29th Annual
PEDIATRIC RESEARCH SYMPOSIUM

May 13-14, 2019
Towsley Center

University of Michigan
DEPARTMENT OF PEDIATRICS
Michigan Medicine

C.S. MOTT
CHILDREN’S HOSPITAL
MICHIGAN MEDICINE

1500 East Medical Center Drive
Ann Arbor, MI 48109-5718
(734) 764-5173
http://medicine.umich.edu/dept/pediatrics/
## PROGRAM-AT-A-GLANCE

### MONDAY, MAY 13

<table>
<thead>
<tr>
<th>Time</th>
<th>Location</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>3:00 – 6:00 PM</td>
<td>Towsley Lobby</td>
<td>Poster Session</td>
</tr>
</tbody>
</table>
| **Valerie Opipari Endowed Lectureship** | Dow Auditorium | Cytokine signaling restrains inflammatory bowel disease development: the bright side of cytokine signaling  
D. Brent Polk, MD, AGAF |
| 4:00 – 5:00 PM   | Dow Auditorium   | (Poster Session continues after lecture)                            |

### TUESDAY, MAY 14

<table>
<thead>
<tr>
<th>Time</th>
<th>Location</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30 - 8:00 AM</td>
<td>Towsley Lobby</td>
<td>Refreshments (coffee, tea, bagels)</td>
</tr>
<tr>
<td>8:00 - 10:00 AM</td>
<td>Dow Auditorium</td>
<td>Grand Rounds / Plenary Session</td>
</tr>
<tr>
<td><strong>Grand Rounds</strong></td>
<td>Dow Auditorium</td>
<td>Shining a Light on an Old Problem: Neonatal Jaundice</td>
</tr>
<tr>
<td>8:00 - 9:00 AM</td>
<td>Dow Auditorium</td>
<td>Alex Kemper, MD, MPH, MS</td>
</tr>
<tr>
<td>9:00 - 10:00 AM</td>
<td></td>
<td>Plenary Session Presentations</td>
</tr>
<tr>
<td>10:00 – 10:30</td>
<td></td>
<td>Awards Ceremony</td>
</tr>
<tr>
<td>10:30 - 11:30 AM</td>
<td>Sheldon &amp; Dow Auditoriums</td>
<td>Breakout Session 1 (DEI) - Sheldon Breakout Session 2 - Dow</td>
</tr>
<tr>
<td>11:30 - 12:30 PM</td>
<td>Sheldon &amp; Dow Auditoriums</td>
<td>Breakout Session 3 - Sheldon Breakout Session 4 - Dow</td>
</tr>
<tr>
<td>12:30 - 1:30 PM</td>
<td>Towsley Dining Room (lower level)</td>
<td>Lunch Networking-Research Roundtables</td>
</tr>
</tbody>
</table>
TABLE OF CONTENTS

Welcome......................................................................................................................... 3
Symposium Program Objectives ....................................................................................... 3
Speaker/Presenter Disclosures ........................................................................................ 3
Acknowledgments ........................................................................................................... 4
Awards ............................................................................................................................. 5
Keynote Speakers ............................................................................................................ 6-7
Poster Session ............................................................................................................... 8
Valerie Opipari Endowed Lectureship ............................................................................ 9
Plenary Session .............................................................................................................. 8-10
Breakout Sessions
  Breakout Session 1 ....................................................................................................... 11
  Breakout Session 2 ....................................................................................................... 12
  Breakout Session 3 ....................................................................................................... 13
  Breakout Session 4 ....................................................................................................... 14
Research Round Tables / Lunch ..................................................................................... 15
Printed Abstracts ............................................................................................................. 16-154
Pediatric Research Office ......................................................................................... 137-139
(Pre- and Post-Award Contacts & Services)
WELCOME

This symposium has been made possible by the research efforts of faculty, fellows, residents, medical, graduate and undergraduate students, and research personnel. We are very proud of the extent and breadth of our research programs and activities, and we trust you will enjoy the day's activities.

This year we are pleased to host keynote lectures from D. Brent Polk, MD (Keck School of Medicine, USC; Children’s Hospital of Los Angeles), and Alex R. Kemper, MD, MPH, MS (Ohio State University College of Medicine; Nationwide Children’s Hospital).

140 abstracts were submitted by Michigan Medicine faculty, fellows, residents, students, and staff performing research in pediatric medicine.

SYMPOSIUM PROGRAM OBJECTIVES

This event has been planned for faculty, residents, students and others performing research in pediatrics at the University of Michigan. Our goal is to provide an opportunity for participants to (1) be informed of state-of-the-art research in Pediatrics by inter/nationally recognized keynote lecturers; (2) present and discuss their current research in an educational forum; (3) compete for awards promoting young investigators in Pediatric research; (4) be informed of peers’ research across all Pediatric specialties; and (5) have the opportunity to interact and form collaborations with other Pediatric investigators.

The objective of the Pediatric Research Symposium is to present new research in the Pediatric world that can be taken back to the clinics for practical implementation.

Disclosure of Relevant Financial Relationships with Commercial Interests. The following symposium planners and speakers have no relevant financial relationships:

| Brigid Gregg, MD | D. Brent Polk, MD |
| Sarah Reeves, PhD | Alex Kemper, MD |
ACKNOWLEDGEMENTS

Donna M. Martin, MD, PhD
Department of Pediatrics, Interim Chair

Julie C. Lumeng, MD
Associate Chair for Research

Brigid E. Gregg, MD    Sarah L. Reeves, PhD, MPH
Symposium Program Chairs

We thank our faculty who served as symposium advisory panel members, abstract reviewers, and session moderators for their time and effort in the planning and review process of this important endeavor.

<table>
<thead>
<tr>
<th>PRS Advisory Panel</th>
<th>PRS Ad Hoc Reviewers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heather Burrows, MD, PhD</td>
<td>Jeremy Adler, MD, MS</td>
</tr>
<tr>
<td>Louis Dang, MD, PhD</td>
<td>Margeaux Naughton, MD</td>
</tr>
<tr>
<td>Naomi Laventhal, MD, MA</td>
<td>Ryan Barbaro, MD</td>
</tr>
<tr>
<td></td>
<td>Jenni Bermick, MD</td>
</tr>
<tr>
<td></td>
<td>R. Alex Blackwood, MD, PhD</td>
</tr>
<tr>
<td></td>
<td>Heather Burrows, MD, PhD</td>
</tr>
<tr>
<td>Gabriel Cara-Fuentes, MD</td>
<td>Gabriel Cara-Fuentes, MD</td>
</tr>
<tr>
<td>Erin Carlton, MD</td>
<td>Karl Desch, MD</td>
</tr>
<tr>
<td>Lindsay Caverly, MD</td>
<td>MacDonald Dick II, MD</td>
</tr>
<tr>
<td>Melissa Cousino, PhD</td>
<td>Lindsay Ellsworth, MD</td>
</tr>
<tr>
<td>Louis Dang, MD, PhD</td>
<td>David Hanauer, MD, MS</td>
</tr>
<tr>
<td>Karl Desch, MD</td>
<td>Catherine Keegan, MD, PhD</td>
</tr>
<tr>
<td>Jordan Shavit, MD, PhD</td>
<td>Carl Koschmann, MD</td>
</tr>
<tr>
<td>Renée Shellhaas, MD, MS</td>
<td>Naomi Laventhal, MD</td>
</tr>
<tr>
<td>Kanakadurga Singer, MD</td>
<td>Kera Luckritz, MD</td>
</tr>
<tr>
<td>Mark Russell, MD</td>
<td>Zubin Modi, MD</td>
</tr>
<tr>
<td>Matthew Sampson, MD</td>
<td></td>
</tr>
<tr>
<td>Ellen Selkie, MD, MPH</td>
<td></td>
</tr>
<tr>
<td>Shane Quinonez, MD</td>
<td></td>
</tr>
<tr>
<td>Jenny Radesky, MD</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Michael Watson Jr, MD, PhD</td>
</tr>
<tr>
<td></td>
<td>Jason Weinberg, MD</td>
</tr>
<tr>
<td></td>
<td>Angela Weyand, MD</td>
</tr>
<tr>
<td></td>
<td>Esther Yoon, MD</td>
</tr>
<tr>
<td></td>
<td>Julie Zibro, MD, PhD</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4
### 2019 ABSTRACT AWARDEES

<table>
<thead>
<tr>
<th>Name</th>
<th>Award</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kao-Ping Chua, MD, PhD</td>
<td>Faculty Award for Health Services Research</td>
</tr>
<tr>
<td>Robin Cook, MD, PhD</td>
<td>Resident Research Award</td>
</tr>
<tr>
<td>Melissa Cousino, PhD</td>
<td>Faculty Award for Clinical investigation</td>
</tr>
<tr>
<td>Hannah Hafner, BS</td>
<td>Staff Award for Basic Science Research</td>
</tr>
<tr>
<td>Prashanthi Kandavel, MS, MD</td>
<td>Award for Diversity, Equity, and Inclusion Research</td>
</tr>
<tr>
<td>Edwin Klein, BS</td>
<td>Medical Student Research Award</td>
</tr>
<tr>
<td>Theresa Kowalski-Dobson, MPH</td>
<td>Staff Award for Health Services Research</td>
</tr>
<tr>
<td>Rohini Majumdar, BS</td>
<td>Undergraduate Student Research Award</td>
</tr>
<tr>
<td>Daniel Peltier, MD, PhD</td>
<td>Faculty Award for Basic Science Research</td>
</tr>
<tr>
<td>Elaine Ritter, PhD</td>
<td>Fellow Award for Basic Science Research</td>
</tr>
<tr>
<td>Liza Rosenbloom, BS</td>
<td>Undergraduate Student Research Award</td>
</tr>
<tr>
<td>Andrew Singer, MD</td>
<td>Faculty Award for Clinical Investigation</td>
</tr>
<tr>
<td>Ian Thomas, MD</td>
<td>Fellow Award for Clinical Investigation</td>
</tr>
<tr>
<td>Jeffrey Weatherhead, MD</td>
<td>Fellow Award for Quality Improvement</td>
</tr>
<tr>
<td>Huey-Fen Chen, MHA</td>
<td>Honorable Mention</td>
</tr>
<tr>
<td>Amelia Gavulic</td>
<td>Honorable Mention</td>
</tr>
<tr>
<td>Elena Holley, BS</td>
<td>Honorable Mention</td>
</tr>
<tr>
<td>Krittika Pant, BA</td>
<td>Honorable Mention</td>
</tr>
<tr>
<td>Anjali Sura, MD</td>
<td>Honorable Mention</td>
</tr>
</tbody>
</table>
Keynote Speaker – Valerie Opipari Endowed Lectureship

D. Brent Polk, MD, AGAF

Dr. Polk is Professor of Pediatrics and Biochemistry & Molecular Medicine and vice dean for child health at the Keck School of Medicine of University of Southern California; he is the immediate past chair of the Department of Pediatrics for USC and served as Chair of Pediatrics, Physician-in-Chief, Vice President for Academic Affairs and Director of The Saban Research Institute of Children’s Hospital Los Angeles.

His research focuses on the regulation of growth and development of the intestine, making important contributions to our understanding of the relationship between injury, repair and inflammation relevant to inflammatory bowel disease. Polk is a Fellow of the American Gastroenterological Society, the American Association for the Advancement of Science, the Royal College of Physicians of Edinburgh and the Association of American Physicians. He is a member of several professional organizations, including the American Pediatric Society, Crohn’s and Colitis Foundation, the American Society for Biochemistry and Molecular Biology and the Society for Pediatric Research. He is chair of the National Scientific Advisory Board for the Crohn’s & Colitis Foundation and chair of the Gastrointestinal Mucosal Pathobiology initial review group for NIH. He is certified by the American Board of Pediatrics and the Subspecialty Boards in Gastroenterology.

Dr. Polk previously served as chief of the D. Brent Polk Division of Pediatric Gastroenterology, Hepatology and Nutrition, director of the Digestive Disease Research Center and a tenured professor of Pediatrics and Cell and Developmental Biology at Vanderbilt University Medical Center. He received a bachelor’s degree in biology and chemistry from Ouachita University in Arkadelphia, Ark., and his medical degree from the University of Arkansas for Medical Sciences.
Alex R. Kemper, MD, MPH, MS

Dr. Kemper is the Division Chief of Ambulatory Pediatrics at Nationwide Children’s Hospital and Professor of Pediatrics at the Ohio State University College of Medicine. Dr. Kemper completed his pediatric residency training at Duke University followed by combined fellowship training in health services research and medical informatics with residency training in preventive medicine at the University of North Carolina. In 2000, Dr. Kemper joined the faculty at the University of Michigan where he developed an active research program evaluating the delivery and outcomes of preventive services. In 2006, Dr. Kemper returned to Duke University for 11 years, where he expanded his work related to pediatric preventive services, serving as the Chair of the Condition Review Workgroup for the U.S. Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children and as a consultant to Bright Futures. Dr. Kemper is also a member of the U.S. Preventive Services Task Force. In 2011, Dr. Kemper joined the Executive Editorial Board of Pediatrics and developed a new section for the journal focusing on quality improvement. In 2013, he was appointed Deputy Editor of Pediatrics.
Cytokine signaling restrains inflammatory bowel disease development: the bright side of cytokine signaling

D. Brent Polk, MD, AGAF
Keck School of Medicine
Children’s Hospital of Los Angeles

* The poster session continues after Dr. Polk’s presentation.
8-10:00 AM  PLENARY SESSION - Dow Auditorium, Towsley

Welcome

Donna M. Martin MD, PhD

Shining a Light on an Old Problem:
Neonatal Jaundice

Alex Kemper, MD, MPH, MS
Ohio State Univ College of Medicine
Nationwide Children's Hospital

* Plenary Session continues after Dr. Kemper's presentation.
9:00 – 10:00 AM

**PLENARY SESSION (cont)**

**Dow Auditorium**

9:00  **GLOBAL RNA SEQUENCING OF T CELLS AFTER HEMATOPOIETIC STEM CELL TRANSPLANT INDENTIFIES LINC00402 AS A NOVEL REGULATOR OF MOUSE AND HUMAN T CELL FUNCTION**  
~ Daniel Peltier, MD, PhD  
Abstract 3

9:15  **COMMUNICATION ABOUT PROGNOSIS AND END-OF-LIFE IN PEDIATRIC ORGAN FAILURE AND TRANSPLANTATION**  
~ Melissa Cousino, PhD  
Abstract 42

9:30  **OPIOID PRESCRIBING PATTERNS AND OPIOID OVERDOSE RISK IN ADOLESCENTS AND YOUNG ADULTS**  
~ Kao-Ping Chua, MD, PhD  
Abstract 101

9:45  **ESTABLISHING A LEARNING HEALTH SYSTEM FOR CHILDHOOD OBESITY AT MICHIGAN MEDICINE**  
~ Joyce Lee, MD, MPH  
Abstract 118

10:00 – 10:30

**PLENARY SESSION (cont)**

**Dow Auditorium**

Sarah Reeves and Brigid Gregg
Symposium Program Chairs

**AWARD PRESENTATIONS**

*Introduction to Breakout Sessions & Lunch research roundtables*
<table>
<thead>
<tr>
<th>Time</th>
<th>Session Title</th>
<th>Presenters</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:30</td>
<td>TRENDS IN CORTICOSTEROID USAGE AMONG PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN A LARGE LEARNING HEALTH SYSTEM</td>
<td>Prashanthi Kandavel, MS, MD</td>
</tr>
<tr>
<td></td>
<td>PANEL ON DIVERSITY, EQUITY, AND INCLUSION IN RESEARCH</td>
<td>Susan Woolford, MD, MPH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Julie Lumeng, MD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Toby Lewis, MD, MPH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sarah Reeves, PhD, MPH</td>
</tr>
</tbody>
</table>
10:30 – 11:30 AM

**Breakout Session 2 – Dow Auditorium**
Moderators: Naomi Laventhal, MD and Louis Dang, MD, PhD

10:30  **DECREASING EPINEPHRINE DOSING ERRORS DURING NEONATAL RESUSCITATION: A RANDOMIZED SIMULATION TRIAL**
~ Kate Brune, DO  
Abstract 51

10:45  **IMPACT OF DOCUMENTATION ON RESPIRATORY INTERVENTION AMONG NEWBORNS WITH CONGENITAL HEART DISEASE**
~ Ian Thomas, MD  
Abstract 63

11:00  **ELECTROGRAPHIC SEIZURES AND BRAIN INJURY IN CHILDREN ON EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)**
~ Robin Cook, MD, PhD  
Abstract 79

11:15  **IMPLEMENTATION OF A STANDARDIZED SEIZURE ACTION PLAN TO IMPROVE COMMUNICATION AND PARENTAL EDUCATION**
~ Kerri Neville, MD  
Abstract 133
11:30 – 12:30 AM

Breakout Session 3 – Sheldon Auditorium
Moderators:  Antonia Popova, MD and  Lindsay Ellsworth, MD

11:30  SIMPLIFYING SOMATIZATION: REDUCING HEALTHCARE UTILIZATION WITH A CLINICAL PRACTICE GUIDELINE FOR PEDIATRIC SOMATIC SYMPTOM AND RELATED DISORDERS
~ Edwin Klein, BS / Kristin Kullgren, PhD  Abstract 70

11:45  HIGH FAT DIET DURING LACTATION PROGRAMS OFFSPRING RISK FOR NAFLD AND INTESTINAL MICROBIOME AND THE IMPACT OF METFORMIN RESCUE
~ Hannah Hafner, BS  Abstract 29

12:00  RISK FACTORS FOR DEVELOPMENT AND PREVENTION OF PERIANAL FISTULAE IN PEDIATRIC CROHN’S DISEASE
~ Andrew Singer, MD  Abstract 37

12:15  POTENTIAL MULTIFACTORIAL MECHANISMS FOR HORMONE-INDUCED VENOUS THROMBOEMBOLISM
~ Xinge Yu, PhD  Abstract 18
11:30 AM – 12:30 PM

Breakout Session 4 - Dow Auditorium
Moderators: Kimberly Monroe, MD and Michael Watson, MD, PhD

11:30  CONSERVED ROLES FOR CHD7 IN TRANSCRIPTIONAL ELONGATION OF GENES INVOLVED IN NEURAL CREST AND INNER EAR DEVELOPMENT
   ~ Elaine Ritter, PhD       Abstract 23

11:45  QUALITATIVE ANALYSIS OF ADOLESCENTS’ PERSPECTIVES ON TAILORED MESSAGES AND IMAGES
   ~ Theresa Kowalski-Dobson, MPH  Abstract 99

12:00  NEW MEDICAL DEVICE PLACEMENT DURING PEDIATRIC SEVERE SEPSIS HOSPITALIZATION- A NATIONWIDE ESTIMATE
   ~ Erin Carlton, MD            Abstract 100
12:30 PM – 1:30 PM

Lunch
Research Round Tables
(Networking & Resource Sharing)
Towsley Dining Room

This session provides an opportunity for investigators and trainees to ask questions and discuss issues relevant to ‘practicing research.’

The intent of this session is to inform about resources and services, stimulate discussion around different topics, and to survey research needs.

Faculty and staff with knowledge and experience in these areas will be available for discussion and information exchange.

The Children’s Clinical Trials Support Unit
Department Funded Biostatistics/Data Architect Team
Corporate & Foundation Relations
Pediatrics Research Office (PRO)
Pediatrics Diversity, Equity & Inclusion Action Committee
PRINTED ABSTRACTS
Abstract 1

β1 INTEGRIN ACTIVATION AND SIGNALING IN ENDOTHELIUM-INITIATED PODOCYTE INJURY
G. Cara-Fuentes1, M. Venkatareddy2, R. Verma2, S. Turkmen1, P. Garg2
1Pediatric Nephrology, University of Michigan; 2Nephrology, University of Michigan.

Background: Integrins are heterodimeric transmembrane proteins that anchor cells to the extracellular matrix but also play a key role as bidirectional (outside-in and inside-out) signaling mediators. Our aim is to determine the activation state and role of podocyte β1 integrin in a transient model of podocyte injury.

Methods: 8-10 week-old mice were injected intraperitoneally with LPS (10 µg/g) or PBS (control) and urine collected prior to and after injection. In another set of experiments, mice were injected with a β1 integrin “blocking” antibody (HMβ, 2.5 µg/g) 20 hours prior to LPS. Albuminuria was measured by ELISA. Mouse kidney tissue was processed for immunohistochemistry. Glomerular isolation was performed for western blotting and RT-PCR.

Results: LPS injected mice had significantly higher albuminuria than controls. β1 integrin activation, FAK and nephrin phosphorylation occurred on podocytes 18 to 32 hours after LPS injection. The “prophylactic” administration of HMβ1 significantly reduced albuminuria 24 h following LPS, suggesting that activation of podocyte β1 integrin plays a role in albuminuria. HMβ1 bound to glomerular endothelial cells and podocytes, suggesting a possible crosstalk between these cells. Since β1 integrin activation can occur due to outside-in and inside-out signaling, we investigated the timed involvement of endothelial, glomerular basement membrane (GBM) and podocytes. By immunohistochemistry, western blotting and RT-PCR, we found that endothelial and GBM injury preceded β1 integrin activation, nephrin phosphorylation and foot process effacement, suggesting an outside-in β1 integrin activation.

Conclusion: LPS activates β1 integrin on podocytes and leads to nephrin phosphorylation in vivo. Targeting endothelial/podocyte β1 integrin reduces albuminuria. Changes in glomerular endothelial cells and GBM precede podocyte injury, suggesting that activation of podocyte β1 integrin may be triggered by an outside rather than inside signal in this model of podocyte injury.
Abstract 2

POSTNATAL LACTATIONAL EXPOSURE TO POLYCHLORINATED BIPHENYLS AND INFANT GROWTH

L. Ellsworth, H. McCaffery, S. Liu, V. Padmanabhan, B. Gregg

1Neonatal-Perinatal Medicine, University of Michigan
2Center for Human Growth and Development, University of Michigan
3Pediatric Endocrinology, University of Michigan
4Department of Pediatrics, University of Michigan

Background: Infant exposure to environmental chemicals, such as polychlorinated biphenyls (PCBs), may contribute to developmental programming of long-term metabolic disease risk. PCBs persist today given their lipophilic, long half-life state, allowing them to bio-accumulate in adipose tissue with excretion into maternal breast milk. The objective of this study was to test the hypothesis that concentrations of PCBs in breast milk were higher in overweight / obese (OW/OB) compared to normal weight (NW) mothers and milk PCB levels were negatively associated with infant growth trajectory over the first year of life.

Methods: Two-week milk samples from mothers with NW (pre-pregnancy body mass index (BMI) <25 kg/m²; n=11) and OW/OB (pre-pregnancy BMI ≥25 kg/m²; n=8) were examined. Infants were primarily breast fed with 3 infants of mothers with OW/OB receiving formula supplementation at 2 weeks of age. PCB congeners 138+163, 153+132, 180 and the congener sum were measured using gas chromatography/mass spectrometry adjusted for milk fat content. Infant growth parameters from birth to one year were assessed using World Health Organization Z-scores and associations with milk PCB congeners determined. Data were analyzed by Welch’s t-test and Pearson’s correlation.

Results: Total fat content in the milk adjusted for maternal pre-pregnancy BMI did not differ between the two groups. Milk from mothers with OW/OB had significantly higher PCB congener sum (p=0.020) and PCB 138+163 (p=0.029). Milk PCB 180 was negatively associated with change in weight-for-age (p=0.006) and BMI (0.036) Z-score from 2 weeks to 2 months. The PCB congener sum was negatively associated with change in head circumference Z-score from 2 weeks to 6 months (p=0.033).

Conclusions: Breast milk from mothers with pre-pregnancy overweight and obesity had higher levels PCB congener sum (132, 138, 153, 163, 180) at two-weeks post-partum. The negative associations between breast milk PCB and infant growth trajectory provide proof of concept for the potential lactational endocrine disrupting chemical programming of offspring health.

*Supported by: P30 ES017885
GLOBAL RNA SEQUENCING OF T CELLS AFTER HEMATOPOIETIC STEM CELL TRANSPLANT IDENTIFIES LINC00402 AS A NOVEL REGULATOR OF MOUSE AND HUMAN T CELL FUNCTION

Daniel Peltier1, M. Radosevich1, G. Hou2, and Pavan Reddy2

1Division of Pediatric Hematology/Oncology, University of Michigan Medical School, Ann Arbor, MI.
2Division of Hematology/Oncology, University of Michigan Medical School, Ann Arbor, MI.

Background: Long non-coding RNAs (lncRNA) are emerging regulators of immune responses. Compared to mRNAs, lncRNAs have greater tissue and context-specific expression, which may make them attractive therapeutic targets or biomarkers. However, little is known about how lncRNAs influence T cell-mediated processes. Allogeneic hematopoietic stem cell transplantation (HSCT) is a powerful treatment for high-risk pediatric malignancies, and HSCT success hinges on the precise control of donor (allogeneic) T function. Unfortunately, the mechanisms governing allogeneic T cell function remain incompletely understood.

Methods: We hypothesized that lncRNAs influenced allogeneic T cell responses, and to test this we performed total RNA-seq on donor T cells from HSCT recipients. These donor T cells received either an absent, mild, or moderate strength allogeneic stimulus. We confirmed our results in an independent patient cohort and explored molecular mechanisms using various in vivo (murine) and ex vivo (human and mouse) experimental systems. Results: RNA-sequencing showed that T cell lncRNAs were dysregulated in proportion to the strength of the allogeneic stimulus they received. These data were confirmed by qRT-PCR in an independent patient cohort, multiple in vivo murine HSCT models, and primary mouse and human T cell cultures. Linc00402 was chosen as the lead lncRNA due to sequence and synteny conservation, which are associated with bona fide functional lncRNAs. In addition, its expression was enriched 88 fold in T cells, which may increase its clinical utility relative to more broadly expressed genes. Importantly, knockdown of Linc00402 limited the proliferation of both human (55% of control, \( p < 0.01 \)) and murine (32% of control, \( p < 0.01 \)) alloantigen-stimulated T cells, but not the proliferation of T cells activated with a strong global T cell stimulus. Conclusions: These results indicate that Linc00402 is a novel regulator of T cell function. In light of its tissue specific expression, Linc00402 could be an attractive target for improving outcomes after allogeneic HSCT and other T cell-mediated disorders.
Abstract 4

THE UNIQUE HISTONE MODIFICATION LANDSCAPE OF NEONATAL CD4+ T CELLS CONTRIBUTES TO DECREASED T CELL RECEPTOR SIGNALING

Jennifer Bermick1, Aaron denDekker2, Steve Kunkel3, Nicholas Lukacs3, Matthew Schaller4
1Neonatal-Perinatal Medicine, Michigan Medicine, Ann Arbor, MI
2Vascular Surgery, Michigan Medicine, Ann Arbor, MI
3Pathology, Michigan Medicine, Ann Arbor, MI
4Pulmonary, Critical Care & Sleep Medicine, University of Florida, Gainesville, FL

Background: Neonatal CD4+ T cells have reduced or delayed immune responses when compared to adult cells, but the mechanisms behind these differences are poorly understood. We have previously shown that neonatal monocytes gain the activating histone tail modification H3K4me3 at promoter sites of immunologically important genes as development progresses from preterm neonate to adult and that this gain is associated with more mature immune responses. It is unknown if T cells experience a similar gain in H3K4me3 that could explain developmental differences in function.

Methods: H3K4me3 ChIP-seq was performed on umbilical cord blood purified CD4+ T cells from extremely preterm (under 30 weeks’ gestation), late preterm (30-36 weeks’ gestation), and term neonates (37+ weeks gestation) and was compared to peripheral blood naïve CD4+ T cells from healthy adults (Adult). CD4+ T cells were incubated with anti-CD3 and anti-CD28 antibodies to initiate T cell receptor signaling and T cell responses were measured using flow cytometry for the activation markers CD69 and CD25 and ELISA for IL-2 cytokine expression.

Results: CD4+ T cells gained H3K4me3 in promoter regions over the course of development from extremely preterm neonate to adult. Adult CD4+ T cells had significantly more H3K4me3 in pathways associated with T cell receptor signaling and T cell co-stimulation than neonatal CD4+ T cells. This H3K4me3 enrichment was associated with increased markers of T cell activation after engagement of the T cell receptor in adult CD4+ T cells, including increased cell surface CD69 and CD25 expression and increased IL-2 cytokine expression (p<0.05).

Conclusion: CD4+ T cells demonstrated a developmental gain in H3K4me3 in pathways associated with T cell receptor signaling and co-stimulation. This gain was associated with increased T cell activation and cytokine expression in adult CD4+ T cells after engagement of the T cell receptor. These findings provide some mechanistic insight into why neonatal CD4+ T cells demonstrate defects in T cell receptor signaling.
Abstract 5

AGE-DEPENDENT EFFECTS OF IMMUNOPROTEASOME ACTIVITY ON MOUSE ADENOVIRUS TYPE 1 PATHOGENESIS
W Trim, A Chandrasekaran, H Seltzer, K Pant, and JB Weinberg
Department of Pediatrics, University of Michigan, Ann Arbor, MI

Background: CD8 T cells promote airway inflammation during acute mouse adenovirus type 1 (MAV-1) respiratory infection and are essential for efficient virus clearance. MAV-1 infection induces activity of the immunoproteasome (IP), an inducible form of the proteasome that shapes CD8 T cell responses by enhancing peptide presentation by MHC class I. Objective: We used mice deficient in all three IP subunits (triple knockout, or TKO mice) to determine whether IP activity modulates control of MAV-1 replication or inflammatory responses to acute infection. Methods: Adult (6-8 weeks old) and neonatal (7 days old) B6 mice and mice deficient in all three IP subunits (TKO mice) were infected with MAV-1. Mock infected controls included B6 and TKO mice inoculated with conditioned media. Some mice were re-challenged with a second infection at 28 dpi. qPCR was used to measure viral loads. RT-qPCR was used to measure viral and host gene expression. Bronchoalveolar lavage fluid (BALF) total protein and cytokine concentrations were measured using Bradford assay and ELISA, respectively. Flow cytometry with intracellular cytokine staining was used to quantify CD4 and CD8 T cell IFN-γ production. Western blot was used to detect IP subunit levels in organ homogenate. In vitro infection with virus preincubated with serum from infected mice was used to assess neutralizing antibody production. Results: Complete IP deficiency in adult TKO mice had no effect on MAV-1 replication, virus-induced lung inflammation, or adaptive immunity compared to B6 controls. In contrast, IP deficiency in neonatal TKO mice was associated with decreased survival and decreased lung IFN-γ expression compared to B6 controls, although without substantial effects on viral replication, histological evidence of inflammation, or expression of the pro-inflammatory cytokines TNF-α and IL-1β in lungs or other organs. T cell recruitment and IFN-γ production by CD4 and CD8 T cells was similar in lungs of infected B6 and TKO mice. In lungs of uninfected B6 mice, we detected low levels of IP subunit mRNA and protein that increased with age. IP subunit expression was less in lungs of adult IFN-γ-deficient mice compared to B6 controls. Conclusion: Developmental regulation of the IP is associated with age-dependent effects of the IP on MAV-1 pathogenesis. Marked effects of IP deficiency in neonatal mice are likely due to the relative immaturity of other aspects of immune function during early life that are capable of compensating for effects of IP deficiency in adult mice.
HUMAN BRONCHIAL EPITHELIAL CELLS BIND RHINOVIRUS VIRAL PROTEIN (VP4) THROUGH TLR2 TO STIMULATE TRANSCRIPTION OF CHEMOKINES. J. K. Bentley, M. Han, T. Ishikawa, A. Goldsmith, C. Rajput and M. B. Hershenson. Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI

Background: Rhinoviruses (RV) bind to ICAM-1 or LDL family receptors, ultimately leading to asthma exacerbation. Binding induces conformational translocation of myristoylated VP4 (MyrVP4) to the virion surface. The altered viral particle interacts with membranes without further involvement of the virus receptor. We have shown macrophage TLR2 expression is required for RV-induced airway inflammation and hyperresponsiveness in allergen-sensitized and -challenged mice (Han et al, J Allergy Clin Immunol. 2016). We hypothesize MyrVP4 binds and activates TLR2, leading to cytokine expression. We sought to determine whether VP4 derived from RV-infected cells could specifically bind and activate human bronchial epithelial cells. Methods: Beas2B cells were obtained from ATCC. Normal human bronchial epithelial cells (HBEs) were isolated from unused human lung explant tracheobronchial trimmings. Beas2B cells were cultured in tissue culture plates or glass coverslips, but HBEs were cultured and mucociliary-differentiated at air-liquid interface on Transwell membranes. Native RV-A1B MyrVP4 was isolated by urea solubilization of infected HeLa cells, differential centrifugation, isoelectric precipitation, and anti-VP4 affinity chromatography. Responses to native MyrVP4 were compared to intact virus, recombinant MyrVP4 (bacterial), and chemically synthesized MyrVP4 (Genscript). MyrVP4 binding to Beas2B cells was examined by immunofluorescence microscopy using anti-VP4 (Genscript) and anti-TLR2 (BioLegend). Beas2B and HBE transcripts were assessed by reverse transcript-quantitative polymerase chain reaction. Results: RV-A1B and MyrVP4 colocalized with TLR2 in Beas2B cells and primary HBEs at the cell surface and cytoplasm. Anti-TLR2 and anti-VP4 blocked cell entry and co-localization of RV and MyrVP4 with TLR2. MyrVP4 (100 ng/mL, 12 h) increased chemokine mRNA in Beas2B cells and HBEs. mRNA of CXCL1, CXCL2 and CXCL8 was increased over sham by RV and all forms of MyrVP4, but CXCL10 was only significantly increased by RV-A1B. In all cases cytokine responses were attenuated by anti-TLR2 and anti-VP4. Conclusions: RV binds and enters airway epithelial cells in a TLR2-dependent manner. MyrVP4 binds TLR2 and is required for the RV-TLR2 interaction. VP4 is also required and sufficient for RV-induced CXCL1, CXCL2 and CXCL8 expression. RV-dependent stimulation of other cytokines such as CXCL10 may not share this mechanism. Supported by NIH R01 HL134369.
Abstract 7

**DAILY DYNAMICS OF CF AIRWAY MICROBIOTA DURING BASELINE CLINICAL STATE**

L.J. Caverly¹, J. Lu¹, L.A. Carmody¹, S. Cahalan¹, M. Azar¹, L.M. Kalikin¹, R. Simon², J.J. LiPuma¹

¹Dept. of Pediatrics & Communicable Diseases, University of Michigan
²Dept. of Internal Medicine, University of Michigan

**Rationale:** Differences in cystic fibrosis (CF) airway microbiota between periods of baseline health and pulmonary exacerbations have been investigated in efforts to better understand the microbial triggers of CF pulmonary exacerbations. Many of these studies have relied on a single or a limited number of samples to represent airway microbiota at baseline. However, the variability in microbial community structure during periods of clinical stability is not well known.

**Objectives:** We sought to determine the temporal variability of measures of airway microbiota using sputum samples collected daily from adults with CF during periods of clinical stability and to identify factors associated with this variability.

**Methods:** Sputum samples were obtained daily from six adults with CF during ten periods of baseline health. Samples (n= 527) underwent sequencing of the V4 region of the bacterial 16S rRNA gene. The average of the pairwise Bray-Curtis similarity measures of each sample to every other sample within the same baseline period was calculated, with outlier samples defined as being ≥ 1.5 times the interquartile range. Total bacterial load was measured with droplet digital PCR.

**Results:** Variation in airway microbiota among daily samples was greater than variation observed in technical replicate control samples. Overall, 6% of samples were identified as outliers in beta diversity. Within baseline periods, changes in bacterial community structure occurred coincident with changes in maintenance antibiotics (p<0.05, AMOVA). Within subjects, bacterial community structure changed between baseline periods (p<0.01, AMOVA). Sample-to-sample comparisons of bacterial community structure within baseline periods were more similar when interval days were fewer between sampling.

**Conclusions:** During periods of clinical stability, airway bacterial community structure vary among daily sputum samples from adults with CF. This day-to-day variation has bearing on study design and interpretation of results, particularly in analyses that rely on single samples to represent periods of interest (e.g., baseline health versus exacerbation of symptoms). These data emphasize the importance of accounting for maintenance antibiotic use and granularity of sample collection in studies designed to assess the dynamics of airway microbiota relative to changes in clinical state in persons with CF.
BIOPHYSICAL CHARACTERISTICS OF SICKLE CELL DISEASE: UNDERSTANDING HOW RED CELL RIGIDITY ALTERS DISEASE SEVERITY
M Shamoun1, M Gutierrez2, A Banka2, O Eniola-Adefeso2
1 Pediatric Hematology/Oncology, University of Michigan; 2 Chemical Engineering, University of Michigan.

Background: Sickle cell disease (SCD) is an inheritable blood disorder characterized by an abnormal sickled shape of red blood cells due to a mutation in hemoglobin. SCD affects nearly 100,000 patients in the United States and life expectancy in homozygous patients is often reduced to the 4th or 5th decade. Sickled cells lead to pain crises, end organ damage, stroke, and early death. The objective of this study was to characterize how the rigidity of patient’s red blood cells (RBCs) affects disease severity in hopes of improving current therapeutic treatments such as blood transfusions.

Methods: Sickle cell patient blood was collected in accordance with our IRB at Michigan Medicine. Physical characteristics of red blood cells and blood flow were measured using flow cytometry, ektacytometry, parallel plate flow chambers and blood smears. Artificially rigid blood was also used as a model to mimic sickle cell patient blood.

Results: 15 patients were studied with either hemoglobin SS or SC disease. Of these patients, about half use chronic transfusions and the others used hydroxyurea to help control disease symptoms. Patients showed an elongation index (EI), which helps measure cell rigidity, between 0.266 and 0.606 with healthy controls at 0.620. Patient white blood cell adhesion showed a decrease in adhesion at three different shear stresses compared to healthy controls with an increase in MAC1 expression and decrease in L-selectin, PSGL-1, LFA-1, and sLea expression. Artificial rigidity models showed similar characteristics of white blood cell and platelet adhesions as actual patient blood.

Conclusions: It appears that patient blood red cell rigidity affects white blood cell and platelet adhesion, adhesion receptor expression and blood flow dynamics. Our patients with the highest rigidity also seem to suffer significantly from their disease compared to patients with more deformable red cells. Using this knowledge, we hope to continue to understand how treatment modalities can be individualized to a specific patient to yield the best outcomes for infections, pain crises, and strokes.
Abstract 9

CRRT FILTER PRIMING CONDITIONS INFLUENCE BRADYKININ RELEASE: AN EX VIVO STUDY
S. Gorga¹; M. Dahmer¹; K. Plomaritas²; K. Luckritz²
¹Pediatric Critical Care Medicine, University of Michigan, Ann Arbor, MI
²Pediatric Nephrology, University of Michigan, Ann Arbor, MI

Background: The use of renal replacement therapy (RRT) techniques in critically ill children is on the rise, with continuous renal replacement therapy (CRRT) becoming the preferred modality in pediatric intensive care units (PICUs). Severe anaphylactoid reactions to CRRT initiation have been described in animals and humans that are related to bradykinin release at the blood-membrane interface when using AN-69 based membrane dialysis filters. This reaction is pH-related and time limited but carries morbidity and mortality risks. The objective of this study is to develop an ex vivo closed circuit model of CRRT initiation to evaluate the bradykinin release potential of various components during the initiation procedure while augmenting the pH at the filter-level.

Methods: An ex vivo PrismaFlex CRRT machine with an AN-69 membrane based dialysis filter set in the continuous venovenous hemodiafiltration (CVVHDF) mode was connected via dialysis catheter to a reservoir of whole blood approximating a 6 kg patient. The circuit was primed with either normal saline or PlasmaLyte-A per experimental protocol. After priming, the whole blood replaced the priming solution in the circuit using a blood-bypass procedure with 50 mEq of sodium bicarbonate infusing over 7 or 15 minutes per protocol. Blood samples were taken at time 0 and set times after circuit flow initiation and evaluated for bradykinin, pH, and pCO2 via a commercially available bradykinin ELISA kit and standard blood gas. Circuit set ups were run in triplicate and bradykinin analysis was run in duplicate.

Results: Baseline parameters of the whole blood were not physiologic. There was significant variability in amount of bradykinin within individual circuit setups at different time points (p = 0.002), as well as among different setups at individual time points (p = 0.004). Baseline pH was similar (p = 0.65), but through the experiment, pH varied based on circuit setup (p = 0.007), over time in individual setups (p < 0.0001), between setups at individual time points (p < 0.0001), and were influenced by the priming conditions and rate of sodium bicarbonate. pCO2 varied based on circuit setup (p = 0.043), among time points in individual setups (p < 0.0001), between setups at individual time points (p < 0.0001), and were influenced by priming conditions and rate of sodium bicarbonate.

Conclusions: Filter priming conditions influence bradykinin release, pH, and pCO2 in an ex vivo, closed circuit model. The clinical implications require further investigation.
Abstract 10

THERAPEUTIC STRATEGIES FOR ATAXIA-TELANGIECTASIA LUNG DISEASE

T Michniacki1, R Saunders2, M Kuo3, C Hames2, J Nguyen4, H Moale2, & J Sekiguchi2

1University of Michigan Department of Pediatric Hematology/Oncology; 2University of Michigan Department of Internal Medicine; 3University of Michigan Medical School; 4University of Michigan, Ann Arbor, MI

Background: Ataxia-Telangiectasia (A-T) is an autosomal recessive disorder caused by mutations in the ATM gene, which encodes a protein kinase that plays crucial roles in the regulation of cellular responses to DNA double strand breaks and oxidative stress. A-T patients suffer from various clinical manifestations, including neurologic dysfunction, immunodeficiency, risk of hematologic malignancies and pulmonary disease. The pathophysiology of pulmonary disease in A-T is poorly understood and currently there are no effective therapies to cure or prevent progression of the respiratory aberrations of A-T. We have developed a murine model of A-T lung disease to gain further insights into the mechanisms underlying pulmonary complications in A-T and to test potential therapeutic interventions.

Methods: Acute lung injury was induced in wild-type and ATM null mice by oropharyngeal exposure to bleomycin. The animals were then treated intraperitoneally with either normal saline, the irreversible myeloperoxidase (MPO) inhibitor, 4-aminobenzoic acid hydrazide (ABAH), or the CXCL1/2 receptor antagonist, reparixin. Inflammatory responses and intrinsic lung phenotypes were assessed via flow cytometry and ELISAs of bronchoalveolar lavage (BAL) fluid and histologic examination of lung tissues.

Results: ATM null mice exhibit significantly decreased survival, reduction in weight and severe hypoxia in response to bleomycin compared to wild type mice. We observed increased pulmonary neutrophil recruitment, elevated apoptosis of alveolar epithelial cells, and increased levels of pro-inflammatory factors, including MPO and CXCL1/KC, within the BAL fluid of ATM-deficient mice. MPO inhibition reduced protein levels in ATM-deficient BALs; however, it did not result in decreased inflammation or improvement in pulmonary function. We observed that CXCL1/2 receptor antagonism decreases alveolar epithelial apoptosis, BAL neutrophilia and TNF-alpha driven inflammation in ATM null mice.

Conclusions: ATM deficiency appears to cause prolonged and amplified inflammation in response to acute lung injury, which may underlie the severely impaired pulmonary function. Our results additionally suggest that reparixin could offer a potential therapeutic intervention in those with A-T pulmonary manifestations. We have now begun studies to probe the molecular mechanisms underlying the exacerbated inflammatory responses seen in ATM-deficient mice.
Abstract 11

CONTRIBUTIONS OF TUMOR NECROSIS FACTOR ALPHA TO MOUSE ADENOVIRUS TYPE 1 PATHOGENESIS
K Pant, W Trim, and JB Weinberg
Department of Pediatrics, University of Michigan, Ann Arbor, MI

Background: During mouse adenovirus type 1 (MAV-1) respiratory infection, CD8 T cells are recruited to the lungs of infected mice and contribute to effective virus clearance and virus-induced pulmonary inflammation. The antiviral function of CD8 T cells in MAV-1 infection is independent of CD8 T cell effectors such as IFN-γ, perforin, and Fas/FasL interactions. The role of TNF-α, another cytokine produced by CD8 T cells that is upregulated during MAV-1 infection, has not yet been examined. Objective: We used a combination of in vitro and in vivo approaches to determine the effect of TNF-α on MAV-1 replication and pulmonary inflammation. Methods: Mouse 3T12 fibroblasts were infected in vitro with MAV-1 in the presence of TNF-α, and RT-qPCR was used to assess viral gene expression. Adult B6 mice, TNF-α-deficient mice, and B6 mice treated with anti-TNF-α or isotype control antibody were infected intranasally with MAV-1. Mice were weighed every day. qPCR was used to measure lung viral loads at 7 and 14 days post infection (dpi), and RT-qPCR was used to measure viral and host gene expression. Bronchoalveolar lavage fluid (BALF) total protein and cytokine concentrations were measured using Bradford assay and ELISA, respectively. Results: TNF-α used at a wide range of concentrations significantly inhibited MAV-1 replication in 3T12 cells. In vivo, TNF-α deficiency or immunoneutralization had no effect on peak levels of viral gene expression or viral loads in lungs at 7 dpi, or on virus clearance from the lungs by 14 dpi. All mice survived infection, but TNF-α deficient and immunoneutralized mice were protected from weight loss over the course of the study. However, virus-induced increases in BALF total protein concentration (a measure of lung injury) and virus-induced expression of proinflammatory cytokines and chemokines such as IFN-γ, IL-1β, CXCL1, CCL2, and CCL5 were not affected by TNF-α deficiency or immunoneutralization. Conclusion: TNF-α inhibits viral replication in vitro. However, that effect is not seen in the absence of TNF-α in vivo, likely because of multiple redundant CD8 T cell effectors and other aspects of innate and adaptive immune function that exert an antiviral effect. Although our data suggests that TNF-α is not essential for the proinflammatory effects of CD8 T cells during MAV-1 respiratory infection, TNF-α is essential for another relevant aspect of disease, weight loss, that is present during acute infection. TNF-α inhibition may be an appealing therapeutic strategy to consider for severe disease caused by adenoviruses.
Abstract 12

EWS/FLI1 ACTIVATES HOXD13 EXPRESSION THROUGH ENHANCER REPROGRAMMING
A. Apfelbaum1, L. Svoboda2, B. Magnuson3, Mats Ljungman4, Elizabeth Lawlor1,2,3

1Cancer Biology Program, University of Michigan; 2Department of Pediatrics and Communicable Diseases, University of Michigan; 3Department of Biostatistics, University of Michigan; 4Department of Radiation Oncology, University of Michigan; 5Department of Pathology, University of Michigan, Ann Arbor, MI, 48109.

Background: Ewing sarcoma is an aggressive bone and soft tissue tumor that primarily affects children and adolescents. Ewing sarcoma is characterized by EWS/ETS fusions, most commonly EWS/FLI1, which initiates tumorigenesis via enhancer reprogramming. The posterior HOXD genes, specifically HOXD13 are highly over-expressed in Ewing sarcoma and function as cooperative oncogenes. HOXD13 is important for limb development and is activated by long-range enhancers. Here, we describe insights into the mechanism of HOXD13 activation by hijacking of developmental enhancers by EWS/FLI1.

Methods: Interrogation of publicly available ChIP-seq, NRO-seq, RNA-seq, and BruUV-seq data. Subsequent ChIP-qPCR and RT-qPCR validation analyses were performed.

Results: Interrogation revealed an EWS/FLI1 binding site, posterior HOXD enhancer (PHE), within the developmentally conserved enhancer region. The PHE was marked with poised (H3K4me1) and active enhancer (H3K27ac) histone marks. The PHE has eRNA expression, indicating it’s a functional enhancer. Knockdown of EWS/FLI1 led to loss of PHE activation and loss of HOXD13 gene expression. EWS/FLI1-transduced mesenchymal stem cells (MSCs), the putative cell of origin, revealed activation of the PHE, which was inactive in the parent MSC line.

Conclusion: These data indicate that EWS/FLI1 hijacks a developmentally conserved enhancer that controls posterior HOXD gene expression. The presence of eRNA and active histone marks implies the PHE to be functional in controlling HOXD13 expression, but future studies will provide definite mechanistic proof using innovative CRISPRi technologies.
Abstract 13

LOSS OF TISSUE FACTOR IN ZEBRAFISH DISRUPTS HEMOSTASIS AND RESULTS IN SYNTHETIC LETHALITY, BUT IS COMPATIBLE WITH EMBRYONIC DEVELOPMENT

S.J. Grzegorski; J.A. Shavit
Department of Pediatrics, University of Michigan, Ann Arbor MI

**Background:** Tissue factor (TF) is responsible for initiation of the extrinsic coagulation pathway through binding to activated factor VII. TF-null mice are embryonic lethal at an earlier timepoint than other procoagulant knockouts, suggesting additional functions beyond coagulation, including suspicions of abnormal angiogenesis and loss of perivascular support. External development and optical transparency make zebrafish a powerful tool to study coagulation and development. Zebrafish have two TF paralogs (TFa and TFb) with unknown spatial and functional differentiation.

**Methods:** We used genome editing with CRISPR/Cas9 to produce null alleles for TFa and TFb. Laser-induced endothelial injury was used to assess thrombus formation. We tracked vascular development using a fluorescent endothelial reporter and angiography.

**Results:** TFb, but not TFa, is present in the zygotic transcriptome, indicating maternal deposition. It has been shown that transcription of both genes increases following gastrulation and we have confirmed transcript presence at the initiation of circulation. Single mutants survived well into adulthood with no gross phenotypes and were able to reproduce. However, double mutants died by 9 weeks of age due to hemorrhage. Loss of TFa resulted in delayed induced thrombus formation in the venous system at 3 days old while TFb had no observable effect. Double mutants demonstrated a complete inability to form thrombi. Fluorescent vascular studies demonstrated normal vasculogenesis, angiogenesis, and vascular integrity throughout embryonic development.

**Conclusions:** Overall, our data suggest that the hemostatic role of TF is conserved in fish while its loss is compatible with normal development, but early adult mortality. Interestingly, maternal deposition of TFb suggests a developmental function prior to vasculogenesis. Our results indicate that the duplication provides an additional layer of quantitative regulation, and creates a titratable TF level that will allow the interrogation of the role TF in perivascular development, cardiovascular stability, remodeling and regeneration.
Abstract 14

CHD7 IS CRITICAL FOR NEURONAL LINEAGE DIFFERENTIATION BY CHANGING CHROMATIN ACCESSIBILITY AND RNA EXPRESSION

D.F. Hannum\(^1\); H. Yao\(^2\); K.E. Ritter\(^2\); S. Hill\(^3\); J.M. Skidmore\(^2\); R. Albanus\(^5\); G. Sanchez\(^2\); M. Ljungman\(^6\); S. Parker\(^4,5\); S. Bielas\(^4\); D.M. Martin\(^2,3,4\)

Departments of \(^1\)Biostatistics, \(^2\)Pediatrics, \(^3\)Neuroscience Program, \(^4\)Human Genetics, \(^5\)Bioinformatics, \(^6\)Otolaryngology-Head and Neck Surgery; University of Michigan, Ann Arbor, MI

Background: CHARGE syndrome, a rare multiple congenital anomaly condition, is caused by haploinsufficiency of the ATP-dependent chromatin remodeling enzyme Chromodomain Helicase DNA binding protein 7 (\textit{CHD7}). Heterozygous loss of \textit{CHD7} in humans and in mice results in highly variable phenotypes, and homozygous loss is embryonic lethal. Brain abnormalities and intellectual disability are commonly observed in individuals with CHARGE. In addition, neuronal differentiation is reduced in CHARGE patient-derived iPSCs and in conditional knockout mouse brains. Here we explored the underlying mechanisms of \textit{Chd7} function in nervous system development using mouse embryonic stem cell-derived neurons.

Methods: \textit{Chd7}\(^{+/+}\) and \textit{Chd7}\(^{Gt/Gt}\) mouse embryonic stem cells (ESCs) were derived from sibling blastocysts in the Transgenic Animal Model Core (TAMC). ESCs were differentiated to neural progenitor cells (NPCs) and neurons. Quantitative RT-PCR, cell growth assays, immunostaining, ATAC-seq, and Bru-seq were performed on ESCs and NPCs.

Results: \textit{Chd7} expression increased during ESC to NPC transition and neuronal differentiation. Loss of \textit{Chd7} did not affect ESC or NPC identity nor proliferation, but significantly reduced \textit{Tuj1}\(^+\) neurons. ATAC- and Bru-seq experiments showed changes in neural specific gene expression and chromatin accessibility with \textit{Chd7} loss.

Conclusions: \textit{Chd7} is required for ESC-derived neuronal differentiation via changes in chromatin accessibility at neural specific genes. Our data suggest that \textit{Chd7} acts preferentially during the transition of NPCs to neurons and likely works in concert with key neuronal regulators to promote differentiation.
Abstract 15

MENIN AND ATF4 COOPERATE TO DRIVE SERINE BIOSYNTHESIS IN EWING SARCOMA

Jennifer Jiménez1, Laurie K. Svoboda2, Sudha Sud2, Samuel Kerk1, Jolanta Grembecka3, Costas A. Lyssiotis4,5, Elizabeth R. Lawlor2,3

1Cancer Biology Program, 2Department of Pediatrics, 3Department of Pathology, 4Department of Molecular and Integrative Physiology, 5Department of Internal Medicine, University of Michigan, Ann Arbor, MI

Background: Ewing sarcoma (ES) is an aggressive bone and soft tissue tumor. We previously reported that the scaffolding protein menin is overexpressed by ES and drives ES cell proliferation, survival, and tumorigenicity. Additionally, our recent studies revealed a previously undescribed role for menin in the activation of the serine biosynthetic pathway (SSP), a critical metabolic pathway that is aberrantly activated in many human cancers. In other cancer types, activation of the SSP has been shown to result from activation of the master transcriptional regulator, ATF4. The biologic functions of menin are largely determined by its protein-binding partners, the best characterized of which is the histone methyltransferase MLL. In the current study, we are investigating the mechanistic link between menin, ATF4, and the SSP to determine whether menin activates the SSP via epigenetic trithorax complexes.

Methods: Lentiviral shRNA knockdown and overexpression of ATF4 were performed in several ES cell lines, and Q-RT-PCR and western blot were used to assess effects on PHGDH, PSAT1, and PSPH expression. Chromatin immunoprecipitation (ChIP)-qPCR was performed to determine ATF4 and menin enrichment at SSP and ATF4 gene promoters, respectively, and H3K4me3 enrichment associated with menin binding. Menin was inhibited pharmacologically in ES cells using MI-503, a menin:MLL interaction inhibitor, and effects on ATF4 and SSP expression and ATF4 enrichment at SSP gene promoters were assessed. Results: ATF4 is overexpressed in ES, and ATF4 loss of function leads to growth inhibition. Q-RT-PCR and western blot of ES cells following ATF4 knockdown revealed down-regulation of PHGDH, PSAT1, and PSPH. In addition, ChIP-qPCR showed enrichment of ATF4 binding at SSP gene promoters, which is diminished by treatment with MI-503. Menin inhibition with MI-503 also led to loss of ATF4 expression, coincident with loss of SSP expression. Additionally, ChIP-qPCR shows enrichment of menin binding at the ATF4 gene promoter, which is associated with H3K4me3 enrichment. Preliminary studies show that ATF4 over-expression via lentiviral transduction may rescue the loss of SSP gene expression induced by MI-503. Conclusion: Together these findings support the hypothesis that ATF4 acts downstream of menin to drive SSP activation in ES. Ongoing studies are assessing whether this is mediated by trithorax-dependent or –independent functions of menin.
Abstract 16

TUMOR NECROSIS FACTOR ALPHA DISRUPTS PLATELET DERIVED GROWTH FACTOR RECEPTOR ALPHA SIGNALING IN NEONATAL LUNG MESENCHYMAL CELLS: IMPLICATIONS FOR BPD DEVELOPMENT. Rosenbloom L, Fulton CT, Cui TX, Popova AP, Dept. of Pediatrics, Michigan Medicine.

Background: Inflammation has been associated with the development of bronchopulmonary dysplasia (BPD). Tumor necrosis factor (TNF)-α, a proinflammatory cytokine, is increased in tracheal aspirates from premature infants with BPD. However, a causal relationship has not been established. During lung development, platelet-derived growth factor receptor (PDGFR)-α-expressing mesenchymal cells migrate to the tips of secondary crests to form alveoli. Impaired alveolar development in BPD is associated with interstitial myofibroblast accumulation and paucity of PDGFRα-positive mesenchymal cells at the tips of secondary crests. We have isolated mesenchymal stromal cells (MSCs) from tracheal aspirates of premature infants with RDS. The expression profile of these cells is consistent with lung-resident mesenchymal cell progenitors. While the effect of TNF-α on neonatal lung MSC gene expression is unknown, in mouse embryonic fibroblasts, TNF-α reduces PDGFRα expression. In this study, we hypothesized that TNF-α reduces neonatal lung MSC expression of PDGFRα and other genes involved in lung development.

Methods: MSCs were isolated from tracheal aspirates of premature infants mechanically ventilated for RDS in the first week of life. Cells grown to 80-90% confluence were treated with recombinant human TNF-α (1 and 5 ng/mL) and TGF-β1 (5 ng/mL). Gene expression was analyzed by qPCR or immunoblotting. Microdissected E16 fetal mouse lungs were cultured in transwells in the presence or absence of recombinant mouse TNF-α (5 and 10 ng/mL). Image analysis was performed using ImageJ software. Results: TNF-α decreased PDGFRα mRNA expression and protein levels in a dose dependent manner. Also decreased was the mRNA expression of WNT2, SPRY1 and FOXF2, genes involved in lung and mesenchymal cell development and the proliferation marker Ki-67. TGF-β1, a known profibrotic factor implicated in BPD pathogenesis, potentiated the effect of TNF-α on neonatal lung MSC expression of PDGFRα, FOXF2 and SPRY1. To further examine the effect of TNF-α on lung growth we used an in vitro culture model with fetal mouse lungs. Recombinant TNF-α inhibited saccular lung growth as represented by reduced airspace chord lengths of mouse E16 fetal lung explants. In mechanically ventilated premature infants, tracheal aspirate TNF-α levels during week of life 3 are significantly higher than week of life 1 levels. Conclusions: In neonatal lung MSCs, TNF-α reduced the expression of PDGFRα and other genes required for normal lung development. TNF-α also inhibited saccular lung development in fetal mouse lungs. Blocking TNF-α may be an attractive new target to prevent or treat BPD.
Abstract 17

*LHX1 IS REPRESSED BY THE ATP-DEPENDENT CHROMATIN REMODELER CHD7 IN THE DEVELOPING MOUSE INNER EAR*

M. Situ1; J. Skidmore2; D. F. Hannum3; D.M. Martin1,2,4
1Neuroscience Graduate Program, University of Michigan, Ann Arbor, MI.
2Pediatrics, University of Michigan, Ann Arbor, MI.
3Biostatistics, University of Michigan, Ann Arbor, MI.
4Human Genetics, University of Michigan, Ann Arbor, MI.

**Background:** *LHX1* is one of several genes that cause Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome, characterized by abnormalities of the female reproductive system. MRKH syndrome type 2 can also present with clinical features of CHARGE syndrome, including skeletal abnormalities, hearing loss and heart defects. Most cases of CHARGE syndrome are associated with pathogenic variants in the *CHD7* gene, which encodes chromodomain helicase DNA binding protein 7. *CHD7* is expressed in the eye, ear, and brain before birth and known to regulate expression of many other genes through chromatin remodeling. Here we characterized inner ear *Lhx1* expression in embryonic mice with heterozygous and homozygous loss of *Chd7* using RNA–seq and immunohistochemistry.

**Methods:** Timed-pregnant crosses were established between male and female *Chd7Gt/+* mice and embryos collected at e9.5 or e10.5. E10.5 otocysts were microdissected for RNAseq analysis. Embryos were embedded in paraffin and sectioned for immunohistochemistry with anti-LHX1 antibody.

**Results:** RNAseq analysis demonstrated upregulation of *Lhx1* in heterozygous mutant embryos. LHX1 immunostaining was increased in otocysts of both heterozygous and homozygous *Chd7* mutant embryos.

**Conclusions:** Upregulation of *Lhx1* in *Chd7* mutant inner ears suggests *LHX1* is a genetic target of *CHD7* and may help explain the phenotypic overlap between MRKH and CHARGE syndromes.
Abstract 18

POTENTIAL MULTIFACTORIAL MECHANISMS FOR HORMONE-INDUCED VENOUS THROMBOEMBOLISM

Xinge Yu1, Steve Grzegorski1, Angela C. Weyand,1 and Jordan Shavit1
1Department of Pediatrics, University of Michigan, Ann Arbor, MI

Background: Hormone-induced venous thromboembolism (HI-VTE) affects thousands of women worldwide, causing significant morbidity and mortality. Combined oral contraceptives are the most commonly used form of birth control in adolescent females. Estrogens pose the major thrombotic risk, while the impact of progestins is less clear. Although sex hormones alter expression of coagulation factors, the pathways that connect hormones to thrombosis are unknown. Mice do not develop HI-VTE and an animal model has been lacking. External development, the ability to generate thousands of offspring at low cost, and optical transparency all make zebrafish a powerful tool to study coagulation.

Objectives: Dissect the mechanisms underlying HI-VTE.

Methods: 5-6 day old zebrafish were treated with therapeutics for 4 hours, evaluated for fluorescent thrombi in our transgenic line (which generates GFP-tagged fibrinogen that is incorporated into fibrin-rich thrombi) using standard and confocal microscopy, and scored by a blinded observer.

Results: Estradiol-treated zebrafish developed venous thrombosis within 4 hours. Pre-incubation with warfarin, rivaroxaban, and dabigatran inhibited estrogen-induced VTE by 50-80%. Fibrin deposition was reduced by 35% in a factor X-knockout background which has severely defective hemostasis. To evaluate the role of progestins, fish were treated with levonorgestrel, drospirenone, or norethindrone, alone and in combination with estradiol. Progestins alone did not cause thrombosis, but increased estrogen-induced VTE by ~20%. Estrogen-induced VTE was decreased by fulvestrant, an estrogen receptor (ESR) antagonist. Treatment of ESR1, ESR2a, and ESR2b knockout fish, demonstrated reduced, unchanged, and increased estrogen-induced VTE respectively.

Conclusions: Our data are consistent with human HI-VTE, although the rapidity of thrombosis development was surprising. We found that progestins do not cause thrombosis, but exacerbate this phenomenon, consistent with human data. The inability to completely inhibit HI-VTE through genetic/pharmacologic anticoagulation or estrogen disruption suggests that the mechanisms mediating HI-VTE are multifactorial. The zebrafish model is uniquely suited to dissect such complex pathways. Results of further studies could lead to novel therapeutic targets and ascertain patients at higher risk for thrombosis.
Abstract 19

SELECTIVE EXPRESSION OF GLP-1R IN GLUTAMATERGIC NEURONS IS SUFFICIENT FOR A FULL ANORECTIC RESPONSE TO LIRAGLUTIDE

Jessica M. Adams1, Paul Sabatini2, Carol F. Elias3, Martin G. Myers2, Darleen A. Sandoval3, Randy J. Seeley4, and David P. Olson1

Departments of 1Pediatrics, 2Internal Medicine, 3Molecular and Integrative Physiology, and 4Surgery, University of Michigan, Ann Arbor, MI

Background: Glucagon-like peptide-1 receptor (GLP1R) agonists are one of only a few classes of currently available anti-obesity drugs, but their mechanism of action is not well understood. By using broad cell type-specific knockouts in mice, we recently demonstrated that Glp1r expressed specifically in vGlut2-expressing glutamatergic neurons is necessary for the appetite suppression and weight loss associated with liraglutide (a GLP1R agonist). Further, we found two specific brain regions that express both vGlut2 and Glp1r and were activated by liraglutide: the area postrema (AP) and lateral parabrachial nucleus (LPBN) (Adams JM et al, 2018, Diabetes).

Methods: We used a complementary approach to further investigate these candidate regions for the primary site of liraglutide action. We utilized a new mouse model in which Glp1r is constitutively absent but can be reactivated in the presence of Cre recombinase (Glp1rRA). In the absence of Cre, we found no detectable Glp1r in the hypothalamus or brainstem. We crossed Glp1rRA to several candidate mouse strains that express Cre in the AP and/or LPBN: Penk (preproenkephalin), Prokr2 (prokineticin receptor 2), Calcr (calcitonin receptor), and Gfra1 (GNDF family receptor alpha-like), as well as vGlu2-Cre, and measured the food intake and body weight response to peripheral liraglutide administration.

Results: We found that vGlu2-Cre-mediated reactivation of Glp1r restored a normal physiological response to liraglutide. In contrast, Glp1rRA mice crossed to each of the other Cre lines responded to liraglutide identically to non-Cre controls.

Conclusions: These results show that Glp1r in glutamatergic neurons is both necessary and sufficient for the appetite and weight loss effects of liraglutide. However, identification of the crucial subpopulation of glutamatergic neurons has been unsuccessful to date and additional work is needed. Further elucidation of this anorectic network will aid our understanding of physiological body weight maintenance and could lead to more effective anti-obesity treatments.
Abstract 20
ABLATION OF NOS-1 NEURONS IN THE PVH REVEALS AN ESSENTIAL ROLE IN SUSTAINING METABOLIC HOMEOSTASIS, INDEPENDENT OF MELANOCORTIN FUNCTION
L. Faulkner1, I. Gonzales1, T. Meek2, D. Olson1

1Division of Endocrinology, Department of Pediatrics and Communicable Diseases, University of Michigan, Ann Arbor, MI 2Novo Nordisk Research Center, Seattle, WA.

Background: The paraventricular hypothalamus (PVH) is vital for energy balance regulation, as developmental or mechanical lesions targeting the PVH lead to massive obesity. We have shown that activation of PVH neurons expressing nitric oxide synthase-1 (Nos1PVH) suppresses food intake and increases energy expenditure. This differentiates these neurons from the well-studied melanocortin 4 receptor expressing population (Mc4R PVH), as activation of Mc4R PVH neurons suppresses feeding but does not alter energy expenditure. In situ hybridization studies in our laboratory show that Mc4R and Nos1 mRNAs do not overlap in the PVH, suggesting that these cell populations may regulate energy balance independently. In this project, we will test the hypothesis that the contributions of Nos1PVH neurons to maintaining metabolic homeostasis are independent of Mc4R PVH neurons. Our overall goal is to unravel the cellular and neurobiological mechanisms engaged by Nos1PVH neurons and open new avenues for treating obesity.

Methods: We used established Nos1 and Mc4R Cre-expressing lines to create a Nos1Cre+Mc4RCre dual recombinase model. Then, we inactivated Nos1PVH and Mc4R PVH neurons alone or in combination. Feeding behavior and body weight were monitored for 8 weeks post injection. These experiments allowed us to examine the interdependency of Nos1 and Mc4R PVH populations in energy balance control.

Results: Silencing the Nos1PVH population alone resulted in the acute onset of obesity without effecting feeding behavior. This phenotype was exacerbated when we simultaneously silenced both Nos1 and Mc4R PVH neurons, suggesting an additive interaction between the two populations.

Conclusion: We demonstrated that simultaneous inactivation of Nos1 and Mc4R PVH neurons results in a significant increase in body weight in comparison to either group alone. This suggests an additive interaction between the two populations; a synergistic effect cannot be excluded. Future studies will focus on the effects of Nos1PVH inactivation on energy expenditure and defining the Nos1 neurocircuitry that facilitates PVH-mediated metabolic regulation.
Abstract 21

IL-1β PREVENTS TYPE 2 INFLAMMATION, ILC2 EXPANSION AND ASTHMA DEVELOPMENT FOLLOWING EARLY LIFE VIRAL INFECTION BY SUPPRESSING EPITHELIAL CELL INNATE CYTOKINE EXPRESSION

M. Han, J. K. Bentley, J.R. Bermick, C. Rajput, T. Ishikawa, J. Lei, A.M. Goldsmith, C.R. Jarman, J. Lee and M.B. Hershenson. Departments of Pediatrics and Molecular and Integrative Physiology, University of Michigan Medical School

Background: Early-life respiratory viral infection has been associated with asthma development. We have shown that human rhinovirus (RV) infection of six-day old immature mice causes the development of a chronic asthma-like mucous metaplasia phenotype which is associated with expansion of IL-13-producing type 2 innate lymphoid cells (ILC2s) and dependent on IL-25 and IL-33.

Objective: We examined the regulation of this phenotype by IL-1β.

Design/Method: Wild-type and IL-1β -/- six day-old immature mice were inoculated with sham-infected cell lysate or RV-A1B. Selected mice were treated with anti-IL-1β, recombinant IL-1β or IL-1 receptor antagonist (IL-1RA).

Results: RV infection induced mRNA and protein expression of pro-IL-1β and NLRP3 as well as cleavage of caspase-1 and pro-IL-1β, together indicating inflammasome priming and activation. IL-1β-/- mice showed attenuation of RV-induced Il25, Il33, Il4, Il5, Il13, muc5ac and gob5 mRNA expression, ILC2 expansion, mucus metaplasia and airway responsiveness. However, in wild type mice, inhibition of IL-1β signaling with IL-1RA or anti-IL-1β had the opposite effect, increasing RV-induced type 2 immune responses, ILC2 number and mucus metaplasia. Accordingly, treatment with IL-1β was protective against type 2 inflammation. In addition, IL-1RA reduced and IL-1β enhanced Il17 transcription. Finally, IL-1β and IL-17 each suppressed Il25, Il33 and muc5ac mRNA expression in cultured airway epithelial cells.

Conclusions: IL-1β regulates the airway response to early life respiratory virus infection. IL-1β deficiency during development prevents RV-induced ILC2 expansion and mucous metaplasia. On the other hand, in wild type mice, IL-1β reduces RV-induced type 2 responses by suppressing epithelial cell innate cytokine expression.

Supported by R01 AI120526 and R01 HL134369.
Abstract 22

EARLY LIFE HETEROLOGOUS RHINOVIRUS INFECTIONS INDUCE AN EXAGGERATED ASTHMA-LIKE PHENOTYPE

C. Rajput, T. Ishikawa, M. Han, J. Lei, J.K. Bentley and M.B. Hershenson. Department of Pediatrics, University of Michigan, Ann Arbor, MI

Background: Early-life wheezing-associated respiratory tract infection by rhinovirus (RV) is considered a risk factor for asthma development. Infants are infected with many different RV strains per year. We have previously shown that RV infection of 6 day-old BALB/c mice induces a mucous metaplasia phenotype which is dependent on type 2 innate lymphoid cells (Hong et al. J Allergy Clin Immunol 2014).

Objectives: In this study, we address the hypothesis that early life heterologous RV infections induce an exaggerated asthma-like phenotype.

Design/methods: BALB/c mice were treated on day 6 of life with RV-A1B and day 13 of life with RV-A2 as follows: 1) day 6 sham+day 13 sham; 2) day 6 RV-A1B+day 13 sham; 3) day 6 sham+day 13 RV-A2; and 4) day 6 RV-A1B+day 13 RV-A2. At day 20, lungs were harvested and analyzed for mRNA, histology, flow cytometry, BAL cells and airways responsiveness. We also performed selected experiments with Rora^fl/fl^IL7R^cre^ (RORα^-/-) mice lacking functional ILC2s.

Results: Mice infected with RV-A1B at 6 days and sham at 13 days of age showed increased mRNA expression of IL-13 but not IFN-γ, indicative of a type 2 immune response. Mice infected with sham on day 6 and RV-A2 on day 13 of life showed increased mRNA expression of IFNγ but not IL13, a mature antiviral response. In contrast, mice infected with sham on day 6 and RV-A2 on day 13 of life demonstrated increased IFN-γ expression, a mature antiviral response. Mice undergoing heterologous infection with RV-A1B and RV-A2 showed additive increases in IL-13, IL-5, Gob5, Muc5b and Muc5ac, expansion of IL-13-producing ILC2s and exaggerated mucus metaplasia and airways hyperresponsiveness compared to RV-A1B alone. Finally, Rora^fl/fl^IL7R^cre^ (RORα^-/-) mice showed suppression of IL-5, IL-13 and mucin genes compared to Rora^fl/fl^ mice.

Conclusions: Early-life heterologous infection with RV-A1B and RV-A2 induces intensified type 2 inflammation and an exaggerated asthma-like phenotype.

Supported by R01 AI120526 and R01 HL134369.
CONSERVED ROLES FOR CHD7 IN TRANSCRIPTIONAL ELONGATION OF GENES INVOLVED IN NEURAL CREST AND INNER EAR DEVELOPMENT

K. Elaine Ritter1; D.F. Hannum2; G.J. Sanchez1; E.D. Sperry3,4; A. Saiakhova5; D.R. Fuentes6; M.E. Bowen7; A.N. Niederriter-Shami3,4; J.M. Skidmore1; A. Srivastava3; L.D. Attardi7; T. Swigut6; J. Wysocka6,8,9; P.C. Scacheri5; and D.M. Martin1,3,4

Departments of Pediatrics1, Biostatistics2, and Human Genetics3, and the Medical Scientist Training Program4, University of Michigan, Ann Arbor, MI. Department of Genetics5, Case Western Reserve University, Cleveland, OH. Departments of Chemical and Systems Biology6, Radiation and Cancer Biology7, and Developmental Biology8, and the Howard Hughes Medical Institute9, Stanford University, Stanford, CA.

Background: Heterozygous pathogenic variants in CHD7, an ATP-dependent helicase, cause multiple organ system malformations and CHARGE syndrome. Hearing, balance, and peripheral nervous system impairment are common in CHARGE, yet the underlying mechanisms of CHD7 action in early inner ear and neural crest development are not well understood.

Methods: Otocysts from E10.5 Chd7+/+ and Chd7Gt/+ mutant mouse embryos were microdissected and subjected to RNA-Seq and differential gene expression analysis via DESeq2. Fibroblasts from a patient with a pathogenic variant in CHD7 were collected, converted to induced pluripotent stem cells (iPSCs), and split into two cell lines. In one line, the variant was left intact; in the other, the variant was corrected via CRISPR/Cas9 gene editing. Both iPSC cell lines were differentiated to neural crest cells (NCCs) and subjected to RNA-Seq and differential gene expression analysis via CuffDiff.

Results: Otocysts from E10.5 Chd7+/+ and Chd7Gt/+ embryos showed a length-dependent effect of CHD7 on gene transcription, with preferential effects on longer (>100 kb) genes. Notably, a similar length dependent effect was observed in heterozygous CHD7 mutation-positive human iPSCs differentiated into NCCs when compared to isogenic patient derived iPSCs in which the variant was corrected.

Conclusions: Reduced Chd7 function in the ear disrupts expression of genes involved in developmental patterning and neurogenesis, particularly genes of long length (>100 kb). Our findings support roles for CHD7 in chromatin events that regulate transcriptional elongation.
Abstract 24
RHINOVIRUS C15 INFECTION INDUCES EOSINOPHILIC
INFLAMMATION AND AIRWAYS HYPERRESPONSIVENESS IN
NAÏVE AND ALLERGEN-CHALLENGED MICE
T. Ishikawa, C. Rajput, M. Han, J. Lei, J.K. Bentley and M.B.
Hershenson. Department of Pediatrics, University of Michigan, Ann
Arbor, MI

Background: Infections with rhinovirus C (RV-C) have been associated
with severe asthma exacerbations in children.

Objectives: We sought to develop a mouse model of RV-C15 airway
disease to study underlying mechanisms of airway inflammation.

Design/methods: Full length cDNA encoding RV-C15 was reverse
transcribed and the resulting RNA transfected into HeLa-H1 cells. Live
virus was propagated in HeLa-E8 cells expressing the human CDHR3
529Tyr allele (associated with increased RV-C15 binding and
replication). Virus was concentrated and partially purified by
ultrafiltration. 8-10 wk old naïve BALB/c mice were treated with 5x10⁶
PFU RV-C15, RV-A1B or sham HeLa cell lysate and lungs harvested 4-
48 hours later for analysis of viral copy number, BAL cells, histology,
cytokine expression and airways responsiveness. Selected mice were
sensitized with 100 μg house dust mite (HDM) and challenged with 10
μg HDM (on days 10 and 11 after sensitization) one day prior to infection.

Results: Mice inoculated with 5 x 10⁶ PFU RV-C15 showed 10⁷ copies
of vRNA/μg lung RNA up to 16 h after infection, with levels declining
thereafter. IFNs-α, β and λ mRNA peaked 48-72 hrs after infection.
Immunofluorescence verified localization of RV-C15 in airway epithelial
cells. Compared to RV-A1B, mice infected with RV-C15 showed higher
bronchoalveolar eosinophils, lung mRNA expression of IL-5, IL-13, IL-25
and Muc5ac, peribronchial deposition of IL-25 and IL-33, and expansion
of type 2 innate lymphoid cells. Similar results were found after allergen
treatment, including greater airway methacholine responsiveness. UV-
irradiation of RV-C significantly reduced cytokine mRNA expression.
RV-C15 infection of differentiated mouse airway epithelial cells induced
mRNA expression of IFNs, IL-25, CXCL1 and CXCL2.

Conclusions: RV-C15 infects mouse airways. Compared to RV-A1B,
RV-C15 induces greater type 2 airway inflammation. Our findings
provide insight into the pathophysiology of RV-C asthma exacerbation.

Supported by R01 AI120526 and R01 HL134369.
Abstract 25

USE OF Sd MUTATION TO IDENTIFY CELL POPULATIONS THAT DIRECT CAUDAL ORGANOGENESIS

Peedikayil E. Thomas, Peter Orchard, James S. White, Anna Mychalowych, Stephen C.J. Parker and Catherine E. Keegan

The homozygous Danforth’s short tail mutant (Sd) mouse phenotype includes severe malformations of axial skeleton with absent tail, kidney agenesis, anal atresia, and persistent cloaca. Sd is an excellent model to study human caudal malformations. The Sd mutation is an endogenous retrovirus (ERV) insertion 12.5 kb upstream of the Ptf1a gene on mouse chromosome 2 and is inherited in a semi-dominant manner with complete penetrance. We have demonstrated substantial transcriptome changes in E9.5 Sd embryos resulting in down regulation of SHH pathway genes. In addition, the effect of the ERV insertion on Ptf1a expression may be mediated by increased chromatin accessibility at a conserved Ptf1a enhancer near the ERV insertion. To examine the effect of ectopic Ptf1a on neuro-mesodermal progenitors, we compared the expression patterns of Ptf1a and T (Brachyury) in wild type and mutant embryos at E7.5-E10.5 by RNA whole mount in situ hybridization. The majority of the cells ectopically expressing Ptf1a are distinct from the T expressing primitive streak cells although they overlap at the node, neural tube, posterior notochord, and some mesodermal progenitors. To determine the direct targets of ectopic Ptf1a activation in Sd mutant tailbuds, we are in the process of epigenomic profiling using CUT & RUN and CUT & Tag analyses. We are also analyzing Ptf1a downstream targets in embryos E8.5-E10.5 by in situ hybridization to evaluate cell fate changes due to ectopic Ptf1a. We plan to perform single cell RNA-sequencing to generate single cell molecular maps in discrete cell populations in wild type and Sd mutant E9.5 tailbuds. We propose that the Sd mouse is an excellent model to study cell fate and the single-cell transcriptional landscape of caudal birth defects.
DNA METHYLATION ACTIVATES VIRULENCE FACTOR EXPRESSION AND PROMOTES DISEASE IN EXPERIMENTAL STREPTOCOCCUS PYOGENES INFECTION

E Holley¹, J Nevarez¹, T Nye², L Simmons², and M Watson¹
¹Division of Pediatric Infectious Diseases, Department of Pediatrics
²Department of Molecular, Cellular, and Developmental Biology, University of Michigan, Ann Arbor, MI, USA

Background: DNA methylation has been extensively studied as a regulator of gene expression among eukaryotes, but the regulatory role for DNA methylation has been far less studied in bacterial pathogens. *Streptococcus pyogenes*, or Group A Streptococcus, is an important bacterial pathogen of children. Our group has recently shown that *S. pyogenes* utilizes DNA methylation at N6-methyladenine (m6A) as a regulatory mechanism modulating gene transcription and influencing the expression of several genes recognized as potential virulence factors.

Objectives: Our goal was to determine if DNA methylation impacts virulence properties of *S. pyogenes* in experimental models of bacterial pathogenesis. Methods: *S. pyogenes* strain MEW123 is a pediatric pharyngitis isolate expressing m6A DNA base modifications. An in-frame genetic deletion of a 3-gene operon encoding the only Type-I Restriction-Modification locus in the genome was constructed, producing strain MEW513 (ΔRSM). The virulence potentials of *S. pyogenes* strains were assessed via *in vitro* human tissue culture assays, and *in vivo* murine models of mucosal colonization and skin and soft tissue infection.

Results: The ΔRSM mutant lacked essentially all m6A DNA base modifications. RNA sequencing found that ~20 genes were strongly down-regulated in the mutant strain compared to the MEW123 parent, most notably genes in the core Mga regulon involved in tissue adherence and evasion of the host immune response. The ΔRSM mutant was attenuated for adherence to human epithelial cells, and was attenuated for intracellular survival within human neutrophils compared to the MEW123 parent. The ΔRSM mutant strain failed to suppress the host immune response, producing significantly larger skin lesions with greater host neutrophil recruitment and cytokine expression in a murine soft tissue infection model compared to the MEW123 parent. Conclusions: DNA m6A modifications regulate gene expression at the transcriptional level in *S. pyogenes* and influence virulence in both *in vitro* and *in vivo* experimental models of infection. Future work will identify the mechanisms of m6A-sensitive transcriptional regulatory proteins, including Mga. Work supported by the Charles Woodson Collaborative Research Award, and NSF awards MCB1714539 and DGE 1256260.
THE ATP-DEPENDENT CHROMATIN REMODELER CHD7 IS CRITICAL FOR PROPER COCHLEAR LENGTH, HAIR CELL STRUCTURE, AND AUDITORY NERVE ORGANIZATION

V. Balendran¹, J. Cimerman¹, L.A. Beyer³, J. M. Skidmore¹, E.A. Hurd⁴, Y. Raphael³, and D. Martin¹,² Departments of ¹Pediatrics; ²Human Genetics; ³Otolaryngology; University of Michigan, Ann Arbor.
⁴University of Edinburgh, Edinburgh, Scotland, UK.

Background: Epigenetic regulation of gene transcription by chromatin remodeling proteins has emerged as having a significant role in inner ear development. Pathogenic variants in the Chromodomain Helicase DNA-binding protein (CHD7) cause CHARGE syndrome, which presents with malformation in the developing mammalian ear. Germline deletion of Chd7 mice is embryonic lethal, whereas heterozygous Chd7 loss-of-function mice display mild mixed sensorineural/conductive hearing loss. CHD7 is broadly expressed in the mouse auditory epithelium as early as E13.5, yet the pathogenic effects of cochlear Chd7 loss have not been fully defined.

Methods: Here we characterize cochlear and auditory epithelial phenotypes after Foxg1Cre, Atoh1Cre, and Ngn1Cre-mediated deletion of Chd7. Inner ear morphology was assessed using paint-fill and the Scanning Electron Microscopy (SEM) as well as immunofluorescence staining. Auditory Brainstem Responses (ABR) and distortion Product Otoacoustic Emissions (DPOAE) have been applied to evaluate the peripheral auditory function.

Results: Deletion of Chd7 in Foxg1Cre; Chd7⁷⁴⁻/Flox mice resulted in disorganized, ectopic, and supernumerary rows of hair cells as well as disrupted innervation with excess axonal looping. Cochlear whole mount dissection and staining of P1 Atoh1Cre; ZsGreen/+ and Ngn1Cre; ZsGreen/+ cochleae revealed that in the early postnatal cochlea, Chd7 expression is restricted to the hair cells. P42 Atoh1Cre; Chd7⁷⁴⁻/+ and Atoh1Cre; Chd7⁷⁴⁻/Flox mice displayed disrupted hearing compared to wildtype controls as measured by ABR and DPOAE. Deletion of Chd7 in developing neuroblasts by Ngn1Cre did not preclude neuronal differentiation, but Chd7 deletion in the P1 organ of Corti disturbed hair cell organization resulting in supernumerary hair cells in the apex.

Conclusions: These observations suggest the presence of dosage-, tissue-, and time-sensitive roles for CHD7 in hair cell morphology, epithelial organization, and cochlear neuronal guidance. Interestingly, the otocyst and maturing neurons appear uniquely sensitive to Chd7 deficiency, whereas the surrounding otic mesenchyme is not. These studies indicate that CHD7 acts to regulate cochlear size and epithelial and neuronal organization, providing novel information about roles for CHD7 in the development of both auditory epithelia and neurons.
Abstract 28

TOLL-LIKE RECEPTOR 4-MEDIATED MYOFIBROBLAST DIFFERENTIATION AND SUPPRESSION OF PDGF RECEPTOR SIGNALING: A NOVEL MECHANISM FOR INFLAMMATION-INDUCED HYPOALVEOLARIZATION

Brady AE, Cui TX, Fulton CT, Rosenbloom L, Popova AP, Dept. of Pediatrics, Michigan Medicine.

Background: Infection and inflammation have been associated with the development of bronchopulmonary dysplasia (BPD). Pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6 are higher in tracheal aspirates of infants who develop BPD. Furthermore, premature infant airway colonization with Gram-negative bacteria is associated with longer supplemental oxygen need. The histopathologic changes in BPD include hypoalveolarization and interstitial myofibroblast accumulation. We have also shown that platelet-derived growth factor receptor (PDGFR) expression is decreased in BPD. Whether early-life infection or inflammation directly impairs lung growth is unknown. In this study, we hypothesize that LPS exposure of immature mice promotes myofibroblast differentiation and inhibits PDGFRα expression in a TLR4-dependent manner, thereby disrupting lung alveolarization.

Methods: Immature C57BL/6J mice were inoculated with 3ug/10ul of LPS from E. coli O26:B6 or PBS intranasally on day of life 3, 5, 7, and 10. Selected mice were injected intraperitoneally with the TLR4 inhibitor TAK-242 or control. Mouse E16 fetal lung explants were cultured in vitro in the presence of LPS. Saccular and alveolar growth was assessed by lung morphometry. Lung gene expression was analyzed by qPCR, ELISA and immunostaining.

Results: Neonatal LPS induced lung mRNA and protein expression of pro-inflammatory TNF-α, IL-6 and IL-17a. In addition, LPS disrupted alveolar growth leading to larger alveoli and increased alveolar chord length. LPS reduced PDGFRα mRNA and protein expression, also reduced were Fgfl, Spry1 and Pdgfrb mRNA expression, each of which are involved in alveolarization. LPS induced accumulation of α-smooth muscle actin (SMA)-positive myofibroblasts in the lung interstitium. Treatment with the TLR4 inhibitor TAK-242 protected immature mice from LPS-induced hypoalveolarization, preventing increases in alveolar chord length, and attenuated the effect on α-SMA and PDGFRα expression. Finally, in mouse fetal lung explants, LPS prevented growth (increase in area) and reduced saccular airspace chord lengths. LPS also induced fetal lung explant α-SMA mRNA and protein expression.

Conclusions: Our findings demonstrate that in immature mice, LPS induces a pro-inflammatory response and hypoalveolarization with reduced PDGFRα expression and interstitial myofibroblast accumulation in a TLR4-dependent manner. Future studies will determine the mechanisms by which TLR4-dependent pro-inflammatory signals control PDGFRα expression, promote myofibroblast differentiation and impair lung growth.
Abstract 29

HIGH FAT DIET DURING LACTATION PROGRAMS OFFSPRING RISK FOR NAFLD AND INTESTINAL MICROBIOME AND THE IMPACT OF METFORMIN RESCUE

H Hafner1, Carlson Z1, H Reynolds1, E Chang1, K Singer1, B Gregg1
1Division of Pediatric Endocrinology, University of Michigan

Background: Research has shown that maternal high fat diet and obesity during pregnancy and lactation can have significant effects on offspring metabolic programming and risk for developing Non-alcoholic fatty liver disease (NAFLD). Isolating the early postnatal period of development may offer a window for intervention to reduce these risks.

Objective: Our objective was to investigate the potential of maternal metformin exposure to ameliorate the adverse effects of a high fat diet confined to the lactation period on offspring intestinal microbiome, insulin sensitivity and their susceptibility to NAFLD in adulthood.

Methods: C57/Bl6J females were fed a normal diet (ND-Lac), a 60% kCal from fat diet (HFD-Lac), or a 60% kCal from fat diet with 3 mg/mL metformin HCl administered in water (HFD+Met-Lac) starting at parturition through postnatal day 21 at which point offspring were weaned onto a normal diet. Male offspring were monitored for weight gain and insulin sensitivity. Stool was collected at 4 weeks of age and analyzed for microbial content. At necropsy liver tissue was collected, weighed and analyzed by H&E staining and quantitative RT-PCR for genes related to lipid accumulation and metabolism.

Results: HFD+Met-Lac male offspring weighed less than ND-Lac and HFD-Lac mice starting at 4 weeks of age. This group also exhibited improved HOMA-IR at 8 weeks of age and improved insulin sensitivity at 10 weeks of age compared to HFD-Lac. Stool microbial community analysis at 4 weeks of age showed an overall change in the intestinal microbiome of HFD+Met-Lac mice with an increase in alpha diversity and a rescue of the bacteroidetes:firmicutes ratio compared to HFD-Lac mice. Micro-steatosis observed in livers of HFD-Lac mice was partially reversed by concurrent metformin exposure. Expression of genes relating to lipid accumulation, metabolism and insulin sensitivity were altered between HFD-Lac and HFD+Met-Lac.

Conclusion: These results suggest that metformin exposure during lactation may reverse alterations in intestinal microbiota, programmed insulin resistance, and hepatic lipid accumulation caused by lactational high fat diet exposure.
Abstract 30

EPIGENETIC HIJACKING OF PRENATAL BRAINSTEM ID1 EXPRESSION IN DIPG DRIVES INVASION AND RESPONSE TO CANNABIDIOL

Lowenstein1, R. Mody1, A. Chinnaiyan1, C. Hawkins3, P. Desprez2, S. McAllister2, S. Venneti1, C. Koschmann1
Micah Harris1, R. Woo2, R. Siddaway3, B. Mullan1, V. Yadav1, S. Stallard1, Z. Miklja1, K. Kasaian1, X. Cao1, A. Pasternak1, M. Castro1, P.
1University of Michigan Medical School, Ann Arbor, MI, 48109, USA.
2California Pacific Medical Center Research Institute, San Francisco, CA, 94107, USA.
3The Hospital for Sick Children, Toronto, Ontario, M5G 1X8

Background: Diffuse intrinsic pontine glioma (DIPG) is a devastating brain tumor with median survival of less than 15 months. Treatment options are limited, and there is a desperate need to identify novel therapeutic targets.

Objectives: (1) Analyze ID1 expression in human and murine DIPG by genomic and regional variables. (2) Characterize the epigenetic regulation of ID1 expression. (3) Characterize ID1 impact on invasion, migration, and proliferation. (4) Target ID1 with cannabidiol (CBD).

Methods: RNA-seq data was integrated across multiple human and mouse DIPG datasets. Chromatin immunoprecipitation-quantitative polymerase chain reaction (ChIP-qPCR) was performed to quantify H3K27ac and H3K27me3 at CpG islands associated with the ID1 gene. Pre-natal murine ENCODE data was analyzed for H3K27ac by brain region. A primary DIPG cell line (DIPG007) was used for genetic and pharmacologic (CBD) knockdown of ID1 and analysis of cell invasion (Matrigel), migration (scratch assay), and viability (MTT).

Results: Integrated RNA-seq dataset analysis demonstrated that ID1 is significantly elevated in DIPG compared to normal brain and cortex tumors. ChIP-qPCR of DIPG at autopsy (n=10) revealed elevated H3K27ac at the ID1 promoter region, suggesting an epigenetic basis for the ID1 upregulation seen in DIPG. H3K27ac and ID1 expression was found to be elevated in prenatal mice, primarily in pontine hindbrain. Knockdown of ID1 in DIPG007 significantly reduced invasion and migration, while proliferation was maintained. Consistent with this, multifocal RNA-seq on a DIPG autopsy demonstrated ID1 expression correlates with regional invasion. Finally, treatment of DIPG007 with CBD decreased ID1 expression and cell viability in a dose-dependent manner, highlighting CBD as a potential drug to target ID1.

Conclusion: Our results indicate that DIPGs epigenetically re-activate prenatal pontine ID1 signaling to promote invasion, and preliminary data indicate that CBD may be used to therapeutically target ID1. These exciting results introduce a novel therapeutic target in DIPG, which may be used to shape future therapies.
Abstract 31

ATRX LOSS IN PEDIATRIC GLIOMA RESULTS IN EPIGENETIC DYSREGULATION OF G2/M CHECKPOINT MAINTENANCE AND SENSITIVITY TO ATM INHIBITION

B. Mullan1, T. Qin2, R. Siada1, C. Danussi2, J. Brosnan-Cashman3, D. Pratt2, T. Garcia1, V.N. Yadav1, X. Zhao1, A. Rehemtulla3, M. Morgan1, S. Venneti1, A. Meeker3, J. Huse2, P. Lowenstein1, M. Castro1, C. Koschmann1

1University of Michigan Medical School, Ann Arbor, MI, USA; 2University of Texas MD Anderson Cancer Center, Houston, TX, USA; 3Johns Hopkins University School of Medicine, Baltimore, MD, USA

Background/Objectives: ATRX is a histone chaperone protein recurrently mutated in pediatric glioma. We previously confirmed its role in tumor progression and mutational burden in glioma. However, the mechanism which mediates the proliferative advantage of ATRX loss in pediatric glioma remains unexplained. Here, we describe the dysregulation of G2/M checkpoint maintenance in ATRX mutated HGG and a means to inhibit tumor growth in ATRX deficient glioma cells through ATM inhibition with in vitro and in vivo brain tumor models.

Methods/Results: Analysis of ATRX ChIP-seq performed in p53 -/- mouse neuronal precursor cells (mNPCs) demonstrated that ATRX binding sites were significantly enriched in gene promoters (p < 0.0001) and CpG islands (p < 0.0001) compared with random regions. Gene set enrichment (GSE) analysis identified that cell cycle and regulation of cell cycle were among the most significantly enriched gene sets (p=2.52e-16 and 1.61e-9, respectively). In line with this, the master cell cycle regulator CDKN1A was significantly down-regulated (p =0.0024) in human pediatric high-grade gliomas with ATRX mutation (PedsCbioPortal, n=247). We found that ATRX loss resulted in dysfunction of G2/M checkpoint maintenance: (1) ATRX-deficient pediatric glioma cells exhibited a seven-fold increase in mitotic index at 16 hours after sub-lethal radiation, and (2) murine glioma cells with ATRX knockdown demonstrated impaired pChk1 signaling on western blot at multiple time points after radiation compared to controls (p=0.0187). Notably the ATM signaling (pChk2) remained intact in those cells, suggesting a potential therapeutic target. ATRX-deficient mouse cells were uniquely sensitive to ATM inhibitors at 1 uM alongside 8 Gy radiation compared to controls with intact ATRX (AZD0156: p=0.0027 and AZD01390: p=0.0436). Using an ATM-luciferase reporter assay, AZD0156 demonstrated stronger ATM inhibition when compared to AZD1390. Mice intra-cranially implanted with ATRX-deficient glioma cells showed improved survival (n=10, p=0.0018) when treated with AZD0156 combined with radiation. Conclusion: Our findings show that ATRX loss in glioma results in unique sensitivity to ATM inhibition via epigenetic dysregulation of G2/M checkpoint maintenance.
INDUCIBLE CONDITIONAL DELETION OF GJB2 LEADS TO REDUCTION OF ENDOCOCHLEAR POTENTIAL AND ELEVATION OF ABR THRESHOLDS WITHOUT LOSS OF HAIR CELLS OR NEURONS

JM Skidmore1, L Beyer2, DL Swiderski2, X Ma2, L Kabara2, D Dolan2, Y Raphael2 and DM Martin1,3; Departments of Pediatrics1, Otolaryngology2, and Human Genetics3, U of Michigan, Ann Arbor, MI

Abstract 32

Background: Mutations in GJB2, encoding Connexin26 (Cx26), are the most common cause of autosomal recessive hereditary deafness. It has been challenging to model GJB2-related deafness in mice due to differences in disease progression. In humans with GJB2-related deafness, spiral ganglion neurons (SGNs) typically survive, whereas mice with Cx26 deletion in supporting cells (Sox10-Cre;Gjb2fl/fl) exhibit profound loss of SGNs. Here we tested an innovative mouse model for the delayed degeneration of hearing in the human ear using a temporally controlled Sox10-Cre to delete Cx26.

Methods: Reporter assay was used to confirm Cre expression in supporting cells of the organ of Corti in Sox10-CreERT2 mice after early (E11.5) or late (P14) tamoxifen exposure. To delete Gjb2, tamoxifen was administered by gastric gavage of postnatal day 1 (P1) Sox10iCreERT2;Gjb2fl/fl and Gjb2fl/fl littermate mice or intraperitoneally at P14. Hearing was analyzed using ABR audimetry and ears were collected from the same animals and analyzed histologically. At least 8 mice were analyzed for each experimental condition. Other animals in the cohort underwent surgery to determine the endocochlear potential. Ears from these animals were used to examine histology of the SGNs. Independent experimental pups were injected with AAV1.CMV.GJB2-GFP as a first step for testing phenotypic rescue by gene replacement therapy in these mice.

Results: Deletion of Gjb2 was confirmed by reduced anti-Connexin26 staining in ears. Consistent with Sox10-CreERT2 reporter activity, Gjb2 deletion reduced Cx26 staining was reduced in non-sensory cochlear cells and did not affect hair cell organization. Gjb2 deletion at P1 inhibited the development of hearing and led to coat hypopigmentation. Gjb2 deletion at P14 resulted in progressive decreased hearing and endocochlear potential over the next 3 weeks. The potential gene therapy treatment of injection of AAV1.CMV.GJB2-GFP into the cochlea of young pups led to gene expression in supporting cells.

Conclusions: Reduced Gjb2 dosage has important developmental stage- and cell type-specific effects on coat color and on auditory epithelial function, demonstrating important roles for Cx26 in development and maintenance of hearing.
Abstract 33

ROLES FOR SOX11 AND CHD7 IN A COMMON GENE REGULATORY NETWORK TO PROMOTE INNER EAR DEVELOPMENT

J. Cimerman1; E. D. Sperry1,2; R. Hojjati1; L. Lei5; D. L. Swiderski3; Y. Raphael3; and D. M. Martin1,3,4

Departments of 1Pediatrics, 2Medical Scientist Training Program, 3Otolaryngology – Head and Neck Surgery, and 4Human Genetics, University of Michigan, Ann Arbor, MI; 5Department of Biology, University of New England, ME.

Background: SoxC transcription factors represent a class of proteins involved in developmental regulation of inner ear morphogenesis. Prior studies in neural stem cells demonstrated that SOX11 is a genetic target of Chromodomain-helicase-DNA-binding protein 7 (CHD7), an ATP-dependent chromatin remodeler. Haploinsufficiency of CHD7 results in CHARGE syndrome, which presents with hearing loss and balance impairment related to inner ear dysplasia. The specific mechanisms by which loss of CHD7 results in inner ear malformation are not well understood. Here, we explored potential molecular genetic pathways of Sox11 and Chd7 in the developing mouse inner ear.

Methods: We performed inner ear paintfilling to reveal morphological semicircular canal abnormalities, histologic analyses of Sox11 and Chd7 mutant embryos, and qRT-PCR studies. Results: Lateral and posterior canal abnormalities were detected in Sox11+/− and Sox11−/− E14.5 ears. E12.5 Sox11−/− embryos revealed a failure of lateral canal fusion plate formation and canal projections, consistent with Chd7Gt/+ inner ear phenotypes. In situ hybridization showed spatiotemporal expansion of Bmp4 expression in E10.5 Sox11−/− embryos. Localization of the canal fusion plate markers Netrin1 and Laminin was unchanged in E12.5 Sox11−/− ears. QRT-PCR on microdissected E10.5 and E12.5 Chd7Gt/+ and Chd7Gt/Gt ears showed dosage-dependent reductions in Sox11 mRNA, consistent with restricted SOX11 protein expression in Chd7Gt/+ and Chd7Gt/Gt inner ears, respectively. Chd7Gt/+; Sox11+/− mice exhibited malformed semicircular canals, similar to those observed in Chd7Gt/+ mice. Conclusions: Sox11 is necessary for lateral and posterior semicircular canal morphogenesis, through control of cellular proliferation around the canal fusion plate. Additionally, Sox11 regulates Bmp4 in the presumptive lateral crista ampullaris. These results suggest that Sox11 is a putative effector of CHD7 function in the developing ear and reveal a novel Chd7-Sox11 regulatory network that promotes vestibular system development.
Abstract 34

RAPID, ULTRA-DEEP SEQUENCING OF DIPG FROM CSF USING A NOVEL HAND-HELD ELECTRONIC DNA ANALYSIS PLATFORM


1Neurosurgery, 2Department of Pediatrics, 3Department of Statistics, University of Michigan, Ann Arbor, MI

Background: Brain tumors release tumor DNA (tDNA) into cerebrospinal fluid (CSF), allowing for detection and serial monitoring of tumor-associated genetic mutations by CSF sampling. For midline and brainstem tumors such as diffuse intrinsic pontine glioma (DIPG), surgical biopsy risks neurological deficits. As such, liquid biopsy is needed. Current platforms for CSF tDNA analysis are limited by their requirement for assay development for each mutation (digital droplet PCR), or cost and timeliness (Illumina sequencing). We hypothesized that direct, electronic analysis of DNA with a novel hand-held platform (Oxford Nanopore) could provide real-time, ultra-deep (>1,000x reads) sequencing of DIPG CSF tDNA. Methods: We performed amplicon-based PCR on DNA from normal brain (n=6), normal CSF (n=13), tumor brain (n=3), and tumor CSF (n=10) to amplify wildtype and mutant H3F3A K27M, HIST1H3B K27M, and ACVR1 G328E genes from normal controls and pediatric patients with DIPG. We performed parallel barcoded sequencing of multiple samples run in duplicate or triplicate using NanoPore MinION technology and determined variant allele fraction (VAF) of each amplicon via an expeditious pipeline using MinKNOW, Guppy, MiniMap2, and Integrated Genome Browser. Results: NanoPore sequenced 30 amplicons with average depth of 17,244 reads per amplicon in under 80 minutes. H3F3A K27M VAF was 49.14% (S.D. 0.49) in tumor tissue and 13.63% (S.D. 0.35) in CSF. VAF was 10.42% (S.D. 1.11) for HIST1H3B K27M and 7% (S.D. 0.46) for ACVR1 G328E in CSF. VAF were comparable to biopsy results by Illumina. Sensitivity and specificity were >80% and 99%, respectively, with p-values of < 0.05 for normal versus tumor samples. Conclusions: NanoPore MinION technology rapidly, reliably, and efficiently sequences tumor mutations in pooled tissue and CSF from patients with DIPG with high sensitivity and specificity. NanoPore is more efficient, and cost and time effective than digital droplet PCR and Illumina.
Abstract 35
IMPAIRED FERTILITY IN MICE WITH ACD/TPP1 TEL PATCH MUTATION
A. Mychalowych1, P. Thomas1, D. Poltavski1, J. Graniel2, A. Friedman3, J. Nandakumar2, I. Maillard4, C. Keegan1
1 Department of Pediatrics, Division Genetics, University of Michigan
2 Department of Molecular, Cellular, and Developmental Biology, University of Michigan
3 Department of Interior Medicine, University of Michigan
4 Department of Medicine, Division Hematology-Oncology, University of Pennsylvania

Background: The Shelterin complex has important roles in the end protection and end replication of telomeres; lack of normal Shelterin function results in genomic instability and cell death. One of the proteins in this complex is TPP1, which binds to POT1 and recruits telomerase to the telomere via the TEL patch domain. Objective: To create a mouse model of dyskeratosis congenital. We previously reported a patient with Hoyeraal-Hreidarsson syndrome (HH)—a severe form of dyskeratosis congenita (DC)—characterized by cerebellar hypoplasia, immunodeficiency, intrauterine growth retardation, and bone marrow failure due to extremely short telomeres and identified a deletion of a single amino acid (K170) in the TEL patch domain of the Acd gene encoding Tpp1 (Kocak 2014). Methods: We generated the AcdTpp1 mouse model via CRISPR/Cas9 deletion of the K82 residue, the equivalent of K170 in humans. Results: We have demonstrated telomere shortening with successive generations in homozygous K82/K82 mutants by Flow-FISH. After intercrossing K82/K82 mutants and wild-type control mice for five generations, we observe impaired fertility as the number of mutant litters and litter size decreased while wild-type breeding pairs have had no reduction in fertility. Further studies have revealed smaller testes and abnormal testis histology in mutant males compared to wild-type males. Conclusions: Our data suggests that telomeres in germ cells are shortening faster than in somatic cells in our mouse model. Further experiments will explore the mechanism by which this occurs.
Abstract 36
INVESTIGATING THE GENETIC ETIOLOGY OF CHARGE SYNDROME
J. Eisenberg¹; A. Moccia²; S. Bielas²; D.M. Martin¹,²
¹Pediatrics and ²Human Genetics, University of Michigan, Ann Arbor, MI.

Background: Solving the genetic basis of developmental disorders is necessary to gain a better understanding of the underlying pathogenesis, as evident from the discovery of the role of $CHD7$ variants in CHARGE syndrome (Coloboma, Heart defects, Atresia of the choanae, Retardation of growth and development, Genital abnormalities, and Ear anomalies including deafness). To date, $CHD7$ pathogenic variants are not present in 5-30% of individuals with CHARGE, suggesting additional genetic and/or environmental etiologies including epigenetic changes or changes in non-coding regions of the genome.

Methods: We performed whole exome sequencing (WES) on 28 families in whom at least one individual presented with features highly suggestive of CHARGE syndrome.

Results: Pathogenic variants in $CHD7$ were present in 15 of 28 individuals (53.6%), whereas four individuals (14.3%) had pathogenic variants in genes ($RERE$, $KMT2D$, $EP300$, or $PUF60$) associated with other Mendelian disorders. These results illustrate a higher degree of oligogenicity than previously recognized for individuals with clinical CHARGE features.

Conclusions: Notably, $CHD7$ and the other four genes ($RERE$, $KMT2D$, $EP300$, and $PUF60$) encode proteins that act to remodel chromatin and regulate transcription. The overlapping phenotypes and the regulatory roles of these genes raise the possibility that regulatory elements modulating or modulated by these developmentally important genes may be shared and contribute to the pathology of CHARGE. Discovery of these such regions, coupled with sequencing of our WES-negative CHARGE cohort (32.1%), will be critical for understanding the contribution of non-coding variants and structural variations to human disease through an influence on gene regulation. In collaboration with the University of Washington, we plan to screen the 19 WES-negative individuals in our CHARGE cohort for variants in CHD7 cis-regulatory elements.
Abstract 37

RISK FACTORS FOR DEVELOPMENT AND PREVENTION OF PERIANAL FISTULAE IN PEDIATRIC CROHN’S DISEASE

A. Singer1; J. Adler 1,2

1. Pediatric Gastroenterology; 2. Susan B. Meister CHEAR Center, University of Michigan, Ann Arbor

Background: Perianal fistulae are among the more severe complications of Crohn’s disease (CD). Little data exist on risk factors for their development and no evidence-based preventive strategies exist. We aimed to identify risk factors for perianal fistula development among pediatric CD patients.

Methods: We retrospectively examined records of patients diagnosed with CD at Michigan Medicine or transferred within a month of diagnosis and prior to starting therapy. To ensure lack of occult fistula, inclusion required cross-sectional imaging confirmation of absence of penetrating perianal disease (MRI is standard of care at diagnosis). Patients were followed for up to three years after diagnosis with the primary outcome of perianal fistula development. Variables including non-penetrating perianal lesions (skin tags, fissures), disease location, age, race, sex, inflammatory markers, steroid use, and medication were analyzed. We performed cox proportional hazard models assessing time free from perianal fistula.

Results: In total, 130 patients met inclusion criteria. The cumulative incidence of perianal fistulae at 12, 24, and 36 months after CD diagnosis was 7.5%, 9%, and 11%, respectively. Development of perianal fistulae was associated with presence of non-penetrating perianal lesions (hazard ratio [HR], 10.23, [95% confidence interval [CI] 1.99–52.55) and non-white race (HR 5.12, 95%CI 1.15–22.67). Treatment with anti-TNFα medications prevented perianal fistula formation compared with other treatments in the entire study population (HR 0.11, 95%CI 0.03–0.34) and in the cohort with non-penetrating perianal lesions at diagnosis (HR 0.09, 95%CI 0.04–0.37).

Conclusions: Non-penetrating perianal lesions at diagnosis and non-white race are risk factors for perianal fistula development among pediatric CD patients. Treatment with anti-TNFα prevents perianal fistula development. The increased risk of non-penetrating perianal lesions is modifiable with early anti-TNFα treatment.
Abstract 38
THE RELATIONSHIP BETWEEN PATIENT-REPORTED OUTCOMES AND LONGITUDINAL CLINICAL CHARACTERISTICS AMONG PATIENTS WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS
J. Troost1; A. Waldo1; N. Carlozzi2; E. Herreshoff1; D. Gipson1
1Division of Nephrology, Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA
2Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI, USA

Background: Understanding the relationship between clinical and patient reported outcomes (PROs) will help support future clinical trial design for novel therapies of focal segmental glomerulosclerosis (FSGS). Objectives: to assess HRQOL in children and adults with FSGS and to identify associations between key clinical and laboratory data and these important outcomes in children and adults.

Design/method: FSGS patients age 8 and older enrolled in the Nephrotic Syndrome Study Network completed several PROMIS® PRO measures (Children: Global Health, Mobility, Fatigue, Pain Interference, Depression, Anxiety, Stress, Peer Relationships; Adults: Physical Functioning, Fatigue, Pain Interference, Sleep Impairments, Mental Health, Depression, Anxiety, Social Satisfaction) at baseline and during longitudinal follow-up for a maximum of five years. Linear-mixed effects models were used to determine which demographic, clinical, and laboratory features were associated with PROs for each of the 8 child and adult PROMIS measures studied.

Results: There were 45 children and 114 adult FSGS patients enrolled that had at least one PRO assessment and a total of 519 patient-visits. Multivariable analyses among children found edema was associated with Global Health (-7.6 points \( p=0.02 \)) and Mobility (-4.2 \( p=0.02 \)); number of reported symptoms with Depression (-2.7 per symptom \( p=0.009 \)) and Anxiety (-2.3 \( p=0.02 \)) and number of emergency room visits in the prior 6 months with Mobility (-2.8 per visit \( p<0.001 \)) and Fatigue (-2.4 \( p=0.03 \)). Among adults, number of reported symptoms was associated with all 8 measures with effect size estimates ranging from -0.9 to -1.5 per symptom. Number of emergency room visits was associated with worse Fatigue, Pain Interference, Sleep Impairments, Depression, Anxiety, and Social Satisfaction. Laboratory markers of disease severity (i.e., proteinuria, estimated glomerular filtration rate, and serum albumin) did not predict PRO in multivariable analyses, with the single exception of complete remission and better Pain Interference scores among Children (+9.3 \( p=0.03 \)).

Conclusions: Findings indicate that PROs provide important information about health related quality of life for persons with FSGS that is not captured solely by the examination of laboratory-based markers of disease. As such, including PROs in clinical care and research may provide a more comprehensive assessment of the patient experience.
Abstract 39

IMPLEMENTING STANDARDIZED PSYCHOSOCIAL SCREENING FOR PEDIATRIC INPATIENTS
Dana Albright, PhD1, Allison Gornik, MA2, Melissa Andersen, PhD1, Kimberly Monroe, MD, MS1, Kristin Kullgren, PhD1

1 University of Michigan/Mott Children’s Hospital, Department of Pediatrics
2 Michigan State University, Department of Psychology

Background: Pediatric consultation-liaison (C-L) behavioral health providers receive referrals for concerns such as adjustment to hospitalization, treatment adherence, and/or psychological support (Carter, Thompson, & Townsend, 2014). While C-L providers educate medical colleagues on biopsychosocial factors affecting hospitalized children, C-L providers rely on their medical colleagues to identify patients needing evaluation and intervention. The aim of this study was to examine the feasibility and utility of a standardized psychological screening tool for pediatric patients admitted to a tertiary pediatric hospital, in order to identify patients at high risk for adjustment difficulties and optimize referrals to C-L behavioral health providers.

Methods: The PROMIS Parent Proxy 25 (PROMIS) was administered to parents of youth ages 5 to 17 years (N = 127) admitted to the general medicine floor of an inpatient children’s hospital. The PROMIS 25 Parent Proxy was developed by the NIH to capture the psychosocial needs (anxiety, depression, fatigue, pain, peer relations, and mobility) of pediatric populations. Chart review was used to dichotomize children into those who received behavioral health consultation during their admission and those who did not.

Results: Results indicate that the PROMIS Anxiety and Depression scales consistently differentiated between children’s consultation status ($\chi^2(1)=11.68, p=.001, R^2 = .128$ and $\chi^2(1)=15.61, p<.001, R^2 = .172$ respectively). Pediatric inpatients referred for C-L behavioral health services had higher rates of both anxiety and depression on parent-report (OR = 4.2 and OR = 5.85 respectively).

Discussion: Results suggest that the PROMIS may be a useful screening tool to determine pediatric patients who need behavioral health referrals. Parent report may be useful for medical providers to identify patients with behavioral health needs and may optimize C-L referrals. Throughout the process of implementing psychological screening, several opportunities and challenges for systematic psychological screening in a pediatric hospital setting to facilitate C-L services were identified.
VENTRICULAR-VENTRICULAR INTERACTIONS IN LONG-TERM FOLLOW-UP AFTER THE PEDIATRIC ROSS PROCEDURE
Mehul Patel1; Adam Dorfman1; Sunkyung Yu1; Ray Lowery1; Maryam Ghadimi Mahani2; Prachi Agarwal2; Jimmy Lu1 (1Michigan Congenital Heart Center, 2Radiology, University of Michigan, Ann Arbor, MI)

Background: Patients post Ross procedure are at risk for right (RV) and left ventricular (LV) dilation and dysfunction. Previous studies have shown a relation between aortic root dilation and neo-aortic insufficiency with LV dysfunction, but potential interaction of RV and LV parameters has not been evaluated in this population. Methods: Patients who underwent Ross procedure under 19 years of age and evaluated by cardiac magnetic resonance (CMR) from 2007-2018 at our center were retrospectively reviewed. Exclusion criteria included neoaortic valve replacement prior to CMR. Residual neo-aortic and conduit stenosis gradients were obtained from echocardiograms. RV and LV peak longitudinal (LS) and circumferential strain (CS) were measured using tissue tracking software (cvi42). Multivariable linear regression or logistic regression controlling for patient characteristics was performed for CMR variables associated with LV function. Results: In 58 patients (median 9.7 years post Ross procedure) the median neo-aortic regurgitant fraction (RF) was 12%, median conduit RF was 8%, and median conduit gradient was 33 mmHg. Lower LV ejection fraction (EF), LV CS and LV LS were each associated with male gender and longer time since Ross procedure. There was no association with LV late gadolinium enhancement, neo-aortic/conduit regurgitation, or neo-aortic gradient. In univariate analysis, LVEF ≤55% was associated with lower RVEF, greater aortic root size, and LV but not RV dilation. LV CS and LV LS both correlated with RV CS and RV LS. Relation of aortic root, RV and LV function remained significant in multivariable analysis (Table). Conclusion: In long-term follow up after the Ross procedure in the pediatric age range, there are significant ventricular-ventricular interactions. Such interactions may impact decision-making on timing of intervention. Long term clinical follow up and evaluation with CMR is warranted to evaluate possible association with clinical outcome in this population.

<table>
<thead>
<tr>
<th>Table. Independent association between RV and LV dysfunction in multivariable analysis, controlling for gender, time since Ross procedure, additional cardiac surgery, and hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure</td>
</tr>
<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>LV ejection fraction ≤55%</td>
</tr>
<tr>
<td>Aortic root dimension</td>
</tr>
<tr>
<td>RV longitudinal strain</td>
</tr>
<tr>
<td>RV circumferential strain</td>
</tr>
<tr>
<td>LV longitudinal strain</td>
</tr>
<tr>
<td>LV circumferential strain</td>
</tr>
</tbody>
</table>
“EAT YOUR GREEN BEANS!” MATERNAL VERBAL PROMPTS AND CHILD VEGETABLE INTAKE: THE MEDIATING ROLE OF PICKY EATING
A Jordan1; DP Appugliese2; AL Miller3; JC Lumeng4; MH Pesch4

1Moorhouse University Medical School; 2 Appugliese Professional Advisors; 3 School of Public Health, University of Michigan; 4Department of Pediatrics, University of Michigan

Background: Maternal prompting has been associated with child vegetable intake. It is unknown if different maternal prompting types are associated with vegetable intake in children perceived to be picky versus non-picky eaters. Objectives: 1) To identify the different prompting types mothers use with their children when presented a familiar vegetable, and 2) to test the correlation of counts of maternal prompting types with child vegetable intake in picky vs. non picky eaters. Design/Methods: 199 low-income mother-child dyads (mean child age 6.0 years) participated in a videotaped standardized laboratory eating protocol, during which each participant was presented with green beans. A coding scheme was developed and reliably applied to categorize mothers’ prompting types. The prompting types were: Coercive Control (Sub-Categories: Reward and Pressure to Eat) and Autonomy Promotion (Sub-Categories: Modeling, Reasoning, Praise, and Choice). Anthropometrics were measured. Mothers completed questionnaires. Bivariate analyses were constructed to test the association between counts of maternal prompting types with amount of green beans eaten in the whole sample, and stratified by child picky eater status. Results: Mothers used on average 1.66 prompts. Greater use of Coercive Control, Modeling and Total Prompts were all inversely correlated with amount of green beans eaten by the child. Greater use of Praise was positively correlated with amount of green beans eaten by the child. In stratified models, greater use of Coercive Control prompts was inversely associated with amount of green beans eaten by the child in non-picky eaters, but not in picky eaters. There was no interaction between other prompting types and child picky eater status in predicting amount eaten. All p-values <0.05. Conclusions: Mothers use different prompting types to encourage their children to eat vegetables, most of which may be correlated with reduced intake.
Abstract 42
COMMUNICATION ABOUT PROGNOSIS AND END-OF-LIFE IN PEDIATRIC ORGAN FAILURE AND TRANSPLANTATION
Melissa K. Cousino1,2, Kurt R. Schumacher1,2, John C. Magee2,3, Joanne Wolfe4,5, Sunkyung Yu1, Sally J. Eder1, & Emily M. Fredericks1,2

1Department of Pediatrics, Michigan Medicine, Ann Arbor, Michigan, 2University of Michigan Transplant Center, Ann Arbor, Michigan, 3Department of Surgery, Michigan Medicine, Ann Arbor, Michigan, 4Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, Massachusetts, 5Department of Pediatrics, Boston Children’s Hospital, Boston, Massachusetts

Background: Despite advancements in treatment and survival, pediatric organ failure and transplant populations continue to face significant risks of morbidity and mortality. Little scientific attention has been given to addressing the end-of-life care needs of this growing population of young people. This study characterized current practices, beliefs, and challenges specific to the disclosure of prognosis and end-of-life care topics among providers caring for pediatric organ failure and transplant populations.

Methods: This cross-sectional study included 144 healthcare providers actively caring for children, adolescents, and young adults with organ failure or solid organ transplant history. Participants completed an electronic survey measuring frequency and comfort in discussing the following topics with patients and parents: prognosis/survival statistics, re-transplantation, advance care planning (ACP), and death/dying. Descriptive statistics, two-sample t tests, and analysis of variance were used.

Results: Fewer than half of respondents regularly discuss prognosis/survival statistics and potential need for re-transplantation with their pediatric and young adult patients. Less than 20% of providers engage their pediatric patients in ACP discussions, and approximately 30% facilitate such discussions with young adult patients. Pediatric organ failure and transplant providers endorse a number of barriers specific to discussing these topics.

Conclusions: Pediatric organ failure and transplant providers do not regularly discuss prognosis or end-of-life care topics with this patient population. Communication-focused intervention research is needed to improve honest and compassionate discussion of these topics that is aligned with both patients’ and parents’ needs and preferences.
Abstract 43
UMBILICAL GRANULOMA AND ASSOCIATED PATIENT CHARACTERISTICS
Paramjeet Kochhar, David Hanauer, Esther Yoon
Division of General Pediatrics, University of Michigan

Background: Umbilical granulomas are the most common anomaly of the umbilicus in neonates. These lesions are characterized by an overgrowth of granulation tissue that persists at the base of the umbilical cord after its separation. However, it is unclear why some infants develop an umbilical granuloma while others do not.

Objective: The objective of this study was to describe patient characteristics associated with umbilical granulomas.


Results: We evaluated 202 infants with diagnosis of umbilical granuloma in 2016. We estimate that the incidence of umbilical granuloma in infants born at Michigan Medicine in 2016 was 10%. All 202 infants were treated with silver nitrate cautery. Seven patients needed multiple silver nitrate treatments and 2 were referred to pediatric surgery for further evaluation and treatment. 48% were male (N=97). The majority (76%) were born by vaginal delivery (N=154); 70% had negative maternal GBS status (N=142); 60% of males were circumcised (N=58); 87% did not use biliblankets (N=176).

Conclusion: We describe patient characteristics of infants diagnosed with and treated for umbilical granuloma. The vast majority of umbilical granulomas required only single treatment with silver nitrate cautery.
EFFECT OF MATERNAL EDUCATION ON BIRTH WEIGHT, WEIGHT GAIN AND BREAST FEEDING PRACTICES IN A COHORT OF PREMATURE AND LOW BIRTH WEIGHT INFANTS IN KUMASI, GHANA.

Y.A. Civil1; A. Bakari2; A. Campbell3; Hart-Johnson, T.4; E. Parker5; R.A. Blackwood4,6
1General Pediatrics, University of Michigan; 2Ghana Health Service, 3Children’s National Health System, 4Office for Health Equity and Inclusion; 5University of Michigan, 6Pediatric Infectious Diseases.

Background: Maternal education has been shown to be a positive predictor for reducing child and infant mortality in Sub-Saharan Africa. Increased maternal education raises a mother’s awareness of good health care practices including prenatal care, recognition of children’s illnesses, vaccinations and utilization of available health services, which all work towards positively affecting a child’s health. Few studies have been done in Ghana to evaluate the strength of correlation between maternal education and low birth weight or premature infants, who are at higher risk for neonatal death.

Objective: The goal of this study is to examine the effects of maternal education on birth weight, weight gain, and feeding practices during the post-natal period within a group of premature and low birth weight infants hospitalized at MBUs in Sunreso Hospital and Kumasi South Hospital.

Methods: The study population includes premature and low birth weight infants from both hospitals. Retrospective chart review of the infants’ hospital record was done. A WHO validated infant feeding survey containing socio-demographic information was given at postnatal visits. To evaluate birth weight and weight change, variables were created by subtracting weight at 48 hours from weight at 3, 6 and 12 months. Paired sample t-tests comparing means provide an initial look at weight gain in the sample. To assess differences in weight-gain by education level, a Pearson correlation test between education and the computed variable was used.

Results: 4.8% of the participants have no formal education or just have primary school education; 55.3% have achieved JHS level; 24.5% have achieved SHS level, and 15.4% have tertiary level education (n=188). To date, preliminary findings have already shown a correlation between maternal education and infant weight gain. However, birth weight was not found to be statistically significant based on mother’s educational level.

Conclusion: Health providers caring for these infants in Sub-Saharan Africa or any low resource setting should be more patient with mothers that have limited or no formal education, particularly when providing instructions on caring and feeding the infant at home.
Abstract 45
TAKING THE PAIN OUT OF MANAGING PEDIATRIC SOMATIC SYMPTOM AND RELATED DISORDERS IN THE ED: EVALUATION OF A STANDARDIZED PROTOCOL
Pardon A1, Pomeranz E1,2, Sroufe N1,2, Malas NM1,3, Monroe KK1,4, Sturza JS1,4, Klein J1,5, Hutton D1,5, Kullgren KA1,4

University of Michigan1, Department of Pediatric Emergency Medicine2, Department of Psychiatry3, Department of Pediatrics4, School of Public Health5

Background: Somatization often contributes to youth presenting to the Emergency Department (ED; Cozzi et al. 2017). When these complaints rise to the level where they cause significant distress and functional impairment, a diagnosis of somatic symptom and related disorders (SSRD) is considered. While the standard of care for treatment of pediatric SSRDs is a combination of outpatient medical and mental health care, there are no published accounts of ED treatment protocols nor their outcomes. Objectives: To describe a pediatric SSRD treatment protocol in the ED and associated costs and utilization-related outcomes. Methods: Pre-protocol (control) patients were identified as youth presenting to the CS Mott Children’s Hospital of the University of Michigan ED with an SSRD diagnosis in the year prior to protocol implementation (n = 19). Protocol patients (n= 33) were placed on the ED SSRD protocol from October 2015 to December 2017. The time-matched control group (n=20) consists of patients with an SSRD diagnosis who were seen in the ED during the protocol time period but not placed on protocol. Data was extracted from the Pediatric Health Information Systems (PHIS) database and MiChart and included: demographics, presenting complaint, cost, and utilization (<30-day readmission). Results: There were no significant demographic differences by group. The pre-protocol group had statistically significant higher ED costs relative to the protocol and time-matched control groups ($8,704 vs. $2,628 & $2,029). Other results are pending. Conclusions: The SSRD protocol had significant impact on patient costs relative to pre-protocol, suggesting that a standardized SSRD protocol can positively impact patient care in the ED.
Abstract 46

ROMANTIC AND SEXUAL HEALTH, EXPERIENCE AND EXPECTATIONS IN TRANSGENDER YOUTH

A. Araya1; E. Selkie2,3; D. Shumer1
1Division of Pediatric Endocrinology, University of Michigan Health System
2Division of Adolescent Medicine, University of Michigan Health System
3Susan B. Meister Child Health Evaluation and Research (CHEAR) Center, University of Michigan

Background: Adolescence is a developmental period for romantic and sexual competency as noted by the fact that nearly 40% of youths in 9th to 12th grade have had sexual intercourse. There is a paucity of information regarding romantic and sexual relationships among transgender youths despite availability of gender-affirming therapy. Knowledge surrounding our patients’ sexual education and expectations is required to shape best practices for schools and providers. Objective: We will explore and describe the shared experience of transgender adolescents’ romantic health, sexual health, experience and expectations, and explore engagement with providers and non-providers when seeking information pertaining to sexual health, as well as describe potential barriers to care. Methods: This is a phenomenological qualitative study. A total of 30 English-speaking transgender and gender non-conforming youth will be recruited from a single pediatric gender services clinic to participate in semi-structured interviews. Interviews are audio recorded and transcribed to text for data analysis utilizing NVivo software. Transcription and data analysis will occur concurrently in an iterative nonlinear process as new commonalities/themes arise with disagreement in coding of transcripts addressed by a third reviewer. Results: Currently we have recruited 20 of a planned 30 participants, comprised of 11 transmen and 9 transwomen between ages 16 and 20. Recruitment, interviews, and analysis will be complete by the end of April 2019. Preliminary themes include lack of inclusion in sexual education: “it’s not very LGBT inclusive, it’s a public school”; seeking reputable websites for sexual education: “I don’t look for a dot com, I make sure it’s coming from a university”; having romantic and/or sexual contact after medical and/or social transitioning: “I’ve been dating a man for 9 months now […] We’re in love”; and variable definition of sexual intercourse: “penetrative or oral” vs “I don’t know”. Further themes and representative quotes are to be determined and will be present in final presentation. Conclusion: In this qualitative interview study, we discussed sexual and romantic health, and education among transgender adolescents. Results, currently pending, may have implications for future sexual research and intervention regarding sexual health and wellbeing in this vulnerable population.
TRENDS IN CORTICOSTEROID USAGE AMONG PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN A LARGE LEARNING HEALTH SYSTEM

Kandavel P1, Adler J1,2. 1Pediatric Gastroenterology, 2Susan B. Meister CHEAR Center, Michigan Medicine, Ann Arbor, MI.

BACKGROUND: Corticosteroids can reduce inflammation in inflammatory bowel disease (IBD). However, corticosteroid use is associated with serious adverse effects. Immunomodulators and biologic agents are considered steroid sparing treatments (SST) and are recommended by society guidelines to minimize use of systemic corticosteroids. Despite these recommendations and increasing use of SST, it remains unknown whether corticosteroid usage has decreased. We aimed to determine whether the point prevalence of corticosteroid use 3 months or more after diagnosis of IBD has decreased over time and to determine if there are any disparities in corticosteroid usage across race, sex, age at diagnosis, disease type or phenotype.

METHODS: We performed a retrospective cohort study of all pediatric IBD patients enrolled in the ImproveCareNow (ICN) Network, a multicenter pediatric IBD quality improvement collaborative. Steroid use was defined as any systemic corticosteroid given beyond 3 months after IBD diagnosis. Bivariate analyses were performed with chi-square and Student t-test.

RESULTS: We included 29,832 patients (69% Crohn’s disease [CD], 31% ulcerative colitis [UC]) in our study. Steroid use was found among 2,562 patients (26%) and was more common among patients with UC than CD (35% vs. 22%; p<0.001). Older patients were less likely to be on steroids (>17 yr 24%, 10-17 yr 26%, <10 yr 27%; p=0.006). Black patients were more often on steroids than white patients (30% vs 25%; p<0.001). There were no meaningful sex differences in steroid use. CD patients with an inflammatory phenotype were more likely to be on steroids (22% vs. stricturing 19%, penetrating 15%; p<0.001). Patients with more extensive UC used more steroids than limited proctitis (36% vs. 22%; p<0.001). Steroid use declined from 38% in 2007 to 30% in 2018. The racial disparity in steroid use has decreased over time (Figure 1).

CONCLUSIONS: Overall, steroid use is decreasing among ICN centers and racial disparities are improving. Strategies are needed to further reduce steroid use within the ICN network. Additional analyses are ongoing.
DECISIONAL CONFLICT IN DIFFERENCES/DISORDERS OF SEX DEVELOPMENT (DSD)
K. I. Suorsa-Johnson1,2; M. m. Ernst3; M. Gardner1; D. E. Sandberg1,2
1Susan B. Meister Child Health Evaluation and Research Center, University of Michigan
2Department of Pediatrics, Michigan Medicine, University of Michigan
3Behavioral Medicine and Clinical Psychology, Cincinnati Children’s Hospital Medical Center

Background: Supporting decision-making in parents of children with chronic conditions may enhance family resilience. Decision-making in DSD is complicated by reports of harm stemming from standard clinical practices. We report on the worries experienced by caregivers during decision-making. Methods: Caregivers (N=129; Mage=34.82) of children with a DSD (N=94; Mage=3.63; Range=0-7 years) were recruited from 11 US pediatric hospitals. Participants completed the Decisional Conflict Scale (DCS) as part of a questionnaire battery. The 16 DCS items are rated on a 5-point scale (higher scores=higher decisional conflict).

Results: A third (31%) of caregivers reported on-going decision-making, whereas 68% had already made a decision. DCS scores for current and past decisions (M=37.11; SD=11.05 and M=30.43; SD=9.76, respectively, p<0.001) were higher than ratings by parents considering surgery for sons with distal hypospadias (M=16.1; SD=12.00 in mothers; M=18.3; SD=12.6 in fathers; Lorenzo et al., 2012). The highest DCS ratings were observed for caregivers currently making decisions and included: “this decision is hard for me to make” (M=3.20; SD=1.42); “I need more advice and information about the choice” (M=3.20; SD=1.38); and “it’s hard to decide if the benefits are more important to my child than the risks, or if the risks are more important than the benefits” (M=3.00; SD=1.40). Decisions under consideration when completing the DCS included: surgery (85%); surgery+hormones (5%); finding a new primary care provider (2.5%); surgery+meeting with an endocrinologist about height/weight (2.5%); hormones (2.5%); and how to share surgical history with the child (2.5%). Conclusions: Caregivers of young children with DSD identify surgery as the most common decision they face. Difficulties include arriving at a decision, wanting more information, and questioning adequately weighing risks and benefits for their child. Decision aids have proven to be useful in such situations. Building caregiver strengths around the most difficult treatment decisions can enhance family resilience.
PREPARING FOR PERIVIABILITY: WHEN DOES LIFE BEGIN IN A GLOBAL CONTEXT?
Sharla Rent, MD1, Cheryl Moyer, MPH, PhD1, Ashura Ba’Kari, MD2, Sara Haimanot, MD3, Solomie Deribessa, MD3, Stephanie Kukora, MD1
1University of Michigan, Ann Arbor, Michigan, USA, 2Suntreso Hospital, Kumasi, Ghana, 3St Paul’s Hospital, Addis Ababa, Ethiopia

Background: Throughout the past decade, the global pediatric community has focused significant attention to both the neonatal and the under-five mortality rates. While the overall under 5 mortality has improved in the past two decades, the ratio of neonatal death comprising this population has increased dramatically. While advances in neonatal care in the US and other developed countries has led to progressive lowering of the viability threshold, now down to 22 weeks gestation in certain cases, many low-resource countries have nationally imposed “viability” thresholds of 28 weeks or higher, based on arguments of resource allocation and likelihood of infant survival. While individual centers attempt resuscitation on infants more premature than these thresholds, there are few survivors. Until recently there has been little need to challenge this definition of viability; however, with the globalization of resuscitation technology and training, many low-resource countries will soon be able to intervene on behalf of extremely premature infants.

Aim: To understand what factors influence resuscitation decisions of premature babies across two hospitals in sub-Saharan Africa.

Methods: Semi-structured qualitative interviews (n=38) of physicians, nurses, and midwives were conducted in neonatal in Addis Ababa, Ethiopia and in Kumasi, Ghana. Interview topics focused on definitions of viability, management of premature infants, and the influence of local values and beliefs on care provision to newborns. Interviews were audio-recorded and then transcribed verbatim. Thematic analysis was conducted to delineate core themes related to these topics.

Results: Provider perceptions regarding neonatal viability fell under two major themes – “duty to resuscitate” and “awareness of resource limitations”. Sub-themes included “respect for life”, “religious beliefs”, “professional responsibility”, “awareness of local outcome data”, “lack of training”, “resource limitations”, and “cultural stigma of disabled children”. Overlying many of these themes was a desire to meet global standards balanced with a desire to “avoid extraordinary measures”. “Extraordinary measures” varied by center, with resources present at delivery and in the NICU being the primary driver of decision making regarding resuscitation attempts, viability, and ongoing care.

Conclusions: The definition of “viability” varies between countries in sub-Saharan Africa, with local beliefs, resource limitations, and national guidelines contributing to decision making at the time of delivery.
SOCIAL ANXIETY AND AGGRESSIVE BEHAVIOR IN TEENS
Shannon L Brothers¹ and Douglas W. Nangle²
¹Pediatric Psychology, University of Michigan, Ann Arbor, MI
²Department of Psychology, University of Maine, Orono, ME

Background: Social anxiety is linked to reactive and relational aggression in early adolescent and young adult samples. Socially anxious teens who engage in reactive relational aggression (RRA) are more likely to have difficulties regulating emotions and maladaptive cognitive coping styles. Objective: The goal of the present study is to assess the relationship between social anxiety and RRA in teens, combining the form and function of aggression and to examine trait anger and anger rumination as factors that may explain this relationship. Method: Teens 14-17 (N=105; M_age = 15.43; 61% female) were recruited through their local high school and community to complete a 30-minute, battery of questionnaires examining social anxiety, trait anger, anger rumination, and RRA. Results: Simple regression analyses found that social anxiety was positively related to RRA (b = .06, p = .001) and anger rumination (b = .44, p < .001). Anger rumination was also positively correlated with RRA (b = .10, p < .001). A conditional process analysis was conducted. Teens with social anxiety were more likely to engage in RRA if they ruminated about experiences that created anger (b = .04, BC 95% CI: .011, .069), and this relationship was present in teens with higher levels of trait anger (b = .03, BC 95% CI: .009, .063). Conclusions: Socially anxious teens were more likely to engage in RRA, had difficulties regulating negative emotions, like anger, and showed ineffective cognitive coping strategies, such as anger rumination. Research purports that socially anxious individuals who engage in aggressive behavior tend to have lower quality of life and poorer health outcomes. Targeted clinical interventions to reduce perseveration and promote emotional expression in teens with social anxiety is warranted to decrease potential negative health outcomes.
Abstract 51
DECREASING EPINEPHRINE DOSING ERRORS DURING NEONATAL RESUSCITATION: A RANDOMIZED SIMULATION TRIAL
K. Brune1, V. Bhatt-Mehta1, D. Rooney1, J. Adams2, G. Weiner1
1 Division of Neonatal-Perinatal Medicine, University of Michigan
2 Department of Pediatrics, St. John Hospital and Medical Center

Background: A previous study demonstrated errors in 43% of intravenous epinephrine doses prepared by nurses for neonatal resuscitation. Subjects chose the wrong epinephrine solution, made calculation errors and were unable to assemble the ABBOJECT® syringe. We developed a cognitive aid that depicts the correct solution, instructions for syringe assembly, and a weight-based table with doses expressed in milliliters (Figure). We hypothesized that the aid would decrease errors and increase efficiency. Methods: In a simulation setting, 100 labor and delivery nurses were randomized to prepare epinephrine with or without the cognitive aid. They received a standardized order, read-back the order, wrote the intended dose and prepared the medication in a syringe. Labeled bottles with 2 epinephrine solutions commonly available on code carts (0.1 mg/ml and 1 mg/ml), a calculator and all necessary supplies were provided. Scenarios were video-recorded for time analysis. The time required and the accuracy of prepared doses were compared. Variables influencing dosing errors were investigated using logistic regression. Results: Demographics were similar in both groups. Using the cognitive aid significantly reduced errors choosing the correct epinephrine solution (12% aid vs. 44% no aid, RR 0.27, CI 0.12-0.59) and preparing the correct dose (22% aid vs. 48% no aid, RR 0.46, CI 0.25-0.81). There was no difference in time to prepare the dose (median 166 seconds with aid vs. 141 seconds without aid, p= 0.16) or in errors calculating the intended dose (8% vs. 8%, RR 1, CI 0.29-3.48). Years of experience, self-perceived math comfort, and self-perceived anxiety were not predictive of dosing errors. Conclusion: This trial demonstrated that a simple cognitive aid decreased epinephrine dosing errors during simulated neonatal resuscitation but did not increase efficiency. Despite availability of the aid, 22% of doses were prepared incorrectly. This is a serious patient safety threat. Additional measures such as stocking only dilute epinephrine where newborns are resuscitated, use of pre-filled unit-dose syringes for neonatal resuscitation, and including pharmacists on neonatal resuscitation teams must be investigated.
Abstract 52
OUTCOMES OF TREATMENT OF ANAEROBIC BACTERIA DURING CYSTIC FIBROSIS PULMONARY EXACERBATION
L. Castner1; M. Zimbric1; S. Cahalan1; L. Caverly1
1Pediatric Pulmonology, University of Michigan, Ann Arbor, MI.

Background: Cystic fibrosis (CF) is an autosomal recessive genetic disorder associated with impaired airway mucus clearance, airway inflammation, and chronic airway infection with pathogens such as Pseudomonas aeruginosa. In recent years, culture-independent studies have identified facultative and obligate anaerobes as being highly prevalent and abundant in CF respiratory samples, and certain studies have identified positive associations between anaerobes and exacerbations of CF lung disease. However, potential benefits of targeting anaerobes with antibiotic treatment at the time of CF exacerbation are unknown. The purpose of this study is to compare outcomes of pulmonary exacerbation treatment between persons treated with intravenous (IV) antibiotics with broad activity against anaerobes to those treated with other IV antibiotic regimens.

Methods: This is a retrospective study of patients admitted to UMHS between 2004 and 2017 with a diagnosis of CF exacerbation and treatment with IV antibiotics. Demographics, co-morbidities, lung function data (forced expiratory volume in 1 second (FEV1)), and antibiotic data were collected from the medical records. Statistical analyses were performed with R using linear mixed effects models, with lung function recovery after exacerbation as the primary outcome.

Preliminary results: A total of 207 patients and 791 CF exacerbations met inclusion criteria. Of these exacerbations, 37.7% were treated with antibiotics with broad anaerobic coverage. On univariate analyses, patients treated with antibiotics with broad anaerobic coverage were older, more likely to be female, and had lower baseline lung function than patients treated with other antibiotic regimens (p<0.01 for all comparisons). Broad anaerobic coverage was not associated with greater recovery of lung function following exacerbation treatment compared to other antibiotic regimens (89.9% vs 92.6% of baseline lung function recovered, respectively, p=0.019).

Conclusions: IV antibiotics with broad anaerobic coverage are used for treatment in the minority of CF exacerbations. Patients treated with antibiotics with broad anaerobic coverage differ in demographics and lung function from those treated with other antibiotic regimens. Multivariate analyses to control for potential confounders of lung function recovery and antibiotic selection (e.g., CF pathogens, baseline lung function, patient effect) are in process and will be reported at the research symposium.
Abstract 53

PARENTAL PREFERENCE FOR PHYSICIAN ATTIRE IN THE NEONATAL INTENSIVE CARE UNIT

P. Cham1; N. Laventhal1; H. Burrows2; V. Chopra3; G. Weiner1

1Neonatal-Perinatal Medicine; 2Department of Pediatrics, 3Department of Internal Medicine, University of Michigan

Background: A positive parent-physician relationship can improve outcomes and parental satisfaction. In addition to technical expertise and quality of care, professional attributes such as the physician’s attire may influence parental perceptions and impact the relationship. In previous studies, adult patients preferred physicians wearing formal attire with a white coat (WC), but preferences varied based on the patient’s age, setting and clinical context. Because of the intensive care context and the younger age of NICU parents, we aimed to study whether parents preferred formal attire with WC to other ensembles.

Methods: Parents of infants admitted in a level IV, Midwestern NICU completed a survey eliciting preferences for physician attire. They were randomized to surveys with male or female models wearing 3 to 4 different ensembles with or without a WC. Parents rated each ensemble in 5 domains (knowledgeable, trustworthy, caring, approachable, makes me feel comfortable) on a 10-point scale and were asked to choose which single ensemble they preferred.

Results: Composite domain scores between formal attire + WC and other ensembles were compared using the Kruskal-Wallis test with Dunn’s multiple comparisons. Surveys were distributed by research staff on paper or using an anonymous electronic link. Participants provided informed consent; no personal identifying data were collected. 45 parents completed the survey; no parent declined to participate. Most respondents (n=25; 57%) indicated that physician attire was important to them, but few (n=10; 21%) asserted that physician attire influenced their satisfaction with the care provided. There was no difference in composite scores between formal attire + WC and any other ensemble. The two most preferred ensembles were scrubs with WC (33%) and formal attire with WC (33%). No parent preferred a formal business suit.

Conclusion: Physician attire is important to NICU parents, but most do not report it influences their satisfaction with care. Scrubs with a white coat or formal attire with a white coat are the most preferred attire for NICU physicians, in contrast to adult patients who favor formal attire with a white coat compared to all other ensembles. This suggests that empirically informed NICU physician dress codes should not be extrapolated from adult patient research findings, and supports the need for larger scale study of NICU parental preferences for physician attire.
Abstract 54
TRANSPORT EDUCATION REQUIREMENTS AMONG NEONATAL-PERINATAL FELLOWSHIP PROGRAMS
C. Gisondo1, K Stanley1, G Weiner1
1University of Michigan, CS Mott Children’s Hospital, Division of Neonatal-Perinatal Medicine, Ann Arbor, MI

Background: Over 68,000 neonatal transports occur annually. Practicing neonatologists frequently participate in referral management and patient retrieval. The American Academy of Pediatrics (AAP) states that transport medicine is an essential part of neonatal fellowship training; however, the current state of transport experience among neonatal-perinatal medicine (NPM) fellows and the requirements for transport education are not well characterized.

Objective: To describe neonatal transport participation and education among NPM fellowship programs in the United States and assess the need for a standardized curriculum.

Methods: Using the Organization of Neonatal Training Program Directors (ONTPD) listserv, an anonymous web-based questionnaire containing 22 questions was distributed to fellowship program directors/associate program directors representing all 96 NPM fellowship programs. Results: 52 ONTPD members responded, representing all 10 AAP districts. The majority of respondents strongly agree that neonatal transport is an important part of fellowship training. However, fellow participation in transport activities varies widely among programs. The majority report that trainees participate in referral intake (83%) or medical management by telephone (75%). Less than half of programs require participation in patient retrieval and 2 programs report that fellows are not allowed to participate in patient retrieval. Educational requirements to lead a transport team also vary. Less than half of programs require fellows to complete a structured curriculum or training program (44%), demonstrate competence in specific procedural skills (38%), participate in safety training (28%) or complete a defined duration of training prior to leading a transport team (44%). Sixteen percent of programs have no requirements. Most respondents indicated that the ability to assist with patient referral, perform medical management by telephone and understand transport physiology are the most important skills for fellows to acquire during fellowship training, while learning to operate transport equipment is the least important.

Conclusion: Although the AAP recommends that all NPM fellows receive education and training in neonatal transport, there is wide variation in transport participation, educational requirements and curriculum among training programs. This survey supports the need for development of a structured curriculum that includes training in referral intake, medical management and transport physiology to fill this educational gap.
MEASUREMENT OF PULMONARY AND SYSTEMIC BLOOD FLOW IN SINGLE VENTRICLE PATIENTS BY CARDIAC MAGNETIC RESONANCE VS CARDIAC CATHETERIZATION

M Hart, R Lowery, M Ghadimi, W Whiteside, S Yu, P Agarwal, A Dorfman, J Lu
University of Michigan, Ann Arbor, MI

Background: Cardiac magnetic resonance (CMR) or cardiac catheterization (cath) may be used to assess patients with single ventricle physiology prior to stage II or Fontan palliation. However, these patients sometimes develop collaterals which may invalidate assumptions of the Fick method, and alter estimates of pulmonary blood flow (Qp) or the ratio of pulmonary to systemic blood flow (Qp:Qs). We assessed agreement and correlation of CMR and cath measurements, and the relation to collateral flow. Methods: This single-center, retrospective study included all pre-stage II and pre-Fontan patients between 2010-2017 who underwent CMR and cath within one month. Cath Qp and Qs were calculated by the Fick method. CMR Qp was calculated by the sum of pulmonary venous flow, and Qs by the sum of vena caval flow. Collateral flow by CMR was the difference of pulmonary vein and pulmonary artery flow. Agreement of cath and CMR was assessed with mean difference (MD), and correlation by Pearson correlation coefficient. Results: In 26 studies (16 pre-stage II and 10 pre-Fontan) in 21 patients (median age 0.6 years, interquartile range 0.4-1.7), collateral flow was higher in pre-Fontan patients (1.8±0.6 vs 0.9±0.8 L/min/m², p=0.01). Overall, CMR and cath had good agreement for Qs (MD 0.14 L/min/m²) and Qp:Qs (MD 0.01), with moderate correlation (r=0.44, p=0.02 for Qs, r=0.48, p=0.02 for Qp:Qs). In pre-Fontan but not in pre-stage II patients, CMR had higher Qp (MD -1.71 L/min/m²) and Qp:Qs (MD -0.36). Agreement improved by using only pulmonary arterial flow on CMR (Qp MD 0.10 L/min/m², Qp:Qs MD 0.05). The difference in Qp by cath vs CMR correlated with amount of collateral flow (r=-0.47, p=0.02). Neither cath nor CMR measures of Qp, Qs, or Qp:Qs correlated with duration of chest tube drainage or length of stay in this small cohort. Conclusion: Collateral blood flow leads to systematically higher Qp and Qp:Qs measurements by CMR compared to cath in single ventricle patients. This likely reflects differences in methodology, such as total vs effective pulmonary blood flow. Measurements may not be used interchangeably, with potential clinical significance in estimation of pulmonary vascular resistance. Further study is necessary to evaluate prediction of clinical outcomes in a larger cohort.
IMMUNOLOGIC PROFILE AND PROPERTIES OF DEFATTED VS. FULL FAT HUMAN MILK

B. Jackson¹; J. Bermick¹; B. Gregg²; S. Tutor³; K. Stanley¹
¹Neonatal-Perinatal Medicine, Michigan Medicine, Ann Arbor, MI;
²Pediatric Endocrinology, Michigan Medicine, Ann Arbor, MI;
³Patient Food & Nutrition Services, Michigan Medicine, Ann Arbor, MI.

Background: In neonatal chylothorax, thoracic lymphatic drainage is ineffective. The resultant effusions often require drainage, leading to a loss of immune components. Affected infants can be managed with feedings low in long chain triglycerides to decrease lymph production. Studies have shown that defatted human milk is effective for chylothorax resolution without significantly impacting growth, as compared to traditional formula. We fill a gap in the literature by comparing the immunological profile and antibacterial effect of full fat and defatted human milk.

Methods: Milk from lactating mothers was divided into two aliquots. One aliquot was defatted via centrifugation with the full fat aliquot as control. Flow cytometry was used to measure immune cell populations. Lactoferrin, lysozyme, IgA and IgG values were determined using ELISA. The antibacterial properties were determined by inoculating paired full fat and defatted milk samples with Escherichia coli or Streptococcus pneumoniae bacteria. Bacterial colony counts were assessed at 24 hours. Differences between defatted and full fat milk samples were compared using paired T-tests.

Results: Compared to full fat milk, defatted milk demonstrated a significant decrease in all immune cell populations. There was no difference in IgA, IgG, lysozyme or lactoferrin concentrations between the full fat and defatted milk samples. Full fat and defatted human milk demonstrated equivalent growth inhibition of Escherichia coli and Streptococcus pneumoniae (Figure 1).

Conclusions: Unexpectedly, defatted human milk contained significantly less leukocytes than full fat milk. In contrast, IgA, IgG, lysozyme and lactoferrin concentrations were preserved. We speculate that the loss of leukocytes is due to the defatting process in which the cell pellet containing the leukocytes is separated from the defatted milk and thus not collected during decanting. The loss of leukocytes did not affect the ability of defatted milk to inhibit bacterial growth, suggesting that the antibacterial benefits of human milk remain after the defatting process. Further investigation regarding the clinical effect of leukocyte loss in defatted milk is warranted.
Abstract 57

DO ETHICAL CULTURES DRIVE PERINATAL CARE?

C. Lawrence1, N. Laventhal1,2, and D. Feltman3 with the INDEED (Investigating Neonatal Decisions for Extremely Early Deliveries) Group

1Neonatal-Perinatal Medicine, University of Michigan 2Center for Bioethics and Social Sciences in Medicine, University of Michigan 3Pediatrics, Division of Neonatology, NorthShore University Health System Evanston Hospital, Evanston, IL

Background: Our previous 6-center retrospective study examined decisions for periviable deliveries from 2011-2015 (Investigating Neonatal Decisions for Extremely Early Deliveries-INDEED). Higher rate of resuscitation centers (HR) versus lower resuscitation rate centers (LR) differed in clinical practice and patient characteristics. Some studies suggest ethical cultures may also drive clinical practice.

Objective: To understand attitudes toward perivable newborn outcomes and management across perinatal care teams at 6 U.S. sites and determine whether clinicians at HR centers have more optimistic views of outcomes and favor more aggressive perinatal care.

Methods: An anonymous online survey of attitudes toward interventions and outcomes for perivable newborns was designed and piloted. Medical team members at the 6 INDEED sites treating mothers delivering at periviable gestational ages and their newborns were invited by email to participate. Self-reported respondent characteristics were compared to patient data collected from the INDEED study. Survey responses were compared by multivariable logistic and linear regression to assess how center rates of planned resuscitation and respondent characteristics related to preferences for perinatal care and outcome predictions.

Results: 986 of 2964 (33%) invited participants responded. Respondents at HR vs. LR sites reported lower estimates for survival to NICU discharge, but did not differ in estimates for survival without neurodevelopmental impairment. HR vs. LR respondents agreed 1.4 times more often (CI 1.1-1.8, p=0.01) to seeing more suffering of perivable neonates in their NICUs. HR vs. LR respondents less frequently reported an acceptable quality of life was likely/very likely at 23 weeks (OR 0.7, CI 0.53-0.93, p=0.012). For a woman facing 22-week delivery, HR vs. LR respondents were less likely to favor antenatal steroids and resuscitation over comfort care only as the best approach.

Conclusion: Contrary to our hypothesis that provider outlook drives practice for perivable newborns, respondents from high resuscitation centers had a less favorable outlook than those in low resuscitation centers, instead suggesting, that provider views are shaped by experience.
RESIDUAL PROCTITIS IS COMMON WHILE ON TREATMENT FOR ULCERATIVE COLITIS
T. Lulgjuraj1; H. Neef1; S. Eder1, 2; J. Adler1, 2
1Pediatric Gastroenterology, University of Michigan, Ann Arbor, MI.
2Susan B. Meister CHEAR Center, University of Michigan;

Background: Residual proctitis (RP), including proctosigmoiditis, is commonly encountered in practice among patients being treated for ulcerative colitis (UC). To our knowledge, there are no published reports on this seemingly common clinical problem. We aimed to describe the characteristics of pediatric UC patients who develop RP.

Methods: All patients with UC diagnosed at 2-18 years at University of Michigan (UM) between 2007-2017 had electronic medical records (EMR) searched using the UM EMR Search Engine (EMERSE) for terms related to proctitis or proctosigmoiditis. Cases with endoscopic evidence of inflammation were categorized as “Endoscopic RP.” Cases of RP diagnosis in EMR but without endoscopic exam were categorized as “Clinical RP”. Clinical information, evaluation, and medical therapies were abstracted. Patients with limited proctitis at diagnosis were excluded. Chi square and Student’s t-test were used, and p<0.05 was considered significant.

Results: 181 patients met inclusion criteria. In total, 36 (20%) had at least one episode of RP; 25 (69%) clinical and 11 (31%) endoscopic RP. Two patients were initially suspected of having RP but were found to have extensive disease on endoscopy (not classified as RP). There were no differences in sex (p=0.11), race (p=0.07), or age (p=0.3) at UC diagnosis. Most patients (78%) were on systemic therapies at the time of RP diagnosis (Figure 1). Most patients (61%) were started on a new therapy to treat RP, often a rectal suppository or enema. Other treatments included new or changed immunosuppression (17%), or oral 5-aminosalicylate (5ASA; 17%).

Conclusions: RP commonly occurs among 1 in 5 pediatric patients with UC, apparently regardless of therapy. Diagnosis is most commonly made clinically. However clinical impression can be inaccurate. Endoscopic evaluation for suspected RP may change diagnosis and management. Larger multi-center study is warranted.
PROGRESSION TO KIDNEY FAILURE IN CHILDHOOD ONSET NEPHROTIC SYNDROME

D. Marchel1; J. Troost1; A. Waldo1; P. Gipson1; H. Desmond1; S. Attalla1; R. Eikstadt1; D. Gipson1
1Division of Nephrology, Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA

Background: Nephrotic syndrome represents a substantial cause of kidney failure, particularly among children. Little is known on the rates of disease progression during childhood and as patients transition into adulthood. Objectives: The goal of this study is to study nephrotic syndrome. Design/method: This analysis was conducted on patients enrolled in the Kidney Research Network with onset of nephrotic syndrome during childhood (before age 18). Encounters, diagnoses, medication, labs, and vitals were extracted from participating centers' electronic health records. Time to end-stage kidney disease was estimated using Kaplan-Meier curves and adjusted Cox-proportional hazards models analyses were conducted from onset to end-stage, and from age 18 to end-stage among those who survived into adulthood.

Results: There were a total of 348 patients with disease onset in childhood. Seventy-seven patients (22%) reached kidney failure during follow-up (26 per 1,000 person-years). Higher age at onset (Hazard ratio (HR) per year=1.1 95% confidence interval (CI)=1.1 to 1.2) and diagnosis of focal segmental glomerulosclerosis (HR vs. non-biopsied nephrotic syndrome=7.3 95% CI=2.6 to 20.7) or membranous nephropathy (HR=7.0 95% CI=1.7 to 28.7) were associated with higher rates of kidney failure. Of the 84 patients with follow-up data and native kidney function past age 18, 22 (26%) progressed to end-stage kidney disease during adulthood (43 per 1,000 person-years), 26 (31%) had resolution of disease for one year at last follow-up, and 36 (43%) had native kidney function but active disease. Differences in progression by disease among those who survived to age 18 were modest compared to differences in survival from onset (HR focal segmental glomerulosclerosis vs. non-biopsied nephrotic syndrome=2.1 95% CI=0.9 to 5.1).

Conclusions: This study provides novel estimates of disease trajectories among patients with childhood onset nephrotic syndrome. Rates of progression appear higher during adulthood, although this difference may be attributed to selection biases where those who reach sustained control of disease before adulthood might not be seen in clinic as adults and thus did not have data during adulthood and did not contribute to the adult-specific estimates.
Abstract 60

ILLNESS SPECIFIC ANXIETY FOLLOWING PEDIATRIC HEART TRANSPLANT
AD McCormick¹, KR Schumacher¹,², M Zamberlan¹, K Uzark¹, S Yu¹, R Lowery¹, N Rottach¹, MK Cousino¹,²
¹Department of Pediatrics, Michigan Medicine
²University of Michigan Transplant Center

Background: Illness specific anxiety, unique from general anxiety, is known to affect psychosocial function and health outcomes in many disease states but not well studied in pediatrics or following heart transplant (HTx) despite significant psychosocial distress among these populations.

Objectives: To evaluate specific fears related to HTx in adolescent and young adult (AYA) patients and parents, and to evaluate associations between illness specific anxiety and clinical features.

Methods: This single-center cross-sectional study administered a novel 12-item multidisciplinary team derived “Post Heart Transplant Fears” (PHTF) questionnaire about specific fears of complications after HTx. Responses were scored on a 5-point Likert scale ranging from “never” (1) to “always” (5). The Generalized Anxiety Disorder-7 (GAD-7) and Pediatric Quality of Life Inventory (PedsQL) were also administered. PHTF scores were totaled. For PHTF items, answers of “often” or “always” were considered reporting fear. Univariate associations between PHTF scores and demographics, clinical features, and medication adherence as measured by immunosuppression level standard deviation (SD) were analyzed. Internal consistency and validity of the PHTF were examined.

Results: In total, 30 patients (12 years) and 42 parents participated. The most common fears reported were retransplantation (20% of patients, 43% of parents), graft rejection (27% of patients, 36% of parents), and post-transplant complications (20% of patients, 36% of parents). Patient female sex (p = 0.01) and immunosuppression SD 2 (p = 0.07) were associated with a higher illness specific anxiety. Patients with an immunosuppression SD 2 were more likely to report fear of graft rejection (p = 0.04). The PHTF had good internal consistency for patients (Cronbach α = 0.88) and parents (Cronbach α = 0.85). Construct validity was demonstrated with medium to high correlations between total PHTF score and GAD-7 (r = 0.62 and 0.69) and PedsQL (r = -0.42 to -0.71).

Conclusion: The PHTF is a brief, valid and reliable instrument demonstrating significant illness specific anxiety in AYA patients and parents after HTx. Specific fears of HTx patients and parents include retransplantation, graft rejection, and post-transplant complications. Associations between the PHTF with metrics of anxiety, quality of life, and medication adherence highlight illness specific anxiety as an important intervention target for improving overall post HTx care.
THIRD TRIMESTER FETAL PREDICTORS OF INTERVENTIONAL TIMING IN TETRALOGY OF FALLOT IN A MULTI-CENTER COHORT

A. Rodenbarger1, T. Thorsson1, C. Stiver2, D. Jantzen3, M. Chevenon3, S. Yu1, R. Lowery1, S. Gelehrter1  
1University of Michigan. 2Nationwide Children’s Hospital. 3Children’s Hospital of Illinois

Background: Tetralogy of Fallot (TOF) is frequently diagnosed prenatally, but predicting the timing of repair remains challenging. Despite multiple small, single-center studies, published fetal echocardiographic (echo) predictors of timing of intervention are not consistently reproducible, complicating fetal counseling. This study evaluated previously reported echo markers, a new predictor, and fetal anticipatory counseling in a multi-center population. Methods: This was a multi-center, retrospective study of 112 prenatally diagnosed patients with TOF or TOF-like double outlet right ventricle at 3 centers from 2005 to 2018. All patients underwent postnatal intervention in the first year of life and had a 3rd trimester fetal echo. Patients with single ventricles, pulmonary atresia, and complex additional cardiac defects were excluded. Fetal echo, fetal consultation, demographic, and outcome data were compared between infants requiring neonatal intervention (Early, before 30 days) and those undergoing later intervention (Late). Receiver operating characteristic curves were used to determine optimal echo values associated with neonatal intervention. Results: Third trimester fetal echo was done at a median of 33.7 weeks with no difference between sites. The Early group included 26 infants (23%); half had a complete TOF repair. The Early group had significantly different pulmonary valve (PV) z-score (Early: -4.0±0.86 vs Late: -3.5±0.95, p=0.01), PV:AoV (aortic valve) ratio (Early: 0.59±0.13 vs Late: 0.66±0.10, p=0.003), PV:AoV z-score difference (absolute difference between z-scores. Early: 5.9±1.7 vs Late: 5.1±1.3, p=0.01), and, when present (10 of 112 patients), were more likely to have retrograde ductus arteriosus flow (23% in Early vs. 5% in Late, p=0.01). Counseling at the time of fetal echo regarding expected timing of postnatal intervention was made in 86% of cases; intervention timing was correctly predicted in 38% of the Early group and 76% of the Late group (p=0.002). The best predictors of early intervention were a PV:AoV ratio of <0.6 and fetal cardiologist counseling of likely early intervention. A PV:AoV z-score difference ≥ 5 provided an 89% negative predictive value for detecting patients that do not need neonatal intervention. Conclusions: Identifying patients that are unlikely to require neonatal intervention can be accomplished via 3rd trimester fetal echo. The best predictors for needing neonatal intervention are PV:AoV ratio <0.6, PV:AoV z-score difference ≥5, and the counseling cardiologist’s overall assessment that neonatal intervention was likely.
Abstract 62
THE EFFECTS OF A GLUTEN-FREE DIET IN JUVENILE IDIOPATHIC ARTHRITIS – A PILOT STUDY
A Sura1; S Fogarty-Brown2; M Riebschleger1
1Pediatric Rheumatology, University of Michigan
2Pediatric Hematology, University of Michigan

Background: The gluten-free diet is rapidly gaining popularity in the non-celiac disease population for its presumed health effects, but very little data exists on its effect in juvenile idiopathic arthritis (JIA).

Objective: To conduct a pilot study of the gluten-free diet in patients with JIA over six months, with the primary outcomes of the components of the JADAS-27, pain scores, and growth parameter changes.

Methods: Patients with non-systemic JIA, without inflammatory bowel or celiac disease, were recruited at a single center to trial a gluten-free diet for 6 months. Celiac disease screening was performed and patients were excluded if positive. Outcome measures were collected at enrollment, 3 months, and 6 months of the diet. Adherence and barriers to adherence were assessed at both follow-up visits, and patients were withdrawn if their adherence was poor. Outcomes were interpreted via mixed-effects analysis.

Results: 32 patients enrolled in the trial, and 2 of these screened positive for occult celiac disease and were excluded. 20 (67%) and 16 (53%) patients remained adherent to the gluten-free diet at 3 and 6 months, respectively. There were statistically significant reductions (p ≤ 0.05) in pain score and ESR. Reductions in patient GAS and JADAS-27 trended towards statistical significance (p ≤ 0.10). There were no significant differences in physician GAS, active joint count, or growth parameters.

Conclusion: A gluten-free diet may be beneficial for a subset of JIA patients. There also may be utility in screening for celiac disease in patients with newly diagnosed JIA. Larger studies are needed to confirm our findings.
Abstract 63

IMPACT OF DOCUMENTATION ON RESPIRATORY INTERVENTION AMONG NEWBORNS WITH CONGENITAL HEART DISEASE

I. Thomas¹; N. Laventhal¹; S. Yu¹; R. Lowery¹; S. Gelehrter¹
¹University of Michigan, C.S. Mott Children’s Hospital, Ann Arbor, MI

Introduction: Maternal-infant bonding in the immediate postnatal period has been shown to have beneficial effects for both mother and infant. Because patients with ductal dependent congenital heart disease (CHD) are a heterogeneous group with varying physiologies and expected oxygen saturations, resuscitation team unfamiliarity with the expected postnatal course may put these neonates at risk for unnecessary early respiratory intervention and decreased bonding time. We examined the effects of standardized pre-delivery documentation of prenatal cardiology consultation on immediate postnatal respiratory intervention and maternal-infant bonding in patients with ductal dependent CHD.

Methods: A single center retrospective cohort study was performed on patients prenatally diagnosed with ductal dependent CHD from 2005 to 2017 who delivered at our center. Premature infants (<37 weeks) and those with cardiac or congenital lesions known to require immediate advanced resuscitation and/or intervention were excluded. Standardized documentation (starting in 2015) included the specific fetal cardiac diagnosis, expected postnatal oxygen saturations and whether the lesion was thought to be conducive to a period of parental bonding prior to placement of umbilical catheters and initiation of PGE. Pre-standardized (2005-2014) and standardized (2015-2017) documentation epochs were compared using appropriate statistical methods.

Results: The study cohort included 386 patients; 289 in the pre-standardized note group and 97 in the standardized note group. The groups showed similar patient characteristics, including sex, birth weight, race, insurance type, and Apgar scores. Fewer infants were born by cesarean delivery in the later epoch (32.2% to 21.6%, p=0.049). After standardized delivery note implementation there was a decrease in any respiratory intervention, from 38.1% to 25.8% (p=0.03), with a nearly four-fold decrease in provision of blow-by oxygen (15.2% to 4.1%). The percentage of patients who had any bonding time increased significantly in the standardized note epoch, from 38.1% to 25.8% (p=0.03), with a nearly four-fold decrease in provision of blow-by oxygen (15.2% to 4.1%). The percentage of patients who had any bonding time increased significantly in the standardized note epoch, from 22.1% to 74.2% (p<0.0001), without an increase in the proportion of patients requiring CPAP or intubation in the first two hours of life (6.9% in the pre-standardized group vs 7.2% in the standardized group, p=0.92). Conclusion: The easily implemented strategy of a standardized pre-delivery note which clarifies the expected immediate postnatal course in neonates with ductal dependent cardiac lesions may decrease unnecessary respiratory intervention and increase maternal-infant bonding.
Abstract 64

RISK FACTORS PREDICTING NEED FOR IMMEDIATE POSTNATAL RESUSCITATION IN INFANTS WITH PRENATALLY DIAGNOSED CONGENITAL HEART DISEASE

I. Thomas1; N. Laventhal1; S. Yu1; R. Lowery1; S. Gelehrter1
1University of Michigan, C.S. Mott Children’s Hospital, Ann Arbor, MI

Introduction: Although most infants with congenital heart disease (CHD) requiring neonatal surgical repair do not require advanced resuscitation, as the ductus arteriosus is still patent, these deliveries are often identified as high risk. This may disrupt the maternal-infant dyad and overuse hospital resources. We sought to determine the frequency and risk factors for immediate adverse perinatal outcomes of neonates with prenatally diagnosed ductal-dependent CHD expected to need neonatal surgery. Methods: A single-center retrospective cohort of patients prenatally diagnosed with ductal dependent CHD during 2005-2017 was assembled. Infants born <37 weeks or with conditions known to require immediate advanced intervention were excluded. The cohort was divided into pre- and post- standardized fetal cardiology documentation (started in 2015). The primary outcome was need for CPAP or intubation in the first 2 hours of life. Results: A total of 386 patients (289 early era, 97 late era) were included. The groups were similar in sex, birth weight, race, and Apgar scores. Risk factors for early onset sepsis (EOS) of 28%, neonatal respiratory distress (RD) of 14%, and non-reassuring fetal heart rate (NRFHR) during labor of 11% were present, with no differences between eras. A total of 27 patients (7%) required CPAP (n=8) or intubation (n=20) in the first 2 hours of life with no difference between the eras (p=0.92); 1 infant required CPR. In the late era there was a decreased incidence of any respiratory intervention from 38% to 26% (p=0.03), with a decrease in provision of blow-by oxygen (15% to 4%). Presence of risk factors for EOS and NRFHR were associated with need for CPAP or intubation in both eras (all p<0.05), but presence of a risk factors for RD was only associated in the early era (p = 0.0002 early era vs 0.10 late era). At least one risk factor of EOS, RD, and/or NRFHR associated with CPAP or intubation was present in 41% and 46% of neonates in early and late eras, with 85% sensitivity in the early era vs. and 86% late era and a 98% negative predictive value in both eras. Conclusion: Typical neonatal risk factors associated with the need for postnatal advanced resuscitation can predict risk for neonates with ductal dependent CHD. In absence of these risk factors, our findings support lower-risk delivery stratification for this patient population to support parental-infant bonding and improve resource utilization.
Abstract 65

FUNGAL SEPTIC SHOCK WITH MULTIPLE ORGAN FAILURE ON VA-ECMO COMPLICATED BY INTRACRANIAL HEMORRHAGE AND CRANIECTOMY
Jeffrey Weatherhead 1, Dana Steien1, Kristen Smith1
1 Michigan Medicine, University of Michigan, Ann Arbor, Michigan

Case Report: Systemic fungal infections dramatically increase mortality on ECMO. We report a case involving a 5-year-old female with mitochondrial disorder, immunodeficiency on IVIG, functional intestinal failure with 100% total parenteral nutrition (TPN) dependence and moderate-severe autism spectrum disorder who presented with septic shock secondary to Candida parapsilosis. Her course was complicated by severe Acute Respiratory Distress Syndrome (ARDS) and multiple organ failure requiring veno-arterial extracorporeal membrane oxygenation (VA-ECMO) and continuous renal replacement therapy (CRRT). She was cannulated onto VA-ECMO and endured a 7-day run. Her fungal sepsis was treated with micafungin and fluconazole through the ECMO circuit. The infection cleared after 4 days of therapy. By day 7 she was ready to trial off of ECMO however suffered a right-sided intracranial hemorrhage with evidence of stroke in the right MCA distribution. She was removed from ECMO and underwent emergent decompressive craniectomy. She was kept in a pentobarbital coma to help control intracranial pressure (ICP) and underwent a prolonged sedation wean. As she emerged from the pentobarbital coma she demonstrated a remarkably intact neurologic exam with left upper and lower extremity weakness and dysconjugate gaze as the major deficits manifested. She underwent tracheostomy in preparation for rehabilitation. She was ultimately transferred to Pediatric Gastroenterology (GI) service after a 53-day stay in the PICU. Her tracheostomy was decannulated after 16 days. She remained on the Pediatric GI service for 60 days where she continued physical therapy and returned close to her neurologic baseline with some residual left upper and lower extremity spasticity. Her bone flap was replaced 90 days post craniectomy. While working with the intestinal rehabilitation team, enteral feeds and oral feeds were advanced and TPN was discontinued for the first time in over 2 years and has remained off TPN. Equally surprisingly, her autism has almost completely resolved, according to family and outpatient providers.

Conclusions: The mortality facing this patient on ECMO was estimated to be 90% and almost 100% without ECMO. This case illustrates how difficult it can be to make timely decisions on ECMO candidacy as well as short and long term outcomes in the pediatric population.
Abstract 66
SURGERY IN CHILDREN WITH VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE
Aimee G. Kim\textsuperscript{a}, Jeremy Adler\textsuperscript{b}, Ronald B. Hirsch\textsuperscript{b}, Samir K. Gadepalli\textsuperscript{a}

\textsuperscript{a} Department of Surgery, Section of Pediatric Surgery, University of Michigan; \textsuperscript{b} Division of Pediatric Gastroenterology, University of Michigan

Background: Literature on surgical management in children with Very Early Onset Inflammatory Bowel Disease (VEO-IBD) is scarce.

Methods: A retrospective chart review of prospectively collected quality improvement data was conducted to identify all cases of VEO-IBD (diagnosed <6 years) enrolled at our institution between 01/2009-07/2018. Data on patients were excluded for non-IBD conditions, surgery at another institution, or surgery as adults. Patient demographics, diagnoses, medical management, timing of first IBD-related surgical intervention, complications, and outcomes were analyzed.

Results: Of 723 children with IBD, 73(10\%) were VEO-IBD. Thirteen (18\%) underwent IBD-related surgical intervention at median 7.5 years (interquartile range[IQR]:5.6-11.4) of age, with 7/13(54\%) occurring ≤2 years after diagnosis. Ten were initially diagnosed as ulcerative colitis and 3 Crohn’s disease; however, 4 patients (31\%) had their diagnosis changed at least once. Most common (92\%) indication for initial surgery was disease refractory to medical management. Combination therapy (≥2 agents) was used for 11/13(85\%). Median length-of-stay was 6 days(IQR:4-8) with one major complication (anastomotic leak requiring diverting ileostomy), and 2 complications related to ileostomies.

Conclusions: In the first study on surgery for VEO-IBD, we found nearly 20\% of children required surgical intervention, most within 2 years of diagnosis, and frequent (31\%) changes to initial diagnosis.
Abstract 67
MIDDLE EASTERN NORTH AFRICAN ADOLESCENT’S RESPONSES TO DISCLOSURES OF SEXUAL ASSAULT
M. Ismail BA1,2, F. Obeid1,2, S. Shaker1,2, R. A. Blackwood MD PhD2,3
1University of Michigan, College of Literature, Science, and the Arts
2Office for Health Equity and Inclusion
3University of Michigan, Department of Pediatrics

Background: As the discussion and reporting of sexual assault continues to increase, it is necessary to educate adolescent’s and better prepare them to provide support to survivors of sexual assault. The current study evaluates the influence of education, age, gender, cultural experiences, and sexual assault training on the responses of Middle Eastern/North African (MENA) adolescent’s responses to disclosures of sexual assault. Methods: An anonymous, bilingual, digital survey conducted through Qualtrics software was distributed to high school and college students between the ages of 16-25 (with a focus on MENA identifying students) within Wayne and Washtenaw County, Michigan. The University of Michigan IRB granted exemption status for this study. Results: Data was collected between May 2018 and into December 2018, 364 participants took part in the study, 84% (271/321) of participants currently enrolled in a public university. About 77% (274/364) of respondents identified as being of being MENA origin or descent. About 61% (99/162) of MENA participants reported that they had not received formal sexual assault awareness or prevention training and of the non-MENA participants 46% (95/205; p<0.01) reported they did not receive formal training as well. Additionally, 36% (53/147) of MENA participants reported that they had experienced sexual assault or had an unwanted sexual experience and 55% (119/214; p<0.0001) of non-MENA participants reported experiencing sexual assault as well. Next steps include analyzing the influence of factors such as the respondent’s race, gender, cultural experiences, or exposure to sexual assault on the types of responses given to survivors after disclosing their assault. Conclusion: Our study is an important step in understanding the social, environmental, educational, and cultural factors that contribute to disparities in the responses of sexual assault disclosures within the MENA adolescent population. By conducting this research, educational information will be available to this community including the effects of cultural values and norms on sexual assault views and coping mechanisms.
Abstract 68

DSD EDUCATION FOR PATIENTS AND PARENTS: ARE PRINCIPLES ALONE ADEQUATE?

A. S. Baskin1; K. I. Suorsa-Johnson1,2; M. Gardner2; T. Schafer-Kalkhoff3; E. M. Weidler4; M. M. Rutter3; K. van Leeuwen4; D. E. Sandberg1,2

1Department of Pediatrics, Michigan Medicine, University of Michigan
2Susan B. Meister Child Health Evaluation and Research Center, University of Michigan
3Department of Pediatrics, Cincinnati Children’s Hospital Medical Center
4Pediatric Surgery, Phoenix Children’s Hospital

Background: Understanding of one's medical condition, its implications, and capacity to meaningfully share with important others are considered imperative to health and well-being. The objective was to understand perceptions of positive DSD outcomes and develop strategies for how providers can better educate parents and patients about DSD.

Methods: Stakeholders (n=28) in DSD care (patients, n=5; parents, n=3; healthcare specialists, n=12; and non-provider stakeholders, n=8) completed audio-recorded interviews exploring features of successful outcomes and how to achieve them. Recordings were thematically coded and analyzed using NVivo.

Results: A majority of participants (82.1%) identified patient knowledge of the DSD as an indicator of both successful process and outcome. Sharing information “repeatedly” in “bits” was mentioned (39.1%). Thirteen participants stressed “developmentally appropriate” sharing, but without further specifics. Some participants insisted sharing all information, while others discouraged “overwhelming” patients with details. Only a single participant mentioned “receiving” information is distinguished from “understanding” it, with ideal communication including “clearly articulating” without “vague terminology.” Although participants rarely specified what information patients and families should receive, knowing “what to expect” was noted. Conclusions: Although recommendations call for educating children about their condition, both provider and non-provider study participants suggested predominantly general and principle-oriented approaches (e.g., providing “age-appropriate” and “repeated” information). The 2006 DSD Consensus Statement stated “studies are needed to evaluate the effectiveness of information management with regard to timing and content” (p. e496), however such research has yet to be conducted. Future work should focus on specific educational strategies to meet the cognitive, emotional, and social informational needs of children with a DSD and their parents.
Abstract 69

PRIMARY CARE DETECTION AND MANAGEMENT OF RAPID INFANT WEIGHT GAIN

K. Asta1; C. Tan2; H. McCaffery2; J. Lumeng2,3; L. Meyyappan4; K. Paternoster4; MH. Pesch 2,3

1University of Michigan Medical School, 2Center for Human Growth and Development, 3Department of Pediatrics, 4University of Michigan Medical School, Ann Arbor, MI

Background: Rapid infant weight gain (RIWG) is a known risk factor for later childhood obesity. The American Academy of Pediatrics suggests close monitoring and evaluation of food intake/literacy for infants identified with RIWG.

Objective: To examine differences between diagnosis and discussion surrounding infant weight gain across growth pattern groups.

Methods: Electronic medical records were reviewed for infants receiving primary care at birth and 6 months in the Michigan Medicine system between 2013-2016. Infants were selected randomly within Growth Pattern Groups: 150 Overweight (Ovwt) (≥85th percentile weight-for-age at birth and 6 months regardless of RIWG), 150 RIWG (weight-for-age z-score gain of ≥0.67 standard deviations from birth to 6 months of age), and 150 matched controls. Extracted data from physician documentation of 6-month well-child visit included: RIWG/Ovwt Diagnosis (defined by any International Classification of Disease 9 or 10 diagnosis related to weight gain or weight status), Weight Discussion Topic (defined as mention of slow weight gain, Ovwt, RIWG, or weight gain reassurance in history, assessment, or plan). Bivariate analyses examined associations between Appropriateness of Weight Discussion Topic by Growth Pattern Group.

Results: Only 1 infant (0.67%) of RIWG Group had a diagnosis and only 3 infants (2.00%) of the Ovwt Group had a diagnosis. 1 (0.67%) of RIWG Group, 9 (6.00%) of Ovwt Group, and 140 (93.33%) of Control Group had a weight discussion that was weight-status appropriate (p<0.001).

Conclusion: There was limited diagnosis and discussion for Ovwt infants, and even more limited diagnosis and discussion for infants with RIWG in this sample. The reason for lack of diagnosis and appropriate weight discussion in RIWG infants may be due to physician beliefs around infant weight gain and dietary recommendations or lack of awareness of negative health outcomes associated with RIWG. Next steps include exploring physician perceptions and beliefs of RIWG with qualitative interviews and surveys.
Abstract 70
SIMPLIFYING SOMATIZATION: REDUCING HEALTHCARE UTILIZATION WITH A CLINICAL PRACTICE GUIDELINE FOR PEDIATRIC SOMATIC SYMPTOM AND RELATED DISORDERS
Klein EJ1,2, Malas N1,3, Hutton D2, Sturza J4, Sroufe N5, Pardon A6, Monroe K4, & Kullgren KA4

University of Michigan Medical School1, School of Public Health2, Department of Psychiatry3, Department of Pediatrics4, Department of Pediatric Emergency Medicine5, University of Michigan6

Background: Somatic Symptom and Related Disorders (SSRDs) are common yet complex conditions in pediatric medicine that can result in significant loss of functionality, poor quality of life, and high healthcare costs and utilization. This study describes the outcomes of an interdisciplinary clinical practice guideline (CPG) for evaluation and management of pediatric SSRDs in an academic children's hospital. Specific outcome measures include hospital cost, time to mental health consultation, length of stay (LOS), and readmission rates.

Methods: Data were collected via electronic health record review and PHIS cost estimates. The control group included patients admitted with a diagnosis of a SSRD in the year prior to protocol implementation (n=53). Patients admitted with a SSRD diagnosis for two years after CPG implementation were either in the time-control, non-protocol group (n=54) or the protocol group (n=55). Analysis included comparison of demographics, cost, LOS, number of procedures, readmission rate and delay to mental health consultation among the three groups. Aggregate measures were compared using unpaired t-tests or non-parametric tests. Results: Cost estimations were significantly less in both the protocol and time-control groups when compared to pre-protocol costs ($8,926 and $12,695 vs. $60,369; p<.0001). LOS was also significantly less in the protocol vs. control (1 vs 2; p=.04). Further results presented include cost reductions by subtype (including procedures, imaging, labs, clinical care), and time to mental health consultation.

Conclusions: Use of an interdisciplinary CPG significantly reduced estimated costs and LOS for children admitted with SSRDs. Cost reductions were also significant in the non-protocol post-implementation group, which suggests an institutional culture-shift for inpatient pediatric SSRD management. Further analysis is needed to determine where costs were most reduced, whether these findings are sustainable over a longer period of time and if there are any biases in care provision in protocol vs non-protocol groups. This study supports standardization of inpatient pediatric SSRD care as a means of reducing healthcare utilization in a population of youth that are often high utilizers of care.
Abstract 71

TRAJECTORIES OF PICKY EATING: PREDICTORS AND LONGITUDINAL ASSOCIATIONS OF CHILD WEIGHT AND MATERNAL FEEDING BEHAVIORS

Carmen Fernandez1, Harlan McCaffery2, Alison Miller2,3, Niko Kaciroti2,3, Julie C. Lumeng1,2,4, and Megan H. Pesch2,4

1) Medical School, 2) Center for Human Growth and Development, 3) School of Public Health, 4) Division of Developmental and Behavioral Pediatrics, University of Michigan

Background: Picky eating is common in childhood, however little is known about longitudinal trajectories of picky eating behavior. Objectives: The objectives of this study were to examine 1) trajectories of picky eating behaviors, 2) predictors of picky eating trajectory membership at baseline, 3) associated trajectories in child body mass index z-score (BMIz), and 4) associated trajectories in maternal feeding behaviors in a longitudinal cohort of low-income children. Methods: Mother-child dyads (N=380) participated in a longitudinal cohort with four data collection points (at child ages 4, 6, 8 and 9 years). Mothers completed the Child Eating Behavior Questionnaire and the Child Feeding Questionnaire. Anthropometrics were measured. Latent class analysis was used to determine trajectories of picky eating behaviors. Baseline correlates of picky eating trajectory membership were examined. Latent class analysis was used to examine trajectories of child BMIz and maternal feeding behaviors. Fisher’s exact tests and ANOVA examined the association of picky eating trajectory membership with child BMIz and maternal feeding behavior trajectory membership. Results: Three trajectories of picky eating behaviors emerged: persistently high (n=51, 29%), persistently medium (n=220, 58%), and persistently low picky eaters (n=51, 13%). Membership in the high picky eating trajectory was associated with more child negative lability, and lower child emotional regulation. High picky eating trajectory membership was inversely correlated with high BMIz trajectory membership (p=.03), and positively correlated to high maternal restriction trajectory membership (p=.004). Low picky eater trajectory membership correlated with medium and high BMIz trajectory membership (p=.03) and low pressure to eat trajectory membership (p=.001). Conclusions: The stability of picky eating behaviors may suggest that this behavior is more of a trait, rather than a state. Picky eating may be protective against higher BMIz.
THE HEALTH OF HAITIAN SCHOOL CHILDREN: A LONGITUDINAL ANALYSIS

Emma Gaboury¹, Mary Starrs¹, Jamarie Geller¹, Andrew Bartholomew¹, Sara Kaliszak¹, Dr. Jeri Kessenich²

¹Michigan State University College of Human Medicine, East Lansing MI
²Helen DeVos Children’s Hospital, Grand Rapids, MI

Background: Little is known about the health of the Haitian population. A local non-profit organization, Kids Health for Haiti, has gathered health data on a population of children grades K-9 in Port au Prince, Haiti and provided longitudinal health care. The objective of this study was to document the prevalence of anemia in a subgroup of Haitian children and investigate the relationship between anemia and BMI. Methods: A retrospective chart review was conducted on health care data collected on 221 Haitian children age 5-19 who attended the Power of Education Foundation (PEF) between the years 2012 and 2017. Primary outcome variables investigated were BMI and Hgb levels. All information was collected as part of routine health provision. Summary statistics were calculated, and means were compared using appropriate tests. We compared BMI and Hgb in Haitian children to African American school children in the US using information supplied by the Centers of Disease Control and Prevention (CDC). Results: In October 2012, 90 students (7.2±3.4 [mean age, SD]) were initially evaluated for BMI, and 77.8% of students (p<0.001) students were below the CDC 50th percentile. The mean Hgb of the 69 students tested in 2012 was 9.9±1.5 g/dL, indicating significant anemia. Of the 127 students evaluated in 2017 (11.6±3.4 [mean age, SD]) there were still significantly more (64.6%, p = 0.001) students below the CDC 50th percentile for BMI than above. The mean Hgb of the 87 students tested in 2017 was 10.8±1.1 g/dL, while the average Hgb of African American males and females ages 11-15 in the US is 13.06±1.09 and 12.61±1.76, respectively. Conclusions: 78% of Haitian school children in this study were below the 50th percentile in BMI on initial evaluation. Despite the increasing number of children over the 50th percentile on subsequent visits, the majority have not achieved adequate BMI. Hemoglobin also mirrored this trend, with low initial values that have improved with time. Our results reveal the likely multifactorial nature of poor growth and nutrition in Haitian children, including poverty and uneven access to health care. The provision of well-child care and treatment of medical conditions has resulted in improvement in these outcomes, suggesting that broader implementation of our strategies may be beneficial.
Abstract 73

EVEROLIMUS TREATMENT IMPROVES THE CNS PENETRATION AND EFFICACY OF DASATINIB IN PDGFRA-DRIVEN PEDIATRIC HIGH-GRADE GLIOMA

Zachary Miklja1, Brendan Mullan1, Ruby Siada1, Stefanie Stallard1, Viveka Nand Yadav1, Amy K. Bruzek1, Taylor Garcia1, Marcia Leonard1, Patricia L. Robertson1, Alyssa Paul1, Manjunath P. Pai2, Timothy Phoenix3, Bernard Marini2, Carl Koschmann1*

1Michigan Medicine, University of Michigan, Ann Arbor, MI. 2Clinical Pharmacy, College of Pharmacy, University of Michigan, Ann Arbor. 3Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Background: High-grade glioma (HGG) and diffuse intrinsic pontine glioma (DIPG) frequently harbor alterations in PDGFRA. The CNS penetration of PDGFRA inhibitors, such as dasatinib, is limited by the tumor-efflux protein P-glycoprotein (P-gp). We hypothesized that co-treatment with everolimus, which has been shown to block P-gp in non-tumor models, will increase CNS penetration and efficacy of dasatinib in PDGFRA-driven pediatric HGG and DIPG. Method: Dasatinib effectively treated mouse DIPG cells generated from an intra-uterine electroporation (IUE) model (TP53, PDGFRA and H3K27M mutations), with an IC50 of 100 nM and a dose-dependent reduction in PDGFRA and pPDGFRA by western blot. Using an in vitro P-gp inhibitor assay, we confirmed that everolimus strongly blocks P-gp activity at 1 μM (p=0.0028 vs untreated, and NS vs complete P-gp block). Results: Treatment studies using the IUE model demonstrate a prolonged life in mice treated with a one week course of dasatinib and everolimus compared to control treatments. Brief treatment with everolimus resulted in sub-IC50 dasatinib average mouse cortex (23 nM) and tumor (65 nM) concentrations by mass spectroscopy, but prolonged (>24 hours) everolimus exposure resulted in improved average cortex (235 nM) and brainstem tumor (509 nM) concentrations. Based on this promising pre-clinical data, we established a phase 2 trial employing dasatinib and everolimus in children with HGG and DIPG that contain PDGFRA alterations (NCT03352427). The first two patients, with recurrent HGG (PDGFRA-amplified) and recurrent DIPG (PDGFRA D842V) respectively, survived 6 months and 9 months (ongoing) after progression, which compares very favorably to historical controls. Paired CSF samples (before and after addition of everolimus) from the PDGFRA-amplified patient showed a 50% increase in CSF dasatinib level after addition of everolimus. Conclusion: In summary, we demonstrate that dasatinib treatment of PDGFRA-driven pediatric HGG and DIPG is improved with everolimus blockade of P-gp. This represents a novel route for improving the CNS penetration and efficacy of precision therapeutics for pediatric HGG.
USE OF AN RNA-SEQ FUSION PIPELINE RESULTS IN SUSTAINED CLINICAL RESPONSE OF CHILDREN WITH RECURRENT HIGH-GRADE GLIOMA

Kallen Schwark1, Amy K Bruzek, MD2, Chandan Kumar-Sinha, PhD3,4, Sylvia Escolero1, Bernard Marini, PharmD5, Amy Pasternak, PharmD5, Marcia Leonard, NP1, Patricia Robertson, MD1, Rajen Mody, MD1, Arul M. Chinnaiyan, MD PhD3,4, Carl Koschmann, MD1

1Department of Pediatrics, Michigan Medicine, Ann Arbor, MI; 2Department of Neurosurgery, Michigan Medicine, Ann Arbor, MI; 3Department of Pathology, Michigan Medicine, Ann Arbor, MI; 4Michigan Center for Translational Pathology, Michigan Medicine, Ann Arbor, MI; 5College of Pharmacy, University of Michigan, Ann Arbor, MI

BACKGROUND: Pediatric diffuse intrinsic pontine glioma (DIPG) and recurrent high-grade glioma (HGG) have an average progression-free survival (PFS) of 3 months. Gene fusions in cancer are being targeted with promising results. However, targeting fusions in DIPG and HGG has largely been unexplored – in part due to lack of clinical RNA-seq and/or low sensitivity in fusion calling. METHODS: We performed DNA sequencing (1700 genes) and RNA-seq analysis with the MI-ONCOSEQ CODAC fusion pipeline designed for improved fusion detection regardless of breakpoint within gene body. We identified three targetable gene fusions in patients with DIPG or recurrent HGG and retrospectively compared treatment and outcome to 19 patients with HGG and DIPG targeted with non-fusion DNA alterations. RESULTS: The first patient is an 11-year-old with anaplastic oligodendroglioma carrying a novel FGFR3-PHGDH fusion. The patient was treated with the FGFR inhibitor ponatinib, resulting in 24 months PFS. The second patient is a 15-year-old with a thrice recurrent mixed glioneuronal tumor despite multiple tumor resections and radiation; their tumor was found to carry a ROS1-GOPC fusion. The patient was treated with the ROS1 inhibitor entrectinib and remains progression-free after 44 months. The third patient is a 5-year-old with DIPG carrying a novel CTTNBP2-MET fusion who was treated with the MET inhibitor cabozantinib but passed away after 9 months from diagnosis (of note, tumor carried 15 other gene fusions). Our patients with HGG and targeted fusions had more favorable clinical response in comparison to our targeted non-fusion patients (12 months PFS) and historical controls (3 months PFS). CONCLUSIONS: RNA-seq analysis with advanced fusion calling can result in the identification of promising treatment regimens for DIPG and HGG. We also show that patients with targeted fusions have potential for superior clinical response in comparison to therapies targeting other alterations.
Abstract 75

CLINIC DISPARITIES OF ADOLESCENT RISKY BEHAVIOR
Y. Lee1, Y. Civil1,2, T. Hart-Johnson1, A. Bahamonde3, R.A. Blackwood1,4
1Office of Health Equity and Inclusion, University of Michigan, 2Division of General Pediatrics, University of Michigan, 3 University of Michigan Medical School, 4Division of Pediatric Infectious Diseases, University of Michigan

Background: The majority of adolescent morbidity and mortality can be attributed to risky behavior.1 The Rapid Assessment for Adolescent Preventive Services (RAAPS) is a 21-item questionnaire designed to aid physicians to quickly assess the most common risk factors and address them during a clinic visit.2 The objective of this study was to assess for the disparities of presence and addressed rate of adolescent risky behavior between several pediatric clinics and examine the demographic predictors of the disparities. Methods: 1,256 RAAPS questionnaires were collected from nine pediatric clinics. Each questionnaire assessed risk and was then reviewed whether the risk was addressed by the provider. Demographic data included race, gender, age, insurance, and religion. Clinic differences in individual risks were assessed via cross-tabs and Chi Squared Analysis and Risk total was assessed with ANOVA. Logistic Regression was then used to test for combined effect of clinic and demographics. Results: Overall, participants had 2.11 risks. Those presenting risk had 2.7 or 85% of risks addressed at their visit. 14 behaviors were statistically different between the clinics. Additionally, 4 behaviors were addressed significantly differently by clinic. Logistic Regression showed demographic differences such as race, age, socioeconomic status, and gender which were partially confounded by clinic. Conclusions: Clinics located in areas of lower socioeconomic status and with higher percentages of underrepresented minority populations, display greater risk than other communities. Special attention and appropriate culturally competent care should be paid towards addressing risky behaviors for providers practicing in such areas. Future studies should also be conducted into more specificity regarding each risky behavior and demographic variable.
MOOD AND HYPERACTIVITY DISORDERS IN CHILDREN WITH GLOMERULAR DISEASE

H. Desmond1; A. Waldo1; S. Attalla1; P. Gipson1; J. Troost1; N. Carlozzi2; R. Eikstadt1; J. Lavigne1; Z. Modi1; D. Gipson1

1Division of Nephrology, Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA
2Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI, USA

Background: Children with chronic conditions are at heightened risk for mood disorders; yet little is known about the prevalence or relationship to disease characteristics in the glomerular disease population.

Objectives: The goal of this study is to assess the prevalence of mood disorders and attention deficit disorder (ADD) in children with glomerular disease, and their association with kidney disease and treatment characteristics.

Design/method: This analysis was conducted on the Kidney Research Network, a multisite patient registry and included patients from four sites with childhood onset glomerular disease. The registry includes encounter, diagnoses, medication, labs, and vitals extracted from participant’s electronic health records. Mood disorders were identified using ICD9/10 diagnosis codes, including a spectrum of anxiety and depressive disorders as well as ADD. Time to diagnosis of interest was estimated using Kaplan-Meier curves and Cox proportional hazards models. Potential covariates in the models include age at kidney disease onset, sex, race, ethnicity, and time-varying treatment, eGFR, and urine protein: creatinine ratio (UPC).

Results: Data was available on 429 children with a median follow-up time of 54 months and a median age of 4 years at kidney disease onset. Of these, 95 (22.1%) were diagnosed as having a mood disorder or ADD, with 43 of those having two or more disorders of interest. The most common disorders were anxiety (n=58, 19.4 per 1000 patient-years), depression (n=35, 11.7 per 1000 patient years), and ADD (n=25, 8.4 per 1000 patient-years). Older age (HR per year: 1.2, 95% CI: 1.1-1.3) steroid treatment (HR: 3.9, 95% CI: 2.4-6.5) and higher UPC (HR per log g/g: 1.2, 95% CI: 1.0-1.3) were associated with mood disorder onset. White children were more likely to be diagnosed with a mood disorder than Black (HR: 3.4, 95% CI: 1.3-8.4) or Asian children (HR: 2.4, 95% CI: 1.0-5.5).

Conclusions: Mood disorders and ADD were documented in approximately one quarter of children with glomerular disease and were associated with concurrent steroid therapy. This may be an underrepresentation as the estimates are based on what was documented in the participant’s electronic health record. A difference of prevalence by child race may suggest a difference in assessment and diagnosis rather than a true difference in prevalence. Once replicated, these findings suggest mental health screening may be warranted in children with glomerular disease.
URINARY EGF AS A PREDICTOR OF PROGRESSION OF RENAL DISEASE IN CHILDREN WITH NEPHROTIC SYNDROME
A. Waldo¹; W. Ju²; S. Eddy²; M. Kretzler²; J. Troost¹; D. Gipson¹
D. Marchel¹; J. Troost¹; P. Gipson¹; H. Desmond¹; S. Attalla¹; R. Eikstadt¹; D. Gipson¹
¹Division of Nephrology, Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA
²Division of Nephrology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA

Background: Low urinary epidermal growth factor (uEGF) has been shown to be predictive of loss of estimated glomerular filtration rate (eGFR) in children with Alport syndrome and adults with chronic kidney diseases. Objectives: The goal of this study is to evaluate uEGF as a predictor of eGFR slope in children with nephrotic syndrome.

Design/method: This analysis was conducted on 144 children enrolled in the Nephrotic Syndrome Study Network (NEPTUNE) with minimal change disease, focal segmental glomerulosclerosis, or childhood onset nephrotic syndrome-not biopsied and had a baseline uEGF measurement. Patients had a median follow-up time of 29 months (IQR: 12-54 months). Longitudinal eGFR measurements were Winsorized to 120ml/min/1.73m² to reduce the effect of outlier measurements during periods of hyperfiltration. Longitudinal mixed models with random intercepts were fitted to the Winsorized eGFR measurements with a dummy variable for hyperfiltration at that time point, and potential baseline predictors of eGFR slope were examined to reach a final model. Predictors included age, sex, race, ethnicity, maternal education, kidney disease diagnosis and duration at baseline, prior therapy at baseline, urine protein: creatinine ratio, serum albumin, and uEGF at baseline, interstitial fibrosis, and APOL1 and monogenic etiology status.

Results: There was a significant relationship between baseline uEGF and eGFR slope over time (Figure 1). Children with a high baseline uEGF (log₂ uEGF = 7 ng/mL), had stable eGFR during follow-up (eGFR slope: 0.3, 95% CI: -1.0 to 1.6 mL/min/1.73m²/year). Children with a moderate baseline uEGF (log₂ uEGF = 5 ng/mL) showed loss of kidney function (eGFR slope: -1.7, 95% CI: -2.5 to -1.0), and children with low baseline uEGF (log₂ uEGF = 1 ng/mL) had a greater loss of kidney function during follow-up (eGFR slope: -5.9, 95% CI: -8.1 to -3.6). uEGF was a robust predictor of eGFR slope after adjusting for age, APOL1, biopsy diagnosis, baseline proteinuria, and interstitial fibrosis. Conclusions: Urinary EGF was found to be a significant predictor of eGFR change over time in children with nephrotic syndrome. This novel biomarker was informative in both biopsied and non-biopsied children with nephrotic syndrome, and further validation may support the use of this non-invasive prognostic marker to routine clinical care.
Abstract 78
(withdrawn)
Abstract 79

ELECTROGRAPHIC SEIZURES AND BRAIN INJURY IN CHILDREN ON EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)
Robin J. Cook1, Stephanie Rau1, Shannon Lester1, Tim Vesper2, Yuki Peterson2, Therese Adamowski2, Renée Shellhaas1, and Faye Silverstein1
1Division of Pediatric Neurology, Department of Pediatrics, Michigan Medicine, Ann Arbor, MI
2ECMO Department, Michigan Medicine, Ann Arbor, MI

Background: Single-center studies suggest that up to 30% of pediatric patients on extracorporeal membrane oxygenation (ECMO) have electrographic seizures. The aim of this study was to characterize seizure prevalence and risk factors, brain injury prevalence, and seizure treatment response in the pediatric ECMO population at a tertiary care children's hospital.

Methods: Eighty-six consecutive patients who received Neurology consults and underwent continuous video-EEG while on ECMO were identified from a registry of patients in critical care units over a 35-month period. A systematic chart review was performed to identify reasons for ECMO initiation, prevalence of electrographic seizures, response to treatment, prevalence of brain injury on neuroimaging, and clinical outcome in this population.

Results: Continuous video-EEG was initiated in 86 of 170 children who were on ECMO from November 2015 to September 2018 (51%). Of 86 children who underwent EEG monitoring, 19 had seizures (22%). Of these, 17 (89%) had subclinical seizures, and 7 (37%) had electrographic status epilepticus. ECMO indication, ECMO access site, and EEG background were not significant risk factors for seizures. Children with interictal epileptiform discharges were significantly more likely to have seizures (p = 0.03). Fifty of 78 children who underwent brain imaging had abnormal studies (64%). Seizures were associated with subsequent presence of hemorrhage on imaging (p = 0.04). Thirty-nine children (45%) died, including 8 of 19 patients with seizures; seizures were not significantly associated with mortality.

Conclusions: Currently, approximately half of children on ECMO at our institution are receiving continuous video EEG monitoring, and nearly a quarter of these have seizures. Seizures are more common in those with interictal epileptiform discharges and are associated with intracranial hemorrhage on imaging. Further research is needed to determine the relationship between seizures and overall outcome. Clinical practice pathways that include EEG monitoring for children on ECMO should also include neuroimaging and neurodevelopmental follow-up.
Abstract 80

CENTRAL CATHETER ASSOCIATED VENOUS THROMBOEMBOLISM IN TWO PEDIATRIC PATIENTS WITH NF-kB ESSENTIAL MODULATOR (NEMO) DEFICIENCY SYNDROME

Christie Atchison MD, Kelly Walkovich MD, Amanda Sankar MD, Angela Weyand MD. Pediatrics, Michigan Medicine

Mutations in Nuclear Factor kB Essential Modulator (NEMO) is a known cause of several X-linked immunodeficiencies including incotinentia pigmenti and ectodermal dysplasia, anhidrotic (1). Due to recurrent infections, patients with NEMO often require central venous access for intravenous antibiotics, frequent phlebotomy, and parenteral nutrition. Need for central access, prolonged hospitalizations, systemic inflammation and systemic infection, common in patients with NEMO, are well known risk factors for development of venous thromboembolism (VTE) (2). Patient A, a 17-year-old male with inflammatory bowel disease, NFkB1A mutation, anhidrotic ectodermal dysplasia, disseminated Mycobacterium avium complex infection, and recurrent soft tissue and blood infections, had a peripherally inserted central catheter (PICC) placed for extended therapy. He developed multiple vessel, catheter-associated VTE, requiring treatment with low molecular weight heparin (LMWH). Given subsequent bleeding complications, he was transitioned to daily Aspirin and heparin line flushes for VTE prevention. Patient B, a 9-month-old male with IKBKG mutation-associated-immunodeficiency, Pneumocystis jiroveci pneumonia and failure to thrive, developed multiple vessel, PICC-associated VTE, requiring therapeutic treatment with LMWH. Given multiple risk factors and history of catheter associated VTE, he continues to receive prophylactic LMWH with any indwelling central lines. While there is no clear association between NEMO deficiency and VTE in the literature, we demonstrate two patients requiring systemic anticoagulation and prophylaxis due to recurrent central-line associated VTE, suggesting that these patients may be at increased risk for VTE. Caution should be taken in prescribing prophylactic anticoagulation, as newer agents such as Rivaroxaban function via the modulation of NFkB pathway and may be ineffective in this patient population (3).

MORAL DISTRESS AMONG PEDIATRIC RESIDENTS: INCIDENCE AND RISK FACTORS
Katie R. Baughman¹, Michele Gornick², Naomi T. Laventhal²,³
¹Pediatrics Residency, University of Michigan
²Center for Bioethics and Social Sciences in Medicine, University of Michigan
³Department of Neonatal-Perinatal Medicine, University of Michigan

Background: Moral distress (MD) among healthcare providers is well described. Unique hierarchical and situational risk factors might impact or heighten residents’ experience of MD, but MD among pediatric trainees is not well studied. Methods: We designed and piloted an electronic survey, querying whether MD was present and quantifying potential contributing causes. 1st - 4th year pediatrics, med/peds, and combined pediatrics/subspecialty residents on their PICU, NICU, and inpatient pediatric heme-onc rotations at a single quaternary academic medical center were surveyed weekly for three consecutive months (July - Sept 2018). Chi-squared tests were performed to examine the relation between trainee characteristic and responses. Results: We collected 114 surveys (response rate 86%). Roughly one quarter of respondents affirmed MD (25%/n=29), providing medically futile care (29%/n=33), provided care was not in the patient’s best interest (25%/n=28), feeling weighed down by past MD (moral residue) (24%/n=27), and inadequate staffing for proper patient care (26%/n=30). Roughly one third reported not feeling adequately involved in medical decision-making (32%/n=36) and carrying out order(s) they did not understand and/or agree with (33%/n=37). When analyzed by clinical service, there were statistically significant differences between services in the number of residents who felt adequately involved in the care of and decision making for their patient(s) (p=0.05) (Figure 1), who felt staffing was adequate (p=0.022) (Figure 2), and who felt weighed down by moral residue (p=0.038) (Figure 3). When analyzed by year of training, there was a significant difference in number of residents who felt they had to carry out order(s) they did not understand and/or agree with (p=0.049) (Figure 4); more senior residents experienced this more often than more junior residents. Conclusions: We identified hierarchical disengagement with medical decision-making, a sense of providing futile or non-beneficial treatment, and perceived inadequate staffing at rates similar to or higher than reported rates of experienced moral distress and moral residue. This suggests that we have begun to identify tangible risk factors for MD among pediatric residents, but that wellness, resilience, and ethics resources at our institution might be effective in mitigating MD. Further investigation is needed to understand MD across time, hospital settings, and specialties.
THE SENSITIVITY AND SPECIFICITY OF PROVIDER PREDICTIONS OF MULTIPLE ORGAN DYSFUNCTION SYNDROME

Close JS1, Dews A2, Paice K1, Cornell TT4, Carlton E2
1Department of Pediatrics and Communicable Diseases, University of Michigan, Ann Arbor; 2Division of Pediatric Critical Care Medicine, Department of Pediatrics and Communicable Diseases, University of Michigan, Ann Arbor; 3University of Michigan, Ann Arbor, Michigan 4Lucile Packard Children’s Hospital, Stanford University

Background: Multiple Organ Dysfunction Syndrome (MODS), a progressive dysfunction of two or more organ systems, is a significant risk factor for morbidity and mortality among critically ill children. Clinician recognition and prediction of MODS is imperative for early interventions to prevent or mitigate MODS development and guide treatment decisions. However, no data exist as to the accuracy with which clinicians can identify or predict the development of MODS. Objective: To determine the accuracy with which bedside clinicians identify and predict MODS based on the two sets of criteria.

Design/Methods: PICU patients with anticipated stay of >48 hours were eligible for inclusion. Direct providers, from residents to attendings, were surveyed in the first 24 hours of admission to identify if the patient had MODS and predict whether a patient would develop new or progressive MODS (NP-MODS). Patient data were collected from the medical record using both the Goldstein and Proulx MODS Diagnostic Criteria. Statistical analysis using McNemar’s test was utilized to determine accuracy of MODS identification and predictions.

Results: Data from 440 patients were included with 1,138 clinician surveys. By Goldstein, 178 patients were found to have MODS on PICU admission and 273 had NP-MODS. By Proulx, 80 were identified as initially having MODS and 170 had NP-MODS. Clinician identification was consistent with Proulx (81%, p=0.12), but not Goldstein (67%, p=0.00). The sensitivity for clinician prediction of NP-MODS was 20% and 21% for Goldstein and Proulx criteria, respectively, while specificity was 87% and 86%. There were 31 deaths, with provider prediction sensitivity of 1.3% and specificity of 98%.

Conclusions: Clinicians correctly identified MODS between 67-81% of the time and were more accurate by Proulx criteria. Overall, clinician prediction of NP-MODS demonstrated a moderate specificity but low sensitivity. Future directions include identifying whether either clinical severity scores, clinician prediction, or a combination thereof are best able to predict development of NP-MODS and if prediction is associated with practice patterns of implementation of therapies.
HUMAN PAPILLOMA VIRUS (HPV) VACCINE INITIATION RATES IN ADOLESCENTS AFTER IMPLEMENTATION OF NEW CDC GUIDELINES

Alison Colonna, Esther Yoon
University of Michigan, Department of Pediatrics

Background: The Human Papilloma Virus (HPV) vaccine was first recommended in the United States as a three dose vaccine series in 2006. It has been shown to be highly effective in preventing HPV infections, specifically the strains that have been shown to cause various types of cancer and genital warts. HPV vaccine rates, both initiation and completion, have trailed behind other adolescent vaccine rates. In October 2016, the CDC released new guidelines for HPV vaccines, recommending two doses of the vaccine for all children who start the series before the age of 15 years compared to the previous 3 dose recommendation.

Purpose: The purpose of this study was to compare HPV vaccine initiation rates in adolescents 11-14 years old one year before and after the release of new CDC vaccine guidelines.

Methods: A retrospective electronic medical record review of patients 11-14 years old seen at Canton Health Center for urgent and well visits. We evaluated HPV vaccine initiation rates of patients receiving their first dose before age 15 years, one year prior to and one year after the release of the CDC’s new guidelines.

Results: Of 1670 adolescents 11-14 years old, 518 patients had already initiated their HPV vaccine thus excluded from analyses. There was no difference in HPV vaccine initiation rates for 11-14 year olds prior to and after the new vaccine guidelines. Of 467 patients seen before the new guidelines, 52% initiated HPV vaccine at that visit. Of 480 patients seen after the new guidelines, 51% initiated HPV vaccine at that visit. Of 205 patients seen in both time periods, 26% initiated the HPV vaccine after the new guidelines were released despite refusing at first. There was no statistically significant difference in HPV vaccine initiation rates by gender nor HPV completion rates by gender.

Conclusion: Our study did not find any significant difference in overall HPV vaccine initiation rates among young adolescents after the release of the CDC’s new 2-dose HPV guidelines. However, among those seen in both time periods, a quarter of young adolescents initiated HPV vaccine despite initial refusal. This suggests that HPV vaccine initiation rates are modifiable and further study is warranted to evaluate various parent, patient and vaccine factors involved.
INFANT PEANUT ALLERGY TESTING IN THE POST-LEAP WORLD

S Volertasa, M Couryb, G Sandersa, M McMorrisa, and M Guptaa
aUniversity of Michigan Department of Allergy and Immunology
bUniversity of Michigan Department of Pediatrics

Background: Peanut allergy prevalence in children has been increasing over time and is present in 2% of children nationally based on a survey performed in 2010. National Institute of Allergy and Infectious Diseases (NIAID) addendum guidelines for early peanut introduction and screening for at-risk populations were introduced in 2017. We hypothesize that in practice, these guidelines are not being followed consistently by pediatricians and allergists. The objective of this study is to review adherence to peanut allergy screening practices following LEAP implementation.

Methods: Retrospective chart review was conducted of infants <12 months of age tested for peanut allergy in the University of Michigan outpatient allergy clinic between January 1, 2017 to January 30, 2018.

Results: Eighty-three patients were screened for peanut allergy with skin prick testing (SPT) or peanut IgE, of which 40 patients (48%) met NIAID screening guidelines. Sixty-seven patients were referred by pediatricians. Of SPT patients, 22 had negative SPT (23% introduced peanut successfully, 2 patients have yet to undergo oral food challenge, 1 was recommended avoidance), 9 patients had a wheal 3-7mm (56% were recommended avoidance), and 6 patients had a wheal >7mm (100% were recommended avoidance). Screened patients that did not meet criteria included those with a history of food allergy or mild-moderate eczema. Twenty-eight additional patients were referred for reaction to peanut after early introduction at home without prior screening. Five would have met criteria for screening.

Conclusions: Less than half of patients screened for peanut allergy met NIAID guidelines regarding testing. Physician management was variable for patients with SPT wheals at 0-7 mm. Reasons for screening in those who did not meet criteria included mild-moderate eczema or family history of allergy. Home peanut introduction elicited reactions in 5 patients who would have met NIAID criteria for screening. These results indicate the need for further education regarding the application of NIAID guidelines for early peanut introduction and screening.

Abstract 85

TUBERCULOSIS SCREENING IN PEDIATRIC PRIMARY CARE

A. Garcia, M. Coury
Department of Pediatrics, University of Michigan, Ann Arbor, MI

Background: In Washtenaw County, the rate of tuberculosis (TB) infection in 2017 was 2.2 per 100,000, which is among the highest case rates within the state of Michigan and approaches the national case rate of 2.8 per 100,000 in the same year. As latent tuberculosis infection (LTBI) is the primary driver of active tuberculosis infections in the U.S., national TB elimination efforts have focused on early identification and treatment of LTBI. Currently, there is no standardized TB risk assessment (screening) tool employed across the University of Michigan (U of M) Pediatrics primary care clinics. We conducted a survey of U of M Pediatric primary care providers to assess provider familiarity with evidence-based TB screening practices. The goal of this survey was to identify barriers to evidence-based screening and areas for improving standardization of TB screening across the U of M Pediatric primary care clinics. Methods: We conducted a qualitative survey of provider experiences with tuberculosis screening practices in the Pediatric primary care setting. This study was conducted by voluntary survey using Qualtrics data collection software and distributed via a secure, anonymous email link. Eligible participants included all U of M primary care Pediatricians as well as all Pediatric residents within the University of Michigan system. Results: We collected a total of 92 discrete responses. Twenty-seven respondents (29.6%) indicated that they did not screen for TB exposure according to AAP recommendations. Overall, respondents indicated lack of comfort assessing risk factors (only 44% of respondents “extremely” or “moderately” comfortable”), lack of time for performing appropriate screening (30% of respondents), and lack of knowledge regarding next steps following positive screens (23%). Additional comments indicated lack of an available standardized risk assessment tool as well as perceived low local prevalence of TB as barriers to appropriate screening. Conclusion: In this survey, U of M primary care providers identify time constraints and lack of knowledge regarding appropriate screening and testing practices as barriers to conducting regular TB risk assessments. Thus, the implementation of a standardized, evidence-based risk assessment tool in the University of Michigan Pediatric primary care system will be a valuable next step toward improving our rates of TB screening and targeted testing. Next steps include assessing screening rates following implementation of this tool as well as rates of targeted testing and treatment.
FACTORS ASSOCIATED WITH AND RESIDENT PERCEPTION OF CODE STATUS ORDERING IN HOSPITALIZED CHILDREN
E. Jacobson1, M. Malakh2

1Medicine-Pediatrics, University of Michigan, Ann Arbor, MI
2Pediatric Hospital Medicine, University of Michigan, Ann Arbor, MI

Background: Hospitalization of ill children can lead to questions surrounding appropriate care. Although data exist on code status ordering in adults along with timing of discussions and rates of DNR orders in pediatric populations, less is known about overall code status ordering in hospitalized children.

Objective: The objective of this study was to characterize current practice as well as identify resident perception of code status ordering in pediatric patients.

Methods: Retrospective chart review of pediatric patients (age 0 – 21 years old) admitted to Michigan Medicine over one year (November 1, 2017 through October 31, 2018) in addition to survey of all Michigan Medicine house officers with subgroup analysis of pediatric and medicine-pediatric (MP) resident responses. ANOVA, 2-sample t-tests, and chi-square tests were used to compare results.

Results: In total, 8,033 encounters for 5,953 pediatric patients were reviewed. Code status was ordered in 4.4% of admissions with 36.3% of orders placed by residents. Factors such as age, length of stay (LOS), admitting service (type along with pediatric versus adult service), and discharge location were associated with documentation of code status. Timing of code status ordering as calculated by ratio of time to order over total LOS occurred statistically later in admission for DNR orders (0.52 for DNR vs 0.19 for full; p<0.001) and in patients admitted to pediatric versus adult services (0.35 vs 0.14; p<0.001). A total of 51 pediatric and MP residents responded to the survey (response rate 51%). Compared to all house officers, they were less likely to report important to discuss (63% vs 85%; p<0.001) along with less likely to choose responsibility of resident to discuss code status (63% vs 81%, p<0.05). The top three reasons for not discussing code status were patient characteristics, forget to discuss, and code status discussion not relevant.

Conclusions: The majority of pediatric patients admitted to the hospital have no code status ordered. Code status ordering varies by patient, provider, and service characteristics.
RETROSPECTIVE STUDY OF NEUROLOGIC, BEHAVIORAL, AND OPHTHALMOLOGIC SIDE EFFECTS OF DINUXUTIMAB THERAPY AT A SINGLE INSTITUTION

H. Lust\textsuperscript{1}, G. Ney\textsuperscript{1,2}, M Shamoun\textsuperscript{1,2}, R. Mody\textsuperscript{1,2}, R. Jasty Rao\textsuperscript{1,2}
\textsuperscript{1}Michigan Medicine Department of Pediatrics, \textsuperscript{2}Division of Pediatric Hematology/Oncology

BACKGROUND: Chimeric anti-GD2 antibody ch14.18 (dinutuximab) therapy has improved the survival of children with high-risk neuroblastoma. Acute neuropathic pain is a well-documented side effect of dinutuximab. Additional adverse effects including sensorimotor neuropathy, ocular symptoms, and behavioral changes have been described. The incidence and severity of these side effects are not well-documented in pediatric patients. With improved survival of patients receiving this modality it is important to look for the potential long-term effects of dinutuximab. OBJECTIVE: To determine the incidence and severity of neurologic, ophthalmologic, or behavioral changes after dinutuximab at our institution. METHODS: We performed a retrospective chart review using our electronic medical record. We included patients with high-risk neuroblastoma between the ages of 1 and 21 years diagnosed between 1997 and 2017 who received dinutuximab. Patients with history of opsoclonus-myoclonus syndrome or gross sensorimotor neuropathy prior to receiving dinutuximab were excluded. We examined clinical documentation for subjective reports and objective exam findings of neurologic, ophthalmologic, or behavioral changes. We also looked for referrals made to neurology, ophthalmology, physical medicine & rehabilitation (PM&R), and psychology. RESULTS: Twenty-two patients met inclusion criteria. 18 patients received dinutuximab per ANBL0032; 5 patients received dinutuximab per ANBL1221. One patient received dinutuximab per both protocols. Of these 22 patients, 11 patients reported symptoms of interest; 5 patients reported multiple symptoms. Seven patients reported symptoms that began at least 6 months after completing dinutuximab; six of these patients reported symptoms at least 12 months after completing therapy. Nine patients had objective findings on exam, including decreased deep tendon reflexes, abnormal pupils, and nearsightedness. For 10 patients, 15 referrals were made to ophthalmology, PM&R, and neurology. CONCLUSION: Neurologic, ophthalmologic, and behavioral symptoms were commonly reported and demonstrated on exam among pediatric patients with high-risk neuroblastoma who received dinutuximab. It is important to identify these effects so that appropriate specialist referrals can be placed for adequate management. These symptoms may not be solely due to dinutuximab as these patients receive other agents including opioids, so a prospective trial is needed to further evaluate the long-term effects of dinutuximab and to determine how best to screen for these effects.
Abstract 88

A 2 YEAR REVIEW OF POSITIVE BLOOD CULTURES IN HOSPITALIZED CHILDREN EVALUATING TIME TO CULTURE POSITIVITY AND GRAM STAIN RELIABILITY

J.A. Metcalf1, E. Telega2, J. Blase1, K. Klein2, A. Tribble3

1Pediatrics Residency Program, U of Michigan, Ann Arbor, MI
2Department of Pharmacy, U of Michigan, Ann Arbor, MI
3Division of Pediatric Infectious Diseases, U of Michigan, Ann Arbor, MI

Background: Hospitalized children undergoing evaluation for sepsis are typically monitored with or without antibiotic therapy while awaiting blood culture results. Although the time needed to observe blood cultures in febrile neonates has been well studied, data are limited in other pediatric populations. There are also limited data on the reliability of early microbiologic data, such as Gram stains, which could guide earlier narrowing of antibiotic therapy. Such information is needed to minimize excess hospital stays and antibiotic use, while ensuring adequate treatment for those ultimately found to have positive blood cultures.

Methods: All positive blood cultures from inpatients aged 0-18 years at the University of Michigan were reviewed over a two-year time period. Individual episodes were defined as a positive blood culture obtained from a hospitalized or emergency room patient, with no other positive blood cultures in the preceding 30 days. De-identified patient data were collected through an IRB-approved retrospective chart review. Bivariate comparisons were made using Mann-Whitney U test and multivariate comparisons were modeled with logistic regression.

Results: 344 patients with a median age of 2.3 years (interquartile range 0.4 – 7.7 years) had 417 discrete episodes of positive blood cultures over the two-year study period. Median time to positivity (TTP) was 22.7 hours (h), (interquartile range 16.0 – 31.9 h), with contaminants (as determined by the primary team) growing more slowly than true pathogens (median TTP 28.1 h versus 19.5 h, P <0.0001). Of true infections, 66% (95% confidence interval: 60.0%-70.7%), 85% (80.3%-84.8%), and 93% (89.6%-93.0%) of cultures were positive by 24 h, 36 h, and 48 h, respectively. In a logistic regression model of clinical characteristics, patients with a chronic illness were more likely to have earlier TTP than those without. There was no correlation between TTP and race, sex, neutropenia, or recent major surgery. Only 0.7% (0.2%-2.1%) of cultures had an incorrect initial Gram stain report. 2.6% (1.5%-4.7%) of cultures were polymicrobial with initial Gram results not reflecting all species in final culture.

Conclusions: These results support the practice of 48h of blood culture observation for pediatric patients undergoing a sepsis evaluation. We found Gram stains to be extremely reliable in our setting, and in clinically improving patients, strategies to narrow antibiotics based on Gram stain could be considered.
Abstract 89

TNF-α INHIBITION WITH ADALIMUMAB IN REFRACTORY IDIOPATHIC SEVERE APLASTIC ANEMIA

M. Rees1, K. Walkovich1,2, M. Vander Lugt1,2, D. Frame3

1Department of Pediatrics, University of Michigan; 2Division of Pediatric Hematology/Oncology, University of Michigan; 3Department of Clinical Pharmacy, University of Michigan

Background:
Aplastic anemia is an acquired marrow failure characterized by peripheral pancytopenia and a hypoplastic bone marrow. In vitro and animal model experiments have implicated TNF-alpha dysregulation in the pathogenesis of aplastic anemia.1

Case Summary:
A 13-year-old female with severe idiopathic aplastic anemia underwent induction with ATG and cyclosporine, and cell counts initially stabilized. However, following relapse, pharmacokinetic studies revealed erratic cyclosporine absorption, and she failed an alternative formulation. She also failed trials of eltrombopag, tacrolimus, re-induction with rabbit ATG and G-CSF, and basiliximab.

Adalimumab was initiated based on previous laboratory work supporting a role of TNF-alpha in aplastic anemia. Since initiating monthly injections of adalimumab, she has had significant count recovery without transfusions through 24 months of follow up. CECR1 sequencing showed no mutations.

Conclusion:
We describe a case of refractory idiopathic severe aplastic anemia with response to a TNF-alpha inhibitor. While such response has been shown in ADA-2 deficiency2, this response in a patient with negative CECR1 mutation testing supports the role of TNF-alpha in the pathogenesis of idiopathic aplastic anemia. Further investigation of the use of TNF-alpha inhibitors in aplastic anemia is warranted.

References:
RESPIRATORY CILIARY DYSFUNCTION AMONG PATIENTS WITH HETEROTAXY SYNDROME

F Sherman¹, M Wodrich², J Zampi¹, H McCaffery³, TG Saba¹
¹Department of Pediatrics, University of Michigan, Ann Arbor, MI
²University of Michigan School of Medicine, University of Michigan, Ann Arbor, MI
³Center for Human Growth and Development, University of Michigan, Ann Arbor, MI

Background: Primary ciliary dyskinesia (PCD) is an inherited disorder of impaired ciliary function characterized by chronic rhinosinusitis, bronchiectasis and situs abnormalities. An estimated 6-12% of patients with PCD have heterotaxy syndrome, defined as situs ambiguous and complex cardiovascular malformations (CVM). The incidence of ciliary impairment among patients with heterotaxy syndrome is not known although evidence supports that patients with heterotaxy have more post-operative respiratory complications. Cilia have been found to play a critical role in cardiogenesis. Objectives: This study explores the hypothesis that there is a greater incidence of ciliary impairment among patients with heterotaxy syndrome. Methods: Patients were identified by an electronic medical record search and divided into 4 groups: 1) situs ambiguous and a complex cardiovascular malformations; 2) situs ambiguous and a simple cardiovascular malformations; 3) situs solitus and a complex cardiovascular malformation; and 4) situs solitus and a simple cardiovascular malformation. Patients completed a questionnaire to evaluate their incidence of sino-pulmonary symptoms. Spirometry and nasal nitric oxide, an indirect marker of ciliary function, were measured for each patient. A combination of ANCOVA for continuous variables and logistic regression for binary variables was used to compare the groups. A spearman correlation was used to determine whether or not there is an association between respiratory symptoms and nasal nitric oxide result. Results: Mean nasal nitric oxide levels were significantly lower among subjects in groups 1 and 3, which included patients with complex CVM. There was no significant difference in respiratory symptoms or spirometry among the 4 groups. Conclusions: These results suggest that there is ciliary impairment among patients with complex CVM but not among those with situs abnormalities. However, this ciliary impairment was not severe enough to contribute to abnormal lung function or pulmonary symptoms.
INFLAMMATORY BOWEL DISEASE-UNCLASSIFIED, WHY ARE SOME GIVEN THIS AMBIGUOUS DIAGNOSIS?
R. Smith¹, S. Mar², J. Adler²³
¹Department of Pediatrics; ²Pediatric Gastroenterology; ³Susan B. Meister CHEAR Center, University of Michigan, Ann Arbor

Background: Inflammatory bowel disease (IBD) generally consists of either Crohn disease (CD) or ulcerative colitis (UC). Those with colitis who cannot be definitively classified, are called IBD-unclassified (IBD-U). Prevalence of IBD-U in pediatrics varies (5-15%) with significant rates of reclassification occurring later in the disease course. Most studies of IBD-U are either relatively small or in adult populations, and few explore the reasons for indeterminate diagnosis. We aimed to evaluate defining features of IBD-U in comparison to UC or CD to gain insights into this ambiguous diagnosis in a large, multi-center cohort.

Methods: The data were obtained from the ImproveCareNow (ICN) Network, a multicenter pediatric IBD quality improvement collaborative. The ICN registry consists of prospectively collected data for pediatric IBD patients from over 100 centers. We limited inclusion to patients enrolled after June 2012, and only those who were enrolled in ICN within 90 days of IBD diagnosis. Patients were categorized as CD, UC, or IBD-U by the provider. Baseline patient characteristics (gender, age at diagnosis, race, insurance status, height, weight velocities, body mass index (BMI) and extent of disease were compared for each group using Chi-squared analysis and Bonferroni significance adjustment.

Results: 9,298 patients meeting inclusion criteria: 5,787 (62%) with CD, 2,601 (30%) with UC, 838 (9%) with IBD-U (72 were excluded for missing diagnosis). IBD-U patients were younger than other patients with 24.8% of children with IBD-U diagnosed under the age of 10 compared to <17% of UC or CD (p<0.0001). Perianal involvement was documented in 29% of patients with IBD-U compared to 22% in CD (p<0.0001). Perianal involvement does not occur with UC. Upper tract involvement was noted in 29% of IBD-U patients.

Conclusions: Pediatric patients with colitis are more likely to be diagnosed with IBD-U if they are younger, have growth failure, upper tract findings and perianal findings. Better characterization of the presenting features of IBD-U may lead to improved diagnostic accuracy with important implications for treatment and counseling. Further research is necessary to determine if any of the significant differences might be able to predict reclassification into Crohn disease or ulcerative colitis in the future.
Abstract 92

DIABETIC KETOACIDOSIS WITH ALTERED MENTAL STATUS: IS IT ALWAYS CEREBRAL EDEMA?

Tim Visclosky a, Marisa Coury a, Joseph Kohne b, and Joseph Custer b
aUniversity of Michigan, Department of Pediatrics
bUniversity of Michigan, Department of Pediatric Critical Care Medicine

Background: Diabetic ketoacidosis (DKA) is characterized by severe insulin deficiency that results in hyperglycemia, ketosis, and acidosis. The role for head imaging in evaluation of such patients presenting with altered mental status is controversial. A recent study suggests head imaging does not change management and could delay therapy. We present a case of severe DKA who was found to have an unusual intracranial pathology. Imaging in this case was crucial for the diagnosis and management. Case: An 18-year-old male presented to the emergency department in severe DKA with minimal responsiveness. Initial blood chemistry was notable for blood glucose 802, pH 6.8, pCO2 24 mmHg, bicarbonate <10 mmol/L. In combination with an insulin infusion and fluid resuscitation, hyperosmolar therapy was started to treat suspected cerebral edema (CE). He remained unresponsive to painful stimuli, with intermittent pupil asymmetry. A non-contrast head CT demonstrated multiple bilateral intraparenchymal hematomas and a small subarachnoid hemorrhage without evidence of edema (Figure). His mental status gradually improved and he was ultimately discharged on hospital day 8 at his baseline level of cognition with no focal findings on neurologic examination. Discussion: This case underscores the role that select imaging can serve as an adjunct in the neurologic assessment of an obtunded pediatric patient in DKA. The most common and well defined neurologic sequelae is CE. However, thrombotic and hemorrhagic strokes should be considered. Differentiating these cases is difficult based on clinical features alone with the majority of cases of hemorrhagic and ischemic changes presenting with global neurologic dysfunction. This case is an example of the value of head imaging in the management of obtunded patients with DKA.

Abstract 93

POINT OF CARE ULTRASOUND IN AN ETHIOPIAN PEDIATRIC EMERGENCY DEPARTMENT: A NEEDS ASSESSMENT

J. White1, C. Wallace2

1Department of Pediatrics, and 2Department of Emergency Medicine, University of Michigan, Ann Arbor, MI

Background: Use of point of care ultrasound (POCUS) is expanding rapidly in pediatric emergency departments (EDs) in the United States. Though the World Health Organization first recommended use of ultrasound (US) in low and middle-income countries (LMIC) in 1985, its use has grown exponentially in the past decade as US technology has become more portable. Prior studies have explored the expansion of POCUS training to resource limited adult EDs. However, there is brevity of data regarding pediatric POCUS training in LMIC. Our objective was to evaluate the current state of US training and use in a resource-limited pediatric ED in Ethiopia. Methods: This was a survey-based study conducted at St Paul's Hospital Millennium Medical College (SPHMMC) in Addis Ababa, Ethiopia. Surveys were developed in conjunction with the departments of pediatrics and emergency medicine at the University of Michigan and distributed to 1st, 2nd, and 3rd year Ethiopian pediatric residents. Data was then analyzed using Microsoft Excel. Results: 27 pediatric residents at SPHMMC completed the survey. 63% were male and ages ranged from 23-32 years. On a global self-assessment of US knowledge, 80.8% of respondents had no knowledge or rated their knowledge as poor or very poor. Despite a perceived lack of knowledge, 60% of residents report using US at least a few times per month, and 24% use US daily. Areas which residents most frequently had prior training included use of the US machine (59.3%) focused assessment with sonography in trauma (FAST) (40.7%), US physics (29.6%), and obstetric US (29.6%). Zero residents reported prior training in US guided nerve blocks, estimation of cardiac ejection fraction, or testicular, musculoskeletal, pediatric abdominal, and airway US. Areas with one responder (3.7%) with any prior training include thyroid, aorta, ocular, soft tissue, gallbladder and hepatobiliary ultrasound. When surveyed on interest in further training, 96.3% reported being “extremely interested” in receiving further training in point of care ultrasound. Conclusion: Point of care ultrasound plays an important role in the routine care of pediatric patients in the resource limited country of Ethiopia. Residents have limited training and a perceived lack of knowledge but are extremely interested in learning to use the ultrasound. Next steps include further work on curriculum development, teaching methods, skills assessments and skill maintenance.
Abstract 94
TRANSCUTANEOUS BILIMETER USE BY NEWBORN HOME VISITING NURSES.
A. Wojciechowski, R. Pandit, L. Pavlek, S. Fried, M. Skoczylas,
Michigan Medicine Department of Pediatrics

Background: Jaundice remains a concern in the neonatal period, studies have shown that approximately 0.4-6.2% of healthy >35 week infants require phototherapy to treat jaundice.

Objectives: To evaluate the outcomes of transcutaneous bilimeter use by home visiting nurses for assessment of jaundice in newborn infants during the first week of life.

Methods: A database of newborns born between March 2017-June 2017 at the University of Michigan Mott Children’s Hospital was created. Only healthy newborns born at >35 weeks gestational age were included. Four Drager JM-105 transcutaneous bilimeters were obtained and distributed between 9 Michigan Visiting Nurses (MVN). The MVN group was divided into 2 groups, the first group used the bilimeter for the first 7 weeks of data collection, then the second group used the bilimeter for the second 7 weeks of data collection. When each group did not have a bilimeter, they used visual inspection to assess for jaundice. This was to help minimize bias. MVNs then collected transcutaneous bilirubin (TcB) measurements depending on clinical indication for monitoring and documented their findings in a prepared note phrase in the electronic medical record. Data was then gathered via chart review to assess for clinically relevant outcomes.

Results: Of the 1000 charts reviewed, 607 newborns had a MVN complete a home visit. Of these home visits, the MVN elected to screen 48 newborns using the transcutaneous bilimeter. The most common indication for screening was Clinical Jaundice on nursing assessment (48%). The average TcB reading was 11.1 mg/dl. There were a total of 4 clinic visits and 4 ED visits for hyperbilirubinemia that were a direct result of MVN TcB screening, which then resulted in 3 hospitalizations for phototherapy and 2 treated with outpatient phototherapy. There were a total of 3 clinic visits for jaundice as a direct result of MVN clinical exam, which then resulted in 0 hospitalizations for phototherapy or outpatient phototherapy.

Conclusion: Assessment of jaundice in term neonates by home visiting nurses using transcutaneous bilimeters identified 5 of 587 infants (0.85%) who needed phototherapy treatment for hyperbilirubinemia compared to 0 infants based on clinical exam alone.
**Abstract 95**

**EFFECT OF REQUIRED RAPID RESPONSE EVALUATION IN PEDIATRIC INTENSIVE CARE ADMISSIONS**  
Wummel, J.¹, Sorkin, T.²  
¹Departments of Internal Medicine and Pediatrics, University of Michigan, Ann Arbor, MI  
²Pediatric Critical Care Medicine, University of Michigan, Ann Arbor, MI

**Background:** Rapid response teams have become an integral part in evaluating a clinically deteriorating child in many hospitals. In 2017, a tertiary care children’s hospital made rapid response evaluation a requirement prior to transfer to the pediatric intensive care unit in an effort to improve timely ICU transfer and have multidisciplinary team evaluation to see if efforts could be made to keep the patient out of the ICU. This study was designed to evaluate this system on change in number of ICU transfers, number of RRTs and need for advanced care interventions.

**Methods:** This is a retrospective cohort, interrupted time series study. Patients were identified via data on rapid response calls and pediatric intensive care admissions obtained from hospital RRT/code logs and Virtual PICU Systems database, respectively. Data was collected from July 2016 and July 2018, one year before and after required RRT change. Electronic medical record chart review was used for supplemental information on patients including reason for admission, reason for transfer, patient outcome and need for advanced care interventions (advanced respiratory support, vasopressors, chest compressions, etc) both before and after RRT requirement.

**Results:** TBD

**Conclusions:** TBD
SEXUAL HARASSMENT DURING MEDICAL INTERNSHIP: A CLOSER LOOK AT GENDER REPRESENTATION & DEPRESSION

F. Obeid¹, E. Frank¹, S. Sen¹

¹Department of Psychiatry, University of Michigan, Ann Arbor, MI

Background: Due to the #MeToo movement, there has been a rise in attention on sexual harassment and how it may affect mental health. In the medical profession, sexual harassment is often under-reported, with specific factors of depression prevalence in medical interns not well understood. Considering the demographics of residential programs, specifically those with lower female representation of residents and faculty, is necessary in further understanding how sexual harassment experiences correlate with change in depressive symptoms. The main purpose of the study is: 1) to determine if lower female representation in residency programs correlate with higher occurrence of sexual harassment experience, and 2) determine whether higher occurrence of sexual harassment experience correlates with an increase in depressive symptoms.

Methods: Internal medicine interns (Response: 62.7%, 283/451) were given a baseline survey one to two months before internship, quarterly Patient Health Questionnaires (PHQ-9), and a sexual experiences questionnaire at the end of internship. The sexual experiences questionnaire scales for gender harassment, unwanted sexual attention, and sexual coercion. Female faculty and resident information collected from FREIDA and two hierarchical linear regressions were performed through SPSS to test the hypotheses.

Results: The following significant correlations were found: 1) among female interns, lower representation of female residents did correlate with an increase in gender harassment (P= 0.023), 2) among female interns, an increase in unwanted sexual attention did correlate with a decrease in depressive symptoms (P= 0.008) and 3) among male interns, an increase in gender harassment did correlate with an increase in depressive symptoms (P= 0.012).

Conclusions: Overall, our results support the association between lower female representation and greater occurrence of sexual harassment experiences. However, further research is necessary in understanding the correlation between occurrence of sexual harassment experiences and depression. Additional studies may take into consideration factors such as social support, mentorship, and intern compliancy.
Abstract 97

EFFECTS OF POSTOPERATIVE INFECTIONS, TREATMENT, & HEALTH SYSTEM PERSPECTIVES ON HIGHER CRC INCIDENCE IN BLACK PATIENTS

S. Shaker1,2, A. Berjaoui BA2,3, M. Ismail BA1,3, R. A. Blackwood MD PhD3,4.
1University of Michigan, College of Literature, Science, and the Arts
2University of Michigan Medical School
3Office for Health Equity and Inclusion
4University of Michigan, Department of Pediatrics

Background: Previous studies have shown that mortality rates in black patients undergoing resection are higher than their white counterparts. Despite both groups taking part in oncologic consultations, black patients were less likely to undergo chemotherapy treatment. This study explores how postoperative infections, treatment, and perspectives within the health system affect the mortality and morbidity rates of CRC patients. Socioeconomic, racial, and institutional factors are analyzed to determine their role in increasing CRC rates. Methods: Following IRB approval a retrospective chart review examining the socioeconomic and demographic variables was conducted. Patients between ages 30-85 diagnosed with CRC were reviewed. Quantitative and qualitative analysis was done using Excel and SPSS. Results: A total of 200 patients were reviewed. Preliminary analysis demonstrates an underrepresentation of African American patients within our health system based on study population and relative disease burden. African American patients tended to have more advanced disease burden at presentation and postoperative complications. Conclusion: There appears to be a lower appreciation of the consequences of CRC within the local African American population within the Michigan Health System. It is uncertain at this time, if the physician-patient communication barrier is patient or physician based, patient priority or failure to develop appropriate means of communication. However, a disparity in outcomes exists which negatively impacts the African American population.
UNDERSTANDING MATERNAL PERCEPTIONS OF TODDLER FOOD TANTRUMS
Lydia Thornburg1, Clare Lauer BA1,2, Abigail Allmacher3, and Megan Pesch1,2
1) Department of Pediatrics; 2) Center for Human Growth and Development; 3) School of Nursing, University of Michigan

Background. Food tantrums in early childhood are common and have been associated with later obesity. There is limited current research about the circumstances that may promote food tantrums in children, parental perception of food tantrums, or potential strategies to resolve food tantrums.

Objectives. 1) To examine themes of mothers’ perspectives of toddler food tantrums; and 2) to examine the correlation of participant characteristics with presence (vs. absence) of each theme.

Methods. Mothers of toddlers (N=35, mean child age 24 months) participated in a semi-structured interview about child feeding. Interviews were audio recorded, transcribed and coded reliably for themes identified. Illustrative quotes were identified. Mothers completed questionnaires. Anthropometrics were measured. Interviews are currently being coded for the presence/absence of each theme. Bivariate analyses will examine the correlation of participant characteristics with presence (vs. absence) of each theme.

Results: Six themes of child food tantrums emerged from the transcripts: 1) Perceived causes of a food tantrum; 2) Tantrum for food versus against eating food; 3) Children tantrum for a specific type of food; 4) Mother’s management techniques used to resolve a tantrum; 5) Mother’s emotions in response to a food tantrum; and 6) Mother’s established feeding rules/expectations.

Conclusions: Mothers reported that food tantrums were emotionally distressing for both themselves and their children. Management strategies such as distraction with devices or giving in to the tantrum were reported to be effective in the short-term but not long term. Future research should examine healthful strategies for mothers to help their children cope with food tantrums in the short and long term.
QUALITATIVE ANALYSIS OF ADOLESCENTS' PERSPECTIVES ON TAILORED MESSAGES AND IMAGES

T. Kowalski-Dobson1; J. Villegas1; C. Singer1; A. Gabowski1; J. Williams1; S.J. Woolford1

1Susan B. Meister Child Health Evaluation and Research Center, University of Michigan, Ann Arbor, MI.

Background: Black youth are more likely to live in communities with a high density of fast food restaurants (FFR) than Caucasian youth. To inform the development of a mobile app to help Black adolescents make healthy choices in FFRs, we conducted focus groups to explore adolescents' perspectives on tailored messages and images.

Methods: Focus groups (N=6) with Black adolescents (13-17 years old) with a BMI at or above the 85% were conducted in three cities in Michigan: Detroit, Flint, and Benton Harbor (N=38). Adolescents rated sample messages and images to be used in the app. A focus group guide addressed differences in message content/format (e.g., direct vs motivational interviewing (MI) tone). Groups were recorded and transcribed. Members of the study team independently coded the transcripts (line-by-line). Discrepancies were resolved by discussion. Data were entered into Microsoft Excel and common themes related to tailored content were identified across all focus groups.

Results: Most participants (66%) were female and the mean BMI was 34.8 (mean percentile was 96.2%). The participants preferred messages that provided the specific reasons why a suggested item was healthy (e.g., number of calories, portion sizes, recommended fruit/vegetable intake) rather than messages that merely suggested an item without this information. Participants equally liked both messages that used a direct and a MI tone. In regard to images, overall, adolescents preferred images that were diverse and had people their own age. More specifically, they liked images that showed people who were 1) displaying healthy behaviors, 2) enjoying making healthy choices, and 3) physically attractive. Of note, participants’ perceptions of attractiveness varied. Images where food did not look appealing or were perceived to be staged were disliked by most of the adolescents.

Conclusions: These findings suggest that among our study population, there was a consensus on using messages that were informative for making healthy decisions and included images of authentically happy healthy people. However, there were distinct differences regarding which people/food were attractive leading to the need for a greater degree of individual tailoring to meet the needs of the adolescents in the study. The pilot trial will test whether tailored messages and images, incorporating these findings, encourage Black adolescents to make healthy choices in FFRs.
NEW MEDICAL DEVICE PLACEMENT DURING PEDIATRIC SEVERE SEPSIS HOSPITALIZATION- A NATIONWIDE ESTIMATE

Erin Carlton1, John Donnelly2,3, Matt Hensley3, Hallie Prescott3,4

1Department of Pediatrics, University of Michigan
2Department of Learning Health Sciences, University of Michigan
3Department of Internal Medicine, University of Michigan
4VA Center for Clinical Management Research, Ann Arbor, MI

Background: Severe sepsis is a significant cause of health care utilization and morbidity among pediatric patients. However, little is known about the rate at which survivors develop new medical device dependence. Objective: We sought to determine the rate of surgical procedures resulting in device dependence, including tracheostomy, gastrostomy tube, hemodialysis catheter, vascular access device placements, ostomy procedures and amputation among children surviving hospitalizations for severe sepsis, and to determine whether procedural rates differ compared to survivors of all-cause pediatric hospitalizations. Methods: Using the Nationwide Readmissions Database (2014), we compared the rate and nationwide estimates of surgical procedures which occurred during pediatric severe sepsis hospitalizations to all-cause pediatric hospitalizations with live discharge. We also examined the difference in device placement during severe sepsis hospitalization in children with versus without pre-existing complex chronic conditions. Nationwide estimates of the rates of new device dependence placement during severe sepsis versus all-cause hospitalizations were compared using Rao-Scott corrected chi-square tests. Results: Among 3,954 eligible pediatric severe sepsis hospitalizations, 383 (9.7%) had new device dependence. Specifically, 137 (3.9%) had a new gastrostomy, 110 (2.9%) new tracheostomy, 88 (2.2%) new hemodialysis catheter, 63 (1.6%) new vascular access devices, 49 (1.3%) new ostomy, and 13 (0.3%) amputation. 1,119 (28.3%) severe sepsis survivors had no pre-existing complex chronic conditions. The rate of new device placement for these patients was just 1.3% versus 13.0% among patients with at least one pre-existing complex chronic condition, (p<0.001). After applying the NRD sampling weights, there were 12,640 pediatric severe sepsis hospitalizations and 1,646,914 all-cause hospitalizations with live discharge nationwide in 2014. Compared to all-cause pediatric hospitalizations, severe sepsis hospitalizations were 6-fold more likely to acquire new device dependence (10.6% vs. 1.7%, p<0.001). Conclusions: In this nationwide, all-payer cohort of US pediatric severe sepsis hospitalizations, one in ten children surviving severe sepsis experienced new device placement during sepsis hospitalization.
Abstract 101

OPIOID PRESCRIBING PATTERNS AND OPIOID OVERDOSE RISK IN ADOLESCENTS AND YOUNG ADULTS

K. Chua1, C. Brummett2, A. Bohnert3
1Child Health Evaluation and Research Center; 2Department of Anesthesiology; 3Department of Psychiatry, University of Michigan

Background: In older adults, opioid overdose risk increases with daily dose, concurrent benzodiazepine use, and extended-release/long-acting opioid use. The objective of this study was to assess whether these findings generalize to adolescents and young adults.

Methods: This was a retrospective cohort study of privately insured patients aged 12-21 years without cancer in the 2009-2015 IBM MarketScan Commercial Claims and Encounters database, a national sample of patients with employer-sponsored insurance. Prescription drug claims for opioids between July 1, 2009 and July 1, 2015 were converted to “person-days”, days on which opioid exposure would occur if opioids were taken as prescribed. For example, a drug claim on January 1 for a three-day supply of opioids was converted to three person-days (January 1-3). Person-days were the unit of analysis. The outcome was a claim with a diagnosis code for opioid overdose. Logistic regression with clustered standard errors at the patient level was used to model the outcome as a function of daily opioid dose category, concurrent benzodiazepine use, and extended-release/long-acting opioid use. Dose categories represented 20 morphine milligram equivalent (MME) increments up to 200 MME, 200-299, 300-399, 400-499, and ≥500 MME. Regressions controlled for demographic characteristics, year, prior opioid use, mental health conditions, substance use disorders, and other chronic conditions. Analyses were repeated among subgroups defined by prior opioid use status.

Results: The sample included 3,791,703 opioid prescription drug claims by 2,205,286 patients, corresponding to 17,797,906 person-days. During the study period, 213 patients (0.01%) had ≥1 overdose. In regressions, each increase in daily opioid dose category was associated with 7% higher odds of overdose (AOR: 1.07, 95% CI: 1.02-1.12). Compared to no use, concurrent benzodiazepine use was associated with 95% higher odds of overdose (AOR: 1.95, 95% CI: 1.35-2.82). Compared to no use, extended release/long-acting opioid use was not associated with significant differences in overdose risk in the overall sample (AOR: 1.59, 95% CI: 0.94-2.72), but was significantly associated with increased overdose risk in the absence of prior opioid use (AOR: 4.09, 95% CI: 1.73-9.66).

Conclusions: In adolescents and young adults, opioid overdose risk could potentially be mitigated by using the lowest effective daily dose, minimizing concurrent benzodiazepine use, and avoiding extended-release/long-acting agents among opioid-naïve patients.
Abstract 102

BEREAVED PARENT PERSPECTIVES ON END OF LIFE CARE FOR PEDIATRIC ONCOLOGY PATIENTS

L. Sedig1; J. Spruit1,2; T. Paul3; M. Cousino4; K. Pituch5; R. Hutchinson1

1Pediatric Hematology/Oncology/Bone Marrow Transplant, UM; 2School of Nursing, Wayne State Univ.; 3Pediatrics, Univ. Minnesota; 4Pediatric Psychology, UM; 5Pediatric Palliative Care Program, UM

Background: Approximately 1 in 5 children diagnosed with cancer will die of their disease, despite advances in treatment. While services such as palliative care are known to improve the experiences of children at the end of life, it is not clear what components of palliative care or similar end-of-life care are most beneficial. Objective: To identify what is most helpful, what is least helpful and what is lacking in end of life care from the perspective of bereaved parents. Methods: We convened focus groups of bereaved parents who lost their child to malignancy within the past seven years. A clinical psychologist guided discussion about their experiences at the end of their child’s life. Results: Two focus groups of six parents each met in June 2017. The parents were predominantly female (11 female, 1 male) and had lost their children an average of 2.8 years prior (range 1-5.3 years). Two parents were in the same family. Nearly all patients were offered palliative care (10/11), all were offered hospice and most died at home (9 at home, 2 in the ICU). Parent discussion uncovered six broad themes: beneficial provider qualities, optimal communication, helpful systematic supports, struggles to feel like a good parent, struggles with a loss of control and unmet needs. Parents appreciated providers who were consistent, reliable and honest. Parents desired communication that was sensitive to the needs of the patient and family with a balance of hope and realism. Parents appreciated the tangible supports provided by social work and the emotional support of child life both for the patient and their siblings. Some parents struggled to define and advocate for their child’s quality of life, especially when it led to disagreeing with the medical team. Several parents expressed frustration with unfamiliar caregivers in the hospital, especially trainees. They expressed a strong desire for more anticipatory guidance about the end of life including how to discuss it with their children. They also wished for a cancer-specific support group for bereaved parents. Conclusion: Bereaved parents of pediatric oncology patients in our focus groups appreciated consistent, reliable providers who communicated with a balance of realism and hope. They appreciated the tangible and emotional support they received and wanted more anticipatory guidance at the end of their child’s life. These results can help guide clinical care, especially in communities without strong palliative care support. Further research is needed to develop interventions to improve end of life care.
Abstract 103

ASSESSING RECEIPT OF PREVENTIVE CARE AMONG CHILDREN WITH SICKLE CELL ANEMIA USING ICD-10 DIAGNOSIS CODES

Reeves, SL1; Madden, B1; Miller, L2; Wu, M2; Anders, D2; Freed, GL1; Dombkowski, KJ1. 1Susan B. Meister Child Health Evaluation and Research Center, 2New York State Department of Health

Background: Sickle cell anemia (SCA) is associated with an increased risk for stroke and infection. Receipt of transcranial Doppler (TCD) screening to detect stroke risk and antibiotics to prevent infection significantly reduces the risk of these outcomes. Evaluating these preventive services using administrative claims has been hampered by ICD-9 coding limitations, which prevents accurate identification of the SCA subtype. Recently, a method to accurately identify SCA cases using ICD-10-CM diagnosis codes was developed and validated.


Methods: The study population consisted of children with SCA continuously enrolled in Michigan Medicaid in 2016 or 2017. Children with SCA were identified as those with ≥1 outpatient visit with a D571, D5700, D5701, or D5702 diagnosis code. This definition was validated using newborn screening records with a high degree of sensitivity (95%) and specificity (92%) for identifying cases of SCA. The annual proportion of children with SCA that received at least one TCD screening was calculated among children ages 2-16 years. The annual proportion of children receiving at least 300 days of dispensed antibiotic prophylaxis was calculated among children ages 0-5 years. The reliability of this method was evaluated using 2016-2017 New York Medicaid claims.

Results: A total of 699 children were eligible for TCD screening in Michigan Medicaid in 2016 or 2017. Rates of TCD screening were 38% in 2016 and 36% in 2017. Among 239 eligible children, 20% received antibiotic prophylaxis in 2016 and 8% in 2017. In New York Medicaid, TCD screening rates were 39% (2016) and 42% (2017) among 2,196 children; antibiotic prophylaxis rates were 18% (2016) and 19% (2017) among 714 children.

Conclusion: Rates of preventive care among children with SCA were found to be low in two large state Medicaid programs. Medicaid administrative claims can be used to monitor trends in preventive services use among children with SCA. Sustainable strategies to address gaps in quality of care among children with SCA are needed.
IDENTIFYING PERIANAL FISTULA COMPLICATIONS IN PEDIATRIC PATIENTS WITH CROHN’S DISEASE USING ADMINISTRATIVE CLAIMS

J Adler1,2, H Jary2, S Eder2, S Dong2, E Brandt1, K Dombkowski2
1Pediatric Gastroenterology, 2Susan B. Meister CHEAR Center, University of Michigan, Ann Arbor

Background: Although perianal fistulas occur commonly in pediatric Crohn’s disease (CD), evaluations of health services have been limited since no validated claims-based methods exist for identifying cases. We aimed to develop and validate accurate case definitions for perianal fistulas among pediatric patients with CD from administrative claims.

Methods: We developed and tested candidate case definitions for perianal fistula in a retrospective cohort study. Patients age 5-21 yr with CD enrolled in Michigan Medicaid with healthcare at University of Michigan 2005-2012 were identified via claims. Electronic Health Records (EHR) were obtained and abstracted. EHR evidence for perianal fistula was considered the “gold standard” against which candidate case definitions were compared. The reference case definition of perianal fistula (ICD9 565.1) and candidate case definitions were evaluated.

Results: 843 patients were identified via claims. Of these, 288 (34%) met inclusion criteria. The true perianal fistula rate among CD patients was 17% (n=48). The highest-performing candidate case definition identified 13% (n=37), had sensitivity 62.5%, specificity 97.1%, positive predictive value (PPV) 81.1%, and area under receiver operator characteristic curve (AUC) 0.80. In contrast, the reference case definition identified 9% (n=26), sensitivity 43.5%, specificity 98.6%, PPV 90.9%, and AUC 0.71.

Conclusions: We developed and validated accurate claims-based methods for identifying pediatric CD patients with perianal fistulas. These methods outperform those used previously with claims data and enable more accurate evaluations of health services utilization and comparative effectiveness studies of prevention and treatment strategies.
Abstract 105

COST-EFFECTIVENESS ANALYSIS OF NEWBORN SCREENING AND TREATMENT OF PHENYLKETONURIA

HF. Chen1; A.M. Rose2; L.A. Prosser1,2,3
1Department of Health Management and Policy, School of Public Health, University of Michigan; 2Susan B. Meister Child Health Evaluation and Research Center, University of Michigan; 3Department of Pediatrics, University of Michigan, Ann Arbor, MI.

Background: Phenylketonuria (PKU) is a rare metabolic disorder in which patients lack the ability to properly metabolize the amino acid phenylalanine (Phe) and was the first disorder to be screened for nationally. Given new data on adherence to recommended diet treatment and a newly available drug treatment option for some patients, sapropterin, the objective of this study was to evaluate the cost-effectiveness of newborn screening and treatment for PKU in the context of these developments. Methods: A computer simulation model for PKU patients was developed assuming a hypothetical cohort of newborns as the target population (n=4,000,000). The intervention, newborn screening (NBS) and treatment for PKU, was compared with clinical identification (CI) and treatment. Four strategies were compared: (1) NBS/diet treatment; (2) CI/diet treatment; (3) NBS/diet with medication (sapropterin); and (4) CI/diet with medication (sapropterin). Data sources included primary data from a survey of PKU patients and parents and secondary data from published literature supported by expert opinion. The primary outcomes included costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios. Analyses were conducted from the societal and health care sector perspectives using a lifetime time horizon. Sensitivity analyses explored robustness of results to changes in input assumptions. Results: Assuming partial diet adherence observed in recent studies, newborn screening strategies overall had higher costs and higher QALYs when compared to the clinical identification strategies. Costs increased significantly when sapropterin was added to diet treatment. When compared with CI/diet, NBS/diet had an incremental cost-effectiveness ratio of $7,000/QALY. When compared to NBS/diet, CI/diet with medication was dominated due to its significantly higher costs and fewer QALYs. Adding medication to NBS/diet resulted in an incremental cost-effectiveness ratio of more than $16,000,000/QALY. Uncertainty analysis did not yield different ranking results. Conclusions: Compared to clinical identification, newborn screening for PKU with diet treatment yields a cost-effectiveness ratio lower than many other recommended childhood prevention programs. Including medication treatment yields cost-effectiveness results that are unlikely to be considered to be within a favorable range. Future research should explore under what conditions the addition of sapropterin to diet treatment would be considered to be cost-effective.
THRESHOLD ANALYSIS OF TREATMENT EFFECTIVENESS FOR NEWBORN SCREENING FOR KRABBE DISEASE

E. Kim DeLuca1,2, A. Gebremariam2, J. Richardson1,3, A.M. Rose2, L.A. Prosser1,2,4

1Department of Health Management and Policy, School of Public Health, University of Michigan; 2Susan B. Meister Child Health Evaluation and Research Center, University of Michigan; 3RTI International, Research Triangle Park, NC; 4Department of Pediatrics and Communicable Diseases, University of Michigan, Ann Arbor, MI.

Background: Though the Secretary’s Advisory Committee for Heritable Disorders in Children and Newborns did not recommend adding Krabbe disease to the recommended uniform screening panel, New York State initiated newborn screening for Krabbe disease in 2006. The New York pilot program found that the incidence of Krabbe disease is lower than predicted, and the outcomes from treatment are worse than expected. A key area of uncertainty is the effectiveness of early diagnosis and treatment on health outcomes for Krabbe disease. The objective of this study was to estimate how effective early intervention (i.e. hematopoietic stem cell transplantation) would have to be to justify newborn screening for Krabbe disease from an economic or clinical perspective.

Methods: A decision analytic simulation model using hypothetical cohorts of newborns was developed to project lifetime outcomes of newborn screening for infantile-onset Krabbe disease compared to clinical identification. Both potential harms and benefits of screening were included in the model. Input parameters were derived from published and unpublished sources supplemented by expert opinion. The primary outcome was the incremental cost-effectiveness ratio (ICER) in dollars per quality-adjusted life years (QALYs) gained. Secondary outcomes were the number of deaths averted, QALYs, and net costs.

Results: In order to determine how effective early intervention must be to justify newborn screening for infantile-onset Krabbe disease, this study will estimate the ICER for a range of screening and treatment effectiveness values.

Conclusion: The health and economic outcomes evaluated from this study for infantile-onset Krabbe disease detected through newborn screening will provide information to decision makers considering the expansion of newborn screening programs.
Abstract 107

RELATIONSHIP BETWEEN SOCIAL INFLUENCES AND SUBSTANCE USE AMONG ARAB AMERICAN YOUTH

F. Bazzi¹, M. Ayyash¹, M. Nasrallah¹, A. Nasrallah², R.A. Blackwood³
¹University of Michigan Medical School, Ann Arbor, MI
²Department of Family Medicine, Beaumont Hospital, Wayne, MI
³Department of Pediatrics, Michigan Medicine, Ann Arbor, MI

Background: Research investigating substance use among Arab Americans is very limited to this point. Yet, substance use remains a taboo topic within Arab communities. Our research aims to investigate contributing factors to substance use within a young cohort of Arab Americans. In particular, to determine whether Arab American substance use is associated with similar social influences when compared with other ethnicities.

Methods: Following exempt determination by the IRB board at the University of Michigan, a survey was distributed throughout multiple community and social media outlets in Dearborn, MI. The survey targeted patterns of substance use among Arab American youth between the ages of 18-30. Inclusion criteria included age parameters and self-identification as Arab American. Categorical data was compared using chi-square testing.

Results: 423 participants, with mean age of 23.4. 40% of alcohol users reported a family history of mental or substance use disorder as compared to 26% in the non-user categories. All tobacco, alcohol, and other substance users had a statistically significant higher percentage of co-substance use by significant others and close friends as compared to the respective non-user categories. It was also demonstrated that previously accepted protective factors, such as higher educational attainment and Muslim religious affiliation were not significantly associated with active substance use within our cohort.

Conclusion: The social influences on young Arab-American substance use are complex. Some factors within our cohort differed from previous norms established within other ethnicities. Other factors that were highlighted, such as substance use as a means of stress coping present particular challenges to Arab Americans due to the seclusion of such practices in the setting of strong taboo. Such information can aid in the development of increasingly effective intervention programs, especially in adolescents.
DISPARITIES IN THE EMERGENCY CARE OF CHILDREN
A. Reardon¹, GL. Freed ¹,²
¹ University of Michigan School of Medicine; ² Child Health Evaluation and Research Unit, University of Michigan

Background: Variation in the care of children can have a negative impact on the process of care and/or outcomes. This review examined the current understanding of associations between patient race and ethnicity and the evaluation and management of children’s chief concerns in the emergency department. Methods: PubMed and Google Scholar databases were searched for peer-reviewed articles published between 01/01/2009 and 02/01/2019. Search terms used were ‘health, disparity, pediatric, pain’. Additional studies were identified from the references of selected articles. Results were limited to studies available in English and performed in the US. Results: The search yielded 72 articles. Of those, 10 studies evaluated whether patient race and ethnicity was associated with the evaluation and management of pediatric illness in the ED and are the focus of this analysis. One study of pediatric ED visits found non-Hispanic (NH) white race independently predicted receipt of higher-acuity triage scores among children with abdominal pain, asthma, or fever. Six other studies examined the treatment of pediatric pain. Three of these found that children of black NH and Hispanic race/ethnicity were less likely to be provided opioid analgesia within subgroups given the same diagnosis and overall. Two retrospective studies found NH white race was independently associated with higher rates of CT scans in children with abdominal pain. One study demonstrated the same effect associated with receipt of CBC, ECG and/or chest x-ray for children with chest pain. Two multi-center studies identified disparities in the management of infectious disease. In one, NH white children received more antibiotic prescriptions for diagnosed acute viral respiratory infections, and in another, symptomatic NH black adolescent females were significantly more likely to be tested for STIs. One trial attempted to delineate why white children received cranial CT at rates inappropriately high for their predicted risk of traumatic brain injury. In this study all treating physicians completed a structured case report form. Parental anxiety or request was cited as influencing physician to order CT scans in low risk patients significantly more frequently among white NH children. Conclusions: The recent literature suggests racial and ethnic disparities exist in the way emergency department clinicians evaluate and treat children with a variety of ailments. Future research should further examine the influence of nonclinical factors on clinical decision making. This may prove particularly important in the care of children in the emergency department due to the acuity of patients’ presentations and the time constraints clinicians in the ED often face due to overcrowding.
Abstract 109

CHALLENGES ON A LOCATION-BASED MHEALTH INTERVENTION

J. Villegas¹, T. Kowalski-Dobson¹, A.D. Kauffman¹, P. Brown², A. Grabowski¹, J. Williams¹, J. Moon², S. J. Woolford¹

¹Susan B. Meister Child Health Evaluation and Research Center, University of Michigan, Ann Arbor, MI; ²MEI Research Ltd., Edina, MN.

Background: Mobile applications enhance wellness interventions. Applications that depend on location for intervention delivery may experience challenges associated with functionality. This analysis hopes to share information learned while developing a smartphone program that uses technology to deliver tailored prompts to users upon entry into an eating venue to encourage them to make healthy choices.

Methods: Our application uses location services (including GPS, Bluetooth, Wi-Fi) to detect users’ locations relative to location coordinates in a database of known eating venues. The location radius was originally set to deliver a notification within 50 meters of an eating venue (entries measured at this distance, N=62) and later was restricted to 25 meters (N=62) of an eating venue. During testing we compared the coordinates of the location services marker (A) with the location of the user (B), see Figure 1. We then 1) recorded whether or not notifications were received on the users’ phones, 2) noted whether the notifications were received inside or outside of the eating venue, and 3) compared the variance of notification receipt at 50 meters compared to 25 meters.

Results: Overall, out of 124 tests, the location services tracking was accurate approximately two thirds of the time (67%,) with accuracy defined as whether the marker correctly indicated where the user was at the time of the test (i.e., the marker indicated the user was in a FFR and the user was actually there). During this test, users received notifications 82% of the time (total number of notifications received N=102). Using the 50-meter radius setting, 79% of notifications were received inside the FFR with the remainder received outside of the FFR. Whereas, using the 25-meter radius setting, 85% of notifications were received within the FFR vs outside of it.

Conclusion: Using location services for message delivery is a promising way to enhance health behavior interventions. However, limitations exist in regard to the ability of mobile phone technology to successfully detect a users’ exact location. Adjusting the geo-fence radius may reduce ‘false positives’ and avoid delivery of a message at a location that was not intended. Further work is required to explore factors that might impact accuracy.
Abstract 110
FLU VACCINE AS A FACILITATOR OF ADULT VACCINATION: THE COLLEGE FLU CHALLENGE
H. Jary1, K. Dombkowski1, S. Clark1
1Susan B. Meister Child Health Evaluation and Research Center, University of Michigan

Background: From 2014-2018, the Michigan Department of Health and Human Services (MDHHS) hosted the College and University Flu Vaccination Challenge (Flu Challenge), a friendly competition between schools to address the historically low flu vaccination rates among young adults. The objective of this study was to assess the extent to which the 2016-17 Flu Challenge facilitated receipt of other adult vaccines.

Methods: We used the Michigan Care Improvement Registry (MCIR) site table to identify 13 college health centers participating in the Flu Challenge; three participating colleges did not have unique site IDs for their health centers and were not included in the analysis. The Flu Challenge target population was identified as adults who received a flu vaccine from a participating college health center during the Flu Challenge (8/1/2016 – 3/31/2017). For each Flu Challenge target recipient, we acquired MCIR records for other vaccinations administered on the same or subsequent date, through 3/31/2017; we excluded any dose considered invalid, deleted, or duplicated, as well as doses of rabies or tuberculin. We summarized results stratified by vaccine type, administering site, and age.

Results: During the 2016-17 Flu Challenge, 15,077 adults received a flu vaccine; this included 62% aged 18-26 years, 27% aged 27-59, and 11% aged ≥60. Among adults receiving a flu vaccine from a participating college health center, 15% (2261) received another vaccine on the same or later day within the flu season. Same-day vaccinations were received by 9% (1411) of adults, ranging from 0.9% to 19.9% across sites; subsequent-day vaccinations were received by 8% (1130) of adults, ranging from 0.9% to 15.9% across sites. The most common vaccines administered on a same or subsequent date to the flu vaccine were Td/Tdap (25% of same-day, 19% of subsequent-day) and HPV (19% of same-day, 20% of subsequent-day). Two-thirds (66%) of vaccines administered later in the season were administered at college health centers, and 22% were administered at primary care sites. Conclusions: We found that the 2016-17 Flu Challenge facilitated receipt of other adult vaccines on the same or subsequent date to flu vaccination. The variation of additional vaccines received among adults at participating colleges demonstrates that the College Flu Challenge facilitates the administration of other types of adult vaccines. Results of this analysis can help immunization staff recognize promising strategies and best practices, and identify sites in need of technical support in order to maximize impact.
Abstract 111

MEDICAL RECORD VERSUS SELF-REPORTED
SOCIODEMOGRAPHIC INFORMATION

J. Samalik1, S. Eder2, I. Moncion1, E. Fredericks2,3, C. Goldberg4,
J. Adler1,2.

1Pediatric Gastroenterology, 2Susan B. Meister CHEAR Center,
3Pediatric Psychology, 4Pediatric Cardiology, University of
Michigan, Ann Arbor

Background: Racial and ethnic disparities are found broadly
within healthcare. Population-based studies into these disparit ies
commonly rely on the accuracy of sociodemographic information
recorded in the electronic health record (EHR). There is little
evidence about the accuracy of EHR data. The objective of this
study was to determine the accuracy of race and ethnicity data in
the UM EHR as compared to self-report.

Methods: We used patient/parent self-reported
sociodemographic data obtained prospectively from prior pediatric
gastroenterology (GI) studies. Sociodemographic information was
also abstracted from the corresponding EMR. We used
descriptive statistics for overall findings. Kappa statistic was used
to determine agreement between self-report and EHR data.

Results: 112 patients were identified (49% inflammatory bowel
disease, 19% liver transplant, 32% other GI condition). Race
agreement was substantial (Kappa 0.79, p<0.0001). Race did not
match among 7 (6%). Hispanic/Latino ethnicity had moderate
agreement (Kappa 0.66, p<0.001), but only 2 patients identified
as Hispanic/Latino in EHR, 1 self-reported white race, and the
other multiracial. Among those who self-identified as Middle
Eastern (N=8), 2 selected Asian while 4 selected white and 2
selected other. Data collection is still ongoing.

Conclusions: In this study, we found that within the UM EHR race
agreement was generally strong. There were some discrepancies
identified between the EHR and patient/parent reported ethnicity
and race. Accurate sociodemographic data are critically important
to identifying and understanding disparities that may impact
patient care and outcomes and to developing mitigation strategies
to improve healthcare disparities. This study supports the use of
EHR documented race. Larger multicenter studies are needed to
corroborate this finding.
Abstract 112

DEMOGRAPHIC COMPARISON BETWEEN VACCINATED AND UNVACCINATED POPULATIONS ACROSS MICHIGAN COUNTIES
S. Irani1, T. Hart-Johnson1, R. Blackwood1,2
1Office for Health Equity and Inclusion, 2Department of Infectious Diseases, C.S. Mott Children’s Hospital, University of Michigan

Background Despite the fact that inoculations have been proven as safe and effective in preventing countless diseases, many families choose not to vaccinate. Currently, Michigan has a rate of 4.2% unvaccinated amongst school children, one of the highest rates in the United States.

Objectives The primary aims of this study are to: (1) Determine any significant changes in vaccination coverage between 2016 and 2018 (2) Determine any correlations between demographic variables and vaccination coverages (3) Look into causes resulting in any trends

Methods The Michigan Department of Health & Human Services county report cards were used to gather vaccination coverages. This report measures coverage for vaccines administered at ages 19-35 months, 13-17 years, and adults (19 or older). The 2016 U.S. Census Bureau estimates measures such as population demographics, education levels, median household income, and percent of individuals/families below the poverty line. This study will investigate if there is a correlation between vaccination rates and income, education and race among other demographics.

Results Average percent coverage significantly increased for nearly all reported Michigan child, teen and adult vaccinations vaccines between 2016-2018 (p ≤ 0.001). Coverage for DTap, PCV and Flu (6mos-17 years) declined. As median household income and % high school graduation increased, % coverage for birth dose Hep B decreased (p ≤ 0.001). However as % of White individuals increased, % coverage for birth dose Hep B also increased (p ≤ 0.001). Differing trends were observed by vaccine, with all correlations being significant with p values ≤ 0.001.

Conclusion Differing correlations were found between county vaccination coverages and county demographics. This research on health disparities and vaccination rates within Michigan counties will be critical to overall state health. Due to current significant findings, further research analyzing which populations are vulnerable is recommended to help guide better solutions to combat low vaccine rates.
Abstract 113
(withdrawn)
Abstract 114

DECISIONAL AUTHORITY AND VALUES IN SHARED DECISION-MAKING: ARE THEY ENOUGH?
R Majumdar,1 H Yan,2 K Piltch,3 P Deldin,2 C Arslanian-Engoren,4 S Kukora3
1: University of Michigan, Ann Arbor, Michigan, 2: Department of Psychology, University of Michigan, Ann Arbor, Michigan, 3: Department of Pediatrics, University of Michigan, Ann Arbor, Michigan, 4: School of Nursing, University of Michigan, Ann Arbor, Michigan

Design: Shared decision-making (SDM) between physicians and parents is recommended for high-stakes, values-based medical decisions in critically ill pediatric patients. Policy Statements on SDM encourage physicians to identify parents' desired level of decisional authority and personal values to support decisions with the appropriate medical recommendations based on parents' values. To identify whether aligning physician recommendations with parents' desired level of decisional authority and self-reported values prioritizing quality of life (QOL) vs length of life (LOL) impacts decisions.

Method: Parents were electronically surveyed regarding a hypothetical scenario in which they have a critically ill child and must decide whether to pursue a tracheostomy. Before exposure to the case, participants indicated whether they prioritized QOL or LOL, as well as their preference for decisional authority: assume the decision themselves, share it with physicians, or defer it to physicians. They were then assigned to one of 9 decision scenarios based on these responses. Participants were matched to a vignette aligning the provided physician recommendation with their preferred level of decisional authority, but were randomized to whether this recommendation matched their reported values.

Results: 1763 participants completed the survey. The majority expressed preferences for shared decisional authority with parents responsible for the ultimate decision; most indicated values prioritizing QOL. Though a higher percentage of participants who prioritized QOL chose comfort care than those who prioritized LOL, more than one-third of both groups were unable to decide. Of participants given recommendations counter to their reported values prioritization, 39.3% chose the option recommended by the physician. Even when given a physician recommendation aligning with their stated values, 10.6% made choices opposing the values and recommendation. Receiving a recommendation consistent with reported values did not reduce indecisiveness for participants.

Conclusion: Physician recommendations influenced decisions when inconsistent with parental values. Even when recommendations were consistent with reported values, participants did not universally choose the option aligning with their values/the recommendation. Further research on SDM approaches in clinical care is warranted.
Abstract 115

COMPLIANCE WITH EMERGENCY ROOM REFERRALS DIFFERS BY GENDER, INSURANCE TYPE, AND REFERRAL DEPARTMENT

BA Palleiko¹, JV Lynn², A Achkar¹, T Hart-Johnson, M Perry³, RA Blackwood¹

¹Office For Health Equity and Inclusion, University of Michigan
²University of Michigan Medical School
³University of Michigan Department of Emergency Medicine

Background: Outpatient referrals constitute a critical component of emergency medical care. However, barriers to care following emergency room (ER) visits have not been thoroughly investigated. The purpose of this study is to determine the impact of sociodemographic variables on referral compliance following ER visits.

Methods: A retrospective, non-interventional QA/QI study was designed and determined “Not Regulated” by University of Michigan Medical Institutional Review Board. Patients age 0-17 who visited the C.S. Mott Children’s Hospital ER in 2016 and received a referral were included. Multiple referrals for one patient were counted as independent encounters for statistical analysis.

Results: Chart review was performed on 6,120 pediatric emergency room encounters, of which 811 culminated with referral for outpatient follow-up within Michigan Medicine. A total of 853 referrals were placed. Thirty-one referrals were excluded giving a total of 822 referrals included in analysis. Referral attendance did not significantly differ by race, ethnicity, language, religion, or age. Black females (p=0.015), beneficiaries of medicaid (p=0.004), or patients referred to neurology (p=0.012) demonstrated significantly decreased attendance rates.

Conclusions: This study provides an overview of the impact of sociodemographic factors on attendance at outpatient follow-up referrals. Patients who are female or Medicaid beneficiaries experience significantly lower attendance at referral appointments. Informed resource allocation may be utilized to improve care for these at-risk patient populations. Further work should be done to further investigate why these groups are less likely to attend referrals and what can be done to improve patient compliance with ER referrals.
IMPLEMENTING INFANT DRIVEN FEEDING PRACTICES ON TWO MEDICAL UNITS LEADS TO A DECREASE IN LENGTH OF STAY

S. Crane¹, C. Rothermel¹, K. Monroe¹, R. Pehovic¹, M. Cox¹, D. Roberts¹, S. Meyer, R. Pehovic, M. Andersen¹
¹University of Michigan, C. S. Mott Children’s Hospital, Ann Arbor, MI

Background: Premature infants on 12E and 11W have traditionally been fed on provider-driven feeding (PDF) schedules, predicated upon the patient taking a set volume every three hours (orally, via an enteral tube, or a combination of both). This practice, focused on quantity consumed, ignores behavioral cues for feeding readiness and reduces feeding to a scheduled task, rather than a pleasurable and developmentally appropriate experience. Current literature provides compelling, evidence-based support for infant-driven feeding (IDF) protocols, in which infants are scored for readiness to feed and allowed to eat when demonstrating associated behavioral cues. Infants fed in this manner have been shown to achieve full oral feeds sooner, experience fewer feeding-associated adverse events, and have a shorter length of stay than those on a PDF schedule. IDF encourages skilled nursing judgment and also provides an excellent opportunity to empower parents by teaching them how to identify their child’s feeding cues and make feeding a nurturing, positive experience. **Methods:** We developed IDF protocols for preterm infants and those with cardiac defects. Implementation of IDFs started in July 2017 on 12E and November 2018 on 11W. This was done through a variety of actions, including: nursing education (one on one, small group, posters), resident education (house officer lunch, just in time education during rounds), hospitalist education (journal club topic, education on the protocol), review of process at DMS huddles, identification of infants on DMS board, and process and outcome measures shared on DMS board for audit and feedback loop. **Results:** Infants fed utilizing the IDF Protocol had a decrease in length of stay by four days compared to infants fed utilizing PDF. Infants fed with IDF achieved 100% PO intake 1-day sooner. (Will have 11W preliminary data by May). **Conclusion:** Implementation of infant-driven feeding practices has consistently led to a decrease in length of stay and time to full PO feeds.
Abstract 117

AN INTEGRATED CARE APPROACH TO IMPROVING QUALITY OF ADHD CARE IN GENERAL PEDIATRICS

B. Lancaster1, K. Orringer2, A. Cook1, B. Felt3, D. Hanauer2, R. Thompson4, G. Koehn3, R. Birnbaum1, M. Koval1, & B. Griffor1

1Pediatric Psychology, 2General Pediatrics, 3Developmental Behavioral Pediatrics, Michigan Medicine; 4Thriving Minds, Chelsea MI

Background: ADHD is the most common behavioral health problem in primary care and the second most expensive pediatric healthcare expenditure. Current American Academy of Pediatrics (AAP) guidelines for ADHD care recommend objective measures across multiple settings be used as part of the diagnostic assessment and behavior therapy be delivered to all children diagnosed with ADHD. Unfortunately, most patients do not receive evidence-based (EB) care for ADHD at the national and state-level. The purpose of the ongoing initiative is to evaluate and improve ADHD assessment and treatment practices in the four General Pediatric clinics with Integrated Behavioral Health (IBH) services.

Methods: An interdisciplinary ADHD task force was established to train pediatricians in EB care for ADHD, use of resources created in EPIC to promote efficient documentation for providers and education for patients, and proposed clinic workflow changes to leverage clinic psychologists and MAs to reduce burden on pediatricians. Medical records were reviewed for all patients with new ADHD diagnoses during the 14 months of baseline for each clinic and post-training for one clinic (A). A knowledge assessment (pre/post) and satisfaction survey (repeated post) were completed by pediatricians. All four clinics will receive training by the end of 2019.

Results: Of the 137 children diagnosed with ADHD during baseline in all four clinics, 31% completed objective measures from home and school, and behavior therapy was suggested for 36% of patients. Pediatricians in Clinic A showed improved knowledge of EB practices for ADHD post-training, whereas satisfaction feedback has been mixed. They were much more likely (29% vs. 64%) to use an unspecified (F90.9) ADHD diagnosis and have not prescribed medication to these patients (28% vs. 0%) post-training. For all other ADHD diagnoses, pediatricians were more likely to objective measures (36% vs. 50%), less likely to prescribe medication (78% vs. 75%), and less likely to recommend behavior therapy (51% vs. 25%).

Conclusions: Similar to state and national data, the quality of care for ADHD at UM falls below best practice standards. A QI initiative, currently underway, has shown some promise for improving care at the one clinic provided intervention, though several challenges have presented during its implementation. Additional data is needed to draw conclusions. Up-to-date data and changes to the initiative will be discussed.
ESTABLISHING A LEARNING HEALTH SYSTEM FOR CHILDHOOD OBESITY AT MICHIGAN MEDICINE

J.M. Lee1,2, K.E. Peterson3, K. Orringer1,4, K. Dombkowski1,4, E. Dhadphale1, A. Garrity1,2, C. Runge1, V. Gavrila1
1Susan B. Meister Child Health Evaluation and Research Center; 2Division of Pediatric Endocrinology, Michigan Medicine; 3Department of Nutritional Sciences, University of Michigan School of Public Health; 4Department of Pediatrics, Michigan Medicine.

Background: Over 30% of children in Michigan are overweight or obese – making it the most common chronic condition in childhood. There are numerous barriers to addressing this epidemic, including the lack of an ongoing surveillance system, the lack of a reliable system-wide approach and missed opportunities for collaborative learning. Methods: We are creating a Learning Health System (LHS) focused on childhood overweight and obesity at Michigan Medicine (MM), for which there are three priority activities: Results: Quality Improvement: We have assembled a local leadership team. Key accomplishments include: 1) Developed a key driver diagram and outcome measures for childhood overweight and obesity. 2) Engaged the UM Pediatric Preventative Quality Improvement Committee to include identification of overweight/obesity as a key metric 3) Convened subspecialists and pediatricians to determine universal screening guidelines for comorbidities among overweight/obese children that will be deployed using clinical decision support in the electronic medical record (EMR). Health IT/Informatics: Using data from the MM EMR’s Clarity database, we measured processes and outcomes for 8,000 overweight/obese patients between 2 and 17 years old seen at MM General Pediatrics clinics in 2018. Overall, 14.3% were overweight and 12.6% were obese, with a disproportionate burden in the African American and Hispanic populations. Only 5% of overweight children and 8% of obese children had abnormal BMI percentile flagged on their problem list and only a subset of children had tests ordered and completed for screening for comorbidities including diabetes, nonalcoholic fatty liver disease, and hypercholesterolemia. Collaborative Engagement: We are engaging with other stakeholders (e.g. pediatricians, dietitians, community stakeholders, and obesity researchers) to support the creation of nutrition behavior interventions and opportunities for cross-talk on real-world clinical issues and future translational research. Conclusion: These data confirm that childhood obesity is a pressing problem locally, which a LHS could address. We see great opportunity in bringing this model to childhood overweight and obesity and believe that this approach will be transformative for tackling the silos of clinical care delivery, quality improvement, and research.
Abstract 119

DELIRIUM IN A PEDIATRIC INTENSIVE CARE UNIT AND A NONPHARMACOLOGIC BUNDLE TO REDUCE DELIRIUM
Jeffrey Weatherhead¹, Matthew Niedner¹, Nasuh Malas¹, Toni Owens¹, Yu Kawai²
¹ Michigan Medicine, University of Michigan, Ann Arbor, MI, ² Mayo Clinic, Rochester, Minnesota

Background: Pediatric delirium is a common, often under recognized condition in the Pediatric Intensive Care Unit (PICU). Delirium can lead to increased length of stay, increased costs, posttraumatic symptoms and higher mortality rates. The objective of this study was to evaluate the prevalence of delirium in our quaternary PICU and to analyze the effect of a non-pharmacologic bundle to decrease the prevalence of delirium in the PICU. Methods: Patients were screened for delirium using the validated Cornell Assessment of Pediatric Delirium (CAPD) screening tool every 12 hours. CAPD scores of ≥ 9 are considered at risk for delirium. Nursing compliance with the screening tool as well as prevalence of CAPD scores ≥ 9 were recorded. Additionally, a non-pharmacologic bundle to eliminate delirium (B.E.D.) was piloted and implemented unit wide and nursing compliance with the bundle was recorded. Over a 16-month period (05/2015 – 08/2016) the data was analyzed and compiled into a “Pre-B.E.D. Pilot” phase, “Pilot” phase, “Early Post Pilot” phase “Late Post Pilot” phase. Results: During the “Pre Pilot” phase nursing CAPD compliance was 67.3% (night) and 71.7% (day). Compliance increased during the “Pilot” phase to 81.6% (night) and 77.4% (day). Compliance remained at 80.5% (Night) and 80.5% (day) during the “Early Post Pilot” phase. However, during the “Late Post Pilot” phase compliance fell to 70.2% at night and 73.9% during the day. Patients at risk for delirium (CAPD ≥ 9) were 32.2% (night) and 71.7% (day). Compliance increased during the “Pilot” phase to 81.6% (night) and 77.4% (day). Compliance remained at 80.5% (Night) and 80.5% (day) during the “Early Post Pilot” phase. However, during the “Late Post Pilot” phase compliance fell to 70.2% at night and 73.9% during the day. Patients at risk for delirium (CAPD ≥ 9) were 32.2% during the “Pre-Pilot” phase and 35.3% during the “Pilot” phase. During the “Early Post Pilot” phase, patients at risk for delirium fell to 29.6%. However, during the “Late Post Pilot” phase CAPD prevalence increased to 32.2%. Nursing compliance with the B.E.D. started off around 55% after the pilot phase and decreased by approximately 5% each week over the ensuing 2 months until compliance was essentially 0%. Conclusion: The prevalence of patients at risk for delirium was slightly higher in our PICU than the national average of 25%. Nursing compliance with the CAPD was impressive at about 75% on average for the 16-month period. We also noted a correlation with CAPD scores and B.E.D. compliance during the post pilot phase. As B.E.D. compliance fell, patients at risk for delirium (CAPD ≥ 9) returned back to Pre-Pilot baseline demonstrating that the B.E.D. may have a positive effect on reducing delirium in the PICU.
Abstract 120
DIABETES BARRIER ASSESSMENT QUESTIONNAIRE TO IMPROVE GLUCOSE MONITORING IN HIGH-RISK TYPE I DIABETES MELLITUS PATIENTS

E. Chang1; A. Garrity1; D. Albright2; B. Carey1; J. Florek1; I. Thomas1; J. Lee1

1Department of Pediatric Endocrinology, University of Michigan; 2Department of Pediatric Psychology, University of Michigan

Background: Type I diabetes mellitus is a chronic medical disease that causes hyperglycemia due to insulin deficiency. Maintaining good glycemic control is crucial in avoiding microvascular and macrovascular complications. At the same time, it is important to minimize the risk of hypoglycemia. The current American Diabetes Association guideline is to monitor gluoses at least 4 times per day with a goal Hemoglobin A1c (HbA1c) of <7.5% in pediatric patients. There is evidence of a strong association between increase frequency of self-monitoring of blood gluoses and lower HbA1c. However, less than 50% of individuals are achieving the recommended frequency of glucose monitoring. There is a need to develop support and solutions to improve self-monitoring of blood glucose in these high-risk individuals. Individualized goal-setting and problem-solving interventions have been shown to be effective to improve diabetes care behaviors.

Methods: A barriers questionnaire was iteratively developed with feedback from the diabetes team as well as patients and caregivers. The tool was provided to high-risk diabetes patients, who were identified as having an average daily glucose check of less than 4 times per day. After the questionnaire was provided, a goal was selected with the patient and documented. At the follow up clinic visit, the effectiveness of the goal was assessed objectively by any changes in the daily average glucose checks and HbA1c.

Results: To date, the barriers assessment has been administered to 34 patients. The average HbA1c at baseline for these patients was 10.9% and the average number of daily glucose checks was 2.3. The top barriers to self-monitoring of blood glucose were “I forget to check” and “I’m too busy with other activities to check.” Since this intervention was recently introduced, we are still gathering follow up data from the patients' quarterly visits.

Conclusions: This quality improvement project is still in its early phase. From the data that has been gathered, we were able to identify the most common barriers to adequate glucose monitoring which is consistent with other studies in the past. The administration of the barrier assessment and goals may be a helpful tool to foster discussion between the patient, family members, and the providers.
Abstract 121

TIMELINESS OF CLEFT LIP AND PALATE REPAIR: IMPACT OF SOCIODEMOGRAPHIC FACTORS
JV Lynn1, K Ranganathan2, MH Bageris3, H Tursak3, BA Palleiko3, T Hart-Johnson3, SR Buchman2, RA Blackwood3

1University of Michigan Medical School
2Section of Plastic Surgery, University of Michigan
3Office for Health Equity and Inclusion, University of Michigan

Background: The timing of surgical cleft lip and/or palate repair impacts long-term patient outcomes, yet clinically accessible predictors of delayed intervention remain ill-defined. We hypothesize that age at which patients reach interventional milestones, mainly cleft lip repair and cleft palate repair, vary based on sociodemographic factors.

Objective: to identify the impact of sociodemographic and health care variables on the age at which patients undergo cleft lip repair and/or cleft palate repair, to enable multidisciplinary teams to support at-risk individuals via efficient resource allocation.

Method: A retrospective, non-interventional quality assessment quality improvement (QA/QI) study was designed. The study was determined “Not Regulated” by the University of Michigan IRB. All patients born between 2012 and 2014 (3 years) who received surgical cleft repair at Michigan Medicine were included. Adopted patients were excluded. Sociodemographic and care variables were collected.

Results: One-hundred twenty-two individuals were included. Female patients accounted for over half the population (59%). Approximately three-quarters of patients identified as white (76%) with the remaining twenty-nine patients identifying as black, Asian, or Other. Fifty-two patients indicated a religious affiliation (43%) and twenty-three reported unstable social history (19%). Over half of patients were Medicaid beneficiaries (61%). Diagnoses included cleft lip only (n=20; 16%), cleft palate only (n=44; 36%), and cleft lip plus cleft palate (n=58; 48%). Average age at cleft lip repair and cleft palate repair was 27-weeks (median 22=weeks) and 64-weeks (median 59=weeks), respectively.

Conclusions: These data provide an initial overview of the patient population affected by cleft lip and/or palate which receives care at the University of Michigan C. S. Mott Children’s Hospital. Statistical analysis via hierarchical linear regression will be performed to delineate the impact of each sociodemographic variable on timeliness of surgical cleft repair while controlling for confounding factors. Results will be utilized to facilitate more efficient allocation of resources among patients affected by cleft lip and/or palate.
DIFFERING EXPERIENCES WITH BREASTFEEDING IN RESIDENCY BETWEEN MOTHERS AND CO-RESIDENTS

E. Ames¹, S. Tomlinson², and H. Burrows¹
¹Pediatrics, University of Michigan; ²Emergency Medicine, University of Michigan, Ann Arbor, MI.

Background: Returning to work and lack of support for expressing breastmilk (pumping) at work is often cited as a reason that mothers discontinue breastfeeding, particularly among female physicians. It is unclear how these perceived difficulties affect resident mothers and how resident teams perceive co-residents who choose to pump at work. The goal of this study was to identify differences in perception of resident mothers and their co-residents about breastfeeding residents pumping.

Methods: An online survey in 2017 was sent to 413 residents in Pediatrics, Internal Medicine, Family Medicine, and Anesthesia at the University of Michigan Health System.

Results: A total of 82 residents completed the survey (20% response rate). Resident mothers (15% of respondents self-identified as a mother) were asked specific questions regarding their experiences with breastfeeding. Almost all mothers (92%) encountered difficulty breastfeeding after returning to work. The majority of mothers reported that their mood was affected by these difficulties (85%). The most common challenge that breastfeeding residents encountered was not enough time to pump. The majority of all residents surveyed (74%) have worked with a breastfeeding resident. Forty percent of breastfeeding residents felt that their pumping adversely affected the team, while only 10% of co-residents felt the same.

Conclusions: Breastfeeding residents encountered significant difficulties that affected their well-being when breastfeeding while returning to work. They also felt that their pumping can be detrimental to their job. However, their co-residents felt that pumping had no major setbacks to team efficiency or patient care and did not create additional work.
Abstract 123

IMPROVING SOCIAL DETERMINANTS OF HEALTH BY STRENGTHENING MEDICAL-LEGAL PARTNERSHIPS: THE PROMISE OF THE ADVOCACY LETTER PROJECT (ALP)

Background: Inevitably, medical problems intersect with patients' social and legal conditions. While medical providers may screen for these social determinants of health, they often lack the time, knowledge, tools and agency to play an active role in advocating for their patients. Currently, the University of Michigan's medical-legal partnership with the Law School's Pediatric Advocacy Clinic (PAC) allows providers to refer low-income patients with legal needs to lawyers and law students for consultation. The PAC has very limited capacity and, anecdotally, a significant proportion of patients who would benefit fall through the cracks. Our purpose is to characterize the types of unmet legal needs and understand which patients we are failing to care for in order to ultimately design advocacy template letters to allow high throughput legal consultation in our clinics. Methods: Our multidisciplinary team consists of physicians, lawyers, and law students who sent out an initial survey to the Briarwood Clinic providers (n=11) to identify common medical-legal issues and understand the potential significance of an intervention. Results: Initial needs assessment showed that 73% of providers encounter patients struggling with legal problems that negatively impact their health at least 2-6 times per week. 100% of providers report that these hardships would be solved with legal advocacy. 82% of providers somewhat/strongly agree that having pre-written letters for medical-legal issues would be useful for patients. 90% of providers somewhat/strongly agree that having pre-written advocacy letters for medical legal issues would improve efficiency for providers. Conclusions: Clearly, medical providers often struggle to identify and intervene on legal issues affecting their patients' health. As a part of larger efforts to synergize Michigan Medicine and the Law School's efforts to improve social determinants of health, the ALP plans to strengthen existing medical-legal partnerships and make patient advocacy letters easily accessible. We will present workshops to providers and integrate template advocacy letters with our EMRs to improve the capacity of physicians to better address their patients' needs. The next step is broadening access to and utilization of these letter templates in our community. This is a part of a larger effort to strengthen the Medical Legal Partnerships between Michigan Medicine and the University of Michigan Law School by jointly addressing social determinants of health.
Abstract 124

EVALUATION OF AN INTERNAL MEDICINE INTERN WELLNESS CURRICULUM
J. Barrett¹, R. Perlman¹
¹ Department of Internal Medicine, University of Michigan

Background: Physician burnout is a hot topic in medical education, and residency programs have responded with various initiatives about resident wellness. However, these programs are seldom evaluated.

Methods: Internal medicine interns were surveyed at the end of a monthly wellness session with three statements related to the utility and enjoyment of the session. The statements were assessed by a Likert scale on agreeability. The sessions covered topics such as gratitude, forgiveness/making mistakes, awe/wonder in medicine, humor, and privilege/ableism. Six of the sessions had a “narrative medicine” theme.

Results: In process. Thus far, >95% agree or strongly agree with the following 3 statements: “attending this session was a good use of my time” “our program should continue to have sessions on resident wellness” and “I would recommend attending wellness report to my co-interns.”

Conclusions: The Internal Medicine intern wellness curriculum has been well-received by their intended audience.
Abstract 125
TAKING THE STAGE: A CASE-BASED CONFERENCE CURRICULUM FOR RESIDENTS
Elise Gross, MD, Marie Pfarr, MD, Kayla B. Phelps, MD, MPH, Heather Burrows, MD, PhD, David A. Stewart, MD, University of Michigan, Ann Arbor, MI

Background: Case-based conferences provide an interactive setting for resident physicians to develop skills in oral presentations, diagnostic evaluation, and patient management. Residents find these conferences highly valuable to their education. In the last two years, our pediatric residency curriculum included 906 didactic conferences, and 209 (23%) were case-based. Only 21 (10%) of these case-based conferences were facilitated by residents.

Objectives: We aimed to evaluate residents’ experiences and perceptions with case-based conferences to help us improve our curriculum.

Methods: An anonymous 9 question web-based survey was sent to all pediatric residents in October 2018. Residents were asked to rate their perceptions of and experience with case-based conferences (a conference that centers around a clinical case and includes discussions pertaining to the presentation, diagnosis, workup, and/or management).

Results: Of the 58 respondents (56% response rate), 97% felt that case-based conferences were either important/very important for resident education, and 80% felt that it is important/very important for residents to lead these conferences. 40% were dissatisfied with the frequency of case-based conferences currently offered, and 62% of respondents felt that there are too few opportunities for residents to lead these conferences. 50% of respondents indicated that they were "not at all" or only "slightly" comfortable in leading or helping to lead a case-based conference. Only 19% of our pediatric seniors have led or helped to lead a case-based conference.

Conclusions: Pediatric residents place high educational value in facilitating and learning from case-based conferences, but our current curriculum does not provide enough opportunity to do so. We have implemented curricular changes to provide more of these opportunities, including bimonthly inpatient case presentations, senior-led intern-only morning reports, and co-facilitation of chief resident morning reports. We plan to re-survey current residents in June 2019 to assess the effectiveness of these interventions.
Background: Historically, our institution has not had a resident orientation for the Children’s Emergency Services (CES) rotation. Published data supports simulation-based orientations for new trainees. Our group previously surveyed the pediatric and medicine-pediatric (MP) residents and found that a majority of junior residents near the end of the academic year lacked confidence in independent decision-making and initial patient stabilization in CES.

Objectives: To create a CES orientation curriculum and assess its ability to improve self-confidence in independent decision-making and patient stabilization among participating interns.

Methods: This was a two-part study performed across two years. A one-hour orientation session was designed employing high fidelity simulation mannequins and utilizing near-peer teaching by senior residents with assistance from CES faculty. In the pilot year, interns were randomized to control (standard orientation) or intervention (simulation orientation) group. Pre- and post-rotation surveys focusing on self-confidence in independent decision-making and stabilization of unstable patients were completed using internet-based (Qualtrics), 5-point Likert scales. In the second year, all interns were included in the orientation and surveyed.

Results: In the first year, 7/13 interns in the intervention and 10/15 in the control group completed surveys. There was a significant increase in self-reported confidence in independent decision making (p=0.01) and preparedness to assess and stabilize unstable patients (p=0.03) in the intervention group. Such differences were not significant in the control group. In the second year, 14/21 participating interns completed both surveys. Paired t-tests of their linked responses revealed similar significant increases in confidence in independent decision making (mean increase 0.6, p=0.01) as well as self-reported preparedness to assess and stabilize unstable patients (mean increase 0.6, p=0.02).

Conclusions: Creation and implementation of a high-fidelity simulation-based orientation curriculum demonstrated durable improvement in self-reported confidence and preparedness during interns’ first rotations in CES. Future directions can look at implementing similar curricula to improve resident experience on other rotations.
Abstract 127

RESIDENT PREPAREDNESS FOR MANAGING ONLINE SAFETY AND CYBERBULLYING IN THE PRIMARY CARE SETTING

V. B. Jayasundera¹; R. Pandit²; E. Selkie³;

¹Department of Pediatrics, University of Michigan, Ann Arbor, MI
²Pediatrics, Yakima Valley Farm Workers Clinic, Woodburn, OR
³Division of Adolescent Medicine, Department of Pediatrics, University of Michigan, Ann Arbor, MI

Background: Cyberbullying is a growing public health concern within the United States and amongst adolescents has been associated with physical and mental health issues, including pain, anxiety, depression, and suicidal ideation. These findings suggest there are additional opportunities to screen for online safety and cyberbullying, including in the primary care setting. Identifying adolescents experiencing cyberbullying through routine screening and then offering resources or support within the office or community has the potential to mitigate the effects of cyberbullying which include both physical and mental health consequences. Here we aim to assess pediatric resident preparedness for screening for cyberbullying in the primary care setting.

Methods: Michigan Medicine categorical pediatric and combined medicine-pediatric residents were emailed a Qualtrics survey assessing their frequency of screening for cyberbullying, comfort level with cyberbullying screening and perceived barriers to discussing online safety in the primary care setting. All responses were anonymous though information regarding the respondent’s post-graduate year and primary care continuity site was requested.

Results: A total of 33 residents from six Michigan Medicine Pediatric Primary Care sites responded (34% response rate). Of the 33 respondents, 24% were in their PGY 1 year of training, 45% PGY2, 21% PGY3, and 9% PGY4. Fifty-five percent reported not screening for online safety or cyberbullying in clinic. Thirty-nine percent of residents reported feeling somewhat comfortable with inquiring about online use. The majority of residents (82%) felt there were barriers to discussing cyberbullying and online safety, with time (37%) and lack of education (28%) the most commonly identified barriers. Overall, 91% of respondents felt their clinic did not adequately screen for cyberbullying.

Conclusion: Residents do not always screen for online safety and cyberbullying in the primary care setting and identify time and lack of education as major barriers to screening. Future work should focus on incorporating screening and management guidelines to resident education and potentially designing a patient handout with local resources for ongoing support and management.
CHALLENGES AND OPPORTUNITIES OF POST PARTUM DEPRESSION SCREENING IN A PEDIATRIC PRIMARY CARE CLINIC

S. Lemke1, M. Orringer4, K. Orringer2, M. Muzik3, S. Kileny2

1Pediatric Residency Program; 2Division of General Pediatrics; 3Department of Psychiatry; University of Michigan, Ann Arbor, Michigan; 4Brown University, Providence, Rhode Island

Background: Postpartum depression (PPD) is a prevalent issue affecting pediatric patients and their mothers, with rates reported as high as 11-18% nationally. PPD has been linked to behavior and attachment issues, early cessation of breastfeeding, and overuse of healthcare services. The AAP recommends screening for PPD at the 1, 2, 4, and 6-month visits using a validated tool, such as the Edinburgh Postpartum Depression Scale (EPDS).

Objectives: We aimed to 1) Introduce PPD screening at a pediatric primary care practice, 2) Evaluate the rate of PPD, 3) Identify barriers to PPD screening and documentation, and 4) Examine referral practices for mothers who screen positive for thoughts of self-harm.

Methods: PPD screening was introduced at a pediatric primary care practice with co-located OB and perinatal psychiatry, using the EPDS. EPDS rated a positive screen as either a score of 10+, or any response other than “never” to the question about self-harm. The project was carried out in 3 phases, 1) a pilot period using a paper screen at 2-week and 2-month well visits, 2) a study period which screened at 2-week, 2, 4, 6, 9, and 12-month visits, and 3) a follow-up period evaluating rates of screening at the 2-week, 2, 4, and 6-month visits. Chart review was performed to evaluate rates of PPD, rates of EMR documentation, and follow-up practices for any positive response to the question about thoughts of self-harm. Value stream mapping (VSM) for the screening process was performed, including input from clinic medical assistants.

Results: 1119 mother-baby dyads were screened during the pilot and study periods. 72% of the paper forms were missing partial patient identifiers. 8.6% (96) had elevated scores of 10+. 2% (22) screened positive for thoughts of self-harm and of those, 2 were unable to be identified for further review, 2 received no intervention, and the remaining received social work referral, Maternal Infant Health Program referral, or both. During the follow-up period, EPDS documentation averaged 48% (range 40%-71% each month). VSM revealed several points for potential intervention in the current screening process.

Conclusions: Rates of PPD at our clinic were similar to reported rates in the literature. However, our overall rates of screening are below 50%, and some patients in distress received no intervention. A failsafe workflow is needed to ensure that screening is administered, documented, and followed-up appropriately. EMR-linked, tablet-based screening has the potential to improve this process.
Abstract 129

NEAR-PEER LED OUTPATIENT TEACHING AND RESIDENT CONFIDENCE

Kayla McAleenan, MD, Sarah Allexan, MD, Rebecca Northway, MD, Sarah Platte, MD, Namita Sachdev, MD
Michigan Medicine Internal Medicine-Pediatrics

Background: Near-peer education experiences can be defined as senior learners assuming the role of coach or instructor. In medical students, near-peer experiences have demonstrated sustained improvement in self-efficacy (1). On a curricular needs assessment survey among Michigan Medicine (MM) Medicine-Pediatrics (M-P) residents, 50% of respondents indicated occasionally participating in near-peer teaching in the outpatient setting and 59% reported a great deal of participation in near-peer teaching in the inpatient setting (scale: never-rarely-occasionally-a moderate amount-a great deal). This demonstrated a significant difference between near-peer experiences in the inpatient and outpatient settings, and identified an area for intervention.

Methods: MM M-P residents were surveyed regarding satisfaction with the outpatient curriculum and teaching confidence. Following that survey, residents were asked to lead two outpatient teaching sessions over the 12-month period. Following all teaching sessions, residents were asked to complete a brief survey regarding medical decision making (MDM) confidence. If a resident led the session, resident and attending physicians also completed a four-question Observed Structured Teaching Evaluation (OSTE). The responses were analyzed for correlations between teacher and MDM confidence.

Results: To date, 73 responses (19% response rate) have been collected. This assumes that every resident attends every teaching session, which is not possible and therefore underestimates the response rate. Using a Chi-Square test, there was no statistically significant difference between who taught the session and resident MDM confidence (n=73; p=0.502).

Conclusions: In this limited study of near-peer teaching and resident confidence, there is no correlation between MDM confidence and resident led sessions. However, the study is limited by small sample size and poor survey response rates. In the future, this study could include residents designing the teaching sessions instead of using pre-created templates to promote further autonomy, which may translate into increased self-efficacy and confidence. Emails could be sent to remind residents to complete the survey after teaching sessions and improve response rates. Additionally, further evaluation of the OSTE and post-survey results is pending.

CHECK YOUR OWN PULSE FIRST: MOCK CODE SIMULATION CURRICULUM FOR PEDIATRIC TRAINEES

M. Pfarr¹, D. McAree¹, H. Mehta¹, J.G. Kohne¹, E. Gross¹, K. Phelps¹, J. Hemberg², K. Paice¹
¹Department of Pediatrics, University of Michigan, Ann Arbor
²Primary Children’s Hospital, Intermountain Healthcare, Salt Lake City

Background: Care for the hospitalized child in cardiopulmonary arrest can be anxiety-provoking even for the most experienced providers. The initial actions of providers responding to a pediatric code are critical. In-hospital pediatric cardiac arrest is associated with poor survival, with approximately 1 in 4 children with an in-hospital arrest surviving to discharge, and one-third of those surviving children suffering a permanent neurological deficit. Even at the largest centers, in-hospital pediatric cardiac arrest is uncommon. Unfamiliarity with pediatric codes may lead to increased provider discomfort, particularly among resident physicians. A well-designed simulation-based training curriculum can help address trainee and provider discomfort and improve communication during real-life events. Objective: The primary aim of this project was to develop a simulation-based mock code training curriculum that increased trainee comfort in participating in and leading cardiorespiratory arrests. Design: Pediatric and Medicine-Pediatric residents were surveyed prior to participating in a simulation to identify their level of comfort participating in and leading cardiorespiratory arrests. Residents were scheduled to participate in a three-hour simulation session, that included a variety of mock patient code scenarios followed by debriefing with chief residents and faculty. Additionally, residents rotated through an airway skills station and reviewed crash cart equipment. Results: Of the 61 residents who completed the pre-survey, 26% “disagreed” or “strongly disagreed”, when asked if they were comfortable participating in a code blue. When asked if they were comfortable being a code team leader, 69% “disagreed” or “strongly disagreed”. 27 residents have participated in the simulation training, and 74% rated the session as very helpful. There was an increase in resident comfort with practical resuscitation skills following the training including: locating items in the code cart (11% comfortable to 59% comfortable), recognizing and treating cardiac arrhythmias (42% comfortable to 63% comfortable), running the defibrillator (21% comfortable to 59% comfortable), and selecting an appropriate airway device (10% comfortable to 70% comfortable). Conclusion: Pediatric residents report a lack of comfort participating in and leading cardiorespiratory arrest codes. We designed and implemented a high yield simulation-based training curriculum that improved resident comfort with resuscitation skills. Further work is needed to apply this training and investigate whether the comfort achieved helps in applied practice.
Background: Standardized handoff tools have been shown to decrease medical error rates and increase communication efficiency. We aim to improve handoff quality, defined as inclusion of essential handoff information, over a one-year period by implementation and education of a standardized handoff tool where one previously did not exist, while maintaining provider satisfaction and handoff efficiency.

Methods: An interdisciplinary group from the departments of emergency medicine and pediatrics created a modified I-PASS tool. Visual aids were placed in workspaces and providers received badge buddies depicting the tool. Education was provided at department conferences and a virtual lecture was created for providers rotating through the ED to view prior to the start of their rotation.

Results: Measures evaluated included: quality of handoff, as determined by inclusion of essential components based on published literature, provider satisfaction, and duration of handoff. A pre-intervention web based survey was completed by 87 providers representing all groups solicited; 69 providers completed a post-intervention survey. Post-intervention, most providers remained neutral or somewhat satisfied with current handoffs in regard to efficiency, detail, safety, and length. Individual handoffs were assessed by inpatient teams, and results of post-intervention handoff assessments showed improvement in inclusion of nearly all essential handoff items (Figure 1). Average time of individual handoffs remained similar (4.6 min pre vs 4.3 min post). On a subjective rating scale of 1 (poor) - 5 (excellent), the average rating of handoffs increased from 3.8 to 4.0.

Conclusions: More providers are now “somewhat satisfied” with most aspects of handoffs, compared to before the handoff tool was implemented. Inclusion of essential patient care information has increased, while still maintaining time efficiency. Next steps include teaching our tool to all oncoming new residents during summer orientation 2019.
Abstract 132

APPLICATION OF A VIDEO ORIENTATION TOOL IN PEDIATRIC RESIDENT CONTINUITY CLINICS
Meyer S 1, Tobin D 1, Burrows H 1
Department of Pediatrics, University of Michigan, Ann Arbor, MI 1

Background and Objectives: One challenge to the resident experience in the outpatient continuity clinic setting is awareness of the logistics and resources in the training physician’s particular clinic setting. The purpose of this project is to create a standardized video orientation template that can be adapted to individual continuity clinic sites, as well as a pilot video specific to the University of Michigan’s Briarwood pediatric continuity clinic. Our hypothesis is that implementation of such a video will enhance residents’ understanding of clinic operations, facilitate better resident awareness of clinic resources, improve resident efficiency, and ultimately optimize patient care.

Methods: Senior residents and faculty identified a list of topics that were challenging to learn or not apparent in clinic during their training experiences, which was used to guide video content. A video introducing the Briarwood continuity clinic to residents was created and distributed to Briarwood residents (interns and senior residents) via an email link. The video included objective information about the clinic site processes, patient visit navigation in the electronic medical records, and other key elements of routine pediatric patient encounters. Briarwood residents were instructed to fill out a 20 question pre-video survey, which consisted of both objective questions about clinic protocols, as well as resident self-assessment of clinic-specific knowledge. They were then instructed to watch the video orientation, and immediately fill out a post-video survey regarding perceived utility of the video as an orientation tool.

Results/Conclusions: The results of this evaluation are pending, but expected to be available by May 2019. Further post-video evaluation of efficacy of this video as an orientation teaching tool is planned for the upcoming academic year, with potential customization and application to additional UM pediatric clinic sites.
IMPLEMENTATION OF A STANDARDIZED SEIZURE ACTION PLAN TO IMPROVE COMMUNICATION AND PARENTAL EDUCATION

K. Neville1, H. McCaffery2, Z. Baxter3, R. Shellhaas1, and E. Fedak Romanowski1

1Division of Pediatric Neurology and 2Center for Human Growth and Development, 3University of Michigan, Ann Arbor, MI

Background: The American Academy of Neurology quality measures highlight the need for efficient treatment of status epilepticus. The first intervention is prevention of refractory status epilepticus through individualized seizure action plans (sZAP). As a quality improvement project, we implemented a standardized sZAP to improve the delivery of key information to families of children with seizures.

Methods: We implemented a new standardized sZAP using plan-do-study-act (PDSA) cycles. The form was distributed to parents of children (0-18 years) seen for seizures in the Michigan Medicine Pediatric Neurology Clinic. Families were given a questionnaire at each visit to gauge their understanding of their child’s diagnosis, treatment, and comfort in emergency seizure management. We analyzed these responses over time to assess effectiveness of the sZAP.

Results: Providers improved their utilization of the sZAP from 0% to 51.44% of visits after the first cycle, and to 58.12% after the second cycle. There were 505 patient encounters where both a sZAP was given and a parent questionnaire were completed; of these, 193 had a second questionnaire completed at a subsequent visit (38.2%). There were 226 encounters where no sZAP was given, but a parent questionnaire was still completed; of these, 72 had a second questionnaire (31.8%). Combining these groups for the first questionnaire, 31.5% of parents indicated that they did not know their child’s epilepsy syndrome or seizure type, 29.6% did not know the emergency protocol at their child’s school, 9.2% did not know when to consider a seizure an emergency or what to do if their child’s seizure had become an emergency, and 17.5% were not comfortable administering rescue medication. On the follow up questionnaire, responses were 13.4%, 18.8%, 3.0%, and 13.0% respectively. Further, parents who received the standardized sZAP had a significant improvement in responses to the questions on knowledge of epilepsy and seizure types, and seizure emergencies (p ≤ 0.001) while those who did not receive the sZAP did not have a significant improvement.

Conclusion: We successfully implemented a standardized sZAP. In contrast to those who received usual care, parents who received the sZAP indicated on follow up questionnaires that they were significantly more knowledgeable about their child’s epilepsy diagnosis and treatment. These results suggest that standard provision of a sZAP in pediatric neurology clinic improved key elements of parental education regarding epilepsy diagnoses and seizure emergencies.
Abstract 134

INSTITUTING NOTE TEMPLATES TO IMPROVE RESIDENT EFFICIENCY WITH INPATIENT DOCUMENTATION

Allison C. Shewmake1; Kayla Bronder Phelps1; Heather L. Burrows1
1Michigan Medicine Pediatrics Residency Program, Ann Arbor, MI

Background Creating de novo documentation for every common pediatric admission is inefficient. Michigan Medicine pediatric residents previously developed their own template notes, i.e. “dot phrases” to improve efficiency. Residents frequently shared personal templates with peers but they were not standardized nor optimized for quality or efficiency. Objectives We sought to improve resident efficiency, quality, fidelity to institutional clinical practice guidelines (CPGs), and consistency of documentation by creating a set of assessment and plan (A&P) templates for common pediatric admission diagnoses. Design/method A web based, anonymous pre-intervention needs assessment survey asked pediatric residents about utilization of template notes perception of need for standardized templates. We then created twenty templates as Epic “dot phrases”. A post-intervention survey will ask residents for changes in efficiency, quality of documentation, and confidence in medical decision-making. Results The survey (response rate 37%) showed that 76% of residents use a dot-phrase. Reasons for not using them included inability to recall the dot phrase and insufficient knowledge in creating or accessing them. 100% of respondents would use standardized dot-phrases for common admission A&Ps; 88% thought they would decrease the risk of missing documentation details. Preliminary data post-rollout suggests that residents regularly use the dot-phrases and experience increased efficiency. Attendings report overall satisfaction with documentation. Conclusions Residents regularly use templates for documentation report that having standardized templates would be beneficial. Created standardized templates have improved efficiency in note writing. Next steps include a post-intervention survey assessing frequency of use, and impact on documentation, efficiency, errors, and overall resident satisfaction.
THE RESIDENTS AS TEACHERS LONGITUDINAL CURRICULUM: A NEEDS ASSESSMENT
A. Zhou, J. Schiller, H. Burrows
Department of Pediatrics, University of Michigan, Ann Arbor, MI

Background: The Liaison Committee on Medical Education and Accreditation Council for Graduate Medical Education both require residents to be trained in and evaluated on teaching skills. The Accreditation Council for Graduate Medical Education also mandates programs provide resources for residents to develop skills for educating students and other health care professionals. It is estimated that residents spend 20% of their time teaching. Despite this, there is no standardized Residents as Teachers (RAT) curriculum for residency programs. While the majority of programs surveyed have existing curricula in place, they take individualized approaches and the effectiveness remains largely unknown. This project assessed the RAT curriculum needs of pediatric residents at our institution.

Methods: We surveyed pediatric residents and medical students to elicit feedback about the existing RAT curriculum using free text and 5-point Likert scale questions addressing relevance, content, format, and effectiveness of the curriculum. Based on responses, we redesigned content topics and changed from an 18-month to 12-month curriculum cycle. Residents were surveyed again 3 months after intervention. Using Mann Whitney testing, we assessed for differences in pre- and post-intervention survey scores. This study was IRB exempt.

Results: 104 residents were invited to complete surveys, response rate was 18% for the pre-survey and 20% for the post-survey. After intervention, scores did not show a statistically significant difference in residents’ perception of relevance of the RAT curriculum (p = 0.54), quality of the curriculum (p = 0.59), or effectiveness in preparing residents to teach (p = 0.68). Free-text responses in both surveys highlighted barriers related to the format for delivery of curriculum, such as inability to attend conferences despite interest in the material. We were unable to address these barriers within the scope of this study. Limitations of this study include late implementation of new curriculum, varying prior teaching experiences, small sample, and recall bias.

Conclusion: Residents indicated interest in the RAT curriculum, however, increasing the number of RAT lectures and refining towards more relevant topics failed to significantly change resident perception regarding the quality or effectiveness of the curriculum. Next steps to pursue improvement would include a more detailed look at the format for curriculum delivery given existing barriers for attendance. Future directions for this work would include repeating the study at other academic residency programs and ultimately using this data to develop a national core RAT curriculum.
Abstract 136
ADHERENCE TO OTITIS MEDIA GUIDELINES IN A LARGE ACAMEDIC PRIMARY CARE NETWORK
M. Bradley1, A. Bacharouch2, T. Hart-Johnson3, H. Burrows4, R. A. Blackwood3,4
1University of Michigan College of Literature, Science, and the Arts; 2University of Michigan Medical School; 3Office for Health Equity and Inclusion; 4University of Michigan Department of Pediatrics

Background: Otitis media (OM) is the infection of the middle ear. Two major types of ear infection are acute OM (AOM) and OM with effusion (OME). Symptoms of AOM include pain, erythema or bulging of the tympanic membrane, fever, and hearing loss. OME is a middle ear effusion without acute symptoms, where fluid remains in the ear after the infection has resolved.

Objective: This study evaluates adherence before and after implementation of a guideline for diagnosis and treatment of pediatric otitis media. Patient cohorts from 2013 and 2016 were evaluated and compared. Our priority predictors of age, symptoms, diagnosis and treatment were analyzed to determine which were significantly associated with adherence or non-adherence to the guideline. Patient demographics, such as race and age, were compared to determine potential disparities in treatment.

Methods: This study performed a retrospective chart review to collect encounter information for pediatric patients seen within a network of ten primary care clinics and diagnosed with otitis media. Abstracted data elements included demographics (age, gender, race), presence of pain or fever, duration of symptoms, middle ear appearance, risk factors, and treatment plan.

Results: Comparison of encounters from 2013 (n = 418) to 2016 (n = 1148) revealed a significant difference in adherence to the Michigan Medicine 2013 Otitis Media Guideline. Adherence increased from 61.2% in 2013 to 68.9% in 2016 ($\chi^2 = 8.111, p = .004$). The prescription of antibiotics for otitis media with effusion decreased significantly from 62.1% of cases in 2013 to 20.4% in 2016 ($p < .001$).

Conclusion: Having a specific guideline for otitis media management was associated with a significant increase in appropriate treatment. However, treatment did not improve equally for all forms of otitis media nor for all ages. Future studies should evaluate treatment disparities across patient age and race, study the effect of guideline promotion and education on compliance, and incorporate perspective design.
INTUSSUSCEPTION PROTOCOL IMPLEMENTATION: SINGLE INSTITUTION OUTCOMES WITH CLINICIAN AND FAMILY SATISFACTION

Amelia E. Gavulic¹, Jennifer S. McLeod MD¹, Wendi Wendt MD², Matthew H. Hilu¹, Erin Dunbar MD MSc², Michelle Macy MD MS², Nicole Sroufe MD MPH²,³, Erin E. Perrone MD¹

¹University of Michigan, Michigan Medicine Department of Surgery, Section of Pediatric Surgery
²University of Michigan, Michigan Medicine Department of Emergency Medicine
³University of Michigan, Michigan Medicine Department of Pediatrics

Background: The use of radiologic enema reduction has become the standard of care in uncomplicated pediatric intussusception. Traditionally, children were admitted for observation to capture early recurrences and prophylactic antibiotics were administered. Recent literature suggests that discharge after a successful enema reduction followed by an observation period in the emergency department (ED) is a safe and effective way of managing uncomplicated intussusception and that antibiotics are unnecessary. Methods: In March 2017, an intussusception protocol was implemented for children with ultrasound findings of ileocolic intussusception. Patients that met inclusion criteria were observed after successful air enema reduction in the ED and discharged after a 6 hour observation period. Retrospective chart review was done for all identified cases 2 years before and 22 months after protocol implementation for clinical outcomes and costs. Providers and parents were surveyed to assess overall satisfaction. Results: Charts were reviewed before (42 encounters, 37 patients) and after (30 encounters, 23 patients) protocol implementation. Admission rates decreased from 95% (40/42) to 23% (7/30; p<0.001) and antibiotic use was eliminated (91% to 0%, p<0.001). There was not a significant difference in recurrence rates (17% vs 23%, p=0.44). Median total length of stay (LOS) decreased from 18.87 to 9.52 hours (p<0.001), but median ED LOS increased from 4.37 to 9.87 hours (p<0.001) as expected due to the observation taking place only in the ED. There was a decrease in cost of over $2000 ($9,595 ± 3424 to $7465 ± 3723; p=0.009) per encounter. The surveyed clinicians and parents were satisfied with the protocol, and parents of pre-protocol and post-protocol patients did not differ in their satisfaction scores. Conclusion: Discharge after a short observation in the ED is safe, hospital cost was decreased, antibiotic use was eliminated, and parents and providers were satisfied with the protocol.
Abstract 138

TRANSITION READINESS IN DIABETES CARE: AN EVALUATION OF DIABETES KNOWLEDGE IN TEENAGERS WITH TYPE 1 DIABETES

S. Zhang, S. Sultana, A. Haddad, I. Thomas
Pediatric Endocrinology, University of Michigan, Ann Arbor, MI

Background: The transition from pediatric to adult endocrinology is known to correlate with a decrease in glycemic control and overall quality of health. Children with type 1 diabetes (T1D) rely heavily on their parents to provide educational resources and support to assist with disease management. As the child ages, more responsibility is given to the teen to manage his or her daily tasks without direct supervision. This could result in worsening diabetes control as deficits in education are uncovered.

Objective: This quality improvement study has two immediate goals; identifying gaps in the knowledge of our teens with T1D and testing the feasibility and accessibility of a tracking tool. This information will ultimately improve the transition process and provide more customized information to adult endocrinology care teams.

Methods: A survey comprised of 14 questions related to basic diabetes knowledge was created and administered to T1D patients between the ages of 11 and 18 years during clinic visits. Responses were recorded in real-time and results were provided to diabetes educators. Participants were then debriefed by their diabetes care team and given educational handouts directly related to their incorrect responses.

Results: Data collection is ongoing. We anticipate data from 50 participants. Several areas so far have been identified as lacking in sufficient knowledge. Questions regarding insulin correction factors, carbohydrate counting, and distinctions between basal and bolus insulin generated the least amount of correct responses.

Conclusions: The current educational materials used in the transition from pediatric to adult care need to be adjusted to give key basic information appropriate for teenagers. Survey results could aid in developing assessment “checkpoints” to allow pediatric care teams to track a patient’s understanding of their disease and help patients become more independent with their ability to self-manage. This information could then facilitate a smoother transition into adult care by focusing on areas that still need to be reviewed in adult endocrinology.
Executive Officers of Michigan Medicine: Marschall S. Runge, M.D., Ph.D., executive vice president for medical affairs, dean, University of Michigan Medical School, CEO, Michigan Medicine; David A. Spahlinger, M.D., president, UMHS, and executive vice dean for clinical affairs, University of Michigan Medical School; Patricia D. Hurn, Ph.D., dean, School of Nursing.

Regents of the University of Michigan: Michael J. Behm, Mark J. Bernstein, Shauna Ryder Diggs, Denise Ilitch, Andrea Fischer Newman, Andrew C. Richner, Ron Weiser, Katherine E. White, Mark S. Schlissel (ex officio)

The University of Michigan, as an equal opportunity/affirmative action employer, complies with all applicable federal and state laws regarding nondiscrimination and affirmative action. The University of Michigan is committed to a policy of equal opportunity for all persons and does not discriminate on the basis of race, color, national origin, age, marital status, sex, sexual orientation, gender identity, gender expression, disability, religion, height, weight, or veteran status in employment, educational programs and activities, and admissions. Inquiries or complaints may be addressed to the Senior Director for Institutional Equity, and Title IX/Section 504/ADA Coordinator, Office for Institutional Equity, 2072 Administrative Services Building, Ann Arbor, Michigan 48109-1432, 734-763-0235, TTY 734-647-1388, institutional.equity@umich.edu. For other University of Michigan information call 734-764-1817.

© 2019 Regents of the University of Michigan. 05/2019/200