale is a validated questionnaire used to assess daytime sleepiness in adults. The Modified Epworth Sleepiness Scale (mESS) is used in children. Our study aims to assess the utility of the mESS in identifying obstructive sleep apnea (OSA) and hypersomnia in children.

**METHODS:** We performed a retrospective chart review of patients who attended our pediatric sleep clinic in 2015 and 2016 who completed both a mESS and Polysomnography (PSG), with or without Mean Sleep Latency Test. Data points included scores on questions within the mESS, total mESS score, body-mass index (BMI), Apnea-Hypopnea Index (AHI), and mean sleep latency (MSL).

**RESULTS:** 158 patients were included. Total mESS scores significantly correlated with MSL (r= -.302, p<.005), whereas total mESS did not significantly correlate with AHI, but did approach statistical significance (r = -.155, p = .052). Cronbach’s alpha score for the 8-question mESS was α = .796. This value decreased when any of the questions was removed. BMI was able to predict 12% of variance in AHI, but reached to 14% when BMI was combined with mESS score.

**CONCLUSION:** The mESS is a reliable screening tool for hypersomnia, but has limited use in isolation for predicting OSA in children. This may be due to the difference in phenotypic manifestations of sleep-disordered breathing in children compared to adults. The mESS is most reliable when its integrity is maintained. Only when it is considered in conjunction with BMI does it add predictive value for pediatric OSA.
**R05**

**Development of sterile abscesses after long acting GnRH agonist leuprolide-depot injection**

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**Background:** The development of sterile abscesses in children receiving long-acting GnRH agonists is known but not well documented. Serious sterile abscess development in children receiving longer-acting depot preparations may be more common than previously anticipated.

**Cases:** 3 female patients being treated for central precocious puberty ranging from ages 22mo to 3y5mo received Lupron Depot-Ped 30 mg and each developed clinically significant abscesses. Pt1 developed extensive abscesses at two injection sites, both treated with incision and drainage. Cultures from the sites were sterile and biopsy revealed focal areas of granulomatous inflammation and fibrosis. Pt2 developed an abscess 3 weeks after her second injection and was treated symptomatically. Pt3 was initially started on Lupron Depot-Ped 7.5 mg IM monthly x3 months and developed a complex abscess after her first 30 mg Lupron Depot-Ped injection confirmed by ultrasound. Leuprolide injections were suspended in all patients.

**Conclusion:** These cases highlight significant sterile abscess after 30 mg Lupron Depot-Ped injection. Pathogenesis is not well understood, however the polymer present in the depot preparations has been frequently implicated as the inciting agent for local tissue inflammation and granulomatous response. Optimal treatment of these lesions is uncertain. Further research into the incidence of abscess development after long-acting injectables is needed.

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**R06**

**Suspending diagnostic bias: a rare cause of emesis and abdominal pain**

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A 15-year-old male presented to emergency department with one year of emesis and 20% weight loss. During initial hospitalization, he underwent esophagastroduodenoscopy (EGD), which showed esophagitis and numerous gastric and duodenal ulcerations. Fasting gastrin levels were normal, and he was discharged home with PPI and sucralfate. He had 9 admissions over the next 4 months for recurring episodes of emesis and abdominal pain. With each admission, patient displayed non-adherence to medications and tested positive for cannabinoids. His symptoms resolved within 24 hours with bowel rest and intravenous fluids. Cannabinoid hyperemesis was considered the most likely etiology. His first hospital follow-up, repeat EGD was scheduled and again showed numerous ulcerations. Repeat fasting gastrin level showed significant increase from 18 to 1667 pg/ml. Follow up abdominal CT showed two enhancing pancreatic lesions, which was confirmed by endoscopic ultrasound. He underwent surgery with excision of lymph nodes overlying pancreas and extensive exploration for other sites of malignancy. Repeat gastrin levels have remained within normal limits six months after the operation. Patient non-adherence to medications coupled with substance abuse can lead to delayed diagnosis because of availability bias. Proper counseling to encourage medication compliance is essential, and alternative diagnoses should be pursued if symptoms persist over time.
Investigating Barriers to Transition in IBD with Survey of Patient and Parent Perspectives

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Up to one quarter of patients with inflammatory bowel disease (IBD) present before 18 years of age and require transition of care from pediatric to adult gastroenterology (GI). This study hopes provides insights from both patients and caregivers, populations which may have discordant experiences during transition. After identifying the 75 patients that had transitioned from a regional, pediatric GI clinic, a phone survey was administered to patients and parents assessing disease knowledge, current clinical control, and opinions on transition. Of the 75-total contacted patient-caregiver pairs, 13 paired surveys were obtained. In addition, there were 10 from only parents and 3 from only patients for a total response rate of 39 (26%). 23(88%) patients had successfully established care at an adult GI clinic. Three patients had not established care with an adult GI provider; all of whom had public insurance. Five (31%) were able to name a side effect of their medications, however, only two (22%) of those on a biologic agent noted infectious or oncologic side effects. 2 (12%) patients and 12 (52%) parents found the transition process stressful. Patients and Parents had gaps in knowledge including medication dosing and side effects. We also found three patients who had not transitioned successfully had public insurance which could indicate limitations in availability of adult providers. Limitations to this analysis included small sample size resulting in low power to detect differences between groups and a low response rate limiting generalizability. Larger studies are needed to better identify factors predicting difficult transitions to better target interventions.

Analysis of a Series of Patients with Acute Flaccid Myelitis (AFM) Presenting to a Tertiary Care Referral Center

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OBJECTIVES: Acute Flaccid Myelitis (AFM) affects the spinal cord leading to serious flaccid neurologic sequelae. While Enterovirus D68 (EVD68) infections are commonly implicated, its overall management options are poorly described. We present the analysis of a series of children with AFM presenting to a mid-south tertiary care referral center.

METHODS: Retrospective chart review of six cases of AFM admitted from January 2016 to December 2016.

RESULTS: In our series only boys were affected; 50% were less than 6 years, with a mean age of 7.4 years. The peak incidence corresponds to CDC reports in September 2016. Clinical and/or radiographic abnormalities in the brainstem were present in 67% patients with 50% patients requiring mechanical ventilatory support. 67% patients could not ambulate at admission. A gastrostomy tube and tracheostomy was required in 33% patients. MRI abnormalities were predominantly noted in the cervical spinal cord in 83% patients. Peripheral nerve enhancement was determined in 33% patients. CSF pleocytosis was seen in 66%. Only two patients tested positive for EVD68 by nasopharyngeal PCR. All patients had residual neurological deficits at discharge despite immunomodulatory treatments including steroid, intravenous gamma globulin, plasma exchange. Four patients required further inpatient rehabilitation.

CONCLUSIONS: This AFM case series demonstrates variable clinical presentations with brainstem and peripheral nerve involvement with residual neurological deficits. The role of immunomodulatory therapy in AFM requires further investigation. We recommend early recognition and prompt neuro-rehabilitation for patients with AFM to improve their long-term outcomes.
R09  Diagnosis and management of tetanus in an academic pediatric hospital
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Background: The annual incidence of tetanus in the United States is estimated at 0.1 per 1 million with a case-fatality rate of 13.2%. The high mortality rate in resource rich settings stresses the importance of early diagnosis and understanding the clinical course. Because tetanus is rare, and can present gradually with varied symptoms, treatment initiation and optimization may be delayed.

Case: A healthy 3-year-old female with unclear vaccination status presented to Le Bonheur Children’s Hospital with two days of abdominal pain and one day of stiffness and trismus. Physical exam showed episodic bruxism, myotonic spasms and opisthotonus, with a healed cut on the sole of one foot. Laboratory studies revealed elevated creatine kinase, anion gap metabolic acidosis, hypokalemia, and hypoglycemia. While tetanus specific therapy was initiated within 12 hours of admission, final diagnosis and treatment optimization were slowed by clinical uncertainty due to episodic symptoms and lack of clear exposure and vaccine history. Her hospital course included intubation, tracheostomy, autonomic instability, intussusception, and spastic symptoms lasting more than 60 days. She required a long antispasmodic wean complicated by delirium. She was discharged after 76 days with tracheostomy in place, and no residual neurologic deficits.

Conclusion: This case highlights the importance of early recognition and treatment initiation, and potential morbidities associated with tetanus infections.

R10  Quality Improvement in Asthma Care of Pediatric Patients in the Primary Care Setting
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Background: Primary care providers are at the forefront of health maintenance, management of chronic illnesses, and patient education. The ULPS General Pediatrics Clinic has been participating in a statewide quality improvement program to improve care for asthma patients utilizing standardized guidelines and tools.

Methods: Data was collected on asthma severity, asthma action plans, asthma control test use, influenza vaccine administration rates, and follow up plans in 3 month cycles. These results were compared against previous data. Handouts for asthma control tests and types of inhaler devices were placed in exam rooms for utilization during visits, and documentation templates were developed.

Results: Asthma severity documentation improved from 82% to 100%. Asthma Control Test documentation improved from 12% to 97%. Plans for timely follow up of asthma patients improved from 60% to 100%. Administration of influenza vaccine improved from 75% to 93%. Asthma Action Plans given to families during clinic visits improved from 12% to 30%. Conclusions: The overall data shows improvement in asthma management, influenza vaccination rates, and follow up rates. Through the statewide collaborative, physicians can utilize resources and guidelines to improve the quality of patient care.
Decreasing Hospital Discharge Time for Stable Asthmatics

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**Background:** Due to asthma being one of the most common diseases of childhood in the United States, an asthma protocol was instituted in 2016 to help facilitate inpatient therapy and decrease length of hospitalization. Once a patient reaches phase 4 (P4) of this protocol, they are stable for discharge home. We found patients discharge was delayed by several hours after P4.

**AIM:** Our goal was to decrease the time from the first P4 treatment to discharge order by 50% in 6 months.

**Methods:** Several barriers were prohibiting early discharge including transportation needs, timely asthma education, and lack of communication between the respiratory therapist and physician. The team developed interventions and collected data from Cerner for patients with asthma from April 2016 through June 2017. The average hours from P4 to discharge order placed was obtained in two groups: 6am-5pm(day) and 5pm-6am(night).

**Results:** The baseline time to discharge order during the day was 10.6 hours and 12.1 hours at night. Following interventions, the average hours to discharge order were 7.76 during the day and 10.66 at night.

**Conclusions:** We found that discharging a child with asthma from the hospital involves many factors, and although our interventions showed some improvement, there are still many aspects of discharge care to be addressed.

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Lack of Disparities in Screening for Associated Anomalies in Children with Anorectal Malformations

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**INTRODUCTION:** Patients with anorectal malformations often have associated congenital anomalies and should undergo several screening exams in the first year of life. We hypothesized that racial and socioeconomic disparities exist in the screening processes for these patients.

**METHODS:** A retrospective review of patients with ARM born between 2005-2016 was performed at a quaternary care children’s hospital. Demographics including gender, race, insurance, and zip code were collected. Zip code was used as a surrogate for median income. Chart review was performed to identify anomaly type and whether VACTERL screening was performed within one year of age. Descriptive statistics and Chi square analyses were performed.

**RESULTS:** 100 patients (59% male, 68% low malformation) were identified. African-American and Caucasian subjects represented 41% and 40% of the population. Overall, 68/100 patients had at least one screening test for each of the VACTERL associations. Although some minor differences were noted (more African-Americans received skeletal survey than Caucasians, 80.5% versus 60%, p=0.00335), no pattern of systematic bias in the receipt or timing of screening was evident based on race, insurance, or income.

**CONCLUSIONS:** There do not appear to be racial or socioeconomic disparities in screening for associated anomalies in patients with ARM. However, overall gaps in screening still exist, and work must be done to appropriately screen all patients for associated anomalies.
**R13 Using Bradford’s Law of Scattering to Identify the Core Journals of Pediatric Surgery**

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**Introduction:** Bradford’s Law of Scattering defines an exponentially diminishing return when extending a search for references in journals, and can be used to identify the “core” journals in a field. The purpose of this study was to identify the core journals of Pediatric Surgery.

**Methods:** We developed bibliometrics profiles for the top academically-productive Pediatric Surgeons in the US. These profiles included number of publications, journals in which they published, identification of references and their source journals. Bradford’s Law of scattering was applied to identify the core journals of Pediatric Surgery.

**Results:** We identified n=69 Pediatric Surgeons (10±0.2 5-year h-index). These authors published 10031 articles (145±90 per surgeon) which contained 199507 references (2891±176 per surgeon). We analyzed 58310 references (top 20 journals) cited by Pediatric Surgeons. Bradford’s Law identified a single core journal for p=3-10 zones, with p=3 providing the best correlation between predicted and actual values (R²=0.9996). The core journal for Pediatric Surgery is Journal of Pediatric Surgery.

**Conclusion:** We utilized Bradford’s Law to identify the core journals of Pediatric Surgery. These core journals include the two leading Pediatric Surgery-specific journals, as well as the highest impact factor journals in Surgery (Annals of Surgery) and Medicine (NEJM). These findings can help busy Pediatric Surgeons focus their reading to stay current in a rapidly evolving field.

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**R14 Burden of Serious Bacterial Infections in Young Febrile Infants in a Mid South Children’s Hospital**

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**Background:** Various criteria have been proposed to stratify young febrile infants for risk of Serious Bacterial Infection (SBI). Only 8.5-12% of hospitalized infants have an SBI, exposing many infants to unnecessary and potentially harmful hospitalization and parenteral antibiotics.

**Hypothesis:** The use of the Rochester Criteria will allow successful identification of low risk (LR) and non-low risk (NLR) infants for SBI and earlier hospital discharge.

**Methods:** A retrospective chart review was conducted for infants aged 29-60 days admitted with an ICD-9 code of fever. Data collected included demographics, vital signs, laboratories, culture results, antibiotic use and length of stay (LOS). The Rochester Criteria was then applied to determine which infants met LR and NLR categories.

**Results:** Of the eligible 396 patients, 90 were LR and 306 NLR. Statistically significant differences were seen for median temperature (p<0.0001) and LOS (p=0.01) but not age (p=0.09) for LR and NLR infants. 50 SBI were found in 44 patients with a greater proportion seen in NLR than LR (42/44 vs 2/44, p=0.002). 286 patients without an SBI were discharged after 36 hours. Of those, 69 were LR patients who could have been discharged at 36 hours without a missed SBI.

**Conclusions:** Our overall incidence of SBI was low. The Rochester criteria successfully identified LR infants. Using this data, we feel we can safely discharge patients earlier from the hospital without fear of missing an SBI in LR patients.
**R15**

**Diffuse Miliary Rash: How One Child Became Spiderman for Halloween**

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Case Description: An 11 year-old previously healthy male presented to the emergency department with a one-day history of abdominal pain, fever and rash. He was febrile, hypotensive, tachycardic, and tachypneic. Physical exam was significant for a diffuse erythematous rash, edema of bilateral pinna, and a point tender, erythematous and edematous site near the umbilicus. Initial labs were significant for a total bilirubin of 1.3 and an elevated C-reactive protein of 59. Abdominal x-ray and ultrasound were within normal limits. He required fluid resuscitation and was admitted on intravenous antibiotics and fluids. A bacterial toxin mediated process was thought to be most likely. The rash later evolved to a diffuse miliaria, starting on the area near his umbilicus and progressing distally to his face then extremities. On day 5 of hospitalization, an eschar formed near the umbilicus. Labs revealed hemolysis. He was diagnosed with systemic loxoscelism. All medications were discontinued. He received a blood transfusion prior to discharge the next day, Halloween. He followed up closely with his pediatrician and did not require additional transfusions. Loxoscelism is caused by the bite of the recluse spider (genus Loxosceles). Systemic effects of loxoscelism are seen more often in pediatric patients. In areas endemic to *Loxosceles reclusa*, loxoscelism should be considered when local or diffuse rashes are present.

**R16**

**Is maternal magnesium sulfate administration prior to delivery an independent predictor of survival in neonates who weigh fewer than five hundred grams?**

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**Objective:** To determine if maternal magnesium sulfate administration is an independent predictor of survival in neonates whose birth weight is fewer than five hundred grams.

**Methods:** This was a retrospective cohort study of live-born singleton neonates from 2012-2015 at a quaternary referral center. The primary outcome was survival from 12 hours of life until discharge. Severe intraventricular hemorrhage (IVH, grade III-IV) was a secondary outcome. Logistic analyses were performed, and potential confounders such as maternal corticosteroid administration, gestational age, surfactant, and gender were controlled for using multivariable analysis.

**Results:** 57 deliveries were included. Birth weights ranged from 195g to 490g and gestational ages ranged from 20 to 29 weeks. The rate of survival from 12 hours until discharge was 76%. Maternal magnesium sulfate administration was associated with improved survival (OR= 22.3; 95% CI 1.9-607; p=0.023) while controlling for gender; corticosteroid and surfactant administration were removed due to collinearity with the exposure. Magnesium sulfate was not associated with severe IVH (OR= 0.20; 95% CI 0.01-2.4; p=0.21).

**Conclusions:** Maternal magnesium sulfate administration is an independent predictor of survival from 12 hours after birth until discharge with a large effect among neonates who are born weighing less than 500g. This is the first study that has found a survival benefit in the periviable period.
Unzipping of Small Diameter Stents as a Management Strategy for Neonatal Coarctation of the Aorta in a Growing Swine Model

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Background: Coarctation of the Aorta (CoA) is a congenital anomaly requiring surgery. Transcatheter small diameter stent (SDS) implant and angioplasty may be effective in relieving stenosis. SDS circumference does not adapt to vessel growth, but can be longitudinally fractured (unzipped) via angioplasty to adult vessel size. VeriFLEX (VF) and Express (EX) SDS unzipped best in in-vivo studies. This study was to determine long-term effects of SDS to treat CoA in newborn piglets with re-dilatation in adulthood.

Methods /Results: CoA was surgically created in 10 piglets (Mdn wt 2.4Kg) by poly-ethylene terephthalate band (5) or excision of aortic wall with a constricting suture (5). Catheterization of 8 surviving pigs 4wk post-op (Mdn wt 5.8Kg) demonstrated angiographic stenosis (4 ± 1.5mm) and peak systolic gradient (PSG) 34 ± 8mmHg. 4mm VF(5) and 6mm EX(3) were used to treat CoA. Re-catheterization at 26 ± 6Kg revealed re-stenosis PSG 18 ± 12mmHg and was treated by unzipping SDS with no residual gradient or complications. Acute effects of unzipping were assessed via 4 euthanized piglets. Remaining 4 were re-catheterized at 54 ± 8Kg with angioplasty or implantation of a large stent (PalmazXL) to treat residual stenosis.

Conclusion: SDS implantation is a feasible treatment of CoA in piglets and it may be safe to unzip SDS without significant vessel injury. This method may avoid surgery in critically ill neonates and allow for future re-dilatation to treat residual stenosis.
Poster Presentations:
Postdoctoral Fellows
PDF01

**VLCAD deficiency related chronic inflammation pattern is suggestive of systemic mediators**

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Very long-chain acyl-CoA dehydrogenase deficiency (VLCADD) is a life-threatening disorder of fatty acid oxidation. While energy supplementation effectively treats hypoglycemia, rhabdomyolysis and chronic inflammation persist. We theorized rhabdomyolysis susceptibility is related to maladaptive-systemic inflammation independent of energy deficiency. We correlated markers that link VLCADD and inflammation. We collected bone marrow from 10 wk old C57BL/6 and VLCAD-/- mice to create in vitro monocytes/macrophages (Mf) and dendritic cells (DCs). We then stimulated inflammation in half of the cells with lipopolysaccharide (LPS). We analyzed cytokine (CTK) profiles on spent media by Luminex assay. In LPS treated VLCAD-/- Mf, IL-12 and IL-23 were significantly elevated vs wild type (WT). Otherwise VLCAD-/- CTK levels were not notably different from WT. We also showed that in vitro inflammatory changes occur in VLCAD-/- mouse Mf and DCs distinguishing them from WT. Increased production of IL-12 and IL-23 by LPS-stimulated VLCAD-/- Mf cells as compared to WT further supports a monocyte-activation related mechanism. Other CTK changes may be explained by cell-specific production and age-dependent increases. We will test these postulates through time-course CTK measurements in mouse plasma. Chronic inflammation clearly plays a role in VLCADD and offers therapeutic targets with optimized immune modulators (e.g. infliximab) that could significantly improve patient quality of life.

**Funding/Grant Support:**


PDF02

**Contribution of Brain Cytochrome P450 1B1 in Angiotensin II-induced Hypertension in Female Mice**

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Cytochrome P4501B1 (CYP1B1) and catechol-O-methyltransferase (COMT) that sequentially metabolize 17β-Estradiol (E2) to 2-hydroxyestradiol and 2-methoxyestradiol (2-ME) are expressed in the brain. The demonstration that central E2 inhibits angiotensin (Ang) II-induced hypertension, and microglia cells produce 2-ME from E2 led us to hypothesize that 2-ME mediates the inhibitory effect of E2 on Ang II-induced hypertension in the brain of female mice. This study shows that intracerebroventricularly (ICV) administered E2 (1.5µg/2µL/every 2nd day) in ovariectomized (OVX) wild-type (Cyp1b1+/+) mice attenuated the Ang II (700 ng/kg/min, 14 days)-induced increase in mean arterial pressure (MAP) measured by radiotelemetry, but not in the mice injected with COMT siRNA (ICV, 0.4 nmol). ICV injections of 2-ME (1.5µg/2µL/every 2nd day) but not E2 attenuated the increase in MAP by Ang II in OVX Cyp1b1+/+ mice. Furthermore, in the intact Cyp1b1+/+ female mice, injections of adenovirus (Ad)-CYP1B1 shRNA but not Ad-scrambled shRNA (2µL, 1.3X1013 particles/mL), potentiated Ang II-induced increase in systolic blood pressure (SBP) measured by tail-cuff method. In the intact Cyp1b1+/-, but not OVX Cyp1b1+/+ mice reconstitution of CYP1B1 in the brain by transduction with Ad-CYP1B1-DNA (ICV, 2µL, 1.0 X 1013 particles/mL) reduced SBP. These data suggest that central effect of E2 to attenuate Ang II-induced hypertension is dependent on brain CYP1B1 and is most likely mediated via generation of 2-ME.
Resistin-Like Molecule Beta is a Necessary Mediator in Chronic Allergic Asthma

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Asthma is a syndrome of the airways with complicated pathophysiology and traditionally considered to be Th2-biased. Existing therapeutics have benefitted some asthmatics, while others remain non-responsive, thereby necessitating the development of additional novel therapeutics. Herein, we hypothesized that resistin-like molecule (RELM)-beta was necessary for epithelial wound healing in a murine model of Aspergillus-induced allergic airways disease. Hallmarks of allergic asthma including airway wall remodeling occurred in Retnlb−/− mice, albeit reduced. The number of eosinophils and macrophages in the lung infiltrate of Retnlb−/− mice decreased, while neutrophils were more abundant. Contrary to previous reports, airway wall remodeling and goblet cell metaplasia occurred in the absence of RELM-β. While IgE production was comparable to wild-type controls, Retnlb−/− mice had increased systemic IgA at homeostasis. Epithelial wound healing and expression of genes involved in this process was altered in the presence of RELM-β suggesting a role for this molecule in epithelial-mesenchymal transition in allergic airways. Our data suggest a novel function for RELM-β in fungal allergic asthma.

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Modeling pneumococcal transmission dynamics in ferrets

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The pathogen Streptococcus pneumoniae (the pneumococcus) is a significant cause of mortality and morbidity worldwide. Acquisition and subsequent nasopharyngeal colonization are essential prerequisites for invasive pneumococcal disease. However, the mechanics of pneumococcal transmission events have been poorly characterized. Established models are not robust enough to undertake genetic screens due to the small number of bacteria that both transmit and can be recovered. Ferrets have long been used to model transmission of Influenza viruses and support transmission of pneumococcus. Seasonal dynamics of pneumococcal colonization support a role of influenza in transmission of pneumococci. Therefore we hypothesize that we can utilize Influenza infected ferrets to determine pneumococcal transmission bottlenecks and factors. Using a highly saturated transposon library, we recovered sufficient bacterial libraries from directly infected and contact ferrets to determine the bottlenecks of transmission. These data were further leveraged to identify putative bacterial factors necessary for transmission of the pneumococcus, which have been confirmed by the infant mouse transmission model. Transmission of pneumococcus was highly dependent on Influenza strain used, suggesting a role of viral factors in either pneumococcal shedding or acquisition. These data represent the first genetic screen in pneumococcus identifying bacterial factors required for transmission in mammalian hosts.
PDF05  Development of a Streamlined Laser Capture Microdissection Protocol For Stromal-Associated Neural Crest-Derived Cells in the Spleen

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We have recently described a novel population of neural crest-derived cells (NCC) in the spleen. Splenic NCC display markers indicating a glial lineage and are arranged anatomically adjacent to blood vessels, pericytes and nerves, suggesting an astrocyte-like phenotype. The purpose of this study was to develop a technique to isolate these cells in purity for phenotypic analysis. We utilized Wnt1-Cre/R26R-tdTomato mice in which NCC are endogenously fluorescent. We developed a custom workflow for laser capture microdissection (LCM). We encountered numerous challenges, including fluorescence bleaching during sample preparation and dehydration steps with ethanol, successful cells adherence and extraction while using an IR capture/UV cutting protocol without dehydration, and managing a RNA integrity number (RIN>=7) high enough for downstream RNA analysis. Real-Time quantitative PCR demonstrated expression of S100b, a common marker for astrocytes from the Central Neurovascular System, to be greatly increased in LCM extracted samples of Tdtomato+ cells. This protocol will allow phenotypic characterization of splenic NCC. Taken together with our preliminary phenotypic identification, these findings point to an astrocyte-like profile for these newly discovered NCC-derived cells in the spleen.

Funding/Grant Support: APSA Foundation Scholars Award

PDF06  A Macromolecular Protein Complex of Phe508del-CFTR-NHERF2-LPA2 Regulates IL-8 Secretion in Cystic Fibrosis Airway Epithelial Cells

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Rationale: We tested whether the complex of CFTR-LPA2-NHERF2 regulates IL-8 secretion from airway epithelial cells besides inhibiting CFTR-mediated fluid secretion, thereby regulating the inflammatory response dominated by neutrophils in CF.

Methods: Human CF bronchial epithelial cells expressing Phe508del-CFTR (DF CFBE) were used as models. CFBEo-- parental cells (P-CFBE) and CFBEo--WT-CFTR (WT-CFBE) cells were used as controls.

Results: (1) LPA2 expression was elevated in DF CFBE cells. (2) DF CFBE cells exhibited a unique profile of IL-8 secretion at the basal level and in response to stimulations; DF CFBE cells secreted large amount of IL-8 in response to IL-1β stimulation. (3) Rescue of Phe508del-CFTR by using VX-809 slightly decreased the basal level of secreted IL-8 and significantly decreased the IL-1β-stimulated IL-8 secretion (11%). (4) Low temperature (28°C) rescue of Phe508del-CFTR dramatically decreased IL-8 secretion from DF CFBE cells. (5) Specific inhibitor of LPA2 decreased the basal level (44%) and IL-1β-stimulated IL-8 (~39%) secretion by DF CFBE cells.

Conclusions: The study provides the first evidence that CFTR-NHERF2-LPA2 complex also plays a role in modulating IL-8 secretion from airway epithelial cells. Antagonism of LPA2 has potential to augment CFTR function to improve the mucociliary clearance process, and to attenuate the release of IL-8, thereby inhibiting the excessive infiltration of neutrophils and the subsequent lung inflammation.

Funding/Grant Support: NIH grant R01 HL123535
PDF07  Varied Disease Phenotypes and Protein Biomarkers in Two Siblings Homozygous for F508del CFTR

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**Background:** It is known that the pulmonary disease phenotypes do not correlate well with CFTR genotypes, and that other genetic (e.g. modifier genes) and environmental factors (e.g. socioeconomic status, infections) affect disease severity. We have two siblings with cystic fibrosis (CF) and both siblings are homozygous for F508del. Despite having the same CFTR genotype, infection status and similar environment, the two siblings exhibit varied disease phenotypes. In this study, we present the clinical features of these two patients and correlate these parameters with inflammatory mediators measured in the sputum samples.

**Methods:** Clinical findings and history were abstracted from the electronic medical record after IRB approval. Enzyme-linked immunosorbent assays (ELISAs) were used to measure IL-8, neutrophil elastase (NE), and other biomarkers in sputum samples.

**Results:** Clinical summary: The siblings are 364 days apart in age and both have chronic Methicillin-resistant Staphylococcus aureus (MRSA) infections. Patient #1 has FEV1 (% predicted) that varies between 30-50% and patient #2 has FEV1 (% predicted) that varies from 50-90%. Biochemical studies: (1) patient #1 generally had higher IL-8 levels in sputum samples (in the range of 53667 - 87897 pg/ml) than patient #2 (in the range of 20117 - 32830 pg/ml). (2) Patient #1 generally had higher NE levels than patient #2. (3) There are certain correlations between IL-8 and NE levels in sputum samples for both patients. (4) The IL-8 and NE levels increased dramatically during pulmonary exacerbation (~ 7- and 5-fold, respectively).

**Conclusions:** In addition to CFTR, other genetic and environmental factors strongly influence the severity of CF disease. For these two siblings, the severity of the disease correlates with IL-8 and NE levels in sputum samples. Validation of these protein biomarkers will help in routine disease monitoring and could potentially be used as outcome measures in clinical trials.

**Funding/Grant Support:** R01 HL123535

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PDF08  Geo-distinctive Comorbidity Networks of Pediatric Asthma

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Network based comorbidity network studies can generate more realistic pathways and realistically identifying overlapping symptoms. In this study, we first empirically reveal the comorbidity patterns in pediatric asthma and then examine geographical discrepancy between different neighborhood types. Our novel method of geo-parsed comorbidity network analysis enables us to identify distinctive patterns of comorbidity networks in urban and suburban areas. We utilize pediatric asthma encounter records (N=4,914). Using a two-mode network analysis, we transform the matrix of patients by disease to disease by disease networks. As result we found that pediatric asthma evolves with 680 diseases. The extreme heterogeneity of asthma challenges treatment and control of asthma. Foremost, our findings show there is a tight relationship between obesity and asthma in childhood (25% for the suburb and 20% for the downtown) and pediatric comorbidity networks are not identical across different geographical boundaries. Patients living in the suburban area exhibit more complex pattern than those living in the down town area. In suburban network, other frequently co-observed diseases are epilepsy and recurrent seizures, gastro-esophageal re-flux disease, cerebral palsy, and lack of expected normal physiological development. In the downtown, the top five symptoms are abnormal breathing, respiratory disorders, throat and chest pain, obesity and blindness and low vision.
PDF09
Identifying Sociomarkers of Pediatric Asthma Patients at Risk of Hospital Revisiting

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Socio-markers, indicators of social conditions where a patient is embedded in, can help medical practitioners and researchers to reliably identify high-risk individuals in a timely manner. Asthma is one of the most common chronic childhood diseases in the US. Combining medical-social dataset from three different sources, we demonstrate how socio-markers play an important role in identifying patients at risk of hospital revisits due to pediatric asthma within a year. We implemented a Support Vector Machine (SVM) based classification model. The classification outcome is either patient visits the hospital only one-time (class 0) or revisits the hospital within a year (class 1). To avoid overfitting and ensure generalizability, we divided the dataset as training, test, and validation with a proportion of 60%, 20%, and 20%. The proposed socio-marker model resulted in an average classification accuracy of 63.70% for the test set and 63.67% for the validation set. Further, the average specificity and sensitivity is found to be 62.79% and 64.77%, respectively for the test set and 62.79% and 64.83%, respectively for the validation set. Incorporating the socio-marker features such as gender, race, insurance type, age, and zip code, we can identify asthma patients at risk of a hospital revisit with 64% accuracy.

PDF10
Intestinal Epithelial Barrier Alterations in a Mouse Model of Hirschsprung-Associated Enterocolitis (HAEC)

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Background: Hirschsprung disease (HSCR) results from failure of neural crest-derived cells to form the distal enteric nervous system (ENS). HAEC is the leading cause of morbidity and mortality in HSCR, the pathogenesis of which remains unknown. Of the several theories proposed are alterations to intestinal epithelial barrier properties, microbiota composition and gut mucosal immunity. We sought to explore the state of epithelial barrier integrity at different time points of development of HAEC.

Methods: We used a neural crest-conditional deletion of EdnrB (EdnrB-null) and studied the ganglionic and aganglionic bowel in this mouse model of HAEC. mRNA expression levels of major tight junction (TJ) genes – Occludin, ZO-1, Claudins 2 & 3 were compared between EdnrB-nulls and controls using qPCR and TJ integrity analyzed by confocal microscopy. Intestinal permeability in vivo was measured by plasma-to-luminal flux of FITC-Inulin.

Results: An increased expression of TJ genes was observed in the proximal colon (PC) of EdnrB-nulls as early as post-natal day (P) 14. In contrast, the aganglionated distal colon (DC) showed weaker staining and increased inulin permeability.

Conclusions: An earlier maturation of TJ's in PC and an altered development of TJ's and increased permeability in DC of EdnrB-nulls suggest that the epithelial barrier is altered during HAEC. ENS/Microbiome interactions will further help to delineate the role of an impaired epithelial barrier towards development of HAEC.

Funding/Grant Support: NIH/NIDDK; American College of Surgeons; Children’s Foundation Research Institute
Heart Rate Features Can Predict Fever Onset in Critically Ill Children
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Background: Outcomes are worse when patients with brain injury develop fever, and fever can herald sepsis in immunocompromised hosts. The ability to predict fever could allow early, targeted interventions and improve outcomes in select patient populations.

Hypothesis: Features of heart rate (HR) can predict fever in critically ill children.

Method: 62 pediatric ICU patients experienced 124 febrile events (≥ 38°C) in which min-to-min heart rate (HR) data was available for 4 hours prior and 1 hour after each fever. HRs and standard deviations were derived from 15 min epochs – selected sequentially from the 4 hours prior to a fever – to predict the temperature 15 min after the epoch (i.e. 15 min prediction window). Preceding temperatures and their standard deviations were also considered by our machine learning algorithm. Using these as predictors, we trained a random forest classifier with 30 decision trees on 70% of randomly selected febrile events and tested the derived model on the remaining 30%. We repeated this process 100 times to avoid sampling bias.

Results: Our machine learning model correctly anticipated fever in a 15 min prediction window with an average accuracy, specificity, and sensitivity of 92%, 97%, and 71%, respectively. However, for a 5 min. prediction window, the average accuracy, specificity, and sensitivity were observed as 97%, 99%, and 89%, respectively.

Conclusion: It is feasible to predict fever with high fidelity using continuous heart rate data with machine learning. Our model should be modified to optimize performance for greater clinical applicability.

Activin deficiency reduces adiposity, causing aberrant development of white adipose tissue
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Background: Activins A and B are members of the TGF-β family. Activin A is abundant in early adipose anlage, however its expression decreases in differentiating adipocytes and is absent in mature adipose depots. In contrast, activin B is expressed at low levels in early white adipose tissues but is highly expressed in mature fat depots.

Methods: We used mice with adipose-selective knockout of activin A and/or global knockout of activin B to understand the roles of activins in adipose tissue and metabolism. We examined expression of adipocyte markers as well as the bioenergetics of mouse embryonic fibroblasts (MEFs) derived from these mice to assess cell autonomous effects and to better define activins' roles in adipocyte biology.

Results: Activin A and global knockout of activin B individually had modest effects on adiposity; however, the combined mutations resulted in a marked reduction in adipose tissue mass while inducing a browning effect predominantly within visceral white adipose tissues, differentially impacting adipogenic, brown and beige markers. Seahorse analysis indicated a significant change between the mutant and control MEFs, suggesting a cell autonomous effect.

Conclusions: Our study highlights depot-selective activin effects in white adipose tissues. The presence of brown-like cells in very early WAT visceral depots and the enhanced bioenergetic properties of differentiated activin-deficient MEFs are consistent with an altered cell fate decision model as a plausible explanation for this phenomenon.

Funding/Grant support: NIDDK RO1 DK073572
**Metabolic Response to Influenza and RSV**

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Infection with airway respiratory viruses such as influenza and the respiratory syncytial virus triggers an innate immune response aimed at initiating the humoral reaction to halt viral replication and spread. The underlying molecular mechanisms of these processes of change in innate immune cell homeostasis have not been determined. We have identified that upon viral infection both dendritic and epithelial cell metabolism are altered to control the uptake and catabolism of nutrients, fuelling the innate response and viral biomass production. The metabolic response of dendritic cells to viral infection differed from activation via TLR stimulation or infection with an inactive virus. Using quantitative mass spectrometry along with metabolic flux measurements and functional assays, we found that metabolic pathways of glycolysis, glutaminolysis were increased and oxidative metabolism was decreased, preferentially fueling the effector function of the immune cells. Functional analyses of the infected dendritic cells under restricted bioenergetics showed no evidence of altered function to activated T cell, suggesting that immune cells have the capacity to regulate their metabolic state. This metabolic response to viral infection increased the expression of the c-Myc transcription factor, which indicates that the influenza infection has the potential to modulate key metabolic regulatory events. Influenza infection induces a unique metabolic signature in dendritic cells early in the infection process. Limiting these metabolic changes affects T cell activation and migration of infected DCs, suggesting metabolic switching may play a vital role in initiating the innate immune response.

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Poster Presentations: Research Staff
**RS01 Exploring the Use of Extracorporeal Membrane Oxygenation (ECMO) as a Bridge to Organ Donation in a Pediatric Cardiac Patient: a Unique Case Report**

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A 13-year-old male was admitted for a same day procedure, during which the patient decompensated. During fluoroscopy, haziness of the left lung was noted which was not present before the start of catheterization and the procedure was aborted. The patient remained intubated and was transfer to the PICU for further medical management. Immediately upon, the patient acutely decompensated. The patient was volume resuscitated and ventilator support was optimized. The patient showed temporary improvement, but within an hour the patient deteriorated and the decision was made to proceed with ECMO cannulation. The patient remained on ECMO for a total of 3 days, however on ECMO day 2 the patient was transported to CT for suspected neurologic injury which was confirmed. The patient’s family was adamant about not prolonging the patient’s life considering the neurologic devastation and expressed a strong desire for organ donation. Ultimately the patient progressed to brain death and traditional pathways of organ donation were initiated. A comprehensive medical evaluation was completed and organs were procured on day 3 of ECMO. The patient’s organs were successfully transplanted and to this date the recipients show no signs of organ rejection per reports. This patient became the first in the region, of all age groups, to donate an organ while on ECMO support. In our opinion, ECMO as a bridge to organ donation is under-explored and under-utilized. This strategy of utilizing ECMO offers the potential for increasing the number of patients who meet donation criteria and are able to donate viable organs.

**RS02 Dosing of Perampanel in Children: Correlation with Serum Levels**

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**Introduction:** Perampanel (PER) is approved for use in patients 12 and older and has been used extensively in children at LeBonheur. PER is metabolized by CYP3A4 and enzyme-inducing anti-epileptic drugs (EIAED) taken concomitantly are known to influence PER serum levels. This study was designed to investigate PER serum levels of LeBonheur pediatric patients prescribed PER between January 2013 and May 2017. We also want to examine the effect of concomitant EIAEDs on PER levels.

**Methods:** We performed a retrospective chart review and data extraction of patients’ age, gender, PER serum level, weight, prescribed PER dose, and concomitant drugs. Exclusion criteria included patients who were prescribed PER but no serum levels were assayed. Patients were categorized into age groups (0 < 2, 2 < 6, 6 < 12, 12+ years) with an age distribution of 2, 17, 21 and 47 patients respectfully, and organized by serum level and concomitant drug category (on inducing CYP3A4 or not inducing CYP3A4).

**Results:** Of the 140 total patients who have been prescribed PER within the relevant time frame, 87 patients with a total of 155 PER serum levels are included in the study. Unexpectedly, when stratified by age group, the patients on EIAEDs did not require higher PER doses than patients not on EIAEDs to reach similar serum levels. Across the age group study, patients are dosed with between 0.13 and 0.35 mg PER/kg. Patients on higher PER doses were less than age 6 and not on EIAEDs. Serum levels obtained were within the range previously reported for adults as therapeutic dose. The most common daily doses of PER were 8 mg and 6 mg. Data analysis was performed on average mg/kg dose, mg/kg dose range, and average PER level within each age group between concomitant drug categories. We hypothesize that PER levels of patients concomitantly taking EIAEDs will be significantly lower than the PER levels of patients who are not concomitantly prescribed EIAED’s.

**Conclusions:** Dosing and serum levels of PER in children are consistent with what was previously reported in adults, except in children below age 6 not on EIAEDs. This age group exhibited higher PER dosing on average while maintaining similar serum levels.

**Funding/Grant Support:** Neuroscience Institute at Le Bonheur Children’s Hospital
RS03  Alteration of the Brain Network Caused by Sedation in Patients with Epilepsy: A Magnetoencephalography Study

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Background: Brain connectivity analysis using magnetoencephalography (MEG) and other noninvasive methods has been increasingly utilized to investigate the nature of epilepsy. Since young, uncooperative, and developmentally delayed patients cannot be motionless during MEG recordings, these recordings are performed under sedation. Understanding alteration of the brain connectivity caused by sedation is of great importance, but there is no MEG study to investigate this alteration. Aim of this study was to address this deficit.

Methods: Resting state MEG from 41 sedated (24 male, 5.45 ± 4.97 years) and 45 non-sedated (26 male, 10.43 ± 5.07 years) patients with epilepsy were acquired. The weighted phase lag index (wPLI) was used for calculating connectivity matrix between MEG sensors. Then the connectivity matrix was used to calculate four integration and segregation graph measures, i.e., global efficiency, characteristic path length (CPL), transitivity, and modularity, in beta (13-30 Hz) frequency band. The graph measures were used to compare the brain networks in two groups.

Results: Sedated patients showed lower global efficiency (P < 0.001) and higher modularity (P < 0.01) compared to those of non-sedated. The CPL and transitivity did not show any significant differences (P > 0.2) between two groups. Conclusions: We found that sedation shifted brain networks towards a regular network by decreasing its integration and increasing its segregation.

Funding/Grant Support: This study was funded by the Children’s Foundation Research Institute, Memphis, TN.

RS04  Resistin-Like Molecules Reduce Influenza A Virus Morbidity in Mice

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Background: Resistin-like molecules (RELMs) are recently discovered cysteine rich secreted proteins abundant in a variety of organs including the lungs. RELMα has an inhibitory role in the lungs by downregulating inflammation, while RELMβ promotes inflammation. We noted increased expression of RELMs in the lungs of mice with acute asthma and influenza, which were protected against severe influenza morbidity, and hypothesized that RELMα and RELMβ proteins enhance antiviral defenses.

Methods: Recombinant RELMα and RELMβ proteins were administered intranasally to C57BL/6 mice starting three days prior to viral infection and continued daily following viral infection. Mice were infected with influenza A/CA/04/2009 virus. Animals were sacrificed on days 3, 5, 7, and 9 following viral infection for sample acquisition. Animals not treated with exogenous RELMs served as controls.

Results: Administration of RELM proteins reduced airway resistance after influenza virus infection. Airway inflammation was increased in RELM-treated mice with macrophages and neutrophils taking precedence and a prominent increase in CD8+ T cells at late timepoints. A significant reduction in viral burden occurred in the lungs of RELM-treated mice.

Conclusion: The administration of RELM proteins directly impacted the host immune response against influenza A virus. Future studies will investigate the mechanisms by which RELMs mediate protection against influenza.

Funding/Grant Support: Le Bonheur, Young Investigator Award
Do Asymptomatic Respiratory Viral Infections Occur?

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Background: Respiratory viruses are common causes of mild to severe upper and lower respiratory tract infections (RTI). Nucleic acid amplification molecular methods are becoming routine in the detection of community-acquired respiratory viruses allowing the detection of multiple respiratory viruses simultaneously. Multiple pathogens are often co-detected in patients with symptoms of RTI. However, little attention has been given to the detection of respiratory viruses within asymptomatic populations.

Objectives: We assessed the detection of respiratory viruses in a highly screened, asymptomatic adult population.

Study Design: We excluded subjects with a) any symptoms of hay fever b) any respiratory symptoms within 14 days c) asthmatics. We used highly sensitive polymerase chain reaction (PCR) assays to evaluate nasal swabs of the highly screened volunteers from our human respiratory syncytial virus challenge models.

Results: Specimen collections occurred in London, United Kingdom and 190 subjects were evaluated. 124 subjects were analyzed by ProFLU+ PCR and 66 subjects were analyzed by Genmark® PCR. We found that none of our 190 patients were positive for influenza, RSV, human metapneumovirus, or parainfluenza; the only detected virus in either assay was rhinovirus (n = 8/66; 12%).

Conclusions: Respiratory viruses (with the exception of rhinovirus) were not detectable in asymptomatic healthy adults. The detection of these viruses generally indicates a current or recent symptomatic infection.

Funding/Grant Support: Laboratory testing was performed as part of clinical trials published elsewhere (protocol numbers GS-US-218-0103 and ALS-8176-502). This work was supported by internal funds (Grant number: RO73230070) from the DeVincenzo laboratory and University of Tennessee Health Science Center; no external financial support was received for this study.

Innate Immune Responses in Fungal Asthma Enhance Antiviral Immunity During Influenza Virus Infections

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Fungal allergic asthma is a prevalent asthma subtype. Although considered to have an elevated risk of severe influenza, asthmatic patients suffered milder morbidity and mortality compared to non-asthmatics during the 2009 influenza pandemic. We developed a mouse model of fungal asthma and influenza to explore this protection. We hypothesized eosinophils guide antiviral responses against influenza virus infections in the allergic host. Eosinophil immunophenotype was characterized in various niches of mice with asthma and influenza and compared to individual disease conditions. Eosinophils from comorbid mice expressed high MHCI, PIR-A/B and CD62L in the lungs and spleens compared to influenza alone. Adoptive transfer of eosinophils reduced viral burden and increased airway CD8+ T cells in virus-infected recipients. We showed that eosinophils promoted CD8+ T cell activation in vitro and ex vivo, and antigen-loaded eosinophils directly interacted with CD8+ T cells in vitro. Eosinophils have been previously shown to regulate B cells and IgA production in the gut. In our model comorbid mice had more plasma cells in lymphoid organs, but a similar number of mature B cells, compared to influenza alone. Antibody production by plasma cells was more prominent at early time points in comorbidity. Our data suggest eosinophils may promote an antiviral response by trafficking to lungs and spleen where they influence CD8+ T cell and B cell responses.

Funding/Grant Support: National Institutes of Health R01 (Samarasinghe)
RS07 37/67-Laminin Receptor Binding to Laminin-1 Facilities Enteric Neural Crest Cell Migration in Endothelin Receptor-B Mutant Mice

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Enteric nervous system (ENS) development is governed by interactions between neural crest cells (NCC) and their surrounding intestinal microenvironment. The molecular mechanisms of this interaction are incompletely understood. Using the NCC-conditional deletion of Endothelin receptor-B (EdnrB), which models human Hirschsprung disease, we performed a comparative microarray of the distal hindgut at E14.5 between wildtype (WT) and EdnrB-null. Laminin-1, a component of extracellular matrix laminin, was upregulated in EdnrB-null colon (2.58x). Laminin-1 (ligand) is bound by 37/67-laminin receptor (LAMR). We identified 37/67-LAMR in human colonic myenteric plexus, with decreased expression in Hirschsprung patient specimens. We found decreased cell surface expression of the 37/67-LAMR in embryonic and postnatal EdnrB-null NCC. BQ788 (EdnrB inhibitor) decreased surface expression of 37/67-LAMR in WT E13.5 gut slice cultures. Adding YIGSR (pentapeptide laminin-1 analog that binds 37/67-LAMR) to E13.5 EdnrB-null slice cultures resulted in increased NCC 37/67-LAMR expression and re-localization of 37/67-LAMR to lamellopodia. Applying YIGSR to E13.5 EdnrB-null colon explants in organ culture rescued ENS colonization of the colon. These results demonstrate that laminin-1 binding to 37/67-LAMR promotes NCC migration during ENS development and this interaction is altered in Hirschsprung disease. These results may inform therapeutic approaches to aganglionosis.

Funding/Grant Support: Le Bonheur Foundation

RS08 Pervasive Motor Deficits Beyond Lesioned Hemisphere in Pediatric Arterial Ischemic Stroke

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Introduction: Pediatric arterial ischemic stroke (AIS) carries significant consequence of persistent motor deficits. However, the cortical mechanisms of motor recovery following stroke in children are seldom assessed.

Hypothesis: We hypothesized that the behavioral and neurophysiological motor measures in the lesioned hemisphere would be altered.

Methods: Motor (indexed by TMS and fMRI) and behavioral measures were obtained in 8 children with AIS and 10 healthy age matched cohort (HC).

Results: When compared to HC, patients with AIS demonstrated increased inhibition measured as ipsilateral silent period by TMS in both lesioned and contra-lesional hemispheres, while the measures of cortical excitation, in both hemispheres were found to be similar. fMRI during a finger-tapping task showed decreased strength and volume of activation in the primary motor cortex, supplementary motor area and cerebellum in the lesional, compared to the contra-lesional hemisphere. Clinical motor evaluation showed gross functional recovery, but fine motor control was significantly impaired in both sides.

Conclusions: Consistent with our hypothesis, we observed network-wide hemodynamic decrease in the lesioned hemisphere. In addition, our data demonstrate, for the first time, impaired inhibitory circuitry and fine motor behavior extending to the non-lesioned hemisphere indicating to pervasive dysfunction of both lesioned and contra-lesional hemispheres in pediatric AIS.

Funding/Grant Support: Le Bonheur Neuroscience Institute
RS09  Characterizing normative motor parameters using Transcranial Magnetic Stimulation (TMS) in typically developing children

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Introduction: The human motor system contains an excitatory network (EN) mediated by pyramidal neurons that reach maturity by age 7. Less is known about the development of inhibitory network (IN) mediated by interneurons in typically developing children. Characterization of EN and IN is crucial to understanding normal trajectories of gross and fine-motor development as well as for recognizing alterations in pediatric motor disorders. We hypothesized that in typically developing 6-7-year-old children, EN parameters would be comparable to that noted in adults, whereas IN parameters would demonstrate continued development.

Methods: Right-handed neurotypical children (N=28, 13F, 6.7±0.5 yrs) were recruited from a Mid-South cohort study. Navigated TMS during Electromyography (EMG) of hand muscles was used to derive EN parameters of corticomotor conduction time (CT) and amplitude of motor evoked potential (MEP), and an IN parameter of cortical silent period (CSP).

Results: No differences in CT, MEP and CSP were seen between hemispheres or between genders. EN parameters of CT (right cortex [R]-18.87ms; left [L]-19.10ms) and MEP (R-1306.07mV; L-1325.32mV) were found to be similar to that reported in adults. Average duration of CSP (R-101.4ms; L-110.9ms) was found to be less than previously reported in adults.

Conclusion: This study provides invaluable information regarding typical motor development indicating a plateau of EN by 7 years and continued evolution of IN.

Funding/Grant Support: Children’s Foundation Research Institute

RS10  Resting State Changes following adjuvant TMS stimulation in Voice Treatment

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We examined how TMS as an adjuvant to voice treatment (VT) in individuals with Parkinson’s disease affected M1arynx (LM1, RM1) connectivity using resting state fMRI (RSMRI). We hypothesized that compared to sham (STMS), TMS applied to LM1 (LTMS) would increase connectivity to the feed forward speech network (FFSN) and treatment effect duration, while TMS applied to RM1 (RTMS) would increase connectivity to the feedback speech network (FBSN) and the rate of learning. Fifteen patients with voice deficits were enrolled. Voice measures and RSMRI scans were performed at baseline, post-treatment, and 16-week follow-up. Adjuvant 5 Hz LTMS, RTMS, or STMS was delivered with VT for 16 sessions. Connectivity of LTMS and RTMS targets was measured by correlating LM1 and RM1 time courses to other regions and contrasting results on individual and group levels. Behaviorally, RTMS group improved fastest during treatment and LTMS group showed the best retention of gains at follow-up. Post-treatment, RSMRI demonstrated greater connectivity of LM1 to FBCS in the LTMS group and of RM1 to FBBCS in the RTMS group versus sham. At follow up, the RTMS group had no further changes while the LTMS group had increased FBBS connectivity. This study used RSMRI to elucidate how TMS can augment behavioral outcomes through connectivity changes in FFSN and FBSN that can be used to elucidate the differential engagement of brain networks during phases of vocal skill learning and retention.

Funding/Grant Support: Michael J Fox Foundation
RS11  Application of Multi-Targeted Metabolic Analysis: High Fat Diet-Induced Altered Brain-Gut Metabolism

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We present an analytical approach using mass spectrometry (MS) to assess the effect of high fat (HF) diets on brain metabolism and the potential association of its alteration with an altered gut-microbiome. Recent findings suggest the gut-brain axis plays fundamental roles in global energy homeostasis. This complex bidirectional communication system can be influenced by the gut microbiota and contributes to obesity development. One clear mechanism of communication is microbial interaction with bile acid (BA) pools and whole body energy balance, occurring through gut and peripheral FXR signaling. What remains to be understood is the role of BAs directly upon CNS metabolism. Using MS methods, the effect of high fat carbohydrate restriction (HFCR) on BA and metabolite profiles in serum and brain of mice fed Western and HFCR diets will be determined. We have recently profiled total serum BAs in a murine model of liver injury following acute parenteral nutrition (PN) and found serum BA compositions to reflect that PN elevates total conjugated primary BA levels (TCA, TCDCA, TbMCA, and TaMCA) compared with chow. In another study, we showed that total serum specific BA changes occurred in colonized germ-free mice fed a HF diet. We have also published changes in brain metabolites of mice and rats fed HF diets compared to controls. We hypothesize that these changes correlate with serum BA changes, such as increased conjugated BAs with Western diet and not carbohydrate restricted diet.

RS12  Evaluation of the impact of antimicrobial stewardship guideline antibiotics on perforated appendicitis outcomes

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Background: Determining the safest, most effective and narrow spectrum antibiotic regimen for perforated appendicitis in children is a challenge. We evaluated the impact of the use of ceftriaxone/metronidazole (CTX/MTZ), compared to meropenem (MERO) or piperacillin-tazobactam (TZP) on post-operative complications.

Methods: This is a retrospective study of children with perforated appendicitis between 1/1/13 and 12/31/16. Patients were divided by antibiotic regimen for comparison. Outcomes collected and assessed included surgical site infection (SSI), 30-day readmit, antiemetic use, length of stay (LOS), antibiotic duration, and discharge antibiotic use.

Results: 374 patients were included: 18% received MERO, 54% TZP, and 28% CTX/MTZ. Collectively, 17% patients developed SSI: 22% who received MERO, 15% TZP, and 17% CTX/MTZ; p=0.359. There was no difference in 30-day readmit across groups: MERO 10%, TZP 13% and CTX/MTZ 6%; p=0.12. Of the 106 patients discharged on antibiotics, 46% had received MERO, 26% TZP, and 22% CTX/MTZ; p=0.001. Median LOS was 6 days for MERO, 5 for TZP and 6 for CTX/MTZ; p<0.0001. The median antiemetic dose was 1 for each group; p=0.278.

Conclusion: There were no differences in SSI, 30-day readmit or number of antiemetic doses. LOS, antibiotic duration, and use of discharge antibiotics were different. Overall, CTX/MTZ had no negative clinical impact compared to MERO or TZP regimens for pediatric patients with perforated appendicitis.
RS13  An Institutional Review of CDH Management Practices and Survival Rates

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An Institutional Review of CDH Management Practices and Survival Rates Jorie Jones MD, Tim Jancelewicz MD MA MS Background: Congenital Diaphragmatic Hernia (CDH) occurs in 2.7 per 10,000 live births. Despite significant advances in supportive medical technology, the mortality rate remains relatively high. This may be due to a lack of standardization of treatment across children's hospitals worldwide. This study aims to review the management practices and survival rates at Le Bonheur Children's Hospital in an effort to optimize care strategies for our patient population. Hypothesis: Morbidity and mortality rates of CDH patients at Le Bonheur may be significantly higher than national statistics. Results: 78 CDH patients treated at Le Bonheur (2204-2017); 50 (64%) survived, and 25 (32%) required ECMO. Survival on ECMO was 28%. Sixty-five patients (83%) were surgically repaired and of those, 61% survived to discharge. Only 46% of patients who received prenatal care were prenatally diagnosed. While 75% of patients who expired received public insurance or were uninsured, lack of prenatal care, patient race, and insurance status were not significantly associated with mortality. Conclusion: There is no evidence of significant socioeconomic healthcare disparities in CDH management and outcomes at Le Bonheur Children's Hospital. Survival at this hospital is similar to other centers worldwide. It is unclear whether the low survivability on ECMO is due to management or patient factors.

RS14  Intestinal Secretory Immunoglobulin A Deficiency in Hirschsprung-Associated Enterocolitis

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Hirschsprung disease (HSCR) is a common cause of intestinal obstruction in the newborn. Hirschsprung-Associated Enterocolitis (HAEC) is a significant and life-threatening complication of HSCR, affecting up to 60% of patients. We previously demonstrated intestinal dysbiosis and a gut-specific deficiency of B-cell produced Secretory Immunoglobulin A (sIgA), the primary effector molecule of mucosal immunity, in neural crestconditional deletion of Endothelin Receptor B [EdnrB(NCC-) ] mice that reproducibly model human HAEC. To determine mechanism, we examined intrinsic and extrinsic aspects of B cell development and function: We found that EdnrB is expressed in developing hematopoietic organs and that splenic B cells express EdnrB. Splenic B cells from EdnrB(NCC-) showed no intrinsic defect in survival vs. WT B cells. In vitro stimulation of B cells with LPS demonstrated increased IgA, but not IgM, production in EdnrB(NCC-) vs. WT. However, polymeric Immunoglobulin Receptor (pIgR), which transports and secretes IgA into the lumen, is decreased ~60% in EdnrB(NCC-). Together, our results are consistent with human HAEC observations of decreased luminal sIgA and mouse models of other inflammatory bowel diseases, in which decreased pIgR is seen in concert with a dysregulated microbiota. These results suggest targeting the dysbiotic microbiome and pIgR-mediated sIgA transport as potential therapeutic approaches in prevention and treatment of HAEC.

Funding/Grant Support: NIH/NIDDK, American College of Surgeons
**RS15**  Short Term Outcomes of HIE Patients Needing ECMO for Respiratory Support – ELSO Database Analysis

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**Background:** Therapeutic hypothermia (TH) is the standard treatment of moderate to severe hypoxic ischemic encephalopathy (HIE) with the presence of pulmonary hypertension in 10-25% of these patients. Extracorporeal membrane oxygenation (ECMO) improves survival in pulmonary hypertension but its use is controversial in HIE as “irreversible brain damage” is a contraindication per ELSO guidelines. The inability to predict neuro-outcomes has led to variable ECMO practice. There is an unproven concern that HIE patients may have increased risk of intracranial bleeding, ischemia, stroke or coagulopathy during ECMO.

**Methods:** The ELSO database was queried for patients with diagnosis of HIE and respiratory failure needing ECMO from 2000 to 2016.

**Results:** 606 patients with diagnosis of HIE needed ECMO for respiratory support. Of these patients 509(83%) survived to discharge. The median ECMO run was 137 hours, with Meconium aspiration syndrome (57%) and Primary pulmonary hypertension (14%) being the most common primary diagnoses. There were 205 patients with 5 minute APGAR of 0-3, 241 with APGAR5 of 4-6 and 120 with APGAR5 of 7-10. There were 172 patients in the pre TH group (2000-2008) and 433 in the post TH group (2009-2016). Further analysis of the descriptive characters, short-term outcomes, procedures and complications will be presented.

**Conclusion:** After the widespread use of TH, HIE patients with respiratory failure are increasingly being supported with ECMO.

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**RS16**  Database analysis of CDH patients with HIE needing ECMO for respiratory failure

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**Background:** Congenital diaphragmatic hernia (CDH), in its severe form has poorer outcome due to associated pulmonary hypertension. ECMO is used for respiratory failure associated with CDH with survival between 55-80%. The presence of hypoxic ischemic encephalopathy (HIE) in CDH patients is likely to lead to poorer outcomes. Therapeutic Hypothermia (TH) was widely used for the treatment of HIE from 2009 onwards.

**Hypothesis:** CDH patients with HIE have worse short term outcomes.

**Methods:** The ELSO database was queried for patients with diagnosis of CDH and HIE needing ECMO for respiratory failure from 2000 to 2016.

**Results:** 158 patients with diagnosis of CDH and HIE needed ECMO for respiratory support with 118 left sided and 37 right sided lesions. Of these patients, 107(68%) were repaired and 62(39%) survived to discharge. The median ECMO run was 240 hours. There were 32 patients with 5 minute APGAR of 0-3, 71 with APGAR5 of 4-6 and 43 with APGAR5 of 7-10. There were 74 patients in the pre TH group (2000-2008) and 84 in the post TH group (2009-2016). Further analysis of the descriptive characters, short-term outcomes, procedures and complications will be presented and compared to patients with CDH.

**Conclusion:** ECMO is being used to treat respiratory failure in patients with CDH and HIE. This subgroup has a worse survival to discharge as compared to CDH patients without HIE.
**RS17**

**Understanding rapamycin resistance in Tuberous Sclerosis Complex and Lymphangioleiomyomatosis**

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Tuberous Sclerosis Complex (TSC) and Lymphangioleiomyomatosis (LAM) are tumor suppressor syndromes caused by loss-of-function mutations in TSC1 and TSC2. Despite the identification of mTOR hyperactivation as the main biochemical defect downstream of TSC1/TSC2 inactivation and the approval of rapamycin and rapalogs for the treatment of TSC and LAM, these drugs are cytostatic and continued treatment is required for clinical benefit. The latter raises the possibility of acquired drug resistance. Moreover, a subset of patients does not benefit from rapamycin therapy, and this patient population is left with surgical options that most often result in poor outcomes. To explore the mechanisms leading to such rapamycin resistance in TSC/LAM, we isolated a Tsc2-null cell line from a rapamycin non-responsive xenograft. These cells (termed ELT3-245) have increased tumorigenic potential, compared to parental ELT3, judged both from increased anchorage-independent cell growth and decreased disease-free survival after xenotransplantation. ELT3-245 exhibit decreased expression of epithelial markers and altered migration characteristics on extracellular matrices. Finally, ELT3-245-derived tumors are responding poorly to rapamycin and ELT3-245 cells have delayed mTOR dephosphorylation kinetics upon rapamycin treatment. Of great interest are the signaling pathways that may confer rapamycin resistance in ELT3-245, and we are currently characterizing gene expression differences, compared to ELT3.

**RS18**

**Implementing precision medicine initiatives: considerations for underserved communities**

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**Background:** Precision Medicine promises to improve the quality of health care based in part on patient information at the molecular level, thereby enhancing the accuracy of diagnosis and affecting clinical management decisions. Substantial challenges occur in communities where limited resources preclude access to the technologies that are associated with precision medicine initiatives, potentially creating even greater health care disparities.

**Methods:** We describe a multi-faceted strategy that includes community engagement and education, partnerships with local foundations and industry and facilitating participation in genomic research studies.

**Results:** The Le Bonheur BIG initiative is collecting DNA from patients to support pediatric research. The samples are available to LeBonheur and UTHSC investigators. TtGG, an educational program to implement laboratory based genomics exercises in local high schools, is underway at White Station High School. Gene Chats, a Facebook Live genetics education series began in September 2017 and a 7-week, community based lecture series on sickle cell disease will begin in April.

**Conclusions:** Encouraging precision medicine initiatives in a responsible way will require a robust, multi-faceted approach that recognizes the impact of historical injustice, mistrust of the research enterprise and the potential for creating greater health care disparities. Our approach to implementing precision medicine in the Memphis community is designed to help 'level the playing field' of accessibility and to minimize precision medicine disparities.
RS19  Ways to Enhance Children's Activity and Nutrition (We Can!) in the Healthy Lifestyle Clinic: A Pilot Caregiver-Focused Intervention

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Parents/caregivers (CG) are primary decision makers in the home environment and are key stakeholders in pediatric obesity treatment. This study evaluated We Can! (an NIH developed education program that provides CGs with training and tools to help them support their family goals of living a healthy lifestyle) in families and CGs from the Healthy Lifestyle Clinic at Le Bonheur Children's Hospital. We Can! included pre/post surveys and anthropometrics as well as four 2 hr interactive lectures that included didactic healthy lifestyle education delivered to the CGs and group discussion. Seven female CGs (39.3 ± 5.3 yrs; 6 African American, 1 Caucasian; body mass index 44.3 ± 8.7 kg/m2; body fat 49.9 ± 5.5%) participated in all sessions of the program. All CGs agreed/strongly agreed that they play a large role in their child's eating and activity patterns. After the education sessions, knowledge of nutrition, physical activity, and weight management increased compared to baseline. Specifically, scores on the importance of modeling healthy lifestyle behaviors (p=0.05) and likelihood of making a change in the next 30 days increased in all CGs. All CGs agreed/strongly agreed they would make changes in the next 30 days. CG feedback was positive, and they expressed interest in similar programming in the future. This focused intervention was well received among CGs and improved knowledge and motivation to implement changes consistent with a healthy lifestyle and improved home environment.

Funding/Grant Support: Urban Child Institute; CFRI; UTHSC
Poster Presentations:
Graduate Students
**CD14 in a Murine Model of Asthma and Influenza Comorbidity**

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**Background:** Asthma and influenza are leading causes of worldwide morbidity and mortality. Although these two conditions can co-exist in the same patient, the immune parameters that impact disease outcomes are not fully elucidated. The importance of macrophages to both conditions suggested a role for CD14, a co-receptor for endotoxin, as a regulatory mechanism for innate immune responses during asthma and influenza co-morbidity.

**Hypothesis:** Parameters of morbidity will be reduced in the absence of CD14.

**Methods:** Age and gender matched wild-type (WT) and CD14 knock-out (KO) mice were subjected to our validated model of Aspergillus-induced model of asthma and/or influenza. Characteristics of disease pathogenesis were investigated using standard methods in weight loss, flow cytometry, airway resistance, histology, quantitative real-time PCR, and viral titer quantification.

**Results:** The absence of CD14 did not have an impact on morbidity as these mice were equally susceptible to disease with similar airway resistance. Peribronchovascular inflammation and goblet cell content were equivalent between WT and KO mice in asthma alone and asthma and influenza co-morbidity. Co-morbid KO mice had less lymphocytes and eosinophils in the airways although their lung viral burden was equivalent to WT. Inflammatory gene signatures were altered in co-morbid mice in each genotype.

**Conclusion:** CD14 is necessary for airway inflammation but not for viral pathogenesis in allergic hosts.

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**Effect of genetics on the development of Hypersensitivity Pneumonitis (HP)**

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HP is an interstitial lung disease that develops following repeated exposure to a variety of inhaled environmental antigens. The disease is characterized by alveolitis, granulomas and fibrosis. Children can develop HP, however it is often diagnosed late in the disease course resulting in significant lung injury and, in some cases, death. Not all individuals exposed to HP causative antigens develop disease suggesting that genetic factors play a role in susceptibility. We are using the innovative systems genetics tool, the BXD panel of recombinant inbred mice with the Saccharopolyspora rectivirgula (SR) model of HP to identify genetic loci and candidate genes associated with disease development. We exposed the parental strains, C57Bl/6 and DBA/2, and twenty six BXD strains to SR for 3 weeks and analyzed the lungs 18h after the last exposure. Bronchoalveolar lavage (BAL) was performed and cells recovered from the BAL fluid were analyzed by flow cytometry to determine the frequency of infiltrating immune cells. The results reveal variability in the cellular composition of the BAL and significant differences in the level of activated CD4+ and CD8+ T cells and B cells across the strains. H&E staining of lung tissue revealed significant differences in the extent of granuloma formation across strains. These data support the contention that genetic differences critically influence SR responsiveness given that environmental factors were held constant.
### Functional connectivity in high beta band during object naming

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**Background:** To study functions of the brain during high-level cognitive tasks, it is informative to investigate not only dynamics of the functional connectivity (FC) of a single frequency band, but also the interactions between network dynamics in different frequency bands. It is still unclear how FC dynamics of different beta sub-bands correlate with each other during language processing.

**Methods:** We acquired ECoG data from a patient with epilepsy while performing an object naming task and calculated the time-frequency FC in all beta sub-bands using phase locking value (PLV). We extracted the FC degree in all subdural electrodes which is a graph measure indicating the total number of connections in an electrode. Finally, we calculated the Pearson correlation between the time-courses of the FC degree in all beta sub-bands to evaluate the similarity of FC brain dynamics in these sub-bands.

**Results:** The correlations between the high beta band and other sub-bands were smaller than the correlation between other bands. Moreover, the dynamics of FC in high beta band sustained a truly different pattern from other sub-bands, mostly concentrated on premotor & motor areas, which is consistent with previous studies.

**Conclusions:** These observations indicate that the dynamics of FC in the high beta band may contain specific information, different from other beta sub-bands, about how the brain processes a linguistic task, such as object naming.

**Funding/Grant Support:** Children's Foundation Research Institute

### Application of pattern recognition in four group classification of Alzheimer's disease by integrating sMRI and rs-fMRI

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**Background:** Structural MRI (sMRI) and resting-state functional MRI (rs-fMRI) have provided promising results in the diagnosis of Alzheimer's disease (AD) and its prodromal stage, mild cognitive impairment (MCI). Our aim was to identify patients with MCI who progress to AD (MCI-C) from those with MCI who do not progress to AD (MCI-NC) by integrating features extracted from rs-fMRI and sMRI.

**Methods:** 25 MCI-C, 62 MCI-NC, 34 AD, and 21 healthy controls (HC) were included. The rs-fMRI features were calculated using the graph theory. The sMRI features were based on the volumetric measures, e.g., cortical thickness. We trained and tested support vector machine and decision tree classifiers to classify four groups (MCI-C, MCI-NC, AD, and HC). We utilized the 10-fold cross-validation to evaluate performances of the classifiers.

**Results:** The Bagged decision tree was the best classifier that provided an accuracy of 63.8% in four group classification (the accuracy by chance is 25%). The area under the receiver operating characteristic curve of this classifier for the binary classification of AD, MCI-C, MCI-NC, and HC were 0.86, 0.89, 0.91, and 0.8, respectively.

**Conclusions:** We integrated rs-fMRI and sMRI features and classified four groups with an accuracy of 63.8%. Our results demonstrated potential of an integrated rs-fMRI and sMRI approach for identification of the early stage of AD.

**Funding/Grant Support:** Children's Foundation Research Institute & Alzheimer's disease neuroimaging initiative (ADNI)
**GS05**

Analysis of electrocorticographic recordings by empirical mode decomposition to detect seizure onset zone

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**Background:** Visual inspection of the ictal electrocorticographic (ECoG) recordings is routinely utilized to localize the seizure onset zone (SOZ). However, this procedure is time consuming, subjective, and may not result in seizure-freedom in all patients. The aim of this study was to localize the SOZ based on ECoG recordings using the empirical mode decomposition (EMD)

**Method.** Methods: We retrospectively analyzed 19 seizures in six patients who underwent a Phase II epilepsy surgery evaluation. All patients were seizure-free after a minimum 6-month follow-up. The ensemble EMD method was used to decompose the ECoG signals into intrinsic mode functions (IMF) components. After extracting the IMF components, average power of the first four components across subdural electrodes within the following three groups of electrodes were calculated: 1) visually-detected SOZ (vSOZ) electrodes, 2) resected electrodes, and (3) non-resected electrodes. The vSOZ electrodes were identified by a board certified epileptologist (JW, co-author of this abstract).

**Results:** The powers of IMF components of the vSOZ and the resected electrodes were significantly larger than that of non-resected electrodes in all patients (P < 0.013).

**Conclusions:** Decomposition of ECoG signal to IMF components based on the EMD approach can identify the SOZ electrodes, and this approach may be used as a complement to the conventional approach of visually identifying the SOZ.

**Funding/Grant Support:** Children's Foundation Research Institute

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**GS06**

Investigating role of superior temporal gyrus in speech using ECoG data

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**Background:** Previous studies have demonstrated that superior temporal gyrus (STG) is associated with receptive language; however, our understanding about its function and its interaction with other areas is still limited.

**Methods:** We investigated the role of STG by comparing its function during an auditory and visual verb generation tasks (VGT). Electrocorticographic (ECoG) data were acquired from a patient with epilepsy while performing VGT. Partial directed coherence (PDC) was used to determine time-frequency effective connectivity between ECoG electrodes. Then the bootstrap resampling statistical test was employed to find significant connections (compared to pre-stimulus onset). Finally, inflow and outflow of each electrode were computed in each time to explore information flow of electrodes.

**Results:** Outflow and inflow patterns of both VGTs are similar during verb selection and articulation. Only auditory VGT contained considerable inflow in STG during perception and also outflow in STG appeared earlier and was stronger during this period. Furthermore, outflow in STG was observed in both VGTs even after perception. Conclusions: Our results demonstrated that STG has an important role in auditory perception and this area is also involved in other language processes, like word selection, as we found a connection from STG to Broca's area and motor cortex in our connectivity analysis.

**Funding/Grant Support:** Children's Foundation Research Institute
Poster Presentations:
Health Professional Students
**MS01**

**Perampanel Use in Children with Epilepsy: A Real-World Retrospective Review of Clinical Use in a Tertiary Epilepsy Center**

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**Introduction:** Perampanel, a selective, non-competitive AMPA receptor antagonist, is approved for the treatment of specific seizures types in patients with epilepsy ages ≥12 years. Due to the lack of information regarding the use of perampanel in children, this study was designed to assess the use of perampanel (i.e., retention rate, dosing, and safety) in children with refractory epilepsy.

**Methods:** After obtaining IRB approval, candidates for the study were obtained through a search of the electronic medical record database. The primary efficacy endpoint we obtained was retention rate, along with information on patient demographics, anti-epileptic drug (AED) history, seizure frequency, perampanel dosage data, and adverse events (AEs).

**Results:** In our patient population (N=100), 71% of patients had improvement of their seizures, based on the clinicians’ impression, with 34% of patients remaining on perampanel at 24 months, 21% at 12 months, and 19% at 6 months. The mean perampanel dose (range) was 6.18mg (0.5–16.0mg) and the mean age was ~12 years. AEs were reported by almost half (49%) with the most common being aggression, emotional instability, somnolence, and dizziness.

**Conclusions:** This is the largest clinical trial of real world experience with perampanel. We documented efficacy and a good safety profile in children, consistent with that observed during prospective clinical studies in adolescents and adults.

**Funding/Grant Support:** Jacob Meek Fund, Neuroscience Institute, Le Bonheur Children’s Hospital

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**MS02**

**Antimicrobial Therapy and Subsequent De-escalation in Uncomplicated Urinary Tract Infections in Hospitalized Children**

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**Background:** Urinary tract infection (UTI) is a common indication for antimicrobial therapy in children. We hypothesized that broad spectrum antibiotics are used despite susceptibility to narrow spectrum antibiotics.

**Methods:** Children 0-18 years of age, admitted with uncomplicated, community-acquired UTI from 2013 to 2015 were included. Urine culture results and antibiotics therapy were examined. Proportions were compared using chi-square test.

**Results:** 573 patients diagnosed with UTI received ≥ 5 days of antibiotics (mean of 11.2 days). 525 had growth in urine cultures, 85% of which grew Enterobacteriaceae (E. coli 90%, K. pneumoniae 6%) with the following non-susceptible rates: aminopenicillins (AP) 58%, first generation cephalosporins (1GC) 8%, 3rd generation cephalosporin (3GC) 2%, trimethoprim-sulfamethoxazole (TMP-SMX) 23%; 6 produced extended spectrum beta-lactamases. Common antibiotics used were: 3GC 49%, AP 21%, TMP-SMX 12% and 1GC 5%. 412 UTI pathogens were known to be susceptible to AP, 1GC or TMP-SMX, but broader spectrum agents were used in 220 patients (46.6%). De-escalation to a narrow spectrum agent occurred less frequently when the bacterial count was >10,000 CFU/mL (44.4% vs 64.6%, p = 0.007).

**Conclusion:** Unnecessarily broad-spectrum antibiotic therapy is used in pediatric UTI. These data will help inform antibiotic stewardship strategies to promote use of narrow spectrum antibiotics and thus reduce the development of resistant organisms.
**Poster Presentations- Health Professional Students**

**MS03**

The Role of HSV PCR in the Early Detection and Diagnosis of Neonatal HSV Encephalitis

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**Background:** Signs and symptoms of neonatal Herpes Simplex Virus encephalitis (HSVE) frequently overlap with those of serious bacterial and other more benign infections. Delay in diagnosis and therapy is associated with worse outcomes. The purpose of this study was to determine if reflex HSV polymerase chain reaction (PCR) testing of CSF from neonates improves the timeliness of the diagnosis of HSVE compared with physician ordered PCR.

**Methods:** Data was collected on neonates 2 months of age and younger with CSF PCR for HSV performed between January 2010 to July 2016. Reflex testing of CSF specimens in neonates under 4 weeks of age began March 2013. We compared the rate of positive tests and the time to test completion between the two periods.

**Results:** There were twice as many CSF HSV PCR tests in infants under 2 months post-reflex compared to pre-reflex (1032 vs. 553). There were 5 positives in the pre-reflex period and 6 in the post-reflex period, including one false positive, resulting in a rate of 0.9% in the pre-reflex period and 0.48% in the post-reflex period (p=0.3). The median time from admission to PCR was 4.6 hours pre-reflex and 3.6 hours post-reflex (p=0.1). There was no difference in the outcomes between the two time periods with 3 (60%) having sequelae in the pre and 4 (80%) having sequelae in the post-reflex period (p=0.5).

**Conclusions:** Reflex HSV PCR on CSF of infants under 4 weeks did not improve time to diagnosis on outcomes in infants with HSVE.

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**MS04**

Prolonged viral replication and relationships with clinical factors in respiratory syncytial virus (RSV) infected infants

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We recently showed naturally infected infants have heterogeneous viral clearance patterns with some infants remaining RSV positive for ≥30 days after symptom onset. Such viral persistence may provide insight for future treatments and improvements in clinical care. In our study, we examined potential relationships between clinical factors and viral dynamics over 3 RSV seasons from 2014-2017. We hypothesized infants with higher viral load and delayed viral clearance will have greater disease severity.

We performed linear regression analysis comparing infants’ daily viral loads with their corresponding 12-hour respiratory rate to discharge respiratory rate ratio; no statistically significant relationship was established. Linear regression analysis comparing viral clearance within the first 48 hours of study enrollment and length of stay did not show a statistically significant relationship. We performed unpaired t-tests comparing viral clearance within the first 48 hours and use of mechanical ventilation and admission to Intensive Care Unit (ICU); there were no detected statistically significant relationships. Effects of viral load AUC and statistical control of host-factor differences to evaluate viral quantity-disease severity relationships is pending. Infants hospitalized with RSV infections have viral load measurements persisting for ≥30 days, but the correlation between viral load and viral clearance with clinical factors has yet to be determined.

**Funding/Grant Support:** DeVincenzo Lab Internal Funds
Patient with features of Floating Harbor Syndrome due to a novel mutation in the CREBBP gene

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Rubinstein-Taybi syndrome (RSTS) is a rare autosomal dominant (AD) disorder with typical facial features, microcephaly, broad thumbs and halluces, intellectual disability, and postnatal growth retardation. The diagnosis of RSTS is primarily clinical, mutations attributed to the CREBBP gene (55%) and to EP300 gene (8%). Floating Harbor Syndrome (FHS) is a rare, AD disorder characterized by short stature, delayed bone maturation, clinodactyly/syndactyly, short thumbs, varying degrees of intellectual disability, and distinct craniofacial appearance, caused by heterozygous truncating mutations in the SRCAP gene. It is known that the SRCAP gene is a co-activator of the CREBBP gene. There is clinical overlap between RTS and FHS. We report a 4 year-old female, with failure to thrive, dysmorphia, cataracts, sacral dimple, tethered cord, 2-3 toes syndactyly, hirsutism, and speech and developmental delay. The family and pregnancy history was negative. She had phenotypic features of FHS, however, molecular analysis of the SRCAP gene was negative. Whole Exome Sequencing found a novel change in the CREBBP gene, which has not been previously described in connection with RSTS. This report describes a clinically and genetically novel presentation of RSTS, which suggests that atypical or mild cases of RSTS may be misdiagnosed as FHS. Comprehensive molecular diagnosis of RSTS and FHS will allow a better understanding of the prevalence and phenotypic spectrum of both conditions.

Funding/Grant Support: Le Bonheur Children's Hospital

Gastrostomy tubes in neonates - Indications and 2-year outcomes at a children's hospital

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Purpose: Gastrostomy tubes (G-tubes) are used to aid in the feeding of infants who are unable to swallow or acquire oromotor coordination. Studies have shown that G-tube placement in neonates can indicate adverse outcomes in the infants’ development and neurodevelopmental delay. The objective of our study was to identify the characteristics of infants requiring g-tubes and review their post-discharge outcomes.

Methods: This is a retrospective chart review of all patients receiving g-tubes from March 2013-December 2016 at the NICU at LeBonheur Children’s Hospital. Patients were identified using appropriate ICD/CPT codes. All data were collected from patient charts.

Results: 225 (12%) patients in the NICU were identified as having undergone G-tube placement. Half of this cohort was female and African American. Median age at g-tube placement was 13(6, 24) wk after birth, while 204(91%) had laparoscopic placement. 115(51%) needed g-tube for dysphagia, followed by failure to thrive in 17(8%); 63(28%) infants had multiple indications. Non-malformation infants received G-tubes later (53 vs. 47 wk, p=0.001) than infants with malformations. At 1 year post-surgery, 70% of patients still had G-tubes, and at 2 years post-surgery, 73/177 (41%) developed normal feeding. Conclusions: Both term and preterm infants needed g-tube placement for variety of reasons, primarily dysphagia. Infant with malformations received g-tube at an earlier age and most infants relied on them for at least 1 year.

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**Guidelines for Maternal Chorioamnionitis Evaluation Reduce Antibiotic Use in Neonates**

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**Background:** Chorioamnionitis (CA) complicates up to 4% of all births in the US, however, the diagnosis varies. CDC guidelines (2010) require a CBC, blood culture, and IV antibiotics (ABX) for minimum of 48 h for a neonate born to a mother with CA. With maternal fever as the prevailing clinical diagnostic sign of CA, over diagnosis leading to unnecessary tests and antibiotics in the newborn is an issue. New guidelines by NICHD suggest replacing the term “CA” with the term “Triple I” (Intrauterine infection, inflammation, or both) and provide specific criteria for diagnosis and management. These guidelines were implemented at our NICU in January 2017. The purpose of this study was to evaluate if the guidelines were followed and the efficacy of the guidelines in optimizing the use ABX for neonates.

**Methods:** A retrospective chart review study of late preterm and term infants born to mothers diagnosed with CA from June 1, 2016 through June 14, 2017 was conducted. We collected demographic information, laboratory data, and type and duration of antibiotics given. Data are presented as means ±SD and groups compared with t-test.

**Results:** We reviewed 114 charts—66 infants from before the guidelines implementation, and 48 after. Table shows population characteristics. Guidelines were appropriately followed in 60% of cases, 19% had inadequate documentation and 21% did not appropriately follow guideline. During the post-guideline period we saw 12% reduction in ABX initiation (85% vs 97%, p=.03) and the mean duration of antibiotics use was reduced (41h vs 52h).

**Conclusions:** Implementation of guidelines led to a statistically significant but moderate reduction in the initiation and average duration of antibiotics use. We hope to improve education in the unit to achieve better adherence to the guidelines and decrease unnecessary antibiotic use in neonates.

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**Optimal Nutrition for Extra Uterine Growth in <1250g Birth Weight Infants**

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**Background:** Extra uterine growth restriction (EUGR) is a common problem in premature infants. Higher caloric intakes have been associated with improved growth. As their remains variability among reports describing optimum recipe associated with least degree of EUGR, our objective was to review the effect of higher caloric intakes on anthropometric measurements (AM) at our hospital. We hypothesized that in premature infants, higher caloric intake is associated with improved growth.

**Methods:** Retrospective chart review of infants discharged from Regional One Hospital 2016-2017 with BW <1250. Detailed nutritional daily intakes were collected including parenteral alimentation, milk type, volume, and milk fortification. Head circumference (HC), length, and weight measurements were collected at birth and at 1500g. Data are reported as z-scores.

**Results:** Data were available for 32 infants with mean birth weight of 948 ±220 g and 27 ±2 weeks gestational age. At 1500g weight, there was a significant decrease in all three AM z-scores. Higher mean daily protein intake was significantly associated with better weight z-score growth, p=0.02 and trended towards significance on length, p= 0.06, and on HC, p=0.08 after adjusting for fat intake and baseline birth z-scores.

**Conclusion:** Higher protein intakes are associated with a lower severity of EUGR in premature infants. Future studies should focus on finding saturation levels of this benefit and investigate development of side effects with higher protein intakes.
Using Bibliometrics to Analyze the State of Academic Productivity in US Pediatric Surgery Training Programs

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Background: The Accreditation Council for Graduate Medical Education (ACGME) Common Program Requirements state that faculty must establish and maintain an environment of inquiry and scholarship. Bibliometrics, the statistical analysis of written publications, assesses scientific productivity and impact. The goal of this study was to understand the state of scholarship at Pediatric Surgery training programs.

Methods: Following IRB approval, Scopus was used to generate bibliometric profiles for US Pediatric Surgery training programs and faculty. Statistical analyses were performed.

Results: Information was obtained for 430 surgeons (105 female) from 48 US training programs. The mean lifetime h-index/surgeon for programs was 14.4 +/- 4.7 (6 programs above 1SD, 9 programs below 1SD). The mean 5-year h-index/surgeon for programs was 3.92 +/- 1.5 (7 programs above 1SD, 8 programs below 1SD). Programs accredited after 2000 had a lower lifetime h-index than those accredited before 2000 (p=0.0378). Female surgeons had a lower lifetime h-index (p<0.0001), 5-year h-index (p=0.0049), and m-quotient (p<0.0001) compared to males. Mean lifetime h-index increased with academic rank (p<0.0001), with no gender differences beyond the assistant professor rank (p=NS).

Conclusion: Variability was identified based on institution, gender and rank. This information can be used for benchmarking the academic productivity of faculty and programs and as an adjunct in promotion/tenure decisions.

Papillary muscle mass quantification using cardiovascular magnetic resonance for the diagnosis of pediatric left ventricular non-compaction

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Introduction: Cardiovascular magnetic resonance (CMR) is commonly used to diagnose left ventricular noncompaction (LVNC), but few studies focus on papillary mass as potential diagnostic criteria. This study was performed to compare papillary mass in LVNC with normal controls.

Methods: From 2013-2017, a retrospective cohort study of 86 children (27 LVNC myopathy, 21 isolated LVNC, and 38 controls) was performed. Left ventricular (LV) volumes, ejection fraction (LVEF), non-compacted mass percentage (LVNCM%), and papillary mass indexed (LVPMI), were measured. LV papillary mass percentage (LVPM%) was calculated as a percentage of the compacted mass. CMR measurements were compared using a non-parametric test. Receiver operating characteristic curve (ROC) analysis was performed.

Results: There was no difference in median age in isolated LVNC (14.7 years) compared to controls (14.6, p=0.59) but LVNC myopathy (17.3) were older (p<0.01). The LVNCM% was higher while the LVPMI and LVPM% were lower in isolated LVNC compared to controls. There was no difference in LVNCM%, LVPMI, or LVPM% between isolated LVNC and LVNC myopathy. The ROC analysis using standard CMR diagnostic criteria of LVNC revealed that a LVPM% lower than 5.6% was predictive of LVNC with a specificity of 92% (CI: 86-98) and a sensitivity of 88% (CI: 82-94).

Conclusions: A papillary mass percentage less than 5.6% is diagnostic for LVNC with high sensitivity and specificity in children.
Prediction of Seizure Outcome Using Presurgical DTI Structural Connectivity

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Rationale: Up to 80% of temporal lobe surgical resection comes out with seizure remission in which complete seizure freedom occurs in approximately 40%. Diffusion tensor imaging (DTI) has been applied in evaluating brain network malfunctions in patients with temporal lobe epilepsy (TLE). It has been demonstrated that hippocampus and thalamus have an important role in TLE. We hypothesize that the brain network topology in these areas constructed using DTI can predict seizure outcome.

Methods: Ten TLE patients who underwent resection for treatment of intractable epilepsy were included. Seven patients were seizure-free and 3 patients were non-seizure-free after 6-month follow-up. White matter fiber tractography was performed on preoperative DTI data to extract the structural connectivity. Two local graph measures, i.e. betweenness centrality and node strength, in hippocampus and thalamus were calculated. Using these graph measures in two areas as input features of a support vector machine (SVM), we trained and cross-validated a classifier to predict seizure outcome.

Results: The SVM classifier was able to predict the surgical outcome with 90% accuracy and false classification of only a single case.

Conclusions: Noninvasive methods can have a pivotal impact on the field by providing insight into the prediction of surgical outcome in seizure freedom. Our results suggest that the structural connectivity metrics of DTI may have clinical value for predicting surgical outcome.

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Innate Lymphoid Cell (ILC) Populations in Hirschsprung-Associated Enterocolitis (HAEC)

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Hirschsprung Disease (HD) is a common cause of neonatal bowel obstruction resulting from failure of enteric nervous system development (aganglionosis) in the distal bowel. HAEC is a potentially life-threatening inflammatory condition that affects infants pre- and post-surgery, suggesting defects in HD extend beyond the aganglionic segment. Innate Lymphoid Cells (ILC) are a recently characterized population of tissue-resident innate immune cells that contribute to gut homeostasis and protection. We hypothesized that gut ILC numbers would be altered in mice with HD prior to HAEC. Using the neural crest-conditional deletion of EdnrB murine model of HD, we performed flow cytometry to characterize ILC1, ILC2 and ILC3 in small and large intestine. Our results confirm that ILCs are small populations of cells in the small and large intestine. No statistically significant differences in ILC1 or ILC3 were seen between genotypes. However, we noted decreased ILC2 in the small intestine of HD mice vs WT. ILC2 secrete type 2 cytokines and play a pro-inflammatory role in gut inflammation. Ongoing work is focused on the functional consequences of these findings, including ILC2 function (cytokine production) in HAEC, and understanding the complex relationship between the enteric nervous and mucosal immune systems.

Funding/Grant Support: Office of the Executive Dean, College of Medicine
In complex surgical procedures, operating room time contributes to a large amount of total costs with perioperative-operative delays directly contributing to these. While multiple surgical subspecialties have undertaken studies to address OR efficiency, little has been done regarding pediatric spine surgery. The purpose of this study is to evaluate OR efficiency in posterior spinal fusion (PSF) surgery for scoliosis at a large, high volume private children’s hospital, focusing on the effect of surgeons, anesthesiologists, and nurse anesthetists (cRNAs), both individually and as teams. These findings will allow us to study the high-performing teams in order to improve efficiency for all surgical teams.

Methods: An IRB approved review of 183 consecutive PSFs were performed over a 2 year period were reviewed and multiple perioperative/intraoperative time intervals were recorded. There were 4 fellowship trained pediatric orthopedic surgeons, 7 pediatric anesthesiologists, and 5 (cRNA) were evaluated individually and as teams based time on various time intervals. Mean time intervals were compared using ANOVA adjusted for etiology, BMI, fusion levels and osteotomy. Patient wait time was also adjusted for patients’ distance from the hospital, and intraoperative intervals were also adjusted for the occurrence of a staff switch. Results: Adjusted for confounding factors, there was a significant difference between surgeons in mean surgery time (p=0.01; adjusted means: 284-329 min) In regards to prep time (surgery start minus in room time) there were significant differences between surgeons (p<0.001, adjusted means 90-107min) and between surgeon/anesthesia pairs (p=0.03, adjusted means 856-115min). In regards to wait time (in room minus arrival time) there were also significant differences between anesthesiologists (p<0.001, adjusted means 53-95 min) and between surgeon/anesthesia pairs (p<0.001, adjusted means 53-95 min). Conclusion: Consistent with other surgical subspecialties, we found that the surgeon in the pediatric orthopedic operating room has a significant effect on multiple OR time intervals. The results also suggest that certain surgeon-anesthesiologist teams work more efficiently together than others. Significance: This is the first study to our knowledge in pediatric orthopedics to specifically address OR personnel factors related to perioperative efficiency and the first to evaluate surgeon/anesthesiologist pairs. These findings will allow future study of these high/low performing teams to determine the factors affecting these variables in order to improve the performance of all surgical teams.
Computed Tomography Findings Predict the Need for Intervention in Children with Blunt Liver Injuries

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Introduction: A standardized method for classifying blunt solid organ injury in adults has existed for nearly three decades. However, there is not a standard approach for pediatric patients and management varies widely among centers. We hypothesize that radiologic findings in pediatric abdominal trauma can be used to predict the need for intervention.

Methods: Following IRB-approval, a retrospective study was performed at an ACS-verified Level 1 Pediatric Trauma Center for 134 children (<18 years) who had sustained liver injuries. Radiologic findings were extracted from CT reports or, when missing, measured from original imaging. Radiologic variables included liver laceration size, number of Couinaud segments involved, presence of hemoperitoneum, hepatic vessel involvement, lobe involvement, and the presence of subcapsular or pericapsular hematoma. Interventions included surgical intervention, angiography, or blood transfusion. Continuous variables were compared with a t-test, and a chi-square analysis was used for categorical variables.

Results: The mean age was 7.5 +/- 5.2 years with 59% male and 52% African-American. Hemoperitoneum, length of liver laceration and number of Couinaud segments involved predicted the need for intervention in children with blunt liver injuries (table). Normalizing continuous variables by age did not change the significance. However, the presence of hematoma and the proximity of the injury to the major hepatic vessels, important variables in the adult grading system, did not predict the need for intervention in children.

Conclusions: Pediatric patients who present with liver injury from abdominal trauma with hemoperitoneum, larger laceration and more liver segments involved are more likely to require intervention. Contrary to the adult trauma guidelines, hematoma and proximity to the major hepatic vessels did not predict the need for intervention in children. These findings build upon the expanding literature indicating the need for pediatric-specific guidelines for trauma management.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention (+)</th>
<th>Intervention (-)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Hemoperitoneum</td>
<td>41 (30.60%)</td>
<td>21 (15.67%)</td>
<td>0.0013</td>
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<tr>
<td>Liver Laceration length (mm)</td>
<td>45.6 36.8</td>
<td>0.04</td>
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<tr>
<td>Couinaud segments (mean, n)</td>
<td>2.44 2.00</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Hepatic Vessels</td>
<td>18 (13.43%)</td>
<td>10 (7.46%)</td>
<td>0.1574</td>
</tr>
<tr>
<td>Subcapsular Hematoma</td>
<td>22 (16.42%)</td>
<td>12 (8.96%)</td>
<td>0.1238</td>
</tr>
</tbody>
</table>
Acknowledgements

Abstract Judges

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