<table>
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<tr>
<th>TIME</th>
<th>ACTIVITY AND LOCATION</th>
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<tr>
<td><strong>WEDNESDAY, OCTOBER 3, 2012</strong></td>
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<tr>
<td>4:45 pm – 6:15 pm</td>
<td>MWSPR Council Meeting&lt;br&gt;1525 Research Building II&lt;br&gt;Nationwide Children's Hospital</td>
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<tr>
<td>6:30 pm – 9:30 pm</td>
<td>MWSPR Council Dinner&lt;br&gt;Lindey's&lt;br&gt;169 East Beck Street, Columbus, OH 43206</td>
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<tr>
<td><strong>THURSDAY, OCTOBER 4, 2012</strong></td>
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<tr>
<td>7:00 am – 8:00 am</td>
<td>MWSPR Registration&lt;br&gt;Continental Breakfast&lt;br&gt;<em>ED131</em></td>
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<tr>
<td>7:00 am – 8:00 am</td>
<td>Put Posters Up&lt;br&gt;Research Building II Lobby</td>
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<tr>
<td>8:05 am – 9:00 am</td>
<td>Pediatric Grand Rounds&lt;br&gt;Stecker Auditorium</td>
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<tr>
<td>9:15 am – 11:45 am</td>
<td>MWSPR Plenary Session I&lt;br&gt;The Research Institute Auditorium</td>
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<tr>
<td>11:50 am – 12:10 pm</td>
<td>MWSPR Business Meeting&lt;br&gt;The Research Institute Auditorium</td>
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<tr>
<td>12:15 pm – 1:30 pm</td>
<td>Founder and Sutherland Award Luncheon&lt;br&gt;<em>ED025 A and B</em></td>
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<tr>
<td>1:30 pm – 2:20 pm</td>
<td>State of the Art Lecture&lt;br&gt;The Research Institute Auditorium</td>
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<tr>
<td>2:30 pm – 4:45 pm</td>
<td>MWSPR Plenary Session II&lt;br&gt;The Research Institute Auditorium</td>
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<tr>
<td>4:45 pm – 6:30 pm</td>
<td>Reception and Combined Poster Session&lt;br&gt;Research Building II Lobby</td>
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<td><strong>FRIDAY, OCTOBER 5, 2012</strong></td>
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<tr>
<td>7:00 am – 8:00 am</td>
<td>MWSPR Registration&lt;br&gt;Research Building II Lobby</td>
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<tr>
<td>7:00 am – 7:50 am</td>
<td>Trainee Breakfast and Lecture&lt;br&gt;(open to all)&lt;br&gt;<em>ED025 A and B</em></td>
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<tr>
<td>8:00 am – 8:50 am</td>
<td>State of the Art Lecture&lt;br&gt;The Research Institute Auditorium</td>
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<tr>
<td>9:00 am – 12:15 pm</td>
<td>MWSPR Plenary Session III&lt;br&gt;The Research Institute Auditorium</td>
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<tr>
<td>12:15 pm – 1:30 pm</td>
<td>MWSPR Kenny, Metcoff, and Student Research Award Luncheon&lt;br&gt;The Research Institute Auditorium</td>
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<tr>
<td>1:30 pm</td>
<td>Optional Tour of New Hospital and Research Building</td>
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<tr>
<td>1:30 pm</td>
<td>Take Posters Down</td>
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</tbody>
</table>
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.

MWSPR Planning Committee
Joyce M. Koenig, MD – President
Robert Hoffman, MD – President-Elect
Pamela Kling, MD – Secretary-Treasurer

Acknowledgements

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

Abbott Nutrition
Mead Johnson Nutrition
Nationwide Children’s Hospital
53rd Annual Midwest Society for Pediatric Research Scientific Meeting

THURSDAY, OCTOBER 4, 2012
8:00 am – 6:30 pm

Nationwide Children’s Hospital
Research Building II
700 Children’s Drive
Columbus, Ohio

7:00-8:00 am  REGISTRATION AND CONTINENTAL BREAKFAST – Room ED131

8:00-8:05  WELCOME AND INTRODUCTION – Stecker Auditorium
Joyce Marie Koenig, MD
President

8:05  PEDIATRIC GRAND ROUNDS – Stecker Auditorium

Understanding NF-1 and Neurofibromatosis: Translating Molecular Mechanisms to Cutting-Edge Therapy
D. Wade Clapp, MD
Richard L. Schreiner Professor and Chair, Department of Pediatrics
James W. Riley Hospital for Children

MWSPR PLENARY SESSION I
The Research Institute Auditorium

INFLAMMATION AND IMMUNITY

Laura Haneline and Joyce Marie Koenig, Presiding

9:15  MYELOID CELLS ARE THE PRIMARY EFFECTORS OF NEUROFIBROMATOSIS TYPE 1 ANEURYSM FORMATION VIA INCREASED ACTIVATION OF THE NADPH OXIDASE SYSTEM.
BD Downing, F Li, W Bessler, B Stansfield, J Mund, M Distasi, and DA Ingram, Indianapolis, IN.
Indiana University School of Medicine  Abstract 1

9:30  HETEROZYGOUS INACTIVATION OF THE NF1 GENE IN MYELOID CELLS ENHANCES NEOINTIMA FORMATION VIA A ROSUVASTATIN-SENSITIVE CELLULAR PATHWAY.
BK Stansfield, WK Bessler, JA Mund, B Downing, R Mali, SJ Conway, R Kapur, and DA Ingram, Indianapolis, IN. Indiana University  Abstract 2

9:45  DECREASED MIR-17~92 CLUSTER EXPRESSION IS ASSOCIATED WITH INCREASED PROMOTER HYpermethylation IN HUMAN INFANTS WITH BPD.
M Robbins, D Dakhlallah, M Piper, C Marsh, and T Tipple, Columbus, OH. Nationwide Children's Hospital  Abstract 3

10:00  OXIDATIVE STRESS IN YOUTH AND ADOLESCENTS EXPOSED TO SECOND-HAND SMOKE.
L Lewis, H Huang, B Schanbacher, J Kuck, N Eastman, R Hoffman, J Groner, and JA Bauer, Columbus, OH.  Abstract 4
10:15 am-10:30 am – BREAK

10:30  MEASUREMENT OF MARKERS OF OXIDATIVE INJURY IN RAT MODEL OF ACUTE LUNG INJURY WITH EXHALED BREATH CONDENSATE.
   *HS Sandhu, R Solomom, S Phumeetham, KM Narayananagowda, and S Heidemann, Troy, MI and Detroit, MI.*  Wayne State University
   Abstract 5

10:45  BREATH CARBON ISOTOPE DELTA VALUE MAY BE A BIOMARKER OF CATABOLIC INFLAMMATORY ACUTE PHASE RESPONSE IN MECHANICALLY VENTILATED PEDIATRIC PATIENTS.
   *JP Boriosi, DG Maki, RA Yngsdal-Krenz, ER Wald, WP Porter, ME Cook, and DE Bütz, Madison, WI.*  University of Wisconsin, Madison
   Abstract 6

11:00  TARGETED REPLACEMENT OF UROPATHOGENS WITH PROBIOTIC NISSLE 1917.
   *EJ Lucas, DW Storm, SA Koff, DJ Horvath, B Li, and SS Justice, Columbus, OH.*  Abstract 7

11:15  THE BEST OFFENSE IS A GOOD DEFENSE: EXPRESSION AND FUNCTION OF BETA DEFENSINS IN THE INFECTED KIDNEY AND URINARY TRACT.
   *B Becknell, A Carpenter, A Schwaderer, DS Hains, SS Justice, and KM McHugh, Columbus, OH.*  Ohio State University
   Abstract 8

11:30  SODIUM CITRATE MODULATES T-CELL ACTIVATION.
   *E Winnega, JJ Pituch, TT Cornell, TP Shanley, and NB Blatt, Ann Arbor, MI.*  University of Michigan
   Abstract 9

11:50  MWSPR BUSINESS MEETING – The Research Institute Auditorium

12:15  FOUNDER & SUTHERLAND AWARD LUNCHEON -- Rooms ED025 A/B

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**FOUNDER AWARD RECIPIENT**

*Alan H. Jobe, MD, PhD*
*Cincinnati Children’s Hospital*

*Introduction by Suhas G. Kallapur, MD*
*Cincinnati Children’s Hospital*
**MWSPR PLENARY SESSION II**
*The Research Institute Auditorium*

**GROWTH AND DEVELOPMENT**

*Robert Hinton and Robert Hoffman, Presiding*

1:30  | State-of-the-Art Speaker  
| *From Lung Maturation to FIRS, Fetal Inflammatory Response Syndrome*  
| Alan H. Jobe, MD, PhD  
| Professor and Director, Division of Perinatal Biology  
| Cincinnati Children’s Hospital

2:30  | **POMEGRANATE JUICE MODULATES GENE EXPRESSION IN HUMAN PLACENTAL TROPHOBLASTS.**  
| *P Zaveri, MS Longtine, B Chen, and DM Nelson, St Louis, MO. Washington University*  
| Abstract 10

2:45  | **ENDOGENOUS ESTROGEN INHIBITION USING LETROZOLE IN OVINE PREGNANCY REDUCES FETAL WEIGHT AND DECREASES IN FETAL IRON.**  
| *MY Sun, KM Meyer, JL Austin, SE Blohowiak, RR Magness, and PJ Kling, Madison, WI. University of Wisconsin-Madison*  
| Abstract 11

3:00  | **OXYTOCINERGIC SIGNALING IN RETINAL COMMUNICATION.**  
| *PJ Halbach, Madison, WI. University of Wisconsin-Madison*  
| Abstract 12

3:15  | **SONIC HEDGEHOG PATHWAY EXPRESSION IN NORMAL AND MEGABLADDER MICE DURING DEVELOPMENT.**  
| *KR DeSouza, M Saha, AR Carpenter, M Scott, and KM McHugh, Columbus, OH. Nationwide Children’s Hospital*  
| Abstract 13

3:30 pm-3:45 pm – BREAK

3:45  | **MIR-205 EXPRESSION CORRELATES WITH SEVERITY OF RENAL INVOLVEMENT IN A MOUSE MODEL OF CONGENITAL OBSTRUCTIVE NEPHROPATHY.**  
| *ME Wilhide, AR Carpenter, K McHugh, and SE Ingraham, Columbus, OH.*  
| Abstract 14

4:00  | **ACTIVATION OF TGFβ/SMAD3 SIGNALING IN MEGABLADDER MICE WITH CONGENITAL OBSTRUCTIVE NEPHROPATHY.**  
| *AR Carpenter, B Becknell, ME Wilhide, SE Ingraham, and KM McHugh, Columbus, OH. The Research Institute at Nationwide Children’s Hospital and College of Medicine at Ohio State University*  
| Abstract 15

4:15  | **ONTOGENY OF ENDOTHELIN RECEPTORS ON RAT BRAIN, HEART AND KIDNEY AT DIFFERENT POSTNATAL AGES.**  
| *IA Awan, B Puppala, S Briyal, A Gulati, and L Schewig, Park Ridge, IL and Downer’s Grove, IL. Lutheran General Children’s Hospital*  
| Abstract 16

4:30  | **DOES NEONATAL GROWTH RESTRICTION PROGRAM AUTISM-LIKE BEHAVIOR IN C57BL/6 MICE?**  
| *LR Meyer, V Zhu, A Miller, and R Roghair, Iowa City, IA. University of Iowa*  
| Abstract 17
4:45 POSTER SESSION AND RECEPTION – Research Building II Lobby

See page 8 for posters

FRIDAY, OCTOBER 5, 2012
7:00 am – 2:00 pm
Nationwide Children’s Hospital
Research Building II

7:00 TRAINEE BREAKFAST SESSION - Rooms ED025 A/B

Transitioning from Trainee to Training of Trainees; Now I am a Mentor?!...
Pamela J. Kling, MD
Associate Professor
University of Wisconsin

MWSPR PLENARY SESSION III
The Research Institute Auditorium

GENERAL NEONATOLOGY AND PEDIATRICS

Caroline George and David B. Kershaw, Presiding

8:00 State-of-the-Art Speaker
Childhood Antecedents of Adult Heart Disease – Tobacco Smoke Exposure and Obesity
Judith A. Groner, MD
Clinical Professor
The Ohio State University, Nationwide Children’s Hospital

9:00 THE ROLE OF ENDOTHELIAL PROGENITOR CELL NUMBERS IN INFANTS AND CHILDREN ON VASCULAR REACTIVITY.
W Ahmed, J Mund, J Case, and L Haneline, Indianapolis, IN. Indiana University School of Medicine
Abstract 18

9:15 ENDOTHELIAL FUNCTION IN HIV INFECTED ADOLESCENTS AND YOUNG ADULTS ON HAART THERAPY.
SL Meyer, AS Dye, LB Rauch, MT Brady, and RP Hoffman, Columbus, OH and Charleston, WV. The Ohio State University
Abstract 19

9:30 POOR GLUCOSE CONTROL IMPAIRS MAXIMAL POST-OCLUSION VASODILATION IN ADOLESCENT TYPE 1 DIABETES.
RP Hoffman, AS Dye, H Huang, and JA Bauer, Columbus, OH and Charleston, WV. The Ohio State University
Abstract 20
9:45  EFFECT OF FITNESS ON GLYCEMIC VARIATION IN TYPE 1 DIABETES.
A Singhvi, M Tansey, K Janz, and E Tsalikian, Iowa City, IA. University of Iowa  Abstract 21

10:00  A NOVEL NEONATAL PROGRAM STRATEGY ACCELERATES FEEDING MILESTONES AND SAVES RESOURCES: THE HOLY GRAIL?
SR Jadcherla, J Dail, L Nelin, R McClead, E Vaughn, and K Kelleher, Columbus, OH. Nationwide Children's Hospital  Abstract 22

10:15  VITAMIN D STATUS IN PRETERM INFANTS AND THE EFFECTIVENESS OF CURRENT VITAMIN D INTAKE DURING HOSPITAL STAY.
NK Monangi, JL Slaughter, H Akinbi, and A Dawodu, Cincinnati, OH and Columbus, OH. University of Cincinnati  Abstract 23

10:30 am - 10:45 am – BREAK

10:45  IMPACT OF DELAYED UMBILICAL CORD CLAMPING AT THE LIMITS OF VIABILITY.
C Backers, H Huang, B Schanbacher, JA Deverse, K Copeland, JP Iams, PJ Giannone, and JA Bauer, Columbus, OH. Research Institute at Nationwide Childrens Hospital, Ohio State University Medical Center  Abstract 24

11:00  SERIAL IRON MEASURES AT BIRTH, 6 AND 12 MONTHS: PREDICTION OF IRON STATUS.
SE Blohowiak, CL Coe, and PJ Kling, Madison, WI. University of Wisconsin-Madison  Abstract 25

11:15  COMPARISON OF METHODS TO MEASURE RED CELL VOLUME (RCV) IN NEONATES USING FETAL HEMOGLOBIN (HBF) AND BIOTIN LABELING OF RBCS (BIORBC).
P Bhandary, D Nalbant, AM Altawalbeh, DJ Kuruvilla, R Schmidt, and JA Widness, Iowa City, IA. University of Iowa  Abstract 26

11:30  SAFETY AND EFFECTIVENESS OF WHOLE BODY COOLING THERAPY FOR NEONATAL ENCEPHALOPATHY ON TRANSPORT.
EM McNellis, T Fisher, and HW Kilbride, Kansas City, MO. University of Missouri-Kansas City School of Medicine  Abstract 27

11:45  TWO YEAR PROSPECTIVE EVALUATION OF HUMAN PARECHOVIRUS AND ENTEROVIRUS CNS INFECTIONS IN INFANTS LESS THAN 90 DAYS OF AGE.
M Klatte, U Kallemuchikkal, CJ Harrison, B Pate, and M Jackson, Kansas City, MO. University of Missouri-Kansas City  Abstract 28

12:00  COUGH IN BPD NEONATES: MECHANISMS OF ORIGIN AND RESOLUTION.
K Hasenstab, D Chen, R Castile, and SR Jadcherla, Columbus, OH. Nationwide Children's Hospital  Abstract 29

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12:15  MWSPR KENNY, METCOFF, AND STUDENT RESEARCH AWARD LUNCHEON
The Research Institute Auditorium
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<th>Institution</th>
<th>Abstract No.</th>
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<tr>
<td>1</td>
<td><strong>AN ACTIN MUTATION THAT CAUSES PATENT DUCTUS ARTERIOSUS ALTERS REGULATION BY PROFILIN.</strong></td>
<td>HL Bartlett, PA Rubenstein, EW Wedemeyer, ND Vanderpool, and K Wen, Iowa City, IA.</td>
<td>University of Iowa</td>
<td>Abstract 30</td>
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<td>2</td>
<td><strong>POST-PRANDIAL MESENTERIC HYPEREMIC RESPONSE IN LACTOSE CONTAINING VERSUS LACTOSE-FREE INFANT FORMULA.</strong></td>
<td>VA Schroeder, T Kilkenny, L Mattioli, and JM Belmont, Kansas City, KS.</td>
<td><em>University of Kansas Medical Center</em></td>
<td>Abstract 31</td>
</tr>
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<td>3</td>
<td><strong>COMMON ALLEGATIONS OF PROFESSIONAL LIABILITY AGAINST PRACTITIONERS OF NEONATAL MEDICINE.</strong></td>
<td>SM Van Nostrand, GS Navon, JC Morrison, and JK Muraskas, Chicago, IL and Jackson, MS.</td>
<td>Loyola University Medical Center</td>
<td>Abstract 32</td>
</tr>
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<td>4</td>
<td><strong>EFFECTIVENESS OF A PEER COUNSELOR-BASED BREASTFEEDING PROGRAM AMONG HIGH-RISK INFANTS.</strong></td>
<td>AD Bhatia, C Smith, and R Oza-Frank, Columbus, OH.</td>
<td><em>Northeast Ohio Medical University</em></td>
<td>Abstract 33</td>
</tr>
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<td>5</td>
<td><strong>END-OF-LIFE DECISIONS ENTER A GREY ZONE AT THE EDGE OF VIABILITY.</strong></td>
<td>JA Weiner and H Kilbride, Kansas City, MO.</td>
<td><em>Children’s Mercy Hospital &amp; Clinics</em></td>
<td>Abstract 34</td>
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<td>6</td>
<td><strong>ASSOCIATION OF GER WITH COUGH, IRRITABILITY AND ARCHING IN INFANTS WITH CHRONIC LUNG DISEASE (CLD).</strong></td>
<td>CY Chan, RK Moore, and SR Jadcherla, Columbus, OH.</td>
<td><em>Nationwide Children’s Hospital</em></td>
<td>Abstract 35</td>
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<td>7</td>
<td><strong>OXYGEN DELIVERY IN VERY LOW BIRTHWEIGHT (VLBW) AND EXTREMELY LOW BIRTHWEIGHT (ELBW) INFANTS DURING TRANSPORT.</strong></td>
<td>EM McNellis, C Sitzman, EK Pallotto, D Willis, and JK Jackson, Kansas City, MO.</td>
<td>University of Missouri-Kansas City School of Medicine</td>
<td>Abstract 36</td>
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<td>8</td>
<td><strong>RELATIONSHIP BETWEEN TOTAL PARENTERAL NUTRITION AND OSTEOPENIA IN INFANTS WITH BRONCHOPULMONARY DYSPLASIA.</strong></td>
<td>MJ Shareef and K Thomas, Lombard, IL and Maywood, IL.</td>
<td>Loyola University Medical Center</td>
<td>Abstract 37</td>
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<td>9</td>
<td><strong>PREDICTORS OF GASTROTOMY TUBE (G-TUBE) IN CHRONIC LUNG DISEASE OF INFANTS (CLDI).</strong></td>
<td>MB Malkar, W Gardner, E Shepherd, A Gest, L Nelin, SE Welty, and SR Jadcherla, Columbus, OH and Houston, TX.</td>
<td>Nationwide Children’s Hospital</td>
<td>Abstract 38</td>
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<td>39</td>
<td>POST DISCHARGE EMERGENCY ROOM (ER) VISITS DURING THE FIRST MONTH OF LIFE IN AN URBAN INNER CITY POPULATION.</td>
<td>Constance Asiedu-Ofei, M Newman, K Ali, M Aslam, S Hari, and S Gopal, Chicago, IL. Rosalind Franklin University</td>
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<td>11</td>
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<td>40</td>
<td>CHANGE IN THORACO-ABDOMINAL ASYNCHRONY IN SPONTANEOUSLY BREATHING PREMATURITY INFANTS BETWEEN 32 AND 36 WEEKS.</td>
<td>LN Ulm, J Kemp, C Cleveland, L Linneman, and J Hoffmann, Glencoe, MO and St. Louis, MO.</td>
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<td>12</td>
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<td>41</td>
<td>READMISSION OF HEALTHY TERM INFANTS WITH HYPERBILIRUBINEMIA IN AN URBAN INNER CITY HOSPITAL.</td>
<td>S Ramarao, OG Okonkwo, G Srinivasan, and H Srinivasan, Westmont, IL and Chicago, IL. Sinai Children’s Hospital</td>
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<td>13</td>
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<td>42</td>
<td>NEONATAL INTENSIVE CARE UNIT BED CONFIGURATION HAS NO EFFECT ON RATES OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS COLONIZATION OR NECROTIZING ENTEROCOLITIS.</td>
<td>SF Julian, B Warner, A Hamvas, W Shannon, PI Tarr, St. Louis. Washington University in St. Louis</td>
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<td>14</td>
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<td>43</td>
<td>THE EFFECTS OF SEQUENTIAL COLOSTRUM VS. EARLY RANDOM BREAST MILK ADMINISTRATION IN PRETERM INFANTS: A QI STUDY.</td>
<td>S Nuthakki, S Knouff, C Smith, C Drake, and S Jadcherla, Columbus, OH. The Ohio State University</td>
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<td>15</td>
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<td>44</td>
<td>EXPLORING THE RELATIONSHIP BETWEEN METABOLIC ACID-BASE STATUS AND THE NUMBER OF APNEA, BRADYCARDIA, AND DESATURATION ALARMS IN INFANTS 27-32 WEEKS GESTATION IN THE FIRST TWO WEEKS OF LIFE.</td>
<td>R Hohle, A Warheker, PA Hummel, and CH Sajous, Maywood, IL and Aurora, IL. Loyola University Medical Center</td>
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<td>16</td>
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<td>45</td>
<td>GLUCOSURIA DURING PACKED RED BLOOD CELL TRANSFUSION IN PRETERM INFANTS.</td>
<td>AS Kiefer, T Fleming, A Bierhaus, P Nawroth, B Poindexter, and M Yoder, Indianapolis, IN and Heidelberg, Germany. Indiana University</td>
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<td>17</td>
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<td>46</td>
<td>FACTORS INFLUENCING SUCCESSFUL DISCONTINUANCE OF CAFFEINE AT 34 WEEKS CORRECTED GESTATIONAL AGE IN PREMATURE INFANTS TREATED FOR APNEA OF PREMATURITY.</td>
<td>R Vimawala, PA Hummel, and CH Sajous, Maywood, IL. Loyola University Medical Center</td>
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<td>18</td>
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<td>47</td>
<td>READMISSION OF HEALTHY TERM INFANTS WITHIN ONE MONTH OF AGE IN AN URBAN INNER CITY HOSPITAL.</td>
<td>OG Okonkwo, S Ramarao, G Srinivasan, and H Srinivasan, Westmont, IL and Chicago, IL. Sinai Children’s Hospital</td>
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</table>
19 PILOT STUDY OF SYMPTOM BURDEN AND QUALITY OF LIFE AMONG FAMILIES OF CHILDREN IN PALLIATIVE CARE OR HOSPICE.  
ML Eversole, S Manring, S Snyder, M Gilmer, M Walsh, J Winters, and C Gerhardt, Lewis Center, OH, Columbus, OH, and Nashville, TN. The Ohio State University  

20 CARDIOPULMONARY RESUSCITATION CERTIFICATION IN HIGH SCHOOL COACHES: A SURVEY OF WISCONSIN HIGH SCHOOL ATHLETIC DIRECTORS.  
MW Harer and JP Yaeger, Madison, WI. University of Wisconsin-Madison  

21 PILOT STUDY OF A PRIMARY CARE INTERVENTION ON THE MANAGEMENT OF CHILDHOOD OBESITY- “A POUND OF CURE”.  
SA Anzeljc, RD Murray, and AR Sternstein, Columbus, OH. The Ohio State University  

22 HOSPITALIZED SUSPECTED CHILD ABUSE-RELATED TRAUMATIC BRAIN INJURIES AMONG CHINESE CHILDREN.  
H Xiang, J Xiang, X Xin, H Zhu, J Shao, and GA Smith, Columbus, OH and Wuhan, HUB. Case Western Reserve  

23 EPIDEMIOLOGICAL CHARACTERISTICS OF PEDIATRIC INPATIENTS WITH TRAUMATIC BRAIN INJURY IN WUHAN, CHINA.  
H Xiang, J Shao, H Zhu, H Yao, L Stallones, K Yeates, and K Wheeler, Columbus, OH, Wuhan, China, Beijing, China, and Fort Collins, CO. The Ohio State University, College of Medicine  

24 PEDIATRIC HYPERTENSION: DEFINING THE EDUCATIONAL NEEDS OF PRIMARY CARE PEDIATRICIANS.  
SD Cha, D Chisolm, H Patel, and JD Mahan, Columbus, OH.  

25 DURATION OF CHILDHOOD OBESITY AND MARKERS OF CARDIOMETABOLIC DISEASE.  
H Huang, M Mohamed, B Schanbacher, J Kuck, N Eastman, L Lewis, R Hoffman, JA Bauer, and J Groner, Columbus, OH. Nationwide Children’s Hospital and Research Institute  

26 RELATIONSHIP OF CALCIUM INTAKE WITH FRACTURE INCIDENCE IN THE PEDIATRIC EMERGENCY DEPARTMENT.  
ME Dulaurier and M Henwood-Finley, Columbus, OH. The Ohio State University  

27 INCREASED FREQUENCY OF SEVERE, ATYPICAL POST STREPTOCOCCAL GLOMERULONEPHRITIS AT A PEDIATRIC TERTIARY CARE CENTER.  
RM Ayoob and AL Schwaderer, Columbus, OH. Ohio State University  

28 PATIENT PERCEPTIONS OF CONGENITAL HEART DISEASE: THE ROLE OF ILLNESS UNCERTAINTY IN ADOLESCENTS AND YOUNG ADULTS.  
KM Tierney, J Jackson, C Daniels, and K Vannatta, Columbus, OH. The Ohio State University
29 **THE EFFECT OF TUMOR TREATMENT AND TYPE ON SOCIAL OUTCOMES OF PEDIATRIC BRAIN TUMOR SURVIVORS.**
BM Misiti, C Gerhardt, K Vannatta, AF Patenaude, M Kupst, and M Barrera, Columbus, OH, Boston, MA, Milwaukee, WI, and Toronto, ON. *Ohio State University* Abstract 58

30 **CRICOPHARYNGEAL ACHALASIA IN CHILDREN: BOTULINUM TOXIN INJECTION AS A TOOL FOR DIAGNOSIS AND TREATMENT.**
MA Scholes, HM Mousa, and GJ Wiet, Columbus, OH. *Ohio State University* Abstract 59

31 **adolescents’ understanding of their cancer prognosis.**
SA Manring, M Eversole, S Snyder, B Misiti, M Ranalli, K Vannatta, B Compas, and C Gerhardt, Columbus, OH and Nashville, TN. *The Ohio State University* Abstract 60

32 **MULTIPLEX FAMILIES WITH SEVERE LUPUS NEPHRITIS IN SUBJECTS WITH HLA A30 B18 DR7 AND COMPLEMENT C4 DEFICIENCY.**
SK Lawrance, M Rudnicki, YL Wu, B Zhou, and CY Yu, Columbus, OH and Innsbruck, Austria. *The Ohio State University* Abstract 61

33 **FAST LEARNING OPTIMIZED PREDICTION METHODOLOGY FOR MOLECULAR THERAPY RESPONSE CLASSIFICATION.**
S Sundararajan, B Geier, E García-Gonzalo, R Kurmasheva, JL Fernández-Martínez, AKloczkowski, and P Houghton, Blacklick, OH, Oviedo, Spain, and Columbus, OH. *The Ohio State University* Abstract 62

34 **INCIDENCE OF NECROTIZING ENTEROCOLITIS IN PREMATURE INFANTS < 32 WEEKS GESTATION WITH NEUTROPENIA IN THE FIRST 24 HOURS OF LIFE.**
RKampanatkosol, J Muraskas, and E Carlos, Chicago, IL and Maywood, IL. *Loyola University Medical Center* Abstract 63

35 **ELUCIDATION OF THE PATTERN OF VARIATION FOR THE AMYLASE LOCUS IN TYPE 1 DIABETES PATIENTS.**
AM Rutherford, B Zhou, Y Wu, S Kingery, J Germak, S Bowden, R Hoffman, and CY Yu, Columbus, OH. *The Ohio State University* Abstract 64

36 **SERUM MARKERS OF BONE HEALTH IN NEUROFIBROMATOSIS TYPE I.**
CJ Murillo, KC Zobrist, BA Speckhart, and MM Al-Rahawan, Peoria, IL. *University of Illinois College of Medicine at Peoria* Abstract 65

37 **SUCCESSFUL TRANSITION TO ORAL SULFONYLUREA THERAPY IN TWO PATIENTS WITH NEONATAL DIABETES MELLITUS WITH NOVEL MUTATIONS IN GENES ENCODING THE K-ATP CHANNEL COMPLEX REGULATING INSULIN SECRETION.**
LB Rauch, WB Zipf, and JA Indyk, Columbus, OH. *Ohio State University* Abstract 66
<table>
<thead>
<tr>
<th>No.</th>
<th>CHARACTERISTICS OF PATHOGENS IN MYELOMENINGOCELE PATIENTS WHO USE CLEAN INTERMITENT CATHETERIZATION.</th>
</tr>
</thead>
<tbody>
<tr>
<td>38</td>
<td>CE Kozlovich, C Singh, C Baxter, B Li, and SS Justice, Columbus, OH. The Research Institute at Nationwide Children’s Hospital</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>IDENTIFYING DIFFERENCES BETWEEN PNEUMOCOCCAL STRAINS THAT MAY CONTRIBUTE TO DEVELOPMENT OF HEMOLYTIC UREMIC SYNDROME.</th>
</tr>
</thead>
<tbody>
<tr>
<td>39</td>
<td>SA Woodiga, JD Rohr, CM Buckwalter, JD Mahan, and SJ King, Columbus, OH. Abstract 68</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>CONTRIBUTION OF STRUCTURAL DOMAINS TO RIBONUCLEASE 7’S GRAM-POSITIVE AND GRAM-NEGATIVE ACTIVITY AGAINST UROPATHOGENS.</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>H Wang, A Schwaderer, J Kline, J Spencer, and D Hains, Columbus, OH. Nationwide Children’s Hospital</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>INTERCALATED CELLS MAINTAIN STERILITY OF THE HUMAN URINARY TRACT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>41</td>
<td>JD Spencer, A Schwaderer, and D Hains, Columbus, OH. Nationwide Children’s Hospital</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>ESTABLISHMENT OF BLADDER WHOLE ORGAN EXPLANT IN VITRO CULTURE SYSTEM.</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td>KR DeSouza, MB Becknell, M Scott, and KM McHugh, Columbus, OH. Nationwide Children’s Hospital</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>INCREASED NA+/H+ EXCHANGER ISOFORM 1 ACTIVITY IN HIPPOCAMPAL ASTROCYTES RESULTS IN INCREASED RELEASE OF GLUTAMATE AND CYTOKINES AFTER IN VITRO ISCHEMIA.</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>P Cengiz, DB Kintner, V Chanana, P Kendigelen, B Gulnaz, E Fidan, E Akture, P Ferrazzano, and D Sun, Madison, WI and Pittsburgh, PA. University of Wisconsin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>THE EFFECT OF HEAT STRESS ON INFLAMMATION MEASURED IN EXHALED BREATH CONDENSATE IN A RAT MODEL OF ACUTE LUNG INJURY.</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>K Narayana Gowda and SM Heidemann, Detroit, MI. Wayne State University</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No.</th>
<th>THE EXPRESSION OF FATTY ACID BINDING PROTEIN 4 (FABP4) IN THE MURINE PLACENTA.</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>A Makkar, Y sadovsky, and T Mishima, Pittsburgh, PA. University of Pittsburgh</td>
</tr>
</tbody>
</table>
Background: Neurofibromatosis Type 1 (NF1) affects 1 in 3500 individuals resulting from mutations in the *NF1* tumor suppressor gene encoding the protein neurofibromin. Neurofibromin is a GTPase activating protein (GAP) negatively regulating Ras activity. NF1 cardiovascular disease (CVD) is an under-studied manifestation resulting in morbidity and mortality (M+M). A common result of NF1 CVD is aneurysms, which can lead to death. Despite these observations, the molecular and cellular mechanism of NF1 aneurysms is incomplete. To identify the cellular role, myeloid cells and vascular smooth muscles cells (VSMCs) were studied due to their role in vascular homeostasis. Purpose: Our first objective was to test if *Nf1* heterozygosity in VSMCs or myeloid cells was the primary effectors of *Nf1* aneurysms. Additionally, increased active Ras has been linked to elevated reactive oxygen species (ROS) levels, potentially through *NADPH* oxidase activation. Given the link between ROS and aneurysms, we tested if heterozygosity of *Nf1* increases ROS via NADPH oxidase activation, leading to aneurysms. Methods: *Nf1flox/+-LysMcre* (LysM) and *Nf1flox/+-SM22cre* (SM22) mice, which have one allele of *Nf1* ablated specifically in myeloid cells or VSMCs, respectively, as well as wild type (WT) and *Nf1* heterozygous (HET) mice were administered angiotensin II (AngII, 1500 ng/kg/min) to induce aneurysms. After 35 days aortas were excised and scored for aneurysms. *Nf1+/−* and WT mice were also administered apocynin (100mg/kg/day), an NADPH oxidase inhibitor, for 7 days prior to AngII infusion continuing until sacrifice to inhibit ROS via the NADPH oxidase. Results: We demonstrate that LysM mice develop aneurysms at a rate similar to *Nf1+/−* mice (77.7% and 75.0%, respectively). Incidence in both SM22 and WT mice (37% and 33%, respectively) were significantly lower than LysM and *Nf1+/−* mice (p<0.05). Together, these results indicate heterozygous inactivation of *Nf1* in myeloid cells is sufficient to recapitulate aneurysms of *Nf1+/−* mice. Finally, apocynin treatment of *Nf1+/−* mice undergoing AngII infusion dramatically reduced aneurysm incidence from 75% in vehicle treated to 14.2% in apocynin treated mice (p<0.05). Conclusions: These data demonstrate heterozygous inactivation of *Nf1* in myeloid cells is sufficient to induce aneurysms. Moreover, pharmacologic inhibition of the NADPH oxidase system significantly reduces aneurysms in *Nf1+/−* mice. Implications for Practice: Newly expanded knowledge of the cellular and biochemical mechanisms of NF1 CVD will allow therapeutics to be tested to prevent and treat major causes of M+M in NF1 patients.

2 HETEROZYGOUS INACTIVATION OF THE *Nf1* GENE IN MYELOID CELLS ENHANCES NEOINTIMA FORMATION VIA A ROSUVASTATIN-SENSITIVE CELLULAR PATHWAY.

B Stansfield, W Bessler, J Mund, B Downing, R Mali, R Kapur, D Ingram, Indiana University School of Medicine, Indianapolis, IN

Background: Mutations in the *NF1* tumor suppressor gene cause Neurofibromatosis Type 1 (NF1). Some NF1 patients develop arterial stenosis resulting in sudden death, particularly younger patients. Murine studies demonstrate that heterozygous inactivation of *Nf1* (*Nf1+/−*) in bone marrow cells is necessary and sufficient for neointima formation following arterial injury and that macrophages populate *Nf1+/−* neointimas. Purpose: We tested the hypothesis that heterozygous inactivation of *Nf1* in myeloid cells alone enhances neointima formation through Ras-Mek-Erk signaling and that treatment of *Nf1+/−* mice with daily rosvastatin would reduce neointima formation *in vivo*. Methods: We generated mice with heterozygous or homozygous deletion of *Nf1* in myeloid cells by intercrossing *Nf1ββ* mice with *LysMcre* mice. Carotid artery ligation was performed on *Nf1+/−*, wild type (WT), *Nf1ββ;LysMcre* and *Nf1ββ;LysMcre* to compare neointima formation and peripheral blood mononuclear cell populations. Functional assays of *Nf1+/−* and WT macrophages were performed following incubation with rosvastatin. Separately, *Nf1+/−* and WT mice were administered daily PD0325901, a specific Mek inhibitor, and rosvastatin prior to arterial injury and through tissue harvest to evaluate effect on neointima formation. Results: Heterozygous or homozygous inactivation of *Nf1* in myeloid cells mobilized a discrete inflammatory murine monocyte population in a cell autonomous and gene-dosage dependent mechanism. Ablation of a single *Nf1* allele in myeloid cells is sufficient to reproduce the enhanced neointima formation observed in *Nf1+/−* mice compared to WT mice. Similar to *Nf1+/−* neointimas, macrophages invest *Nf1ββ;LysMcre* neointimas. Deletion of both *Nf1* gene copies results in complete arterial occlusion. *Nf1−/−* neointima...
formation is mediated through the canonical Ras-Mek-Erk signaling pathway and inhibition of this pathway reduces neointima formation in vivo. Cultured Nf1⁻/⁻ macrophages demonstrate abnormal function that is restored with rosuvastatin incubation. Finally, treatment of Nf1⁻/⁻ mice with daily rosuvastatin reduced neointima formation compared to placebo. Conclusions: These data provide genetic and cellular evidence that myeloid cells are critical cellular regulators of Nf1⁻/⁻ arterial stenosis and provide a potential therapeutic intervention. Clinical Implications: NF1 is an independent risk factor for early, debilitating cardiovascular disease and statins may be an important preventative therapeutic in NF1 patients without overt cardiovascular disease.

3
DECREASED MIR-17~92 CLUSTER EXPRESSION IS ASSOCIATED WITH INCREASED PROMOTER HYPERMETHYLATION IN HUMAN INFANTS WITH BPD
M. Robbins, D. Dakhllalah, M. Piper, C. Marsh, T. Tipple, The Research Institute at Nationwide Children’s Hospital, Columbus, OH and Department of Critical Care and Pulmonary Medicine, The Ohio State University Wexner Medical Center, Columbus, OH.

Background: Bronchopulmonary Dysplasia (BPD) is a chronic lung disease that causes significant morbidity and mortality in prematurely born infants. Specific pro-fibrotic pathways have been implicated in the development of BPD in infants and idiopathic pulmonary fibrosis (IPF) in adults and miR-17~92 cluster is predicted to suppress activation of these profibrotic pathways. In IPF, pulmonary miR-17~92 cluster expression is decreased, appears to be mediated via promoter hypermethylation, and directly correlates with diminished pulmonary function. Hypothesis: The present studies tested the hypothesis that miR-17~92 expression is decreased and promoter methylation increased in lungs from human patients that died with BPD when compared to lungs from patients that died from without BPD. Methods: Lung samples (BioRepository for Investigation of Neonatal Diseases of the Lung, University of Rochester) obtained at autopsy from patients who died with BPD or without BPD were analyzed for individual miR-17~92 cluster expression by qRT-PCR (n=3). miR-17~92 promoter methylation was determined in lung samples using Methyl-Profiler™ Assay (n=7-8). Results: Expression of individual members of the miR-17~92 cluster was decreased by 40% in samples from patients with BPD when compared to non-BPD controls. In promoter methylation analyses, miR-17~92 promoter was 50% methylated and 50% unmethylated in non-BPD control samples. In contrast, miR-17~92 promoter was 98% methylated and 2% unmethylated in lung samples from patients with BPD. Conclusions: Our novel data indicate that miR-17~92 cluster expression is significantly decreased and promoter methylation significantly increased in lungs from patients who died with BPD compared to non-BPD controls. We speculate that decreased miR17~92 cluster expression in BPD occurs due to promoter methylation and contributes to previously reported elevations in pro-fibrotic gene expression in these patients. Thus, therapies directed at restoring miR-17~92 cluster expression by attenuating DNA methylation could be therapeutically beneficial in prematurely born infants.

4
OXIDATIVE STRESS IN YOUTH AND ADOLESCENTS EXPOSED TO SECOND-HAND SMOKE
L. Lewis, H Huang, B Schanbacher, J Kuck, N Eastman, R Hoffman, JA Bauer, and J Groner, Center for Perinatal Research and Section of Ambulatory Pediatrics, Nationwide Children’s Hospital and Research Institute, Columbus, OH

Background: Active smoking contributes to the progression of atherosclerotic heart disease by causing endothelial dysfunction. Increased free radicals and consequent oxidative stress is one of the major contributors to this disease process. While it is known in adults that there is a strong relationship between secondhand smoke (SHS) and cardiovascular disease, the exact mechanism of this relationship is uncertain. In the present study the effect of SHS exposure on systemic oxidative stress was investigated in a group of youth and adolescents. We hypothesized that subjects with higher levels of SHS exposure would have greater evidence of inflammation and oxidative stress.

Methods: A total of 90 healthy non-smoking youth and adolescents (9-18 years of age) were recruited. SHS exposure was determined by questionnaire and hair nicotine levels. Oxidative stress was measured by malondialdehyde (MDA), a natural bioproduct of lipid peroxidation, modified protein levels in plasma. Inflammation markers (high-sensitive C-reactive protein and adiponectin) were measured with ELISA. Soluble intracellular cell adhesion molecule-1 (sICAM-1), an indicator of endothelial stress, was also measured. Results: The subjects recruited had a range of hair nicotine levels from 0.004 to 11.5 ng/mg hair. Since hair nicotine was not normally distributed, log hair nicotine was used for the analyses. Log hair nicotine was positively correlated to plasma protein- MDA adduct (Pearson r = 0.2333, p<0.05), as well as to plasma hsCRP (Pearson r = 0.2756, p<0.05). Although BMI had a strong correlation with hsCRP, it wasn’t associated with protein-MDA, suggesting obesity was not the reason for increased oxidative stress in this population. A weaker correlation was detected between the oxidative stress parameter and sICAM-1 (Pearson r = 0.2046, p=0.0530).

Conclusions: Our findings demonstrate that in children SHS exposure is strongly associated with oxidative stress and systemic inflammation, independent of BMI. These mechanisms may be important contributors to vascular endothelial injury in this early phase of life and thereby may contribute to later disease risks in adulthood.
5

MEASUREMENT OF MARKERS OF OXIDATIVE INJURY IN RAT MODEL OF ACUTE LUNG INJURY WITH EXHALED BREATH CONDENSATE

H Sandhu, R Solomon, S Phumeetham, K Narayanagowda, S Heidemann, The Children’s Hospital of Michigan, Detroit, MI

Purpose: During acute lung injury (ALI), reactive oxygen species cause damage to the lung and produce mediators such as leukotriene B4 (LTB4) and 8-isoprostane (8-IP). Bronchoalveolar lavage can be used to measure these mediators, however it is invasive, samples a small part of the lung and is associated with nosocomial infection. Exhaled breath condensate (EBC) is a newer method that is non-invasive and may reflect the production of mediators from the entire lung. Our objectives are to determine: 1) whether LTB4 and 8-IP can be measured in EBC of rats with ALI; 2) the change in LTB4 and 8-IP in EBC and total lung lavage (TLL) over time; and 3) the extent to which LTB4 and 8-IP concentrations correlate between EBC and TLL.

Methods: Rats were divided into 3 groups: control (n=9), and 4 hr (n=9) or 24 hr (n=9) after administration of 1mcg/kg of Staphylococcal enterotoxin b (SEB). All rats were ventilated and EBC was collected via a cooled tube attached to the ventilator exhalation port. Rats were sacrificed and TLL was performed. EBC and TLL were analyzed for LTB4 and 8-IP and cell count was performed on the TLL.

Results: LTB4 was elevated at 24 hours post-SEB compared to controls in the EBC (**p<0.05) and TLL, (* p<0.01). The LTB4 was not elevated in the 4 hour post-SEB compared to the 24 hr post –SEB or the control groups in both the EBC and TLL. (fig) 8-IP tended to be elevated in EBC 24 hours post-SEB compared to controls (9[5-32] vs. 7[5-11] pg/ml, p=0.07) but not in TLL (57[34-289] vs. 59[41-242] pg/ml, p=0.28). 8 IP was increased in the TLL of the 4 hour post-SEB group but not in the EBC (114[36-316] vs 59[41-242]pg/ml p<0.05 and 7[0-18] vs 7[5-11] pg/ml, p=0.34 respectively). White cell counts were higher in TLL at 24 hours post-SEB compared to controls (1500[466-4990] vs 444 [148-928], p<0.01) but not for 4 hour post SEB(p=0.07). LTB4 and 8 IP levels did not correlate between EBC and TLL.

Conclusions: LTB4 and 8-IP were measured in the EBC of rats with acute lung injury. LTB4 was higher 24 hrs post-SEB compared to 4 hrs or controls in both the EBC and TLL. 8-IP was elevated 24 hrs post-SEB in the TLL but not in the EBC. Correlation of these mediators was not observed between the EBC and TLL.

6

BREATH CARBON ISOTOPE DELTA VALUE MAY BE A BIOMARKER OF CATABOLIC INFLAMMATORY ACUTE PHASE RESPONSE IN MECHANICALLY VENTILATED PEDIATRIC PATIENTS.


*University of Wisconsin, Madison, Wisconsin.

The present work was performed at American Family Children’s Hospital, Madison, Wisconsin.

Purpose: To determine baseline variability of exhaled breath delta value (i.e. ¹³CO₂/¹²CO₂ delta value) in a population of mechanically ventilated pediatric patients with and without systemic inflammatory response syndrome (SIRS).

Methods: Observational pilot study in Pediatric intensive care unit (PICU) at an urban, tertiary children’s hospital. Subjects: seventeen mechanically ventilated pediatric patients underwent measurement of exhaled breath delta value at study enrollment and every 8 hours thereafter for a total of 72 hours. Results: At the time of enrollment 8 subjects met SIRS criteria and 9 subjects did not meet SIRS criteria. The mean breath delta value was lower, though not statistically significant, in the SIRS group compared to the non-SIRS group at the time of enrollment (mean breath delta value in SIRS -21.57‰ SEM 0.93 vs. mean breath delta value in no-SIRS -20.76‰ SEM 0.76; p=0.51). The mean breath delta value was significantly lower in subjects with active sepsis or trauma/post-op status compared to subjects with No-infection/trauma/sepsis (No-I/T/S) or improving sepsis (mean breath delta value of -22.94‰ SEM 1.42, -23.43‰ SEM 0.82 respectively; p=0.0062). There was no statistical difference in the mean breath delta value between patients with No-I/T/S and patients with improving sepsis. Trend analysis of individual cases showed that the breath delta value correlated with catabolic inflammatory acute phase response, and was a leading indicator for the onset of infection in two patients who developed ventilator associated pneumonia.

Conclusions: The breath delta value does not correlate well with SIRS status, however, when patients are classified based on the severity of their catabolic inflammatory acute phase response the breath delta value appears to correlate with the severity of inflammation. The breath delta value may be a leading marker of catabolic inflammatory acute phase response related to infection.
TARGETED REPLACEMENT OF UROPATHOGENS WITH PROBIOTIC NISSEL 1917.

EJ Lucas1, DW Storm2, SA Koff2, DJ Horvath J1, B Li3, SS Justice1. 1Section of Infectious Disease, Nationwide Children’s Hospital, Columbus, OH. 2Division of Pediatric Urology, Nationwide Children’s Hospital, Columbus, OH. 3Center for Microbial Pathogenesis, Research Institute at Nationwide Children’s Hospital, Columbus, OH. 

**Purpose:** The usefulness of prophylactic antibiotics to prevent recurrent urinary tract infections (UTI) in children has recently come into question. Furthermore, prophylaxis antibiotics is a risk factor for selecting out more resistant uropathogens. Some groups have attempted to use gram positive based probiotics, like lactobacillus, to prevent recurrent infections by altering the intestinal bacterial reservoir with variable results. Mutaflo® is a possible alternative probiotic in which the active agent is the gram negative Nissle 1917. Nissle 1917 is a commensal *Escherichia coli* strain that eradicates pathogenic bacteria from the gastrointestinal tract. Due to its ability to alter the intestinal biome we hypothesized that Mutaflo may have the potential to prevent recurrent UTIs in children with normal urinary tract anatomy and children requiring urinary catheterization to empty their bladders. Thus, we used an *in vitro* assay to analyze the effectiveness of Nissle 1917 for eradicateing pediatriuc uropathogens and catheter associated uropathogens. **Materials and Methods:** We established a collection of 43 bacterial pediatric uropathogens and collected discarded urinary catheters. With each isolate a microcin-type assay was performed to determine the effectiveness of Nissle 1917 on bacterial growth inhibition and competitive overgrowth. **Results:** Nissle 1917 adversely affected the growth of 34 of the 43 isolates (79%) isolates. It inhibited the growth of 21 isolates and overgrew 13. The percent of species adversely affected by Nissle 1917 was 40% for *Pseudomonas*, 50% for *E. coli*, *Enterococcus* and *Staphylococcus*, 100% for * Klebsiella *and *Enterobacter*, and 0% for *Citrobacter* and *Serratia*. Pending trial conclusion, results from the discarded urinary catheter assay are anticipated to show similar replacement patterns. **Conclusions:** Nissle 1917, the active agent in Mutaflo, inhibited or out competed most bacterial isolates. These mechanisms could be used in vivo to eradicate uropathogens from the gastrointestinal tract. Pending trial conclusion, the discarded urinary catheter assay could provide an alternative to preventing UTIs in a population greatly burdened with frequent infections and multiple courses of antibiotics. Further study is needed to determine whether Mutaflo can prevent recurrent urinary tract infections in children.

THE BEST OFFENSE IS A GOOD DEFENSE: EXPRESSION AND FUNCTION OF BETA DEFENSINS IN THE INFECTED KIDNEY AND URINARY TRACT

B Becknell1, A Carpenter2, AL Schwaderer1, DS Hains1,3, SS Justice4, KM McHugh5,†1Division of Nephrology, Nationwide Children’s Hospital; 2Integrated Biomedical Sciences Program, Ohio State University; 3Center for Clinical and Translational Research, The Research Institute at Nationwide Children’s Hospital; 4Center for Microbial Pathogenesis and 5Center for Molecular and Human Genetics, The Research Institute at Nationwide Children’s Hospital, Columbus, OH.

**Background:** Beta defensins (BDs) comprise a large family of 50+ genes encoding cationic peptides with immunomodulatory and antimicrobial properties. BD expression and function in mucosal immunity of the kidney and urinary tract are incompletely defined. The goals of this study were to quantify and localize the expression of BDs in naïve and infected kidney and urinary tract, and to measure their bactericidal activity *in vitro* and *in vivo*. **Methods:** Kidneys, ureters, bladders and urine were collected from female C57BL/6 mice that remained naïve or experienced experimental urinary tract infections (UTIs) mediated by uropathogenic *Escherichia coli* (UPEC). The magnitude of BD mRNA and protein expression was evaluated by quantitative RT-PCR and immunoblotting, respectively. Tissue distribution of BD protein and mRNA was determined by immunohistochemistry and *in situ* hybridization, respectively. The bactericidal activity of recombinant BD peptides toward UPEC was evaluated *in vitro* and *in vivo* by quantifying the bacterial burden following transurethral challenge of wildtype versus *BD1* knockout mice with UPEC. **Results:** In naïve mice, *BD1* mRNA was preferentially expressed in kidney, whereas *BD3* and *BD14* mRNAs were enriched in ureter and bladder. BDs displayed unique localization patterns within the naïve kidney and lower urinary tract. *BD1* mRNA was expressed in renal collecting ducts and bladder urothelium. *BD3* was localized to endothelial cells and papillary collecting ducts of naïve kidneys. Within the bladder, *BD3* was restricted to the apical surface of umbrella cells, whereas *BD14* was expressed homogeneously throughout the urothelium. UPEC specifically decreased bladder expression of *BD1* mRNA, whereas *BD3* mRNA levels increased following inoculation. *BD1* peptides are detectable in urine following UPEC inoculation. Recombinant BD peptides demonstrated differential bactericidal activity toward UPEC *in vitro*. *BD1* knockout and wildtype mice had comparable UPEC colony counts in bladder and kidney homogenates following transurethral challenge. **Conclusions:** BDs are differentially expressed throughout the naïve kidney and urinary tract, and are subject to unique local regulatory changes following challenge with UPEC. BDs exhibit microbicidal activity toward UPEC, and further *in vivo* studies are required to evaluate their bactericidal and potential immunomodulatory roles in the infected kidney and urinary tract.
SODIUM CITRATE MODULATES T-CELL ACTIVATION.

E Winnega1, J Pituch1, T Cornell2, T Shanley3, and N Blatt1 University of Michigan, Department of Pediatrics, Sections of Nephrology1 and Critical Care2, Ann Arbor, Michigan

Acute kidney injury (AKI) is common in intensive care patients with 50% mortality rates. AKI often requires continuous renal replacement therapy (CRRT) to regulate fluid and electrolytes and clear waste products. Regional anti-coagulation with citrate during CRRT increases circuit lifetimes and decreases bleeding. However, the effect of citrate on immune function is unknown. Since lymphocyte activation requires the opening of membrane calcium channels, we hypothesized that the ability of citrate to chelate calcium will result in altered lymphocyte responses. **Objective:** Evaluate the effect of sodium citrate on T-cell activation. **Methods:** Jurkat cells, a human leukemia T-cell line, were pre-treated with sodium citrate prior to activation with antigenic [anti-CD3 + anti-CD28 (aCD3)] or pharmacologic [phorbol12-myristate 13-acetate with ionomycin (PMA)] agents. Cells were treated in media with 0.4 mM or 1.4 mM Ca\(^{2+}\) to model conditions both within a CRRT circuit or within the patient. Interleukin-2 (IL-2) levels were measured by ELISA and expression of CD25 was determined by flow cytometry. **Results:** Pre-treatment of Jurkat cells with sodium citrate (1 mM) decreases IL-2 production in low and high Ca\(^{2+}\) media: aCD3 (50% reduction in 0.4 mM Ca\(^{2+}\), 86% in 1.4 mM Ca\(^{2+}\)) PMA (65%, 60%). Following aCD3 stimulation, citrate inhibits CD25 expression in a dose-dependent manner (Table 1). However, citrate augments CD25 expression following PMA stimulation in low Ca\(^{2+}\) media. **Conclusions:** The ability of citrate to augment and inhibit responses indicates that it may act as a metabolic substrate as well as calcium chelator. These findings suggest that regional anti-coagulation with citrate may influence immune responses in patients on CRRT.

<table>
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<tr>
<th>[Citrate], mM</th>
<th>0.4 mM Calcium</th>
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<td>aCD3</td>
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<tr>
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Table 1: Jurkats were stimulated with aCD3 or PMA for 24 h prior to analysis of CD25 expression. Data is mean ± SD

MWSPR PLENARY SESSION II

GROWTH AND DEVELOPMENT

POMEGRANATE JUICE MODULATES GENE EXPRESSION IN HUMAN PLACENTAL TROPHOBLASTS.

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**Background:** Placental function and dysfunction determine pregnancy outcome. We showed pomegranate juice protects human villous trophoblast from exogenous stressors in vivo and in vitro (Chen et al. Am J Physiol 302:E1142, 2012). The mechanisms for pomegranate to render this protective action are unknown. **Objective:** We tested the hypothesis that pomegranate juice modulates expression of a cassette of genes important for the functions of human villous trophoblasts. **Methods:** Primary human trophoblasts isolated from term placentas of uncomplicated pregnancies were cultured in DMEM with 1% (v/v) pomegranate juice, or DMEM with glucose as control, from 4-24 h after plating (n=7), when the cytotrophoblast phenotype predominates, or from 24-72 h after plating (n=6), when cultures had differentiated into the syncytiotrophoblast phenotype. RNA was isolated and gene expression analyzed by quantitative rtPCR, normalized to 18S as a housekeeping gene. Comparisons were by t-test. We examined candidate genes in apoptosis/autophagy (bad, bak, bax, beclin, bid, bnip3, P53, puma, noxa, mcl1 and mdm2), altered in hypoxia (hyp, sflt, ndrg1, plgf and vegfA), involved in differentiation (ppary, syncytin and bhcg), or affected by oxidative stress (cox2, iNos, eNos, pon2). **Results:** Pomegranate juice compared to glucose control significantly (P < 0.05) enhanced cytotoxicphoblast expression of bid (2-fold), bak (1.6-fold), bhcg (2.5-fold), iNos (1.6-fold) and ndrg1 (9-fold) and decreased expression of eNos (0.3-fold), noxa (0.3-fold) and syncytin (0.5-fold), with expression of other genes unchanged. In syncytiotrophoblasts, pomegranate juice, compared to glucose control, significantly (P < 0.05) enhanced expression of iNos (2.5-fold), ndrg1 (7-fold), vegfA (4-fold), and decreased expression of pon2, with no effect on the other genes evaluated. **Conclusions:** Pomegranate juice modulates gene expression in primary human trophoblasts in a phenotype dependent manner: ndrg1 and iNos are increased by pomegranate in both phenotypes; bak, bid and bhcg are increased, and noxa, syncytin, and eNos expression are decreased, by pomegranate juice in cytotrophoblasts but not syncytiotrophoblasts; vegfA is increased and pon2 is decreased by pomegranate juice treatment of syncytiotrophoblasts but not cytotrophoblasts. **Implications for practice:** We suggest that the phenotype-dependent modulation of gene expression is an important mechanism by which pomegranate juice protects human trophoblasts from injury by external
stressors. We speculate that antenatal pomegranate juice supplementation for women may improve pregnancy outcomes. (Supported by NIH RO1 HD 291909)

11 ENDONUOUS ESTROGEN INHIBITION USING LETROZOLE IN OVINE PREGNANCY REDUCES FETAL WEIGHT AND DECREASES IN FETAL IRON.
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Purpose: Estrogen levels from the placenta rise dramatically during increasing gestation, impacting fetal growth and development. Limited data show that estrogen modulates iron homeostasis by increasing cellular iron uptake. Letrozole is a potent clinical aromatase inhibitor that suppresses estrogen production. Therefore we hypothesized that Letrozole-mediated decreases in estrogen production during pregnancy decreases both fetal weights and fetal iron levels.
Methods: In late gestation (day 120±5 Term=147 days) sheep we studied the effects of prolonged administration of Letrozole 20mg IM (day 0) then 125ug/kg/day for 12 days vs. Control (Vehicle). Fetuses were weighed and crown rump, abdominal girth, and thoracic girth measured. Fetal plasma hormones by ELISA and LC-MS and whole blood was analyzed for red blood cell (RBC) count, hemoglobin, and Zinc Protoporphyrin (ZnPP), a measure of incomplete RBC iron incorporation.
Results: Two hours after giving the Letrozole loading dose, we observed lower maternal and fetal circulating estrogen (P<0.05); whereas progesterone levels were not affected. Reductions in estrogen were confirmed using LC-MS, however, the C19 steroid levels of testosterone, DHEA and androstenedione were not altered by Letrozole. Compared to Vehicle Controls, ovine fetuses were 11.4±0.051% lighter and the ponderal index was 10.0±0.43% lower in the Letrozole group (P<0.05). Although Letrozole did not alter the crown rump length, abdominal girth was 6% lower within fetuses of this group (P<0.05). Moreover, Letrozole fetuses exhibited higher ZnPP levels, but similar RBC count and hemoglobin.
Conclusions: Estrogen reduction with aromatase inhibition by Letrozole produced leaner fetuses and impeded RBC iron incorporation, indicating a role for estrogen in controlling fetal growth, body composition, and iron metabolism during pregnancy. NIH HL87144-Supplement (PJK), HL49210, HD50578, and HD38843 (RRM).

12 OXYTOCINERGIC SIGNALING IN RETINAL COMMUNICATION
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Purpose: Oxytocin (OT) is a pertinent birth hormone that increases throughout the third trimester of gestation. Best studied for its role in parturition and lactation, OT elicits its response via oxytocin receptor (OTR), which activates a cellular phosphatidylinositol-calcium second messenger. In the retina, the retinal pigment epithelium (RPE) is hypothesized to communicate with the neural retina through a similar phosphatidylinositol-calcium mechanism and thereby, mediate in utero retinal development and maturation. Interestingly, we have found OTR transcripts to be present and functional in cultured human RPE (hRPE) cells. Therefore, we investigated oxytocinergic signaling in the retina to elucidate its potential role in retinal development. Methods: Frozen rhesus and human retinal sections were used to determine location and expression of OT and OTR in the retina by standard immunofluorescence methods. Determination of RPE oxytocinergic signaling was conducted on hRPE cells cultured as a tight monolayer using 1% serum-containing media. Cultures were maintained at 37°C and 5% CO2 with a media change every 2 days. Intracellular Ca2+ ([Ca2+]i) mobilization in response to 100nM OT was conducted via live-cell imaging and FURA-2AM ratiometric measurements. Results: OTR was expressed in the RPE of human and rhesus retinal tissue. OT was heavily concentrated in the photoreceptors, in close proximity to the RPE. Cultured hRPE cells, when stimulated with OT, exhibited a reversible 70-120 nM increase of [Ca2+]i. Conclusions: Our novel proximal localization of OT and OTR, together with the observed OT-activated increase in hRPE [Ca2+]i, supports the use of oxytocinergic signaling in RPE-retinal communication. Since retinal development is facilitated by an interdependent maturation of the RPE and photoreceptors, we suggest in utero RPE-photoreceptor oxytocinergic signaling underlies retinal development.

13 SONIC HEDGE HOG PATHWAY EXPRESSION IN NORMAL AND MEGABLADDER MICE DURING DEVELOPMENT
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1The Research Institute at Nationwide Children’s Hospital, Columbus OH, USA.
In this study, we present the first comprehensive assessment of the expression pattern of the Sonic Hedge Hog (Shh) signaling pathway in the bladders of normal mice at consecutive stages during development. Additionally, we compared the expression pattern of the Shh signaling pathway in mgb-/mice to normal mice to determine if this
critical signaling pathway is altered in the mutant bladders of these animals. We characterized the expression pattern of the Shh pathway’s ligand (Shh), receptor (Ptc.), and transcription factors (Gli 1-3) and the key smooth muscle regulatory gene, Myocardin (MyoC), in the bladders of male and female wild type and mgb-/- mutant mice at embryonic days 12, 13, 14, 15, and 16 (E12-E16), by in situ hybridization analysis. This study provides evidence that the Shh pathway exhibits a canonical pattern of expression in wild type bladders, with each molecule displaying a specific spatial localization within the bladder. Shh expresses exclusively in the urothelium of the developing bladder. Ptc. expresses in the proximal mesenchyme immediately adjacent to the urothelium, while Gli expresses in the distal mesenchyme, where smooth muscle cells develop. MyoC, a key smooth muscle regulatory gene, expresses in the distal mesenchyme, the presumptive smooth muscle cells in the bladder. Our study shows the Shh pathway is functional in mgb-/- mutant bladders but shows a potential developmental delay with poorly restricted signal boundaries. In contrast, our results indicate that MyoC is absent to minimally expressed in mgb-/- bladders when compared to controls. This study represents the first comprehensive analysis of the Shh signaling pathway during normal bladder development in mice. In addition, we show the Shh pathway is functional in mgb-/- bladders but the key smooth muscle regulator, MyoC, is drastically reduced or absent. This finding suggests that the lack of detrusor smooth muscle development in mgb-/- bladders is not due absent short axis patterning but appears to result from a dramatic reduction in the expression of MyoC.

14 MIR-205 EXPRESSION CORRELATES WITH SEVERITY OF RENAL INVOLVEMENT IN A MOUSE MODEL OF CONGENITAL OBSTRUCTIVE NEPHROPATHY.

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Background: Congenital obstructive nephropathy (CON) is a leading cause of chronic kidney disease (CKD) and end stage renal disease (ESRD) in children. CON is a complex disease process involving pathological changes in kidney development and function that occur as a result of obstructed antegrade urine flow beginning in utero. We hypothesize that microRNAs (miRs) play important roles in the renal response to urinary obstruction and in regulating gene expression in the pathogenesis of CON. Thus, miRs may represent an important novel class of potential biomarkers and therapeutic targets in CON. Methods: The megabladder (mgb-/-) mouse is an animal model of CON that develops kidney disease secondary to a bladder development defect. Specific miR expression levels were measured by quantitative PCR (qPCR) of kidney samples from wild type and mgb-/- mice. Results: There was increased expression of miR-205 across an unstratified panel of mgb-/- kidneys compared to wild-type controls (Relative Quantitation [RQ] =3.49, P=0.004). Furthermore, upon stratification of the mgb-/- population by severity of kidney involvement, relative miR-205 expression levels rise with worsening grade of hydronephrosis (Mild: RQ=1.60, P=0.59; Moderate: RQ=2.73, P=0.007; Severe: RQ=6.32, P=0.001; all values are relative to wild-type control). This suggests that miR-205 expression correlates with the severity of CON in this animal model. Additional preliminary studies indicate that miRs, including miR-205, can be measured by qPCR from urinary exosomes, including human urine samples. Conclusions: In summary, our results show that miR-205 correlates with disease severity in a mouse model of CON, and is quantitatively detectable in urine samples. Future studies will explore the target molecules and pathways affected by miR-205 in the mgb-/- model of CON, as well as the potential of miR-205 as a non-invasive biomarker of renal injury in congenital urological obstruction.

15 ACTIVATION OF TGF-β/SMAD3 SIGNALING IN MEGABLADDER MICE WITH CONGENITAL OBSTRUCTIVE NEPHROPATHY

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Purpose: Congenital obstructive nephropathy (CON) is the leading cause of chronic kidney disease in children. The megabladder (mgb) mouse serves as a unique animal model of CON. Mutants develop a functional lower urinary tract obstruction due to a lack of proper detrusor muscle organization in utero. This leads to formation of a massively distended hypomuscular bladder, renal failure and death in early adulthood. To better understand the molecular mechanisms responsible for the pathophysiology of CON, we performed transcriptome analysis of mgb kidneys compared to wild type controls. Methods: Kidneys from age-matched adult mgb-/- (mutant) and mgb+/+ (control) mice were harvested and prepared for evaluation by the Agilent cRNA microarray, qPCR and immunohistochemistry (IHC). ELISA was performed on embryonic day 15 (E15), E18, postnatal day 1-3 (P1-P3), P10, and adult kidney lysates. Gene expression data was analyzed using Ingenuity’s IPA software. Results: Transcriptome analysis of mgb kidneys identified a number of changes in genes involved in the canonical TGF-β pathway. Specifically, the expression of receptor-regulated Smad3 and Smad4 (p-value of overlap = 2.31 x 10^-9 and 4.42 x 10^-4 respectively) were identified as the most transcriptionally active (regulation z-score = 2.896 and 2.108 respectively) based on number of target genes.
with increased expression. Of the 26 differentially expressed mRNAs regulated by Smad3, 22 were upregulated in mutant kidneys. We confirmed upregulation of Smad3 target genes, Egr1 and Fos by qPCR, and genes implicated in TGF-β-dependent renal fibrosis such as CTGF by IHC. ELISA confirmed a significant increase (p≤0.05) in TGF-β3 and related TGF-β1 secreted proteins in adult mutant kidneys. Preliminary findings suggest that TGF-β1 may be increased as early as P10. Conclusions: In the mgb mouse model of CON, TGF-β and Smad3/4 profiles are upregulated. The unique progression of renal failure observed in the mgb mouse may provide an approach for the investigation of time-point dependent pharmacological inhibition of the molecular pathways responsible for CON.

16
ONTOGENY OF ENDOTHELIN RECEPTORS ON RAT BRAIN, HEART AND KIDNEY AT DIFFERENT POSTNATAL AGES
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Endothelin (ET) receptor analysis in the human placenta has shown that ET_A and ET_B receptor concentrations decrease as pregnancy advances, thus indicating their involvement in the progression of pregnancy. ET as well as ET_A and ET_B receptors have also been implicated in various central nervous system (CNS) functions. We have demonstrated that endogenous ET concentration in the CNS changes with age, however the ontogeny of ET_A and ET_B receptors in the brain, heart and kidney has not been studied. Objective: To determine the expression of ET_A and ET_B receptors in the brain, kidneys and heart of normal newborn rat pups at different postnatal ages. Methods: Eight pregnant Sprague-Dawley rats were used in the present study. In order to avoid hormonal influence, only male rat pups were included and sacrificed randomly on Day of Life 1, 7, 14 and 28. Brain, kidney and heart organs were removed and homogenized in buffer to study the expression of ET_A and ET_B receptor protein levels using western blot technique. Results: The mean body weight, brain, kidney and heart weights increased proportionally with advancing age showing adequate nutrition and growth. The behavioral development of rats during the observational period was normal. The expression of ET_A receptors in the brain, heart and kidneys was similar in rats of postnatal ages 1, 7, 14 and 28 days. However, ET_B receptor expression significantly (p<0.001) decreased by 72 % on day 28 compared to rats of age 1, 7 and 14 days. Conclusions: These results demonstrate that ET_B receptor expression is higher in neonatal rat brain on day 1 through 14 of life and decreases with age (day 28). No change in expression of ET_A receptors was observed. No change in either ET_A or ET_B receptor expression was observed in the heart or kidney suggesting that ET receptors have a more functional role in these organs than a developmental one. We conclude that ET_B receptor ontogeny decreases with age in the brain implicating its involvement in the development of the central nervous system.

17
DOES NEONATAL GROWTH RESTRICTION PROGRAM AUTISM-LIKE BEHAVIOR IN C57BL/6 MICE?
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Background: Autism Spectrum Disorder (ASD) is a group of developmental disabilities that can cause social, behavioral, and communication difficulties. The incidence has increased significantly in the past 20 years, and current prevalence is 1 in 88 children. Prematurity and neonatal growth restriction are associated with an increased risk of ASD. Leptin, an important neurotrophic hormone, is deficient in growth restriction. Previous studies have shown growth restricted mice that received neonatal leptin supplementation have improved adult brain weight, amygdala size, and myelination, factors thought to play a role in ASD. Methods: As a screen for autism-like behavior, we investigated the social interaction of adult C57BL/6 mice using a tripartite chamber assay. At birth, mice were divided into litters of 6 pups (average growth) or 12 pups (restricted growth). From DOL 4-14, the pups were randomized to receive daily injections of saline or leptin. Upon reaching adulthood (4 months), mice underwent social interaction testing (N= 25-38 mice per group). Data were compared by Student’s t-test with P<0.05 considered statistically significant. Results: Independent of leptin supplementation, growth restricted mice spent less time in casual contact with the “stranger mouse” (average growth 103+/−3 sec, growth restricted 94+/−3 sec, p<0.04). Growth restricted mice that did not receive leptin supplementation tended to spend more time in the empty chamber, apart from the “stranger mouse” (control 193+/−7 sec, growth restricted-saline 212+/−13 sec, p<0.02), and more time interacting with the novel object away from the “stranger mouse” (control 67+/−3 sec, growth restricted-saline 74+/−4 sec, p<0.15). These isolation behaviors were normalized by neonatal leptin supplementation: time in empty chamber (growth-restricted-leptin 195+/−8 sec) and time with novel object (growth restricted-leptin 65+/−4 sec). Conclusion: These results suggest a possible effect of neonatal growth restriction on adult autism-like behavior, that is not fully corrected by neonatal leptin administration. Additional behavioral assays are underway to further assess the effects of leptin supplementation on the neurodevelopmental outcomes of growth restricted mice.
THE ROLE OF ENDOTHELIAL PROGENITOR CELL NUMBERS IN INFANTS AND CHILDREN ON VASCULAR REACTIVITY.

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Background: Diabetes Mellitus (DM) is the leading risk factor for early cardiovascular disease. Recent attention has shifted to the predisposing effects of fetal exposure to an intrauterine diabetic environment on long-term cardiovascular function. Critical to vascular health is intact endothelial function and endothelial homeostatic regulation. The endothelium relies on endothelial progenitor cells (EPCs) to orchestrate vascular repair and vessel formation. One population of EPCs, hematopoietic-derived circulating progenitor cells (CPCs), has a major role in facilitating angiogenesis. Recent studies from our laboratory showed that cord blood CPCs are reduced in pregnancies complicated by type 2 or gestational diabetes. Therefore, we hypothesize that infants and children exposed in utero to maternal type 2 diabetes (T2DM) will have reduced CPC numbers and impaired vascular function. Methods: A total of 20 subjects per experimental group is planned. Peripheral venous blood samples were collected from neonates (<7 days of age) and children (5-10 years of age) who were born to women with T2DM or an uncomplicated pregnancy. CPCs were enumerated using 5-color polychromatic flow cytometry. Endothelial-dependent and -independent vascular reactivity were assessed using acetylcholine (Ach) and sodium nitroprusside (SNP) iontophoresis and laser Doppler imaging. Results: Thus far, 24 infants and 22 children have been enrolled. Infants born to mothers with T2DM (n=10) trend towards impaired vasodilation and decreased maximal perfusion in response to SNP compared to controls (n=14). Children born to mothers with T2DM (n=10) trend towards impaired vasodilation in response to SNP and Ach compared to controls (n=12) with more pronounced differences than infant subjects. Preliminary data from flow cytometry studies detect no differences in CPC numbers between experimental groups. Further recruitment and data analysis are ongoing until twenty controls and twenty experimental subjects in each age group are studied. Conclusions: These data suggest that infants and children born to mothers with T2DM may display impaired vascular smooth muscle function, and further analysis is ongoing to investigate whether children also exhibit impaired endothelial function. Studying the impact of intrauterine DM exposure on offspring vascular function is integral to identifying novel therapies to maintain vascular health in these children.

ENDOTHELIAL FUNCTION IN HIV INFECTED ADOLESCENTS AND YOUNG ADULTS ON HAART THERAPY

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Background: The development of highly active anti-retroviral therapy (HAART) has dramatically reduced HIV-associated mortality. HAART therapy, specifically protease inhibitors (PI), in adults with HIV has been implicated as a cause for endothelial dysfunction via its role in decreasing nitric oxide availability. However, numerous other studies have demonstrated an association with decreased endothelial inflammatory markers on HAART therapy with or without the use of PI. Research in the HIV infected pediatric population has been scarce. Objective: To directly evaluate endothelial function in HIV infected pediatric patients on HAART therapy, comparing those on protease inhibitors (PI) vs. those on nucleoside reverse transcriptase inhibitors (NRTIs). Methods: HIV infected subjects between the ages of 12 and 21 years who had reached pubertal Tanner stages of 4-5 were recruited out of the infectious disease clinic at Nationwide Children’s Hospital. Subjects were required to have maintained a stable weight and to have been compliant on stable antiretroviral therapy for 6 months prior to enrollment. 12 subjects were enrolled in total with 6 subjects in the PI group and 6 subjects in the NRTI group. Endothelial function was assessed using reactive hyperemic changes (5 minutes of upper arm vascular occlusion) in forearm vascular resistance (FVR) measured using venous occlusion plethysmography. Endothelial function was assessed as percent change in FVR pre and post upper arm vascular occlusion. Results: We found no significant difference in endothelial function between PI and NRTI treated HIV infected adolescents and young adults (p>0.1). Conclusions: Our data suggests that endothelial function is not impaired in HIV infected adolescents and young adults on PI versus NRTI therapy. Comparison to non-HIV infected adolescents and young adults is warranted to assess the effect on HIV infection on endothelial function independent of therapy type in the pediatric population.
POOR GLUCOSE CONTROL IMPAIRS MAXIMAL POST-OCCLUSIVE VASODILATION IN ADOLESCENT TYPE 1 DIABETES

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Objective: Endothelial dysfunction plays an important role in the pathogenesis of cardiovascular disease and long-term complications in type 1 diabetes (T1D) and is present in adolescents with T1D. How glucose control affects endothelial function in adolescent T1D is unclear. Methods: We used venous occlusion plethysmography to measure forearm blood flow (FBF) and forearm vascular resistance (FVR, mean arterial pressure/FBF) before (Pre) and after (Post) 5 min of upper arm arterial occlusion in 16 adolescents with T1D (age: 13 ± 2 yrs; duration: 5 ± 4 yrs, BMI: 20 ± 3 kg/m2) and assessed their relationship to fasting glucose (FG), 72 hour mean glucose (MG) and standard deviation (STD) (Medtronic Guardian), single hemoglobin A1c (SA1c), and hemoglobin A1c area under the curve (A1cAUC) since diabetes diagnosis. Results: PostFBF negatively correlated (r = -0.54, p = 0.03) and PostFVR (Figure) positively correlated (r = 0.55, p = 0.03) with SA1c. PostFVR also correlated with MG (r = 0.57, p = 0.03). PreFVR (Figure) tended to correlate with SA1c as well (r = 0.48, p = 0.06). Percent change in FVR from pre to post-occlusion tended to decrease as FG increased (r = -0.49, p = 0.07). Vascular performance was not related to STD, A1cAUC, age, duration, or body mass index.

Conclusion: The results indicate that poor diabetes control impairs maximal, shear stress-induced, endothelially-mediated vasodilation. Decreased vasodilatory ability may cause poor tissue blood flow and future complications.

EFFECT OF FITNESS ON GLYCEMIC VARIATION IN TYPE 1 DIABETES

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Background: Extreme glycemic variation has been associated with a high incidence of Type 1 Diabetes Mellitus (T1DM) complications. Glucose variability indicators, such as the mean amplitude of glycemic excursion, are now being considered as methods for identifying worsening glycemic control, perhaps even more accurately than the traditionally accepted HbA1c. While studies on the effects of exercise on hypoglycemia and glucose variation are abundant, little is known about the significance of cardiovascular fitness – a modulator of insulin sensitivity – and its role in glycemic variation. Thus, the goal of this study was to determine if aerobic fitness and exercise workload are associated with glycemic variability in adolescents with T1DM. Methods: Nineteen adolescents with T1DM, ages 14-19, were admitted to the Clinical Research Unit (CRU) and underwent aerobic treadmill fitness testing to determine VO2 max (ml/kg/min). During this admission, a continuous glucose monitor (CGM) was placed on each subject and worn until the subjects returned within 3-5 days. At the return CRU visit, subjects underwent a one hour treadmill exercise challenge at 55% of individual VO2 max and continued wearing the CGM until 24 hours after exercise challenge. Metabolic equivalent (MET), a measure of accumulated metabolic workload during the exercise challenge was calculated. The mean amplitude of glycemic excursion (MAGE) was calculated by identifying the glucose peaks and nadirs from the CGM data collected over a 3-5 day interval between the two study visits. Results: Mean starting glucose value prior to exercise challenge was 116.5 ± 29.3 mg/dL and majority of subjects developed hypoglycemia during exercise challenge. Metabolic equivalent (MET), a measure of accumulated metabolic workload during the exercise challenge was calculated. The mean amplitude of glycemic excursion (MAGE) was calculated by identifying the glucose peaks and nadirs from the CGM data collected over a 3-5 day interval between the two study visits. Results: Mean starting glucose value prior to exercise challenge was 116.5 ± 29.3 mg/dL and majority of subjects developed hypoglycemia during exercise challenge. There was an inverse association between VO2 max and MAGE, calculated from CGM data between the two study visits, with Pearson correlation r = -0.50 (95% CI: -0.78, -0.04; p-value = 0.030). For the same CGM data, MET load and MAGE also had an inverse relationship with r = -0.57, (95% CI: -0.82, -0.14; p-value = 0.010). Conclusions: Glycemic variation in everyday life was inversely associated with both fitness and metabolic workload during an exercise challenge. Thus, fitter subjects had less variation in everyday glucose values. Given that the amount of exercise was relative to individual aerobic capacity (fitness), this suggests that absolute amount of exercise plays an important role in determining post-exercise hypoglycemia. Fitness should be promoted in adolescents with T1DM for its beneficial effects on glycemic variation in everyday life, leading to fewer extremes in hypoglycemia and hyperglycemia to prevent long-term complications.
A NOVEL NEONATAL FEEDING PROGRAM STRATEGY ACCELERATES FEEDING MILESTONES AND SAVES RESOURCES: IS THIS THE HOLY GRAIL?
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Nationwide Children’s Hospital, the Ohio State University Wexner College of Medicine, Columbus OH

Background: Premature infants undergo gastrointestinal and aerodigestive difficulties during gavage-, transitional-, and oral- feedings. No pragmatic infant feeding protocols that can be generalized; thus feeding practices are variable. Feeding-related morbidity, length of stay and economic burden is increasing. Objective: We optimized feeding methods from NICU admission until discharge using an individualized, pathophysiology-based, integrative approach, and tested the hypothesis that a standardized feeding strategy modifies accepted feeding milestones, morbidity and economic burden. Methods: Inclusions: <32 wk GA and <34 wk PMA at admission. Exclusions: Necrotizing enterocolitis (NEC) at admission, neonatal abstinence syndrome, congenital birth defects, and surgical patients. Focused multidisciplinary feeding rounds ensured compliance to feeding strategies. A targeted feeding enhancement strategy focused on attaining feeding milestones set for each infant. Prior baseline data (N=92, collected for 15 mo) were compared with the novel feeding program data (N=69, implemented over next 15 mo). Results: Demographics were similar between groups. Uptake of trophic feeding increased from 34% to 80% (baseline vs. novel feeding program, P <0.002). The proportion of subsequent visits (hospital readmission, Emergency visits), medical or surgical NEC, closure of PDA, and IVH were similar (P=NS).

Characteristics Baseline Novel Feeding Program P-Value
Weight velocity, g/d 24 ±6 27 ±11 0.03
Length of stay (LOS), d 96 ±1 80 ±1 0.005
Trophic feeds to enteral progression onset, d 15 ±10 8 ±8 0.0001
Enteral progression onset to full enteral onset, d 16 ±15 10 ±10 0.01
PO onset to Full PO, d 13 ±17 20 ±16 0.01
Charges at Initial in-patient stay, per patient, $ 511,547 ±$ 298,773 296,782 ±$ 181,706 0.0004

Conclusions: Our novel neonatal feeding strategy minimizes provider practice variability, accelerates feeding milestones, improves growth velocity, lowers LOS and saves health care dollars in NICU.

VITAMIN D STATUS IN PRETERM INFANTS AND EFFECTIVENESS OF CURRENT VITAMIN D INTAKE DURING THE HOSPITAL STAY.
N Monangi, J Slaugther, H Akinbi, A Dawodu, University of Cincinnati

BACKGROUND: Preterm infants are at high risk for vitamin D (vD) deficiency because of inadequate intake, lack of sun exposure and acute illness. It is unclear if current vD intake strategies are adequate in repleting preterm infants with vD. OBJECTIVE: To assess the relationship between maternal and VLBW infant vD status at birth and the effect of current intake strategies on vD status in preterm infants during the NICU stay. DESIGN/METHODS: Maternal blood was obtained postpartum and infant’s specimens collected on admission to NICU, at 4 weeks, and at 36 weeks post menstrual age (PMA). The serum 25(OH)D levels were measured from dried blood spots using LC-MS/MS. Infants were stratified into 2 groups: <28wks weeks and 28 – 32 weeks. Within each group, infants were stratified based on serum 25(OH)D <20ng/ml or >20ng/ml. Data collected on total daily vD intake. RESULTS: A total of 120 infants were enrolled: <28 weeks 67, 28 – 32 weeks 53. The serum 25(OH)D levels at birth were directly correlated with maternal 25(OH)D levels (r=0.65, p=0.001). There was a direct correlation between the 25(OH)D at birth and the level at 36 weeks PMA (r=0.54, p=0.003). With current supplementation strategy, 40% (< 28 weeks) and 30% (28 – 32 weeks) have serum 25(OH)D levels <20 ng/ml at 4 weeks and at 36 weeks of PMA.

Vitamin D Status

<table>
<thead>
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<th>Status</th>
<th>&lt;28 weeks (n = 67)</th>
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<tr>
<td>n (%)</td>
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<td>20 (30)</td>
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<td>Gestation age (wks)</td>
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<td>Birth weight (g)</td>
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<td>864.2 ±202.6</td>
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<td>Maternal 25(OH)D (ng/ml)</td>
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<td>26.5 ±3.9</td>
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<td>25(OH)D at birth (ng/ml)</td>
<td>13.6 ±4.8*</td>
<td>13.9 ±4.3*</td>
</tr>
<tr>
<td>vD supplement (IU/kg/d)</td>
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</tbody>
</table>

Values are Mean ± standard deviation, * p-value <0.01 between Deficient and Sufficient
CONCLUSIONS: Almost two-thirds of preterm infants are VD deficient at birth. Although serum 25(OH)D levels increased from birth to discharge, about one-third are deficient at 4 weeks chronologic age and 36 weeks PMA. Vitamin D levels should be optimized in pregnant women to ensure VD sufficiency in the offspring. Further evaluation of our VD supplementation strategy in VLBW infants is warranted.

24 IMPACT OF DELAYED UMBILICAL CORD CLAMPING AT THE LIMITS OF VIABILITY.

C Backers, H Huang, B Schanbacher, JA Deverse, K Copeland, JP Iams, PJ Giannone, JA Bauer, Research Institute at Nationwide Childrens Hospital, Ohio State University Medical Center, Columbus, Ohio

Background: Immediate umbilical cord clamping (ICC) at delivery is routine practice but delayed clamping (DCC) may improve infant outcomes. The mechanisms involved are unclear but DCC provides enhanced blood volume and cord blood is known to contain progenitor cell types with developmental or reparative value. Infants at highest risk of morbidities such as intraventricular hemorrhage (IVH) are those born <28wks, and DCC may have particular value in this setting. Objectives: We conducted a pilot study to test hypotheses: 1)DCC can be safely implemented in extremely low birth weight infants; 2)DCC is associated with hematological and/or hemodynamic effects and increases pools of circulating progenitor cells; 3)DCC reduces the frequency/severity of IVH. Design/Methods: Randomized, controlled, clinical trial. Pregnant women admitted 23-28wksGA were enrolled & assigned to ICC (<10sec) or DCC (45sec). Neonate blood was obtained at admission, 48hrs, 30d. Additional data collected retrospectively via medical chart. Progenitor cell types (defined as AC133+/CD45-, CD34+/CD45-, or AC133+/CD34+/CD45- cells) were determined by flow cytometry. IVH was determined via head ultrasound; all data was collected by investigators blinded to treatment group at delivery. Survival analysis (logrank Mantel-Cox test) was used to compare IVH incidence (grades 3-4) or death as a combined primary endpoint from day of life 0 to day 30. Blood measures were compared using 2-way ANOVA.

Results: A total of 40 infants were enrolled (n=22 ICC group; n=18 DCC). Birth weight was not different between groups (634±160g ICC vs. 745±193g DCC, range 386-1105g). There was no difference in maternal demographics, vaginal vs. cesarean section, gestational age, Apgar scores, or male/female ratio. DCC was associated with slightly higher hematocrit at 2hr (43 vs. 39%) and 72hrs (40 vs 35%) post-delivery. DCC was also associated with a significantly higher mean blood pressure of ~3-5mmHG over the first 24hr of life, and a 4-fold reduction in use of BP support (saline and/or dopamine infusion). IVH (grade 3 or 4) or death was observed within 30d of life in 6 of 20 (30%) cases of ICC but only 1 of 16 (6%) cases receiving DCC (p=0.006). DCC was also associated with trends of increased prevalence of circulating progenitor cells at day 30. Conclusions: DCC can be safely implemented in extremely premature infants (e.g. <800g), seems to have some impact on initial hematocrit and BP, and apparently substantial benefit in lowering IVH incidence in this extremely vulnerable population, and is associated with increased circulating pools of progenitor cell types. Further studies to extend enrollment of this patient population and define efficacy and mechanistic aspects of DCC in the setting of extreme prematurity are clearly warranted.

25 SERIAL IRON MEASURES AT BIRTH, 6 AND 12 MONTHS: PREDICTION OF IRON STATUS.

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Purpose: Developing iron deficiency (ID) in the first 2 years of life is associated with impaired neurocognitive development. Risk for developing ID at 12 mos. can be increased by prolonged exclusive breastfeeding or other nutritional factors. Several historical maternal or neonatal risk factors also increase risk for infantile ID, because half the iron needed for infant growth is acquired before birth. Two measures of iron status at birth are potential candidates to predict ID in later infancy. We hypothesized that cord blood serum ferritin, a measure of storage iron, and zinc protoporphyrin/ heme (ZnPP), a measure of incomplete erythrocyte iron incorporation would predict iron status at 6-12 mos. of life. Methods: In a prospective study, we enrolled healthy term newborns with risk factors for infantile ID; lower socioeconomic status, maternal minority status, anemia, gestational diabetes, or fetal growth disturbance. Serial measures of ferritin, ZnPP and ZnPP in the reticulocyte fraction (RetZnPP) were measured. Additionally, the lowest 6 or 12 mo. postnatal ferritin was the study endpoint, with ID cutoff of 12.5 ng/mL. Results: Blood was collected from 88 at-risk infants at birth, 6 and 12 mos. Values for cord ferritin, cord ZnPP and cord RetZnPP were all correlated with 6 mo. values of their respective parameters, p<0.05. Both cord ZnPP and cord RetZnPP were correlated with cord ferritin, p<0.05. Of the sample, 29.5% of the postnatal ferritins fell below the ID cutoff of 12.5 ng/mL, with 60% of the low postnatal ferritins predicted by one or more of the cord blood parameters. Conclusions: Our healthy, but at-risk sample exhibited 6-fold higher incidence of biochemical ID in infancy than controls. Although postnatal factors also impact infantile ID, cord blood ferritin and ZnPP can predict a subset of children who ultimately develop biochemical ID later in infancy. Earlier identification can lead to earlier treatment and potential prevention of adverse sequelae.
COMPARISON OF METHODS TO MEASURE RED CELL VOLUME (RCV) IN NEONATES USING FETAL HEMOGLOBIN (HbF) AND BIOTIN LABELING OF RBCS (BioRBC).

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**Background:** Anemia is a common and serious problem in critically ill neonates that is treated with red blood cell (RBC) transfusion. Inability to use radioactive chromium to label RBCs due to concern of radiation exposure in vulnerable populations like neonates has limited our understanding and management of this serious condition. BioRBCs has been used to measure RCV and red cell kinetics accurately however this requires labeling of RBCs with biotin. Since RBCs of neonates predominantly contain HbF while donor RBCs received during RBC transfusion contain HbA, the dilution of HbF by HbA following RBC transfusion can be used to calculate RCV. **Objective:** To compare RCV by three methods using HbF measurement in neonates with BioRBC method. **Design/Methods:** RCV was measured by HbF dilution technique in transfused neonates using the following laboratory techniques: i) cell flow cytometry technique (n=10); ii) HPLC (n=6); and iii) alkali denaturation (n=14) from Hudson et al., 1990, and compared with simultaneous BioRBC RCV measurements. **Results:** The data sets were fitted using linear regression method and the slopes of the lines were compared with the BioRBC method. There was no statistical difference between slopes of alkali denaturation and HbF flow cytometry compared to the BioRBC (Unpaired t-test). However there was a statistically significant difference between the slopes of HPLC method as compared to the BioRBC method (p<0.05). HPLC method overestimates RCV compared to the BioRBC method. **Conclusions:** RCV by HbF flow cytometry and alkali denaturation tend to agree better with BioRBC method than by HbF HPLC method in transfused neonates. HPLC technical limitations could possibly explain lesser agreement when compared to other methods using HbF. RCV by HbF cell flow cytometry technique and alkali denaturation are reasonable alternatives to measure RCV in transfused neonates.

SAFETY AND EFFECTIVENESS OF WHOLE BODY COOLING THERAPY FOR NEONATAL ENCEPHALOPATHY ON TRANSPORT

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**Purpose:** Therapeutic hypothermia is the only treatment currently available for neonatal hypoxic-ischemic encephalopathy proven to decrease morbidity and mortality. Current evidence suggests greater efficacy if hypothermia is initiated within 6 hours of birth. Cooling during interfacility transport would expand this treatment to those infants requiring a prolonged transport. There are currently few studies evaluating the safety and effectiveness of whole body cooling on transport. Our objective was to evaluate the safety and effectiveness of a transport protocol for therapeutic whole body cooling of the neonate with hypoxic-ischemic encephalopathy. **Methods:** This was a single center, retrospective cohort study of neonates who met criteria for and received whole body cooling during transport by the Children’s Mercy Critical Care Transport (CMCCT) team between December 2008 and August 2011. Infants meeting criteria based on the NICHD cooling trial (Shankaran et al. NEJM 2005) were cooled during interfacility transport utilizing both passive and active (ice) interventions based on esophageal temperature parameters followed every 15 minutes. Outcomes of interest included central temperature on admission (desired range 33.5°C to 36.5°C), incidence of hypothermia (<32°C) or hyperthermia (>37°C) during transport, and hour of life upon admission. Infants not transported by CMCCT were excluded. The data were analyzed by means procedure. **Results:** Of 55 infants meeting criteria, 48/55 (87%) had central admission temperatures in the desired range of 33.5-36.5°C, 5/55 (9%) were below (32.5-33.4°C), and 2/55 (4%) were above (36.6-37°C) this range. One infant (2%) had a central temperature reading of 31.9°C while no infants had temperatures >37°C during transport. 11/54 (20%) infants were admitted after 6 hours of life, 5/11 (45%) of which achieved or were maintained at targeted cooling central temperature (33.5±0.5°C) during transport. **Conclusion:** Whole body cooling of neonates with hypoxic-ischemic encephalopathy can be effectively and safely performed during interfacility transport. This expands the availability of a potentially life-saving therapy to those infants for whom admission to a referral facility within six hours is not feasible.
TWO YEAR PROSPECTIVE EVALUATION OF HUMAN PARECHOVIRUS AND ENTEROVIRUS CNS INFECTIONS IN INFANTS LESS THAN 90 DAYS OF AGE

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Affiliations: 1. Children’s Mercy Hospitals and Clinics, University of Missouri-Kansas City School of Medicine, Kansas City, MO

Background: Human Parechoviruses (HPeVs) are increasingly recognized in infants presenting with sepsis and meningitis. Recent retrospective data from our institution noted different clinical characteristics in HPeV vs. Enterovirus (EV), but no prospective study has validated these findings or detailed infant exposure history. We are currently in year 2 of active CSF surveillance for EV and HPeV, expecting renewed activity in summer 2012.

Methods: Hospitalized infants <90 days old, with CSF WBC counts <1000 and negative CSF gram stain are eligible. Mothers were asked about pregnancy history, infant exposures, and infant illness history. Mothers were asked for throat swabs and blood specimens. Infant throat swabs, nasal swabs and stools were obtained. Scavenged infant CSF, blood and urine were batch tested. Demographics, laboratory values, clinical course, and treatment modalities were collected from charts.

Results: Among 281 subjects to date (Jan 2011 – April 2012), specimens tested were 236 CSF, 231 throat, 57 nasal swabs, 148 urine, 210 stool, 210 blood and 233 maternal throat swabs. EV was detected in 20 subjects and HPeV in 5 subjects. EV CSF WBC counts were higher than HPeV (Mn= 102.1/mm³ ± 9.9/mm³ vs. 4.0/mm³ ± 4.0/mm³, p < 0.0001), as were peripheral WBC counts (8929/mm³ ± 1838/mm³ vs. 6118/mm³ ± 2624/mm³, p = 0.0005) and CSF glucose values (46.2 mg/dL ± 3.9 mg/dL vs. 40.9 mg/dL ± 2 mg/dL, p = 0.0002). EV positives had an ill household contact more often than HPeV (p = 0.0403). Compared to controls with neither, HPeV and EV subjects trended to more ill contacts (p = 0.0698). Overall 19/32 (59%) specimens were positive from HPeV subjects and 57/112 (51%) from EV subjects. Permissive sites (throat, stool, nasal) had virus detected in 5/5 (100%) HPeV and 19/20 (95%) EV, while CSF and/or blood isolates were detected in 3/5 (60%) HPeV and 15/20 (75%) EV subjects.

Conclusions: Active surveillance for HPeV and EV CNS infections is ongoing. Prospective analysis has confirmed that mean CSF and peripheral WBC counts and CSF glucose levels were significantly higher in EV vs. HPeV patients. EV subjects also had ill contacts more often than HPeV. We expect HPeV and EV infections to re-appear in summer 2012, permitting more complete 2-year EV to HPeV prospective comparisons.

COUGH IN BPD NEONATES: MECHANISMS OF ORIGIN AND RESOLUTION

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Background: Cough and swallowing are key protective mechanisms that defend against aspiration. Premature neonates with BPD commonly experience swallowing and breathing difficulties and are at risk for aspiration. Aim: To define the cough-triggering and resolving mechanisms in BPD infants. Methods: BPD neonates (N=16, born at 26 ± 1 wks GA, studied at 44.5 ± 1.5 wks PMA) underwent concurrent pharyngo-esophageal manometry, respiratory inductance plethysmography, and nasal air flow to determine the concurrent relationships between esophageal motility patterns and respiratory waveform changes. Cough was defined as audible sound in conjunction with deep inhalation succeeded by forceful exhalation. The triggering mechanisms that resulted in cough reflex were analyzed based on the manometric waveform characteristics. Normalcy restoring esophageal peristaltic mechanisms were also defined succeeding cough reflex. Results: 1) The frequency of cough initiating mechanisms in BPD neonates (N=88 cough episodes) are non-propagating swallow (NPS) in 59%, upper esophageal sphincter contractile reflex (UESCR) in 18%, lower esophageal sphincter relaxation in 14%, esophageal retrograde movement in 6%, and no trigger identified in 3%. 2) The frequency of post-tussive cough resolving mechanisms (N=85 cough episodes) that restored respiratory normalcy were primary peristalsis in 84%, secondary peristalsis in 8%, and none recognizable in 8%. 3) UESCR was the dominant reflex that triggered cough for infants on NCPAP at the time of study, contrasting with NPS for infants on nasal cannula at the time of study (OR=9.13, 95% CI = 1.88-44.24). Conclusions: 1) In BPD neonates, NPS and UESCR are dominant triggers for the cough reflex, indicating upper-aero digestive origins. 2) Primary peristalsis is the most important clearance mechanism for post-tussive restoration of normalcy with respiration and pharyngo-esophageal quiescence. 3) BPD infants on NCPAP are more likely to have coughs triggered by UESCR, while coughs from BPD infants on nasal cannula are more likely to be triggered by NPS.
AN ACTIN MUTATION THAT CAUSES PATENT DUCTUS ARTERIOSUS ALTERS REGULATION BY PROFILIN
EW Wedemeyer, KK Wen, ND Vanderpool, PA Rubenstein and HL Bartlett

More than thirty mutations in ACTA2, which encodes alpha-smooth muscle actin, have been identified to cause autosomal dominant Thoracic Aortic Aneurysm and Dissection. The mutation R256H is of particular interest because it also causes moyamoya disease and patent ductus arteriosus. Based on its molecular location along the inter-strand interface, F-actin conformation may be altered and impact actin regulation by binding proteins. Two such proteins are profilin and formin. Profilin binds and sequesters actin monomers and facilitates nucleotide exchange to ready monomers for polymerization. This profilin-actin complex then interacts with formin to accelerate actin filament assembly. Based on previous data, we hypothesized that the R256H mutation would affect actin regulation by profilin. To investigate the biochemical effects of the mutation, we engineered the R256H mutation into yeast actin, which is 94% similar to human alpha-smooth muscle actin to investigate the effect on actin function in vitro. Mutant actin monomers were less stable as determined by circular dichroism and the conformation profilin-mutant actin complex was altered as assessed by protease digestion. The change in conformation did not affect profilin binding affinity or profilin-actin ATP exchange rates. Polymerization kinetics in the presence of profilin, however, was significantly altered. Relatively independent of concentration, profilin inhibited mutant actin polymerization with a 50% decrease in final extent. At high dose, polymerization was completely inhibited likely due to the additive effect of sequestration. Together, the data suggest that profilin weakly caps mutant actin filaments, an activity not previously identified. Normalization of filament conformation by the addition of phalloidin rescued polymerization in the presence of profilin. Both the inhibition of profilin regulated actin polymerization and rescue with phalloidin were more pronounced in the presence of the formin, Bni. This indicates that the misregulation of mutant actin by profilin is a consequence of filament conformation. Profilin regulates vascular smooth muscle cell proliferation and migration during development. As such, the effects of the R256H mutation on profilin regulation may contribute to inappropriate persistence of the ductus arteriosus.

POST-PRANDIAL MESPENTERIC HYPEREMIC RESPONSE IN LACTOSE CONTAINING VERSUS LACTOSE-FREE INFANT FORMULA
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University of Kansas Medical Center, Kansas City, KS

Background: Fructose and infant formulas containing dextrose and sucrose promote mesenteric vascular inflammation. These sugars may decrease nitric oxide bioavailability and consequently endothelial-dependent function as evidenced by decreases in flow mediated vaso-dilation in adults. Whether certain sugars affect vascular mesenteric function in neonates is unclear. We compared post-prandial superior mesenteric artery (SMA) blood flow in infants following feeds of lactose-containing (LC) and lactose-free (LF) formula (corn syrup solids + sucrose).

Methods: This 2x2 cross-over study included 6 term newborns, the first 3 were assigned LC formula followed by the LF formula. For the remaining 3 the order was reversed. Duplex ultrasound was used to assess pre- and post-prandial SMA blood flow (Q cm/sec), SMA lumen diameter (cm), and vascular resistance. Assessments were made 5 min prior to feed, then 10-, 30, 40-min post-prandial. Doppler information from 5 cardiac cycles was averaged. Data were analyzed using RM ANOVA and t-tests with two-tailed alpha=0.05.

Results: The mean +/- SD age and weight of infants (n=6) was 24.1+/-.23h and 3.1+/-.0.21kg respectively. The volume of formula consumed was 22.5+/-2.8cc for LC and 25+/-1.8cc for LF (p>0.05). Consumption of both formulas was associated with increased SMA flow at 10 and 30 min. Averaged over these times, flow was significantly greater with the LC formula than for the LF (p=0.005) with a maximal difference at 30 min (LC 103ml/min, a 52% increase from pre-prandial vs. LF 92.7ml/min a 31% increase, p=0.028). SMA flow was not significantly affected by the order of the formula ingestion. For both formulas, post-prandial vasodilation was seen up to 30min. Averaged over the 10 and 30 min values, vasodilation was significantly greater for the LC formula than for the LF (LC 9% increase, LF 4% increase, p=0.007). Consumption of both formulas also elicited a significant decrease in SMA vascular resistance for up to 30 min (p=0.016) with peaks of -8 to -10% at 30 min. However, the decrease in resistance did not differ across the formulas.

Conclusion: Consumption of LC formula was associated with a greater post-prandial hyperemic SMA response compared to LF formula. Post prandial flows for both formulas were within expected ranges, thus differences between the two formulas are likely inconsequential for a healthy term newborn. However, differences in post-prandial SMA blood flow in a vulnerable pre-term infant may become significant and merits further investigation.
COMMON ALLEGATIONS OF PROFESSIONAL LIABILITY AGAINST PRACTITIONERS OF NEONATAL MEDICINE

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Background and Significance: The professional liability crisis is highly relevant to all practitioners in neonatal medicine. Identifying the most common events in sick newborns leading to litigation could improve the current professional liability crisis and potentially reduce avoidable devastating outcomes. Objective: To identify the most common allegations brought against practitioners of neonatal medicine and to recommend specific risk-management strategies, which could favorably impact professional liability. Brief Methods: We reviewed 136 closed legal cases of alleged negligence in the care of the newborn as a neonatal expert (JKM) from 1986-2012. A confidential file was kept for each case. Of these cases, 70% were reviewed for the defense and 30% were reviewed for the plaintiff, with 55% of cases in Illinois. Results: A total of 186 allegations were identified. Multiple allegations per case were common. The fifteen most common allegations were: inadequate airway (20%), unrecognized pneumothorax (14%), delayed transfer to a level III NICU (12%), delayed attendance/inadequate personnel in delivery room (11%), inadequate treatment of seizures (10%), medication error (8%), cardiac tamponade (6%), blindness (5%), midgut volvulus (4%), delayed treatment of anemia (3%), hypoglycemia (1%), and hyperbilirubinemia (1%). Conclusions: Specific risk-management strategies can be identified to potentially reduce devastating neonatal outcomes. Residency programs must ensure sustained housestaff proficiency in intubation. Needle thoracentesis far outweighs the risk and can acutely reverse a potentially lethal pneumothorax. Regionalization is in the best interest of the mother and newborn. Low risk newborns can require significant resuscitation. The presence of apnea with desaturations can often represent a seizure. Other risk reduction strategies including computerized order entry, serial x-rays, mandatory eye exams, prompt surgical evaluation for bilious emesis, and immediate access to O negative blood may help reduce poor neonatal outcomes and allegations of professional liability.

EFFECTIVENESS OF A PEER COUNSELOR-BASED BREASTFEEDING PROGRAM AMONG HIGH-RISK INFANTS

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Background: In September 2001, Nationwide Children’s Hospital (NCH) began a lactation program based in the hospital’s neonatal intensive care units (NICU), and in June 2007, a breastfeeding peer counselor program was added. The purpose of the addition was to provide additional lactation support to women during their infants’ NICU hospitalization. The impact of breastfeeding peer counselors in NCH NICUs has not been evaluated. Objective: To assess effectiveness of a peer counselor-based program by comparing the proportion of patients receiving any form of maternal breast milk, exclusive breast milk, or direct breastfeeding during NICU stay, as well as patients discharged on mother’s milk pre- and post-program implementation. Methods: A retrospective chart review was conducted on NICU admissions pre-program implementation (8/1/06-5/31/07) as well as year 1 (1/1/08-6/30/08) and year 4 (1/1/11-6/30/11) post-program implementation. Infants who were not admitted to the NICU within seven days of birth, expired during hospital stay and/or whose mother expired during hospital stay, not admitted long enough to be impacted by peer/lactation counselors, or who attempted direct breastfeeding unsuccessfully were excluded. Chi-squared tests were performed using SPSS statistical analysis software. Results: During hospital stay, infants receiving any maternal breast milk increased from baseline (n=201) to post-program year 1 (n=223) (59% versus 71%, respectively; p=0.01). Infants receiving exclusive breast milk increased from post-program year 1 to post-program year 4 (n=203) (11% versus 19%; p=0.04). Direct breastfeeding increased from baseline to post-program year 4 (38% versus 48%; p=0.05). Infants receiving maternal breast milk at discharge increased overall from baseline (50%) to post-program year 1 (59%) and year 4 (56%). Conclusions: Breastfeeding peer counselors likely contributed to increases in the number of infants receiving any or exclusive maternal breast milk during NICU stay post-program implementation. Increases in direct breastfeeding rates during NICU stay as well as in the proportion of infants receiving breast milk at discharge were also observed post-program implementation. Most outcome rates at both time points post-program implementation were higher than baseline, indicating the sustained impact of the peer counselor breastfeeding program. Implications for practice: NICU lactation programs should consider including peer counselors to facilitate an environment conducive to initiating and sustaining lactation. Future work should focus on ways to further improve breastfeeding rates at discharge.
END-OF-LIFE DECISIONS ENTER A GREY ZONE AT THE EDGE OF VIABILITY.

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**Background:** Prematurity or complications of prematurity account for majority of infant deaths in the Neonatal Intensive Care Units (NICU). We examine trends in end of life care for preterm infants at differing gestational age.

**Purpose:** Determine circumstances and causes of deaths for preterm infants at a referral level IIIc NICU.

**Methods:** Retrospective descriptive study involving very preterm infants (≤32 weeks) that died in the NICU at a children’s hospital from January 1st, 1999 to December 31, 2008. Infants were categorized based on gestational age at birth. Level of stability was categorized using the criteria of Verhagen et al (J Peds, 2010). NICU deaths were further divided by gestational age. The primary outcome was level of clinical service provided at end-of-life (care withheld, care withdrawn, or CPR).

**Results:** Over 10 years, 414 infants died in the NICU, 35% were related to prematurity. Withdrawal of care was more common in infants 25-27 weeks and 28-32 weeks versus infants 22-24 weeks (62.5%, 55.9% vs. 43.8%). Infants 22-24 weeks were more likely to receive CPR and be unstable at the time of death. (Table 1)

**Conclusion:** At the edge of viability, NICU deaths were more unstable and significantly more likely to receive CPR than other preterm infants. This suggest quality of life and medical futility enter a “gray zone” when dealing with the limits of viability. Differences in CPR for infants 22-24 weeks may represent selection bias. Those infants admitted to the NICU had parents who wanted “everything done”. These differences imply end of life care are view differently for preterm infants.

ASSOCIATION OF GER WITH COUGH, IRRITABILITY AND ARCHING IN INFANTS WITH CHRONIC LUNG DISEASE (CLD)

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**Background:** Aerodigestive symptoms (cough, irritability and arching) occurs both in CLD or GER disease (GERD). The prevalence of these symptoms in GERD alone or CLD with GERD is unclear. **Aims:** To evaluate the association of GER with cough, irritability and arching in CLD vs. non-CLD infants. **Methods:** Infants (N=48, 30 ± 0.7 wk GA) were evaluated for GER at 44 ± 0.6 wk PMA. CLD was defined as >30% oxygen requirement at 36 wk PMA. 24-h pH-impedance methods were adopted concomitant with symptom scoring. Tracings were reviewed manually. A symptom was considered associated with GER if it occurred during or within a 2 min window after the completion of GER. Data are shown as mean ± SE or as median (range), and were analyzed using Wilcoxon-Mann-Whitney test. P≤0.05 was considered significant. **Results:** 27 CLD (45 ± 4 wk PMA) and 21 non-CLD neonates (42 ± 0.8 wk PMA) were evaluated. Overall, 1,101 h of pH-Impedance recordings were evaluated in 2-min segments (33,034 segments); 2,586 GER events were analyzed. Frequent symptoms were cough (N=1,156), irritability and arching (N=1,939). Significantly, 1) CLD infants underwent escalated levels of respiratory support (P=0.001). 2) CLD infants are more sensitive in reacting with aerodigestive symptoms (P=0.05). 3) Higher SSI associated with cough of gas acidic GER in CLD infants (P=0.03). 4) Greater proximal GER than distal GER extent in CLD infants (P=0.01). 5) Greater total gas weakly acidic than gas acidic- GER in both CLD (P=0.0001) and non-CLD group (P=0.007). 6) No differences with acid- (P=0.5) or weakly acid- reflux indices (P=1.0) between groups. 7) Total cough (P=0.6), irritability and arching (P=0.06) were similar between groups. **Conclusions:** Lack of relationship of acid and weakly acid GER to CLD is recognized. The clinical relevance of proximal extents of reflux and presence of gas in generating symptoms is debated.

**Table 1: Diagnosis, Clinical Stability and Mode of Death for Infants ≤ 32 WEEKS**

<table>
<thead>
<tr>
<th>Gestational Age, (weeks)</th>
<th>22-24 n=64</th>
<th>25-27 n=48</th>
<th>28-32 n=34</th>
<th>Total N=146</th>
</tr>
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<tbody>
<tr>
<td>Withdrawn, %</td>
<td>43.8</td>
<td>62.5</td>
<td>55.9</td>
<td>52.7</td>
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<tr>
<td>Withheld, %</td>
<td>25</td>
<td>12.5</td>
<td>26.5</td>
<td>21.2</td>
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<td>CPR, %</td>
<td>31.2</td>
<td>25</td>
<td>17.6</td>
<td>26</td>
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<tr>
<td>Unstable%</td>
<td>90.6</td>
<td>62.5</td>
<td>73.5</td>
<td>77.4</td>
</tr>
<tr>
<td>Stable%</td>
<td>9.4</td>
<td>37.5</td>
<td>26.5</td>
<td>22.6</td>
</tr>
</tbody>
</table>

**Characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CLD (N=27)</th>
<th>Non-CLD (N=21)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI cough, %</td>
<td>8 (0-49)</td>
<td>3 (0-18)</td>
<td>0.05</td>
</tr>
<tr>
<td>SSI irritability and arching, %</td>
<td>13 (0-50)</td>
<td>4 (0-28)</td>
<td>0.05</td>
</tr>
<tr>
<td>SI irritability and arching, %</td>
<td>10 (0-50)</td>
<td>4 (0-35)</td>
<td>0.05</td>
</tr>
<tr>
<td>SSI cough associated with gas acidic GER, %</td>
<td>0 (0-100)</td>
<td>0 (0-17)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

GER: gastroesophageal reflux; SSI: Symptom Sensitivity Index; SI: Symptom Index
OXYGEN DELIVERY IN VERY LOW BIRTHWEIGHT (VLBW) AND EXTREMELY LOW BIRTHWEIGHT (ELBW) INFANTS DURING TRANSPORT
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Purpose: Administration of supplemental oxygen is one of the most common interventions in the treatment of critically ill neonates and may lead to oxygen toxicity. Titrating the administration of supplemental oxygen to match the needs of very and extremely low birth weight infants may decrease the risk of excessive oxygen delivery and adverse outcomes such as retinopathy of prematurity, bronchopulmonary dysplasia, and death. While saturation targeting and oxygen titration continues to be critically evaluated in the intensive care setting, this practice has not been evaluated in the transport environment. Our objective was to evaluate the practice, safety and effectiveness of supplemental oxygen delivery during interfacility transport of very and extremely low birth weight infants. Methods: This was a single center, retrospective cohort study of infants less than 1500 grams, <24 hours of age, receiving supplemental oxygen (titrated and nontitrated), transported by the Children’s Mercy (CMH) Critical Care Transport team, and admitted to the CMH Neonatal Intensive Care Unit between January 2000 and December 2009. Outcomes of interest included ABG within the first hour of admission (a measure of oxygen exposure), base deficit (a measure of hypoxemia), and admission mean arterial blood pressure (a measure of cardiovascular stability). Infants with multiple congenital anomalies or cyanotic heart defects were excluded. The data were analyzed by ANOVA and chi-square tests. Results: Of 237 infants, 83 infants received nontitrated and 154 received titrated supplemental oxygen. Both groups had similar gestational age (26±2.3 vs 26±2.3 weeks), birthweight and 5-minute Apgar scores. Excessive oxygen exposure (paO2 >90 torr) occurred in 53% (95% CI: 42.3% to 63.8%) vs 32.5% (25.1% to 39.9%) in nontitrated vs titrated infants, respectively. Mean paO2 was significantly higher in nontitrated than in titrated infants, 114±80 torr vs 87.7±50.9 torr (p<0.005). Admission base deficit and mean arterial blood pressure did not differ between the two groups. Conclusion: Titration of supplemental oxygen during interfacility transport of very and extremely low birth weight infants decreases the risk of hyperoxia (paO2 >90 torr). There is no evidence that titration increases the risk of hypoxia or cardiovascular compromise.

RELATIONSHIP BETWEEN TOTAL PARENTERAL NUTRITION AND OSTEOPENIA IN INFANTS WITH BRONCHOPULMONARY DYSPLASIA
MJ Shareef*, K Thomas*, Loyola University Medical Center, Maywood, IL, USA
Bronchopulmonary dysplasia (BPD) is a chronic respiratory disorder that often occurs in very-low-birthweight (VLBW) infants as a result of treatment for respiratory distress syndrome. Maintaining the appropriate balance of fluid, calories, and nutrients in a formula for these infants is challenging, especially since very little evidence has been collected in order to make specific nutrition recommendations for this population. Research has shown that VLBW infants, including those who develop BPD, are at increased risk for bone fractures and poor bone mineralization. Infants with BPD often receive total parenteral nutrition (TPN) for a prolonged period of time; however, it is unclear whether TPN provides adequate nutrition for bone mineralization. The purpose of this study was to determine whether there was an association between TPN duration and the development of osteopenia in infants with BPD, and to determine whether infants with BPD were at greater risk for fracture than non-BPD infants. This was a retrospective study including 87 infants with BPD and 19 infants without BPD treated in Loyola University Medical Center’s neonatal intensive care unit between 2006 and 2011. Cutoffs for birthweight and gestational age were 1500 grams and 30 weeks, respectively. Of the BPD infants, 41 developed osteopenia. Among infants with BPD, there was a significant positive correlation between duration of TPN and high alkaline phosphatase levels (r=0.48; p=0.000002), and a significant negative correlation between duration of TPN and low phosphorus levels (r=-0.46; p=0.000008). In addition, BPD infants who developed osteopenia received TPN for a significantly longer period of time than infants who did not develop osteopenia (t=3.3; p=0.0008). Finally, there was a significantly higher incidence of fracture in the BPD group (t=2.5; p=0.01), although there was no significant difference in incidence of osteopenia, phosphorus, alkaline phosphatase levels, and TPN duration in the BPD group vs. the non-BPD group.
38
PREDICTORS OF GASTROSTOMY TUBE (G-TUBE) IN CHRONIC LUNG DISEASE OF INFANTS (CLDI)

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* Nationwide Children’s, The Ohio State University, Columbus, Ohio. † Baylor College of Medicine, Houston, Texas

Background: Predictors and indications for G-tube in CLDI are unclear. Objective: To identify risk factors likely to be responsible for G-tube placement in CLDI. Methods: A retrospective study design using hospital database was used. 185 subjects with birth weights < 1500 grams and who received uninterrupted mechanical ventilation for 7 days were included in the study. 14 patients with congenital anomalies were excluded. Indication for G-tube was feeding failure which was arbitrarily defined as inability to safely nipple feed full volume feedings. The characteristics of subjects receiving G-tube versus no G-tube were analyzed. Logistic regression methods were used to compare the groups.

Results: 32 (17.3%) of 185 infants had a G-tube. Using the univariate logistic regression model, cumulative ventilation days (CVD) (OR 1.02, 95% CI 1.01-1.02, p < 0.0001), uninterrupted ventilation days (UVD) (OR 1.03, 95% CI 1.01-1.04, p < 0.0001) and sepsis (OR 2.59, 95% CI 1.09-6.14, p < 0.03) were found to be significant predictors. However multiple logistic regressions revealed that only CVD (p value < 0.0001) and UVD (p value < 0.0001) were significant predictors. Sepsis, IVH grade 3 or 4, PDA ligation and NEC were not significant predictive factors. Among the infants who achieved full oral feedings (data available on N=96), the postmenstrual age at which full oral feeding milestone was achieved was directly related to the number of CVD (p < 0.0001) and UVD (p < 0.0001).

Conclusion: Prolonged ventilation reflecting the severity of CLDI is a significant risk factor for feeding failure necessitating G-tube placement. Infants with shorter duration of ventilation were more likely to achieve successful oral feeding.

39
POST DISCHARGE EMERGENCY ROOM (ER) VISITS DURING THE FIRST MONTH OF LIFE IN AN URBAN INNER CITY POPULATION.

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BACKGROUND: ER crowding is a growing concern in health care. Studies have shown that non-emergent ER use increases waiting time for all patients, health care expenditure and risk of hospital acquired nosocomial infections. OBJECTIVE: To document the chief complaint and pattern of referral of the ER visits during the first month of life. 1) To identify opportunities to decrease nonemergency use by the type of problems which make parents seek unnecessary visit as urgent care. 2) To create and implement appropriate corrective measures and study the impact later. MATERIAL AND METHOD: A retrospective chart review all newborns (<1 month) who visited Mt Sinai Hospital ER between January 2010-December 2011 was done by the authors. RESULTS: During the study period, 576/5,800 (10%) of babies born at Mount Sinai Hospital were evaluated in ER during the first month of life. The average age at visit was 14.3 days; 54.5 % were males. Of the total visits, Self-referred-77.5%, primary physician referred-19.9% and the remaining 2.6% were home births admitted through ER. Disposition- 20.7% of babies was admitted to the hospital for medical care and the remaining 79.3% were discharged home.

The table below shows the major disposition and hospital admission diagnosis.

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Total</th>
<th>Discharged</th>
<th>Admitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaundice</td>
<td>135 (100%)</td>
<td>112 (83%)</td>
<td>23 (17%)</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>116 (100%)</td>
<td>106 (91%)</td>
<td>10 (9%)</td>
</tr>
<tr>
<td>Respiratory illness (URI Symptoms)</td>
<td>80 (100%)</td>
<td>58 (73%)</td>
<td>22 (7%)</td>
</tr>
<tr>
<td>Fever</td>
<td>34 (100%)</td>
<td>20 (59%)</td>
<td>14 (41%)</td>
</tr>
<tr>
<td>Other complaints</td>
<td>211 (100%)</td>
<td>195(92%)</td>
<td>16 (8%)</td>
</tr>
</tbody>
</table>

CONCLUSION: Majority of the newborn visits to the ER were for non-emergent conditions were self-referred. Education of parents and routine transcutaneous bilirubin measurements with a follow up plan, creating an answering service to help parents may decrease the visits. A plan has been developed and implemented for bilirubin monitoring; with follow up appointments is made prior to hospital discharge.
40
CHANGE IN THORACO-ABDOMINAL ASYNCHRONY IN SPONTANEOUSLY BREATHING PREMATURE INFANTS BETWEEN 32 AND 36 WEEKS
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Background: Chronic lung disease (CLD) is defined by the need for supplemental oxygen at 36 weeks postmenstrual age (PMA). Quantitative changes in thoraco-abdominal asynchrony (TAA) using respiratory inductance plethysmography (RIP) may reflect changes in respiratory system resistance and/or compliance and be used to augment the respiratory phenotype of CLD. Methods: 29 spontaneously breathing infants born at 23 to 29 weeks PMA were studied at 32 and 36 weeks PMA. During quiet sleep, rib cage and abdominal excursion were recorded simultaneously using RIP. TAA for each of 60 breaths was quantified using the phase angle (Φ), where 0 degrees represents complete synchrony and 180 degrees represents complete discordance between chest wall and abdominal breathing movements.
Results: At 32 weeks the group mean Φ was 67.7 degrees ± 41.3 (median 69.1, IQR 20.4, 96.3). Comparing 60 breaths at 32 and 36 weeks for each of the 29 subjects (unpaired t-test), 7 had a significant increase in mean Φ (mean change 42.2 degrees ± 15.7), 12 had a significant decrease (mean change 56.7 degrees ± 34.8), and 10 had no significant change. Conclusion: Significant changes in TAA between 32 and 36 weeks PMA occurred in 19 of 29 infants. Changes can be explained by changes in compliance and resistance of the respiratory system, improved chest wall stability, and less frequent use of high flow catheters at 36 weeks.

41
READMISSION OF HEALTHY TERM INFANTS WITH HYPERBILIRUBINEMIA IN AN URBAN INNER CITY HOSPITAL
Department of Pediatrics, Sinai Children’s Hospital Chicago Illinois
BACKGROUND: Post partum hospital stay has dramatically decreased over the past few decades leading to an increase in newborn readmissions. OBJECTIVE: To document incidence of readmission of healthy term infants with hyperbilirubinemia in an urban inner city population. METHOD: Retrospective review of the medical records of neonates (≤ 1 month old) admitted to Sinai Children's Hospital from Jan 2010 to Dec 2011. RESULTS: During the study period 6050 infants were delivered at Mount Sinai Hospital, 700 were admitted to the NICU. The 5350 infants admitted to the nursery formed the study population. 48 infants were readmitted within one month of life with jaundice. The readmission rate was 8.9 per 1000 births. The infants were screened for jaundice in the nursery by measuring Transcutaneous Bilirubin (TCB) levels if the infant was visibly jaundiced on examination. The mean duration of stay in nursery at birth was 44.2 hours with a range of 24-74 hours. The mean age at readmission was 170.8 hours and the range 80-660 hours. The mean readmission serum bilirubin levels was 18.2 mg/dl, with a range of 10.2-23.9 mg/dl. The infant with readmission bilirubin of 10.2 had elevated direct bilirubin of 1.4 mg/dl. Of the 48 infants, 2 were Coomb’s positive. Treatment modality for all patients was phototherapy. 31% of the babies were exclusively breast fed and the rest had either mixed feeding with both the formula and breast milk or just the formula. 4 infants lost >10% of birth weight. CONCLUSION: Screening only the visibly jaundiced infants by a TCB measurement prior to discharge from the nursery resulted in a high readmission rate of 8.9/1000 births in this study population. Routine TCB screening at 24 hours of age may decrease the readmission rate for hyperbilirubinemia.

42
NEONATAL INTENSIVE CARE UNIT BED CONFIGURATION HAS NO EFFECT ON RATES OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS COLONIZATION OR NECROTIZING ENTEROCOLITIS
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Infections continue to be a significant cause of morbidity and mortality within neonatal intensive care units (NICUs). The contributions of environmental factors, including hand hygiene and disinfection techniques are well documented. Less well studied is the effect of nursery design. The St. Louis Children’s Hospital NICU is a tertiary care facility with half of its bedsspaces organized as single patient rooms and the other half in an open unit model. Our setup permits direct comparisons of the incidence of methicillin-resistant Staphylococcus aureus (MRSA) and necrotizing enterocolitis (NEC) between these two models. All patients in the NICU are routinely screened for MRSA on admission and weekly until discharge. We analyzed our admission data from July 1, 2009 through November 30, 2011, representing 1824 patients and >50,000 patient-days and used Cox regression for days to MRSA positivity or the diagnosis of NEC. Comparing single patient rooms and the open unit model, we found no difference in the incidence of MRSA colonization (2.3% vs 3.7%, respectively) or the MRSA-colonization-free survival times (Kaplan Meier survival curve p=0.42). In addition, no significant effect was seen from acuity level, birth weight, estimated gestational age, sex,
or race. Proximity to patients with MRSA did not influence the incidence of new-onset MRSA colonization. The incidence of NEC was similar in the single patient rooms and the open unit model (7.5% vs 6.7%, respectively), and NEC-free survival times between unit layouts did not differ. Again, no significant effect was seen from acuity level, birth weight, estimated gestational age, sex, or race. While the single-patient room provides privacy and has become the standard model in newly constructed hospitals, the effect of this room format for reducing two potentially transmissible morbidities, MRSA and NEC, needs further study.

43
THE EFFECTS OF SEQUENTIAL COLOSTRUM VS. EARLY RANDOM BREAST MILK ADMINISTRATION IN PRETERM INFANTS: A QI STUDY.
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BACKGROUND: Colostrum production continues for up to four days after birth and its composition changes according to infant’s needs for passive protection. Colostrum is rich in protein and its anti-microbial properties are considered beneficial to the high risk neonate. There is a strong correlation between mom’s milk and the decreased incidence of NEC and infections. However, milk collection and administration methods are very variable in the first weeks of life. OBJECTIVE: Our objective was to test the hypothesis that administering sequentially collected colostrum will decrease the incidence of NEC and infections; improve growth velocity; and decrease the number of PICC line days compared to infants receiving random EBM administration. METHODS: We compared the outcomes in infants who received sequential administration of colostrum vs. random expressed breast milk administration. Infants < 28wks gestational age and <7days were included. Sequential colostrum was collected in individual containers, color coded to represent specific days over the first 7 days of lactation. Some infants received milk collected in non-sequential random order. STATISTICAL ANALYSIS: Data were analyzed using ANOVA, chi-squared tests, unpaired t-test. RESULTS: We compared sequential colostrum vs. random breast milk administration methods respectively: a) Central line duration: 23.0 ± 5.4 vs. 15.4 ± 2.0. b) Number of infections 0.5 ± 0.2 vs. 0.3 ± 0.1. c) NEC 2 (14.3%) vs. 2 (12.5%). d) Growth velocity: 23.9 ± 0.8 vs. 22.8 ± 0.7. No statistical differences were observed. CONCLUSIONS: Effects of both methods of milk administration were similar. It would take 5619 patients per group to detect a statistical significance at 80% power. Given the lack of significance and greater economic burden from resource utilization and potential errors in feeding sequential colostrum, may label this as non-beneficial approach. However, this approach may be a useful adjunct with other components of the feeding care bundle.

44
EXPLORING THE RELATIONSHIP BETWEEN METABOLIC ACID-BASE STATUS AND THE NUMBER OF APNEA, BRADYCARDIA, AND DESATURATION ALARMS IN INFANTS 27-32 WEEKS GESTATION IN THE FIRST TWO WEEKS OF LIFE
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*Div. of Neonatology Loyola University Medical Center, Maywood, IL
** Illinois Math and Science Academy, Aurora, IL

Apnea, bradycardia, and desaturation events are common in preterm infants, necessitating the use of positive airway pressure, methylxanthine, or endotracheal intubation. Many factors influence the frequency and severity of these events. Metabolic acidosis is a respiratory stimulant, and metabolic alkalosis can contribute to hypoventilation, potentially increasing the number of monitor alarms in preterm infants or the need for mechanical ventilation. Metabolic acidosis is common in preterm infants, and is corrected by giving acetate or sodium bicarbonate, which may lead to overcorrection of the acidosis. Since severe acidosis can lead to cellular dysfunction, clinicians have the goal of correcting metabolic acidosis in preterm infants, but the optimal pH and bicarbonate levels are unknown. The relationship between metabolic acid-base status and apnea, bradycardia, and desaturation alarms in non-ventilated infants 27-32 weeks gestation in the first two weeks of age was investigated. Charts of 38 babies hospitalized in the NICU at Loyola University Medical Center were reviewed for pH, PCO2, sodium bicarbonate, base excess/base deficit, and serum bicarbonate levels, as well as bradycardia, apnea, and desaturation alarms. Pearson correlation revealed a positive relationship between serum bicarbonate levels and the number of desaturations alarms, supporting the theory that higher bicarbonate levels are associated with hypoventilation and desaturations alarms (p=0.000). This research supports the hypothesis that there is a relationship between acid-base status and the number of monitor alarms. More research is needed to determine the optimum pH and serum bicarbonate levels in preterm infants.
GLUCOSURIA DURING PACKED RED BLOOD CELL TRANSFUSION IN PRETERM INFANTS

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Glucosuria occurs frequently in preterm infants < 30 weeks gestation. Though there is not a defined threshold at which glucosuria occurs across all preterm infants, the amount of glucosuria for a single patient does reflect plasma glucose patterns. Previous research demonstrates standard volume packed red blood cell (RBC) transfusions in preterm infants lead to a mean decline in plasma glucose of 17 mg/dL at the end of the transfusion period, despite the high glucose content of packed RBCs. There are no published reports of the plasma glucose patterns during the transfusion period, which result in this decline. However, exchange transfusions are known to cause hypoglycemia due to initial hyperglycemia followed by prolonged insulin secretion. We hypothesized that the same mechanism occurs in standard volume transfusions to preterm infants and that the glucose patterns could be non-invasively examined through urinary excretion of glucose. We measured glucose concentrations in packed RBC products and in the urine of the transfused preterm infants around the time of transfusion by cotton ball collection. Glucose levels were determined by Aviva glucose monitor (PQQ-glucose dehydrogenase method). 17 transfusion events in 7 preterm patients were studied. The hemolyzed packed RBC samples were hyperglycemic with a mean glucose of 821 mg/dL. In 6 transfusions with no other changes in the glucose delivery to the infant, the change in urinary glucose ranged from -89 to 15 mg/dL during the transfusion. After the transfusion, the change in glucose ranged from -81 to 108 mg/dL, and 67% of the patients had a decline in urine glucose concentration. In 5 additional transfusion events, the patients’ feedings were held during transfusion, but similar patterns of glucosuria were seen. Six observations were incomplete due failed urine collection. We did not observe an initial increase in glucosuria with RBC transfusion. If the drop in plasma glucose is triggered by transient hyperglycemia, it may be too brief to be detected in urine glucose measurements.

FACTORS INFLUENCING SUCCESSFUL DISCONTINUANCE OF CAFFEINE AT 34 WEEKS CORRECTED GESTATIONAL AGE IN PREMATURE INFANTS TREATED FOR APNEA OF PREMATURITY

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*Div. of Neonatology Loyola University Medical Center, Maywood, IL, ** Illinois Math and Science Academy, Aurora, IL

Apnea of prematurity (AOP) is common in infants, particularly those born less than 34 weeks gestation. The benefits of caffeine therapy for AOP are well known, but the appropriate time to discontinue this therapy is unknown, as well as factors that predict success or failure. Several factors that may predict success were evaluated and presented previously, including gestational age at birth, birth weight, race, gender, and oral feeding ability. No significant predictive factors were found. Additional review was done to determine the predictive value of intracranial hemorrhage or periventricular leukomalacia, presence of bronchopulmonary dysplasia (BPD) or necrotizing enterocolitis (NEC). 556 infants had caffeine discontinued before discharge or transfer. 5.9% of the infants failed discontinuance and had caffeine restarted. Additional factors predicting success in stopping caffeine therapy at 34 weeks CGA were not found. Caffeine can be safely discontinued at 33-35 CGA, with a low failure rate of 5.9%. No significant factors were found that predict success or failure with discontinuation of caffeine at 33-35 weeks corrected GA, including the infant’s gender, birth weight, race, gestational age at birth, the infants ability to nipple feed at the time of discontinuance, the presence of intracranial hemorrhage or cysts, BPD or NEC. Further research should include a larger sample size.

READMISSION OF HEALTHY TERM INFANTS WITHIN ONE MONTH OF AGE IN AN URBAN INNER CITY HOSPITAL.

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BACKGROUND: Post partum hospital stay has dramatically decreased over the past few decades leading to an increase in newborn readmissions. OBJECTIVE: To document the incidence and diagnosis for readmission for healthy term and near term infants within one month of age in an urban inner city population. METHOD: Retrospective review of the medical records of neonates (≤ 1 month old) admitted to Sinai Children’s Hospital from Jan 2010 to Dec 2011. RESULTS: During the study period 6050 infants were delivered at Mount Sinai Hospital. 700 were admitted to the NICU. The 5350 infants admitted to the nursery formed the study population. Of these 121 infants were readmitted within one month of discharge. The readmission diagnoses is shown in the table below. Readmission rate was 22.6 per 1000 births.
Table

<table>
<thead>
<tr>
<th></th>
<th>2010 &amp; 2011 by Diagnosis</th>
<th>1\textsuperscript{st} WEEK (0 – 7)</th>
<th>2\textsuperscript{nd} WEEK (8-14)</th>
<th>3\textsuperscript{rd} WEEK (15 – 21)</th>
<th>4\textsuperscript{th} WEEK (22- 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Unconjugated hyperbilirubinemia</td>
<td>17 13</td>
<td>3 3</td>
<td>1 -</td>
<td>1 -</td>
</tr>
<tr>
<td>2</td>
<td>RSV bronchiolitis</td>
<td>- -</td>
<td>3 2</td>
<td>3 3</td>
<td>8 2</td>
</tr>
<tr>
<td>3</td>
<td>Other respiratory infections</td>
<td>1 -</td>
<td>- -</td>
<td>- -</td>
<td>4 1</td>
</tr>
<tr>
<td>4</td>
<td>ALTE</td>
<td>1 2</td>
<td>4 1</td>
<td>- -</td>
<td>- 2</td>
</tr>
<tr>
<td>5</td>
<td>Neonatal fever</td>
<td>3 1</td>
<td>2 -</td>
<td>3 4</td>
<td>4 2</td>
</tr>
<tr>
<td>6</td>
<td>Neonatal sepsis</td>
<td>- 1</td>
<td>1 -</td>
<td>1 -</td>
<td>- -</td>
</tr>
<tr>
<td>7</td>
<td>Neonatal Seizure</td>
<td>- -</td>
<td>2 -</td>
<td>- -</td>
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</tr>
<tr>
<td>8</td>
<td>Miscellaneous</td>
<td>1 2</td>
<td>3 6</td>
<td>4 1</td>
<td>4 -</td>
</tr>
</tbody>
</table>

CONCLUSION: The readmission rate of 22.6 /1000 infants is well above the national average of 18.6/1000 infants. We speculate that this is due to the minority inner city population the hospital serves.

48
PILOT STUDY OF SYMPTOM BURDEN AND QUALITY OF LIFE AMONG FAMILIES OF CHILDREN IN PALLIATIVE CARE OR HOSPICE

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¹The Research Institute at Nationwide Children’s Hospital, ²Vanderbilt University, ³Nationwide Children’s Hospital, ⁴The Ohio State University

Purpose: Despite calls for improvement in pediatric palliative care, children may have significant suffering at end-of-life (EOL). Research is limited and relies heavily on retrospective reports from mothers or nurses. We prospectively assessed symptom burden and quality of life (QOL) among children with life limiting conditions to examine concordance across multiple informants (i.e., mother, father, child, nurse). Method: Families were recruited shortly after their child (ages 5-18) was enrolled in palliative care or hospice. Of 36 eligible families, 8 children died before recruitment. Of the remaining 28, 25 (89%) participated. Participants included 25 mothers, 14 fathers, 12 children (Mage = 11.4, SD = 3.4). On average, the sample of children was White (72%) and female (52%); 60% had complex chronic conditions, and 40% had cancer. Mothers, fathers, nurses, and children (who were able to self-report) completed the Memorial Symptom Assessment Scale (MSAS), and parents and children completed the PedsQL in the home. Results: A similar number of symptoms were reported for children by mother (M = 9.5, SD = 3.3), father (M = 10.3, SD = 3.0), and self-report (M = 10.6, SD = 3.3), but nurses (M = 5.3, SD = 3.3) reported about half as many symptoms (p < .01). For composite symptom scores (i.e., weighted for frequency, severity, bother), nurses reported the highest scores, followed by mothers, fathers, and children. Paired t-tests show differences between nurse and mother (p < .08), nurse and father (p < .01), and mother and father (p < .01) composite scores. QOL was well below normal according to mothers (M = 50.4, SD = 22.1), fathers (M = 40.9, SD = 18.7), and children (M = 53.2, SD = 17.6). Higher symptom burden was strongly and consistently associated with worse QOL across informants (r = -.34 to -.69). Conclusion: Preliminary findings indicate high symptom burden in children at EOL and its negative impact on the child’s QOL. Nurses report significantly fewer symptoms than families but higher composite scores when considering frequency, severity, and bother. Implications for Practice: Discrepant reports on symptom burden indicate significant gaps in communication between families and healthcare providers, as well as the need for future research to inform clinical care and improve the QOL of children at the EOL.

49
CARDIOPULMONARY RESUSCITATION CERTIFICATION IN HIGH SCHOOL COACHES: A SURVEY OF WISCONSIN HIGH SCHOOL ATHLETIC DIRECTORS.

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Purpose: Cardiopulmonary Resuscitation (CPR) has been shown to increase survival in instances of sudden cardiac arrest (SCA). With an incidence of 3.75/100,000 in children aged 14-24 and a survival rate of only 11%, SCA is a devastating event. Data show that US high school coaches are the first responders to SCA in one third of high school athlete collapses, but little is known about their CPR certification status. The primary goal of this study was to assess the prevalence of CPR certification in high school coaches as well as attitudes of Wisconsin athletic directors about CPR certification requirements. Methods: This study was a web-based survey of Wisconsin high school athletic directors. Sixteen multiple-choice questions were created, piloted, and developed into an online survey. An email database from the Wisconsin Interscholastic Athletic Association was obtained and the online survey was sent out to 503 athletic directors. Responses were tabulated through the University of Wisconsin Qualtrics survey website. Results: There were a total of 240 survey responses, a 48% response rate, reporting that Wisconsin coaches are the
primary responders to the vast majority of collapses (78%). Overall, 75% of those answering the survey have an emergency action plan (EAP). Athletic directors with the longest tenure, greater than 12 years, were the most likely to have an EAP in place at their school (p<0.007). The majority of Wisconsin high schools (64%) do not require CPR certification of coaches, with only 50% of coaches currently CPR certified. When given the choice, 86% of athletic directors either agree, or strongly agree, that coaches should be CPR certified. Schools that previously experienced a collapse were more likely to require CPR certification (p=0.11). Comparing schools with a previous high school athlete collapse vs. no collapse, 81% vs. 73% had an EAP (p=0.16). Conclusions: In Wisconsin, the proportion of coaches who act as the primary responder to a collapse is greater than previously reported. Although EAPs are present in 75% of schools, two-thirds of schools do not require CPR certification for coaches. The discrepancy between the number of CPR certified coaches and number of coaches who serve as a primary responder is neither safe nor adequate due to the severe consequences of SCA. Pediatricians should advocate for schools to develop EAPs and mandate CPR certification for coaches as two important steps to protect the safety of high school athletes.

50
PILOT STUDY OF A PRIMARY CARE INTERVENTION ON THE MANAGEMENT OF CHILDHOOD OBESITY “A POUND OF CURE”
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Problem: Primary care providers (PCPs), despite regular access to families with young children, lack a comprehensive model for approaching office visits on pediatric excess weight. In 2007 an Expert Committee comprised of 15 national organizations established guidelines for clinicians on the standard of care for managing pediatric excess weight. Over two years of development, we produced a series of modularized office visits for use by PCPs, founded on the 2007 Expert Committee Recommendations (ECRs). These were piloted at an urban clinic with a diverse, low-income population. The high quality intervention tools, entitled “A Pound of Cure” (POC), provide PCPs with a counseling model and handouts to direct behavior modification within families with overweight children. Methods: 100 families with children 2-11 years old were interviewed on the “Pound of Cure” counseling sessions and resources. The feedback we obtained guided development of the POC office visit modules and resources. Retrospective chart reviews were conducted on those families who attended POC office visits and included analysis of the targeted history collection, weight related discussions and goal setting and patient weight related outcomes. Outcomes: On average, motivated families that returned to the clinic needed to complete only 3 to 4 modules, setting 3 goals per visit, to successfully incorporate recommendations into the child’s daily life. Of families that returned for follow up visits 41.6%, 25.7%, 18.6%, and 14.1%, of families completed 2, 3, 4, or 5+ office visits respectively. Additionally, of families that attended follow up visits 53.2%, 44.8%, 38% and 37.5% of children reduced their BMI percentile as they attended the 2nd, 3rd, 4th, and 5th - 7th office visits, respectively. In total, 46% of children attending follow up office visits have reduced their BMI over an average of 158 days (SD-150.73). Significance: By developing and piloting “A Pound of Cure” we seek to help PCPs establish a standard of care on pediatric weight management within the practice setting, the optimal site for early identification and intervention in childhood obesity.

51
HOSPITALIZED SUSPECTED CHILD ABUSE-RELATED TRAUMATIC BRAIN INJURIES AMONG CHINESE CHILDREN
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Background and Objectives: Abusive head trauma (AHT) is a preventable source of injury with severe morbidity and mortality among young children. Using hospital discharge data, this study investigated abuse-related traumatic brain injuries (TBIs) among patients of Wuhan Medical Care Center for Women and Children in The People’s Republic of China. Methods: De-identified hospital discharge data for patients 5 years old and younger were analyzed, and ICD-10 codes were used to identify cases of TBI. Medical notes provided by doctors in the medical record were used to identify cases of TBI where there was also suspected child abuse. Results: From 2002 to 2011, 3,061 pediatric TBI patients were hospitalized at the Wuhan Medical Care Center for Women and Children, and 4.6% (140) of these cases were suspected child abuse-related. The majority of suspected child abuse cases involved children younger than 1 year of age (68.6%) and usually affected males (63.6%). Physical abuse was responsible for 78.6% of suspected child abuse TBIs for patients 0 to 4 years old, and 91.7% of suspected child abuse TBIs for patients under the age of 1. Only 44.3% of the suspected child abuse patients made a full recovery, compared with 68.3% of TBI patients without suspected child abuse. Conclusions: This is the first comprehensive study highlighting the important role of suspected child abuse in causing TBIs among Chinese children. Child abuse as a major cause of TBIs among infants in China should be studied...
further, and there should be greater awareness of this important social and medical problem in China.

52
EPIDEMIOLOGICAL CHARACTERISTICS OF PEDIATRIC INPATIENTS WITH TRAUMATIC BRAIN INJURY IN WUHAN, CHINA
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Background and Objectives: Pediatric traumatic brain injuries (TBIs) have not been well studied in China. This study investigated epidemiological characteristics of hospitalized TBIs suffered by Chinese children. Methods: Medical records of hospitalized TBI patients (0-18 years of age) from a large urban children’s hospital were analyzed. TBIs were defined using the International Classification of Diseases, Tenth Revision (ICD-10) codes. Age patterns were examined across external causes of TBIs. The proportion of traffic crash-related TBIs was reported for each year from 2002 to 2011. Results: Of 4,230 pediatric TBIs identified, males suffered disproportionately more TBIs than females (65.2% vs. 34.8%). Falls, struck by/against objects, and traffic crashes were the top three external causes of TBIs for all age groups. There were 125 TBIs in 0-2 year olds (5.9% of all TBIs in this age group) that were caused by suspected child abuse. Falls were the leading cause of TBI for all ages, but peaked at 2 years of age. Suspected child abuse was significantly more likely to occur in 0-1 year olds. The proportion of traffic crash-related TBIs increased significantly from 12.99% in 2002 to 19.68% in 2008 but dropped each subsequent year until it reached a level of 8.91% in 2011. Conclusions: Our study confirms that falls, struck by/against objects, and traffic crashes are the top external causes of TBIs in Chinese children. When compared with national data from the U.S., gender patterns are similar, but the ranking of external causes is different. This is the first study to highlight the important role of suspected child abuse in causing TBIs in infants in China. TBIs caused by child abuse warrant further research and government attention as a social and medical problem in China.

53
PEDIATRIC HYPERTENSION: DEFINING THE EDUCATIONAL NEEDS OF PRIMARY CARE PEDIATRICIANS
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Background: Essential hypertension (HTN) is becoming increasingly prevalent in pediatrics, affecting 3-5% of the general pediatric population. Suspected pediatric HTN is evaluated with varying degrees of accuracy by primary care pediatricians (PCP). In an effort to improve recognition, evaluation and treatment of HTN among PCP, the comfort level and educational gaps for PCP need to be understood and addressed. Objective: To identify the educational needs and to develop effective teaching methods to educate and influence practice behaviors of PCP regarding appropriate recognition, diagnostic evaluation, and therapeutic intervention in pediatric essential HTN. Methods: We conducted 4 separate focus group (FG) discussions with pediatric residents, Adolescent Medicine physicians and 2 outpatient pediatric groups associated with Nationwide Children’s Hospital in Columbus, OH. Six to 9 participants in each group discussed approaches to 3 common pediatric HTN scenarios. Sessions were recorded and transcribed for review. Themes were elucidated amongst the focus groups by 4 reviewers. Results: Five major themes emerged from the focus group sessions (utilization of resources to obtain BP, BP measurement method, co-morbidities, barriers to care, and experience level of training) and 6 minor themes also emerged (differences in BP measurement, accuracy of BP, recognition, practice pattern, education, and differences in level of training). Most participants in each FG wanted further education on pediatric HTN but different groups defined varied needs and identified multiple preferences for how to learn this material. Conclusions: These results support the need to develop programs to increase PCP knowledge of specific aspects of pediatric HTN. Based on the varied stated preferences of these PCP, education modules and methods will need to employ multiple presentation methods (e-learning, small group sessions, self-study, large group presentations) to be useful and ultimately improve outcomes in pediatric HTN.

54
DURATION OF CHILDHOOD OBESITY AND MARKERS OF CARDIOMETABOLIC DISEASE.
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Background: Obesity is a major risk factor for adult metabolic and cardiovascular disease, and the rising prevalence of childhood obesity has become a major public health concern. Our previous study has shown that decreased HDL, elevated blood pressure, insulin resistance, and systemic inflammation are all associated with obesity in youth and adolescents and here we investigated if the duration of obesity during childhood affects the severity of these measurable risk markers. Methods: We retrospectively reviewed EPIC charts for forty-two obese adolescents (ages 9-18, BMI >95
vitamin D intake between children with and without fractures, intake of both nutrients still fell short of the National Institutes of Health recommendations. It is critical to encourage adequate calcium intake among all children and adolescents in order to promote accrual of peak bone mass.

Among children with fractures, 36% had a history of previous fracture and not different (980.6 vs. 926.9mg respectively, p=0.79). Median daily vitamin D intake for all fracture cases was 152 international units (IU) and within the control group 128 IU [68-168], p=0.42. Sub-group analysis according to age based on current recommendations for nutrient intake did not show significant differences between the two groups. Gender, age, and sex were found to not be significant correlates of log calcium or vitamin D intake in multivariable analysis (p=0.49 and 0.66, respectively).

Conclusions: Obese adolescents have variable degrees of measurable cardiovascular and metabolic disease risk markers. In this relatively small sample population and within the study confines of ~10yrs years of obesity duration, we did not find relationship between duration and the levels of biomarkers of cardiometabolic disease. Further studies to investigate the impact of obesity duration beyond one decade of life and assess patterns of reversal following weight loss are warranted, as are study of other contributors, such as genetics, lifestyle, and socioeconomic status.

55
RELATIONSHIP OF CALCIUM INTAKE WITH FRACTURE INCIDENCE IN THE PEDIATRIC EMERGENCY DEPARTMENT
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Objective: This study investigated the association between dietary calcium intake and fractures in children presenting to the emergency department (ED). Vitamin D intake was evaluated as a secondary outcome. Patients and Methods: Children 3-18 years old who presented to the emergency department with long bone fractures and healthy controls with no history of fractures were eligible for inclusion in the study. Dietary calcium and vitamin D intake was documented using a food diary completed by study subjects and controls over a 4-day period (3 weekdays/1 weekend day). Results: 194 children (116 fracture group, 78 control group) were enrolled in the study; 63 children (32.5%, including 25 fracture subjects and 38 control subjects) returned the food diary. There were no differences between age or gender between children with and without fractures. Among children with fractures, 36% had a history of previous fracture and 88% were located in the upper extremities. The median daily calcium intake between the fracture and control group was not different (980.6 vs. 926.9mg respectively, p=0.79). Median daily vitamin D intake for all fracture cases was 152 [76-180] international units (IU) and within the control group 128 IU [68-168], p=0.42. Sub-group analysis according to age based on current recommendations for nutrient intake did not show significant differences between the two groups. Gender, age, and sex were found to not be significant correlates of log calcium or vitamin D intake in multivariable analysis (p=0.49 and 0.66, respectively).

Conclusions: Although there was no difference in calcium and vitamin D intake between children with and without fractures, intake of both nutrients still fell short of the National Institutes of Health recommendations. It is critical to encourage adequate calcium intake among all children and adolescents in order to promote accrual of peak bone mass.

56
INCREASED FREQUENCY OF SEVERE, ATYPICAL POST STREPTOCOCCAL GLomerulonephritis AT A PEDIATRIC TERTIARY CARE CENTER
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Background: Post streptococcal glomerulonephritis (PSGN) is the most common form of acute glomerulonephritis in children occurring between 3-12 years old. Gross hematuria is typically present and hypertension is found in up to 70% of hospitalized patients. Proteinuria is common but nephrotic syndrome is rare. Severe PSGN complications are infrequent with hypertensive encephalopathy found in <10% and rapidly progressive glomerulonephritis in <1% of hospitalized children. We report a high frequency of severe atypical PSGN cases seen at a pediatric tertiary care center over 12 months. Methods: Data was collected retrospectively on patients 3-18 years old with the ICD-9 code 580.0 (Acute Glomerulonephritis with lesion of proliferative glomerulonephritis; Acute Post Streptococcal). Patients had hematuria +/- proteinuria, low serum complements (C3) that subsequently normalized and either serologic evidence of infection or household contact with a documented streptococcal infection. Data was analyzed by either a Fischer exact test or by the Student's t-test. Significance was assigned for a P <0.05. Results: Seventeen children (11 males), mean age of 8 years, were analyzed and 76% required hospitalization. Compared to the outpatients, inpatients had significantly lower serum albumin levels (P=0.02), platelets (P =0.01) and glomerular filtration rates (P =0.01). Overall, 70% had nephrotic range proteinuria and 41% had hypertensive complications. Emtn typing was obtained on 2 patients, one of which was a novel serotype for PSGN. Conclusions: Historically PSGN does not frequently present as a severe nephritis. Over the last 12 months, a larger number of severe cases characterized by acute kidney injury, low serum albumin and thrombocytopenia were cared for.
Major treatment advancements for congenital heart disease (CHD) have led to a dramatic increase in the number of adults living with CHD. Unfortunately, low rates of adherence to suggested medical regimens and ongoing follow-up care may place these individuals at risk for further health complications that could be prevented. This poor adherence may be influenced by individual health beliefs and perceptions, including illness uncertainty, or whether a person feels that they understand their illness and can predict events related to a chronic condition. The first aim of this study is to evaluate differences in illness uncertainty as a function of patient age (adolescents, emerging adults, and young adults) and disease severity (simple, moderate, and complex). The second aim is to examine whether illness uncertainty is a barrier to medical regimen adherence, as well as recommended health behaviors (exercise and diet). CHD patients between the ages of 15 and 39 are currently being recruited from the adult and pediatric CHD clinics. Following informed consent, a number of self-report measures are completed, including Mischel’s Uncertainty in Illness Scale, the Medication Adherence Questionnaire, Godin Leisure Time Exercise Questionnaire, and Rapid Eating and Activity Assessment. Medical record reviews are performed for each participant to extract information related to diagnosis, medications, treatment, and history of health care services. This study is currently underway. Since May, 2012, twenty-seven participants have enrolled, three have declined, and recruitment is in progress for sixteen. By September, 2012, we expect to have data from a total of 85 patients. Data analysis will include ANOVA to examine differences in illness uncertainty as a function of patient age and disease severity. Correlation coefficients and linear regression will examine the association of illness uncertainty and medical regimen adherence. Results of the study will identify factors associated with the risk of illness uncertainty for individuals with CHD during the important, yet poorly understood, transition from adolescence to adulthood. In addition, this study will be the first to examine whether individual differences in illness uncertainty account for differences in adherence to prescribed medication and recommended lifestyle behaviors during a period when many patients with CHD seem to disconnect from recommended care. This could help develop methods to better support at-risk patients and improve prevention of many additional health complications.

DISEASE-RELATED INVESTIGATION

THE EFFECT OF TUMOR TREATMENT AND TYPE ON SOCIAL OUTCOMES OF PEDIATRIC BRAIN TUMOR SURVIVORS.

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Advances in surgical techniques, chemotherapy, and radiation have improved survival rates for children with brain tumors. Unfortunately, this progress may come at a price. Many pediatric brain tumor survivors (PBTS) develop significant late-effects, e.g., medical impairments, cognitive delays, and changes in appearance, that threaten social and emotional adjustment. The aim of this study was to examine whether social outcomes for PBTS are accounted for by tumor type, treatment, and late-effects. Data were collected in the classrooms of PBTS (N = 208; 53% male) who were 8-15 and 1-5 years post-treatment at 5 pediatric oncology centers in the United States and Canada. Classmates with consent (87%) completed peer nominations on the Revised Class Play to assess dimensions of social behavior including social sensitivity-isolation, victimization, and leadership. Resulting scores were standardized within gender in each class, giving a Mean = 0 and a SD = 1.0. Classmates also completed peer acceptance ratings and friendship nominations. Data about medical late-effects were obtained from medical records. Estimated IQ scores from the Wechsler Abbreviated Scales of Intelligence assessed cognitive late-effects. In addition, the staff that administered classroom measures also rated whether the appearance of PBTS reflected their diagnosis or treatment, e.g., alopecia, scars. No association was found between social behavior and tumor location, although PBTS with infratentorial tumors had a greater number of medical late effects and a more adversely affected appearance than PBTS with supratentorial or midline tumors (p < 0.05). PBTS who received radiation or chemotherapy were rated as lower in leadership and more sensitive-isolated and victimized than peers (p < 0.05), and PBTS receiving chemotherapy also had fewer reciprocated friendships (p < 0.05). Both chemotherapy and radiation were associated with medical late-effects, altered appearance, and diminished IQ (p < 0.05). Our preliminary analyses show that the risk of negative social outcomes is associated with chemotherapy and radiation. For the final poster, we will expand on these findings to see if the type of late-effects mediates the relationship between type of treatment/tumor and social outcomes. Awareness of the social risks
associated with tumor treatment, type, and different late-effects will help healthcare providers be aware of which PBTS may still need assistance with peer relationships over the long-term.

59
CRICOPHARYNGEAL ACHALASIA IN CHILDREN: BOTULINUM TOXIN INJECTION AS A TOOL FOR DIAGNOSIS AND TREATMENT
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Purpose of study: Cricopharyngeal(CP) achalasia is a well-described entity in adults but less well recognized in the pediatric population. As the experience with botulinum toxin has evolved, it has been found to be a safe and useful method in treating CP achalasia in adults by injection of the cricopharyngeus muscle. There is very limited data in the literature about its utility in children. We have been using botulinum toxin in children at Nationwide Children’s Hospital to treat CP achalasia since 2006. We conducted a retrospective chart review of patients to assess pre-operative, operative and post-operative details about each case. We also conducted a parental survey to gauge overall improvement and satisfaction with the results. Methods: After Institutional Review Board approval a retrospective review was conducted. After confirming the diagnosis and procedure specific parameters were recorded including: patient age at presentation, symptoms, pre-intervention diet, pre-intervention objective studies, operative details, post-operative objective studies, and post-operative diet. A survey of the parents’ satisfaction was conducted with five of six surveys completed. Results: Six children were identified with cricopharyngeal achalasia with an age range of 3 months to 10 years. Symptoms varied but included cough, aspiration, cyanosis, failure to thrive, emesis and abdominal pain. Five of the six children required some form of altered nutrition. Preoperative and postoperative studies varied with each patient. The number of injections ranged from one to three per patient and the mean dose was 4.4 U/kg. There was one major complication that did resolve. Two of the children went on to have cricopharyngeal myotomy, while four of the children resolved symptoms. A parental survey was performed via telephone. All parents reported improvement and would recommend the procedure. Conclusion: 4 of the 6 treated children were treated exclusively with botulinum toxin avoiding a more invasive procedure. In the two children who went on to have cricopharyngeal myotomy performed, the botulinum toxin was useful in confirming the diagnosis of cricopharyngeal achalasia. Parental satisfaction was high. Botulinum toxin injection of the cricopharyngeus muscle is a useful tool to help diagnose and treat pediatric cricopharyngeal achalasia. It has been proven safe, and is less invasive than other surgical procedures. More research is needed to elucidate optimal dosing, frequency of injections, and when to move on to surgical intervention.

60
ADOLESCENTS’ UNDERSTANDING OF THEIR CANCER PROGNOSIS
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Purpose: How adolescents come to understand their cancer prognosis remains relatively unknown. Parents and doctors are often the primary sources of information for teens; however, research has shown that parents often overestimate the chances of successful treatment. We expected that adolescents would report a more favorable prognosis than both parents and oncologists. Furthermore, these discrepancies would be smaller with more direct and frequent communication from oncologists and parents. Methods: Families whose children were: (a) 10 to 17 years old, (b) 3-8 weeks after a new diagnosis or relapse, and (c) English speaking were recruited from cancer registries to complete questionnaires in the home or hospital. Data were reported for 52 families (50 mothers, 30 fathers, 52 adolescents). On average, the sample of adolescents was 13.5 years old (SD = 2.4), 66% female, and 86% White. Diagnoses included leukemia (30%), lymphoma (28%), brain tumors (9%), and other solid tumors (33%); 17% had relapsed. Parents reported on the content and frequency of communication about the child’s prognosis, and adolescents reported on sources of information. Each participant and the child’s primary oncologist rated the child’s chance of 5-year survival on a visual analogue scale from 0-100%. Results: Oncologists discussed prognosis with most adolescents (78%), while 53% of mothers and 62% of fathers discussed it in concrete numbers. Discussing the possibility of cure with their child was more important to parents and occurred more often than the possibility of treatment failure. Adolescents reported getting information about their illness from doctors (83%), parents (62%), and their own research (25%). They reported a more favorable prognosis (M = 92%) than mothers (M = 88%, p < .05), fathers (M = 87%, p < .05), and especially physicians (M = 67%, p < .01). More frequent parent communication about cure was associated with less discrepancy between adolescents and both mother and oncologist estimates. Conclusions: Most adolescents receive prognostic information from oncologists and parents. Parents, understandably, emphasize the chance of cure relative to treatment failure. More frequent communication between parents and adolescents with cancer may be associated with more accurate estimates of cure. Implications for Practice: More research is needed, but clinicians may want to emphasize accurate understanding of prognosis and encourage parents to talk to adolescents so they can be involved in care.
MULTIPLEX FAMILIES WITH SEVERE LUPUS NEPHRITIS IN SUBJECTS WITH HLA A30 B18 DR7 AND COMPLEMENT C4 DEFICIENCY.

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Systemic lupus erythematosus (SLE) is a multi-organ autoimmune disease characterized by the production of autoantibodies against cellular constituents. Multiple genetic susceptibility loci for SLE have been identified but the most significant risk factors reside in the HLA, by which genetic variants of HLA-DRB1 and complement C4 (at the class III region) appear to play important roles. The mechanism underlying this association remains enigmatic. Here we report a clinical and molecular biologic investigation of a Caucasian family of three generations with multiple members detected positive for antinuclear antibodies (ANA) and persistently low levels of complement C4, plus two incidences of lupus-related death. The female proband, now deceased, was diagnosed with SLE in 2001 and progressed to lupus nephritis that required hemodialysis. Kidney biopsy revealed proliferative lupus nephritis class IV. Clinical laboratory data revealed low levels of C4 (6.4 mg/dl; normal: >18 mg/dl) and C3 (35.5 mg/dl; normal: >100 mg/dl), high titer of ANA (1:2560), the presence of anti-dsDNA (1:40), and positivity of anti-Ro. The patient experienced two episodes of generalized seizure and died of fulminant pulmonary infection with a septic shock. One of the proband’s three sisters was also diagnosed with severe lupus nephritis and died of CNS vasculitis with intracranial hemorrhage. The proband’s mother, a male and a female sibling, and a niece (age: 17) were presented with low C4 (12-16 mg/dl) and the presence of ANA (1:80 to 1:640). HLA typing revealed the subjects with low C4 in this family shared a common haplotype with HLA A30, B18 and DR7. Southern blot analysis revealed the presence of two short C4 genes with C4B-specific DNA sequences. However, immunofixation using EDTA-plasma revealed no C4B or C4A proteins were produced from this haplotype. We amplified and sequenced the genomic DNA sequences at the C4d region from six subjects in this family. The proband was heterozygous for a G→A mutation at the donor splice site of intron 28, which abrogated C4 gene expression by bringing a premature termination codon into the mRNA for the two C4B genes. Interestingly, we observed this same mutation in two other independent families with complete C4 deficiency and severe lupus nephritis, inferring multiple incidences of lupus nephritis in subjects with this HLA haplotype. This work highlights the importance of C4 genotyping and phenotyping among subjects with low C4 levels, as genetic deficiency of C4 are strongly associated with SLE with severe outcomes.

FAST LEARNING OPTIMIZED PREDICTION METHODOLOGY FOR MOLECULAR THERAPY RESPONSE CLASSIFICATION

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BACKGROUND: The Pediatric Preclinical Testing Program (PPTP) is a program for evaluating novel anti-cancer agents in pediatric cancer populations. This program is able to determine if an anti-cancer agent should be prioritized in the pediatric domain given clinically relevant observations of toxicity, overall tumor survival, and potential effect relative to current standard of care or in combination with existing agents. Additionally, we have observed that molecularly targeted therapy does not necessarily follow obvious trends in clinical populations and is likely only discernable at a molecular level. In addition to providing a robust drug evaluation pipeline, the PPTP has publicly made available DNA copy-number and mRNA characterization of a diverse pediatric cell line and tumor xenograft collection. Our approach is to apply machine learning techniques to uncover omic features that are predictive of drug sensitivity.

METHODS: Statistical and Genetic Algorithms (GA), machine learning methods and Particle Swarm Optimization (PSO) are used to identify molecular biomarkers that predict efficacy and broad classes of cancers within the context of PPTP childhood cancer populations. RESULTS: Thus far, we have demonstrated that a relatively small gene-expression signature is able to accurately segregate in vitro sensitivity. CONCLUSION: Furthermore, this work is evidence that interrogation of basal gene-expression data can reveal molecular biomarkers that are potentially predictive of in vivo agent efficacy, and can lead to an insightful prioritization of more effective treatments for children with cancer.
INCIDENCE OF NECROTIZING ENTEROCOLITIS (NEC) IN PREMATURE INFANTS ≤ 32 WEEKS GESTATION WITH NEUTROPENIA IN THE FIRST 24 HOURS OF LIFE

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Background: Neutropenia among neonates is a relatively common occurrence, affecting up to 8% of all infants in neonatal intensive care units (NICUs). The incidence of neonatal neutropenia is higher among preterm infants than among term infants, with estimates ranging between 6% and 58% depending on the definition of neutropenia (1). In the pediatric and adult population, neutropenia can be associated with inflammatory damage and necrosis of the intestinal mucosa, often of the terminal ileum and the cecum, known as neutropenic enterocolitis. It occurs more frequently in patients with leukemia and/or undergoing chemotherapy, and the main risk factor is neutropenia <1000/mm³ (7). Neutropenic enterocolitis is not seen in preterm infants, but necrotizing enterocolitis (NEC), the most common life-threatening gastrointestinal disease of preterm infants, has a similar process causing a severe inflammatory disorder of the intestine. Currently, the only common risk factors known for NEC are prematurity and feeding. Unlike in the pediatric and adult population, the relationship of neutropenia and enterocolitis has not been established for neonates.

Methods: Retrospective chart review of all infants ≤ 32 weeks gestation over a three year period were analyzed to determine if there is a higher incidence of NEC in infants who develop neutropenia (defined as an absolute neutrophil count (ANC) < 1800/mm³) in the first 24 hours of life compared to those without neutropenia. A complete blood count with differential taken at birth was reviewed to determine the presence of neutropenia. All infants were then classified into 4 categories, according to Bell and colleagues classification of NEC. Fisher’s exact or Chi-square tests were used to examine the association between neutropenia and the incidence of NEC. Results: 356 charts were analyzed. Of these, 98 infants had neutropenia at birth. 7 of the 98(7%) infants with neutropenia developed NEC. 27 of 258 (10%) infants without neutropenia at birth developed NEC (p=0.73). Conclusions: The presence of neutropenia in preterm infants at birth is not associated with an increased risk for NEC.

ELUCIDATION OF THE PATTERN OF VARIATION FOR THE AMYLASE LOCUS IN TYPE 1 DIABETES PATIENTS.

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Failure to metabolize polysaccharides as an energy source and inability to regulate blood glucose levels are hallmarks of diabetes mellitus. Type 1 diabetes (T1D) is a disease where pancreatic beta cells, producers of insulin that controls blood glucose levels, are destroyed by the immune system. Starch is a major source of glucose. Digestion of starch in humans begins with the enzyme alpha-amylase, which catalytically hydrolyzes alpha-1,4-glycosidic bonds between glucose monomers. Humans express two forms of alpha-amylase that display high tissue specificity. Pancreatic amylase (encoded by AMY2) is expressed by cells of the exocrine pancreas. Salivary amylase (encoded by AMY1) is expressed in the parotid salivary gland. Human amylase genes are one of the first reported instances for inter-individual gene copy number variation (CNV). Six different genes exist in a cluster on chromosome 1 in the human genome – three salivary genes (AMY1A, 1B, and 1C), two pancreatic genes (AMY2A and 2B) and one truncated pseudogene (AMYP1). In an effort to explain diversity of amylase CNV in healthy individuals, Groot and colleagues (Genomics 5:29, 1989) proposed a model with AMY2B-AMY2A-(AMY1A-AMY1B-AMYP1)n-AMY1C, where n = 0 – 2 copies in a diploid individual, but many exceptions are present. The objective of this study was to interrogate the amylase locus in T1D subjects to better understand its pattern of variation. We recruited 344 Type 1 diabetes patients from the Endocrinology Clinic at Nationwide Children’s Hospital in Columbus, Ohio. Genomic DNA from each patient was extracted from peripheral whole blood. PstI digests were paired with pulsed field gel electrophoresis (PFGE) for long range mapping of the amylase locus. TaqI, PvuII/PshAI, and PstI digested genomic DNA were processed with Southern blot analysis to determine copy number of individual AMY genes. Dot-plot analysis of genomic DNA sequences for the amylase locus indicated the presence of four large blocks of duplications ranging in size from 44kb to 64kb. Within these blocks are smaller segments of 7-30kb with sequence similarity. PstI-PFGE revealed a minimum fragment size of 280 kb, with ~20-50kb increments in different subjects. The largest AMY locus has a PstI fragment of 690kb, which would correspond to the presence of 15 copies AMY genes in a haplotype. Comparisons of TaqI, PstI, and PvuII/PshAI genomic RFLP data revealed variable copy number for all amylase genes in individuals. Individuals exist with short haplotypes consisting of AMY2B and AMY1C on each ends, with either AMY2A or AMY1P sandwiched in the middle. Pancreatic AMY2 genes appear to vary in copy number throughout the population. One T1D patient was found to be homozygous deficient for AMY2A. Our T1D population as a whole showed large range of copy number variation for all both AMY1 and AMY2. The human amylase locus undergoes complex variation that was likely generated by non-allelic homologous recombination.
SERUM MARKERS OF BONE HEALTH IN NEUROFIBROMATOSIS TYPE I

C. J. Murillo\textsuperscript{1,2}; K. C. Zobrist\textsuperscript{2,3}; B. A. Speckhart\textsuperscript{1,3}; M. M. Al-Rahawan\textsuperscript{1,3,4}.

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**Background:** Neurofibromatosis Type 1 (NF-I) is an autosomal dominant disorder that affects 1 in 3000 people. Aside from the array of diagnostic criteria, NF-I can also be associated with oncogenic osteomalacia (OM). OM is characterized by defective bone mineralization, susceptibility to bone fractures and deformities, and abnormal levels of serum markers of bone health, specifically, phosphorus (Ph) and alkaline phosphatase (AlkP). The levels of serum bone health indicators in NF-I have not been established. **Objective:** To assess the range of calcium (Ca), magnesium (Mg), Ph and AlkP in patients who have NF-I and compare it to the general population. **Methods:** We conducted a retrospective chart review study of patients with NF-I and controls who were evaluated at our hospital between February 2004 and October 2011. We collected data about cases and controls that included gender, age, and all recorded serum levels of: Ca, Mg, Ph and AlkP. We used a generalized linear model that controlled for gender to analyze differences between cases and controls in the levels of Ca, Mg, Ph, and AlkP. The study was approved by our local IRB. **Results:** We reviewed the charts of 94 patients and 196 controls. There was no difference in gender distribution between the two groups (M:F ratio is 45:49 case and 100:96 control, \(p=0.6\)). The age range was 10.2 to 49.5 years in NF-I cases and 10.4 to 50.9 years in controls. While 31% of the cases were children (<18 years-old), only 10% of the controls were (\(p<0.001\)). Upon comparing each of the four markers between cases and controls, no statistical difference was noted. After stratifying for age, individuals >18 did not have a difference in any of the levels \((p>0.05)\). However, children with NF-I had a significantly higher Ph and lower Mg than their control counterparts \((p=0.02\) and <0.0001, respectively). Neither Ca nor AlkP were different between children with or without NF-I \((p>0.2)\). **Conclusion:** Despite the low numbers of cases, our study demonstrates significant differences in serum levels of Mg and Ph in children with NF-I compared to the controls, yet no significant difference in levels of Ca or Alk-P. This observation is not compatible with the typical picture of OM, which is characterized by an elevated AlkP and a low, rather than high, level of Ph. Our control group had a limited number of children, which may explain our inability to find the typical picture of OM in the serum. Nevertheless, high serum Ph and low Mg can suggest an abnormal bone health in children with NF-I. A larger cohort, prospective design and measurement of bone density in children and adults with NF-I may better evaluate bone health in this group.

SUCCESSFUL TRANSITION TO ORAL SULFONYLUREA THERAPY IN TWO PATIENTS WITH NEONATAL DIABETES MELLITUS WITH NOVEL MUTATIONS IN GENES ENCODING THE K-ATP CHANNEL COMPLEX REGULATING INSULIN SECRETION

LB Rauch, WB Zipf, JA Indyk, Pediatric Endocrinology, Nationwide Children's Hospital, Columbus, OH.

Neonatal Diabetes Mellitus is a rare form of diabetes, frequently caused by mutations in the KCNJ11 and ABCC8 genes coding for the Kir6.2 and SUR1 (Sulfonylurea Receptor) subunits of the pancreatic beta-cell ATP-dependent potassium channel complex that regulates insulin secretion. Oral sulfonylurea therapy has been successfully used to treat many patients with these mutations, and can immensely improve glycemic control and quality of life. Severe mutations result in the DEND syndrome (Development delay, Epilepsy, and Neonatal Diabetes Mellitus), whereas iDEND (intermediate DEND) represents a milder phenotype. Some mutations are not amenable to sulfonylurea therapy and patients must remain on life-long subcutaneous insulin therapy. Methods: We describe two cases of neonatal diabetes with novel mutations in KCNJ11 and ABCC8, which were successfully transitioned from subcutaneous insulin to oral sulfonylurea therapy, including one infant with iDEND Syndrome not previously described in the literature. Findings: An infant male with developmental delay and multiple congenital anomalies was admitted to the Pediatric ICU at 4 months of age with DKA (diabetic ketoacidosis). Gene testing revealed a novel mutation in the ABCC8 gene and at age 15 months he was electively admitted for transition to sulfonylurea (glyburide) therapy. A second case is an infant female admitted to the Pediatric ICU at 3 months of age with DKA. After genetic testing revealed a novel mutation in the KCNJ11 gene, she was electively admitted for transition to sulfonylurea therapy at 8 months of age. Both patients were successfully transitioned and continue to have improved glucose control on oral glyburide therapy. Conclusions: We present two cases of infants with neonatal diabetes mellitus with novel gene mutations, both of which successfully transitioned to oral sulfonylurea therapy after being maintained on subcutaneous insulin. After transition, both have improved glycemic control on this simplified regimen. Though iDEND is very rare and generally less frequently amenable to oral therapy, our patient represents a novel mutation in the ABCC8 gene with an iDEND phenotype responsive to oral sulfonylurea therapy. This case illustrates that novel mutations (of either KCNJ11 or ABCC8 genes) should be considered for trial of oral sulfonylurea therapy.
CHARACTERISTICS OF PATHOGENS IN MYELOMENINGOCELE PATIENTS WHO USE CLEAN INTERMITTENT CATHETERIZATION.

CE Kozlovich1, C Singh2, C Baxter3, B Li1, and SS Justice1,2,1Center for Microbial Pathogenesis, Research Institute at Nationwide Children’s Hospital, Columbus, OH 2Division of Pediatric Urology, Nationwide Children’s Hospital, Columbus, OH 3The Ohio State University, College of Medicine, Columbus, OH

The urinary tract is the second most common site of infections, which can be severe enough to cause lifelong kidney damage in children. Uropathogenic Escherichia coli (UPEC) is the most common causative agent of pediatric urinary tract infections (UTIs). UPEC and other pathogens are becoming increasingly resistant to antibiotics including last resort drugs like levofloxacin, so new infection prevention strategies are needed. LoFric® catheters may decrease the incidence of UTI, but no trials have concluded that in a primarily pediatric population. Additionally, the prevalence of potential UTI pathogens has been described in adults but not in children. We hypothesize that E. coli cause most UTIs and that patients using LoFric® catheters will have a lower incidence of UTI. We have recruited 50 out of 50 consented patients with underlying etiologies necessitating clean intermittent catheterization for an IRB-approved clinical trial; 25 patients are using LoFric® and 25 are using conventional catheters. Clean catheterized urine specimens were collected at recruitment, and bacterial isolates were identified and tested for antibiotic resistance. E. coli, Proteus mirabilis, and Enterococcus spp. have been the most prevalent. E. coli are most frequently resistant to ampicillin, cephalothin, tobramycin and trimethoprim-sulfisoxazole which are also among the most frequently prescribed chemoprophylactics for UTIs. Pending trial conclusion, LoFric® may be a useful non-chemotherapeutic prevention strategy to reduce UTI in children.

IDENTIFYING DIFFERENCES BETWEEN PNEUMOCOCCAL STRAINS THAT MAY CONTRIBUTE TO DEVELOPMENT OF HEMOLYTIC UREMIC SYNDROME.

S A Woodiga1, J D Rohr1, C M Buckwalter1, J D Mahan2,3 and S J King1,3, 1Center for Microbial Pathogenesis, The Research Institute at Nationwide Children's Hospital, 2 Department of Nephrology, Nationwide Children’s Hospital, Columbus, OH, 3The Ohio State University College of Medicine, Columbus, OH

Pneumococcal-associated hemolytic uremic syndrome (pHUS) is a rare but severe sequelae of invasive pneumococcal disease. pHUS patients have higher morbidity and mortality than patients with Escherichia coli associated HUS. Furthermore, studies demonstrate a rise in the percentage of invasive pneumococcal disease patients suffering pHUS over recent years, suggesting this is an increasing problem. Why some patients with invasive pneumococcal disease develop HUS and the host and bacterial factors that contribute development of this disease are unclear. It is proposed that pneumococcal neuraminidases cleave terminal sialic acid from O-linked glycans on red blood and endothelial cells to expose the Thomsen-Friedenreich antigen (T-antigen). As the T-antigen is present on the surface of many bacteria antibodies against this carbohydrate are present in the blood and it is proposed that binding of anti-T-antigen immunoglobulin M to red blood cells leads to agglutination. T-antigen exposure is observed in patients with pHUS, but it is also observed in many bacteremic patients without HUS. Thus far there is no evidence that T-antigen exposure causes pHUS. To determine if pHUS isolates have higher neuraminidase levels and hence expose the T-antigen more efficiently we tested the neuraminidase activity of pHUS and blood non-HUS isolates. Although there was variation in neuraminidase activity between strains this did not correlate with disease manifestation. As the distribution of neuraminidases varies between strains and presence of the gene encoding Neuraminidase C was recently shown to correlate with pHUS in Taiwan, we are currently determining distribution in our strains. Pneumococci also express an O-glycosidase which cleaves the T-antigen and may contribute to pHUS. However, there was no correlation between O-glycosidase activity and disease manifestation. We are now undertaking a genome wide approach to identify pneumococcal sequences which correlate with HUS. We are using multi-locus sequence typing to determining the genetic background of 30 pHUS isolates from the CDC. These data will be used to select 6 strains of distinct genetic backgrounds for sequencing. The presence of sequence variants that correlate with pHUS will then be assessed in a larger number of strains. The long term goal is to define the pathogenic mechanisms of pHUS and aid development of therapeutics that would reduce mortality and morbidity in patients.
69
CONTRIBUTION OF STRUCTURAL DOMAINS TO RIBONUCLEASE 7’S GRAM-POSITIVE AND GRAM-NEGATIVE ACTIVITY AGAINST UROPATHOGENS.

H. Wang1, AL. Schwaderer1,2,3, J. Kline1, JDavidi13 and DS. Hains1,2,3

1The Research Institute at Nationwide Children’s Hospital, Center for Clinical and Translational Medicine. 2 Department of Pediatrics, College of Medicine, The Ohio State University 3 Nationwide Children’s Hospital, Division of Pediatric Nephrology

Background: Ribonuclease 7 (RNase 7) is a 14.5 kDa peptide that possesses potent antimicrobial properties against Gram-negative and Gram-positive bacteria and is expressed in a variety of epithelial tissues. Little is known about its mechanisms of action and the determinants of its antimicrobial properties. The objective of this study is to identify the intrinsic functional domains of RNase 7 that influence its activity against uropathogenic Gram-negative and Gram-positive bacteria. Methods: In this study, a series of RNase 7 fragments were generated that contained different numbers of its secondary motifs starting from both N-terminus and C-terminus of RNase 7. We determined antimicrobial properties of each fragment against both Gram-positive and Gram-negative uropathogenic bacteria. Results: RNase 7 fragments displayed significant differences in their antimicrobial activity profiles. Compared to N-terminal fragments, C-terminal fragments showed uniformly decreased activity against Escherichia coli and Staphylococcus saprophyticus. In addition, the fragments that lack β-sheets 1, 3 and 4 demonstrated significantly decreased activities. We have also identified one fragment with at least four-fold increased potency against both E. coli and S. saprophyticus compared to full-length peptide. We have also identified distinct regions of the peptide that are independently responsible for Gram-negative and Gram-positive activity. Conclusions: Our results suggest that RNase 7 has antimicrobial activity against both Gram-positive and Gram-negative uropathogenic bacteria but with distinct mechanisms. We also have identified a peptide fragment with increased activity compared to the naturally occurring peptide. These findings serve as the foundation to design future novel antimicrobial and therapeutic agents.

70
INTERCALATED CELLS MAINTAIN STERILITY OF THE HUMAN URINARY TRACT

Jim D. Spencer

Background: Although urine is sterile, little is known how the kidney maintains sterility. We have shown that the renal collecting duct produces several antimicrobial peptides (AMP) that help maintain sterility. Intercalated cells (IC) produce one of the most potent human AMPs – Ribonuclease 7 (RNase7). When RNase7 is neutralized in the urinary tract, bacterial growth increases. This study was designed to further characterize the biological relevance of RNase7 and Ribonuclease Inhibitor (RI) in the human kidney during infection. Design/Methods: Gene expression: RNA from non-infected and pyelonephritic kidney tissue was used to quantify RNASE7 and RI using real-time PCR. Protein expression: Immunofluorescence (IF) localized RNase7 and RI production. Western blot (WB) and ELISA quantified RNase7 and RI production in non-infected/infected kidney and urine samples. RNase7 function: Live/Dead kill assays assessed the antimicrobial function of RNase7 on uropathogens in the presence and absence of RI. Results: Gene expression: With pyelonephritis, RNASE7 mRNA expression increased from 1028 ng to 2927 ng/10ng total RNA (p<0.04) while RI mRNA expression decreased from 806 ng to 549 ng/10ng total RNA (p<0.05). Protein expression: IF localized RNase7 production to the apical surfaces of IC and RI to the basolateral surfaces of IC. Extracellular staining showed that IC secrete RNase7 into the urinary space. ELISA showed kidney and urinary RNase7 peptide production increase with infection. WB showed concurrent decreases in kidney RI production with pyelonephritis. RI was not detected in sterile urine. Degraded RI was identified in infected urine. RNase7 function: Recombinant RNase7 rapidly kills Gram-positive/negative uropathogens at micromolar concentrations (0.1-2.5µM). In the presence of equal concentrations of RI, the antimicrobial effects of RNase7 significantly decreased. Conclusions: ICs are important in maintaining sterility of the urinary tract as they produce potent AMPs like RNase7. IC also produce regulatory proteins like RI, which abrogates the antimicrobial effects of RNase7. Further elucidation of the IC factors that regulate production and function of AMPs like RNase7 may lend insight into the pathogenesis of UTIs.

71
ESTABLISHMENT OF BLADDER WHOLE ORGAN EXPLANT IN VITRO CULTURE SYSTEM

Kristin R. DeSouza, Ph.D.1, M. Brian Becknell, M.D., Ph.D.1, Melissa Scott1, and Kirk M McHugh1

1The Research Institute at Nationwide Children’s Hospital, Columbus, OH, USA.

In this study we present an in vitro model system established by our lab, using whole bladder organ cultures to characterize bladder smooth muscle initiation and development. In order to better characterize bladder smooth muscle development, we utilized wild type mice and our unique megabladder (mgb-/-) mouse model that fails to develop smooth muscle specifically in the bladder. Bladders from embryonic day 15 (E15) mice were isolated and transfected
by either soaking or injection with, Ad5, AAV8, or AAV2 viruses containing a GFP reporter gene under the control of the CMV promoter. Following transfection, bladders were cultured for up to 7 days. Over the course of culturing, the bladders were assessed by microscopy for GFP expression and gross smooth muscle cell (SMC) morphology. All the organ cultures exhibited SMC morphological development, including differentiation of sail-shaped myoblasts and spindle-shaped myocytes. Bladders inoculated with Ad5 expressed GFP from days 1-7 in culture and AAV8 expressed GFP from days 5-7. Minimal to no GFP expression was observed in bladders transfected with AAV2. At day 7 of culturing, bladders were collected and assessed by immunohistochemistry (IHC) for -SMA and GFP expression. We found the bladder explant cultures expressed -SMA, indicative of mesenchymal differentiation into smooth muscle under in vitro conditions. Additionally, the -SMA positive cells expressed GFP, indicating SMC were successfully transfected with Ad5 or AAV8 virus. This study demonstrates bladders can be grown in an in vitro culture system where they will initiate smooth muscle cell differentiation and development. This technique establishes a baseline for assessing development of SMC in bladder organ explants. We are utilizing this novel in vitro model system to manipulate expression of key smooth muscle genes in the bladder and investigate their role in bladder smooth muscle cell differentiation and development.

72
INCREASED Na+/H+ EXCHANGER ISOFORM 1 ACTIVITY IN HIPPOCAMPAL ASTROCYTES RESULTS IN INCREASED RELEASE OF GLUTAMATE AND CYTOKINES AFTER IN VITRO ISCHEMIA. 
P. Cengiz1, DB Kintner1, V Chanana1, P Kendigelen1, B Gulnaz2, E Fidan1, E Acture1, P Ferrazzano1, D Sun2.
1Univ.Wis. Madison, Dept. of Pediatrics, Madison, WI. 2 Univ. Pittsburgh, Dept. Neurology, Pittsburgh, Pennsylvania. Neonatal encephalopathy remains a significant cause of mortality and morbidity. Perinatal hypoxia and ischemia (HI), is associated with severe long-term neurologic morbidity. One hallmark of HI in neonates is reactive astrogliosis in the hippocampus. However, the impact of reactive astrogliosis on hippocampal damage after HI is unknown. We have recently shown that inhibition of the Na+/H+ exchanger isoform 1 (NHE-1) resulted in decreased hippocampal neuronal damage and subsequent improvement of learning and memory in adolescent and adult mice after perinatal HI. In the current study, we further investigated the role of NHE-1 protein in hippocampal reactive astrocyte function using an in vitro ischemia model [oxygen/glucose deprivation and reoxygenation (OGD/REOX)]. Primary hippocampal astrocytes were cultured from the hippocampus of 3-4 day old C57/Blk 6 mice. Cells were incubated in 0.2-1 ml of OGD solution for 2 h in a hypoxic incubator containing 1% O2, followed by 1, 5 and 24 h of REOX. NHE-1 and GFAP were detected via immunohistochemical staining and immunoblotting. Intracellular pH and H+ efflux were determined using BCECF. Glutamate release into the media was determined with the amplex® red glutamic acid/glutamate oxidase assay. Cytokine release was determined using cytokine ELISA kits and intracellular Na+ in single cells was determined using Sodium Green. NHE-1 and GFAP expressions, H+ efflux, release of gliotransmitters (glutamate, IL-β, IL-6, and TNFα) and intracellular Na+ peaked at 5 h of REOX. Inhibition of NHE-1 activity with its inhibitor HOE 642 reduced H+ efflux from hippocampal astrocytes. Moreover, HOE 642 reduced intracellular intracellular Na+ accumulation at 5 and 24 h REOX. Lastly, both HOE 642 and the excitatory amino acid transporter inhibitor TBOA significantly attenuated glutamate release. Conclusion: NHE-1 plays an essential role in maintaining H+ homeostasis in hippocampal astrocytes. NHE-1 and GFAP expressions were significantly elevated in hippocampal astrocytes after in vitro ischemia. Inhibition of NHE-1 reduced intracellular sodium accumulation and gliotransmitter release. We speculate that over-stimulation of NHE-1 activity in hippocampal astrocytes may disrupt Na+ homeostasis and trigger the reverse operation of the Na+-dependent glutamate transporter. Therefore, overstimulation of NHE-1 in these cells led to intracellular alkalosis and release of glutamate and cytokines in in-vitro ischemic conditions.

73
THE EFFECT OF HEAT STRESS ON INFLAMMATION MEASURED IN EXHALED BREATH CONDENSATE IN A RAT MODEL OF ACUTE LUNG INJURY. 
K Narayana Gowda SM Heidemann Children’s Hospital of MI, Detroit, MI
Heat stress prior to infection is thought to be protective by either a molecular chaperone effect or by attenuation of inflammatory mediators like TNF-α and IL-6. Cytokines may be measured in bronchoalveolar lavage but this technique has the disadvantage of diluted specimen from a small part of the lung whereas exhaled breath condensate (EBC) may reflect global cytokine production in the lung. Objectives: 1) to determine if TNF-α and IL-6 are produced in the EBC and total lung lavage (TLL) in a rat model of acute lung injury (ALI) with and without prior heat; 2) to find out if prior heat stress resulted in attenuation of TNF-α and IL-6; 3) to correlate the mediators in the EBC to TLL. Methods: Rats were assigned to control (n=4), 4 hr (n=8) or 4 hr + heat stress(n=9). The heated group was warmed to 41C for 15 min, 18 hours
before study entry. 4 hrs after giving 1µg/kg Staphylococcal Enterotoxin B (SEB), rats were by ventilated and EBC was collected in a cooled tube placed in the exhalation limb. After death, the whole lung was lavaged, the supernatant collected and white cell counts were measured. **Results:** The volume of EBC was similar in the control, 4 hr, heat+4 hr SEB groups [1000(560-1430),1320(340-1430),1210 (880-1540)µl p=0.47]. Lung inflammation was shown by white cell counts which were higher in the preheated, 4 hrs after SEB compared to 4 hr after SEB and control rats [1,480 (860-2540) vs. 686 (362-9970) vs. 540 (400-614) 1000cells/ml (p<0.002). TNF-α concentration was elevated in the TLL in the 4 hr and preheated, 4 hr after SEB groups when compared to controls (**p=0.005). IL-6 was higher in the TLL in the 4 hr and preheated, 4 hr after SEB groups when compared to control rats (**p=0.005) (fig). TNF-α in the EBC was similar in the control, 4 hr and preheated, 4 hr after SEB groups [26(14-48) vs. 21(10-40) vs.28(15-69)pg/ml). IL-6 was not detected in the EBC. There was a correlation between the TNF-α in the EBC vs. TLL (r²=0.399, p=0.04). Conclusions: Heat stress prior to ALI did not protect the lung by decreasing inflammatory mediators in the lung. Lack of elevation of TNF-α in the EBC of rats receiving SEB suggests that TNF-α detection in the EBC may require a longer time period than 4 hours. IL-6 may be detected in the EBC using more sensitive methods. The weak correlation of the TNF-α in the EBC and TLL suggests the possibility of release of membrane bound TNF-α during the lavage process.

74

THE EXPRESSION OF FATTY ACID BINDING PROTEIN 4 (FABP4) IN THE MURINE PLACENTA

**Abhishek Makkar,** Takuya Mishima, & Yoel Sadovsky, Magee-Womens Research Institute, Department of OB/GYN and Reproductive Sciences, and Department of Neonatal Perinatal medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA

**Objective:** The aim of the study was to determine the spatial and temporal expression of the fatty-acid-binding protein (FABP4) mRNA and protein in the mouse placenta. **Study Design:** Protein expression of FABP4 in the murine placenta at different gestational age was detected by immunohistochemistry, immunofluorescence and western immunoblotting. The expression of FABP4 mRNA was analyzed using real time PCR. **Results:** Using Immunohistochemistry, we found that FABP4 is expressed in the trophoblast layer of murine placenta. FABP4 expression was also detected in fetal capillaries within the labyrinth of the murine placenta. This finding was confirmed using co-localization of FABP4 with CD31, an endothelial cell marker. We also found that FABP4 expression in labyrinthine layer varied with gestational age, with increased levels of FABP4 with advancing gestational age from E12.5 to E16.5, followed by lower levels of mRNA and protein at E18.5. **Conclusions:** FABP4 is selectively expressed within in the placental labyrinthine trophoblast and endothelial layers suggesting a role for FABP4 in maternal-fetal lipid trafficking.
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 a $1,000 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
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.

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<td>Misty Good, MD</td>
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<td>Andrew Harris, MD</td>
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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.

1994  Bindya S. Singh
1995  Genie E. Roosevelt
1996  Raghavendra Rao
1997  Howard M. Katzenstein
1998  Rajeev Dixit
1999  Jennifer L. Kloesz
2000  Gregory Dalshaug
2001  Lisa K. Kelly
2002  Nancy B. Aspey
2003  Gerhard C. Hildebrandt
2004  Aaron K. Olson
2005  Christopher Linblade
2006  Todd D. Nebesio
2007  Nicholas Von Bergen
2008  Sundan Rajan
2009  Paul Mann, MD
2010  Shaun Ashfield, MD
2011  Dennis Slagel, DO
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.

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<td>2011</td>
<td>Juan F. Sotos, MD</td>
</tr>
</tbody>
</table>
Officers and Council Members
2011

President
Joyce M. Koenig, MD (2011-2013)
Saint Louis University

Past President
J. Carter Ralphe, MD (2010-2012)
University of Wisconsin-Madison

President-Elect
Robert P. Hoffman, MD (2011-2014)
Ohio State University

Secretary-Treasurer
Pamela J. Kling MD (2012-2017)
University of Wisconsin-Madison

Council Members (three-year term)

Patrick D. Brophy, MD (2012)
University of Iowa

Laura Haneline, MD (2013)
Indiana University

David B. Kershaw, MD (2012)
University of Michigan

Heather Bartlett MD (2014)
University of Iowa Carver College of Medicine

Deanne W. Wilson Costello, MD (2011)
Case Western Reserve University

Wendy Luce MD (2014)
Nationwide Children’s Hospital

Maria L. Becker, MD (2013)
University of Missouri-Kansas City

Michael Wilhelm MD (2014)
University of Wisconsin

Caroline George, MD (2013)
University of Minnesota

University of Cincinnati