SAVE THE DATE
September 21-23, 2016
Ann Lurie & Robert Lurie Children's Hospital
Chicago, Illinois
## PROGRAM-AT-A-GLANCE

**56th Annual Midwest Society for Pediatric Research Scientific Meeting**  
Children’s Mercy Hospitals & Clinics  
Kansas City, Missouri

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<th>TIME</th>
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<td><strong>WEDNESDAY, OCTOBER 28, 2015</strong></td>
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| 4:45 pm – 6:15 pm     | MWSPR Council Meeting  
                       Children’s Mercy Kansas City - CM Board Room – 1st Floor                          |
| 6:30 pm – 9:30 pm     | MWSPR Council Dinner                                                                |
| **THURSDAY, OCTOBER 29, 2015** |                                                                                       |
| 7:00 am – 8:00 am     | MWSPR Registration  
                       Continental Breakfast  
                       Children’s Mercy Kansas City – Auditorium – 1st Floor                             |
| 8:00 am – 11:20 am    | MWSPR Plenary Session I  
                       Auditorium – 1st Floor                                                              |
| 11:00 am – 5:00 pm    | Poster Set Up  
                       Must be up by 5:00 pm  
                       Empire Ball Room – Mezzanine Level  
                       Sheraton Kansas City Hotel at Crown Center                                          |
| 11:20 am – 11:35 pm   | MWSPR Business Meeting for Members  
                       Children’s Mercy Kansas City – Auditorium – 1st Floor                             |
| 11:35 am – 1:30 pm    | Founder and Sutherland Award Luncheon  
                       Children’s Mercy Kansas City - Community Room – 1st Floor                          |
| 1:30 pm – 4:45 pm     | MWSPR Plenary Session II  
                       Children’s Mercy Kansas City – Auditorium – 1st Floor                             |
| 5:20 pm – 7:30 pm     | Reception and Combined Poster Session  
                       Sheraton Kansas City Hotel at Crown Center  
                       Empire Ball Room – Mezzanine Level  
                       2345 McGee Street, Kansas City, MO                                                 |
| 7:30 pm               | Poster Take Down  
                       (immediately following Session)                                                     |
| **FRIDAY, OCTOBER 30, 2015** |                                                                                       |
| 7:00 am – 8:00 am     | MWSPR Registration  
                       Children’s Mercy Kansas City – Community Room – 1st Floor                          |
| 7:00 am – 8:00 am     | Continental Breakfast  
                       Children’s Mercy Kansas City – Community Room – 1st Floor                          |
| 7:40 am – 8:30 am     | Trainee Breakfast  
                       The Road Less Traveled  
                       Michael Artman, MD, University of Missouri –  
                       Kansas City and University of Kansas School of Medicine  
                       Board Room – 1st Floor                                                            |
| 8:30 am – 12:15 pm    | MWSPR Plenary Session III  
                       Children’s Mercy Kansas City – Community Room                                       |
| 12:15 pm – 1:30 pm    | Kenny, Metcalf, and Student Research Award Luncheon  
                       Children’s Mercy Kansas City – Community Room – 1st Floor                          |
This meeting has been made possible in part through the generosity of our supporters and the research efforts of the faculty, fellows, residents, medical and graduate students. We are very proud of the extent and breadth of our research programs and activities, and we trust that you will enjoy the activities of the meeting. We would like to thank the abstract reviewers for their time and effort in the review process in this important endeavor.

**Campus Map:**
[http://www.childrensmercy.org/AdeleHallCampus/](http://www.childrensmercy.org/AdeleHallCampus/)

**MWSPR Planning Committee**
- Raghavendra Rao, MD – President
- Heather Bartlett, MD – President-Elect
- Patrick Brophy, MD – Secretary
- Pamela Kling, MD - Treasurer

**Acknowledgements**
The Midwest Society for Pediatric Research would like to thank the following organizations for their generous support:

- Abbott Nutrition
- Mead Johnson Nutrition
- Children’s Mercy Hospital and Clinics & University of Missouri – Kansas City
- University of Minnesota Masonic Children’s Hospital, Minneapolis
- University of Wisconsin-Madison Pediatrics
- University of Iowa Institute of Clinical and Translational Science
- Cleveland Clinic
56th Annual Midwest Society for Pediatric Research Scientific Meeting

THURSDAY, OCTOBER 29, 2015
8:00 am – 7:30 pm
Children’s Mercy Hospital and Clinics
Auditorium – 1st Floor

7:00-8:00 am  REGISTRATION AND CONTINENTAL BREAKFAST

8:00-8:05  WELCOME AND INTRODUCTION
Raghavendra Rao, President

8:05  State-of-the-Art Speaker
WHY GLOBAL CHILD HEALTH NEEDS PHYSICIAN SCIENTISTS
Chandy John, MD, MS, Indiana University

MWSPR PLENARY SESSION I
Auditorium – 1st Floor

Presiding: David Kershaw, MD and Michelle Baack, MD

9:00  SENTINEL1: AN OBSERVATIONAL STUDY OF RESPIRATORY SYNCYTIAL VIRUS HOSPITALIZATIONS AMONG US INFANTS BORN AT 29-35 WEEKS GESTATIONAL AGE NOT RECEIVING IMMUNOPROPHYLAXIS.
ML Forbes, (on behalf of the SENTINEL1 Study Group), Akron Children’ Hospital, Akron, OH. Northeast Ohio Medical University

9:15  ENTEROVIRUS 68 ILLNESS IN CHILDREN WITH ASTHMA AND RECURRENT WHEEZE. JE Schuster, R Selvarangan, F Hassan, K Briggs, L Hays, B Pahud, G Weddle, J Miller, M Thompson, H Puls, M Queen, and M Jackson, Kansas City, MO. Children’s Mercy Hospital

9:30  OVER EXPRESSION OF TYPE II TGF β INTERACTING PROTEIN-1 (TRIP-1) PROTECTS MICE AGAINST ACUTE HYPEROXIA LUNG INJURY.
MF Nyp, A Navarro, SM Mabry, and II Ekekezie, Kansas, MO and Kansas City, MO. University of Missouri, Kansas City

9:45  MATERNAL SSRI EXPOSURE DECREASES CARDIAC 5-HT2B RECEPTOR EXPRESSION AND AKT PHOSPHORYLATION IN NEONATAL MICE.
SE Haskell, C Lo, KA Volk, VA Peotta, B Reinking, and RD Roghair, Iowa City, IA. University of Iowa

10:00 – 10:15 am Break

10:15  FOOD ALLERGY AND ITS IMPACT ON GROWTH: MISSOURI WIC 2014-PRESENT.
MK Nanda and CM Dinakar, Kansas City, MO. Children’s Mercy Hospital
10:30 INTRAUTERINE GROWTH RESTRICTION RESULTS IN PERSISTENT ALTERATIONS IN NEUROTRANSMITTER CONCENTRATIONS IN THE ADULT RAT BRAIN.  
*AM Hall, M Alexander, I Tkac, G Oz, and R Rao, Minneapolis, MN. University of Minnesota*  
Abstract 6

10:45 CHORIOAMNIONITIS AND GESTATIONAL MATURITY MODULATE INNATE IMMUNE SIGNALING IN THE PLACENTA.  
*N Kumar, P Nandula, H Menden, J Jarzembowski, and V Sampath, Grand Blanc, MI and Wauwatosa, MI. Michigan State University*  
Abstract 7

11:00 PANTOPRAZOLE PHARMACOKINETICS IN OBESE CHILDREN.  
*V Shakhnovich, S Abdel-Rahman, C Friesen, J Weigel, R Pearce, A Gaedigk, J Leeder, and GL Kearns, Kansas City, MO. Children's Mercy Hospital*  
Abstract 8

11:20 MWSPR BUSINESS MEETING FOR MEMBERS

11:35 FOUNDER AND SUTHERLAND AWARD LUNCHEON – *Community Room*  
*Presiding: Heather Bartlett, MD, President Elect*

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**Founder Award Recipient**  
Jeffrey Segar, MD  
Professor of Pediatrics – Neonatology  
University of Iowa

*Introduction by: Pamela Kling, MD*

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**MWSPR PLENARY SESSION II**  
Auditorium – 1st Floor

*Presiding: Howard Kilbride, MD and Noah Hillman, MD*

1:30 THE CORRELATION BETWEEN ABO BLOOD GROUP AND NEONATAL DISEASE SEVERITY.  
*KE McMahon, D Jasthi, F Leslie, H Leslie, and J Muraskas, Chicago, IL and Maywood, IL. Loyola University Medical Center*  
Abstract 9

1:45 ASSOCIATION OF HEMOGLOBIN LEVELS WITH NEURODEVELOPMENTAL OUTCOMES AMONG PRETERM INFANTS.  
*F Spyropoulos, OA Ekahguere, TT Colaizy, and EF Bell, Coralville, IA and Iowa City, IA. University of Iowa Hospitals and Clinics*  
Abstract 10

2:00 COMPARISON OF NEAR INFRARED SPECTROSCOPY (NIRS) WITH CAPILLARY REFILL TIME (CRT) IN THEIR ABILITY TO PREDICT SVO2<70%.  
*S Arya and YY Han, Kansas City, MO. Children’s Mercy Hospital*  
Abstract 11

2:15 EVALUATING PERIOSTIN AS A BIOMARKER FOR BRONCHOPULMONARY DYSPLASIA.  
*KJ Kelley, S Ahlfeld, S Davis, and B Poindexter, Indianapolis, IN and Cincinnati, OH. Indiana University School of Medicine*  
Abstract 12
2:30 POLYMORPHISMS IN THE UREA CYCLE ENZYME GENES ARE ASSOCIATED WITH PERSISTENT PULMONARY HYPERTENSION OF NEWBORN.  
DC Kaluarachchi, JC Smith, B Bedell, JM Klein, JM Dagle, JC Murray, and KK Ryckman, Iowa City, IA.  University of Iowa  
Abstract 13

2:45 HYPOXIA ACTIVATION OF EXTRACELLULAR SIGNAL-REGULATED KINASE IN HUMAN PULMONARY MICROVASCULAR ENDOTHELIAL CELLS IS DEPENDENT ON EPIDERMAL GROWTH FACTOR RECEPTOR.  
HA White, Y Jin, LG Chicoine, B Chen, and LD Nelin, Columbus, OH.  Nationwide Children's Hospital  
Abstract 14

3:00 PROPHYLACTIC RAPAMYCIN MODULATES PULMONARY HYPERTENSION AND ALVEOLAR DEVELOPMENT.  
CJ Sitzman, M Nyp, SM Mabry, M Navarro, and II Ekekezie, Kansas City, MO.  University of Missouri - Kansas City  
Abstract 15

3:15 – 3:30 pm Break

3:30 UREMIA AUGMENTS T CELL APOPTOSIS IN CKD MICE.  
EC Winnega and NB Blatt, Ann Arbor, MI.  University of Michigan  
Abstract 16

3:45 CLINICAL IMPACT OF MULTIPLEX PCR FOR RAPID IDENTIFICATION OF STAPHYLOCOCCUS AUREUS BACTEREMIA IN HOSPITALIZED PEDIATRIC PATIENTS.  
S Torres-Torres, JL Goldman, AL Myers, DE Yin, R Selvarangan, and MA Jackson, Kansas City, MO.  University of Missouri Kansas City- School of Medicine  
Abstract 17

4:00 DETAILED CHARACTERIZATION OF ATOMOXETINE METABOLISM AND IMPLICATIONS FOR A BOTTOM-UP PBPK MODEL FOR DOSE INDIVIDUALIZATION IN CHILDREN.  
JC Dinh, L Van Haandel, KT Gibson, RE Pearce, A Gaedigk, and JS Leeder, Kansas City, MO.  Children's Mercy Hospital  
Abstract 18

4:15 VITAMIN D REDUCES PROGERIN EXPRESSION AND RESCUES GENOMIC INSTABILITY AND PREMATURE SENESCENCE IN HUTCHINSON-GILFORD PROGERIA SYNDROME.  
R Kreienkamp, M Croke, M Neumann, and S Gonzalo, St. Louis, MO.  Saint Louis University  
Abstract 19

4:30 MATERNAL DEPRESSION, MATERNAL ASTHMA AND CHILDHOOD ASTHMA IN PUERTO RICANS.  
BH Medsker, E Forno, and JC Celedon, Pittsburgh, PA.  University of Pittsburgh  
Abstract 20

5:20 RECEPTION AND COMBINED POSTER SESSION  
Sheraton Kansas City Hotel at Crown Center  
Empire Ball Room – Mezzanine Level  
2345 McGee Street, Kansas City, MO  
See page 7 for posters  
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FRIDAY, OCTOBER 30, 2015

Children’s Mercy Hospital
7:00 am – 1:30 pm

7:00  MWSPR REGISTRATION

7:40  TRAINEE BREAKFAST SESSION

THE ROAD LESS TRAVELED
Michael Artman, MD, University of Missouri – Kansas City and
University of Kansas School of Medicine
Board Room – 1st Floor

MWSPR PLENARY SESSION III

Children's Mercy Hospital
Community Room – 1st Floor
8:30 am – 12:15 pm

Presiding: Heather Bartlett, MD and Joshua Petrikin, MD

8:30  State-of-the-Art Lecture
INDIVIDUALIZED MEDICINE FOR CHILDREN: FINDING THE DOSE THAT’S
JUST RIGHT.
J. Stephen Leeder, PharmD, PhD, University of Missouri – Kansas City

9:30  RESPIRATORY SEVERITY AND CALORIC CONSUMPTION IN INFANTS ON NEURALLY
ADJUSTED VENTILATORY ASSIST (NAVA). RANDOMIZED CROSSOVER TRIAL OF NAVA
AND SYNCHRONIZED INTERMITTENT MANDATORY VENTILATION WITH PRESSURE
SUPPORT (SIMV (PC) PS)).
JL Rosterman, EK Pallotto, WE Truog, K Meinert, M Allen, A Holmes, and WM Manimtim,
Kansas City, MO. Children’s Mercy Hospital, University of Missouri
Abstract 21

9:45  LONGITUDINAL BODY COMPOSITION TRACKING IN PREMATURE AND TERM
PRECHOOLERS.
JM Scheurer, L Zhang, A Kapur, EW Demerath, and SE Ramel, Minneapolis, MN. University
of Minnesota
Abstract 22

10:00  MATERNAL HIGH-FAT DIET AND GESTATIONAL DIABETES MELLITUS MODIFY
EXPRESSION OF PLACENTAL FUEL TRANSPORT AND STORAGE PROTEINS.
Ej Louwagie, TD Larsen, AL Wachal, K Chaudhary, and ML Baack, Sioux Falls, SD. Sanford
Children’s Health Research Center
Abstract 23

10:15 – 10:30 am Break
10:30 MATERNAL HIGH FAT DIET AND DIABETES AFFECT NEPHROGENESIS IN DEVELOPING OFFSPRING.
K Klippenstein, TD Larsen, EJ Louwagie, K Surrendran, and ML Baack, Sioux Falls, SD. Sanford Children's Health Research Center

10:45 THIOREDOXIN-INTERACTING PROTEIN STIMULATED BY HIGH GLUCOSE INDUCES ENDOTHELIAL CELL APOPTOSIS.
X Li, KL Kover, DP Heruth, DJ Watkins, WV Moore, M Zang, MA Clements, and Y Yan, Kansas City, MO and Boston, MA. Children's Mercy Hospital

11:00 GENETIC RISK FACTORS OF HLA-DRB1 AND COMPLEMENT IN AFRICAN AMERICAN AND SOMALI TYPE 1 DIABETES.
LK Coshwa, S Bowden, KE Lintner, Y Wu, B Zhou, A Alhomosh, R Hoffman, and C Yu, Columbus, OH. Nationwide Children's Hospital

11:15 NONOATE RESTORES DISRUPTED INSULIN SIGNALING IN OFFSPRING EXPOSED TO HYPERGLYCEMIA.
K Kua, S Hu, J Yao, and AW Norris, Coralville, IA and Iowa City, IA. University of Iowa

11:30 GLUCOSE FLUCTUATIONS IN DIABETES HAVE TARGETED EFFECTS ON THE OSTEOCYTE IN VITRO AND IN VIVO.
DM Pacicca, T Brown, J Wirtz, K Kover, Y Yan, D Watkins, P Tong, and L Bonewald, Kansas City, MO. University of Missouri - Kansas City

11:45 QUALITY MONITORING IDENTIFIES CRITICAL GAPS IN ROUTINE PRIMARY CARE AUTISM/DEVELOPMENTAL SCREENING PRACTICES.
CB Nadler, L Pham, C Low-Kapalu, K Williams, G Rahm, and S Nyp, Kansas City, MO. Children's Mercy Kansas City

12:00 SEPSIS-INDUCED LUNG INFLAMMATION IN THE DEVELOPING LUNG IS ATTENUATED WITH NADPH OXIDASE 2 BLOCKADE.
HL Menden and V Sampath, Milwaukee, WI. Medical College of Wisconsin

12:15 pm – 1:30 pm MWSPR Kenny, Metcoff, and Student Research Award Luncheon Community Room

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RECEPTION AND COMBINED POSTER SESSION
THURSDAY, OCTOBER 29, 2015
Sheraton Kansas City Hotel at Crown Center
Empire Ball Room – Mezzanine Level
2345 McGee Street, Kansas City, MO

Poster Number

1 DOCUMENTATION OF NUTRITIONAL STATUS IN PATIENTS AGED ≤ 24 MONTHS ADMITTED TO AN URBAN INNER CITY HOSPITAL.
CS Abrenica, H Vaule, M Philip, R Keilman, and V Geraldo, Chicago, IL. Mount Sinai Hospital Medical Center

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<td>NEURODEVELOPMENTAL FOLLOW UP AND NEUROIMAGING IN NEONATAL HYPOXIC RESPIRATORY FAILURE.</td>
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<td><em>PR Agarwal, D Altinok, J Desai, and B Sood, Detroit, MI. Wayne State University</em></td>
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<td>3</td>
<td>ATTITUDES, BELIEFS AND KNOWLEDGE ABOUT SEX AND CONTRACEPTION AMONG LATINO YOUTH IN RURAL KANSAS.</td>
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<td><em>RL Barral, B Cartujano, P Cupertino, J Cowden, R Manzo, and A Garcia, Kansas City, MO. University of Kansas</em></td>
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<td>4</td>
<td>HUMAN PAPILLOMA VIRUS INFECTION AND VACCINE KNOWLEDGE AMONG YOUNG LATINOS IN WESTERN KANSAS?</td>
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<td><em>RL Barral, J Cowden, B Pahud, P Cupertino, B Cartujano, A Chavez, I Calderon, and J Arteta, Kansas City, MO. University of Kansas</em></td>
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<td>5</td>
<td>PREDICTORS OF EXTREME EARLY RESPONSE TO METHOTREXATE IN JUVENILE IDIOPATHIC ARTHRITIS.</td>
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<td><em>RM Manne, L van Haandel, RS Funk, JS Leeder, and ML Becker, Kansas City, MO. University of Missouri-Kansas City</em></td>
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<td>RATE, CAUSES, AND CIRCUMSTANCES OF DEATH OVER A 20-YEAR PERIOD IN THE SOLE COMPREHENSIVE NEONATAL UNIT IN A RURAL STATE.</td>
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<td><em>MC Michel, TT Colaizy, JM Klein, JL Segar, and EF Bell, Iowa City, IA. University of Iowa</em></td>
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<td>7</td>
<td>BODY TEMPERATURES OF VERY LOW BIRTH WEIGHT INFANTS ON ADMISSION TO A NEONATAL INTENSIVE CARE UNIT.</td>
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<td><em>EA O’Brien, JE Brumbaugh, GA Cress, KJ Johnson, TT Colaizy, JM Klein, and EF Bell, Iowa City, IA. University of Iowa</em></td>
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<td>8</td>
<td>PSYCHIATRIC SYMPTOMS AND EPILEPSY IN A MALE PATIENT WITH PATHOGENIC PCDH19 GENE VARIANT MOSAICISM.</td>
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<td><em>BT Black, S Soden, I Thiffault, J Lowry, L Smith, E Farrow, N Miller, and C Saunders, Kansas City, MO. Children’s Mercy Kansas City</em></td>
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<td>CORD BLOOD ERYTHROPOIETIN LEVELS AFTER MATERNAL OBESITY DURING GESTATION.</td>
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<td><em>SE Blohowiak, AJ Pollock, DD Pham, and PJ Kling, Madison, WI and Kenosha, WI. University of Wisconsin-Madison</em></td>
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<td>10</td>
<td>BIOIMPEDANCE TO MEASURE FETAL BODY COMPOSITION IN AN OVINE UTERINE SPACE RESTRICTION MODEL.</td>
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<td><em>CK Korlesky, SE Blohowiak, RR Magness, and PJ Kling, Madison, WI. University of Wisconsin-Madison</em></td>
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<td>ENOXAPARIN TREATMENT OF VENOUS THROMBOEMBOLISM IN THE NEONATAL INTENSIVE CARE UNIT.</td>
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<td><em>JC Bohnhoff, RK Aneja, JR Shenk, YA Dommina, BR Brozanski, ML Good, and SA Disilvio, Homestead, PA and Pittsburgh, PA. University of Pittsburgh School of Medicine</em></td>
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12 RATES OF NONCONTRAST HEAD CT USE IN PREVERBAL CHILDREN AT AN ACADEMIC HOSPITAL FOLLOWING THE PECARN HEAD INJURY STUDY.
JJ Brown, H Haddad, MS Puffenbarger, JA Heneghan, and H Li, Detroit, MI, Cleveland, OH, and St Louis, MO. Wayne State University

13 NEONATAL AUTOPSY AND PARENTAL GRIEF.
JL Brunkhorst, J Weiner, J Lantos, and H Kilbride, Kansas City, MO. University of Missouri-Kansas City

14 RISK FACTORS FOR ELEVATED GENTAMICIN TROUGH LEVELS IN NEONATES RECEIVING THERAPEUTIC HYPOTHERMIA.
A Oschman, A English, C Elson, BS Carter, EK Pallotto, Kansas City, MO and Highlands Ranch, CO. University of Missouri-Kansas City

15 CHALLENGES IN IMPLEMENTING UNIVERSAL NEWBORN HEARING SCREENING PROGRAM IN AN URBAN INNER CITY POPULATION.
S Chung, H Srinivasan, and C Ngozika Onyelobi, Chicago, IL. Mount Sinai Hospital

16 SUSTAINED IMPROVEMENT IN MEDICATION COUNSELING AND PREGNANCY SCREENING AFTER IMPLEMENTATION OF A TERATOGENIC RISK EDUCATION STRATEGY.
A Cooper, J Harris, and ML Becker, Kansas City, MO. Children’s Mercy/University of Missouri Kansas City

17 EFFECTS OF CUMULATIVE HYPOXIC INJURY DURING DEVELOPMENT OF LUNG STRUCTURE AND FUNCTION.
AM Cox, Y Gao, and SK Ahlfeld, Indianapolis, IN and Cincinnati, OH. Indiana University

18 CONCURRENT METABOLIC CHANGES IN PLASMA AND THE BRAIN DURING ACUTE HYPOGLYCEMIA IN YOUNG RATS.
KM Ennis, E Lusczek, and RB Rao, Minneapolis, MN. University of Minnesota

19 INHIBITION OF NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE POTENTIATES METHOTREXATE TOXICITY IN A LYMPHOCYTE CELL LINE.
LA Pramann, JS Leeder, ML Becker, and RS Funk, Kansas City, KS. University of Kansas

20 METHOTREXATE POLYGLUTAMATION IN SYNOVIAL FIBROBLASTS FROM PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS.
RS Funk, L vanHaandel, ML Becker, and JS Leeder, Kansas City, KS. University of Kansas

21 IMPROVED OUTCOMES FOR INBORN BABIES WITH GASTROSCHISIS.
KW Gonzalez, BG Dalton, SR Reddy, RJ Hendrickson, SD St. Peter, and CW Iqbal, Kansas City, MO. Children's Mercy Hospital
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<td>HIGHER DOSAGES OF BONE MORPHOGENETIC PROTEIN-2 IN ALVEOLAR CLEFT REPAIR RESULT IN HIGHER RATES OF POSTOPERATIVE NASAL STENOSIS.</td>
<td>JA Goss, MS Hunter, ES Armbrecht, and AY Lin, Houston, TX and St. Louis, MO. Saint Louis University</td>
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<td>23</td>
<td>ADOLESCENT CHRONIC PAIN WITH COMORBID CONVERSION DISORDER: AN ANALYSIS OF PAIN, FUNCTION, AND PSYCHOLOGICAL OUTCOMES IN INTENSIVE INTERDISCIPLINARY PAIN REHABILITATION.</td>
<td>CM Hoffart and DP Wallace, Kansas City, MO. University of Missouri at Kansas City/Children’s Mercy</td>
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<td>EPINEPHRINE DOSING INTERVAL AND SURVIVAL OUTCOMES DURING PEDIATRIC IN-HOSPITAL CARDIAC ARREST.</td>
<td>DB Hoyme, SS Patel, RA Samson, TT Raymond, VM Nadkarni, and DL Atkins, Iowa City, IA, Denver, CO, Tucson, AZ, Dallas, TX, and Philadelphia, PA. University of Iowa</td>
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<td>25</td>
<td>CPR TRAINING IN SCHOOLS: WHAT CAN BE LEARNED FROM IOWA’S EXPERIENCE?</td>
<td>DB Hoyme and DL Atkins, Iowa City, IA. University of Iowa</td>
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<td>ATYPICALLY PROLONGED HONEYMOON PHASE IN A 15-YEAR OLD WITH TYPE 1 DIABETES.</td>
<td>L Huerta-Saenz, Wichita, KS. University of Missouri-Kansas City</td>
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<td>MULTIMODALITY IMAGING IN PRENATAL DIAGNOSIS OF AORTIC ARCH ANOMALY.</td>
<td>BM Jepson and S Sivanandam, Minneapolis, MN. University of Minnesota</td>
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<td>COMMON ALLEGATIONS OF PROFESSIONAL LIABILITY AGAINST PRACTITIONERS OF NEONATAL/PERINATAL MEDICINE.</td>
<td>AD Jones and J Muraskas, Chicago, IL and Maywood, IL. Loyola University Medical Center</td>
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<td>DOES COMPUTERIZED PHYSICIAN ORDER ENTRY DECREASE MEDICATION ERRORS IN THE NEONATAL INTENSIVE CARE UNIT?</td>
<td>R Katebian, S Padiyar, Z Khudeira, and H Srinivasan, Chicago, IL. Sinai Children’s Hospital</td>
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<td>30</td>
<td>BREASTFEEDING PRACTICES IN INFANTS WITH CLEFT LIP AND/OR PALATE.</td>
<td>CJ Cattaneo, AE Kaye, and HM Huff, Kansas City, MO. University of Missouri-Kansas City</td>
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<td>CLEFT CARE OF INTERNATIONALLY ADOPTED CHILDREN FROM CHINA.</td>
<td>AE Kaye, EA Stueve, and S Jiang, Kansas City, MO. University of Missouri-Kansas City</td>
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<td>PEDIATRIC RHEUMATOLOGY: INTEREST IN AND EXPENSES RELATED TO TRADITIONAL VERSUS TELEMEDICINE CLINIC VISITS.</td>
<td>EA Kessler, C Smith, A Sherman, and ML Becker, Kansas City, MO.</td>
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**SENTINEL1: AN OBSERVATIONAL STUDY OF RESPIRATORY SYNCYTIAL VIRUS HOSPITALIZATIONS AMONG US INFANTS BORN AT 29–35 WEEKS’ GESTATIONAL AGE NOT RECEIVING IMMUNOPROPHYLAXIS**

**Michael L. Forbes** (on behalf of the SENTINEL1 Study Group), Akron Children’s Hospital, Akron, OH

**Purpose:** To characterize RSV hospitalizations (RSVHs) among US preterm infants born at 29–35 wks’ gestational age (wGA) not receiving RSV immunoprophylaxis (IP) in the SENTINEL1 observational study.

**Methods:** At participating hospitals, all laboratory-confirmed RSVHs among preterm infants 29–35 wGA <12 mo of age, hospitalized ≥24 h during the 2014–15 RSV season, and who did not receive RSV IP within 35 d before the onset of RSV disease symptoms were systematically identified (NCT02273882). Measures included infant wGA, birth month, hospital length of stay (LOS), intensive care unit (ICU) admission, ICU LOS, mechanical ventilation (MV), and survival. Exploratory statistical comparisons were conducted using the Wilcoxon rank-sum test.

**Results:** Data were collected from 39 hospitals between Oct 1, 2014 and Apr 30, 2015. 606 RSVHs were identified: 210 infants 29–32 wGA, 237 infants 33–34 wGA, and 159 infants 35 wGA. Case characteristics are presented in Table. Death occurred in one 29-wGA infant. Infants <6 mo accounted for 75% of RSVHs observed, 83% of ICU admissions, and 89% of those requiring MV. Infants 29–32 wGA were overrepresented relative to their prevalence in US births.

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<th>Variable</th>
<th>29–32 wGA (n=210)</th>
<th>33–34 wGA (n=237)</th>
<th>35 wGA (n=159)</th>
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<td>Median (IQR) age at admission, mo</td>
<td>3 (2–6)</td>
<td>2 (1–5)</td>
<td>3 (1–5)</td>
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<tr>
<td>Median (IQR) hospital LOS, d</td>
<td>6 (3–13)</td>
<td>5 (3–10)</td>
<td>5 (3–7)</td>
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<td>ICU admission, n (%)</td>
<td>112 (53)</td>
<td>100 (42)</td>
<td>51 (32)</td>
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<tr>
<td>Median (IQR) ICU LOS, d</td>
<td>8 (3–14)</td>
<td>6 (3–12)</td>
<td>6 (3–9)</td>
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<td>MV among all admissions, n (%)</td>
<td>56 (27)</td>
<td>42 (18)</td>
<td>21 (13)</td>
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**Conclusion:** Among preterm infants born at 29–35 wGA not receiving RSV IP, RSV illness can be severe, frequently resulting in ICU admissions and MV, particularly during the first few months of life.

**Clinical Correlation:** Consistent with previous RSVH studies, RSV disease severity is greater in infants born at earlier gestational ages.

*This study was sponsored by AstraZeneca.*

2

**ENTEROVIRUS 68 ILLNESS IN CHILDREN WITH ASTHMA AND RECURRENT WHEEZE**

**J Schuster,** R Selvarangan,* F Hassan,* K Briggs,† L Hays,* B Pahud,* G Weddle,* J Miller,* M Thompson,* H Puls,* MA Queen,* MA Jackson*

*Children’s Mercy Hospital, Kansas City, MO, USA, †University of Missouri-Kansas City, Kansas City, MO, USA.

**Purpose:** Enterovirus 68 (EV-D68) is an uncommon cause of pediatric acute respiratory tract infection. Small cohorts of asthmatic children with severe disease have been rarely reported. We compared infection from EV-D68 vs. other enteroviruses/rhinoviruses (EV/RV) in children with a history of asthma and recurrent wheeze.

**Methods:** EV/RV positive specimens by multiplex PCR assay from hospitalized patients, aged 0–17 years, admitted from August 1–September 15, 2014, were retrospectively tested for EV-D68 by sequencing or PCR. Children with parental report of a history of asthma or recurrent wheeze were identified from the larger cohort. Data was obtained from the medical chart.

**Results:** 542 patients were admitted for conditions related to EV/RV testing and had specimens available for further testing. 206/339 (60.8%) EV-D68 positive children had a history of asthma or recurrent wheeze compared with 91/203 (44.8%) children with other EV/RV, P<0.01. Children with EV-D68 were older than those with other EV/RV (median 69 vs. 49 months, P=0.02). EV-D68 infected children were more likely to require supplemental oxygen (92.7% vs. 82.4%, P=0.007), albuterol (99.0% vs. 92.3%, P= 0.004), corticosteroids (97.1% vs. 91.2%, P=0.04), magnesium (42.7% vs. 29.7%, P=0.03), and aminophylline (7.3% vs. 0.0%, P=0.007). EV-D68 positive children required more hours of continuous albuterol (median 3 vs. 2 hours, P=0.03). Need for intensive care unit (ICU) management was more common in EV-D68 children (19.4% vs. 11.0%, P=0.07). Neither ICU length of stay nor overall length of stay was statistically different between the children with EV-D68 and children with other EV/RV.
Conclusions: In children with a history of asthma and recurrent wheeze, EV-D68 can cause severe disease, and EV-D68 infected children are more likely to require therapy for refractory bronchospasm than those with other EV/RV.
Clinical correlation: Aggressive management of bronchospasm is crucial for EV-D68 infected children with asthma and recurrent wheeze, and the availability of a rapid EV-D68 PCR test may have clinically relevant impacts on acute treatment decisions in these children.

3 OVER EXPRESSION OF TYPE II TGFβ RECEPTOR INTERACTING PROTEIN-1 (TRIP-1) PROTECTS MICE AGAINST ACUTE HYPEROXIA LUNG INJURY

MF Nyp, A Navarro, SM Mabry, II Ekekezie
Children's Mercy-Kansas City/University of Missouri- Kansas City, Kansas City, Missouri.

Background: Hyperoxia-induced acute lung injury (ALI) varies depending on whether postnatal growth is complete or not, with adult mice being more sensitive to hyperoxia exposure and favoring profibrotic lung remodel compared to neonatal mouse pups. Transforming growth factor β (TGFβ) signaling has been linked to aberrant lung remodeling, however it is also essential for normal lung development, suggesting cellular responses to TGFβ signaling are developmentally regulated. Type II TGFβ receptor interacting protein-1 (TRIP-1) was identified as a mediator of the TGFβ signaling pathway and our laboratory has observed that TRIP-1 is highly expressed in mouse pup lungs, but expression is lower in lungs of aging mice. We have found that TRIP-1 expression mediates profibrotic morphological changes in epithelial and fibroblast cells in culture. While TRIP-1 expression at the cellular level appears to favor normal epithelial and fibroblast morphologies, its role in preventing in vivo ALI is not known. The purpose of this study is to assess if TRIP-1 expression in Type II epithelial cells model is protective against hyperoxia-induced ALI.

Methods: Type II epithelial cell specific TRIP-1 over expressing mice (G5+) and non over expressing siblings (G5-) were used in this study. Mice were genotyped at DOL 21 and then randomized at 4 wks of age to either >95% O2 or room air for 4 days, at which time mice were sacrificed. Lungs were fixed, embedded in paraffin, and sectioned for H&E or immunohistochemistry studies. Mouse lungs were also collected for RNA, protein, and bronchoalveolar lavage (BAL) analysis.

Results: TRIP-1 over expression mice had normal lung development. The G5+ mice showed less hyperoxia-induced cellular proliferation (36% vs. 43% [p<0.05]) and a lower macrophages count (4.1/hpf vs. 7.6/hpf [p<0.05]) compared to G5- mice. BAL collected from G5+ hyperoxia exposed pups had a lower protein content and lower macrophage count when compared to G5- hyperoxia exposed pups.

Conclusion: Type II epithelial specific TRIP-1 over expression appears to maintain normal lung development and may protect older mice against hyperoxia-induced ALI. The importance of this research is hyperoxia-induced ALI carries a high degree of morbidity and mortality in humans. Therefore, identifying specific proteins that protect against ALI may lead to the development of new therapies.

4 MATERNAL SSRI EXPOSURE DECREASES CARDIAC 5-HT2B RECEPTOR EXPRESSION AND AKT PHOSPHORYLATION IN NEONATAL MICE.

S Haskell, C Lo, K Volk, V Peotta, B Reinking, R Roghair, Pediatrics, University of Iowa Children's Hospital, Iowa City, Iowa.

Background: Selective serotonin reuptake inhibitors (SSRIs) are prescribed in 10% of pregnancies in the United States. Maternal paroxetine therapy has been associated with cardiac malformations, and sertraline has supplanted paroxetine as the most commonly prescribed SSRI during pregnancy. While most fetuses exposed to SSRIs do not develop congenital heart disease, there are no studies evaluating for long-term cardiovascular effects.

Purpose: We hypothesized that perinatal SSRI exposure will negatively affect cardiomyocyte development and lead to decreased adult cardiac function.

Methods: Gravid mice were injected with sertraline (5 mg/kg/d) or saline throughout pregnancy. Pups continued to receive sertraline (1.25 mg/kg/d) or saline on post-natal days 1-14 during the proliferative phase of cardiomyocyte development, with the dose decreased to achieve serum levels consistent with those obtained in utero. Cardiomyocytes were isolated from neonatal mice and adult phenotypes were assessed in remaining mice.

Results: Sertraline exposed mice had decreased left ventricular cardiac expression of the 5-HT2B receptor on post-natal day 21 (Fold Change versus GADPH: saline 1.06 ± 0.09, SSRI 0.67 ± 0.04, p<0.01). Consistent with the reduction in 5-HT2B receptor expression, cardiomyocytes from sertraline exposed mice had decreased Akt phosphorylation compared to control mice, and cardiomyocyte Akt activation was refractory to in vitro 5-HT
stimulation (p<0.05) These findings were associated with a reduction in cardiomyocyte area (saline day 6 - 398 ± 6 µm², day 13 - 1803 ± 69 µm², SSR1 day 6 - 364 ± 5µm², day 13 - 1513 ± 38 µm², p<0.05). As adults, sertraline exposed mice had decreased stroke volumes (saline 48.7 ± 2.5 µL, SSR1 39.4 ± 2.2 µL, p<0.01) and decreased adult exercise capacity (saline 438.6 ± 67.3 m, SSR1 345.6 ± 48.3 m, p<0.01).

**Conclusion:** Sertraline exposure during development decreases cardiac Akt phosphorylation and cardiomyocyte size, leading to decreased left ventricular volumes in adult mice. Investigations are underway assessing if 5-HT2B agonist administration to sertraline exposed mice can reverse this phenotype. These findings suggest the need for closer assessment of cardiac function in children exposed to SSRIs in utero.

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5 FOOD ALLERGY AND ITS IMPACT ON GROWTH: MISSOURI WIC 2014-PRESENT

**MK Nanda*, C Dinakar**

*Children's Mercy Hospital, Kansas City, MO

**Purpose:** Young children with food allergies on restrictive diets may be at increased risk for poor growth.

**Methods:** Demographic, food allergy, weight, height, and dietary data were obtained on 99,610 children ages 0 to 61 months seen by the Missouri Department of Health (MO DOH) Women, Infants, and Children (WIC) Services between January 1, 2014 and June 17, 2015. Descriptive statistics, tests of independence were performed using SAS 9.4. Age-adjusted percentiles for height, weight, body mass index (BMI) were calculated by using the US Centers for Disease Control and Prevention (CDC)'s SAS program with comparison to CDC 2000 reference growth curves. IRB exemption status was obtained from Children's Mercy Hospital IRB and the MO DOH IRB.

**Results:** A physician diagnosis of food allergy was reported in 1,714 (1.7%) of children. Children with food allergy were 57% male, 82% white, with a mean age of 27.6 months (range 12-60 months), mean weight 13.0 kg (4.6-30.8 kg), and mean height 86.9 cm (35.6-118.7 cm). Families with food allergic children had significantly higher mean income of $19,015 (0‐136,968; p<0.0001) compared to mean income of $ 17,623 (0‐326,000) in the non-allergic group. Food allergic children had significantly lower mean weight-for-age of 49.5% (9.7 E-40 to 99.9; p<0.0001), mean height-for-age percentile of 45.2% (4.5 E-43 to 99.9; p<0.0001), mean height-for-age Z score of -0.19 (-14 to 24.5; p<0.0001) and mean BMI-for-age percentile of 61.4% (6.7 E-5 to 100.0; p<0.0001) than children without food allergy. The mean height-for-age Z score in food allergic children was -0.05 (-13.5 to 4.1; p=0.09). Children with food allergy were significantly more likely to have a weight-for-age Z score less than -1 (p<0.001), but not less than -2 (p=0.18).

**Conclusions:** Children with food allergy in the Missouri Department of Health WIC program have significantly lower weight-for-age percentiles, height-for-age percentiles, height-for-age Z scores, and BMI-for-age percentiles than children without food allergy. This raises the concern that the caloric intake in children on food allergen restrictive diets is less than children without food allergies. Future studies may help determine if the observed growth retardation in food allergic children is due to decreased energy intake versus increased expenditure.

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6 INTRAUTERINE GROWTH RESTRICTION RESULTS IN PERSISTENT ALTERATIONS IN NEUROTRANSMITTER CONCENTRATIONS IN THE ADULT RAT BRAIN

**A. Maliszewski-Hall**, **M. Alexander, I. Tkac, G. Oz and R. Rao**

1Department of Pediatrics, Division of Neonatology, University of Minnesota, Minneapolis, MN
2Center for Magnetic Resonance Research, Department of Radiology, University of Minnesota-Minneapolis, MN

**Background:** Children who are born after intrauterine growth restriction (IUGR) are at increased risk for long-term neurodevelopmental deficits including motor, cognitive and attention impairments. The nature of these deficits suggests that the cerebral cortex and hippocampus are particularly vulnerable to injury, however the mechanisms of injury are unknown. Using in vivo, high-field (9.4T) 1H MRS, we recently showed lower concentrations of several metabolites responsible for energy metabolism and neurotransmission in the cerebral cortex of postnatal (P) day 7 IUGR rats vs. normally grown (NG) controls. Whether or not the early changes in neurometabolites persist throughout development is unknown.

**Objective:** To evaluate the neurochemical profile of the cerebral cortex and hippocampus in adult IUGR and NG control rats using *in vivo* 1H MRS at 9.4T.

**Methods:** IUGR was induced using bilateral uterine artery ligation at gestational day 19 in pregnant Sprague Dawley dams (term=22.5d). MR spectra were obtained from the cerebral cortex and hippocampus at P60 in IUGR (N=8) and NG (N=7) pups. All spectra were acquired using previously described methods. The following neurochemicals and ratios were quantified using LCModel: ascorbate, aspartate, creatine (Cr), phosphocreatine (PCr), GABA, glucose (Glc), glutamate (Glu), glutamine (Gln), glutathione (GSH), lactate (Lac), myo-inositol (Ins), N-acetylaspartate (NAA), N-acetylaspartylglutamate...
(NAAG), phosphoethanolamine (PE), taurine (Tau), the sum of glycerophosphocholine and phosphocholine (GPC+PC), total PCr+Cr, PCr/Cr. Differences in neurochemical concentrations in each region were compared between IUGR and NG using Student's t-test.

**Results:** In the P60 cerebral cortex, IUGR resulted in lower concentrations of the excitatory neurotransmitter Gln compared to NG, while in the IUGR hippocampus, lower concentrations of GABA, an inhibitory neurotransmitter, were demonstrated. **Conclusion:** IUGR differentially affects the neurochemical profile in a regional dependent manner in the adult rat brain. Specifically, IUGR resulted in lower Gln concentrations in the cerebral cortex and lower GABA concentrations in the hippocampus. We speculate that these alterations may reflect an imbalance of excitatory vs. inhibitory neurotransmission and might be one underlying mechanism leading to cortex-based long-term cognitive impairments in human IUGR adults.

7  
**CHORIOAMNIONITIS AND GESTATIONAL MATURITY MODULATE INNATE IMMUNE SIGNALING IN THE PLACENTA**

**Navin Kumar**, MD, MS, Padma Nandula*, MD, Heather Menden, MS, Jason Jarzemowski, MD, PhD and Venkatesh Sampath, MBBS, MRCPCh. Medical College of Wisconsin, Wisconsin, United States.

**Background:** Toll like Receptors (TLRs) and Nucleotide Oligomerization Domain (NOD) like Receptors (NLRs) pathways are critical regulators of innate immune responses at the maternal-fetal interface. However, changes in their placental expression in relation to gestational maturity and various inflammatory environments have not been systematically examined. **Objective:** To quantify specific patterns in placental TLR/NLR gene expression with 1) advancing gestational age (ontogeny) and 2) exposure to chorioamnionitis (CA) and preterm premature rupture of membrane (PPROM). **Methods:** mRNA expression of 13 TLR/NLR pathway genes were analyzed by RT-PCR from fetal surfaces of the placental tissue. CA was assessed by an experienced pathologist, blinded to the mRNA results. **Statistics:** 1) **Ontogeny of individual genes:** analyzed by linear regression after excluding samples with CA and PPROM. ROC analysis was then done to find cut-off GA. 2) **Changes with CA and/or PPROM:** analyzed initially by univariate analysis and then logistic regressions to correct for confounders.

**Results:** Of 83 patients enrolled, 61 were preterm (<37 wks.) and 22 were term. 23 (27%) had evidence of CA; and 33 (40%) had PPROM. 15 (18%) had both CA and PPROM (CP). 42 (50%) had neither CA nor PPROM (C/P). Only RIPK2 (p=0.0025; r² 0.46) and TLR4 (p=0.0005; r² 0.55) were found to increase progressively with GA with cut-off at 38 wks. We found prominent changes in TLR5, NFKBIA and NFKB1 with CA and PPROM (Table)

<table>
<thead>
<tr>
<th>Comparison group</th>
<th>GENE</th>
<th>p-value</th>
<th>AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA vs no CA</td>
<td>TLR5</td>
<td>0.01</td>
<td>3.00(1.23-7.33)</td>
</tr>
<tr>
<td>PPROM vs no PPROM</td>
<td>NFKBIA</td>
<td>0.016</td>
<td>1.85(1.11-3.06)</td>
</tr>
<tr>
<td>CA+PPROM vs normal</td>
<td>NFKBIA</td>
<td>0.003</td>
<td>2.53(1.37-4.66)</td>
</tr>
<tr>
<td></td>
<td>NFKB1</td>
<td>0.009</td>
<td>1.79(1.15-2.79)</td>
</tr>
</tbody>
</table>

**Conclusions:** RIPK2 (mediator of NOD-dependent NF-kB signaling) and TLR4 progressively increased with GA. We speculate this upregulation may be involved in initiating labor at term. Increase in NFKBIA seen in PPROM and CA might represent a counter-regulatory mechanism to decrease inflammation in these inflammatory conditions. This study provides new insight into the relationships between GA, CA &/PPROM and TLR/NLR signaling in the placenta.

8  
**PANTOPRAZOLE PHARMACOKINETICS IN OBESE CHILDREN**

**V Shakhnovich**, S Abdel-Rahman, C Friesen, J Weigel, RE Pearce, A Gaedigk, JS Leeder, GL Kearns. The Children’s Mercy, Kansas City, MO; USA

**Background:** Overweight children (~30% pediatric population) are at higher risk for gastroesophageal reflux disease (GERD). Yet, no guidelines exist regarding dose selection of proton pump inhibitors (PPIs), the mainstay of GERD therapy, in this growing patient population. The objective of this prospective study was to evaluate differences in the pharmacokinetics (PK) of pantoprazole (PPI; CYP2C19 substrate) in overweight vs. normal-weight children. **Methods:** Using TaqMan techniques, 51 children (6-17yrs) were genotyped for CYP2C19 loss-of-function (*2, *3, *4) and gain-of-function (*17) alleles. After a single oral dose of pantoprazole (1.2 mg/kg lean body weight), 10 plasma samples were collected over 8hrs, pantoprazole/metabolite concentrations measured by HPLC-UV, and relevant PK parameters [e.g., systemic exposure (AUCtot), apparent clearance (CL/F), etc] generated via non-compartmental methods (Kineta 5.0). Using a two-tailed unpaired t-test, parameters were compared between overweight/obese (n=24) and normal-weight (n=25) children, and the effect of CYP2C19 genotype (*1/*1, n=24; *1/*17, n=15; *1/*2, n=7; *2/*17, n=3; *2/*2, n=2) on PK was
analyzed using a one-way ANOVA; α=0.05. **Results:** Analyzing all CYP2C19 genotypes together, dose-adjusted AUC\textsubscript{tot}, CL/F and other PK parameters were not significantly different between overweight/obese and normal-weight children; however, a positive correlation was observed between AUC\textsubscript{tot} and BMI ($r^2=0.4$; $p=0.01$). Comparing PK parameters in children of the same CYP2C19 genotype (e.g., *1/*1, $n=24$) CL/F was significantly reduced ($0.25\pm0.1$ vs. $0.41\pm0.23$ L/h/kg; $p<0.05$) and AUC\textsubscript{tot} increased ($5.3\pm3.5$ vs. $3.1\pm1.5$ mg*h/L; $p=0.05$) in overweight/obese vs. normal-weight children. Pantoprazole AUC\textsubscript{tot} was significantly increased ($8.1\pm4.6$ vs. $3.1\pm1.5$ mg*h/L; $p<0.05$) in obese (BMI $\geq$ 95th percentile) vs. normal-weight children with the *1/*1 genotype. Independent of obesity status, mean AUC\textsubscript{tot} for pantoprazole was 2-fold greater in children with 1 loss-of-function vs. 1 gain-of-function allele ($p=0.01$), and over 10-fold greater in children with 2 loss-of-function alleles vs. all other genotypes ($p<0.0001$). **Conclusions:** CYP2C19 genotype appears a primary determinant of pantoprazole PK in children, whereas BMI may explain individual variability within genotype groups. An activity score based on CYP2C19 genotype, modified by an obesity factor, may be helpful in the appropriate dose-selection of CYP2C19 substrates (e.g., PPIs); however, further studies are indicated, particularly in children with BMI $\geq$ 95th percentile for age.

**MWSPR Plenary Session II**

9  
**THE CORRELATION BETWEEN ABO BLOOD GROUP AND NEONATAL DISEASE SEVERITY**  
K McMahon, J Divya, F Leslie, H Leslie, J Muraskas  
Loyola University Medical Center, Maywood IL  
AB blood type is associated with an increased risk for adult cardiovascular disease, maternal preeclampsia, and severe neonatal necrotizing enterocolitis. The purpose of our study was to investigate whether maternal and neonatal AB blood type is significantly correlated with increased severity of neonatal and pregnancy-related diseases. We retrospectively collected data on 1,525 mothers and neonates admitted to the NICU at Loyola University Medical Center from the years 1990 to 2005. Neonates with blood types A, B, and O were matched for controls. We compared the severity of neonatal and pregnancy-related diseases in patients with AB blood type to patients with control blood types. Neonatal diseases included neutropenia at birth, culture proven sepsis throughout the hospital course, intraventricular hemorrhage (IVH) grades 3 or 4, respiratory distress syndrome (RDS) requiring surfactant, retinopathy of prematurity (ROP) requiring laser or cryotherapy, patent ductus arteriosus (PDA) requiring surgical ligation, and death. Maternal complications included pregnancy-induced hypertension, preeclampsia, and chorioamnionitis. To assess for significant differences between blood type and disease severity, a Chi-Square test of independence was performed. Of the 1,525 mothers and neonates analyzed, 388 mothers and 94 neonates had the AB blood type. Control blood types included 578 type A, 290 type B, and 563 type O. Between blood types, there was no significant correlation with severe IVH, RDS, ROP, or PDA in neonates or maternal preeclampsia or chorioamnionitis. Correlation between AB blood type and pregnancy-induced hypertension approached significance ($P=0.0732$). Neonatal AB blood type appeared to significantly influence the presence of neutropenia at birth ($P<0.0001$) and culture proven sepsis throughout the hospital course ($P<0.0002$) as opposed to no influence in control blood types ($P=0.0804$; $P=0.9418$, for neutropenia at birth and culture proven sepsis, respectively). Further analysis demonstrated that when compared to each control blood type, neonatal AB blood type was more significantly associated with neutropenia and culture proven sepsis ($P<0.0001$; $P<0.0001$). Our data demonstrates a significant association between AB blood type with neutropenia at birth and the number of culture proven sepsis throughout the hospital course. Correlation between AB blood type and pregnancy-induced hypertension approached significance. Maternal hypertension can lead to in utero bone marrow suppression resulting in neonatal neutropenia and an increased risk for infection. Therefore, mothers and neonates with AB blood type must be closely monitored for complications such as hypertension in mothers and neutropenia and sepsis in children.
ASSOCIATION OF HEMOGLOBIN LEVELS WITH NEURODEVELOPMENTAL OUTCOMES AMONG PRETERM INFANTS.

P Spyropoulos, OA Ekaghure, TT Colaizy, EF Bell
Dept. of Pediatrics, Univ. of Iowa, Iowa City, IA

Background: Anemia is the most common hematologic abnormality of the preterm infant. Transfusion of packed red blood cells (pRBC) is the first line therapy for this disorder. Current transfusion therapy is driven by the hemoglobin (Hgb) levels. However, there is no consensus on the ideal Hgb levels for optimal neurodevelopmental outcome, and only limited data are available comparing Hgb levels with neurodevelopmental outcomes of extremely preterm infants.

Purpose: To determine the association between Hgb levels in the first 30 and 90 days (d) of life and neurodevelopmental outcomes of infants 22 0/7 to 26 6/7 weeks. We hypothesized that a higher mean Hgb level is associated with a better outcome.

Methods: We conducted a retrospective cohort study of infants born from 2005 to 2013 with gestational age (GA) 22 0/7 to 26 6/7 weeks. We included infants that were assessed with Bayley III Scales of Infant Development (BSID III) at 18-24 months corrected age. We excluded infants with major congenital anomalies, NEC, IVH, PVL, HIE, suspected meningitis, critical congenital heart defects, major surgeries and death. We collected all available Hgb levels in the first 90 days and compared mean Hgb in the first 30 d and the first 90 d with cognitive, language and motor composite scores on BSID III. Logistic regression analysis was conducted and a p value less than 0.05 was considered statistically significant. SAS 9.3.3 was used for analysis.

Results: A total of 189 infants were identified that met study criteria. The median GA was 26 weeks. Median Cognitive, Language, and Motor subscale scores on the BSID III were 90, 94, and 88, respectively. We found that a higher mean Hgb concentration during the first 30 days of life was associated with Language [p=0.0053, OR=1.72 (CI 1.18-2.52)] and Motor [p=0.0099, OR 1.97 (CI 1.32-2.92)] scores greater than the sample medians, adjusted for GA. This association was not statistically significant for the Cognitive Composite scores. There was no association between the mean Hgb level and the lowest Hgb level during the first 90 d of hospitalization with the scores on the BSID III.

Conclusions: Among preterm infants born less than 26 6/7 weeks GA, higher mean Hgb level during the first 30 days of life is associated with improved neurodevelopmental outcomes.

COMPARISON OF NEAR INFRARED SPECTROSCOPY (NIRS) WITH CAPILLARY REFILL TIME (CRT) IN THEIR ABILITY TO PREDICT SVO2<70 %.

Arya S., Han YY.
Children's Mercy Hospital, Kansas City, MO.

Background: Shock is a life threatening condition. Early identification and aggressive resuscitation with goal Svo2 >70 % have shown to improve outcomes (1-3). Most critically ill children are initially stabilized by local community physician lacking skills for central line placement hence SvO2 monitoring is not easily available. Since early shock reversal by community physician has been associated with improved survival a need for easy to obtain target point is desirable.

Objective: Comparison of Near Infrared Spectroscopy (NIRS) with Capillary refill Time (CRT) in their ability to predict Svo2<70%

Design: Prospective Cohort Study

Interventions: Non cyanotic, Non hypoxic (>95% saturation) patients, >1 month of age with Central venous catheter and NIRS monitor were enrolled from Oct 2014-January 2015. NIRS value for cerebral and flank NIRS recorded at the time of venous blood gas collection. Peripheral and Central capillary refill Time recorded with stop watch in a standard manner.

Main results:

Correlations:

<table>
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<tr>
<th>Svo2</th>
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<th>Peripheral CRT</th>
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<tr>
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<tr>
<td>P value</td>
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ROC Curve:

<table>
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<tr>
<th>Area Under Curve</th>
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<tbody>
<tr>
<td>Cerebral NIRS</td>
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</tbody>
</table>
Conclusions: Cerebral NIRS showed better correlation with SvO2 compared Flank NIRS and CRT.
Speculation: NIRS may be beneficial as non-invasive monitor during shock resuscitation.

12 EVALUATING PERIOSTIN AS A BIOMARKER FOR BRONCHOPULMONARY DYSPLASIA.
K Kelley and S Davis
Indiana University School of Medicine, Indianapolis, IN. S Ahlfield and B Poindexter, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Background/Purpose: Bronchopulmonary Dysplasia (BPD) is a chronic lung disease associated with extreme prematurity. Biomarkers that can accurately determine which neonates will develop BPD are needed to guide treatment decisions and avoid undesirable side effects on neurodevelopment. Periostin, a matricellular protein secreted by myofibroblasts in the lung, has been identified as a useful biomarker of adult inflammatory lung disease but has not been studied in BPD.

Methods: This prospective observational study enrolled a subgroup of infants consented for the Prematurity and Respiratory Outcomes Program (PROP) study at Indiana University with a gestational age <29 weeks requiring respiratory support >2 liters/minute nasal cannula at Day 7. Whole blood (500uL) was collected at 7 and 28 days of age and analyzed via Bioplex to determine plasma Periostin levels. BPD was defined as the physiological need for supplemental oxygen at 36 weeks corrected gestational age.

Results: 31 babies were enrolled with an average gestational age of 26.4 +/- 1.6 weeks and birthweight 919 +/- 226 grams. Fifteen (48%) neonates developed BPD, 11 (35%) neonates did not develop BPD, and 5 (16%) neonates died prior to classification. When comparing plasma Periostin levels at Day 7 between patients without BPD to those that died or developed BPD, there was no statistically significant difference (p =0.15). However, at Day 28, neonates that would go on to develop BPD had significantly higher plasma Periostin levels (average 291.2 ng/ml for those without BPD and 386.0 ng/ml for those with BPD, p = 0.04). Receiver operating characteristic (ROC) analysis for Day 28 Periostin levels resulted in a c-statistic of 0.7338. Using a cut-off of >325 ng/ml, plasma Periostin levels at Day 28 predicted BPD with 71% sensitivity, 64% specificity, and a positive predictive value of 71%.

Conclusions: An elevated plasma Periostin level at Day 28 is associated with the development of BPD at 36 weeks corrected gestational age. A plasma Periostin level >325 ng/ml at Day 28 provides a fair predictor of future BPD risk. Additional study is needed to determine if Periostin represents a novel biomarker capable of guiding therapy for extremely preterm neonates at risk of developing BPD.

13 POLYMORPHISMS IN THE UREA CYCLE ENZYME GENES ARE ASSOCIATED WITH PERSISTENT PULMONARY HYPERTENSION OF NEWBORN
Dinushan C Kaluarachchi1, Jessica C Smith2, Bruce Bedell1, Jonathan M. Klein1, John M Dagle1, MD, Jeffrey C Murray1, Kelli K Ryckman2
1Department of Pediatrics, University of Iowa, Iowa City, IA, United States; 2Department of Epidemiology, College of Public Health, University of Iowa, Iowa City, IA, United States

Purpose: Persistent Pulmonary Hypertension of the Newborn (PPHN) is characterized by elevated pulmonary vascular resistance with extrapulmonary right to left shunting causing life threatening hypoxemia. Endogenous Nitric Oxide is critical for regulation of pulmonary vascular resistance and the transition of pulmonary circulation at birth. Endothelial cells generate Nitric Oxide from the precursor L-arginine which is an amino acid supplied by the urea cycle. We hypothesized that polymorphisms in Urea Cycle genes and low concentrations of urea cycle intermediates are associated with PPHN.

Methods: We performed a family based candidate gene analysis to study 48 SNPs (single nucleotide polymorphisms) in 6 urea cycle enzyme genes (CPS1, NAGS, ASS, ASL, ARG1, OTC). SNPs were genotyped using the Fluidigm genotyping platform. Genotyping was done on 110 families with infants diagnosed with PPHN based on inclusion/ exclusion criteria (infant and at least one parent). Statistical analyses was performed with a transmission disequilibrium test, using family-based association test software (FBAT, Cambridge, MA) to look for nonrandom allele transmission from parents to offspring. Haplotype analysis using sliding windows of 2-6 SNPs across the region was used to evaluate associations with PPHN.

Results: Three SNPs in Carbamoyl Phosphate Synthetase 1 gene (rs41272673, rs4399666, rs2287599) showed significant association with PPHN (p=0.02). Presence of CCACAT alleles at rs2287599, rs7607412, rs7572146, rs6724941, rs3213784, and rs1047891 of CPS1 was associated with PPHN (P= 0.006). None of the SNPs in other 5 urea cycle enzymes genes were associated with PPHN. SNPs that meet nominal significance, did not reach formal levels of significance when the conservative Bonferroni correction is applied.
Conclusions: This study suggests a potential association between SNPs in the CPS1 gene and PPHN. We will be performing a case control study to identify urea cycle intermediate levels measured by routine newborn screening and association with PPHN to test the functional impact of these findings.

14
HYPOXIA ACTIVATION OF EXTRACELLULAR SIGNAL-REGULATED KINASE IN HUMAN PULMONARY MICROVASCULAR ENDOTHELIAL CELLS IS DEPENDENT ON EPIDERMAL GROWTH FACTOR RECEPTOR
HA White, Y Jin, LG Chicoine, B Chen, LD Nelin
Nationwide Children's Hospital and Pediatrics, The Ohio State University, Columbus, OH USA

Background: We have previously shown that hypoxia-induced proliferation in human pulmonary microvascular endothelial cells (hPMVEC) depends on epidermal growth factor receptor (EGFR)-mediated arginase II induction.

Objective: To test the hypothesis that hypoxia-induced EGFR activation leads to phosphorylation of extracellular signal-regulated kinase (ERK) leading to increased arginase II expression in hPMVEC.

Methods: hPMVEC were incubated in either normoxia (20% O₂, 5% CO₂) or hypoxia (1% O₂, 5% CO₂) for 1 or 24 hours and western blotting was performed for EGFR, phospho-ERK, total ERK and arginase II. In a second set of experiments, hPMVEC were transfected with siRNA against EGFR or scramble siRNA for 24 hours, recovered for 24 hours, and then incubated in hypoxia for 1 or 24 hours. Cells were harvested for western blot analysis of phospho-ERK, total ERK and arginase II. Additionally, hPMVEC were transfected with siRNA against EGFR or scramble siRNA for 24hrs, recovered for 24 hours and then equal numbers of hPMVEC were plated in a 6-well plate and incubated in hypoxia and 48 hours later viable cell number counted using trypan blue exclusion.

Results: hPMVEC exposed to hypoxia had greater EGFR and arginase II protein levels than hPMVEC exposed to normoxia. hPMVEC incubated in hypoxia had greater phospho-ERK protein levels with little effect on total ERK levels. Hypoxic hPMVEC treated with the EGFR siRNA had lower phospho-ERK and arginase II levels than did hypoxic cells treated with a scramble siRNA. Additionally hPMVEC treated with EGFR siRNA had significantly lower viable cell numbers at 48 hours than did hypoxic cells treated with scramble siRNA.

Conclusions: Our findings suggest that in hPMVEC hypoxia activates EGFR which in turn phosphorylates ERK eventually leading to increased levels of arginase II. We speculate that ERK may be a potential therapeutic target to prevent or reverse the vascular remodeling seen in pulmonary hypertension associated with hypoxia.

15
PROPHYLACTIC RAPAMYCIN MODULATES PULMONARY HYPERTENSION AND ALVEOLAR DEVELOPMENT.
C Sitzman, M Nyp, SM Mabry, A Navarro and II Ekekezie.
Children's Mercy: University of Missouri - Kansas City, Kansas City, MO.

Pulmonary hypertension in the neonate bears significant morbidity and mortality. Rapamycin is an antiproliferative agent reported to reverse pulmonary hypertension in adult mice. However, it is not known whether rapamycin could moderate the degree of developing pulmonary hypertension (PH) in newborn mice. Previous work demonstrated no statistically significant change in weight gain in newborn mice in room air injected with rapamycin at a dose of 1 mg/kg every 3rd day compared with normal saline controls. As the next step, we sought to determine rapamycin's effect on weight gain, alveolar development, and cardiac hypertrophy in hypoxic conditions.

Wild type mouse pups were randomized to 4 groups: 1) Rapamycin (1 mg/kg every 3rd day)/room air; 2) Normal saline/room air; 3) Rapamycin (1 mg/kg every 3rd day)/hypoxia (12%); 4) Normal saline/hypoxia (12%). Pups were weighed before each injection (day 1, 4, 7, and 10 of life), and before euthanization on Day 13. After at least 24 hours of fixation, lung and heart sections were embedded in paraffin. Radial alveolar counts (RACs) were done on hematoxylin and eosin stained lung sections. Ratios of the right ventricle wall thickness to left ventricle wall plus septum thickness were used as a measure of right ventricle hypertrophy.

Rapamycin administration under hypoxia led to statistically significant growth impairment when compared with room air normal saline controls (2.97 ±0.39 vs 7.09±0.91). Radial alveolar counts were statistically lower in hypoxia controls compared to room air controls, suggesting significant alveolarization impairment (5.21±1.89 vs 2.0±0.63). Rapamycin administration led to a statistically significant increase in the RACs in the mice exposed to hypoxia (3.8±1.37 vs 2.0±0.63). There was a trend towards increasing right ventricle/left ventricle+septum ratios in mice exposed to hypoxia which was improved with the administration of rapamycin.

Rapamycin administration attenuates alveolar simplification and PH in neonatal mice exposed to hypoxia. Creating a strategy that could provide targeted therapy to at risk premature infants to prevent the development of PH could reduce the morbidity associated with its diagnosis. Preventing the development of PH cannot come at the cost of impairing weight gain, although this hypoxia model may exaggerate the weight gain issue.
16
UREMIA AUGMENTS T CELL APOPTOSIS IN CKD MICE.
EC Winnega, NB Blatt
Pediatrics – Nephrology, University of Michigan, Ann Arbor, MI, United States.
Background: End-stage renal disease (ESRD) affects more than 32 million in the US including over 7500 children. Infection is the second leading cause of death in ESRD, and young ESRD patients with sepsis have 1000-fold increased mortality compared to the general population. Human and animal studies have linked mortality in sepsis to T lymphocyte apoptosis, yet few studies have attempted to assess the impact of chronic kidney disease (CKD) on immune function.

Objective: Determine the effect of uremia on T cell apoptosis ex vivo in a well-established mouse model of CKD

Methods: 129 S1 mice underwent subtotal nephrectomy (SNx) or a sham procedure. Splenic T lymphocytes were isolated from SNx and sham mice, then stimulated mitogenically with Concanavalin A (ConA) or pharmacologically with phorbol 12-myristate 13-acetate + ionomycin (PMA). Apoptosis was assayed by flow cytometry using 3,3’-dioctadecyloxacarbocyanine perchlorate to monitor mitochondrial gradient collapse or a fluorescent caspase substrate (Life Technologies, Grand Island NY).

Results: SNx mice developed blood urea nitrogen values that were approximately two-fold greater than those of the sham-operated cohort within 4 weeks post-surgery that remained stable for at least 6 months (SNx: 42 ± 6 vs Sham: 19 ± 3, p < 0.001), indicating development of uremia. Splenic T lymphocytes from SNx mice showed increased mitochondrial gradient collapse in both unstimulated conditions (SNx: 22.9% ± 0.1 vs Sham: 14.5% ± 2.0, p = 0.027) and following stimulation with PMA (SNx: 28.3% ± 1.5 vs Sham: 22.3% ± 1.8, p = 0.067) or ConA (SNx: 51.5% ± 2.1 vs Sham: 31.3% ± 1.9, p = 0.001). Caspase 3 activation was increased in unstimulated SNx T cells (SNx: 40.1% ± 0.1 vs Sham: 36.0% ± 0.9, p = 0.046) as well as those stimulated with PMA (SNx: 38.7% ± 0.5 vs Sham: 34.9% ± 0.7, p = 0.049) and ConA (SNx: 67.1% ± 0.8 vs Sham: 42.8% ± 0.5, p = 0.005).

Conclusions: We have used a well-established mouse model of CKD to demonstrate that splenic T cells from uremic mice are primed to undergo apoptosis, which suggests that increased apoptosis may explain increased mortality from sepsis in CKD/ESRD. These findings also validate the use of this CKD mouse model to explore the mechanisms that link uremia to lymphocyte apoptosis, as well as the impact of CKD on immune responses in sepsis.

17
CLINICAL IMPACT OF MULTIPLEX PCR FOR RAPID IDENTIFICATION OF STAPHYLOCOCCUS AUREUS BACTEREMIA IN HOSPITALIZED PEDIATRIC PATIENTS
S Torres-Torres 1,2, JL Goldman 1,2, AL Myers 1,2, DE Yin 1,2, R Selvarangan 1,2, MA Jackson 1,2
1Children’s Mercy Hospital and Clinics, Kansas City, MO; 2University of Missouri-Kansas City, Kansas City, MO

Background: S. aureus is a leading cause of invasive disease in children, and for both MSSA and MRSA bacteremia, timely initiation of therapy is the critical factor in decreasing morbidity and mortality. Rapid multiplex PCR testing in blood cultures provides faster identification and detection of the gene for methicillin-resistance in S. aureus isolates compared to traditional laboratory techniques. Hence, we evaluated the impact of management in pediatric patients with S. aureus bacteremia after implementation of the FilmArray blood culture identification (BCID) panel (BioFire, Salt Lake City, UT).

Methods: The FilmArray BCID panel was implemented in July 2014, and as per institutional protocol, all patients with a positive blood culture for S. aureus receive a formal infectious diseases (ID) consult. All patients with S. aureus bacteremia one year before implementation of the FilmArray BCID panel and in the subsequent 6 months after implementation were evaluated.

Results: The total cases of S. aureus bacteremia were 57 and 22, pre and post intervention, and MSSA predominated. The median time to identification of S. aureus from blood cultures decreased from 19 h before to 1 h after the FilmArray BCID panel was implemented. This was associated with a shorter time to initiation of β-lactams (7.0 vs. 3.0 h, p=0.04) and decreased exposure to vancomycin (5.0 vs. 0.2 h, p=0.12) for patients with MSSA bacteremia in the post intervention period.

Conclusions: Rapid multiplex PCR testing resulted in a shorter time to initiation of appropriate therapy and decreased patient exposure to vancomycin in those with MSSA bacteremia. We are in the process of evaluating clinical outcomes including time to ID consultation and infection source control associated with rapid PCR detection.
Detailed Characterization of Atomoxetine Metabolism and Implications for a Bottom-Up PBPK Model for Dose Individualization in Children

**IC Dinh**, L Van Haandel*, KT Gibson*, RE Pearce*, A Gaedigk*, JS Leeder*

*Children’s Mercy Hospital, Kansas City, MO, United States

Atomoxetine (ATX) is a norepinephrine re-uptake transporter inhibitor that is used in the treatment of attention deficit hyperactivity disorder (ADHD). Therapeutic response to ATX in children is highly variable. Contributing to this, is the primary role of CYP2D6, a highly polymorphic enzyme, in ATX clearance. As variable therapeutic benefit may mirror variable active parent exposure, CYP2D6 genotype stratified *in vitro* studies were conducted to determine 

**K<sub>M</sub>, V<sub>max</sub>, and intrinsic clearance (Cl<sub>int</sub>)** for 4′-OH-ATX (the major ATX metabolite) formation in single-donor human liver microsomes of known CYP2D6 genotype, and pooled human liver microsomes. 

**K<sub>M</sub>, V<sub>max</sub>, and Cl<sub>int</sub> values determined from pooled microsomes were 2.4 µM, 478.5 pmol/min/mg protein, and 201.8 µL/min/mg protein respectively.**

To identify CYPs responsible for 4′-OH-ATX formation in PM and IM microsomes, a screen of ATX with heterologously expressed P450 isoforms and specific chemical inhibitor studies in pooled and single donor HLMs with CYP2D6 intermediate and poor metabolizer status was performed. CYP2E1 and CYP3A4 contributed to 4′-OH-ATX formation in livers with intermediate and poor CYP2D6 status. In livers with lesser CYP2D6 activity, 2′-methyl-OH-ATX and n-desmethyl-ATX formation (NDM-ATX), the metabolite formed by CYP2C19 metabolism, became more predominant pathways of metabolism. CYP2B6 appeared to be responsible for the formation of 2′-methyl-OH-ATX and NDM-ATX. Lastly, to better estimate metabolism in a clinical setting, an ATX screen at metabolism became more predominant pathways of metabolism. CYP2B6 appeared to be responsible for the formation of 2′-methyl-OH-ATX. CYP2E1 and CYP3A4 contributed to 4′-OH-ATX formation in livers with intermediate and poor CYP2D6 status. In livers with lesser CYP2D6 activity, 2′-methyl-OH-ATX and n-desmethyl-ATX formation (NDM-ATX), the metabolite formed by CYP2C19 metabolism, became more predominant pathways of metabolism. CYP2B6 appeared to be responsible for the formation of 2′-methyl-OH-ATX. Lastly, to better estimate metabolism in a clinical setting, an ATX screen at previously published goal ATX Cmax concentration (3 µM) and relevant ATX *in vivo* concentrations (1 and 10 µM) was conducted in a human liver microsome bank comprising of both pediatric (n = 73) and adult (n = 25) livers of known CYP2D6 genotype. Formation of 4′-OH-ATX was strongly associated with CYP2D6 activity. Formation of 2′-methyl-OH-ATX and NDM-ATX were consistent among livers of different CYP2D6 activity. However, relative contribution of 2′-methyl-OH-ATX and NDM-ATX to overall metabolite formation increased with lesser CYP2D6 activity. These data will be used to develop a physiologically based pharmacokinetic model (PBPK) to aid in individualizing dosing by predicting ATX exposure based on CYP2D6 genotype and knowledge of competing pathways of ATX metabolism.

VITAMIN D REDUCES PROGERIN EXPRESSION AND RESCUES GENOMIC INSTABILITY AND PREMATURE SENESCENCE IN HUTCHINSON-GILFORD PROGERIA SYNDROME.

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Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare, but devastating, premature aging disease. Patients present with a constellation of abnormalities, including cardiovascular disease, which lead to patient death in their teenage years. HGPS is caused by mutations in the *LMNA* gene, which encodes nuclear proteins lamin A/C. These mutations prevent the normal processing of lamin A, producing a permanently farnesylated and carboxymethylated toxic product called progerin. Progerin elicits profound nuclear morphological abnormalities, altered cell signaling, genomic instability, epigenetic alterations, and other cellular disturbances, all of which contribute to disease. New treatment strategies, specifically those aimed at reducing progerin levels, are desperately needed to treat this universally fatal disease, as current treatment regimens offer only modest benefits.

Recently, we observed that HGPS cells become vitamin D receptor (VDR) deficient before entering premature senescence. This is significant because VDR is a nuclear receptor that regulates approximately 3% of the transcriptome and mediates actions of vitamin D within the cell. Interestingly, VDR-deficient mice also exhibit abnormalities similar to those seen in progeria, including a premature aging phenotype, atherosclerosis, and cardiovascular complications. As a result, we investigated if VDR deficiency might contribute to HGPS disease phenotype.

Here, we show that HGPS cells treated with active vitamin D (1,25D) not only escape VDR deficiency but also display a greatly improved phenotype. 1,25D treatment prevents HGPS cells from entering premature senescence and endows them with enhanced replicative potential. Cells treated with 1,25D also show strikingly improved nuclear morphology and decreased genomic instability compared to vehicle treated cells. Most excitingly, we find that the vitamin D/VDR axis regulates *LMNA* gene expression through a vitamin-D responsive element downstream of the *LMNA* gene transcription start site. Consequently, prolonged treatment of HGPS cells with 1,25D results in a profound down-regulation of progerin expression. Thus, vitamin D/1,25D emerges from these studies as an exciting new therapeutic strategy to ameliorate defects and reduce progerin...
in HGPS cells. New studies must now be initiated to determine if 1,25D can improve phenotype and reduce progerin levels in in vivo models of disease.

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MATERNAL DEPRESSION, MATERNAL ASTHMA AND CHILDHOOD ASTHMA IN PUERTO RICANS
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Background: Asthma is the most common chronic disease of childhood and a major public health concern. Asthma burden is unequally distributed, with Puerto Ricans and non-Hispanic Blacks more heavily affected. The possibility of an interaction between maternal depression and asthma to explain disparities in childhood asthma remains unknown.
Objective: To examine the relationship among maternal depression, maternal asthma and childhood asthma in Puerto Ricans.
Methods: Cross-sectional study of 678 children (ages 6-14 years) with (n=351) and without (n=327) asthma in San Juan, Puerto Rico. Recruitment utilized a multistage probability sampling design. Maternal depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale (CESD), with depression defined as a CESD score ≥ 16. Cases were defined as physician-diagnosed asthma with ≥1 wheezing episode in the past year. Logistic regression was used for multivariate analysis of maternal depression and/or maternal asthma and childhood asthma. Since maternal depression and maternal asthma may be correlated, we analyzed these variables in separate models, the same model, and as a composite score (0=neither maternal depression nor maternal asthma, 1=either maternal depression or maternal asthma, and 2=both maternal asthma and maternal depression). Parental consent was obtained. Institutional Review Board approval was granted from University of Puerto Rico and University of Pittsburgh.
Results: Compared to controls, cases were younger, more likely to have maternal asthma, environmental tobacco smoke (ETS) exposure before age 2, and maternal depression. Multivariate analysis adjusting for age, gender and income, maternal depression was associated with 1.4 times higher odds of asthma (95% CI 1.03-2.03). However, this association was not significant after adjustment for maternal asthma (which was significantly associated with childhood asthma). In a multivariate analysis adjusted for age, gender, income and ETS exposure before age 2, children with either maternal depression or maternal asthma had 1.7 times higher odds of asthma than those with neither maternal depression nor maternal asthma (p=0.0027). Moreover, children with both maternal asthma and depression had 5.3 times higher odds of asthma than those without maternal asthma or maternal depression (p<0.0001).
Conclusions: Maternal asthma and maternal depression may impact the pathogenesis of childhood asthma in Puerto Ricans making recognition and treatment of maternal depression important.

MWSPR Plenary Session III

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RESPIRATORY SEVERITY AND CALORIC CONSUMPTION IN INFANTS ON NEURALLY ADJUSTED VENTILATORY ASSIST (NAVA). RANDOMIZED CROSSOVER TRIAL OF NAVA AND SYNCHRONIZED INTERMITTENT MANDATORY VENTILATION WITH PRESSURE SUPPORT (SIMV (PC) PS).
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Background: NAVA, a novel ventilatory support mode, delivers ventilator pressure assistance proportional to and in synchrony with the electrical activity of the diaphragm. NAVA has shown improvement in peak inspiratory pressures and dynamic compliance (DC) and decreased estimated work of breathing (WOB) in infants with respiratory failure. While this may benefit infants’ breathing, the impact of NAVA on respiratory severity or energy expenditure is unknown. Does the cost of increased caloric consumption with NAVA outweigh the benefits of its use?
Objective: To determine whether infants have improved respiratory severity scores (RSS) (MAP X FiO2) and/or resting energy expenditure (REE) on NAVA compared to SIMV (PC) PS.
Study Design: This crossover study included premature and term infants who were enrolled, randomized and ventilated with NAVA or SIMV (PC) PS for 12 hours then crossed over to the alternative mode for 12 more hours. A washout period up to 3 hours was allowed between each mode. The primary outcomes were RSS and caloric consumption/REE. Secondary outcomes included peak inspiratory pressures (PIP), mean airway pressures (MAP), tidal volumes (TV) respiratory rates (RR), fraction of inspired oxygen (FiO2), DC and estimated WOB.
Results: Twenty-two infants completed the 24-hour study. The RSS and measured REE were not significantly different between NAVA and SIMV (PC) PS. PIPs were significantly lower on NAVA (17.8 ± 20.1 cmH2O (p<0.05)) without increasing oxygen requirements (35.71 vs. 35.73 % (p NS)). Respiratory rates were higher on NAVA (52 vs. 39 bpm (p<0.05)) but WOB and DC was improved (0.66 vs. 0.73 J/L; 0.02 vs. 0.04 mL/cmH2O respectively (p<0.05)) on NAVA versus SIMV (PC) PS.

Conclusion: When compared to SIMV (PC) PS, infants ventilated with NAVA showed no increase in RSS or caloric consumption/REE. Our data suggest that NAVA can be a beneficial mode of ventilatory support for infants with respiratory failure.

22 LONGITUDINAL BODY COMPOSITION TRACKING IN PREMATURE AND TERM PRESCHOOLERS.
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Background: Rapid infancy weight gain is implicated in later life obesity for children born both prematurely and full-term. However, poorer growth is implicated in poorer neurodevelopmental outcomes for preterm children. More recent attention has focused on understanding body composition and proportionality in order to characterize optimal growth patterns in the preterm population. To date, only one other study has followed premature children’s body composition longitudinally beyond infancy.

Objective: To investigate associations between early body composition changes and preschool body composition in children born prematurely versus full-term.

Methods: A longitudinal cohort of appropriate-for-gestation preterm (n=20, mean gestational age 31.5 weeks) and term (n=50) infants were followed at three visits—1: near term (preterm’s corrected age (CA)), 2: at 3-4 months (preterm’s CA), 3: near 4 years. Assessments at all visits included body composition via air displacement plethysmography and anthropometrics. Associations between body composition measurements at and between visits 1 and 2 with visit 3 measurements were quantified using Spearman correlation coefficients adjusting for sex and visit 3 age.

Results: Although body composition differed between the two groups in infancy, measurements were similar by 4 years. Between visits 1 and 2 preterm infants demonstrated greater fat-free mass gain than term infants (5.02 vs. 4.58kg, p=0.01) and less %body fat gain (6.84 vs. 10.3%, p=0.04). In preterm children visit 3 %body fat moderately correlated with change in %body fat from visit 1 to 2 (r=0.51, p=0.03); visit 3 fat mass moderately correlated with visit 2 fat mass (r=0.54, p=0.02) and change in fat mass from visit 1 to visit 2 (r=0.59, p=0.01). Respective correlations were less robust in term children (r=0.35-0.36, p=0.01).

Discussion: Infancy to preschool age body mass accretion differs between those born prematurely versus at term. Similar to rapid weight gain, increased fat mass gains in infancy may be associated with later obesity. The associations at visit 2 and between visits 1 and 2 suggest interventions to promote optimal body mass accretion may be best applied following NICU discharge. Further, intervention to increase preterm infant’s growth prior to term CA may be less detrimental to long-term metabolic health than later catch-up growth. Future studies with additional subjects followed at more time points and with attention to interventions will enable best practices to optimize these children’s metabolic health.

23 MATERNAL HIGH-FAT DIET AND GESTATIONAL DIABETES MELLITUS MODIFY EXPRESSION OF PLACENTAL FUEL TRANSPORT AND STORAGE PROTEINS
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Purpose of study: The mammalian placenta plays vital roles in the maintenance of pregnancy and fetal nutrient transport. Maternal diabetes and obesity are associated with increased circulating fuels and fetal hyperinsulinemia that may affect the expression of various placental transport and storage proteins and contribute to adverse effects of the pregnancy and fetus. To better understand fuel-mediated consequences, this study aimed to determine alterations in placental nutrient transport and storage in response to maternal high-fat diet and diabetes, specifically through qualitative, quantitative and mechanistic measures.

Methods used: Female Sprague-Dawley rats received control (CD) or high-fat (HF) diet for 28 days before timed breeding. On gestational day (GD) 14, pregnant dams were given citrate buffer (CB) or streptozotocin (STZ) to induce diabetes which was then treated twice daily with sliding-scale insulin. On GD21, placentae were harvested via Cesarean-section from four groups: CD-CB (controls), CD-STZ (diabetes exposed), HF-CB (diet exposed), and HF-STZ (combined). Placental lipids were stained with Oil-Red-O for qualitative comparison of lipid droplet accumulation. Storage was analyzed using chloroform:methanol lipid extraction and triglyceride assay. qPCR evaluated expression of key placental fatty acid and glucose transport and storage genes. Groups
were compared using linear mixed models and by ANOVA with significance set at 0.05. **Summary of results:** Qualitatively, lipid droplets increased on both the fetal and maternal sides of the placentae in all exposed groups with the greatest increase in the HF-STZ group. Quantitatively, placental triglyceride levels increased 40.9% (p=0.0132) with diabetes (n=15), 44.4% (p=0.0044) with HF-diet (n=7), and 68.7% (p=0.0095) in combination (n=11). Unexpectedly, expression of FAT/CD36, FABP3, FATP1, PPARγ, ADRP decreased with HF-diet and diabetes exposure, expression of GLUT3 decreased with HF-diet alone, and expression of GLUT1, HSL, and LPL was unaffected. **Conclusions reached:** Excess lipid droplet accumulation in placentae exposed to excess circulating fuels cannot be explained by increased storage mechanisms; indeed expression of active transporters are decreased, implicating a placental protective role against lipotoxicity.

**Clinical correlation:** Our findings along with the increased risk of stillbirths in infants of obese or diabetic mothers, suggest that decreased placental lipid utilization could affect hormone production and placental metabolism necessary for maintenance of the pregnancy. These mechanisms should be further explored.

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MATERNAL HIGH FAT DIET AND DIABETES AFFECT NEPHROGENESIS IN DEVELOPING OFFSPRING.

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**Purpose of study:** Offspring of diabetic mothers have an increased risk of hypertension as early as adolescence. Hypertension often has an underlying renal pathogenesis. Diabetes and dyslipidemia are associated with altered circulating fuels which over time may lead kidney injury in adults. The effects of in utero exposure on kidney organogenesis are largely unknown. This study used a rodent model to characterize fuel-mediated differences in the developing kidney, specifically via lipid deposition, nephrogenesis, and expression of key proliferative genes/proteins.

**Methods used:** Female rats were fed high fat (HF) or control diet (CD) for 28 days before mating and throughout pregnancy. On gestational day 14, dams were given either citrate buffer (CB) placebo or streptozotocin (STZ) to induce diabetes. Hyperglycemia was partially controlled with twice daily sliding scale insulin. Kidneys were harvested from 1-day-old offspring (NBD1) and sections were stained for lipid droplets with Oil-Red-O; for proliferation with Ki67; and for nephrogenesis with PAX2 and NCAM. Stained sections were imaged using a Nikon 90i microscope and qualitatively compared between groups. RNA was purified from NBD1 kidneys using Quiagen RNeasy mini kit. qPCR was performed on cDNA using ABI 7500 system and data was analyzed using student's t-test. Significance was set at p<0.05.

**Summary of Results:** HF and diabetes exposed NBD1 kidneys demonstrated decreased lipid deposition compared to controls (CD-CB). Diabetes exposed offspring demonstrated much fewer Ki67 positive cells; the effect was most striking in the HF-STZ group. NCAM/PAX2 staining revealed abnormal ureteric bud and tubular alignment in the HF-STZ group. qPCR revealed a 1.64 fold increase in IRS-1 in the HF-CB group (p<0.05). Downstream activated protein comparisons are ongoing. There was no significant difference in gene expression of FGFR2, GDNF, PAX2, SIX2, or PTEN.

**Conclusions Reached:** Late gestation diabetes is associated with decreased nephrogenesis in developing rat offspring and the effect is exacerbated alongside a maternal HF diet. Abnormal ureteric bud branching and connectivity with the developing tubules may explain additional pathogenic mechanisms.

**Clinical Correlation:** The study adds to a growing body of evidence that maternal dyslipidemia during diabetic pregnancy exacerbates developmentally programmed disease and likely includes a renal pathogenesis of hypertension. Additional human studies and preventative measures should be investigated.

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THIOREDOXIN-INTERACTING PROTEIN STIMULATED BY HIGH GLUCOSE INDUCES ENDOTHELIAL CELL APOPTOSIS

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**Background:** Thioredoxin-interacting protein (TXNIP) inhibits cell growth and induces apoptosis. Our lab previously found that high glucose increases TXNIP mRNA and protein expression in primary human aortic endothelial cells (HAEC) and mouse aortic endothelial cells (MAEC). However, the role of endothelial TXNIP and the detailed mechanism of its regulation by glucose remain to be elucidated.

**Objective:** To dissect the underlying mechanism of apoptosis in endothelial cell induced by high glucose and TXNIP.
Materials and Methods: HAECs or MAECs were randomly divided into normal glucose (5.5 mM) and high glucose (30 mM), and then treated for 24 hours. We used the full-length TXNIP promoter as template and constructed a series of truncated or mutated TXNIP promoter mutants. The full-length- or mutated-TXNIP-promoter-driven pGL3-luciferase-reporter constructs were co-introduced with a Renilla-luciferase-reporter-expressing vector into HAECs or MAECs followed by the 24 h high glucose treatment. The relative firefly luciferase activities were measured following the manufacturer’s instructions. To confirm the effects of carbohydrate response element-binding protein (ChREBP), the major transcription factor responsible for glucose-dependent transcription, on endothelial TXNIP expression, we transfected HAECs with pcDNA-CMV-ChREBP or pcDNA-CMV-Laz constructs prior to the 24 h high glucose treatment. The normal-glucose- or high-glucose-treated HAECs were then subjected to western blot analysis, TUNEL staining and caspase-3 activity assessment.

Results: High glucose significantly increased TXNIP promoter activity. Promoter truncation assay suggests that 200 bp upstream of the TXNIP promoter, which contains the carbohydrate response element site is the most important part responsible for promoter activity induction by high glucose. ChREB mutation significantly decreases the stimulatory effect of high glucose. We also found that the TXNIP over-expression in HAECs caused by ChREBP over-expression accelerated high-glucose-induced apoptosis.

Conclusion: TXNIP expression may have major implications for endothelial biology especially in the responses to altered glucose homeostasis as seen in diabetes and insulin resistance. ChREBP plays an important role in high glucose induced TXNIP promoter activity through binding to the ChoRE site in the promoter region, which may link glucotoxicity and endothelial cell apoptosis. Our data provide potential therapeutic target for cardiovascular complications in the patients with diabetes.

26 GENETIC RISK FACTORS OF HLA-DRB1 AND COMPLEMENT IN AFRICAN AMERICAN AND SOMALI TYPE 1 DIABETES

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Background: Human Leukocyte Antigen (HLA) genes carry the highest genetic risk for type 1 diabetes in European American patients, but more study is needed of HLA and complement mediated diabetes risk in African American and Somali populations. Columbus has the second largest Somali population in the USA.

Methods: We studied 195 healthy black controls and 32 black T1D subjects (26 African American and 6 Somali). Total gene copy number (GCN) of C4, C4-long, C4-short, C4A, and C4B were determined by genomic Southern blot. HLA DRB1 genotypes were determined by sequence-specific-primer PCR. We used t-tests to compare continuous data, and report odds ratios (OR) with 95% confidence intervals (CI).

Results: DRB1*0301/DRB1*04 heterozygosity was present in 25% of T1D patients but absent in controls (p=1.2x10^-12). DRB1*15 and DRB1*08 were both absent in T1D and protective in controls (DRB1*15: 28.2% controls, p=6.8 x 10^-5; DRB1*08: 12.3% controls, p=.036). DRB1*04 alone was a risk factor [T1D 56.3%, control 13.9%, OR=4.1 (CI: 1.6—10.3); p=.0014]. After excluding patients with DRB1*0301 to control for linkage disequilibrium, C4A deficiency and single short C4 remained significantly more frequent in T1D patients (p=.006 and .015 respectively). Multiple logistic regression identified 6 independent genetic risk factors associated with T1D, including DRB1*0301/DRB1*04 heterozygosity, DRB1*04, DRB1*15, DRB1*08, total C4, and single short C4 haplotype (R²=0.49; p=1.7 x 10^-14, AUC=92.2). Regression analyses suggested that DRB1*0301 was secondary to total C4 GCN and the mono-short haplotype.

Conclusions: We found many traditional European American diabetes risk factors in African American and Somali T1D, including DRB1*0301, DRB1*04, and additionally low C4 GCN.

27 NONOATE RESTORES DISRUPTED INSULIN SIGNALING IN OFFSPRING EXPOSED TO HYPERGLYCEMIA.

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Background: Human and animal studies show that offspring of diabetic mothers are at higher risk for diabetes. However, the underlying mechanism is unclear. Due to complicated nature of maternal diabetes, the isolated role of fetal hyperglycemia has been uncertain. We and others have shown that maternal hyperglycemia decreases relative uterine blood flow.
Purpose: We hypothesized that maintaining normal uterine blood flow with the vasodilator NONOate, a nitric oxide donor, during maternal hyperglycemia would restore normal offspring skeletal muscle insulin sensitivity.

Methods: A left-sided arterial catheter was placed via the femoral artery placing the tip just upstream of the uterine artery take-off. Fetal rats on left uterine horn were exposed to hyperglycemia (HG) ± NONOate infusion for 48 hours via 4mg/min glucose infusion. C-section was performed at completion of infusion and offspring raised by foster-mothers. Insulin sensitivity was evaluated at postnatal day 21 by determining insulin stimulated Akt Phosphorylation in skeletal muscle and glucose tolerance testing (GTT).

Results: Fetal rats exposed to HG infusion were smaller (Normalized weight 13±2 % lower). At postnatal day 21, offspring exposed to HG infusion exhibited mild glucose intolerance during GTT (iAUC 33.7±33% increase, P<0.05, n = 9 vs 19) with decreased pAkt level (Normalized pAkt 24.4±10% decrease, P<0.05, n= 9 vs 19). By contrast, fetal rats exposed to HG+NONOate infusion had similar weight (3.40±0.11 vs 3.38+0.08 gram, P<0.05, n=20 vs 30) with no significant changes in pAkt level. At postnatal day 21, offspring exposed to HG+NONOate had normal GTT and similar skeletal muscle pAkt level compared to controls (n =12 vs 12).

Conclusion: Maternal hyperglycemia alone is sufficient to program offspring insulin sensitivity permanently. One of the underlying mechanisms is disruption of uterine blood flow during maternal hyperglycemia. Ultimately, rescuing uterine blood flow with a vasodilator prevents offspring insulin resistance.

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GLUCOSE FLUCTUATIONS IN DIABETES HAVE TARGETED EFFECTS ON THE OSTEOCYTE IN VITRO AND IN VIVO
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Though Type 1 diabetics have increased fracture risk, the effect of glucose fluctuation on bone cells has not been well-studied. While we have noted little effect of high and low glucose on osteoblasts, we have observed dramatic effects in osteocytes. In this study we used the streptozotocin (STZ)-induced diabetic rat model to test in vivo our hypothesis that elevated glucose and increased glucose variation would result in increased SOST/sclerostin expression in osteocytes and increased circulating serum sclerostin.

Male Sprague-Dawley rats were divided into diabetic and control groups. Diabetic animals were given one dose of STZ (70 mg/kg), resulting in elevated blood glucose within 2 days and were treated with insulin via osmotic pump. We recorded blood glucose measurements. At 8 weeks, long bone and serum samples were taken, and primary osteocytes isolated from long bones. Osteocytes were cultured under 5.5mM and 25mM glucose conditions. qPCR for SOST mRNA was performed on whole bone and cultured osteocytes and ELISA for sclerostin protein was performed on serum samples and culture media.

Glucose variability and maximum glucose were significantly increased in the diabetic vs. control animals (670/796 vs. 102/142 mg/dL). Immunostaining of bone showed greater sclerostin levels in diabetic compared to control animals. Relative SOST mRNA expression was increased 4 fold in the long bones of diabetic animals. SOST mRNA and sclerostin were elevated in cultured osteocytes from diabetic animals compared to normal. This 60+ fold increase was comparable to that seen in the IDG-SW3 osteocytic cell to high glucose. Surprisingly, serum sclerostin from the rats was decreased in diabetics compared to controls.

Diabetic rats express higher levels of SOST in bone, correlating with both high glucose levels and increased variability. Cultured osteocytes from diabetic animals continue to express higher levels of SOST and sclerostin in culture, showing retention of the in vivo phenotype. Despite this, the diabetic animals have lower serum sclerostin, reflecting retention of sclerostin in bone matrix. These data suggest that high glucose and glucose variability have a detrimental effect on bone through a dramatic increase in sclerostin production by osteocytes. Local elevation in sclerostin may be a contributor to increased fractures in diabetics.

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QUALITY MONITORING IDENTIFIES CRITICAL GAPS IN ROUTINE PRIMARY CARE AUTISM/DEVELOPMENTAL SCREENING PRACTICES.
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Significance: The American Academy of Pediatrics (AAP) recommends general developmental screening at 9, 18 and 24/30 month well-child visits, and autism-specific screening at 18 and 24/30 month visits. Standardized screening tools perform well when implemented correctly, but the AAP does not provide recommendations on how to monitor screening and referral implementation.
Objective: To develop and implement a novel quality monitoring plan in the primary care clinics of a large urban hospital in order to examine the real-world outcomes of AAP-recommended autism/developmental screening practices.

Methods: Electronic health records (EHRs) for 9, 18 and 24/30 month well-child visits from two one-month samples (n = 731) were manually coded to quantify the extent to which providers (faculty, residents, and nurse practitioners) correctly administered screeners for autism (Modified Checklist for Autism in Toddlers; M-CHAT) and general development (Parents’ Evaluation of Developmental Status; PEDS), as well as the rate of referrals for children who screened positive.

Results: When implemented according to published administration standards, the sensitivity and specificity for both the M-CHAT (>85%; >99%) and PEDS (>74%; >70%) are strong. However, real-world implementation of both measures in this sample resulted in provider sensitivity well below acceptable clinical standards (22.2% correctly identified positive M-CHATs; 33.8% correctly identified positive PEDS). Moreover, only 33% of children who screened positive on either measure received a referral for further evaluation or early intervention.

Conclusions: Clinics that routinely use evidence-based screening tools may unknowingly use these forms incorrectly, and may not respond to positive screens appropriately. Quality monitoring can identify these implementation problems, and guide systems-based quality improvement interventions to correctly identify children at risk for developmental problems. While efforts to improve screening at this hospital are ongoing, the quality of screening administration is universally overlooked in clinical and research settings elsewhere.

Implications for practice: AAP autism/developmental screening guidelines fail to consider how clinicians and researchers should monitor and quantify the implementation of these tools. We propose that a quality improvement and monitoring approach can bridge this gap, ensuring that screening efforts in primary care actually result in the identification and referral of children at risk.

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SEPSIS-INDUCED LUNG INFLAMMATION IN THE DEVELOPING LUNG IS ATTENUATED WITH NADPH OXIDASE 2 BLOCKADE

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Background: Although sepsis is a major risk-factor for lung inflammation and bronchopulmonary dysplasia (BPD) in preterm infants the key molecular players that regulate sepsis-induced lung inflammation remain understudied. We hypothesized that NADPH oxidase 2 (NOX2) regulates Toll-Like Receptor (TLR, bacterial recognition receptor) mediated neonatal lung inflammation in sepsis.

Methods: Sepsis was induced in 6-day C57Bl/6J mice using i.p lipopolysaccharide (LPS, Invivogen, 1mg/kg), and lung inflammation was assessed after 20hr. For NOX2 inhibition, the specific NOX2 inhibitor gp-91 ds tat (Nox2-I, Anaspec, 5mg/kg) was i.p injected 2.5hrs prior to LPS injection. Harvested lung homogenates were used for PCR and western blot to look at inflammatory genes and TLR signaling.

Results: Sepsis robustly induced lung expression of IL-1β and ICAM-1 protein, as well as TNF-α, IL-1β, and KC RNA at 20hr (p<0.04, n=4). Lung phosphorylation of IKKβ, p38, and JNK; markers of TLR pathway activation were also demonstrated with sepsis. Mice treated with Nox2-I showed decreased lung inflammation as evidenced by decreased TNF-α, IL-1β, and KC RNA, and ICAM-1 and IL-1β protein after sepsis (Fig. 1). Lung IKKβ-phosphorylation, p38-phosphorylation, and JNK-phosphorylation were also attenuated with Nox2 inhibition in sepsis (Fig. 2).

Conclusions: These data demonstrate that NOX2 regulates inflammation in the developing lung during sepsis by regulating the IKKβ-MAPK pathways. Targeting NOX2 during sepsis might inhibit lung inflammation and decrease BPD in premature infants.

Fig. 1

Fig. 2
31
DOCUMENTATION OF NUTRITIONAL STATUS IN PATIENTS AGED <24 MONTHS ADMITTED TO AN URBAN INNER CITY HOSPITAL

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Background: Malnutrition prevalence rate in hospitalized children over the last 10 years in US and Europe has ranged from 6-14%. Determining the nutritional status of patients in the hospital and clinic setting, can lead to better clinical outcomes.

Objectives: 1) To determine the prevalence of malnutrition (MN) in inpatients <24 months of age. 2) To review chart documentation of MN diagnosis.

Methods: Retrospective chart review of patients <24 months admitted at Sinai Children’s Hospital from January 1, 2014 to December 31, 2014. Demographic data on admission and documentation of diagnosis for MN were obtained from the patients’ electronic medical records. The indicator and criteria for MN was Weight-for-length (WFL) and Z score ≤-2, respectively. Using PediTools to determine Z-scores based on the 2006 WHO Growth Standard for 0-24months, each patient’s Z-score was calculated. Nutrition status categories were: a) Healthy, Z-score above -1, b) Healthy at risk, Z -1 to -1.99, c) Moderate-MN, Z-score -2 to -2.99 and d) Severe-MN, Z below -3.

Results: 508 infants were included in the analysis, 39% were Female, 80% Term, 60% African American and 40% Hispanic. 73% (n=371) were classified as Healthy, 14% (n=71) Healthy at risk, 7.5% (n=38) Moderate-MN and 5.5% (n=28) Severe-MN. No significant differences in gender (12.9% male vs. 13.1% female, p=0.9), race (12.2% Hispanic vs. 13.5% African-American, p=0.6) and gestational age (11.8% term vs. 18% preterm, p=0.4) were observed among those identified as malnourished. Of 13% (66/508) patients identified as malnourished, 1.5% was diagnosed Moderate MN with chart documentation and 98.5% (Moderate-MN 56.1% and Severe-MN 42.4%) had no documentation of MN diagnosis. Table 1. Malnutrition Diagnosis and Documentation

<table>
<thead>
<tr>
<th>MN Criteria Met n(%)</th>
<th>Documentation n(%)</th>
<th>No Documentation n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate 38(7.5)</td>
<td>1(1.5)</td>
<td>37(56.1)</td>
</tr>
<tr>
<td>Severe 28(5.5)</td>
<td>0(0)</td>
<td>28(42.4)</td>
</tr>
<tr>
<td>Total 66(13)</td>
<td>1(1.5)</td>
<td>65(98.5)</td>
</tr>
</tbody>
</table>

Conclusion: Prevalence rate of MN was 13% in our patient population. The high percentage of underrecognition may be due to practice inconsistencies in measuring nutritional risk on patients upon admission and its subsequent chart recording. Encouraging the use of screening tools and initiatives to educate clinicians on the proper identification and documentation of MN diagnosis should be promoted.

32
NEURODEVELOPMENTAL FOLLOW UP AND NEUROIMAGING IN NEONATAL HYPOXIC RESPIRATORY FAILURE

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Background: Patients with Neonatal hypoxic respiratory failure (NHRF) are at risk of future neurodevelopmental delay. Currently there is limited data of neuroimaging and neurodevelopmental outcome in this patient population.

Objective: To define the pattern of MRI abnormalities in NHRF and to establish the predictive accuracy of Neuroimaging for neurodevelopmental outcome in this patient population.

Design/Methods: This is a retrospective study from 2009-2012. Eligibility criteria: All patients ≥ 34 weeks gestation and ≤ 14 days of age, who were admitted to NICU with NHRF and required either inhaled nitric oxide (iNO) or Extracorporeal membrane oxygenation (ECMO). Neurodevelopmental data was collected from the developmental assessment clinic (DAC). Disability was defined as either: Bayley III Cognition, Language or Motor score <85, GMFCS grade 2-5, Hearing impairment, Blindness or Speech delay. All MRI were read by a single pediatric radiologist.

Results: A total of 75 patients (iNO=47, ECMO=28) were included in the study. Mortality was 14.6% (N=11) and 46.6%(N=35) were followed in the DAC. Of the patients who followed in DAC, 54.3% (N=19) had atleast one disability. 40% (N=30) patients had MRI performed (iNO=12, ECMO=18), out of which 80% (N=24) patients had an abnormal MRI. 73% had focal/diffuse white matter lesions, 46.6% had basal ganglia/thalamic lesions, and 53.3% had focal parenchymal/intraventricular hemorrhage. 23 patients had both MRI and neurodevelopmental data. There was no difference in MRI findings among patients with or without disability. 17% of these 23 patients had normal MRI but had disability on follow up.
Conclusions: There is high risk of neurodevelopmental disability among patient with NHRF. There was no difference in MRI findings among patients with or without disability.

33
ATTITUDES, BELIEFS AND KNOWLEDGE ABOUT SEX AND CONTRACEPTION AMONG LATINO YOUTH IN RURAL KANSAS.

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1Children’s Mercy Hospital, Kansas City, MO; 2University of Kansas, Kansas City, KS.

Purpose: Although pregnancy rates for Latino adolescents in Western Kansas are three times higher than the rate for White non-Hispanics, limited studies have focused on this vulnerable group. We aim to describe attitudes, beliefs, and knowledge about family planning among this group.

Methods: Latino adolescents aged 15-24 years in rural Western Kansas completed an anonymous self-administered survey and focus groups stratified by age and gender (15-19 and 20-24 years old). Groups discussed attitudes, subjective norms, and perceived behavioral control of sex, teen pregnancy and contraception. Bi-lingual moderators conducted, audiotaped and transcribed sessions verbatim. Reviewers evaluated the data using an open coding process.

Results: Participants (125) completed an anonymous self-administered survey and participated in 25 focus groups. Their mean age was 18 [SD=2.72], mostly Christian or Catholic [86.2%]. More than half (53%) of participants were female; had been living in the USA for over 10 years (54%) and 47% spoke only Spanish at home. Roughly half (56.2%) of the participants had attended Sexual education classes. Out of the sexually active participants (41%), 75% never received sexual health care. Focus groups discussed Sex viewed by all as a “taboo” topic, ”prohibited before marriage”. Adolescents were more likely to talk to their older siblings or cousins about sex, than to parents or doctors; Teen pregnancy: although frequent, was viewed as disrespect to their families. However, the birth was “a new life” and eventually embraced; Contraception: Girls reported it is difficult to access confidential reproductive health services and seeking contraception was viewed by the community as a sign of “being easy”. Contraceptive knowledge primarily consisted of condoms and oral contraceptive pills. Boys described contraception as “having an abortion”, “killing the sperm”, and that “it means someone doesn’t have a chance to live”. Although condoms were more accepted among boys, withdrawal was the main contraceptive method.

Conclusions: Latino teens in rural Kansas grow up with community, religious, and familial expectations of “staying virgins till matrimony.” Despite engaging in sexual behaviors counter to this expectation, limitations on health care knowledge and access to family planning services likely contribute to the high rates of unplanned pregnancy in this region. Clinical correlations: These findings underscore the need for a culturally-relevant community-based pregnancy prevention strategy to reduce disparities in this disadvantaged youth.

34
“HUMAN PAPILLOMA VIRUS INFECTION AND VACCINE KNOWLEDGE AMONG YOUNG LATINOS IN WESTERN KANSAS”.

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1Children’s Mercy Hospital, Kansas City, MO; 2University of Kansas Medical Center, Kansas City, KS.

Purpose: Human papilloma virus (HPV) is the most common sexually transmitted infection (STI) in the US, with estimated 79 million Americans currently infected. Although most infections resolve on their own, infections are associated with warts, oral and anogenital cancers. Hispanic women have higher HPV-associated cervical cancer incidence rates than non-Hispanic women in the US. Although HPV vaccines are safe and effective, national HPV immunization coverage is low among 13-17 years old (57%) with the lowest percentage in Kansas (39%). Latinos have become the fastest growing minority group in the Midwest. The purpose of this study was to better understand knowledge about HPV infection and HPV vaccine among rural Latino youth in southwest Kansas.

Methods: Latino youth aged 15-24 residing in southwest Kansas were recruited to complete an anonymous self-administered survey that assessed acculturation, reproductive health care access and knowledge about HPV infection and vaccine.

Results: A total of 125 participants (mean age 18.2; SD=2.72) completed an anonymous self-administered survey. Most subjects described themselves as Christian or Catholic (86.2%), living in the US for over 10 years (54%). More than half were female (52.8%), attended sexual education classes (56.9%) and had health insurance (67.5%). However, most participants did not know that: HPV is the primary cause of cervical cancer (69.7%); HPV infections can lead to anal and throat cancers (63.9%); HPV vaccine is safe (79%), it protects against various HPV related cancers (67.2%) and it is not associated with sterilization (90.7%). Also, more than half of the subjects did not know that HPV viruses may cause genital warts (53.8%). However, 61.3% knew HPV
is a STI. Half of the participants (43%) reported being sexually active, but the majority (91.1%) of the sexually active population had never received sexual health care.

**Conclusions:** Kansas population has the lowest HPV vaccination rates of the country. There is an important growing Latino population in Western Kansas. Regardless of insurance coverage and sexual education, Latino youth in Western Kansas seem to lack basic knowledge about HPV infection and immunizations.

**Clinical Correlations:** Targeted education to the growing Latino youth in Western Kansas on HPV infections and HPV vaccines could impact immunization rates in the state of Kansas and improve Latino health, the most affected group by cervical cancer.

### 35

**PREDICTORS OF EXTREME EARLY RESPONSE TO METHOTREXATE IN JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Intracellular methotrexate polyglutamates (MTXGlu) have been proposed to be effective biomarkers of clinical response in rheumatoid arthritis and juvenile idiopathic arthritis (JIA). However, response and toxicity to MTX in patients with JIA remains unpredictable. This study aims to identify predictive biomarkers of early extreme response and non-response to MTX in children with JIA.

**Methods:** This is a single center prospective cohort study of newly treated JIA patients on standardized doses of MTX (15mg/m²) and folic acid (1mg/day). After obtaining informed consent, samples for intracellular erythrocyte folate ([total folate]; comprised of 5-methyl-tetrahydrofolate + 5-10 methenyl-tetrahydrofolate) and MTXGlu measurements by ultra-performance liquid chromatography-tandem mass spectrometry are collected prior to MTX (baseline), and after 3 and 6 months on therapy. Clinical data are collected at each time point and include the juvenile arthritis disease activity score (JADAS) and the American College of Rheumatology (ACR) core set criteria. Extremes of response include “poor responders”, defined as subjects who did not achieve 30% improvement from baseline (< ACR Pedi 30 response) and “optimal responders” who achieved more than 70% improvement from baseline (ACR Pedi 70 +). Statistical significance was tested using ANOVA, t-test, and chi square, utilizing Wilcoxon Rank Sum or Spearman’s correlations in non-normally distributed data.

**Results:** Of the 53 subjects who completed a 3 month visit, 14 (26%) were poor responders, and 13 (25%) were optimal responders. Age, gender, route of MTX, and baseline JADAS scores were similar between the two extreme response groups. Baseline and 3 month mean (±SD) [total folate] were higher in optimal responders compared to non-responders (baseline: 1159.6 (± 377) vs. 797.7(± 307) nmol/L, p=0.01 and 3 month: 794 (±216) vs. 610.9 (±192) nmol/L, p=0.03). Optimal responders had a greater decline in folate from baseline (p=0.04) and had a higher proportion of long chain MTXGlu₃₋₅ (0.63 (±0.16) vs. 0.48 (±0.15), p=0.04).

**Conclusion:** Differences in baseline cellular folate concentrations and the degree of folate depletion differentiate optimal from poor responders to MTX. Better characterization of the impact of MTX upon the folate pathway may improve individualization of JIA treatment in the future.

### 36

**RATE, CAUSES, AND CIRCUMSTANCES OF DEATH OVER A 20-YEAR PERIOD IN THE SOLE COMPREHENSIVE NEONATAL UNIT IN A RURAL STATE**

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*Department of Pediatrics, University of Iowa, Iowa City, IA, USA

**Purpose:** To examine changes in the principal causes and circumstances of all consecutive neonatal deaths in a Level IV neonatal intensive care unit (NICU) over a 20-year period.

**Methods:** We analyzed data for 551 infants who died before discharge out of 13,952 infants admitted to our NICU during a 20-year period between July 1, 1993 and June 30, 2013. The principal cause of death was determined by the NICU medical director, and deaths were classified into 13 categories. Circumstances of death were classified into four categories: 1) died with CPR, 2) died on ventilator without CPR, 3) life support interventions withheld, and 4) life support interventions withdrawn. Data were compared across four distinct 5-year epochs.

**Results:** The mortality rate decreased over the 20-year period: 5.9%, 4.0%, 3.4%, 2.6% (P<0.0001). The leading cause of death in all four epochs was congenital anomalies, with the percentage of deaths due to this cause trending upward. The percentage of deaths due to all other categories either decreased or remained stable. The most common circumstance of death involved withdrawal of life support (74.6%). The decision to withhold care occurred in 1.8% of deaths. Death while ventilated without CPR occurred in 7.8% of deaths. CPR preceded 15.8% of deaths. Parents were involved in the end-of-life decision-making process in 90% of cases.
The most commonly documented reasons for limitation of care were futility of treatment in the face of limited life expectancy (65%) and poor developmental prognosis (32%).

**Conclusion:** The mortality rate per admission declined significantly between 1993 and 2013, consistent with improvements in neonatal intensive care during this 20-year period. In our NICU, withdrawal of life support interventions was the most common circumstance of death, with only 15.8% of deaths occurring despite maximal intensive care. Futility of treatment and poor developmental prognosis were common reasons for limitation of care. These results indicate that, in our unit, perceived futility of continued treatment and concerns for quality-of-life are important considerations in the end-of-life decision-making process. Parental involvement in end-of-life decision-making remains a priority at our institution.

37

**BODY TEMPERATURES OF VERY LOW BIRTH WEIGHT INFANTS ON ADMISSION TO A NEONATAL INTENSIVE CARE UNIT**

**Ea O’Brien,** JE Brumbaugh,† GA Cress,† KJ Johnson,† TT Colaiazy,† JM Klein,† EF Bell†

*College of Liberal Arts & Sciences and †Department of Pediatrics, University of Iowa, Iowa City, IA, USA*

**Background:** Low body temperature is a common finding in preterm infants, especially during the first hours of life. Because preterm infants have immature thermoregulatory capacity, they require a protected thermal environment to limit body heat loss and avoid hypothermia, a potentially harmful complication.

**Methods:** We examined the frequency and degree of low and high body temperature among very low birth weight (VLBW) infants on admission to the University of Iowa Children's Hospital neonatal intensive care unit (NICU) and compared inborn and outborn patients. Normothermia was defined as 36.5–37.4°C (Mayfield SR et al, *J Pediatr.* 1984;104:271). Severe, moderate, and mild hypothermia were defined as <35°C, 35.0–35.9°C, and 36.0–36.4°C, respectively.

**Results:** We studied 667 infants (532 inborn and 135 outborn) who were admitted to the NICU from May 1, 2008 through April 30, 2013. The distribution of admission temperatures among all VLBW infants was:

<table>
<thead>
<tr>
<th></th>
<th>Inborn</th>
<th>Outborn</th>
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<tbody>
<tr>
<td>&lt;35°C</td>
<td>11.7%</td>
<td>11.1%</td>
</tr>
<tr>
<td>35.0-35.9°C</td>
<td>40.4%</td>
<td>21.5%</td>
</tr>
<tr>
<td>36.0-36.4°C</td>
<td>27.1%</td>
<td>20.0%</td>
</tr>
<tr>
<td>36.5-37.4°C</td>
<td>19.4%</td>
<td>43.7%</td>
</tr>
<tr>
<td>≥37.5°C</td>
<td>1.5%</td>
<td>3.7%</td>
</tr>
</tbody>
</table>

There was a lower prevalence of moderate hypothermia and a higher prevalence of normothermia (both P<0.0001) among outborn infants compared with inborn infants.

**Conclusion:** Hypothermia at the time of admission to the NICU is common among very low birth weight infants. Outborn infants were less likely to be hypothermic, presumably because they were older at the time of admission, had been provided thermal support during transport, and had had more time for thermal adaptation. Infant body temperature and its regulation within the first hours of life are crucial to health and survival. Reducing hypothermia soon after birth has the potential to reduce mortality and improve outcome of preterm infants.

38

**PSYCHIATRIC SYMPTOMS AND EPILEPSY IN A MALE PATIENT WITH PATHOGENIC PCDH19 GENE VARIANT MOSAICISM.**

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Children's Mercy Kansas City, Kansas City, Mo.

**Background:** PCDH19 encodes protocadherin-19, a calcium dependent cell adhesion molecule expressed throughout the central nervous system, associated with brain development and synaptogenesis. Through cellular interference, females with heterozygous PCDH19 variants develop early infantile epileptic encephalopathy-9 (EIEE9), also known as epilepsy and mental retardation restricted to females (EFMR), while carrier males are usually affected only by psychiatric symptoms. EIEE9 is characterized by early normal development followed by febrile seizures that tend to occur in clusters. The phenotype arises in heterozygous females who have two populations of neurons: wild type, and PCDH19-. Hemizygous males who have a homogeneous PCDH19- population of neurons remain carriers, however mosaicism has the potential to confer susceptibility to the EIEE9 phenotype in males.

**Methods:** A six year old male with obsessive compulsive symptoms, ADHD, and epilepsy was enrolled in a genome sequencing program for diagnosis of monogenic disorders. The patient had onset of seizures at 9-months, which were initially refractory to treatment. Anxiety based behavioral issues emerged by age 3, with subsequent development of obsessive compulsive symptoms. Exome sequencing was performed on an Illumina HiSeq 2500 with 2 x 100 nucleotide sequences. Sequence was aligned to the human reference 37 and variants were detected and genotyped with the Genome Analysis Toolkit. Variants were annotated with the Rapid Understanding of Nucleotide variant Effect Software.
**Results:** A truncating mutation was identified in PCDH19, c.605C>A (p.Ser202*). The variant was not detected in the patient’s mother, and was presumed de novo. The patient appeared to have an admixture of the variant and normal nucleotides at this position, which is atypical of a hemizygous male. Sanger sequencing confirmed that the variant was present in approximately 50% of the lymphocyte derived DNA, and PCDH19 variant mosaicism was determined to be the etiology of this patient’s presentation. **Discussion:** Increased use of next generation sequencing has resulted in an expanded phenotype for many genes associated with neuropsychiatric disorders. In the era of phenotype driven serial gene testing, patients with atypical features for a disorder were often undiagnosed. However, the capacity of whole exome / genome sequencing to detect pathogenic changes in all genes enables clinicians to quickly diagnose such patients. This case illustrates an unusual case of a male presenting with both psychiatric symptoms and a female-specific form of epilepsy secondary to PCDH19 mosaicism.

**39**

**CORD BLOOD ERYTHROPOIETIN LEVELS AFTER MATERNAL OBESITY DURING GESTATION**

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**Background:** Maternal obesity during pregnancy complicates up to 30% of pregnancies in the U.S. Complications include higher risk for diabetes, fetal overgrowth, labor and delivery complications, and higher risk for cesarean deliveries. We previously found that iron status in cord blood (CB) was poorer after maternal obesity in pregnancy, with evidence for stimulated erythropoiesis vs. controls. Erythropoietin (Epo) stimulates erythropoiesis. Other than acute hypoxia, little is understood about programming of fetal Epo production. In adults, iron depletion directly stimulates renal Epo transcription, rising blood levels, but Epo is produced in the liver and it is not known if iron regulates fetal Epo.

**Objective:** To examine CB plasma erythropoietin (Epo) level in a 202-member cohort at-risk for developing iron deficiency anemia in infancy.

**Methods:** We compared CB-Epo, CB-Ferritin, and CB-Reticulocytes with fetal and maternal morphometric parameters.

**Results:** CB-Epo was unrelated to fetal growth indices, weight, baby BMI or baby z-score for weight, nor was CB Epo higher if baby was LGA vs. not. CB Epo was directly related to maternal BMI at delivery, \( p<0.01 \). When dichotomized by obese (BMI≥30 kg/m\(^2\)) or lean BMI<30kg/m\(^2\) at delivery, CB-Epo was higher in obesity, \( p<0.01 \). Similarly, CB-Epo was higher if dichotomized by excessive pregnancy weight gain (>18 kg) vs. not, \( p<0.05 \). CB Epo levels were higher with maternal diabetes vs. not, \( p<0.03 \), but this relationship was stronger if maternal obesity and diabetes was combined with an LGA baby (LOD), \( p<0.02 \). CB Epo levels were higher in those with the lowest quartile of CB-ferritin, \( p<0.002 \). Multivariate analysis showed that the combination of LOD and poor CB-ferritin equally impacted CB-Epo.

**Conclusion:** Greater fetal tissue growth did not independently impact CB-Epo, but placental dysfunction in LOD may lead to a hypoxic fetal environment in LOD, while poor placental iron delivery depletes fetal tissue iron. Oxygen consumption due to tissue growth did not appear to stimulate hypoxia, but placental dysfunction in LOD and fetal iron depletion may work in concert to determine CB-Epo levels.

**Clinical Implication:** Continued work in understanding the nutritional regulation of Epo in obesity is needed in order to decrease fetal complications of obesity during gestation.

**40**

**BIOIMPEDANCE TO MEASURE FETAL BODY COMPOSITION IN AN OVINE UTERINE SPACE RESTRICTION MODEL**

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**Background:** Ovine pregnancy can model aspects of human intrauterine growth restriction (IUGR) resulting from multifetal gestation. IUGR offspring exhibit morphological changes in organ size and development, as well as physiological changes, including decreased vascular volumes. However, the effect of multifetal IUGR on fetal lean mass and body composition is unknown. Bioimpedance analysis (BIA) is an established method to non-invasively measure body composition in adult humans and adult animals, however, no fetal species-specific formulae or constants exist for commercial BIA meters.

**Purpose:** To use BIA, including resistance, reactance, impedance, and phase angle to predict lean and fat mass in fetal sheep to test the hypothesis that body composition is altered in fetuses born uterine space restricted.
**Methods:** Using MATLAB software, several formulae were generated based on near-total fat weights during fetal harvests and previous ovine BIA equations. IUGR (<10th % of singleton population) was defined at each of three gestational day (GD) ages, GD120, GD130, GD140, with term at 147 days.

**Results:** First attempts at formulae generation using BIA indices showed abnormally high variability among animals. Resistance, proportional to lean body mass, did not vary using singleton, twin, triplet, and quad/quint group-wise comparisons. However, when contrasting growth percentiles, IUGR fetuses had higher resistance (ohms) than normal fetuses (57.2±2.3 vs. 52.5±1.1, p<0.03), while small fetuses, <25th, also had higher resistance than larger fetuses (56.3±1.6 vs. 51.5±1.3, p<0.01). IUGR fetuses also had a lower phase angle than normal fetuses (5.97±0.54 vs. 14.5±2.13, p<0.001).

**Discussion/Conclusions:** Proportionately more fat or bone than lean body mass and/or dehydration would increase BIA resistance. Phase angle combines reactance (measures cell membrane integrity) and impedance (integrates reactance and resistance) to measure cell viability. Increased cell death and breakdown cause lower phase angles. Significant differences in BIA measures in the anticipated directions in IUGR vs. normal ovine fetuses supports ongoing work in this field. More detailed validation of fetal fat, bone, lean, and water mass compartments would aid generation of formulae. Further work defining formulae and constants in the sheep model is needed.

**Clinical Correlation:** BIA in neonatology clinical practice would be a simple and easy-to-perform biomarker of fetal well being in premature and term IUGR newborns that assesses cell catabolism and lost lean body mass.

**Support:** NIH HL117341 and HD38843.

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**41**

**ENOXAPARIN TREATMENT OF VENOUS THROMBOEMBOLISM IN THE NEONATAL INTENSIVE CARE UNIT.**

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Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh, Pittsburgh, Pennsylvania.

**Background:** Venous thromboembolism (VTE) is a significant cause of morbidity in the neonatal intensive care unit (NICU), and is often managed with low molecular weight heparins such as enoxaparin. Ideal treatment of VTE in the NICU setting likely differs from that of older patients because of the unique features of neonatal vasculature, hemostasis and thrombosis, and may differ for NICU patients of different gestational and corrected ages. However, relatively few studies have looked at VTE in the NICU setting, and fewer still have focused on enoxaparin treatment and long-term follow-up. Objective: To describe the presentation, treatment, and follow-up of NICU patients diagnosed with VTE.

**Methods:** Infants admitted to the Children's Hospital of Pittsburgh NICU between 2007 and 2013 were retrospectively screened for development of venous thromboembolism. Data was collected on patient demographics, medical comorbidities, hospital course, VTE development, treatment, and sequelae up to 6 months. Enoxaparin dosage, dosage adjustment, and monitoring was compared based on gestational age, corrected age, and medical comorbidities.

**Results:** We identified 33 VTE in 27 NICU patients with a mean age of 20 days and gestational age of 32 weeks. Enoxaparin treatment was initiated in 19 (70%) infants, with a mean initial dose of 2.8 mg/kg/day. This dose was increased a mean 2.3 times over 4.5 days before target anti-factor Xa levels were reached, which occurred at a mean enoxaparin dose of 4.0 mg/kg/day. Gestational age did not have a significant impact on enoxaparin dosing or anti-factor Xa levels. Infants with a corrected age less than 40 weeks received a significantly higher initial enoxaparin dose and required higher dosing to achieve target anti-factor Xa levels. However, these infants reached target levels after fewer days of therapy. Review of hematology and other evaluations up to 6 months after hospital discharge identified no incidences of major bleeding, heparin-induced thrombocytopenia, osteoporosis, or other adverse events associated with enoxaparin.

**Conclusions:** In the NICU setting, VTE is frequently managed with enoxaparin. More aggressive dosing for younger neonates may result in earlier therapeutic levels of anti-factor Xa without an increase in adverse events. This suggests that more aggressive initial dosing or dosing adjustment may be safe and beneficial in older infants, and should be evaluated in future studies.

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**42**

**RATES OF NONCONTRAST HEAD CT USE IN PRE-VERBAL CHILDREN IN AN ACADEMIC HOSPITAL FOLLOWING THE PECARN HEAD INJURY STUDY**

**Brown JB, Haddad H, Puffenbarger M, Heneghan J.**

Rainbow Babies and Children's Hospital, Cleveland, OH.

**Background:** Kupperman et al and PECARN published a prospective study in 2009 demonstrating that the use of a clinical guideline algorithm could identify patients at very low risk for ciTBI after head trauma without the
use of head CT. Our aim was to determine whether PEM physicians at a pediatric teaching hospital were
ordering fewer Head CTs after these guidelines were published.

**Methods:** Retrospective chart review of patients <2 yrs age with head injury identified by discharge diagnosis
code 959.01 (head injury, unspecified). Chi-squared comparisons of CT use in years before and after clinical
guidelines were published.

**Results:** CT use amongst all subjects decreased from 49.7% in 2007-2008 pre-guideline (“Before”) group to
26.3% in 2012-2013 post-guideline (“After”) group. A similar pattern was observed when patients were
excluded for pre-existing neurologic or hematologic conditions, altered mental status, shunt, CNS tumor, or
signs of severe penetrating injury. Odds of CT use was higher in patients less than 6 months age, compared to
patients between 6 and 24 months. Odds of receiving CT in Before group were more than two times higher than
After group (Table 2). CT use decreased among all age groups evaluated.

Interpretation: PEM physicians appear to be decreasing CT use in accordance with published clinical head
injury guidelines.

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**NEONATAL AUTOPSY AND PARENTAL GRIEF**

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**Background:** Details surrounding the death of child leave a lasting impression on families. The decision to have
an autopsy is one aspect of end-of-life care that can be particularly troublesome. The medical benefits of
autopsy have been well documented, but the autopsy's impact on parental grief and bereavement is less clear.
No study has compared grief between parents who chose to have an autopsy examination and those who did
not.

**Purpose:** This is a single site, cross sectional survey of human behavior, utilizing a qualitative questionnaire to
evaluate parental views on autopsy examination and compare grief between those who chose to have an
autopsy and those who did not

**Method:** Parents who endured the death of an infant in a referral level 4 NICU, between January 1, 2009 and
July 31, 2013 were eligible to participate. A questionnaire was created and consisted of six parts: 1.
Demographic information, 2. End-of-life experience Likert-type questions, 3. Autopsy Likert-type questions, 4.
Texas Revised Inventory of Grief (TRIG)- Past Behavior, 5. TRIG- Present Feelings, 6. Open ended questions and
Safety questions. Parents were sent the questionnaire via standard postal mail

**Results:** 218 deaths occurred during the study period. Current addresses could not be determined for 43
families. 5 families opt-ed out. 69 subjects completed a study questionnaire. 25 subjects completed the autopsy
questions. The majority respondents Agreed or Strongly Agreed that every family should be offered an autopsy
(80%) and that if they had to make the same choice today, they would chose to have an autopsy (84%). Few felt
guilty or regretted that their baby had an autopsy (4% and 8%, respectively). 48% felt that the autopsy helped
with their grief. Mean TRIG Present Feelings scores were higher in the autopsy group, indicating more intense
grief at the present time (48 vs 43, p= 0.04).

**Conclusions:** Although the majority of respondents viewed the autopsy in a positive manner, there was a
correlation between having an autopsy examination and worse parental grief. This finding warrants study in a
larger population.

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**RISK FACTORS FOR ELEVATED GENTAMICIN TROUGH LEVELS IN NEONATES RECEIVING THERAPEUTIC
HYPOTHERMIA.**

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**Purpose:** Gentamicin trough concentrations[G]T are typically not monitored until 48 hours of therapy unless
decreased renal function is suspected. Recent data suggests that hypothermia treatment for HIE may alter the
pharmacokinetics of gentamicin, particularly with respect to renal clearance. This study aims to determine risk
factors for elevated [G]T in neonates undergoing therapeutic hypothermia in order to identify which patients
may benefit from earlier therapeutic drug monitoring.

**Methods:** Retrospective cohort study of neonates receiving therapeutic hypothermia for hypoxic-ischemic
encephalopathy at a regional level IV neonatal intensive care unit. Subjects (n=36) were partitioned into Group
1 ([G]T < 2 mcg/mL) or Group 2 ([G]T ≥ 2 mcg/mL. Risk factors indicating disease severity or impacting [G]T
were compared between groups.
Results: Demographic data was similar between both groups. Mean gentamicin half-life was longer in group 2 versus group 1 (10.98±1.61 hours vs. 7.56 ± 0.96 hours; p < 0.01). On admission, serum creatinine (SCr) was not different between group 1 and 2 (SCr 1.1±0.07 mg/dL vs. 1.3±0.22 mg/dL; p = 0.09). At 72 hours, group 2 had a higher mean SCr (1.3±0.3 mg/dL vs 0.65±0.03 mg/dL; p=<0.0001). Urine output was not different between the two groups at 24, 48, and 72 hours. Baseline transaminases were significantly higher in Group 2 compared to group 1 with regard to AST (664 vs 188; p = 0.001) and ALT (354 vs 72; p = 0.007). At the time of initial birth resuscitation (33/36), there was no significant difference in rates of asystole (19% vs. 27%; p=0.44) or chest compressions (33% vs. 46%; p=0.43) between Groups 1 and 2. Multivariate logistic regression showed patients requiring epinephrine at birth or needing inotropic medications during therapeutic hypothermia were more likely to have an elevated [G]T (OR –4.6, 95% CI 1.03 to 20.35 and OR –6.5, 95% CI 1.32 to 31.83, respectively).

Conclusions: Elevated [G]T during therapeutic hypothermia is associated with epinephrine use in delivery room resuscitation or inotropes while on therapeutic hypothermia. SCr is elevated in patients that have elevated [G]T, but may not be clinically useful as an indicator for early monitoring. These neonates may benefit from earlier drug therapeutic monitoring.

45 CHALLENGES IN IMPLEMENTING UNIVERSAL NEWBORN HEARING SCREENING PROGRAM IN AN URBAN INNER CITY POPULATION.
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Background: UNHS has been shown to be effective in early identification of hearing impairment in neonates. In an urban inner city population, follow up of infants failing the initial testing poses a significant challenge.

Objective: To determine the incidence of infants failing the initial hearing screen done prior to discharge from the hospital. To document the follow up rate of these infants in the outpatient audiology clinic. In those infants with no follow up, to determine the reason for not following up.

Methods: This study included all infants admitted to the newborn nursery of Sinai Children's Hospital between January 2009 through December 2013. Infants were tested using the Clarity System Auditory Screener by the Oto Acoustic Emission technique. Infants who failed the screen were referred to the audiologist for an outpatient follow up. The parents of those infants who failed to follow up at audiology clinic were contacted over the telephone to determine the reasons.

Results: During the study period 14,765 infants were delivered at Mount Sinai hospital. Of these, 13,271 [89.9%] were admitted to the normal newborn nursery, who formed our study population. 12,619 [95.1%] infants were screened prior to discharge. 12,194 [96.6%] infants passed and 425 [3.4%] failed the screen. Of the 425 infants who failed, 273 [64.2%] have documented follow up with the audiologist and 152 [35.8%] infants have no documented follow up. 4 infants were diagnosed to have hearing loss. The parents of the infants who did not follow up were contacted over the telephone. 103 [67.8%] of the parents could not be contacted as either the telephone was disconnected or the number was wrong.

Conclusions: In this urban inner city population, 35.8% of infants who failed the initial hearing screening did not follow up with an audiologist. The parents of 67.8% of these infants could not be contacted. Further resources are needed to ensure better tracking mechanisms to follow up infants failing the hearing screen.

<table>
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<th>Reasons for not following up with audiology</th>
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<td>Followed up at a different institution</td>
<td>25 (16.5%)</td>
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<tr>
<td>Not informed of the failed screen result</td>
<td>12 (7.9%)</td>
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<tr>
<td>No follow up appointment given</td>
<td>8 (5.3%)</td>
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<td>Felt no follow up was necessary</td>
<td>2 (1.3%)</td>
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<tr>
<td>Did not recall</td>
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SUSTAINED IMPROVEMENT IN MEDICATION COUNSELING AND PREGNANCY SCREENING AFTER IMPLEMENTATION OF A TERATOGENIC RISK EDUCATION STRATEGY.

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Purpose: This quality improvement project aimed to increase patient education and pregnancy screening in girls of childbearing age prescribed teratogenic medications in the pediatric rheumatology clinic.

Methods: This project was conducted in a single center tertiary care rheumatology clinic with 7 providers averaging 3500 visits per year. The medical records of 89 girls age 10 and older taking teratogenic medications were reviewed for teratogen education and pregnancy screening to establish our baseline practice. Six Plan-Do-Study-Act (PDSA) cycles were completed to test interventions (Figure 1). Run charts were created for each aim to display improvement over time, and data reflecting overall improvement was analyzed by chi-square analysis.

Results: At baseline, 42/89 (47.2%) girls age 10 and older taking teratogenic medications had education documented in the last 12 months, and 21/89 (23.6%) had pregnancy screening performed at the visit. Implementation of our interventions resulted in improvement in documentation of education (616/767, 80.3%) and pregnancy screening (630/767, 82.1%), (p<0.0001). Annotated run charts depict shifts indicating special cause (Fig 1).

Conclusions: Development of a standardized education template in the electronic health record has helped sustain initial improvements in teratogen education and urine pregnancy screening.

EFFECTS OF CUMULATIVE HYPEROXIC INJURY DURING DEVELOPMENT OF LUNG STRUCTURE AND FUNCTION.

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Background: Bronchopulmonary dysplasia (BPD) is the most prevalent long-term consequence of preterm birth and leads to adverse pulmonary outcomes. Mechanical ventilation and supplemental oxygen has been shown in animal studies to disrupt the development of the alveolar-capillary membrane. Despite clinical improvement, survivors of BPD have reduced pulmonary diffusing capacities. Understanding which components of abnormal alveolar structural development (septal versus vascular) contribute to diffusion deficits may direct therapies aimed at optimizing lung functional recovery.

Methods: Neonatal mice were continuously exposed to room air (RA) or >90% hyperoxia (O2) for the first 4, 7, or 14 days after birth, then recovered in room air until day 56. At day 56, functional gas exchange was assessed using the diffusing factor for carbon monoxide (DFCO). The relative contributions of the membrane and vascular components of pulmonary gas diffusion were obtained by performing DFCO under both normal and high-oxygen conditions. Hemoglobin concentration was measured and lungs were inflation-fixed for determination of left lung volume by water displacement and morphometric analysis of alveolar surface area. Staining for von Willebrand Factor was used to assess vascular volume.

Results: Hyperoxia exposure resulted in a step-wise increase in the mean airspace size directly proportional to the duration of exposure. While 7 days of hyperoxia exposure did not affect lung volume, exposure for 14 days significantly increased lung volume. As a result, compared to RA controls, both 7 and 14 days of exposure resulted in a similar decrease in total alveolar surface area. Hyperoxia exposure for 7 or 14 days did not significantly reduce pulmonary microvascular density or affect hemoglobin concentration. DFCO was significantly reduced in 7 and 14 day-exposed animals, resulting from a reduced membrane component but, surprisingly, normal vascular component.

Conclusions: Neonatal hyperoxia exposure results in a step-wise increase in airspace enlargement. Due to a concurrent increase in lung volume with prolonged exposure, there is a threshold effect on alveolar surface area. Both histological and functional analysis following neonatal lung injury indicate that vascular function is...
maintained and a reduced alveolar surface area is the predominate factor contributing to impaired diffusing capacity.

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CONCURRENT METABOLIC CHANGES IN PLASMA AND THE BRAIN DURING ACUTE HYPOGLYCEMIA IN YOUNG RATS  
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Background: Hypoglycemia (HG) is a risk factor for brain injury during development. The current diagnosis and treatment of HG is based on plasma glucose level, which does not reflect the dynamic metabolic state in the brain. A better knowledge of the concurrent metabolic changes in plasma and the brain would optimize therapy for HG.  
Objective: Determine the concurrent metabolic changes in plasma and the brain during HG using NMR-based metabolomics in young rats.  
Methods: HG was induced using insulin in 4-week-old rats (blood glucose: 37±4 mg/dL). Brain metabolism was terminated at 120 min of HG using focused microwave fixation (4kW for 1.1 sec). The metabolomic profiles of the brain and concurrently obtained plasma were determined using 1H NMR spectroscopy (MRS) at 16.4T and partial least squares - discriminant analysis (PLS-DA) and compared with age-matched Control group (blood glucose: 86±7 mg/dL) (N=7).  
Results: MRS determined the absolute concentration of 37 metabolites in plasma and 28 metabolites in the brain. PLS-DA demonstrated clear separation of the HG and Control groups in both plasma and brain (Q², ≥ 0.7). The inter-group differences were due to β-hydroxybutyryate (βHB), acetoacetate, glucose, proline, glutamine (all lower in HG), phenylalanine and formate (both higher in HG) in the plasma, and glucose, alanine, valine, threonine, serine, ascorbate, βHB, glutamine (all lower in HG), 2-methylglutarate, phenylalanine and choline (all higher in HG) in the brain (VIP score ≥ 1 for all).  
Conclusions: HG causes concurrent metabolic changes in plasma and the brain. The changes reflect depletion of substrate pool (lower glucose, βHB and acetoacetate) and gluconeogenic amino acids (lower alanine, proline, valine, threonine and serine) in both compartments, and depletion of antioxidants (lower ascorbate), impaired choline incorporation into acetylcholine (increased choline) and impaired TCA cycle activity (increased 2-methylglutarate, a metabolite of the TCA cycle intermediate, succinate) in the brain. The parallel changes in plasma and brain metabolites suggest the potential use of plasma metabolomics for predicting the risk of brain injury and designing preventive therapies for HG.

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INHIBITION OF NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE POTENTIATES METHOTREXATE TOXICITY IN A LYMPHOCYTE CELL LINE  
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¹University of Kansas Medical Center, Kansas City, KS; ²Children’s Mercy-Kansas City, University of Missouri Kansas City School of Medicine, Kansas City, MO  
Background: Recent work by our group has demonstrated that reduced plasma levels of nicotinamide phosphoribosyltransferase (NAMPT) are associated with therapeutic response in juvenile idiopathic arthritis (JIA) patients treated with methotrexate (MTX). Although these findings suggest that reduced NAMPT activity may potentiate the clinical response to MTX, the mechanistic basis for this observation has not been evaluated and is the focus of this study.  
Methods: Pharmacologic activity of MTX was assessed as cytotoxicity in the Jurkat lymphocyte cell line. Cell viability was measured as the reduction of resazurin into its fluorescent product resorufin in a 96-well plate format using a BioTek Cytation 3™ fluorescence plate reader λex:560nm, λem:590nm. Modulation of NAMPT activity was accomplished by treating cells with FK866, a potent competitive inhibitor of NAMPT. Synergism between FK866 and MTX was determined using the Chou-Talalay method, in which cytotoxicity was measured in cells exposed to varying concentration ratios of MTX and FK866 for 96 hours. The IC50 values of FK866, MTX, and the selected drug ratios were calculated using CompuSyn™ software by Chou and plotted on an isobologram based on observed and predicted IC50 equivalents for each agent. Observed and predicted IC50 values for each drug concentration ratio were used to determine the fold potentiation of MTX activity by FK866.  
Results: The IC50 values for FK866 and MTX were found to be 0.76±0.35 nM and 25.25±2.12 nM, respectively. Potentiation of MTX toxicity by FK866 was observed as a reduction in the dose of MTX needed to produce a 50% reduction in cell viability. Thirteen concentration ratios of MTX to FK866 between 12.5:1 and 100:1 had an average MTX dose reduction of 1.93±0.45, indicating that in the presence of FK866 1.93-fold less MTX was needed to elicit the same pharmacologic effect as predicted by simple additive toxicity.
**Conclusion:** Pharmacological inhibition of NAMPT by FK866 potentiates the pharmacologic activity of MTX in a lymphocyte cell model. These finding suggest that reductions in NAMPT activity may result in enhanced pharmacologic response to MTX in the treatment of JIA.

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**METHOTREXATE POLYGLUTAMATION IN SYNOVIAL FIBROBLASTS FROM PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Intracellular methotrexate polyglutamates (MTXGlu) have been proposed to be the pharmacologically active form of the drug in juvenile idiopathic arthritis (JIA). However, the formation of these active metabolites in disease tissue (i.e. synovial fibroblasts) has not been previously demonstrated. This study aims to measure the capacity of synovial fibroblasts to transport MTX and metabolize it into its pharmacologically active form in a subset of JIA patients.

**Methods:** This is a single center prospective study of synovial fibroblasts isolated from JIA patients by arthrocentesis during routine intra-articular steroid injections. After obtaining informed consent, synovial fluid samples were maintained under sterile culture conditions and the resulting fibroblast cell lines were maintained in culture for a total of 6 passages prior to experimentation. Synovial fibroblasts from four patients were treated in triplicate with concentrations of MTX between 1 and 1000 nM for 24 hours. At the completion of the study cells were washed twice with phosphate-buffered saline (PBS), re-suspended in 80% acetonitrile in PBS, vortexed and centrifuged at 16,100xg. The resulting supernatant was analyzed by ultra-performance liquid chromatography-tandem mass spectrometry for MTXGlu1-5 and markers of inhibition of nucleotide biosynthesis, including: aminimidazole carboxamide ribonucleotide (ZMP) and deoxyuridine monophosphate (dUMP). Differences in uptake and polyglutamation between tested cell lines were determined. Statistical significance was assessed by unpaired t-test analysis.

**Results:** MTX uptake and polyglutamation in all cell lines tested was concentration dependent with minimal polyglutamate formation at MTX concentrations below 30 nM. At 1000 nM total cellular MTX levels varied greater than 17-fold (range: 51±4 to 892±438 fmole/mcg of protein, p < 0.05) with MTXGlu2-5 representing between 6.6±2.7% and 90.2±3.0% of total cellular MTX (p<0.0001). Despite the accumulation of MTXGlu, MTX exposure did not result in the accumulation of ZMP or dUMP.

**Conclusion:** MTXGlu is formed in synovial fibroblasts, but displays a large degree of inter-individual variability and has no measurable effect on cellular ZMP or dUMP. An improved understanding of clinical, genetic, or environmental factors that influence MTX polyglutamation and pharmacological activity at the target end organ may be leveraged to improve outcomes with MTX.

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**IMPROVED OUTCOMES FOR INBORN BABIES WITH GASTROSCHISIS**

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**Introduction:** Gastroschisis (GS) is a common abdominal wall defect necessitating neonatal surgery and intensive care. Since the opening of a delivery center within our free-standing children’s hospital in 2011 the majority of patients treated for GS at our center are inborn. We hypothesized that inborn patients had improved outcomes compared to patients born at an outside hospital (outborn) and transferred to our center for definitive treatment.

**Methods:** A single center retrospective chart review at a pediatric tertiary care center was performed from 2011 to 2014. All patients whose primary surgical treatment of GS was performed at this center were included. Findings are reported in mean ± standard deviations. Comparative analysis was performed using student t test for continuous variables and Fishers exact for binary variables. Significance was defined as a p ≤ 0.05.

**Results:** During the study period 79 patients with GS were identified. Of these, 53 were inborn and 26 were outborn. The rate of complicated GS was higher in the outborn group (32%) compared to the inborn population (11%) (p=0.03). Given the expected wide variability in outcomes for patients with complicated GS, outcomes for uncomplicated GS were analyzed. Length of stay (30±15 vs 40±26, p=0.03), 90 day readmission rate (11% vs 22%, p=0.02) and TPN duration (23±13 vs 32±23, p=0.04) were all significantly decreased for inborn patients, while time to definitive closure was similar. Mortality was 0% for both inborn and outborn patients.

**Conclusion:** Benefit is derived for patients with GS who are inborn rather than outborn.
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HIGHER DOSAGES OF BONE MORPHOGENETIC PROTEIN-2 IN ALVEOLAR CLEFT REPAIR RESULT IN HIGHER RATES OF POSTOPERATIVE NASAL STENOSIS

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A former surgeon at our institution preferentially used bone morphogenetic protein-2 (BMP-2) instead of autograft for alveolar cleft repair. Clinically, his patients who received BMP-2 appeared to have higher rates of postoperative nasal stenosis. To determine if this relationship was dose-dependent, a content analysis was performed comparing different dosages of BMP-2 in alveolar cleft repairs. BMP-2 had six levels of concentration depending on the size of kit used in the alveolar cleft (mg): 0, 1.05, 2.1, 4.2, 8.4, 12. Postoperative outcomes were examined by content analysis of clinical notes. Nasal stenosis was defined as any mention of clinical signs of stenosis, and indeterminate responses counted as no stenosis. Patients with nasal stenosis prior to their primary alveolar repairs were excluded. 60 consecutively enrolled patients underwent 115 surgeries that met criteria: surgeries involving BMP-2 (BY) 48%, those without BMP-2 (BN) 52%. The average age at surgery (years): BY 3.53, BN 3.43, P = 0.890. The incidence of postoperative nasal stenosis: BY 61.8% (34/55), BN 30.0% (18/60), ***P < 0.001. Some surgeries involved a concurrent nasal repair: BY 69.1%, BN 31.7%, ***P < 0.001. Using the predictor variables BMP-2 status, concurrent nasal repair status, and their interactive effect, a logistic regression indicated that only BMP-2 status was a statistically significant predictor of postoperative nasal stenosis: OR 3.49 (95% CI = 1.06, 11.46) *P = 0.04. BMP-2 concentration was then used as a predictor variable with 6 continuous levels in a logistic regression, adjusting for concurrent nasal surgery. The regression indicated that BMP-2 dose level was a dose-dependent predictor of postoperative nasal stenosis with an odds ratio of 1.244 (CI = 1.030, 1.503), *P = 0.023. In patients who received BMP-2 during alveolar cleft repair, higher rates of postoperative nasal stenosis were observed as greater doses of BMP-2 were used. A logistic regression showed that the effect of BMP-2 on nasal stenosis is dose-dependent and statistically significant, whereas concurrent nasal surgery is not a significant predictor. Possible etiologies include BMP-2 exacerbating septal deviation or hypertrophic bone deposition, and both need to be investigated further. These results suggest that BMP-2 has a dose-dependent effect with certain clinical outcomes, such as postoperative nasal stenosis.

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ADOLESCENT CHRONIC PAIN WITH COMORBID CONVERSION DISORDER: AN ANALYSIS OF PAIN, FUNCTION, AND PSYCHOLOGICAL OUTCOMES IN INTENSIVE INTERDISCIPLINARY PAIN REHABILITATION.

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Purpose: Chronic pain compromises quality of life in adolescents, illuminating a critical need to identify the natural history of pain and disability, particularly in association with conversion symptoms. While there is increasing recognition of comorbid conversion disorder in pediatric chronic pain, few studies investigate the effect of interdisciplinary treatment on outcomes in children with chronic musculoskeletal pain and conversion disorder. We hypothesized youth with conversion disorder would have greater pain, disability, and catastrophizing at baseline and throughout treatment, leading to worse function, pain, and psychological outcomes.

Methods: This outpatient program provides 5-6 hours of daily intensive PT and OT in addition to self-regulation, and behavioral health intervention. 70 participants age 11-18 (58 female) with chronic musculoskeletal pain completed Functional Disability Inventory (FDI), PROMIS anxiety, depression, and peer relationships, PRCQ-catastrophizing, CPAQ-A, and reported pain using a 100mm Visual Analog Scale (VAS 0-100) at program start, end of each week, and at 1, 6, and 12-mos follow-up. ANOVA and Hierarchical linear modeling (HLM) was used to conduct time-series analyses.

Results: 19 participants (15 female) had conversion disorder, which included sensory and/or motor symptoms. Patients with conversion had greater physical disability upon program entry (P=.02). Functional differences decreased during the program, with trends toward faster improvement among those with conversion (P=.089), and these differences resolved by follow-up. All patients significantly improved function from baseline to program end (P<.001) and continue to improve following treatment (P=.002). Similar patterns were found for peer relationships and pain acceptance. Patients with conversion had similar pain severity (M=61.5) as those without conversion (M=58.4) at baseline (P=.48) and at all time points. Both groups demonstrated significant decrease in pain through follow-up (P=.001). There were no differences between groups in depression, anxiety, or catastrophizing.

Conclusion: Children with chronic pain and comorbid conversion disorder have increased disability, poorer peer relationships, and decreased pain acceptance compared to those without conversion at baseline, though
differences resolve post-treatment. Patients with conversion have similar pain severity and no differences in depression, anxiety, or catastrophizing to those without conversion. Both groups demonstrate significant improvement in function, pain, and psychological outcomes post-treatment. Prospective studies are warranted to determine best practices for diagnosis and treatment of comorbid conversion symptoms in children with chronic pain.

54 EPINEPHRINE DOSING INTERVAL AND SURVIVAL OUTCOMES DURING PEDIATRIC IN-HOSPITAL CARDIAC ARREST

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++University of Iowa, Iowa City, IA, Denver, CO*, Tucson, AZ**, Dallas, TX, Philadelphia*+

Background: American Heart Association (AHA) guidelines recommend administration of epinephrine (epi) every 3 to 5 minutes during CPR to improve systemic blood pressure and coronary perfusion pressure. In adults with in-hospital cardiac arrest (IHCA), longer dosing intervals are associated with improved survival to hospital discharge. The purpose of this study is to investigate whether longer epi dosing intervals are associated with improved survival to hospital discharge.

Methods: A retrospective review of the AHA Get With The Guidelines-Resuscitation registry identified 1,260 pediatric IHCA that met our inclusion criteria: index IHCA event; no vasoactive infusion in place or alternate vasoactive medication boluses; > 1 dose of epi administered; not located in delivery room, nursery, NICU or obstetrical units. For each arrest, an epi dosing interval was defined by dividing the duration of resuscitation after the first dose of epi by the total doses given. This was necessary as the database does not provide time of individual epi doses. For analysis, epi dosing intervals were categorized as 1 to <5 minutes/dose, 5 to <8 minutes/dose, and 8 to 10 minutes/dose. Multivariable logistic regression models were constructed controlling for age, gender, illness category, location of arrest, and arrest duration to evaluate the relationship of epi dosing intervals on survival to discharge. Odds ratios were calculated using the 1 to <5 minutes/dose interval as the reference.

Results: Adjusted odds ratio for survival to hospital discharge for dosing interval of 5 to <8 minutes was 1.454 (95% CI 1.014-2.084) and for 8 to 10 minutes was 1.945 (95% CI 1.094-3.459).

Conclusions: Longer dosing intervals than those currently recommended by the AHA guidelines for epinephrine administration during pediatric IHCA are associated with improved survival to hospital discharge.

55 CPR TRAINING IN SCHOOLS: WHAT CAN BE LEARNED FROM IOWA’S EXPERIENCE?

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Background: Survival from out of hospital cardiac arrest has remained almost constant at 10-12% over several decades. In a witnessed arrest, prompt initiation of bystander CPR has been demonstrated to double the chance of survival. Overall CPR training rates in the United States are low: 2.4% per year. Currently, 21 states have adopted legislation to increase CPR training in schools. Iowa has required CPR as a high school graduation requirement since 2011 through an unfunded mandate. The objective of this study is to understand the implementation process, practices and barriers to providing CPR education to high school students. We surveyed Iowa high schools to provide guidance for nascent programs based on 4 years of experience.

Methods: A cross-sectional study was performed through surveys sent to 346 Iowa high schools using the Qualtrics™ online platform. A 20 question survey was developed to obtain descriptive data covering general demographics of the school, specifics of the CPR training programs including what year the program was implemented, who performs the training and in which setting it occurs, logistics and barriers to implementation, and AED training and availability.

Results: Response rate was 24.3%, with a mean school size of 100-500 students and a mean faculty size of 25-50. When the law took effect in 2011, 51% of schools had training programs already in place, and currently 96% have successfully implemented CPR training. Perceived barriers to implementation were staffing, time commitment, cost, and equipment availability. The training facilitator was a school official or unpaid volunteer in 81% of schools, only 19% reported a paid instructor. Average estimated time commitment was 2 hours. The average estimated startup costs as well as yearly maintenance costs were <$500 with funds usually allocated from existing school district funds. A low proportion of staff is trained in CPR: 69% of schools have less than 25 staff members who are CPR trained. AEDs are available in 98% of schools while only 61% include AED training in their training curriculum.

Conclusions: Despite perceived barriers, school CPR training programs can be implemented with reasonable resource and time allocations.
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ATYPICALLY PROLONGED HONEYMOON PHASE IN A 15-YEAR OLD WITH TYPE 1 DIABETES
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Background: Type 1 diabetes (T1D) is an immune-mediated form of diabetes characterized by loss of insulin-producing beta cells. Early identification of beta-cell autoimmunity in high-risk populations allows identification of asymptomatic subjects with high risk for T1D development. The “honeymoon period” in patients with T1D is defined as a period with insulin requirements of less than 0.5 units/Kg/day and hemoglobin A1C (HbA1C) level less or equal than 6%. The honeymoon phase typically does not last longer than 1 year, but range has been reported to be between 1 month - 13 years.

Purpose of study: This clinical case describes an atypical case of a 15-year old male who had early diagnosis of T1D at 7 years old and remains on prolonged honeymoon phase since the time of diagnosis.

Methods: Descriptive, observational.

Summary of results: A 5-year old White male patient was initially evaluated for seizures associated with hypoglycemia. Workup for congenital hyperinsulinism, adrenal and growth hormone deficiency was negative. Electroencephalography evaluation showed seizure activity triggered by hypo/hyperglycemia. He underwent IV glucose tolerance test and was found to have impaired glucose tolerance (IGT) with normal HbA1C at 5.3%. Autoimmune screening for T1D, thyroid disease and celiac disease were performed. Glutamic acid decarboxylase (GAD) [1.6 unit/mL] and islet cell antigen (ICA-512) [1.6 U/mL] antibodies were positive confirming beta-cell autoimmunity. Fasting and postprandial glucose monitoring was started. HbA1C and glucometer download were analyzed every 3-4 months. Fasting insulin and C-peptide were normal (6.04 uIU/mL [1.9-23] and 2.6 ng/mL [0-3.3] respectively). After 2 years he developed postprandial hyperglycemia above 200 mg/dL with intermittent polyuria and polydipsia. A diagnosis of T1D was made at 7 years old. HbA1C was still normal at 5.3%, and short acting insulin treatment for meals was started with a carbohydrate ratio of 1:45. Basal insulin was initiated at age 13 when C-peptide was low at 0.55 ng/mL (08-3.9). On May 2015, his total daily dose of insulin was 0.02 units/kg/day; HbA1C was 5.6%, and he does not have any associated metabolic complications.

Conclusion: Early identification of IGT and beta-cell autoimmunity prompted close glycemic monitoring and early diagnosis of T1D in this patient, with early initiation of insulin treatment. Beta cell function was preserved and patient remains on prolonged honeymoon phase.

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MULTIMODALITY IMAGING IN PRENATAL DIAGNOSIS OF AORTIC ARCH ANOMALY.
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Background: Prenatal diagnosis of aortic arch anomaly improves morbidity and mortality. Recently multiple imaging modalities have been integrated into the diagnosis and management.

Aim: To evaluate the impact of fetal/transthoracic echocardiography (FE, TTE) and cardiac CT on the diagnosis, surgical approach, and outcome of fetuses with aortic arch anomaly.

Methods: Review of fetal database for aortic arch anomalies, excluding single ventricle from 2010-2016. FE, TTE, CT, karyotype, and surgeries reviewed.

Results: 25 fetuses with aortic arch anomaly including isolated aortic coarctation and/or hypoplasia (IACH, n=16) and arch hypoplasia with complex cardiac defect (CCD, n=9). 60% female; 32% chromosome anomaly; mean GA at diagnosis, birth (27.2, 37.6 wks); mean wt at birth, surgery (2.92, 3.04 kg); mean surgery age (16 d). CCD group included AVC (n=4), TGA (n=2), DORV (n=2), LVNC (n=1). FE and TTE in all, CT in 80%. Figure 1 shows two anatomical arch configurations (flat vs. candy cane) with implications for surgical technique (Table 1). Two patients are followed for mild coarctation without repair (one with TGA s/p arterial switch; other with aortic stenosis s/p balloon angioplasty). Initial thoracotomy required revision in 1/8 discrete coarctation, 3/7 arch hypoplasia. Initial pre-op CT in 5/7 requiring revision (3/4 IACH, 2/3 CCD) and 13/16 without revision (8/11 IACH, 5/5 CCD).

Conclusion: In CCD, CT complements TTE in surgical planning and may reduce revision rate through evaluation of extent of arch augmentation. In IACH, TTE allows adequate surgical planning and CT may not add further value. Flattened arch may be a proxy for arch hypoplasia; in both, initial repair via sternotomy appears to reduce revision rate compared to thoracotomy likely by better exposure of hypoplastic arch.
COMMON ALLEGATIONS OF PROFESSIONAL LIABILITY AGAINST PRACTITIONS OF NEONATAL/PERINATAL MEDICINE.

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The current professional liability crisis is highly relevant to all practitioners in the medical field. Understanding what allegations are most commonly brought against those involved in caring for sick newborns and why could have profound implications. Addressing these issues could potentially reduce avoidable devastating outcomes. The specific aim of this study is to identify the most common allegations brought against practitioners of Neonatal-Perinatal Medicine. We reviewed 175 confidential closed legal cases of alleged negligence in the care of newborns through the experience of a neonatal expert witness (JM) from 1986-2015. A confidential file was kept for each case including medical records, depositions, expert witness testimony and final legal outcome. In some instances, multiple allegations were found per case. The twenty five most common allegations were included out of 258 total allegations analyzed. A total of 175 cases were reviewed. The twenty five most common allegations were inadequate airway management (16.4%), unrecognized pneumothorax (10.9%), delayed attendance/inadequate personal at delivery (9.5%), delayed transfer to a level III facility (9%), medication error (7%), cardiac tamponade (7%), inadequate treatment of seizures (5.8%), failure to perform eye exam (4.4%), failure to recognize midgut volvulus (3.3%), delay in treatment of acute anemia (3%), improper dosing of delivery room epinephrine (2.7%), improper sized ET tube (2.7%), delayed treatment of sepsis (2.3%), failure to initiate total body cooling within six hours (2.3%), hypoglycemia (1.9%), necrotizing enterocolitis (1.6%), IV infiltrates (1.6%), pronounced dead with return of spontaneous heart rate (1.6%), nasogastric tube perforation of stomach (1.4%), discharge without monitors (1.4%), inadequate informed consent (1.2%), kernicterus (0.8%), delayed treatment of herpes (0.8%), improper isolation (0.8%), and inadequate triage in emergency department (0.7%). Of the 175 cases, 75.2% were reviewed from the defense and 24.8% for the plaintiff; 55% were in state (Illinois) and 45% out of state. Patient safety and professionalism have become a major priority in all fields of medicine, including Neonatal-Perinatal Medicine. Identification of common allegations could help reduce improper performance, inadequate supervision, medication errors and diagnostic errors with the aim of improving patient outcomes. The majority of cases are associated with preventable events. By recognizing these common allegations, we can increase awareness, education and establish new protocols to improve the safety of the workplace and reduce the occurrence of major sentinel events.
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DOES COMPUTERIZED PHYSICIAN ORDER ENTRY DECREASE MEDICATION ERRORS IN THE NEONATAL INTENSIVE CARE UNIT?

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Objective: To determine the incidence of medication error in the Neonatal Intensive Care Unit (NICU). To classify these errors based on the type and severity. To compare the incidence prior to and after the implementation of Computerized Physician Order Entry (CPOE).

Methods: This was a retrospective review of the medical records and an online database of all infants admitted to the NICU of Sinai Children’s Hospital from July 2011 to October 2014. CPOE was implemented on July 1st, 2013. The study was divided into two periods pre CPOE (July 2011 to June 2013) and post CPOE (July 2013 to October 2014). Medication errors are voluntarily reported by all healthcare workers in an online database. The database includes type and severity of the error.

Results: The number of admissions to the NICU was 705 and 590 in pre CPOE and post CPOE period respectively. There were 47 (6.6%) errors pre CPOE and 34 (5.7%) post CPOE. This difference was not statistically significant (p=0.34). The medication errors occurred most frequently in the dispensing and administering phases. Severity of the medication error was classified based on the National Coordinating Council for Medication Error Reporting and Prevention (NCC-MERP).

Conclusions: The incidence of medication errors decreased from 6.6% pre CPOE to 5.7% post CPOE. This decrease was not statistically significant. The medication use process is complex, involves multiple processes and personnel. Hence a comprehensive approach addressing all the processes involved should be used to decrease medication errors in the NICU.

<table>
<thead>
<tr>
<th>Medication Error by Severity</th>
<th>Pre CPOE (N = 39)</th>
<th>Post CPOE (N= 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category A</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Category B</td>
<td>9</td>
<td>4</td>
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<tr>
<td>Category C</td>
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<td>Category D</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Category E</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>23</td>
</tr>
</tbody>
</table>

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BREASTFEEDING PRACTICES IN INFANTS WITH CLEFT LIP AND/OR PALATE

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Background: The Surgeon General, AAP, and WHO are all encouraging increases in the exclusive use of breast milk for at least 6 months via direct breastfeeding. Underscored is the specific need to empower the medical community to support breastfeeding mothers through education, encouragement, and professional assistance. There is, however, scant literature on breast milk (BM) provision for infants with medical conditions other than very low birth weight and prematurity. For infants born with cleft lip and/or palate, breastfeeding is often discouraged. These infants are often considered unable to successfully breastfeed due to anatomical abnormalities and/or frequent concomitant syndromes. Feeding assistance may be required for poor weight gain with changes in feeding strategies and the use of formula for calorie supplementation. The stress of difficult feeding increases maternal anxiety and, as a result, the provision of BM may not be a priority.

Methods: A telephone survey was conducted of mothers of infants with cleft lip and/or palate born in 2012 to determine details of their breastfeeding experiences.

Results: 86 patients were identified and the families contacted. 50 mothers agreed to participate, 32 could not be reached, and 4 refused. Cleft types included 13 cleft lip, 18 cleft lip and palate, and 19 cleft palate. 11 patients had identified syndromes or chromosomal abnormalities; 7 had Pierre Robin Sequence. 39 mothers (78%) initiated breastfeeding or provided expressed BM to their infants. 31 mothers exclusively provided pumped BM for their infant. 23 mothers (58.97%) provided BM for less than 6 months, 16 (41%) provided BM for 6 months or more. On average, patients received BM for 5.59 months. 36 mothers reported receiving lactation support. Poor supply was cited as the most frequent challenge to providing BM and caused cessation in 46.15%. 17 mothers reported supplementing with formula due to poor supply. 17 infants were supplemented due to poor weight gain. Mothers who did not provide BM cited many reasons including: no supply, time constraints, complexity, and stressfulness. 36% of mothers reported individual encouragement of breastfeeding. 28% reported support from “everyone”. 36% reported no specific encouragement. 18% reported they were specifically discouraged from providing breastmilk for their infants.

Conclusions: 78% of mothers initiated providing breast milk for their infants with cleft lip and/or palate, primarily through pumping, but only 41% continued for the recommended 6 months or more. Challenges maintaining supply were common.
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CLEFT CARE OF INTERNATIONALLY ADOPTED CHILDREN FROM CHINA

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Purpose: International adoption from China has previously been common as a result of government-imposed birth restrictions and a large population of abandoned children. The availability of adoptable Chinese infants has significantly decreased in the last several years with lessening of restrictions on family size and increasing domestic adoptions in China. The smaller pool of healthy children available for international adoption has increased the rate of “special needs” adoptions. Relaxed protocols have encouraged the adoption of children with medical conditions including those with clefting conditions. These children have a wide variety of pre-adoption cleft care experiences and often arrive in the United States in mid-treatment for complex issues. There is limited scholarly information available about this population. This study aims to quantify this population and assess the management practices for international adoptees with cleft conditions.

Methods: A retrospective chart review was performed for the 104 Cleft Team patients (50 males; 54 females) adopted from China between 2000 and 2014 at our institution.

Results: Average age at adoption is 31 months with 71% aged 13-36 months at adoption. 86.5% had a combined cleft lip and palate, 68 unilateral and 32 bilateral. Only 4 patients were adopted with isolated cleft palate. 51 patients (49%) had cleft lip repair prior to adoption; 33.6% had both a cleft lip and cleft palate repair in China. 16.3% of adoptees arrived in the US without any prior surgery. In China, the average age at lip repair was 14.41 months and palate repair is 26.71 months. Once in the US, lip repair averaged 23.43 months and palate repair was 27.83 months. 83 revisional surgeries were performed. Only 19 patients (18.2%) have not required further cleft-related surgery after adoption. 74% of patients demonstrate moderate-severe articulation disorders and/or language delays. 33.6% of patients have some degree of velopharyngeal insufficiency with hypernasal speech. 40% of patients with hypernasality required palatal revision surgery to achieve normal resonance. Approximately 10% of patients present with global delays or significant medical issues beyond their anticipated cleft condition.

Conclusions: Chinese adoptees present with a high percentage of complete clefts including bilateral clefts. The average age at surgery for cleft lip or palate is significantly higher than for patients born in the US. Revisional surgery is exceedingly common. Speech and language issues are also frequent and can persist despite therapy.

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PEDIATRIC RHEUMATOLOGY: INTEREST IN AND EXPENSES RELATED TO TRADITIONAL VERSUS TELEMEDICINE CLINIC VISITS.

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Purpose: Nearly 1 in 250 children have arthritis, yet less than 300 board certified pediatric rheumatologists exist in the United States, about 90% of whom work in large cities. Clinic travel can be a significant time and monetary commitment for families. Telemedicine (TM) may improve patient access to pediatric rheumatology (PR) clinics and reduce the cost of care. The objective of this study is to describe the cost to families associated with PR visits and identify interest in TM.

Methods: Surveys were offered to parents and guardians in PR clinics in Kansas City (KC), Missouri (n=256) and at a TM outreach site 160 miles away, in Joplin, Missouri (n=24). Survey questions included the distance traveled to clinic, amount of work and school missed, meal and lodging costs, and interest in TM. Different survey versions resulted in a variable number of total responses for each question. Descriptive and inferential analyses were performed using SPSS 20 and SAS 9.4.

Results: The median distance traveled one-way by the KC population was 41 miles [IQR=20-82]; 61% missed work for the appointment, 52% purchased meals and 6% spent money on lodging. Overall, 42% were interested in a TM option. When stratified by distance, those living at least 50 miles from the KC clinic were more interested in TM than those less than 50 miles away (63% vs. 28%, p<0.0001). Among respondents who missed work, those who spent more hours away from work were more likely to endorse interest in TM (p=0.004).

The median distance traveled by the Joplin population was 60 miles [IQR=20-85] when seen via TM vs. 175 miles [IQR=160-200] when seen in KC (p<0.0001). Joplin respondents were more likely to spend money collectively on food, lodging and/or child care when traveling to KC as compared to Joplin (92% vs. 38%, p<0.0001). Respondents missed an average of 3.2 more hours of work and 3.6 hours of school when seen in KC vs. Joplin TM.
**Conclusion:** Children with rheumatic diseases travel substantial distances to receive subspecialty care and incur significant costs with this travel. Interest in TM is associated with greater distance traveled and more time away from work. In our established TM Joplin clinic, respondents were less likely to spend money on travel, food, lodging and time away from work and school. TM is an effective way to lessen financial burden for families that travel considerable distances for PR care.

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**DEVELOPMENT OF A FETAL HEALTH CENTER WITHIN A FREESTANDING CHILDREN'S HOSPITAL: DESCRIPTION OF INITIAL PATIENT USE 2011-2015.**

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**Background:** Birth anomalies are now considered the leading cause of neonatal and infant mortality. In 2011, Children's Mercy Hospital, a freestanding children’s hospital in Kansas City, Missouri developed a program to address evaluation and management for prenatally diagnosed fetal anomalies. The goal of the “fetal health center” (FHC) was to provide comprehensive care for pregnant women with suspected fetal anomalies. Services included integrated multi- specialty prenatal counseling and comprehensive obstetrical care and delivery availability adjacent to the Level IV NICU when indicated.

**Purpose:** This is a descriptive analysis of fetal conditions cared for in a FHC within a free-standing children's hospital during the first 4 years of operation.

**Methods:** Fetal diagnoses were grouped into one of eight diagnostic categories. The FHC and Intensive Care Nursery (ICN) databases were reviewed to assess the number and diagnostic categories of those delivering during the first 4 years (March 2011 to April 2015). For the 3 year period between July 1, 2011 and June 30, 2014, ICN admissions were reviewed to determine the percentage of infants with fetal anomalies outborn versus those delivering at the FHC. Prenatal consults and FHC deliveries were reviewed for calendar year 2014 to assess diagnostic differences between those receiving prenatal care at the FHC without delivery and those delivering within the FHC.

**Results:** There have been 1046 FHC integrated prenatal consults during the first 4 years, including 155 in 2011 increasing annually to 300 in 2014. There were 468 deliveries in the FHC during that same time period, 57 occurring in 2011, with an annual increase to 133 in 2014. The primary diagnoses resulting in delivery were cardiac (34%), gastrointestinal (17%), CNS (13%), complex (13%) and pulmonary (8%). For pregnancies receiving prenatal consultation in the FHC, those with craniofacial, genitourinary, and skeletal anomalies were statistically more likely to deliver at community hospitals (P< 0.001) and infants with cardiac anomalies were more likely to deliver at the FHC. The overall C-section rate was 53%; there were 13 sets of twins, so the fetal health center had to accommodate some well infants. During the four year period, there were 69 FHC patient deaths (15%). For the 3 year study period 2011-14, 44% of ICN admissions had birth defects (1145/2287). Of these, 278 (24%) were born in the FHC, others were not diagnosed prenatally, were not referred to the FHC or immediate neonatal care was not anticipated.

**Conclusion:** Our fetal health program continues to grow about 15% per year, providing integration of high level pediatric subspecialty and perinatal services for a unique subset of pregnancies with high risk fetal anomalies. There continues to be a large number of infants with congenital anomalies in the referral area not accessing this resource. Further analysis is necessary to determine factors which may present obstacles for use of the FHC.

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**SEX DIFFERENCES IN RIGHT VENTRICULAR GENE EXPRESSION IN A RAT MODEL OF PULMONARY HYPERTENSION.**

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**Background:** Pulmonary arterial hypertension (PAH) is a progressive disease of the pulmonary circulation which ultimately causes right ventricular (RV) failure and death. Females represent up to 75% of patients with PAH. However, most of the animal research conducted on PAH has been conducted on males. We have developed an animal model to analyze genome-wide RV mRNA expression patterns in female and male rats with PAH to better understand sex-specific differences in gene expression.

**Methods:** Female and male Sprague Dawley rats underwent left pneumonectomy or sham surgery and received 50-60 mg/kg monocrotaline or vehicle subcutaneously 7 days later (N = 4 per group). After 10 days, prior to the onset of RV failure or dysfunction, specimens were frozen for mRNA analysis. RNA was then labeled and hybridized to the Illumina RatRef-12 Expression BeadChip, permitting genome-wide expression analysis using 21,910 probes selected primarily from the NCBI RefSeq database (Release 16). QPCR was then performed on
selected genes implicated in pathways affecting cell hypertrophy (EMMP3, S100A4, HSPB1), extracellular matrix (ECM) signaling (TIMP1, FN1, COL1A2), and mitochondrial function (NDUFV2, CYCS). Gene expression was quantified relative to all controls (male and female) and analysis was done with unpaired t-testing.

**Results:** The most significant differences in gene expression were seen in genes involved in ECM signaling: Male PAH rats have increased expression of TIMP1 and FN1 relative to female PAH rats (P < 0.05) and overall male control and PAH rats have increased expression of TIMP1, FN1, and COL1A2 (P < 0.05). Male control and PAH rats also have increased expression of NDUFV2 relative to their female counterparts (P < 0.05), but otherwise there are no significant differences in genes influencing mitochondrial function. Genes studied that are involved in cell hypertrophy pathways do not appear to have differential expression between the two sexes.

**Conclusion & Clinical Correlation:** Prior to the onset of RV failure or dysfunction, preliminary data suggests that there are potential sex-related changes in gene expression. These changes may be related to the differences seen in disease progression between males and females with PAH. We plan to study more genes involved in pathways affecting cell hypertrophy, ECM signaling, and mitochondrial function.

### 65
**NO DO WE THINK? ANALYSIS OF DECISION MAKING FATIGUE IN THE NEONATAL INTENSIVE CARE UNIT**

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**Purpose:** Most adults make hundreds of decisions daily. Decisions are either active (make a change) or passive (maintain the status quo). As the number of decisions increases, individuals subconsciously become susceptible to decision-making fatigue – a state of reduced mental energy associated with increased difficulty making decisions. Previous studies suggest active decisions are less likely to occur with increasing decision-making fatigue. There is limited data regarding the decision making process or the impact of decision-making fatigue for physicians in the NICU. The objectives of this study were to 1) assess whether physicians in the NICU experience decision-making fatigue; 2) evaluate whether decision-making fatigue impacts the time required for both active and passive patient care decisions.

**Methods:** This was a prospective, observational study of daily patient rounds in a 44 bed level III NICU. A non-participatory study investigator attended rounds. For each patient, the type of decision (active versus passive) and amount of time spent making a decision were recorded for decisions regarding nutrition, respiratory support, medications, labs, and discharge planning. Healthcare providers were blinded to study objectives. Statistics were performed with SAS 9.4 to evaluate associations between patient order on rounds, level of acuity (ICD-9 critical versus non-critical code), type of decision (active versus passive), and duration of patient rounds.

**Results:** Data was collected for 1012 patients over 6 months. Rounds decreased by 4.1 ± 2.9 minutes/patient from the first 5 patients (n=328) to patient ≥11 (n=357; p<0.0001). 10.4% of decisions were active decisions. The likelihood of an active decision was not associated with patient order on rounds (p=0.1835). Patient rounds were 2.9 ± 3.1 minutes longer/patient with active vs passive decisions (p<0.0001) and 6.2 ± 3.7 minutes longer for critically ill (n=201) vs non-critically ill patients (n=811, p<0.0001). Rounds were longer with active decisions for both critically ill and non-critically ill infants. Time per patient decreased as rounds progressed even after adjusting for both the type of decision and critical care status (p<0.0001).

**Conclusion:** Active decisions required more time than passive decisions. Critically ill infants required more time than non-critically ill infants irrespective of the type of decisions made. Patient rounds became shorter as rounds progressed even when adjusting for decision type and infant condition. Fatigue may be a factor influencing decision making. Further study of decision making fatigue is needed to determine its relation to infant care.

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**PHARMACOEPIDEMIOLOGY OF OPIATE USE IN THE NEONATAL ICU: INCREASING CUMULATIVE DOSES AND IATROGENIC OPIATE WITHDRAWAL.**

**T Lewis**, B Erfe, T Ezell, E Gauda

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**Objective:** Neonatal ICU (NICU) care involves use of opiates to treat post-operative, ventilated or chronically ill infants. Opiates provide necessary analgesia and sedation, but the morbidities of high or prolonged dosing include prolonged Neonatal Abstinence Syndrome (NAS) and extended length of stay for dose tapering. Our objective was to quantify trends in opiate exposure in a tertiary care NICU. We hypothesize that medical opiate exposure and resultant ICU-acquired NAS would increase over time.

**Methods:** This is a retrospective cross-sectional cohort study performed in a tertiary care NICU among high risk inborn infants admitted in fiscal years 2003-2004, 2007-2008 and 2010-2011. The primary outcome of
average cumulative morphine exposure (all opiate doses converted to morphine equivalents) per time epoch was compared in cohorts of clinically similar infants. Linear regression was used to assess the primary outcome, assessing changes in cumulative opiate exposure over time.

**Results:** 63 infants were included in the final analysis. The primary analysis assessing average cumulative opiate exposure per infant showed an increase of 134 mg per time epoch (95% CI -12, 279 mg, p-value 0.071). A secondary analysis involving quartile regression of median cumulative opiate exposure per infant showed increased exposures from 10 mg to 25 mg and 114 mg over the three epochs studied (p-value 0.038). There was a statistically significant increase in the percent of infants with a diagnosis of iatrogenic NAS, increasing from 9 to 50% (p-value 0.012).

**Conclusion:** This is the first study to quantify medical opiate exposure in neonates. In one tertiary NICU, medical opiate exposure is increasing over time in high risk ICU infants. In association, there are increased diagnoses of ICU-acquired NAS. The etiology of this increase is currently unknown, but may include secular changes in pain perception and management, changes in perception of risk and benefit related to opiate exposure, or changes in weaning practices.

**Clinical Correlation:** This trend should be monitored closely and further studies to assess interventions including more strident pain and sedation monitoring, weaning protocols and other efforts to decrease opiate exposure are warranted.

### 67 PREDICTING DEATH OR SHORT BOWEL SYNDROME IN PRETERM INFANTS WITH SURGICAL NECROTIZING ENTEROCOLITIS


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**Background:** Surgical necrotizing enterocolitis (NEC) is associated with short bowel syndrome, intestinal failure (SBS/IF) and mortality. Factors to predict these outcomes for affected, preterm infants are uncertain.

**Objective:** To estimate the risk of death or SBS/IF in infants with surgical NEC.

**Study Design:** We identified infants born ≤32 weeks' gestation with surgical NEC from 5 regional neonatal intensive care units (NICUs) using the Children’s Hospitals Neonatal Database over 3 years. We excluded infants with intestinal perforation without NEC, volvulus, congenital heart disease, abdominal wall defects, NEC totalis and, as a surrogate for NEC totalis, death within 14 days after NEC surgery. We collected patient demographics, physiologic, and laboratory measurements in the first 24 hours after NEC onset or admission, and determined their association with the primary outcome, mortality or SBS/IF before discharge. Multivariable analyses were used to develop a predictive equation.

**Results:** The mean gestational age and birthweight were 26 weeks' and 845 grams, respectively (n=103). The median age of NEC onset was 16 [9, 28] days. The primary outcome occurred frequently (death or SBS/IF: 30%; death: 8%, SBS/IF:23%). Multivariable analysis showed that death or SBS/IF was related to gender (odds ratio (OR): 2.6, 95% confidence interval (CI): 0.8, 8.2; p=0.10), blood stream infection (BSI) (OR: 3.8, 95% CI: 1.4, 10.7; p=0.01), lowest total leukocyte count (OR: 0.9, 95% CI: 0.9, 1.0; p=0.01) and hematocrit lower than 22% (OR: 12.2, 95% CI 1.2, 129.1; p=0.04) in the first 24 hours of NEC onset or admission and small for gestational age (SGA) (OR: 3.2, 95% CI 0.8, 12.0, p=0.09). This equation modestly predicted the outcome of interest (area under ROC curve 0.81, goodness-of-fit $\chi^2 = 0.30$). Unrelated to death or SBS/IF were blood pressure, pre-transfusion platelet counts, lower pH, blood urea nitrogen, and serum creatinine (p≥0.11 for all).

**Conclusions:** Five routinely-available clinical variables were associated death or SBS/IF in this cohort of preterm infants after surgical NEC. Even though infants with NEC totalis were excluded, these results can be used to assist clinicians in counseling affected families of infants. Future work will focus on validating this equation in another cohort of affected infants.

### 68 ENTERAL NUTRITION AND SHORT-TERM GROWTH OUTCOMES IN PRETERM INFANTS AFTER SURGICAL NECROTIZING ENTEROCOLITIS


1Ann and Robert H. Lurie Children’s Hospital of Chicago and the Feinberg School of Medicine, Northwestern University, Chicago, IL; 2Children’s Mercy Hospitals and Clinics and the University of Missouri School of Medicine, Kansas City, MO; 3Nationwide Children’s Hospital and the Ohio State University College of Medicine,
Background: Even though surgical necrotizing enterocolitis (NEC) is associated with suboptimal growth, a paucity of data exists evaluating post-operative feeding practices and their relation to short-term growth.

Objective: To estimate the association between post-operative enteral nutrition and short-term growth in infants with surgical NEC.

Study Design: We identified infants ≤32 weeks' gestation with surgical NEC from 5 regional neonatal intensive care units (NICUs) using the Children's Hospitals Neonatal Database over 3 years. We excluded infants with intestinal perforation without NEC, volvulus, abdominal wall defects, congenital heart disease, surgical NEC that resolved prior to referral, and death within 14 days after NEC surgery. We collected daily enteral nutrition data including: type of enteral feeds, volume and calories administered for the first 28 post-operative days and weekly thereafter until discharge or death. The primary outcome was the pre-discharge/ death growth velocity (GV) and, secondarily, time to achieve feeding milestones including feeding initiation and reaching 100 kcal/kg/day after surgery.

Results: The cohort's (n=103) mean gestational age and birth weight were 26 weeks' and 845 grams, respectively. Three infants were not fed enterally; other infants received breast milk exclusively (BM: 27%), formula exclusively (F: 53%), or a combination (BM/F: 20%). Of infants receiving formula, 66% received an amino acid-based formula and 69% of those infants were initially fed breast milk. GV (BM: 12 g/kg/day; F: 10 g/kg/day; BM/F: 10 g/kg/day; p = 0.2) and changes in length (1 cm/week, p=0.83) and HC (1 cm/week, p=0.67) through discharge or death were similar between feeding groups. Feedings started at a median [iqr] 14 [10.5, 23] days after surgery (p = 0.5 across groups). Fortification began at 52 [26, 75] d after surgery and when feedings were 125 [99, 145] ml/kg/day. The duration to reach 100 kcal/kg/day via enteral feeds was prolonged (BM: 64 d; F: 49 d; BM/F: 56 d, p = 0.5). Twenty infants never reached this milestone and 8 of those had short bowel syndrome. The median length of stay was 132 [95,180] d.

Conclusions: At five regional NICUs, infants with surgical NEC were slow to reach substantive provisions of enteral nutrition and showed poor weight gain after convalescing from their acute disease. Clinicians' assessment of feeding readiness, feeding advancement rates and intestinal health may be significant contributors to length of stay in infants with surgical NEC.

69 ADHERENCE TO PERINATAL GROUP B STREPTOCOCCAL DISEASE PREVENTION GUIDELINES FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION, 2010

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Background/Objective: Revised 2010 CDC guidelines for prevention of neonatal Group B Streptococcal Disease (GBS) recommend universal maternal screening and intrapartum antibiotic prophylaxis (IAP) when indicated. The algorithm for neonatal disease surveillance recommends routine care for infants born to GBS unknown/no risk factors (RF) mothers and ≥48 hour hospital observation (obs) for infants born to GBS+/inadequate IAP mothers. Our objective is to assess clinicians’ adherence to these recommendations.

Method: Retrospective chart review of newborns ≥ 37 weeks gestation admitted to the Newborn Nursery at Sinai Children’s Hospital from 11/01/2012 to 04/15/2013.

Results: 921 term infants were admitted to the nursery during the study period, 21% (190/921) were born to GBS (+), 60 % (552/921) were born to GBS (–) and 19 % (179/921) were born to GBS unknown mothers. 67 (37%) GBS unknown mothers delivered via elective C‐section (CS). 165 mothers had indication for IAP of which 32% (52/165) received inadequate IAP. To assess neonatal algorithm compliance, 369 infants born to GBS (+) and GBS unknown mothers were analyzed. 127 (34.4%) infants delivered via C-Section (CS) were excluded due to >48 hours routine stay and 22(9%) of vaginally delivered infants (n=242) were excluded due to complex maternal/neonatal issues. Of the remaining 220 infants, 5% had unwarranted laboratory evaluation. 68% infants born to GBS unknown mothers (n=86) stayed for 48 obs and 13% infants born to GBS (+) /inadequate IAP mothers (n=44) were discharged before completing 48hour observation.

<table>
<thead>
<tr>
<th>Table1: Neonatal Algorithm Adherence</th>
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<tr>
<td>Infants (n=220)</td>
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<tr>
<td>GBS(+)/adequate IAP (n=90)</td>
</tr>
<tr>
<td>GBS(+)/inadequate IAP (n=44)</td>
</tr>
<tr>
<td>GBS Unknown/no RF (n=86)</td>
</tr>
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</table>

No IAP or IAP <4 hour prior to delivery,* non adherence.
Conclusion: CDC guideline adherence was suboptimal, especially in the universal maternal screening of mothers delivered via elective CS and in the overzealous management of infants born to GBS unknown mothers with no risk factors. Improvement initiatives to increase compliance in these groups are necessary.

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SHORT-TERM FUNCTIONAL OUTCOMES OF INFANTS WITH CHIARI II MALFORMATION WITH TRACHEOSTOMY AND HOME VENTILATOR-DEPENDENCE.
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Background: Chiari II malformation is associated with reduced life expectancy. The major causes of death during the first few years are related to brainstem dysfunctions which include severe apnea, cardiac arrhythmias and vocal cord paralysis. Our purpose is to report the short-term functional outcomes of a series of seven infants with Chiari II malformation who received tracheostomy for home mechanical ventilation.
Method: Retrospective chart review
Results: Over the last 5 years, a total of 39 infants with Chiari II malformation were discharged from the intensive care nursery. Of these, 7 (18%) had tracheostomy for home mechanical ventilation. All 7 infants were born at term, AGA. Four were males. Myelomeningocele was repaired and VP shunt placed at median ages of 1 day (range 1-5 days) and 5 days (range 1-46 days) respectively. Tracheostomy was placed within 3 months of age (range 1 – 3 months), all but one were due to central apnea and vocal cord paralysis. All infants with central apnea were provided chronic ventilation at parent’s request. The current ages at the time of data collection range from 2 months to 5 ½ years. Of the 7 patients, 1 is decannulated and 6 remain tracheostomy-dependent. Of these 6, two are weaned off the ventilator 24 hours a day, three are receiving nocturnal ventilation, and the youngest patient, a 2 month old is completely ventilator-dependent. All the seven patients are gastrostomy tube-dependent for nutrition, and five are urinary catheter-dependent for neurogenic bladder. Six of the seven patients are now two years or older and all are wheelchair-bound, have significant speech and language delay and are receiving physical, occupational and speech therapy.
Conclusion: In our case series of seven infants with Chiari II malformation, only one is successfully decannulated. All continue to have complex medical needs with significant functional delays. These results underscore the ongoing morbidities, neurodevelopmental impairments, and risk for mortality faced by this vulnerable population.

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CASE SERIES OF NON-INFECTIOUS PAROTITIS IN INFANTS WITH BRONCHOPULMONARY DYSPLASIA.
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Background: Salivary gland inflammation is rare during the neonatal and infancy period and the pathogenesis in this age group is not fully understood. Risk factors for parotitis include: low birth weight, oral trauma, immune suppression, ductal obstruction, sepsis, malnutrition and dehydration.
Objective: We report three extremely premature infants with severe bronchopulmonary dysplasia who had tracheostomy for prolonged mechanical ventilation and presented with non-infectious parotitis in the NICU.
Method: Retrospective chart review
Results: There were 3 infants born at 24-25 weeks with severe BPD who had tracheostomy at 36 -43 weeks PMA and were diagnosed with parotitis between 42 -50 weeks PMA, 2 were bilateral. All 3 did not present with fever, only 1 had leukocytosis at the time of parotitis. All 3 had prolonged use of systemic steroids and chronic diuretics for BPD. All 3 were exclusively G tube fed without feeding by mouth. Two were diagnosed by CT and one by ultrasound. All 3 had full work up to exclude infectious etiology that were all negative. Two infants were treated with empiric course of antibiotics. Two infants had immunologic evaluation and were immune-suppressed. Two had recurrent parotitis. There were no other complications following parotitis.
Conclusion: Non-infectious parotitis can complicate the clinical course of tracheostomized and ventilator-dependent infants with severe BPD. Multiple factors including immune suppression, prolonged steroid exposure, chronic diuretic use, non-oral feeding and tracheostomy may play a role in its pathogenesis. While there was recurrence in 2 cases, the clinical course appeared to be self-limited.
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EVALUATING THE DIAGNOSTIC ROLE OF BRAIN CT SCANS IN CHILDREN WITH NEW ONSET FEBRILE SEIZURES.
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Background: Currently neuroimaging is not part of the recommendations or guidelines set by the American Academy of Pediatrics and American Academy of Pediatric Neurology for evaluating febrile seizures. However, many physicians continue to evaluate patients with febrile seizures using brain computed tomography (CT) for demonstration of cause and exploring prognosis.
Objective: To determine the diagnostic utility of brain CT in children who present to the emergency department (ED) with new-onset febrile seizures (NOFS).
Design/Methods: Retrospective chart review of patients aged 6 months to 6 years who presented to the ED with NOFS during the study period of 2007-2012. Children diagnosed with concomitant seizure disorder, genetic syndrome, brain trauma, encephalitis or meningitis were excluded from the study. All parametric data was analyzed with student t-test.
Results: 86% (131/152) of children presented with simple NOFS and 14% (21/152) had complex NOFS. Table 1 outlines the characteristics between the two groups.
Table 1: Characteristics | Simple NOFS | Complex NOFS | P value
--- | --- | --- | ---
Males | 77/131 (58%) | 13/21 (61%) | 0.07
GA <37wk | 14/131 (10%) | 2/21 (9%) | 0.70
Mean age | 29months ± 43months | 20months ± 52months | 0.88
Brain CT ordered | 23/131 (17%) | 9/21 (42%) | 0.03
Overall 21% (32/152) of children were evaluated with brain CT, of which 9% (3/32) had abnormal findings. 3% (5/152) of our study population were diagnosed with seizure disorder in subsequent months with confirmatory EEG.
Conclusions: Children, who had brain CT ordered, were more likely to have complex NOFS. This suggests that complex NOFS could be a possible predictor for ordering brain CT and warrants further large scale studies.
Implications for Practice: Neuroimaging studies tend to be performed more often in children presenting with complex febrile seizures as compared to those with simple febrile seizures.

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EFFECT OF CLINICAL PRACTICE GUIDELINE IMPLEMENTATION ON FEBRILE INFANT EVALUATION AND MANAGEMENT
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*Children's Mercy Kansas City, Kansas City, MO, USA
Background: One in 10 infants ≤60 days old who present with fever will be diagnosed with a serious bacterial infection (SBI), which includes meningitis, bacteremia, and/or urinary tract infection. However, febrile infant management varies widely among practitioners. A clinical practice guideline (CPG) was implemented in an urban children's hospital with the aim of minimizing practice variation and improving clinical outcomes for febrile infants. The objective of this study is to determine the association of CPG implementation with diagnostic test and medical therapy use and clinical outcomes for febrile infant evaluations.
Methods: Infants ≤60 days old with a documented or caregiver-reported fever ≥38.0°C from 1/1/09 – 1/31/11 (pre-CPG) and 2/1/11 – 1/31/13 (post-CPG) were included. Data on patient demographics, clinical presentation (including whether children met CPG-determined low-risk criteria for SBI), diagnostic tests, medications administered, and patient outcomes were collected. Febrile infants were further divided into two age groups: 0-28 days and 29-60 days old, due to CPG recommendations differing based on this age criterion. Management practices and outcomes were compared between pre- and post-CPG periods.
Results: A total of 967 infants were identified pre-CPG and 843 infants post-CPG. Evaluation of infants 0-28 days old including complete blood count (CBC), blood and urine cultures, lumbar puncture (LP) and herpes simplex virus (HSV) testing did not significantly change after CPG implementation. Post-CPG, more infants 29-60 days old underwent LP (60% pre-CPG vs 69% post-CPG, p=0.0008) while fewer infants underwent HSV testing (14% pre-CPG vs 9% post-CPG, p=0.0055). Other testing (CBC, blood and urine cultures) remained unchanged for older infants. Antibiotic use decreased among low-risk infants 29-60 days old (83% pre-CPG vs 62% post-CPG, p <0.0001). Diagnosed SBI, hospital admission prevalence, and length of stay did not change after CPG implementation.
Conclusion: Antibiotic use and HSV testing decreased and LP obtainment increased for infants 29-60 days old after CPG implementation, representing changes toward adherence to CPG recommendations. These results suggest that CPG implementation reduced practice variation at our institution.
A DE NOVO MISSENSE MUTATION IN THE FORKHEAD DOMAIN OF FOXP1
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Sanford Research, Sioux Falls, SD

Background: FOXP1, a member of the winged-helix motif forkhead box protein family, is a transcriptional repressor that has been linked to development of many tissues throughout the body, particularly within the brain and the immune system. Disruptions in Foxp1 have been shown to have profound phenotypes, including global developmental delay, autism spectrum disorders (ASD), and intellectual disabilities (ID). A two-year-11-month old male presented with a severe phenotype, displaying hypotonia, global developmental delay, seizure-like activity, and recurrent fevers following the seizures. Clinical whole exome sequencing (WES) showed a de novo c.1574G>A (p.R525Q) missense variant of unknown significance. This mutation was compared with a previously reported nonsense mutation (p.R525X) that also occurs in the DNA-binding domain. Results from transfection of the missense and nonsense variants into HEK 293 cells suggest a disruption of FOXP1 activity. Although there was correct localization of the protein to the nucleus in the missense variant, (the nonsense mutation does not) it still loses repression activity. In addition, the DNA was transfected into primary neurons of an E14.5 mouse to show the effects on polarization as well as differences in structure that occur in each variant. The mutations were introduced to mouse embryos at E14.5 using in utero electroporation (IUE) and the tissues were stained with layer specific markers to ascertain localization within the cerebral cortex. The findings from this study show the benefit and importance of conducting basic science analyses on novel mutations and how it can lead to a better understanding of the biological significance, clinical phenotypes, and pathways of neurodevelopmental disorders as a whole.

NEURODEVELOPMENTAL OUTCOME AT SCHOOL AGE OF CHILDREN WITH CONGENITAL HEART DISEASE: A PILOT STUDY.
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Background and Objective: With improved survival for children with complex congenital heart disease (CHD), there has been a heightened awareness that these children are at an increased risk for poor neuropsychological outcome. The goal of this pilot study is to delineate the neuropsychological outcomes at school age of children who have undergone cardiac repair prior to 3 months of age.

Methods: A sample of 20 children at 8-9 years of age with a diagnosis of transposition of the great vessels, hypoplastic left heart syndrome, Tetralogy of Fallot, or coarctation of the aorta will be evaluated using the Wechsler Intelligence Scale for Children (WISC)-IV and PedsQL modules which are questionnaires assessing health-related quality of life. Parents of enrolled subjects will complete the Child Behavior Checklist, PedsQL modules, and the Vulnerable Child Scale.

Results: Assessments have been completed on 9 subjects. The WISC Full Scale Intelligence Quotient scores of these children range from 65-102 with median of 96 (IQR: 85-99). Parents who perceive their child as vulnerable tend to report worse overall health for their child as well as their child having more symptomatic heart disease, and they worry more about their child’s heart condition. Because of their child’s health, this subset of parents tends to have more problems with their own physical and emotional functioning. Child-reported quality of life measures indicate their lives are negatively affected by their CHD, and their responses often differ from those of their parent.

Conclusions: The full scale IQ scores of this population fall in the extremely low to average range. A large percentage of children have repeated a grade and frequently require special services at school. In families where the child is perceived as more vulnerable, there is a lower parent-reported quality of life and greater disease impact on family functioning.

QUALITY IMPROVEMENT PROJECT TO OPTIMIZE USE OF RAPID ANTIGEN DETECTION TESTING AND ANTIMICROBIAL UTILIZATION FOR GROUP A STREP PHARYNGITIS IN OUTPATIENT PRACTICE
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Background: Acute pharyngitis is a common diagnosis in pediatric outpatient clinics. Group A streptococcus (GAS) is the most common bacterial cause of pharyngitis in children but viruses are far more common. The Infectious Diseases Society of America (IDSA) clinical practice guideline for GAS pharyngitis recommends using strict criteria to determine testing, as there is a high rate of colonization (~30%) in school-aged children. This colonization may lead to unnecessary treatment. We suspected many outpatient clinic providers are obtaining
unnecessary testing for GAS and providing antibiotic therapy when it may not be indicated. This provides an opportunity for intervention to reduce unnecessary antibiotic prescribing in outpatient pediatric clinics.

**Methods:** Charts were identified for inclusion from patients with a procedure code for streptococcal rapid antigen detection test (RADT) in 2 community pediatric clinics. Symptom history, exam findings, and patient-specific factors were collected from the encounter where RADT was performed. These data were used to calculate the outcome measure, unnecessary GAS testing. Baseline level of this outcome measure was established by reviewing 20 charts per month for a 1 year period (October 1, 2013–September 30, 2014). Interventions include an educational webinar, a discussion of baseline unnecessary testing results with the clinic providers, and a plan for adopting new office procedures to decrease unnecessary testing. Post-intervention data will be available by the time of presentation.

**Results:** 240 charts were reviewed for the baseline data collection period for each clinic. During this period 81% of GAS testing in Clinic A and 70% of GAS testing in Clinic B were deemed unnecessary using criteria from the IDSA guidelines for testing. The most common reason testing was unnecessary was presence of viral symptoms followed by the absence of sore throat. The unnecessary tests resulted in 55 antibiotic prescriptions that were not indicated in Clinic A and 151 antibiotic prescriptions that were not indicated in Clinic B.

**Conclusions:** The majority of GAS testing in these outpatient clinics may be unnecessary, due to presence of viral symptoms in patients undergoing GAS testing. Testing for GAS in children when it is not clinically indicated can result in unnecessary antibiotic exposure. Interventions focused at reducing unnecessary GAS testing may reduce unnecessary antibiotic use in outpatient pediatric clinics.

**GENTAMICIN DOSING REGIMEN IN NEONATES – HOW MUCH IS TOO MUCH?**

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**Background:** Different Gentamicin dosing regimens in NICUs nationwide have resulted in varying peak level attainment. Our study aims to review variability in Gentamicin dosing and levels in a selected NICU population of <35 weeks gestational age within 7 days of life at Mount Sinai Hospital and look into the possibility of establishing a single dosing regimen which can reach adequate peaks regardless of gestational age.

**Methods:** A retrospective chart review was done, looking at infants <35 weeks GA within 7 days of life between 2009 and 2014. Inclusion criteria were limited to <35 weeks GA infants within post natal age of 1 week of receiving Gentamicin. Data was divided into Variable dosing (4.5mg/kg/dose Q36h for 30-34 weeks GA and 5mg/kg/dose Q48h for <29 weeks GA – Group 1) and Fixed dosing (4mg/kg/dose Q36h for 30-34 weeks GA and Q48h for <29 weeks GA – Group 2) regimens. Goal serum levels were peaks between 6-12 mg/dl and trough level <2. 169 patients in group 1 and 90 patients in group 2 met the inclusion criteria. Categorical data was analyzed with chi-squared/Fisher’s exact test. Parametric data was analyzed with t-test and nonparametric with Mann–Whitney U test. p value of < 0.05 was considered statistically significant.

**Results:** Our study included 259 babies, 169 were in Group 1 and 90 were in Group 2. Although not significant, 88 (97.7%) of the Fixed group attained therapeutic levels compared to 146 (86%) in the Variable group (p<0.08). Conversely, 23 (14%) in the Variable group attained supra-therapeutic levels compared to 2 (2.2%) in the Fixed group (p<0.03).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fixed dosing</th>
<th>Variable dosing</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW</td>
<td>1543 ±534</td>
<td>1447 ±490</td>
<td>Not significant</td>
</tr>
<tr>
<td>GA</td>
<td>31 ± 3.1</td>
<td>30.4 ± 3.1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Gentamicin trough</td>
<td>1 ± 0.35</td>
<td>1 ± 0.46</td>
<td>Not significant</td>
</tr>
<tr>
<td>BUN</td>
<td>19 ± 15</td>
<td>18 ± 14</td>
<td>Not significant</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.9 ± 0.4</td>
<td>0.9 ± 0.28</td>
<td>Not significant</td>
</tr>
<tr>
<td>Urine Output</td>
<td>3.68 ± 1.3</td>
<td>3.69 ± 1.2</td>
<td>Not significant</td>
</tr>
<tr>
<td>Gentamicin peak</td>
<td>9.3 ± 1.8</td>
<td>10.4 ± 1.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** More supra-therapeutic levels occurred with Variable dosing and Fixed dosing achieves more therapeutic levels. Fixed dosing regimen of 4mg/kg/dose successfully attains therapeutic ranges across various gestational age groups.
PREVALENCE OF INFECTION WITH MYCOPLASMA PNEUMONIAE AND CHLAMYDIA PNEUMONIAE IN HOSPITALIZED CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA.

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**Background:** Community-acquired pneumonia (CAP) in children is caused by many organisms including respiratory viruses, typical bacteria and atypical bacteria such as Mycoplasma Pneumoniae (MP) and Chlamydia Pneumoniae (CP). Studies in hospitalized children with CAP done in tertiary care university hospitals have found infection with MP in 8%-25.7% cases in studies using PCR alone, in 7-33% cases in studies using serology alone, and in 11-35% cases in studies using both PCR and serology. Infection with CP has been found in 0-5.9% cases in studies using PCR alone, 3%-9% cases in studies using serology alone and 3%-7% cases in studies using serology and PCR. In our hospital, a panel of PCR assay on nasopharyngeal swab for various respiratory pathogens including MP and CP is frequently used in children admitted with CAP. This study was done to evaluate the prevalence of infection with MP and CP in hospitalized children with CAP in inner-city population of predominately minority children.

**Methods:** Retrospective review of medical records of children 6 months-18 years of age, hospitalized with a diagnosis of Pneumonia from March 2013 to December 2014. Charts were reviewed and included in analysis, if the child had fever (>100F) and/or respiratory symptoms or signs at admission and had radiographic opacity on chest x-ray consistent with diagnosis of pneumonia. Various demographic, clinical, laboratory, radiologic and microbiologic data were collected.

**Results:** 157 patients met the study criteria. Mean age was 3.8 ± 4 years. 87 (55%) were African-American, 25(16%) Hispanic, and 45(29%) of mixed, other or unknown race. Nasopharyngeal swab for respiratory panel PCR was done in 104 (66.24%), and both PCR and MP serology were obtained in 6 patients (3.82%). Of the patients, in which either PCR or serology was obtained (n=104), 8 (7.6%) were positive for MP and 1 (0.9%) was positive for CP. PCR was positive for one or more respiratory viruses in 73 (70%) cases. **Conclusion:** A large majority (70%) of hospitalized children with CAP in this inner-city population had infection with respiratory viruses. Infection with MP or CP in this population was very low, much less than reported in other studies done in tertiary care university hospitals. Prospective study in this specific population is needed to confirm these findings.

ASSOCIATIONS BETWEEN PARENT AND CHILD PERCEPTIONS OF CHILD SLEEP IN OBESE YOUTH.

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**Background:** A growing body of literature indicates sleep has important implications for daytime functioning in youth. Sleep problems have been associated with poorer attention/concentration, cognitive deficits, impaired academic achievement, and greater anxious and depressive symptomology in youth. Obese youth may be particularly susceptible to sleep difficulties. However, up to 80% of children's sleep problems are neither reported to, nor treated by primary healthcare providers. One contributing factor may be the lack of consensus regarding how to assess sleep in this age group efficiently, effectively, and affordably. Objective indicators of sleep quality and quantity, including actigraphy and polysomnography, are cost prohibitive for many providers. Sleep questionnaires completed by children and their parents may provide a cost-effective method for screening for sleep problems in youth in routine clinical care. The present study investigated associations between reports on an abbreviated version of a parent report measure, the Children's Sleep Habits Questionnaire, and the child self-report version, the Sleep Self-Report, in a clinical sample of 45 children with morbid obesity. Total scores demonstrated a strong positive association, r=.525, p<.01. Correlations were strong for items assessing fear of dark (r=.496, p<.01), visits to a family member's bed during the night (r=.461, p<.01), and daytime sleepiness (r=.424, p<.01). There were moderate associations for bedtime consistency (r=.314, p<.05) and falling asleep alone (r=.328, p<.05). Overall, results suggest parent and children's perceptions of sleep behaviors were consistent in a clinical sample of obese youth. Although further validation work is necessary, our study provides preliminary data that the Children's Sleep Habits Questionnaire and Sleep Self-Report may facilitate identification of obese youth who are experiencing sleep problems and would benefit from more extensive evaluation of sleep difficulties.
EVALUATION OF DEEP MUSCULOSKELETAL INFECTIONS: EXPERIENCE OF A CARE PROCESS MODEL APPROACH IN A PEDIATRIC EMERGENCY DEPARTMENT

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Background: Musculoskeletal infections commonly present to the ED and require prompt recognition to provide the best outcomes for children. Evidence-based guidelines have been developed for septic arthritis, but none have tried to develop a guideline to identify all types of deep musculoskeletal infections.

Objective: To describe a musculoskeletal infection care process model in the Emergency Department & Urgent Care Center of a children’s hospital.

Methods: In April of 2014, a multidisciplinary team developed a care process model to standardize the evaluation of patients presenting to the ED with concern for a deep musculoskeletal (MSK) infection (e.g., septic arthritis (SA), osteomyelitis (OM), deep muscle abscess, pyomyositis, or necrotizing fasciitis). A clinical decision rule (CDR) for SA of the hip was used to categorize all suspected patients of a MSK infection into a risk group. The factors included were: temperature >38.3, non-weight bearing, WBC >12.0, CRP >2.0, and ESR >40. Risk stratification was established as follows: High (>3 factors), Moderate (2 factors), or Low (0 to 1 factor). Patients were identified retrospectively through electronic order history for imaging of an extremity and for labs recommended by the CDR. Electronic medical records were reviewed and results of imaging, presence of the CDR criteria & final diagnosis were documented.

Results: From April 2014 to April 2015, 608 patients were evaluated for a deep MSK infection. MSK infections were identified in 68: SA (24), OM (29), SA/OM (8), deep muscle abscess (6), pyomyositis (1). Of the 68 patients, 33 (49%) were categorized as high and 21 (31%) were categorized as moderate. Among 14 patients with an MSK infection categorized as low, OM occurred in 10 & SA in 4. Of patients without an MSK infection (n=540), 387 (72%) were categorized as low & 64 (12%) were considered high. The most common diagnoses for patients without a deep MSK infection were extremity/joint pain (33%), cellulitis/abscess (22%), and transient synovitis (17%). Of 355 patients discharged home, 10 were admitted within 1 week of the ED evaluation however, none were identified to have a deep MSK infection.

Conclusions: The care process model stratified 80% of patients found to have a deep MSK into the high or moderate risk group. Future work will evaluate the factors involved in children that had a MSK infection and were found to be low risk.

HYPOXIA UPREGULATES TYPE II TGFβ RECEPTOR INTERACTING PROTEIN-1(TRIP-1) EXPRESSION IN MOUSE PUPS.

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Exposure to prolonged hypoxia at birth results in arrested alveolar development and vascular changes in mouse pups that mimic the development of bronchopulmonary dysplasia, a human disease with high morbidity and mortality. Central to these pulmonary changes are hypoxia-induced factors including the TGFβ signaling pathway, an important cytokine implicated in lung development and repair as well as vascular development. The type II TGFβ receptor interacting protein 1 (TRIP-1) is a protein that has been shown to modulate gene expression downstream of the TGFβ signaling pathway and has been identified as part of the eIF3 complex. However, the effect of hypoxia on TRIP-1 expression during the alveolarization stage of lung development is unknown. Our lab has previously demonstrated that TRIP-1 mediates cellular processes in wound healing and repair, specifically myofibroblast trans-differentiation and EMT through both TGFβ dependent and independent mechanisms and Yuan et al. recently found that TRIP-1 plays a critical role in embryonic development of Zebrafish and tumorigenesis via vascular endothelial growth factor (VEGF) signaling. In addition, TRIP-1 expression has been implicated in hypoxia-induced angiogenesis in human hepatocellular cells suggesting that TRIP-1 expression may play a role in hypoxia-induced lung injury. Method: Wild type mice were exposed to either room air (21%) or hypoxia (12%) from birth. Pups were sacrificed at 7 and 14 days of treatment with lung tissue harvested. A subset of lung tissue was fixed and embedded in paraffin for morphology, histology and immunohistochemistry studies. Another subset of lung tissue was collected for protein and RNA analysis.

Result: Hypoxia exposed mouse pups have lower radio alveolar counts (RAC) compared to room air exposed pups. Mouse pups exposed to hypoxia for 14 days have higher TRIP-1 expression compared to room air exposed pups (P<0.05). Mouse pups exposed to low O2 for 7 and 14 days have increased TRIP-1 staining compared to controls (P<0.05).
Conclusion: TRIP-1 expression is increased during hypoxia exposure in mouse pup lungs. This increased TRIP-1 expression may reflect either a protective or a pathologic response, the specific ascertainment of which may offer prospect for intervention therapies aimed at mitigating the effect of hypoxia lung injury.

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SUICIDE SCREENING IN A BUSY PEDIATRIC URGENT CARE
Rationale: Suicide is the third leading cause of death in the adolescent population. Many teens are seen in a health care setting shortly before taking their lives. Unfortunately, they are never identified as being at risk for suicide and therefore never set up with appropriate treatment or resources. We have initiated a suicide screen in our busy pediatric urgent care setting with the intention of identifying at risk adolescents and establishing appropriate treatment.
Methods: A two question written survey is administered to all patients 12 years and older presenting to the Urgent Care. Extensive education of the Urgent Care staff was done prior to implementation. Patients with positive screens undergo further mental health evaluation and are either admitted or counseled by Social Work concerning need for outpatient treatment. Social Work follows these patients over a one month time period to facilitate entrance into outpatient therapy.
Results: Screening began in March, 2014. Through March, 2015 we have screened 4808 patients. There were 137 (2.8%) positive screens and 9 (6.6% of those with positive screens, 0.2% of screened patients) patients were admitted. The program is well accepted by staff and is not thought to significantly interfere with patient flow.
Conclusions: Suicide screening in an urgent care setting has not previously been described. Suicide Screening is feasible in a busy Pediatric Urgent Care Center. It is well accepted by nursing staff and providers. Challenges to the system include insufficient mental health resources in the community to provide the necessary follow up. This is being addressed by the Social Work Department and other providers.

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EFFECT OF UNILATERAL PULMONARY ARTERY STENOSIS AND DISTAL LUNG VASCULAR RESISTANCE ON REGURGITATION AT THE BRANCHES-A COMPUTATIONAL STUDY.
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Background and Objectives: Unilateral branch pulmonary artery (PA) stenosis and distal pulmonary vascular resistance (PVR) can affect regurgitation at the PA branches in patients with free pulmonic insufficiency. An ability to predict PVR from the branch PA regurgitation fraction (RF) may assist in clinical decision-making. Prior reports in small patient population with multiple confounders have suggested that unilateral stenosis decreases and elevated PVR increases the RF at the affected branch. This study examines the independent effects of unilateral stenosis and distal PVR on regurgitation at the PA branches by keeping the confounders such as heart rate, cardiac output and PA geometry fixed.
Method: Three-dimensional computational idealized models of non-compliant PA bifurcation with different degrees of left PA (LPA) stenosis and different distal PVR (simulated by porous media) were developed. Pulsatile flow was simulated by applying a fixed time-varying flow at the main PA inlet and zero pressure at each outlet. The RF at each branch was calculated; graphically plotted and analyzed.
Result: For a given RF at the main PA, an increase in unilateral PVR showed a small but consistent drop in RF (figure 1) at the affected branch (% drop from baseline RF after raising the baseline PVR by 5 times was only 11-17% in the left and 5-8% in the right side). An increase in LPA stenosis did not change the ipsilateral RF except when the stenosis was severe (11-19% rise from baseline RF as in figure 2).
Conclusion: Since the RF at PA branches changes minimally with a change in PVR it might not have potential clinical utility in predicting distal PVR. Although the effect is small, RF at the affected side shows a rise with a severe stenosis and a drop with an elevated PVR. Prior study's observation of the drop in RF at the stenotic side could potentially be explained by an unknown but elevated PVR distal to the stenosis. Further studies with simultaneous Magnetic Resonance Imaging and cardiac catheterization in a larger population of relevant patients are needed to explore such effects.
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THE IMPACT OF DEVELOPING A PECTUS CENTER FOR CHEST WALL DEFORMITIES
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†University of Missouri-Kansas City, Kansas City, MO

Introduction: In July 2011, we established a dedicated center for patients with chest wall deformities to allow for more effective consultation and to initiate a bracing program for the carinatum patients. In this study, we evaluated the effect of this center on patient volume and management.

Methods: A retrospective review was conducted for 699 patients seen with congenital chest, rib and sternal anomalies between July 2009 – June 2013. Patient demographics, operative interventions, clinic and bracing visits were compared, based on the date of initial consultation, before the center opened (July 2009‐June 2011, Group 1), versus after (July 2011‐June 2013, Group 2). Comparative analysis was performed utilizing Chi-square and Mann‐Whitney U test.

Results: Three hundred twenty new patients were in Group 1 and 379 in Group 2, for an 18.4% increase in patient volume. The number of excavatum patients increased from 172 (Group 1) to 189 (Group 2). The number of carinatum patients increased substantially from 125 (Group 1) to 165 (Group 2). The number of mixed defects and rib/sternal anomalies was similar between groups. The percentage of patients undergoing operative repair of carinatum/mixed defects dropped significantly from 15.1% (Group 1) to 1.1% (Group 2) (p < 0.01) whereas the percentage of patients undergoing nonoperative bracing for carinatum/mixed defects rose significantly from 20.1% (Group 1) to 62.2% (Group 2) (p < 0.01). Patients traveled between 3 and 1249 miles to visit the center for a single visit suggesting that although the majority of patients are regional, the catchment area has extended beyond adjacent states.

Conclusion: Initiating a dedicated pectus center increased patient volume and provided an effective transition to nonoperative bracing for patients with pectus carinatum. The concentrated focus of medical staff dedicated to chest wall deformities has allowed us to treat patients on a local and regional level.

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CHORIOAMNIONITIS AND THE CORRELATION OF MATERNAL ABO PHENOTYPE AND PREMATURITY.
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There are several studies that show ABO phenotype plays a role in predicting poor outcomes in the adult population. Specifically related to ARDS, pre‐edempia, infection, and thromboembolic disease. The purpose of this study is to identify risk factors for prematurity based on maternal ABO phenotype.

We reviewed 1,462 charts of infants born between January 1st 2008-December 31st 2014, and with gestational ages 22-34 weeks. We looked at multiple dependent variables in our population including maternal age, race, pregnancy-induced hypertension, pre‐edempia, chorioamnionitis, PPROM, and IUGR.

A total of 1,462 charts were reviewed. O+ mothers were found to be 2.53 times more likely to develop chorioamnionitis compared to all other blood types (RR= 2.53, 95% CI= 1.09-5.88; P=.031). Conversely, B mothers are at a 46% decreased risk of developing chorioamnionitis versus all other blood groups (RR= 0.54, 95% CI= 0.36-0.81; P=.003). Rh factor also emerged as a prognostic indicator of disease with Rh-negative mothers having a 58% increased risk of developing chorioamnionitis compared to Rh-positive mothers (RR= 1.58, 95% CI= 1.02-2.43; P=.039).

While there are several reports in the literature on ABO phenotype and disease severity, few studies address maternal ABO phenotype and its correlation to prematurity. Understanding these relationships can help us predict maternal risk factors associated with prematurity based on ABO phenotype. By identifying these risk factors we will be able to provide optimal care for the most at risk neonates.

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HYDROCORTISONE TREATMENT FOR HYPOTENSION IN PRETERM INFANTS AND THE RISK FOR SPONTANEOUS INTESTINAL PERFORATION.
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The administration of low doses of hydrocortisone is the treatment of choice for hypotension in very low birth weight (VLBW) preterm infants, resulting in improvement of blood pressure, decreased administration of vasopressors, decreased days on vasopressors, and decreased volume use of vasopressors. However, one major adverse side effect to this treatment is the increased risk for spontaneous intestinal perforation (SIP). Currently,
there is little information available regarding what factors correlate with a higher instance of SIP following hydrocortisone therapy.

To provide insight on effectively using hydrocortisone to treat hypotension in preterm infants, while minimizing the risk of SIP, and to uncover additional factors associated with an increased risk of SIP in neonates receiving hydrocortisone treatment.

We conducted a retrospective chart review of infants treated for hypotension at Loyola University Medical Center’s Neonatal department from the years of January 2008 to December 2013. Neonates selected for the study received hydrocortisone for the treatment of hypotension, weighed less than 1500 grams at birth, and were less than 32 weeks gestational age. Additional data collected included gender, mode of delivery, APGAR scores, if the mother received steroids in the 24 hours preceding delivery, the number of doses of hydrocortisone each neonate received, the number of days the treatment spanned, the day of life treatment started on, and if there was combined vasopressor treatment. Lastly, it was noted which infants’ treatment resulted in SIP. Infants that died prior to discharge were not included in the study.

The data was analyzed using logistic regression. A total of 54 neonates qualified for the study, of which 9 had SIPs. The only significant association was between birth weight and the incidence of SIP with a p-value of 0.037 (p ≤ 0.05).

The results of our study suggest that the lower the birth weight of the neonate, the higher the incidence of SIP. The primary limitation of the study is the small sample size of 54 cases. In the future, we hope to expand on this sample size to determine if additional correlations can be made between the data collected and the incidence of SIPs.

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INFANT MORTALITY CAUSE OF DEATH IN CORONER CASES

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Background: A coroner must investigate a case if the death is unexpected, sudden, and/or suspicious or violent. All deaths reviewed by the coroner include a scene examination, autopsy process, and review of the medical history. The coroner completes the death certificate after all information from the autopsy process is available. Public health interventions are often based upon epidemiologic data generated from vital records. Infant mortality rate (IMR) is generally regarded as a fundamental indicator of population health and is often used to validate public health interventions. United States IMR is excessively high compared to other developed countries. Hamilton County, Ohio has one of the highest IMR in the nation. The purpose of this study was to analyze the most frequent cause of death (COD) in autopsies performed by the Hamilton County Coroner, to determine if there are target areas to provide public health interventions to decrease its high IMR.

Methods: No IRB was required for this study as all of the information accessed through the Hamilton County Coroner’s office is of public record. We conducted a retrospective review of autopsies conducted by the Hamilton County Coroner from January 1, 2006 through December 31, 2013. The eligible population included live born infants, who died less than one year of age. We excluded cases that were stillborn or intrauterine fetal demise.

Results: There were 217 cases of infant deaths corresponding to 14 cause of death categories identified in this cohort. Unsafe sleep accounted for the majority of infant deaths (n=141, 65%). Over the eight year study period, this is a mean of 17.6 unsafe sleep-related deaths per year. Contributing factors for unsafe sleep are positioning, co-sleeping, excessive bedding, and not sleeping in a crib. Several of these deaths met criteria for more than one category. 43 (30.5%) were due to positioning, 77 (54.6%) were due to co-sleeping, 19 (13.5%) were due to excessive bedding, and 112 (79.4%) were due to not sleeping in a crib.

Conclusions: During the study period, sleep-related deaths comprised the majority of infant deaths referred to the Hamilton County Coroner. Cause of death investigation demonstrated that nearly all of these deaths could be prevented through evidence-based interventions. Our data demonstrate that a specific focus on elimination of co-sleeping, and sleep in a crib could lead to significant reductions in sleep-related death.
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VITAMIN A SUPPLEMENTATION IN VERY LOW BIRTH WEIGHT INFANTS: REVIEW OF LITERATURE
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Purpose of review: Very low Birth Weight (VLBW) babies have a very high risk of mortality and morbidity in United States (US). Vitamin A deficiency is a commonly cited cause. Vitamin A helps maintain integrity of epithelial cells of the respiratory tract and is required for proper development and functioning of the retina, and immune system. Most premature infants have low plasma concentrations of Vitamin A and its active form as compared to term babies since accumulation of Vitamin A by the fetus mostly occurs in the third trimester. If post-natal supplementation is not provided in premature infants the relative Vitamin A deficiency is further aggravated.
Methods: We did a literature review of studies looking at the effect of Vitamin A supplementation in comparison with a placebo or by itself in varying dosing regimens as an intervention were reviewed. Outcomes were manifestations of deficiency like bronchopulmonary dysplasia (BPD), retinopathy, Intraventricular Hemorrhage (IVH), Patent Ductus Arteriosus (PDA) closure. Very low birth weight infants were defined as birth weight less than 1500 grams and less than 32 weeks GA.
Results: Most studies favored Vitamin A supplementation using the parenteral dose of 5000 IU, 3 times a week for at least 4 weeks. Effective reduction was seen in incidence of chronic lung disease due to BPD in VLBW babies. Role of supplementation in preventing retinopathy, IVH, PDA closure remains to be proven. Most studies had a sample size < 150.
Discussion: Definition of BPD used varied in different studies since it has evolved over time. Different surrogate markers were used as assessment but there is no single serological marker to assess Vitamin A stores in the liver. Weight based dosing fortification of milk is an alternative but with questionable role in VLBW infants since they receive parenteral nutrition.
Clinical correlation: Absorption of Vitamin A by enteral or parenteral feeds in premature infants is unpredictable and often times inadequate. Hence the need for parenteral dosing, which is not widely accepted due to concerns for toxicity. In the future, an RCT is warranted before making this standard of care. The goal should be to design a RCT using the current definition of BPD.

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LESION-SPECIFIC PRENATAL DETECTION OF CONGENITAL HEART DISEASE AT A MIDWEST CARDIAC SURGERY CENTER.
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Background: National prenatal detection of congenital heart disease (CHD) is approximately 30%. Prenatal diagnosis depends on detection of a cardiac abnormality at the obstetric (OB) 18-week anatomic ultrasound evaluation. Standard OB cardiac screening includes the 4-chamber view at a minimum, but only ~50% of defects can be identified by this view alone. Detection sensitivity can increase to 90% if outflow tract and 3-vessel views are obtained as well. The purpose of this study was to determine lesion-specific prenatal detection of CHD in our region.
Methods: Our Fetal Cardiology Program has grown robustly in fetal echocardiogram volume and services provided since 2010. Efforts to improve regional prenatal detection of CHD have included annual fetal cardiology symposiums and shadowing opportunities for regional OB sonographers. Retrospective review of prenatal diagnosis of critical CHD (lesions requiring surgery before 31 days of age) from 2010-2014 at our institution was completed through de-identified Heart Center® data.
Results: Prenatal detection of critical CHD improved from 28.1% (2010) to 46.2% (2014). However, prenatal diagnosis continued to vary widely depending on the specific cardiac lesion: diagnosis of hypoplastic left heart increased from 33% to 83%, while total anomalous pulmonary venous return (TAPVR) remained at 0% (see graph).
Conclusion: Regional prenatal detection now exceeds reported national averages, but individual cardiac lesions have varied rates of detection. Continued outreach education to local OB providers and sonographers, with emphasis on improving cardiac screening methods, is fundamental to improve prenatal critical CHD detection in our region.
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RISK FACTORS FOR ORAL STEROID USE IN THE FIRST 2 YEARS OF LIFE IN PREMATURE INFANTS.

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Rationale: 1:8 children in the United States are born prematurely(1). 73% of premature infants require rehospitalization(2) for respiratory illnesses. Oral steroids are commonly used in children; however, they have long-term side effects including diminished bone density, cataract formation, and growth deficits(3).

Methods: A retrospective cohort design (RCD) evaluated risk factors for oral steroid use in premature infants. The cohort (n=157) was born between 01/01/2008 and 12/31/2013 at <29 weeks GA, admitted to our NICU within 24 hours of birth, and had no significant congenital anomalies. Our dataset was compared to a large national dataset representing a similar patient population with similar clinical outcomes(4). Table 1 lists the categorical and continuous variables selected.

Results: Univariate analysis was performed to determine which variables were risk factors for oral steroid use: dysphagia (OR:3.04 p=0.005), transient adrenal insufficiency (OR:3.55 p= 0.006), inhaled steroid use in NICU (OR:3.46 p=0.03), inhaled steroid use at NICU DC (OR:6.44 p=0.04), inhaled steroid use at 6mo (OR:15.23 p<0.0001), birth weight (OR:0.998 for each increase of weight (gm) p=0.04), subsequent number of respiratory infections (OR: 2.04 for each subsequent infection p=0.0007), BPD severity (OR:1.6 p=0.02), oxygen use at NICU discharge, oxygen use at 1yr (OR:3.75 p=0.01) and oxygen use at 2yrs of age (OR:5.65 p=0.04). Gestational age had a protective effect (OR:0.76 p=0.03). Gender, tobacco exposure, NICU pulmonary HTN, Pulmonary HTN post NICU discharge, breast milk, oxygen at NICU discharge, oxygen at 6mo, steroids in the NICU, chronic adrenal insufficiency, and diuretics were not significant. A multivariable model using logistic regression with backward model selection was performed using the above variables and showed that number of respiratory infections, oxygen use at NICU D/C and inhaled steroid use at 6mo and 2 years were predictive of increased oral steroid use (% concordance 87%).

Conclusions: Risk factors for oral steroid use include signs of more severe respiratory disease, namely prescribed inhaled steroids. Other factors known to affect inflammatory processes in the lungs include dysphagia, oxygen use, recurrent respiratory infections, and adrenal insufficiency. It is unclear if oral steroids had a significant impact on the long-term respiratory health in infants with BPD since their wheezing/hypoxia was due to multiple factors causing persistent airway inflammation over time. This is an important clinical question since oral steroid use in this population is more frequent than in term infants and the side effect profile remains detrimental for a population that is already at higher risk for developmental problems.

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MATERNAL DOCOSAHEXAENOIC ACID SUPPLEMENTATION AND BODY COMPOSITION AT AGE 5 YEARS.

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The dietary intake ratio of omega-6 to omega-3 fatty acids in the US has increased dramatically over the last 50 years at the same time of equally dramatic increases in vegetable oil intake and obesity. Omega-6 fatty acids increase adipogenesis. A recent observational study associated higher arachidonic acid (ARA, 20:4 omega-6) in pregnancy with higher fat mass (FM) and higher maternal docosahexaenoic acid (DHA, 22:6 omega-3) with higher fat free mass (FFM) in the offspring at 5 and 7 years, suggestive evidence of early programming of body composition by fatty acid status. The purpose of this study was to determine if providing pregnant women with DHA would affect FM and FFM of their offspring at 5 years of age. The children’s mothers were part of a Phase III placebo-controlled, randomized trial of maternal DHA supplementation (600 mg/ day) starting before 20 weeks gestation and continuing until birth. We determined fat mass (FM) and fat free mass (FFM) by air displacement plethysmography (ADP) using the BodPod™ at 5 years (placebo, n= 75 ; DHA, n= 78 ). All children consumed DHA and ARA either from human milk or infant formula during the first year of life by parent choice. Linear regression was used to explore the effect of DHA supplementation by treatment group and interactions with prospective predictors of child body composition. Children whose mothers were assigned to DHA had significantly higher FM than those whose mothers were assigned to placebo (15.14±2.11 kg vs 14.48±2.22 kg, p=0.051). FM was unaffected by DHA supplementation, however, the association between gestational weight gain (GWG) and FM differed by group (pInteraction=0.043): greater GWG predicted higher FM in the placebo group (p=0.049), but not in the DHA-supplemented group. In summary, DHA supplementation during pregnancy increased offspring FFM at 5 years and attenuated the increase in FM related to gestational weight gain. Both are evidence that maternal fatty acid status during pregnancy has a long term effect on body composition of the offspring that could be altered by altering the balance of maternal omega-3 to omega-6 fatty acid intake.
The Developmental Origins of Health and Disease (DOHaD) hypothesis comes from epidemiologic studies that show a poor nutritional environment in utero can increase the risk of developing chronic diseases including non-alcoholic fatty liver disease (NAFLD). Due to the high prevalence of maternal obesity, maternal high fat diet (HFD) is one nutritional exposure of significant concern. Animal models of maternal high fat diet exposure during the gestational and lactation periods show that offspring have an increased risk for NAFLD. The molecular mechanisms involved in this disease progression are not clear, but a better understanding could help explain why some patients with NAFLD are more likely to develop progressive disease and provide targets for preventative therapy. In this study, female C57Bl6 mice were fed a standard diet (SD) or HFD for 8 weeks and allowed to breed. Dams were continued on the same diet with offspring sacrificed in perinatal period or maintained on either SD or HFD for 12 weeks. Body and liver weights were measured from offspring. Histology, gene, and protein expression analyses of liver from offspring were performed. Both male and female offspring from HF fed dams exhibited significantly larger body and liver weights than controls. Of approximately 30 genes analyzed that are involved in fatty acid and glucose metabolism or fibrosis, only MMP-9 was significantly increased in male offspring exposed to HFD compared to control. Despite not showing any change in gene expression, levels of PPAR-γ protein were significantly higher in both male and female offspring of HF fed dams compared to standard diet. Proteomic analysis performed on 7 day old pup liver supports dysregulation of PPAR-γ signaling after perinatal exposure to HFD. Histologic analysis showed evidence of collagen deposition (Sirius red), stellate cell activation (alpha smooth muscle actin positive), and inflammation (CD45+) in liver of HFD exposed offspring. Offspring exposed to perinatal HFD and then placed on HFD at weaning showed more extensive hepatosteatosis than offspring who were placed on HFD after perinatal SD. Interestingly, offspring exposed to perinatal HFD and then placed on SD for 12 weeks showed evidence of steatosis and significant pericellular fibrosis on sirius red staining. These findings show that perinatal HFD exposure induces pathologic changes that persist into adulthood and impact the response to dietary exposure. Thus, it is likely that perinatal HFD exposure predisposes to disease progression of NAFLD in the adult offspring.

The prevalence of diabetes and obesity during pregnancy is increasing at an astounding rate and the effects extend beyond those of the mother to include devastating consequences to the developing fetus. Infants born to mothers with diabetes (IDM) have poorer neurodevelopmental outcomes than their peers. Normal brain development and function are dependent on the insulin-like growth factor (IGF) signaling pathways. Activation of insulin dependent pathways, including Pi3K/AKT and Ras-Raf-MEK-ERK signaling, is essential for proper neurogenesis, synaptogenesis, neurite outgrowth, myelination and regulation of progenitor apoptosis. Indeed, IGF expression peaks during neuronal progenitor proliferation. Excess fuels in maternal circulation resulting from gestational diabetes can incite fetal hyperinsulinemia and elevated IGF signaling. But, the effects of hyperinsulinemia on the developing brain, resulting in an imbalance in the Pi3K/AKT and Ras-Raf-MEK-ERK signaling pathways, are unknown. The purpose of this study is to analyze changes in pathway activation, neuronal proliferation and differentiation, and neurobehavioral changes in offspring exposed to either maternal diabetes (CD-STZ), a high-fat diet (HF-CB) or the combination (HF-STZ) and to identify the molecular culprit of the insulin receptor that is responsible for these changes. Methods used: Female rats were fed a high fat (HF) or control diet (CD) throughout the study and bred with normal males. Gestational day (GD) 0 was defined as a positive swab for spermatozoa. On gestational day 14, dams were given an injection of either citrate buffer (CB) placebo or streptozotocin (STZ) to induce diabetes. Pups were either sacrificed on newborn day 1 (NBD1) or cross-fostered to normal dams for evaluation at 3 and 10 weeks. Brains were harvested at each time point and stratified for histopathology as well as gene and protein expression analyses. Additionally, animals will undergo behavioral analysis to look for changes in social interaction, anxiety, memory and motor performance. Summary of Results: This study will reveal changes in neurobehavior associated with hyperinsulinemia and dissect the molecular pathways underpinning these changes. Moreover, the results from this study may provide insight into potential therapeutic targets that could be provided to prevent IDM associated impairment in neurodevelopment.
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IRON DEFICIENCY PERTURBS NEURONAL OXIDATIVE STRESS RESPONSE

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Background: Iron deficiency during the fetal and neonatal period is one of the most prevalent nutrient deficiencies worldwide. It causes cognitive and socio-emotional abnormalities in adulthood despite prompt iron repletion in childhood. Many of these effects have been replicated in animal models, which facilitate investigations into the neural basis underlying these long-term neurological effects. Previous transcriptomic analysis of formerly iron deficient (FID) rat hippocampus identified alteration in the NRF2-mediated oxidative stress response, which plays critical role in maintaining cellular homeostasis. Due to multiple cell types in the hippocampus, the extent of this cellular effect in neurons is unclear.

Objectives: We sought to determine if iron deficiency permanently alters the mechanism that mediates the neuronal response to oxidative stress, thereby reducing the ability of neurons to cope with external stressors.

Methods: We used deferoxamine (DFO) to induce iron deficiency in an immortalized neuronal cell line (HT-22) that was derived from mouse embryonic hippocampus. Iron deficient (ID) and FID HT-22 cells were analyzed for expression of genes along the NRF2-mediated oxidative stress response pathway.

Results: Compared to iron sufficient (IS) control, ID and FID HT-22 cells showed alterations in expression of molecules along the NRF2-mediated stress response pathway.

Conclusion: Our finding confirms the diminished activity of oxidative stress response in the adult FID hippocampal neurons. Thus, this in vitro model is suitable to determine the ability of FID neurons in coping with various oxidative stressors, including xenobiotics, inflammation, and free radicals in future studies.

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PROTEOMIC ANALYSIS OF SYNAPTOSOMAL PROTEINS ALTERED BY ISCHEMIA IN DEVELOPING MOUSE BRAIN

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Background: Neonatal encephalopathy (NE) following hypoxic-ischemic (HI) insult remains a major cause of global infant mortality and morbidity. Many surviving infants with HI develop neurodevelopmental disabilities. Given the importance of synaptic growth and plasticity in neurobehavioral development, we focused on investigating the mechanism underlying synaptic dysfunction, an effectual consequence of ischemia.

Objective: We sought to delineate the molecular pathways that may be altered by early ischemia at the synaptic level in a mouse model. This will provide insight into the effects of early ischemia on synaptic development and function.

Methods: We induced ischemia by ligating the right carotid artery of postnatal day (PND) 10 mouse pups. 24-hr post surgery, ipsi- and contra-lateral hemispheres (excluding cerebellum) were collected and used to prepare synaptosomes by a sucrose-gradient method. Synaptosomal proteins were quantified using isobaric tagged for relative and absolute quantitation (iTRAQ). Selected synaptic proteins were validated by Western blots. iTRAQ data were analyzed by the knowledge-based Ingenuity Pathway Analysis (IPA).

Results: We identified 72 proteins, whose expressions were altered by ischemia (Fold change > 1.2, P<0.05). IPA analysis mapped these altered proteins to mechanisms critical for nervous system development and function, notably mTOR signaling, gene regulation by PPAR, and NRF2-mediated oxidative stress response.

Conclusion: Our findings suggest that early-life ischemia induced changes in molecular mechanisms that underlie synaptic dysfunction, which may lead to increased risk for neurological diseases and psychological disorders.

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UNTARGETED METABOLOMIC PROFILING OF BASELINE AND THREE MONTH PLASMA SAMPLES FROM JUVENILE IDIOPATHIC ARTHRITIS PATIENTS WITH EXTREME RESPONSE PROFILES TO METHOTREXATE THERAPY.

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Background: Juvenile Idiopathic Arthritis (JIA) is an immune-mediated clinically heterogeneous inflammatory disease of unknown etiology, although genetic and environmental factors may play important roles. The clinical management of JIA is challenging as response to treatment with methotrexate (MTX) is highly variable and underlying mechanisms of action of MTX are incompletely understood. In order to provide insight into the systemic effects of MTX responsive JIA, we performed a nontargeted high-resolution LC-MS metabolomics
analysis to measure plasma metabolites from individuals with JIA at baseline and after three months of treatment with MTX.

**Methods:** This is a single center prospective cohort study of newly treated JIA patients on standardized doses of MTX (15mg/m²) and folic acid (1mg/day). After obtaining informed consent, blood was obtained during routine lab monitoring at baseline and 3 months. At the 3 months patients were classified according to ACR Pedi criteria. Patients who did not meet ACR Pedi 30 were considered non-responders and those who met ACR Pedi 70 + were considered optimal responders. Plasma samples were extracted and separated on a HSS t3 column and analyzed by a Waters Xevo G2 QTOF mass spectrometer. Metabolites were putatively identified against the human metabolome database utilizing exact mass and MS/MS spectra.

**Results:** OPLS-DA analysis of the baseline plasma metabolome of responders (n=11) and non-responders (n=12) demonstrated a clear separation between the responders and non-responders. Group differences were in part driven by four metabolites in the bile acid biosynthesis pathway. On average, levels of bile acids were higher in MTX non-responders. Specifically levels of taurodeoxycholic acid (3.1-fold \((p = 0.0074)\)), taurohyocholate (4.9-fold \((p = 0.015)\)), tauroursodeoxycholic acid (6.5-fold \((p = 0.0479)\)) and chenodeoxyglycocholic acid (2.4-fold \((p = 0.079)\)). Additional markers were found in the lipid biosynthesis pathway, in addition to significant markers that have yet to be identified.

**Conclusion:** These data suggest that bile acid homeostasis may be related to MTX response in JIA. This finding may be relevant as in-vitro studies have shown bile acids can inhibit the enterohepatic circulation of MTX by impairing intestinal transport, liver uptake and biliary excretion of MTX. Further studies with targeted analytical methods towards bile acids are required to validate these findings.

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THE IMPACT OF INTEGRATING CLINICAL GUIDELINES INTO AN ELECTRONIC MEDICAL RECORD ON DIAGNOSIS AND MANAGEMENT OF ACUTE OTITIS MEDIA: A QUALITY IMPROVEMENT STUDY.

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**Background:** In 2013, the American Academy of Pediatrics and the American Academy of Family Physicians revised their 2004 clinical practice guidelines on acute otitis media (AOM), designed to assist providers in the appropriate diagnosis and treatment of AOM.

**Objective:** To assess the impact of integrating clinical practice guidelines for AOM into an electronic medical record (EMR) workflow.

**Methods:** A summary of the guidelines for AOM were developed and integrated into the EMR, so that when a diagnosis of AOM (ICD-9 382.9) was entered, a hyperlink appeared that opened the guideline summary. A retrospective cohort study was performed by abstracting data from pediatric outpatient and emergency department encounters with the diagnosis of AOM one year prior to and following integration of the guidelines in the EMR. Clinical documentation was evaluated for the presence of diagnostic criteria of AOM, concurrent signs and symptoms, pain control, and antibiotic use. Data were analyzed by tests of equivalence of proportion \((\chi^2 \text{ test})\).

**Results:** Of 1,139 charts abstracted, 579 encounters prior to guideline integration and 328 encounters after integration met inclusion criteria. In the post-guideline period, there was significant improvement in documentation of the diagnostic criteria for AOM (onset of less than 48 hours, middle ear effusion and middle ear inflammation) from 34.4% to 43.6% \((p=0.0059)\), due largely to the improvement in documentation of middle ear effusion (62.9% to 73.8%, \(p=0.0008)\). The data also show a significant increase in the use of first-line antibiotics (or an appropriate alternative in penicillin-allergic patients) for AOM from 49.2% to 63.1% \((p<0.0001)\).

**Conclusion:** This study demonstrated improvement in documentation supporting the diagnosis of AOM and rates of first-line or clinically indicated alternative antibiotic use after guidelines were integrated into an EMR. This suggests that the EMR can be used to positively influence providers and improve patient care. A larger study with inclusion of all encounters with a clinical suspicion for AOM would further elucidate the integrated guidelines’ impact on appropriate diagnosis and treatment of AOM.
NEONATAL PHLEBOTOMY-INDUCED ANEMIA RESULTS IN BEHAVIORAL DEFICITS IN ADULT MICE

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Background: While in the NICU, neonates are often allowed to reach low hematocrits while the brain is still rapidly developing. Early-life phlebotomy results in iron deficiency (ID), hypoxia, and acute alterations to neonatal hippocampal energy metabolism (Wallin et al., 2015). Rodent models of ID anemia and chronic hypoxia in early-life result in long-lasting effects on brain development.

Purpose: Assess the functional behavioral effects of adult mice that underwent phlebotomy-induced anemia in early life during critical developmental periods.

Methods: Postnatal day (P)3 mice (developmental equivalent = 26 weeks gestation in human) underwent twice daily phlebotomy by facial venipuncture to a target hematocrit of 21-25%. Once daily phlebotomy was continued to maintain the anemia until P14 (dev. equiv. = 42 weeks). Mice were then allowed to recover and underwent a battery of behavioral tests beginning at P65 including elevated plus maze (EPM), Barnes maze with a reversal task, and fear conditioning with cue extinction.

Results: Previously anemic (PA) mice had faster fear conditioning acquisition as compared to non-bled control. In addition, there was an interaction between cue extinction day and group (p=0.0258) where cue extinction was delayed in the PA mice. No differences were found in cue and contextual fear. No learning differences were found in the Barnes Maze. However, during reversal probe trials PA mice traveled 103.8% faster (p=0.0089) and traveled 103.5% further (p=0.0087), spending 74.9% less time in the center of the maze (p=0.0059). They reached the goal 78.9% faster (p<0.0001). Similar results were found in the probe trial. PA mice exhibited a trend towards decreased time in EPM open arms.

Conclusions: Non-anemic PA mice exhibit altered behavior as compared to control mice, indicating anemia during neonatal developmental periods alters behavior long-term. The deficits in cued fear extinction, in addition to their behavior in the Barnes maze and increased anxiety behavior in the elevated plus maze could be due to alterations to the dopaminergic system, especially as tyrosine hydroxylase requires iron as a cofactor in dopamine synthesis.

Clinical Correlation: Decisions made about hematocrit levels during neonates’ time in the NICU can have long-lasting effects on the brain.

CARE OF LATE PRETERM (LPT) INFANT: IMPORTANCE OF STANDARDIZED APPROACH

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Background: In 2006, the National Institute of Child Health and Human Development made a push to change the term used for neonates born 35 0/7-36 6/7 weeks from “near term” to “late preterm”, emphasizing the vulnerability and high risk of LPT neonates. Through a quality improvement (QI) project at a community level III Neonatal Intensive Care (NICU), we set out to standardized the approach to LPT neonates with the goal to lower morbidities and facilitate earlier dismissal (<7 days).

Method: Recognizing LPT neonates are at risk for transitional issues, a paper standard order form and protocol was created in 2007, allowing babies to remain with their family. Partnering with the family, the was providing anticipatory support to avoid NICU admit and decrease LOS. A standardized QI method, Plan Do Study Act (PDSA), was used to create cycles of change.

Results: Between the years 2003-2013, there were an average birth rate of 135/year for infants born between 35 0/7 – 36 6/7 weeks, referred to as LPT for the purpose of this project. Prior to the protocol 41% of LPT required NICU admission, with 46% of the overall LPT population requiring a LOS > 7 days. After the implementation of the protocol, both the percent of NICU admission and protocol failure decreased (Table 1).

<table>
<thead>
<tr>
<th>Year</th>
<th>Admitted to NICU (%)</th>
<th>LOS &gt; 7 days (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003-2006</td>
<td>41</td>
<td>46</td>
</tr>
<tr>
<td>2007-2009</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>2011</td>
<td>30</td>
<td>37</td>
</tr>
<tr>
<td>2013</td>
<td>23</td>
<td>31</td>
</tr>
</tbody>
</table>

With the introduction of computer based ordering (CPOE), protocol failure and those infants requiring length of stay (LOS) > 7 day increased. In 2013, with modification of the CPOE system and reintroduction and modification of the education system for parents and health care providers, improvement was seen in LOS and need for NICU admission.
Conclusion: The LPT project allowed for more careful observation and facilitated a shorter hospital stay and decreased NICU admission. With early recognition and support of risk factors, significant issues can be avoided, facilitating an earlier dismissal (< 7 days). An important lesson learned was a standard process must be integrated into the electronic medical record to become a sustained part of a practice culture.

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CLINICAL VIRULENCE OF PROPIONIBACTERIUM SPECIES GROWTH IN CEREBROSPINAL FLUID THIOGLYCOLLATE BROTH CULTURES.

DE Yin,‡ O Adogwa,‡ DD Williams,‡ SF Costa,‡ SA DeLurgio,* RE McKinney,‡ GA Grant§

*Children's Mercy-Kansas City; Kansas City, MO; †University of Missouri-Kansas City, Kansas City, MO; ‡Duke University, Durham, NC; §Lucile Packard Children's Hospital, Stanford University, Palo Alto, CA

Purpose: In patients with cerebrospinal fluid (CSF) shunts, Propionibacterium species in thioglycollate broth may be a true infection or skin contaminant. We aimed to estimate the relative hazard of shunt externalization for infectious reasons after thioglycollate broth-only growth of Propionibacterium vs. coagulase-negative Staphylococcus (CoNS) vs. other microorganisms.

Methods: We performed a retrospective cohort study via manual chart review of all patients with microorganism growth in only thioglycollate broth from CSF culture at Duke University Clinical Microbiology Laboratory between January 1, 1996 and March 31, 2010. We estimated relative hazards of CSF shunt externalization following the first positive broth-only culture, censored at time of non-infectious shunt externalization, positive CSF culture with a different organism, death, 2 years after culture, or end of follow-up. Data were analyzed by Cox models, adjusted for age, co-morbidities, number of shunt manipulations, culture procedure era, and neurosurgeon. Results: The cohort included 379 patients (median age 14.2 years, IQR 1.3-26.8) with 907 CSF broth-only cultures. At presentation, 304 (80%) patients had ≥1 clinical manifestation; 137 (36%) had ≥1 radiographic abnormality. Median CSF values were in the normal range; 14 (4%) patients had a repeat positive culture with the same organism in <90 days. 112 (30%) patients had their shunts externalized for an infectious reason within 2 years. Patients with Propionibacterium had lower point estimates for CSF shunt externalization than patients with CoNS (adjusted HR 0.68 [95% CI 0.35-1.30], P = 0.24) or other organisms (adjusted HR 0.66 [0.32-1.33], P = 0.24). Predictors of shunt externalization included younger age (adjusted HR 0.97 [0.96-0.99], P = 0.001), higher number of shunt manipulations (adjusted HR 1.16 [1.10-1.24, P <0.001], and neurosurgeon. Conclusions: Patients with broth-only cultures for Propionibacterium did not undergo shunt externalization any more frequently than patients with likely contaminants. Later events requiring shunt externalization within 2 years were uncommon. Growth of Propionibacterium from CSF thioglycollate broth may often be a contaminant without major clinical consequences.

Clinical Correlation: Broth-only growth of Propionibacterium may not always require CSF shunt externalization. A predictive model may help guide these clinical decisions but needs validation.
The James Sutherland Award

The James Sutherland Award was named after a neonatologist from the University of Cincinnati, who was instrumental in establishing their neonatal unit. Dr. Sutherland was a renowned teacher, clinical investigator, and role model for trainees. He was active in the Midwest Society for Pediatric Research, and encouraged trainees to submit work at the annual meeting. The award, which recognizes the best investigative work presented by a junior faculty member, was first given in 1991. To be eligible for this award, the junior faculty candidate must be no more than five years out of fellowship training.

The award is accompanied by an honorarium and plaque. The recipient is announced and honored each year at the Founder and Sutherland Awards Luncheon held during the MWSPR annual meeting.

1994 Thomas Scholz, MD
1995 Edward N. Guillery, MD
1996 Michael R. Uhing, MD
1997 Carol Gilmour, MD
1998 Robert H. Lane, MD
1999 I. I. Ekekezie, MD
2000 D. Balkundi, MD
2001 Janine Y. Khan, MD
2002 Steven Pipe, MD
2003 Shruti M. Phadke, MD
2004 J. Carter Ralphe, MD
2005 Michael Blake, MD, PhD
2006 Matthew I. Goldsmith, MD
2007 Jayme D. Allen, MD
2008 Alex Huang, MD and Mara Becker, MD, MSCE
2009 Michael Wilhelm, MD
2010 Celeste Morely, MD
2011 Amy VanMorlan, MD
2012 Juan Boriosi, MD
2013 Craig A. Byersdorfer, MD
2014 Naim Alkouri, MD
2015 Awarded at the MWSPR Meeting
The Frederic M. Kenny Memorial Award

Frederic M. Kenny was instrumental in establishing the Pediatric Endocrinology Clinical and Fellowship Program at the Children’s Hospital in Pittsburgh. Dr. Kenny was a scholarship student at Princeton University, then a medical school student at The Johns Hopkins University School of Medicine, where he received his medical degree in 1955. He completed his general pediatric residency at The Johns Hopkins Hospital in 1958 and then spent two years in the U.S. Navy. He then returned to The Johns Hopkins Hospital where he completed a pediatric endocrine fellowship.

In 1962, Dr. Kenny accepted an invitation to move to Pittsburgh and assume the position of director of the Pediatric Endocrine Division. He developed an outstanding clinical program in pediatric endocrinology and laboratory research focused primarily on normal adrenal function ranges for children and adolescents. He was intensely interested in the pathophysiology of all of the endocrinopathies, and his work led to the description of the course of endocrine diseases. He co-authored approximately 100 papers and made more than 40 presentations at scientific meetings around the world.

The Kenny Award is given for outstanding research presentation by a fellow at the MWSPR, and includes an honorarium and plaque.

1989  Michael S. (Mickey) Caplan, MD
1996  Brenda B. Poindexter, MD
2001  J. Carter Ralph, MD
2002  Indra D. Chandrasekar, MD
2003  Heather Bartlett, MD
2004  Eyal Shteyer, MD
2005  Peter DeYoung, MD
2006  Rinku Mehra, MD
2007  Wendy Luce, MD
2008  Melissa Agoudemous, MD
2009  Suzanne Kingery, MD
2010  Misty Good, MD
2011  Andrew Harris, MD
2012  Brian Becknell, MD
2013  Brittany L. Knipstein, MD
2014  Jessica White, MD
2015  Awarded at the MWSPR Meeting
The Jack Metcoff Award

The Jack Metcoff Award is given for outstanding research presentation by a resident or fellow at the MWSPR. The recipient receives a plaque and honorarium.

Jack Metcoff made a major impact on the field of pediatric nephrology and body fluid physiology. Throughout his career, Dr. Metcoff was the consummate teacher of clinical pediatrics and pediatric nephrology, of a problem-oriented approach to patient care, of the use of computers in medicine, and of investigative attitudes and techniques.

The Annual Conference on the Kidney, which he edited from 1950 to 1967, reflected the best of basic and clinical research progress in those years and remains a hallmark of journalistic excellence. As a leader and catalyst in the development of the Nephrosis Foundation, which evolved into the National Kidney Foundation and the American Society of Nephrology, he helped to lay the foundation for current professional and patient education.

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<thead>
<tr>
<th>Year</th>
<th>Name</th>
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<tbody>
<tr>
<td>1994</td>
<td>Bindya S. Singh</td>
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<td>1995</td>
<td>Genie E. Roosevelt</td>
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<td>1996</td>
<td>Raghavendra Rao</td>
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<td>1997</td>
<td>Howard M. Katzenstein</td>
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<td>1998</td>
<td>Rajeev Dixit</td>
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<td>1999</td>
<td>Jennifer L. Kloesz</td>
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<td>2000</td>
<td>Gregory Dalshaug</td>
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<td>2001</td>
<td>Lisa K. Kelly</td>
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<td>2002</td>
<td>Nancy B. Aspey</td>
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<td>2003</td>
<td>Gerhard C. Hildebrandt</td>
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<td>2004</td>
<td>Aaron K. Olson</td>
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<td>2005</td>
<td>Christopher Linblade</td>
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<td>2006</td>
<td>Todd D. Nebesio</td>
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<td>2007</td>
<td>Nicholas Von Bergen</td>
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<td>2008</td>
<td>Sundan Rajan</td>
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<td>2009</td>
<td>Paul Mann</td>
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<td>Shaun Ashfield</td>
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<td>Dennis Slagel</td>
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<td>Brian Stansfield</td>
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<td>2013</td>
<td>Lauritz Meyer</td>
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<td>2014</td>
<td>Sophia Patel</td>
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<td>2015</td>
<td>Awarded at the MWSPR Meeting</td>
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The William Segar Award

The William Segar Award was initiated in 2012 to be given annually to a student, resident or fellow trainee with a hypothesis driven clinical research or behavioral/social or education project that involves innovative improvement in patient care delivery.

Dr. Segar’s father was the first pediatrician to practice in the state of Indiana. Bill would earn both his BS (1944) and MD (1947) from Indiana University. Dr. Segar has long been an advocate for trainees and had served the MWSPR well as its 5th President and 2nd Founder’s Award winner. Dr. William E. Segar was one of the 38 people who attended the first meeting of the Midwest Society for Pediatric Research in Iowa City on October 27, 1959. He was present for the first business meeting and voted on the bylaws of the Society. He became the 5th president of the MWSPR in 1965. He was an active member and organizer of the Salt & Water Club, an active group that met adjacent to the MWSPR.

Together with Dr. Malcolm Holliday, he developed Holliday-Segar equation for calculating fluid therapy. Other than his time in the US Army at Walter Reed Medical Center, he trained and practiced medicine exclusively in Pediatric Departments within the MWSPR territory, University of Indiana, University of Illinois, Mayo Medical School, and finally the University of Wisconsin, where he became Chair of Pediatrics. This award is sponsored by Friends of William E. Segar.

2012 Carl Backes, MD
2013 Shawna S. Shafer, MD
2014 Emma Austenfeld
2015 Awarded at the MWSPR Meeting
Cleveland Clinic Award

The Cleveland Clinic awards Student Award is given for the most outstanding abstract presentation by a trainee at a level prior to postgraduate training or residency. The Cleveland Clinic has long supported the role of medical, graduate, undergraduate students, and even high school students in the MWSPR and provides ongoing support for this award.

2001 Anthony Ratanproeksa
2002 Liza Cadnapaphornchai
2003 Karen Wiseman
2004 Emily Segar
2005 Amy Hurst
2006 Christopher Lux
2007 Keri Drake
2008 Christa Pittner
2009 Katie Meyer
2010 Emily Peterson
2011 Jeremy Sandgren
2012 Brandon Downing
2013 Richard C. Godby
2014 Micaela Zywicki
2015 Awarded at the MWSPR Meeting
## The Stanley Phillips Award

Awarded for the best poster or posters at the MWSPR meeting. This award is named after Stanley Phillips III, a first year neonatology fellow at University of Wisconsin, who died during a transport in 2013 from a terrible ambulance accident. Dr. Phillips was a kind and compassionate physician, whom loved caring for ill newborns. He was looking forward to his research career and presenting at the MWSPR meeting. However, his research and clinical career was cut short. In the short time as a fellow, he was admired as an enthusiastic, inquisitive, thoughtful and caring physician. This award is sponsored by Meriter Foundation and University of Wisconsin Department of Pediatrics, Neonatology Division.

<table>
<thead>
<tr>
<th>Year</th>
<th>Winner</th>
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<tr>
<td>2013</td>
<td>Frances A. Boyle</td>
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<td>2013</td>
<td>BreAnn Sheehan, MD</td>
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<td>2014</td>
<td>Michael Thompson, MD</td>
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<td>2015</td>
<td>Awarded at the MWSPR Meeting</td>
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The Founder’s Award

The Founders Award is the highest honor given by the Midwest Society for Pediatric Research to a senior member in recognition of contributions made in the development of the careers of academic pediatricians and in the advancement of pediatric research. Since 1986, this award has recognized some of the leaders in our field of pediatric research and academic medicine.

Mead Johnson Nutritionals has generously provided an honorarium and plaque to the recipients during an awards luncheon held in honor of the recipient.

1986  Samuel J. Fomon, MD
1987  William E. Segar, MD
1988  Orville C. Green, MD
1989  Ira M. Rosenthal, MD
1990  Jean Holowach-Thurston, MD
1991  William Weidman, MD
1992  Reginald D. Tsang, MD
1993  Rosita Pildes, MD
1994  Dharmapuir Vidyasagar, MD
1995  Fred G. Smith, MD
1996  Gunner B. Stickler, MD
1997  Dorothy J. Becker, M.B.B.Ch.
1998  Laurence A. Boxer, MD
1999  Robert T. Hall, MD
2000  Sherin U. Devaskar, MD
2001  Edward S. Ogata, MD
2002  Jean E. Robillard, MD
2003  Frank R. Greer, MD
2004  Robert P. Kelch, MD
2005  John A. Widness, MD
2006  James E. Heubi, MD
2007  Edward F. Bell, MD
2008  William E. Truog, MD
2009  Avory A. Fanaroff, MD
2010  Michael K. Georgieff, MD
2011  Juan F. Sotos, MD
2012  Alan H. Jobe, MD, PhD
2013  Howard Kilbride, MD
2014  Margaret K. Hostetter, MD
2015  Jeffrey Segar, MD
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University of Minnesota

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University of Michigan

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Naim Alkhouri, MD (2016)
Cleveland Clinic Foundation
Hotel Information

We are able to offer you a discounted rate at the following Host hotel:

**Sheraton Kansas City Hotel at Crown Center**
2345 McGee Street, Kansas City, MO 64108
Telephone 816-841-1000 or 1-800- 325-3535

We have a block of rooms reserved until **Wednesday, October 7, 2015**. After this time they will be released. The rate is $149 for a Deluxe King. Book online or call.

In addition to the Host hotel, these other hotels listed below are within a close proximity of the conference site:

Westin Crown Center Hotel
KC Marriott Downtown
Hotel Phillips
Hilton President Kansas City
Fairfield Inn KC Downtown/Union Hill by Marriott

**Airport Information:**

The airport is about 20 miles north of the conference facilities. Taxi service and rental cars are available.

**Driving Directions:**
[http://www.mapquest.com/#c91d943837644dbfb14fdf55](http://www.mapquest.com/#c91d943837644dbfb14fdf55)

**Parking**
Onsite parking is available at no cost at Children’s Mercy Hospital. Covered parking is available at the Sheraton Hotel for $17/night.

**Registration for the Meeting:** **Registration deadline is October 13, 2015**
**Preregistration is required** for the meeting and you can register online: [www.medpubinc.com](http://www.medpubinc.com).

The registration fees are as follows:

**Pre-registration Discount Rate** *(register by October 13, 2015)*
- Member: $95
- Trainee: Free
- Nonmember: $140

**Onsite Registration Rates:**
- Member: $150
- Trainee: Free
- Nonmember: $200
Credit Card (MasterCard, Visa or American Express) will be accepted. Please note that by submitting this form with your credit card, you authorize MedPub, Inc. to charge your credit card for the amount as indicated above. Your credit card statement will show the charge from MedPub, Inc. and not from the Midwest Society for Pediatric Research. **You must register in advance.** Please note there are two luncheons offered for MWSPR attendees at no charge – please indicate if you plan on attending one or both of these events so that meals can be planned.

**Cancellation Policy:** Your registration fee, less a $50 administrative fee, will be refunded if written notification is received by MWSPR on or before **October 13, 2015. No refunds will be granted after October 13, 2015.**

Register online: www.medpubinc.com

The Final program will be posted to our Website one month prior to the meeting.  
https://www.aps-spr.org/regions/mwspr/

For Financial Questions, Contact Dr. Kling, below:  
For Programmatic Questions, contact Dr. Brophy below:

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SAVE THE DATE
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Chicago, Illinois