Midwest Society for Pediatric Research

PROGRAM

October 10-11, 2013
Minneapolis, MN
## PROGRAM-AT-A-GLANCE

### 54th Annual Midwest Society for Pediatric Research Scientific Meeting

**University of Minnesota**  
Cancer and Cardiovascular Research Building, Minneapolis, Minnesota

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<th>TIME</th>
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<td><strong>WEDNESDAY, OCTOBER 9, 2013</strong></td>
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| 4:45 pm – 6:15 pm   | MWSPR Council Meeting  
Amplatz Children's Hospital, Room C6-140  
2450 Riverside Ave, Minneapolis, MN 55454 |
| 6:30 pm – 9:30 pm   | MWSPR Council Dinner  
Nicollet Island Inn, Fireside Lounge  
95 Merriam St., Minneapolis, MN 55410 |
| **THURSDAY, OCTOBER 10, 2013** |                       |
| 7:00 am – 8:00 am   | MWSPR Registration  
Continental Breakfast  
Cancer & Cardiovascular Research Building – Atrium & Courtyard |
| 7:00 am – 8:00 am   | **Poster Set Up**  
Cancer & Cardiovascular Research Building – Atrium |
| 8:00 am – 11:50 am  | MWSPR Plenary Session I  
Cancer & Cardiovascular Research Building, Room 1-125 |
| 11:50 am – 12:15 pm | Founder and Sutherland Award Presentation  
Cancer & Cardiovascular Research Building, Room 1-125 |
| 12:15 pm – 12:35 pm | MWSPR Business Meeting for Members  
Cancer & Cardiovascular Research Building, Room 1-125 |
| 12:25 pm – 1:30 pm  | **Lunch**  
Cancer & Cardiovascular Research Building – Atrium & Courtyard |
| 1:30 pm – 4:50 pm   | MWSPR Plenary Session II  
Cancer & Cardiovascular Research Building, Room 1-125 |
| 4:50 pm – 6:15 pm   | Reception and Combined Poster Session  
Cancer & Cardiovascular Research Building, Atrium |
| **FRIDAY, OCTOBER 11, 2013** |                       |
| 7:00 am – 8:00 am   | MWSPR Registration  
Cancer & Cardiovascular Research Building, Atrium |
| 7:15 am – 8:05 am   | **Trainee Breakfast**  
McGuire Translational Research Facility/Lions Research Building,  
Conference room 1-110  
2001 6th St. SE, Minneapolis, MN 55455 |
| 7:15 am – 8:15 am   | Continental Breakfast  
Cancer & Cardiovascular Research Building, Atrium & Courtyard |
| 8:15 am – 12:05 pm  | MWSPR Plenary Session III  
Cancer & Cardiovascular Research Building, Room 1-125 |
| 12:05 pm            | **Poster Take Down** |
| 12:20 pm – 1:30 pm  | Kenny, Metcalf, and Student Research Award Luncheon  
McNamara Alumni Center, Johnson Great Room  
200 Oak St. SE, Minneapolis, MN 55455 |
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**

Robert Hoffman, MD – President
David B. Kershaw, 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
Cleveland Clinic
INO Therapeutics LLC - Ikaria
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University of Minnesota Medical School, Department of Pediatrics
54th Annual Midwest Society for Pediatric Research Scientific Meeting

THURSDAY, OCTOBER 10, 2013

8:00 am – 6:15 pm

University of Minnesota
Cancer and Cardiovascular Research Building
Minneapolis, Minnesota

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

8:00-8:05  WELCOME AND INTRODUCTION
Robert Hoffman, President

8:05  State-of-the-Art Speaker
Gene therapy in muscular dystrophy
Jerry R. Mendell
Professor and Director of the Center for Gene Therapy
Ohio State University

MWSPR PLENARY SESSION I
Cancer & Cardiovascular Research Center – Room 1-125

Wendy Luce and Carrie George, Presiding

9:00  ALLOGENEIC T CELLS INCREASE RELIANCE ON FATTY ACID METABOLISM, WHICH ALLOWS FOR SELECTIVE METABOLIC TARGETING.
CA Byersdorfer, S Sandquist, JL Ferrara, S Goodell, V Tkachev, JL Ferrara, S Goodell, and J Swanson, Ann Arbor, MI. University of Michigan Abstract 1

9:15  PHYSICAL ACTIVITY AND CARDIOMETABOLIC RISK FACTORS IN CHILDHOOD CANCER SURVIVORS.
ME Slater, JA Ross, AR Sinaiko, A Moran, J Lee, JL Perkins, KS Baker, and J Steinberger, Minneapolis, MN and Seattle, WA. University of Minnesota Abstract 2

9:30  PHLEBOTOMY INDUCED ANEMIA ALTERS HIPPOCAMPAL GENE EXPRESSION IN NEONATAL MICE.
TG Zamora, D Wallin, K Ennis, K Thibert, A Stein, R Rao, and M Georgieff, Minneapolis, MN. University of Minnesota Abstract 3

9:45  HEMATOPOIETIC ALTERATIONS IN GESTATIONAL IRON DEFICIENCY.
ZR Smith, MY Sun, HR Zundel, SE Blohowiak, and PJ Kling, Madison, WI. University of Wisconsin-Madison Abstract 4

10:00 – 10:20 am BREAK
(Atrium and Courtyard)
10:20  PRENATAL CHOLINE SUPPLEMENTATION REVERSES THE DOWNREGULATION OF HIPPOCAMPAL GENE EXPRESSION RESULTING FROM GESTATIONAL IRON DEFICIENCY.
KA Thibert, BC Kennedy, AJ Siddappa, PV Tran, JC Gewirtz, and MK Georgieff, Moorhead, MN and Minneapolis, MN. University of Minnesota  
Abstract 5

10:35  PBX1/2 ARE REQUIRED IN LUNG MESENCHYME FOR NORMAL POSTNATAL LUNG DEVELOPMENT.
DJ McCulley, EA Hines, X Sun, and L Selleri, Madison, WI and New York, NY. University of Wisconsin, Madison  
Abstract 6

10:50  EFFECT OF MATERNAL HIGH FAT DIET AND LATE GESTATIONAL DIABETES MELITUS ON FETAL LUNG DEVELOPMENT.
Bj Forred, DN Jensen, CC Evans, TD Larsen, ML Baack, and PF Vitiello, Sioux Falls, SD. USD Sanford School of Medicine  
Abstract 7

11:05  SURVIVAL AND PULMONARY MORBIDITIES FOLLOWING PROLONGED PREMATURE RUPTURE OF MEMBRANES PRIOR TO 24 WEEKS GESTATION.
EA O'Brien, N Nuangchamnong, DK Fleener, TT Colaizy, JM Klein, and JE Brumbaugh, Iowa City, IA. University of Iowa  
Abstract 8

11:20  CHARACTERIZATION OF A NOVEL QUORUM QUENCHING PROTEIN PRODUCED BY MRSA.
MJ Van Dyke, ME Olson, and AR Horswill, Iowa City, IA. University of Iowa  
Abstract 9

11:35  NEONATAL NEUTROPHILS STIMULATED WITH GROUP B STREPTOCOCCUS INDUCE A PRO-INFLAMMATORY BIAS IN CD4+ T CELLS AND T REGULATORY CELLS.
J Lin, SJ Barenkamp, R Weisert, LC Lorenset, G Peng, and JM Koenig, St. Louis, MO. Saint Louis University  
Abstract 10

11:50  FOUNDERS & SUTHERLAND AWARD PRESENTATION
Cancer & Cardiovascular Research Building, Room 1-125

**Founder Award Recipient**

Howard Kilbride, MD  
University of Missouri-Kansas City

*Introduction by: Joshua E. Petrikin, MD*  
University of Missouri Kansas City

12:15  MWSPR BUSINESS MEETING FOR NON-TRAINEES
Cancer & Cardiovascular Research Building, Room 1-125

12:25  LUNCH  -  Cancer & Cardiovascular Research Building – Atrium & Courtyard
Jane Brumbaugh and Robert Hinton, Presiding

1:30 State-of-the-Art Speaker Introduction – Robert Hoffman, President

State-of-the-Art Speaker
Iron Deficiency and Neonatal Development
Christopher L. Coe
W.B. Cannon Professor
University of Wisconsin

2:30 EXCESS GLUCOSE EXAGGERATES AND BETA-HYDROXYBUTYRATE PROTECTS AGAINST HYPOGLYCEMIA INDUCED BRAIN INJURY IN DEVELOPING RATS.
KM Ennis, H Dotterman, K Le, A Stein, and R Rao, Minneapolis, MN. University of Minnesota
Abstract 11

2:45 IUGR ALTERS THE REGIONAL VULNERABILITY TO HYPOGLYCEMIA IN THE NEONATAL RAT BRAIN.
AB Stein, KM Ennis, R Rao, and A Maliszewski-Hall, Minneapolis, MN. University of Minnesota
Abstract 12

3:00 DEVELOPMENTAL CHANGES AND EFFECT OF HYPOGLYCEMIA ON BRAIN REGIONAL ANTIOXIDANTS IN RATS.
AR Rao, H Quach, E Smith, G Vatassery, and R Rao, Minneapolis, MN. University of Minnesota
Abstract 13

3:15 – 3:35 pm BREAK
(Atrium and Courtyard)

3:35 DEVELOPMENTAL PROGRAMMING OF CARDIOMYOCYTE METABOLISM IN OFFSPRING OF DIABETIC MOTHERS.
LJ Weaver, BJ Forred, TD Larsen, AL Cypher, PF Vitiello and ML Baack, Duluth, SD. University of South Dakota
Abstract 14

3:50 MATERNAL HIGH FAT DIET AND DIABETES INCITES LIPID DEPOSITION IN THE DEVELOPING HEART OF OFFSPRING.
MD Schimelpfenig, AL Wachal, TD Larsen and ML Baack Sioux Falls, SD. University of South Dakota
Abstract 15

4:05 PEDIATRIC NONSYNDROMIC THORACIC AORTIC ANEURYSM: CLINICAL STRATIFICATION AND IMPACT OF EARLY MEDICAL THERAPY.
BJ Landis, SM Ware, A Shikany, J Arthur, LJ Martin, and RB Hinton, Cincinnati, OH. University of Cincinnati
Abstract 16

4:20 MACROPHAGES AND REDUNDANTLY-ACTING Fc GAMMA RECEPTORS DRIVE AUTOIMMUNE VALVULAR CARDITIS.
PM Hobday, JL Auger, GR Schuneman, S Haasken, JS Verbeek, and BA Binstadt, Minneapolis, MN, Iowa City, IA and Leiden, The Netherlands. University of Minnesota
Abstract 17
4:35  MECHANOBIOLOGY OF NOTCH IN AORTIC VALVE DISEASE.
RC Godby, C Munj, AM Opoka, DA Narmoneva, and RB Hinton, Cincinnati, OH. University of Cincinnati
Abstract 18

4:50  RECEPTION AND COMBINED POSTER SESSION
Cancer & Cardiovascular Research Building, Atrium
See page 8 for posters

FRIDAY, OCTOBER 11, 2013
7:15 am - 1:30 pm

7:15  TRAINEE BREAKFAST SESSION
McGuire Translational Research Facility/Lions Research Building
Conference Room 1-110
2001 6th St. SE

Statistics
Stephen D. Simon
University of Missouri Kansas City

MWSPR PLENARY SESSION III
Cancer & Cardiovascular Research Center – Room 1-125

David Kershaw and Akhil Maheshwaril, Presiding

8:15  State-of-the-Art Speaker Introduction – Robert Hoffman, President

State-of-the-Art Speaker
Vitamin D and Immunity
Lynda Polgreen
Assistant Professor
The University of Minnesota Amplatz Children's Hospital

9:15  LUMBAR PUNCTURE SIMULATION TRAINING: BRIDGING THE CLINICAL GAP.
SS Shafer, D Rooney, and J House, Ann Arbor, MI. University of Michigan
Abstract 19

9:30  NEONATAL GROWTH RESTRICTION AND THE PROGRAMMING OF ADULT BEHAVIOR IN MICE.
LR Meyer, V Zhu, A Miller, and R Roghair, Iowa City, IA. University of Iowa
Abstract 20

9:45  INTESTINAL ALKALINE PHOSPHATASE IS PROTECTIVE TO THE PRETERM RAT PUP INTESTINE.
NP Heinzerling, SR Welak, JL Liedel, K Fredrich, B Biesterveld, K Pritchard, and DM Gourlay, Milwaukee, WI. Medical College of Wisconsin
Abstract 21
10:00  METABOLOMICS ANALYSIS IDENTIFIES NOVEL PLASMA BIOMarkers OF CF PULMONARY EXACERBATION.
TA Laguna, CB Williams, K Brandy, C Welchlin-Bradford, CE Moen, and CH Wendt, Minneapolis, MN. University of Minnesota

Abstract 22

10:15 – 10:35 am BREAK
(Atrium and Courtyard)

10:35  DENDRITIC CELL MATURATION IS DELAYED IN NEONATES DURING RESPIRATORY VIRAL INFECTION.
LP Shornick, BR Tumala, and S Bhattacharya, St. Louis, MO. Saint Louis University

Abstract 23

10:55  IVH SCREENING BY CRANIAL ULTRASOUND FOR ALL PRETERM INFANTS >30 WEEKS IS NOT COST EFFECTIVE.
C Van der Walt, R Vazzalwar, L Schweig, and R Donovan, Park Ridge, IL. Advocate Children’s Hospital - Park Ridge

Abstract 24

11:05  BODY COMPOSITION AND PROCESSING SPEED OF VLBW INFANTS.
KM Pfister, HL Gray, EW Demerath, MK Georgieff, and SE Ramel, Minneapolis, MN. University of Minnesota

Abstract 25

11:20  IRON MAY BE THE CRITICAL LINK BETWEEN MATERNAL OBESITY AND ASTHMA IN OFFSPRING.
SE Murray, NC Dosch, RM Weigert, EF Guslits, TW Guilbert, CL Coe, and PJ Kling, Madison, WI. University of Wisconsin-Madison

Abstract 26

11:35  PSEUDOTYPED ADENO-ASSOCIATED VIRUS 9 EXPRESSION OF GFP IN MICE USING A TRUNCATED NEPHRIN PROMOTER.
MA Muff-Luett, D Wu, JL Picconi, E Bunchman, and PD Brophy, Iowa City, IA. University of Iowa

Abstract 27

11:50  INTERROGATING THE MECHANISMS OF AFLATOXIN-ASSOCIATED CHILDHOOD STUNTING.
BL Knipstein, B Emily, H Jiansheng, Y Brian, D Dennis, and R David, St. Louis, MO. Washington University

Abstract 28

12:20  MWSPR KENNY, METCOFF, AND STUDENT RESEARCH AWARD LUNCHEON
McNamara Alumni Center, Johnson Great Room, 200 Oak St. SE, Minneapolis MN 55455

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| **1** | **SEGMENTAL PROGERIA AS A MODEL OF CARDIAC AGING.**  
*JL Lohr, MJ Doyle, CS Chapman, FD Kamdar, C Eide, C Lees, N Koyano-Nakagawa, DJ Garry, and J Tolar, Minneapolis, MN. University of Minnesota*  
Abstract 29 |
| **2** | **DETERMINING THE ROLE OF PTPN12 IN CONGENITAL HEART DISEASE AND VASCULAR DEVELOPMENT.**  
*EA Duffy, PR Pretorius, SL Lerach, JL Lohr, B Hirsch, and LA Schimmenti, Minneapolis, MN. University of Minnesota*  
Abstract 30 |
| **3** | **INTRAOPERATIVE TRANSESOPHAGEAL ECHOCARDIOGRAM ASSESSMENT OF LEFT VENTRICULAR TEI INDEX IN CONGENITAL HEART DEFECTS.**  
*S Sivanandam and J Louis, Minneapolis, MN. University of Minnesota*  
Abstract 31 |
| **4** | **SURGICAL REPAIR RESULTS OF ANOMALOUS AORTIC ORIGIN OF CORONARY ARTERY: A MULTI-INSTITUTIONAL PEDIATRIC CARDIAC CARE CONSORTIUM STUDY.**  
*JD St. Louis, BA Harvey, and UK Jodhka, Minneapolis, MN. University of Minnesota*  
Abstract 32 |
| **5** | **RE-ACCESS OF THE LEFT ATRIUM VIA PRIOR TRANSSEPTAL PUNCTURE SITE WITH USE OF THREE DIMENSIONAL NAVX.**  
*AG Unnithan, IH Law, and NH Von Bergen, Coralville, IA and Iowa City, IA. University of Iowa*  
Abstract 33 |
| **6** | **INTRACRANIAL PATHOLOGY IN NEONATES WITH CONGENITAL HEART DISEASE: IS THERE A RISK TO DELAYING CARDIAC SURGERY?**  
*JL Nyholm, S Sivanandam, and A Mello, Minneapolis, MN. University of Minnesota*  
Abstract 34 |
| **7** | **FETAL TAPSE AND TRICUSPID ANNULAR PEAK SYSTOLIC VELOCITY IN FETAL HEARTS.**  
*DB Dixon, K Thammineni, and S Sivanandam, Minneapolis, MN. University of Minnesota*  
Abstract 35 |
| **8** | **USE OF HIGH FIDELITY SIMULATION TO IMPROVE MEDICAL STUDENT CONFIDENCE AND KNOWLEDGE OF PRE-ARREST PEDIATRIC PATIENT.**  
*MD Schimelpfenig and JM Berner, Sioux Falls, SD. University of South Dakota*  
Abstract 36 |
| **9** | **SHARING LIFE ALTERING INFORMATION: DEVELOPMENT OF PEDIATRIC HOSPITAL GUIDELINES AND TEAM TRAINING.**  
*AD Wolfe, SA Friedrich, J Wish, J Kilgore-Carlino, JA Plotkin, and M Hoover-Regan, Madison, WI. University of Wisconsin*  
Abstract 37 |
10 COMPARISON OF MEDICAL STUDENT UNDERSTANDING AND RECALL OF ACUTE MANAGEMENT OF ASTHMA; TRADITIONAL LECTURE VS. INTERACTIVE TEACHING. 
*JC Mosher, S Hagen, and C Gjerde, Mount Horeb, WI and Madison, WI. University of Wisconsin* 
Abstract 38

11 ADMINISTRATION OF LONG-ACTING INSULIN ANALOG IN PEDIATRIC PATIENTS ADMITTED FOR DIABETIC KETOACIDOSIS Ñ DOES TIMING AFFECT OUTCOMES? 
*ER Howe, L Pesce, and A Comellas, Iowa City, IA. University of Iowa* 
Abstract 39

12 FEASIBILITY AND SUCCESSFUL USE OF A HOME COMPUTER SPREAD-SHEET PROGRAM DESIGNED TO HELP MAKE INSULIN DOSE CALCULATIONS AND ADJUSTMENTS TO INSULIN REGIMENS IN CHILDREN WITH TYPE 1 DIABETES. 
*K Stephens and RP Hoffman, Columbus, OH. The Ohio State University* 
Abstract 40

13 VITAMIN D DEFICIENCY IN CHILDREN EXPOSED TO PRENATAL ALCOHOL. 
*AL Taylor, LE Polgreen, JR Wozniak, and JK Eckerle, Minneapolis, MN. University of Minnesota* 
Abstract 41

14 NATURAL LANGUAGE PROCESSING OF CLINICAL NOTES FOR PROBLEM LIST. 
*P Hemmati, G Melton-Meaux, R Bill, S Pakhomov, and LA Pyles, Minneapolis, MN. University of Minnesota Amplatzer Children's Hospital* 
Abstract 42

15 EMERGENCY ROOM(ER)VISIT DURING THE FIRST MONTH OF LIFE IN AN URBAN INNER CITY POPULATION. 
*R Camacho, G Srinivasan, and H Srinivasan, Westmont, IL and Chicago, IL* 
Abstract 43

16 PRIMARY CARE PROVIDER PREFERENCES FOR CLINIC FOLLOW-UP AFTER EMERGENCY DEPARTMENT VISITS. 
*MA Hendrickson, E Obeya, P Gaillard, and A Wey, Minneapolis, MN. University of Minnesota* 
Abstract 44

17 TMEM35 (TUF1): A NOVEL FACTOR IN PAIN PATHWAYS? 
*BC Kennedy, JD Dimova, JD Dimova, KH Reise, KH Reise, PS Marell, PS Marell, W Von Hohenberg, W Von Hohenberg, JC Gewirtz, JC Gewirtz, PV Tran, and PV Tran, St. Paul, MN and Minneapolis, MN. University of Minnesota* 
Abstract 45

18 AUTISM ON THE RISE: SURVEILLANCE OF PREVALENCE TRENDS BY SCHOOL NURSES. 
*ES Armbrecht and R Maxim, St. Louis, MO. Saint Louis University* 
Abstract 46

19 ARE RADIOLOGIC FINDINGS FOR BONE DISEASE ASSOCIATED WITH THE TIMING OF FRACTURES IN YOUNG CHILDREN? 
*V Tchonang, V Goduguchinta, K Dietz, M Murati, and CL George, Minneapolis, MN. University of Minnesota* 
Abstract 47

20 PECTUS CARINATUM TREATED WITH ORTHOTIC BRACING AS FIRST-LINE THERAPY. 
*EA Berdan, J MacDonald, M Hanlon, L Rogers, BJ Segura, DJ Hess, RD Acton, and DA Saltzman, Minneapolis, MN. University of Minnesota* 
Abstract 48

21 EFFECT OF TOPIRAMATE ON BMI IN SEVERELY OBESE ADOLESCENTS. 
*CK Fox, KL Marlatt, and AS Kelly, Minneapolis, MN. University of Minnesota* 
Abstract 49
22 WHAT'S FOR LUNCH? AN ASSESSMENT OF SCHOOL NUTRITION IN INNER CITY MILWAUKEE.
RM Weigert, Madison, WI. University of Wisconsin-Madison

23 GASTROINTESTINAL SYMPTOMS BEFORE AND AFTER TOTAL PANCREATECTOMY AND ISLET AUTOTRANSPLANTATION: IMPACT OF PANCREATIC ENZYME THERAPY.
MD Bellin, J Crosby, DM Radosevich, S Chinnakotla, TB Dunn, TL Pruett, GJ Beilman, ML Freeman, and SJ Schwarzenberg, Minneapolis, MN. University of Minnesota

24 ABNORMAL CHROMOSOME 6 OR EZR GENE IS POSSIBLY RELATED TO INTESTINAL NECROSIS.
MB Ghbeis, LA Schimmenti, JR Hume, DA Saltzman, and DJ Hess, Minneapolis, MN. University of Minnesota

25 A CHILD WITH WORMS IN STOOL (CASE REPORT).
RN Khasawneh, M Varman, and T Karre, Omaha, NE. University of Nebraska Medical Center

26 LONG-TERM SINGLE CENTER DONOR LYMPHOCYTE INFUSION OUTCOMES SHOW A ROLE FOR DURABLE RESPONSE IN HIGH-RISK PEDIATRIC LYMPHOID MALIGNANCIES.
HP Robinson, M Nugent, P Simpson, C Keever-Taylor, D Margolis, J Casper, and M Thakar, Wauwatosa, WI and Milwaukee, WI. Medical College of Wisconsin

27 COAGULASE NEGATIVE STAPHYLOCOCCUS (CONS) AS A PATHOGEN IN PEDIATRIC URINARY TRACT INFECTIONS (UTI).
CM Ilboudo, B Pahud, V Chadha, U Alon, and R Selvarangan, Kansas City, MO. University of Missouri Kansas City

28 THE KETOGENIC DIET AS AN ENERGY TREATMENT OF A COMPLEX I DEFICIENCY.
CH Andrus and PB Andrus, St. Louis, MO. Saint Louis University

29 LARYNGEAL MASK AIRWAY DEVICE PLACEMENT IN NEONATES.
AA Wanous, A Wey, KD Rudser, and KD Roberts, Blooming Prairie, MN and Minneapolis, MN. University of Minnesota

30 MAST CELL-DERIVED FAS LIGAND PROMOTES ENTEROCYTE APOPTOSIS AND DAMAGES THE GUT MUCOSAL BARRIER DURING EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO).
M Krishnan, A Maheshwari, and C Killingsworth, Chicago, IL. University of Illinois at Chicago

31 SYSTEMIC MATERNAL INFLAMMATION PROMOTES INFLAMMATORY INNATE AND ADAPTIVE IMMUNE RESPONSES TO VIRAL LUNG INFECTION IN NEONATAL AND WEANLING MICE.
D Gleditsch, R Weisert, P Gressens, LP Shornick, and JM Koenig, St. Louis, MO and Paris, France. Saint Louis University

32 ENDOGENOUS ERYTHROPOIETIN LEVELS AND BRAIN INJURY IN PRETERM INFANTS.
NM Fahim, MK Georgieff, and TE Inder, Minneapolis, MN and St Louis, MO. University of Minnesota
33 CANCELLED
THE COMPONENT OF TRUST IN END OF LIFE DECISION MAKING IN THE NICU: PARENT PERSPECTIVES.
RN Kearby, Z Salih, A Torke, P Helft, and J Allen, Avon, IN and Indianapolis, IN. Indiana University School of Medicine
Abstract 61

34 NURSES' AND PARENTS' PERCEPTIONS OF AN OPEN UNIT (OU) POLICY IN A NEONATAL INTENSIVE CARE UNIT (NICU).
KC Voos and N Park, Kansas City, MO. University of Kansas City Missouri
Abstract 62

35 SMALL LEUCINE-RICH PROTEOGLYCANS BIND TGFβ2 IN HUMAN MILK AND LIMIT ITS BIOAVAILABILITY.
K Namachivayam, H Coffing, S Srinivasan, GS Veloo, K MohanKumar, R Jagadeeswaran, and A Maheshwari, Chicago, IL. University of Illinois at Chicago
Abstract 63

36 THE GESTATIONAL AGE OF INDEPENDENT ORAL FEEDING IN PRETERM NEWBORNS.
SM Van Nostrand, V Coraglio, FS Seo, LN Bennett, and JK Muraskas, Chicago, IL and Maywood, IL. Loyola University Medical Center
Abstract 64

37 PULMONARY NITRIC OXIDE EXCRETION IN TRACHEOSTOMIZED AND VENTILATOR-DEPENDENT CHILDREN: A PILOT STUDY.
VR Murthy, W Manimtim, M Norberg, C Lachica, L Gratny, and WE Truog, Kansas City, MO. University of Missouri at Kansas City
Abstract 65

38 NEONATAL LENTICULOStrIATE VASCULOPATHY: CHARACTERIZATION OF 42 CASES.
BI Segel, B McLachlan, J Hernandez, A Vade, J Lim-Dunham, and J Muraskas, Forest Park, IL and Chicago, IL. Loyola University Chicago
Abstract 66

39 A NORMATIVE URINARY METABOLOMIC PROFILE OF CARNITINE IN PREMATURE INFANTS.
MN Kompare, M Hanna, and PD Brophy, Iowa City, IA and Lexington, KY. University of Iowa
Abstract 67

40 TRAINING AND DECISIONS REGARDING RESUSCITATION OF EXTREMELY PREMATURE INFANTS AMONG U.S. PEDIATRIC RESIDENTS AND FELLOWS.
HI Myers, JM Dagle, and T Bahr, Iowa City, IA. University of Iowa Carver College of Medicine
Abstract 68

41 UPREGULATION OF HEPCIDIN EXPRESSION BY LACTOFERRIN ADMINISTRATION TO PRE-WEANLING MICE.
JA Cooper, E Memisoglu, and RE Fleming, St. Louis, MO. Saint Louis University
Abstract 69

42 PARENTAL NICU VISITATION IN LOW BIRTH WEIGHT INFANTS DURING THE FIRST 28 DAYS OF LIFE IN AN INNER CITY HOSPITAL.
S Khairkar, P Rajtar, J Chan, V Geraldo, G Srinivasan, and B Lucherne, Chicago, IL. Sinai Children's Hospital
Abstract 70

43 USING CBC AS A MARKER FOR CLABSI IN THE NICU.
H Miltaha, JH Lam, and MJ Shareef, Maywood, IL Mundelein, IL, and Lombard, IL Loyola University
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HYPOCALVARIA AS AN ISOLATED SKELETAL DYSOSTOSIS.  
JM Scheurer, B Zarmbinski, R Temme, R Tibesar, and NJ Mendelsohn, Minneapolis, MN.  
University of Minnesota  
Abstract 72

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W Ratajczak, W de Lange, and J Ralphe, Madison, WI.  
University of Wisconsin - Madison  
Abstract 73

DISTINCT GROUP EXPRESSION PROFILE OF ENDOTHELIAL PROGENITORS EXPOSED IN UTERO TO GESTATIONAL DIABETES.  
FA Boyle, CM Hocutt, E Blue, and LS Haneline, Indianapolis, IN.  
Indiana University  
Abstract 74

THE ROLE OF ALTERED GENE EXPRESSION IN ENDOTHELIAL COLONY FORMING CELLS FROM INFANTS OF DIABETIC MOTHERS.  
BM Sheehan, EK Blue, ZK Nuss, and LS Haneline, Indianapolis, IN.  
Indiana University School of Medicine  
Abstract 75

25-HYDROXY VITAMIN D LEVELS AND IMMUNE FUNCTION IN PRETERM INFANTS.  
VA Navarrete, B Puppala, RL Donovan, LJ Schweig, K Weedon, and C Wagner, Des Plaines, IL.  
Park Ridge, IL, and Charleston, SC.  
Advocate Children’s Hospital, Park Ridge  
Abstract 76

CORD BLOOD VITAMIN D STATUS IN PRETERM INFANTS.  
AS Vasileff and MB Hershenson, Plymouth, MI and Ann Arbor, MI.  
University of Michigan  
Abstract 77

INTESTINAL ALKALINE PHOSPHATASE ADMINISTRATION DECREASES INTESTINAL PERMEABILITY AND BARRIER DYSFUNCTION THROUGH THE ALTERATION OF TIGHT JUNCTION PROTEINS.  
SG Dillman, NP Heinzerling, SR Welak, K Fredrich, and DM Gourlay, Wauwatosa, WI and Milwaukee, WI.  
Medical College of Wisconsin  
Abstract 78

INTESTINAL ALKALINE PHOSPHATASE ACTIVITY IS DECREASED IN NECROTIZING ENTEROCOLITIS.  
BE Biesterveld, RM Rentea, SR Welak, NP Heinzerling, KM Fredrich, and DM Gourlay, Milwaukee, WI.  
Medical College of Wisconsin  
Abstract 79

ASSOCIATION OF NIL PER ORAL (NPO) DAYS AND ANTIBIOTIC USE WITH THE DEVELOPMENT OF NECROTIZING ENTEROCOLITIS (NEC) IN LOW BIRTH WEIGHT (LBW) INFANTS.  
S Indukuri, A Khan, G Srinivasan, and H Srinivasan, Westmont Il and Chicago, IL.  
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1 ALLOGENEIC T CELLS INCREASE RELIANCE ON FATTY ACID METABOLISM, WHICH ALLOWS FOR SELECTIVE METABOLIC TARGETING

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Purpose: Bone marrow transplantation (BMT) remains a curative procedure for children with intractable cancer and inherited blood disorders. But BMT is a highly morbid procedure due to complications such as graft-versus-host disease (GVHD), where donor T cells attack and destroy host tissues. Careful metabolic analysis of the T cells that cause GVHD allows the discrimination of a pathogenic phenotype and the potential for future targeted therapies.

Methods: We investigated the metabolism of T cells that cause GVHD using a parent into F1 murine BMT model. Donor T cells were isolated at several points after transplantation and analyzed by a variety of methods including flow cytometry, ex vivo oxidation and protein analysis via western blotting. Finally, fatty acid (FA) oxidation was inhibited in multiple models to assess key functional pathways. Results: Allogeneic T cells dramatically increased FA metabolism compared to pre-transplant donor cells. FA transport increased in allogeneic T cells, as measured by uptake of a fluorescent FA analog, (44.3% vs. 0.7%, p < 0.003). This increased FA transport correlated with increased fat oxidation in these same cells (2.84 vs. 0.7 x10^5 cpm, p < 0.001). FA oxidation could be pharmacologically inhibited by etomoxir (Eto) and in vivo Eto treatment decreased donor allogeneic T cells (5.4 vs. 3.4 x10^5, p = 0.01) and improved both weight loss and clinical score in a clinically relevant model of GVHD (average clinical score 3.5 vs. 1.4, p < 0.0001, PBS vs. Eto respectively). Finally, changes in FA metabolism were specific to allogeneic T cells, as T cells proliferating after a syngeneic transplant (no GVHD) minimally up-regulated FA transport (45.6% vs. 14.6%, p = 0.004, allogeneic vs. syngeneic) and were not susceptible to treatment with etomoxir (donor T cell number 9.3 vs. 8.8 x10^4, p = 0.67, PBS vs. Eto).

Conclusions: During GVHD, allogeneic T cells adapt to higher energy demands by up-regulating fat metabolism and thus become bioenergetically dependent upon FA oxidation. This property is specific to allogeneic T cells and can be leveraged to selectively eliminate T cells that cause disease while preserving normal immunity. These findings not only change the paradigm for activated T cell metabolism, but also suggest a potential avenue for future therapies against GVHD and other T cell-mediated diseases.

2 PHYSICAL ACTIVITY AND CARDIOMETABOLIC RISK FACTORS IN CHILDHOOD CANCER SURVIVORS


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A growing number of childhood cancer survivors (CCS) are at high risk of developing treatment-related late effects, including cardiovascular disease and diabetes. Late effects can be exacerbated by the low levels of physical activity (PA) commonly observed in CCS and may be mitigated by greater PA. The relationship between PA and cardiometabolic risk (CMR) has not been described in CCS; therefore, we examined associations between PA and CMR factors in 319 CCS and 208 controls aged 9-18 years. The Kruskall-Wallis test, analysis of covariance (continuous factors), and logistic regression were used to detect differences in CMR factors between PA tertiles. No significant differences were noted for triglycerides, cholesterol, blood pressure, fasting glucose, flow-mediated dilation, carotid cross-sectional compliance and distensibility, or carotid intima-media thickness. For male CCS, percent fat mass (PFM), subcutaneous fat, and insulin resistance (independent of PFM) were lower in those reporting high PA versus low PA (p<0.05). For female CCS, waist circumference, PFM, subcutaneous fat, and visceral fat were lower in those reporting high PA versus low PA (p<0.05). Differences were nonsignificant in controls. Our results demonstrate the role of PA in maintaining a healthier bodyweight, especially lower levels of body fat, in CCS. PA may also help males maintain insulin sensitivity. These associations appear stronger in CCS than in healthy children. PA-associated CMR benefits, especially if sustained into adulthood, may reduce the risk and severity of late effects in CCS. Our results also support the importance of PA interventions in this population. Supported by [NCI/NIDDK R01CA113930, NIH T32 CA099936, NIH K05 CA157439, and Children’s Cancer Research Fund Hodder Chair]
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PHLEBOTOMY INDUCED ANEMIA ALTERS HIPPOCAMPAL GENE EXPRESSION IN NEONATAL MICE.
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Background: Anemia is common in preterm infants due to a combination of anemia of prematurity, and anemia induced by frequent blood sampling (ie, phlebotomy induced anemia (PIA)). Since most of total body iron is found in blood, PIA may contribute to total body and, more specifically, brain iron deficiency (ID). Neonatal rodent models of dietary ID anemia have altered hippocampal gene expression, and abnormal learning/memory behavior. However, it is unknown whether PIA causes brain iron deficiency, and whether it affects hippocampal function and development. Purpose: Determine the effects of PIA on hippocampal mRNA expression using qPCR. Methods: Postnatal day (P)3 mice (brain developmental equivalent of a 26 week gestational age infant) underwent daily phlebotomy by facial venipuncture to achieve a hematocrit <25%. This degree of anemia was maintained by daily phlebotomy until P14, when hippocampal tissue was harvested. Control mice were non-phlebotomized littermates. The expression of mRNA relative to controls was determined by qPCR (n=6). Results: Anemic mice had a lower hematocrit relative to controls 20 +/- 2% vs 32 +/-3%, p<0.05. Conclusions: At hematocrit levels similar to those often seen in preterm neonates, PIA in neonatal mice induces hippocampal gene expression consistent with tissue ID and hypoxia. Molecular markers of synaptic plasticity, cytoskeletal structure, mTOR signaling, and inflammation are affected. PIA may be a potentially modifiable cause or contributing factor for the hippocampally-mediated learning and memory deficits in preterm neonates. to hippocampal ID and risk for learning and memory deficits in preterm infants.

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HEMATOPOIETIC ALTERATIONS IN GESTATIONAL IRON DEFICIENCY
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Background: Iron is vital for cell proliferation; therefore, severe gestational iron deficiency (ID) can impair fetal erythropoiesis. However, little is known about the susceptibility of other fetal hematopoietic cell types to ID. In humans, ID increases erythropoietin production, which has been shown increase both red cells and platelets. Additionally, gestational ID may permanently alter the production of hematopoietic cell profiles, leading to future clinical implications in adult life. In newborn rats, we hypothesized that gestational ID stimulated adaptations in all hematopoietic cell types. Methods: The University of Wisconsin – Madison Animal Care and Use Committee approved this protocol. From gestational day 2 to postnatal day (P) 7, dams were fed either iron sufficient (IS) diet (198mg Fe/kg) or ID rat diet (<6mg Fe/kg diet) with the biological lactating dam nursing the pups. Beginning at P7, the IS diet was fed to all dams. At P20, pups were weaned to the IS chow diet. Blood was collected between P2-P10 and again from P30-P45 for hemoglobin, zinc protoporphyrin/heme (ZnPP/H), reticulocytes, white blood count, platelet count and mean platelet volume. Results: From P2 to P10, hemoglobin levels were ID were 20-25% lower than IS (p<0.01 in ID). Erythrocyte iron incorporation was poorer in ID than in IS as measured by ZnPP/H ratio; ZnPP/H was 2-3 fold higher in ID (p<0.01). In addition, reticulocyte production was suppressed immediately after birth (p<0.004) but equalized before P7. Reticulocytes were indirectly related to ZnPP/H in the first 10 days (R^2=0.15, p=0.005). White blood counts were 28% lower at birth in ID and platelet counts were 25% lower at birth (p<0.003 for both). Platelets were directly related to reticulocytes in the first 10 days (R^2=0.31, p=0.0001). However, mean platelet volumes in ID were higher throughout the first 10 days (p<0.05), supporting the presence of immature platelets. After weaning, white blood counts and platelets in the ID rats remained lower than IS (p<0.003). Conclusion: Gestational ID caused anemia and long-term hematopoietic programming alterations in red, white and platelet cell types. Maternal complications during pregnancy often impair fetal iron delivery, thus it is important to better understand how fetal iron depletion impacts all hematopoietic cell types.
Prenatal choline supplementation reverses the downregulation of hippocampal gene expression resulting from gestational iron deficiency

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Background: Early-life iron deficiency results in long-term alterations in the expression of genes involved in synaptic plasticity, which may contribute to learning and memory deficits observed in adult, formerly iron deficient (ID) rats. Choline is an essential nutrient that is critical for early brain development. We have previously shown that prenatal choline supplementation can improve recognition memory in formerly ID animals. However, it is unclear whether the beneficial effects of choline supplementation on cognitive function correspond to similar changes in gene expression in the hippocampus. The current study assessed the effects of prenatal choline supplementation on hippocampal expression of genes critical for neuronal differentiation and synaptic plasticity in rats following gestational iron deficiency. Due to the long-term effects of early-life iron deficiency on gene expression, we sought to determine whether prenatal choline supplementation could offset the effects of iron deficiency at different time points during infancy and adulthood. Sprague-Dawley pregnant dams were given an ID diet from gestational day (G) 2 to postnatal day (P) 7, and then placed on an iron sufficient (IS) diet. Half the dams in each diet group were given choline supplementation from G11 to G18 creating 4 treatment groups: IS, ID, iron sufficient supplemented with choline (ISC), and iron deficient supplemented with choline (IDC). Hippocampi were dissected from P15, P65, and P120 rats for quantitative RT-PCR (TaqmanTM) analysis of mRNA expression. Consistent with previous findings, ID pups and formerly ID adult rats showed reduced expression of genes involved in synaptic plasticity and neurogenesis, such as BDNFIII, EGR1 and IGF, relative to IS controls. Prenatal choline supplementation increased the expression of these genes in formerly ID animals at P65 and P120. These findings suggest that prenatal choline supplementation may be able offset the long-term disruption in gene expression resulting from early life iron deficiency. This protective effect may contribute to the beneficial effects of choline supplementation on recognition memory.

PBX1/2 are required in lung mesenchyme for normal postnatal lung development

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Background: Congenital diaphragmatic hernia remains among the most common, lethal birth defects. Despite improvements in the medical and surgical management of patients with diaphragmatic hernia, the genetic basis of the condition remains unclear. A current hypothesis is that a core group of genes is involved in both the development of the diaphragm and the development of the lung and pulmonary vasculature. Mutation of these genes or disruption of their downstream signaling cascades is likely responsible for the severe pulmonary hypoplasia and pulmonary hypertension that affects a subset of patients with congenital diaphragmatic hernia. Recently, a group of genes was identified as playing an important role in development of the diaphragm. Pre–B-cell leukemia transcription factor 1 (Pbx1) was included in this list and its global deletion in mice results in diaphragmatic hernia. Pbx1 is conserved in humans and plays an important role in the development of several tissues, however the role of Pbx1 in lung and pulmonary vascular development has not been explored. Objective: To study the role of Pbx1/2 in the developing lung mesenchyme, focusing on postnatal alveologenesis and development of the pulmonary vasculature and vascular smooth muscle. Method: Using a conditional knockout approach in a mouse model, we have eliminated the expression of Pbx1/2 in the developing lung mesenchyme. We have analyzed the phenotype at late embryonic and early postnatal stages and studied the effect of loss of PBX1/2 on the developing lung epithelium, airway smooth muscle, vasculature, and vascular smooth muscle. Results: Loss of PBX1/2 in the developing lung mesenchyme results in mice that have normal embryonic lung development, but fail to undergo postnatal lung maturation. These mice die within the first 21 days of life and have a simplified lung architecture that has failed to undergo normal postnatal alveologenesis. Pbx mutant mice also have evidence of right heart failure with right ventricular hypertrophy and right atrial enlargement. Conclusion: PBX1/2 is required for normal postnatal lung alveologenesis and loss of PBX1/2 results in simplification of the postnatal lung and evidence of pulmonary vascular disease.
EFFECT OF MATERNAL HIGH FAT DIET AND LATE GESTATIONAL DIABETES MELITUS ON FETAL LUNG DEVELOPMENT

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Background: Maternal diabetes and obesity are both associated with increased circulation of metabolic fuels such as glucose and lipids that can cross the placenta. While it is known that children of diabetic mothers are more likely to suffer from newborn respiratory distress and that fatty acids regulate lung growth, little is understood about how glucose- and fatty acid-induced fetal programming of lung development occurs and if these events function in parallel or independent pathways. Objectives: Investigate the manner in which gestational diabetes and maternal high fat consumption adversely affect offspring pulmonary development. Design and Methods: A rat model was developed that simulates the human conditions by pharmacologically inducing gestational diabetes with streptozotocin in pregnant dams sustained on a high fat diet to study fetal lung development. Physiological (cardiopulmonary echocardiogram, respiratory mechanics), histopathological (mean chord length, alveolar cell markers), and molecular (protein, fatty acid status) outcomes were determined in offspring of diabetic mothers at birth and after 3 and 10 weeks of age. Results: Offspring of diabetic mothers on a high fatty acid diet had pulmonary hypertension at birth followed by decreased pulmonary compliance and hysteresis with increased elastance and respiratory system resistance. Glucose-dependent pulmonary expression of thioredoxin interacting protein (Txnip), a negative regulator of alveolar growth was increased in offspring of diabetic mothers yet was attenuated by a maternal high fat diet. Conclusions: Altered expression of signaling molecules, such as Txnip, with known responsiveness to glucose and fatty acids that regulate alveolar epithelial and vascular growth may be a primary molecular target responsible for the observed pulmonary pathologies in children of diabetic mothers.

SURVIVAL AND PULMONARY MORBIDITIES FOLLOWING PROLONGED PREMATURE RUPTURE OF MEMBRANES PRIOR TO 24 WEEKS GESTATION.

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Background: Prolonged premature rupture of membranes (PPROM) before 24 weeks gestation was associated with high mortality in the 1990s (35-55%). Aggressive use of high frequency ventilation, nitric oxide, and surfactant may have improved survival for preterm infants affected by PPROM.

Objective: To measure survival and pulmonary morbidities, including chronic lung disease, pulmonary hypertension, and air leak syndrome, following preterm birth complicated by PPROM. Methods: A retrospective case-control analysis of 184 inborn infants (63 cases, 121 controls) born between 2002 and 2012 at a tertiary care facility with a level 4 neonatal intensive care unit was performed. Mothers of cases experienced ≥ 1 week of ruptured membranes prior to 24 weeks gestation (Mean duration= 6.80±4.29 weeks). Mothers of controls experienced <24 hours of ruptured membranes. Cases were matched consecutively 1:2 with controls for gestational age at birth (±1 week), sex, and antenatal corticosteroid exposure. Results: Despite PPROM before 24 weeks gestation, there was no difference in survival between cases (89%) and controls (93%, p=0.40). However, pulmonary hypoplasia was identified in nearly half of cases (49%) versus 1% of controls (p<0.001), pulmonary hypertension was present in 29% of cases compared to 5% of controls (p<0.001), and air leak occurred in 22% of cases versus 3% of controls (p<0.001). High frequency ventilation was used more often in cases (78%) than controls (54%, p=0.002) as were surfactant (cases 92%, controls 78%, p=0.006) and nitric oxide (cases 43%, controls 14%, p=0.001). Chronic lung disease was common in both cases (73%) and controls (63%, p=0.18). Conclusion: There was no significant difference in survival of preterm infants with membranes ruptured ≥ 1 week prior to 24 weeks gestation and preterm infants with membranes ruptured <24 hours when matched for gestational age at birth. However, significant pulmonary morbidities and intensive medical care were more common following PPROM. In the era of high frequency ventilation, nitric oxide, and surfactant, we speculate that the use of these respiratory therapies may have improved survival following high-risk PPROM, and we recommend that antenatal counseling include current center-specific survival data.
CHARACTERIZATION OF A NOVEL QUORUM QUENCHING PROTEIN PRODUCED BY MRSA

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Purpose: Staphylococcus aureus is a versatile pathogen that causes a broad spectrum of acute and chronic infections. Antibiotic resistance in this pathogen is an ongoing concern, and over the past decade methicillin-resistant S. aureus (MRSA) strains have spread to the community, infecting otherwise healthy children. Rates of MRSA infections in children are rising, raising concern over treatment options. Many bacteria control cellular events using cell-to-cell communication mechanisms, a phenomenon called quorum-sensing. We recently discovered that MRSA strains produce a novel protein that has the ability to inhibit quorum-sensing in other bacteria. Our overarching hypothesis is that SqqA is a virulence factor produced by MRSA strains that facilitates colonization and pathogenesis. Disruption of quorum-sensing system function in other commensal bacteria could give MRSA a competitive advantage. Methods/ Results: The Horswill lab has generated a fluorescent S. epidermidis reporter strain to track quorum-sensing system activity. Addition of MRSA supernatants to this reporter strain inhibit S. epidermidis quorum sensing. To eliminate the possibility that autoinducing peptide (AIP) as the inhibitor, a MRSA mutant unable to produce AIP was tested using the S. epidermidis reporter strain. This mutant also inhibited reporter fluorescence, indicating the presence of an additional inhibitory molecule. To identify the inhibitor, we used molecular weight cutoffs, thermostability testing and proteinase K treatments, which indicated the factor is a protein. Next, spent media from MRSA was fractionated using a cation exchange column, and the collected fractions were tested against the S. epidermidis reporter. Those fractions found to be most inhibitory were sent to College of Medicine Proteomics facility for identification. Mass spectrometry analysis indicated that SqqA was the protein of interest. A MRSA transposon mutant strain in the SqqA gene was tested and culture supernatants lost ability to inhibit the S. epidermidis reporter. Further the protein was purified and found to inhibit the S. epidermidis reporter. We also generated rabbit polyclonal antibody to SqqA, and the antibody specifically detects SqqA in the spent media of MRSA strains. Conclusions: The SqqA gene product was identified as inhibitory to the S. epidermidis quorum sensing system. Importantly, SqqA was shown to function independent of AIP production. The SqqA protein was identified by bioactivity-guided fractionation of MRSA spent media, and a transposon mutant in the SqqA gene lost the ability to inhibit the S. epidermidis reporter, confirming the assignment. Finally, purified SqqA inhibits S. epidermidis quorum sensing as predicted. Future Directions: Our preliminary data demonstrate that MRSA strains produce a novel quorum quenching protein called SqqA. However, we do not know the distribution and production of this protein in MRSA strains. Nor do we understand the mechanism by which SqqA inhibits quorum sensing. With our SqqA antibody, we will continue to work on answering these questions. It is our hope that by understanding MRSA interactions with its competitors we can improve management and treatment of infections by this ubiquitous pathogen.

NEONATAL NEUTROPHILS STIMULATED WITH GROUP B STREPTOCOCCUS INDUCE A PRO-INFLAMMATORY BIAS IN CD4+ T CELLS AND T REGULATORY CELLS.

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Background: Group B Streptococcus (GBS), a common agent of life-threatening neonatal sepsis and meningitis, is associated with inflammatory co-morbidities. Enhanced neonatal susceptibility to infection has been attributed to immature adaptive immunity associated with a Th2-type bias. However, new evidence suggests that impaired immune homeostasis related to innate-adaptive immune interactions may play a significant contributory role. We reported that GBS-stimulated neonatal neutrophils (PMNs) promote T regulatory (Treg) cell migration (Heithaus, 2011) and that Tregs convert to Th1/Th17 phenotypes in an inflammatory milieu (Ye, 2011). Objective: We designed studies to test our hypothesis that GBS-stimulated neonatal PMNs can bias the differentiation program of CD4+ T cells or the conversion of Treg cells towards Th1/Th17 phenotypes, potentially augmenting inflammatory responses. Methods: Neonatal (CB) or adult (AD) PMNs were stimulated with GBS (COH1), and the resulting supernatants (PMN-CM) or intact stimulated PMNs were co-cultured with purified CD4+ T cells or Treg cells. T-specific phenotypes in target cells were assessed by measuring intracellular cytokines (IFN-γ, IL-4, Th17) or the transcription factor, Foxp3, using multicolor flow cytometry, and by determining Th-specific transcription factor gene expression with real-time PCR. Results: We observed that: 1) CB PMN-CM promoted greater CD4+ expression of phenotypic markers for Th1, Th17, Treg cells vs. AD PMN-CM. 2) Directive effects of CB-PMN CM on Th-type immunity were dose-dependent and did not occur without GBS stimulation; 3) CB PMN-CM increased the proportion of CD4+Foxp3+ cells that co-expressed IFN-γ (Th1) and/or IL-17 (Th17); 4) Neither direct contact between GBS-stimulated PMN and CD4+ T cells nor incubation of CD4+ T cells with GBS alone influenced Th-type differentiation; 5) CB PMN-CM promoted Th1- and Th17-type immunity in CD4+CD25+ but not CD4+CD25- T effector cells. Conclusion: These novel studies show that GBS-stimulated neonatal PMNs induce CD4+
T cell differentiation and Treg cell conversion towards inflammatory Th1 and Th17 phenotypes. Our data suggest that developmental alterations of innate-adaptive immune cross-talk mechanisms contribute to the inflammatory complications observed in GBS-infected neonates. Studies to characterize the mechanisms underlying these processes are underway. Funded in part by NIH R21AI094478 (JMK, GP) & Saint Louis Cord Blood Bank.

**MWSPR PLENARY SESSION II**

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**EXCESS GLUCOSE EXAGGERATES AND BETA-HYDROXYBUTYRATE PROTECTS AGAINST HYPOGLYCEMIA INDUCED BRAIN INJURY IN DEVELOPING RATS.**

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**Background:** Hypoglycemia (HG) in newborn infants and children is typically treated using 10% dextrose (D). However, 10% D does not ameliorate brain injury. Whether rapid correction using 50% D or an alternative substrate, such as beta hydroxybutyrate (BHB) is protective unknown. In adult rats, excess glucose worsens HG-induced neuronal injury by poly(ADP ribose)polymerase-1 (PARP-1) overactivation and release of apoptosis-inducing factor (AIF). Whether a similar effect occurs during development is not known. **Objectives:** To compare the neuroprotective efficacy of 50% D and BHB with 10% D on HG-induced neuronal injury in developing rats.

**Design/Methods:** Insulin-induced HG was produced on postnatal day (P) 21 or P28, HG was terminated 180 min later using 10% D (HG-10 group) or 50% D (HG-50 group) in Experiment 1, and using 10% D or BHB (HG-BHB group) in Experiment 2 (N=6-9). Neuronal injury was determined 24 hr later using Fluoro-Jade B (FJB) histochemistry. In experiment 1, PARP-1 and AIF mRNA and protein expressions were determined. **Results:** The blood glucose (mean±SEM, mg/dl) levels were comparable in the HG-10 (36.0±4.2), HG-50 (36.2±3.5), and HG-BHB (39.3±3.5) groups. FJB stained (FJB+) cells reflecting injured neurons were present in all the HG groups. In Experiment 1, relative to the HG-10 group, more FJB+ cells were present in the HG-50 group (53±2 vs 90±19, p<0.05). There was greater upregulation of Parp1 (34% vs 17%) and Aif (24% vs 12%) transcripts (p<0.05), and PAR (132% vs 123%) and AIF (23% vs 2%) protein expressions in the HG-50 group, than the HG-10 group. In experiment 2, fewer FJB+ cells were seen in the HG-BHB group, relative to the HG-10 group (20±12 vs 74±17, p<0.05). **Conclusions:** HG caused neuronal injury in the developing cerebral cortex. Contrary to our expectation, rescue with 50% D worsened injury, whereas rescue with BHB was neuroprotective. Greater upregulation of PARP-1/AIF system in the HG-50 group suggests that oxidative stress during glucose reperfusion may have worsened injury in this group. Better neuroprotection with BHB administration suggest the importance of considering alternative substrates for optimizing treatment of HG during development.

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**IUGR ALTERS THE REGIONAL VULNERABILITY TO HYPOGLYCEMIA IN THE NEONATAL RAT BRAIN**

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**Background:** Intrauterine growth restricted (IUGR) infants are at increased risk for cognitive, motor and intellectual deficits as children and adults. The nature of the deficits suggests that specific brain regions (i.e. hippocampus (HPC) and cerebral cortex) may be particularly vulnerable relative to other brain regions. The mechanisms for the region-specific vulnerability are not known. Infants affected by IUGR are at increased risk of neonatal hypoglycemia (HG). Animal studies demonstrate that in normally grown neonatal rats, the cerebral cortex is more affected than other brain regions by acute HG. It is unknown whether IUGR also alters this regional specific vulnerability to HG. **Objective:** To determine whether regional variations exist in response to HG in the developing IUGR brain. **Methods:** IUGR was induced through bilateral uterine artery ligation on gestational day 19 (term = 21 days). On postnatal day (P)14, insulin-induced HG (blood glucose <40mg/dl for 240 min) was performed in IUGR (IUGR/HG, n=5) and control (C/HG, n=5) rat pups. C/C (n=4) and IUGR/C (n=4) pups received an equivalent dose of normal saline. Blood glucose and ketone values were measured at baseline and glucose was measured every 30 minutes. Neuronal injury in the brain regions was quantified on P15 using FluoroJade B (FJB) histochemistry, and groups were compared using student’s t test. **Results:** IUGR rats weighed less at birth (4.5±0.1 g vs. C 5.7±0.2 g, P<0.001). Blood glucose at baseline and severity of HG were similar. Baseline ketone values were higher in IUGR (2.0±0.21 mmol/L vs. C 1.33±0.04 mmol/L, P<0.05). There were fewer FJB+ cells in the cerebral cortex of IUGR/HG (18.4±2.5 vs. C/HG 90.4±16.8 P<0.05); however, there was a trend towards more FJB+ cells in the HPC of IUGR/HG (5.2±1.2 vs. C/HG 2.0±0.9, P<0.07). FJB+ cells were absent in both control groups. **Conclusion:** In the developing IUGR rat brain, the pattern of hypoglycemia-induced injury (Cortex>HPC) is similar to normally grown rats. However, the severity of injury was reduced in the cerebral cortex,
and increased in the HPC. We speculate that adaptations, such as enhanced production and delivery of alternative substrates (e.g., ketones), prioritize the limited resources to the cerebral cortex in IUGR.

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DEVELOPMENTAL CHANGES AND EFFECT OF HYPOGLYCEMIA ON BRAIN REGIONAL ANTI-OXIDANTS IN RATS.

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Background: Ascorbic acid (AA), α-tocopherol (AT), and glutathione (GSH) are major antioxidants (AO) in the brain. The vulnerability to oxidative stress (e.g., during hypoglycemia [HG]) varies among the brain regions and postnatal age in humans and rats. The developmental changes, as well as the effects of HG, on AO levels in the brain regions have not been comprehensively studied. Objective: To determine the influence of postnatal age on AA, AT and GSH levels in the brain regions during normal development and after acute HG in rats. Methods: Brains were harvested from postnatal day (P)7 and P14 (developing), and P60 (adult) male rats (n=6-7). Acute HG of equivalent severity and duration (blood glucose [mg/dl], 26 ± 2 P14; 30 ± 2 P60 for 3h) was induced in separate groups of P14 and P60 rats (n=6), and the brains were harvested. AA, AT and GSH levels in olfactory bulb, cerebral cortex, hippocampus, striatum, cerebellum, hypothalamus, midbrain, pons and spinal cord were determined using HPLC. Results: Postnatal age affected all three AOs in all the brain regions (p<0.001). AO levels were 100-600% higher at P7 than P14 and P60 (P7>P14>P60, p<0.01) with few exceptions. An anterior to posterior regional decrease was present at P14 and P60, but not at P7. Postnatal age also had an effect on regional AOs post-HG. None of the AOs was altered at P14. A differential effect was seen at P60: no changes in AT, a 17% decrease in AA only in the hippocampus, and 12-22% decrease in GSH in all the regions, except hypothalamus (p<0.02). Conclusions: Postnatal age influenced all three AO levels in the brain regions. Higher AO levels at P7 and P14 suggest the potential for oxidative stress during the metabolically active period of neurodevelopment. The age-related and the anterior to posterior regional decrease in AOs likely reflects the parallel changes in the neuron:glia composition of the developing and mature brain regions. The differential effect of HG on P14 and P60 parallels the known vulnerability to HG injury at these ages (P60>P14). A global decrease in GSH with relative sparing of AA and AT post-HG indicates preferential involvement of GSH in at P60.

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DEVELOPMENTAL PROGRAMMING OF CARDIOMYOCYTE METABOLISM IN OFFSPRING OF DIABETIC MOTHERS

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Purpose: Diabetes and obesity are escalating at epidemic proportions; these conditions extend beyond the mother to detrimental, lasting effects on the developing fetus. Offspring of mothers with diabetes (ODM) and/or obesity are at increased risk of cardiovascular disease at birth, continuing throughout life. The presumed mechanism for this risk from mother to fetus is through fuel mediated fetal programming. Alteration in cardiomyocyte substrate metabolism is associated with increased oxygen consumption, poor energy efficiency, and heart failure in adults. The effect of fetal exposure to excess maternal circulating fuels on cardiac fuel metabolism and heart function in the newborn offspring is unknown. Therefore, the goal of this study is to determine the effect of a maternal high-fat diet, in the presence or absence of maternal diabetes, on the developmental programming of cardiac metabolism in cardiomyocytes of offspring. Methods: Sprague Dawley rats were randomized to controlled (CD) diet or high-fat (HF) diet for 28 days prior to breeding and throughout the study. All protocols were approved by the IRB. At gestational day 14, confirmed pregnant dams were further randomized to receive citrate buffer (CB) or streptozotocin (STZ) to induce diabetes. On newborn day 1 (NB1), pups from the following groups were analyzed: Normal controls (CD-CB), diabetic affect (CD-STZ), diet affect (HF-STZ) and combined affect (HF-STZ). Metabolic fuel efficiency was analyzed using Seahorse real-time extracellular flux analyses for aerobic respiration and glycolysis, with and without the presence of insulin, on primary cardiomyocyte cultures from the aforementioned NB1 pups. Variability between the groups was compared using ANOVA with a p-value of 0.05. Results: NB1 cardiomyocytes from HF-STZ mothers showed a significant decrease in maximal aerobic respiration capacity and a 2-fold decrease in reserve capacity. In comparison to CD-CB, in CD-STZ and HF-CB maximal aerobic capacity was not statistically different. Offspring exposed to maternal diabetes (CD-STZ) or high-fat diet (HF-CB) have a 1.6 and 2.3 fold increased capacity for glycolysis compared to controls (CD-CB). HF-STZ was not statistically different from CD-CB. Inner mitochondrial proton leak increases in offspring exposed to maternal diabetes (CD-STZ) in the presence of insulin. Conclusions: Maternal high-fat diet, in the presence of maternal
diabetes, reprograms cardiomyocyte metabolism in the developing heart of offspring. The shift in metabolic preference results in inefficient ATP production. In addition, the inability to metabolize glucose efficiently suggests cardiac insulin resistance and increased oxygen consumption associated with decreased cardiac efficiency.

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MATERNAL HIGH FAT DIET AND DIABETES INCITES LIPID DEPOSITION IN THE DEVELOPING HEART OF OFFSPRING

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Background: Gestational diabetes (GDM) and maternal obesity are both associated with excess circulating fuels that exert adverse effects on a developing fetus. GDM complicates 18% of pregnancies; nearly 35% of women at child-bearing age are obese. Both conditions increase the risk of cardiovascular disease in the offspring. Preventative measures focus on glucose control; however women with normoglycemia have affected infants, implicating other risk factors including circulating maternal lipids. **Objective:** To establish the effects of high-fat diet in the presence or absence of diabetes on the developing neonatal heart through histopathological evaluation of lipid deposition in newborns (day of life 1). **Methods:** Female rats were fed high fat (HF) or control diet (CD) for 28 days before mating and throughout pregnancy. On gestational day 14, dams were given either citrate buffer (CB) control or streptozotocin (STZ) to induce diabetes. Thereafter, hyperglycemia was partially controlled with twice daily sliding scale insulin. Hearts were harvested from 1 day old offspring from the following four maternal groups: Normal controls (CD-CB), diet affect (HF-CB), diabetes affect (CD-STZ), or combined affect (HF-STZ). Neonatal heart sections were stained for lipid droplets (frozen, 10µm) with Oil-Red-O and hematoxylin. Lipid droplets were quantified by point counting using the Nikon 90i microscope, 25 µm grid, and NIS-Elements software. Lipid droplets were compared between groups and regions within the heart (anterior wall, septum, outer wall, and posterior wall) using ANOVA and two-tailed t-tests for dietary, drug, and interaction differences. **Results:** Maternal HF diet and diabetes increased lipid deposition in the developing heart (CD-CB=7.3±1.9, n=14; CD-STZ=17.0±5.4, n=14; HF-CB=28.9±7.3, n=16) and the combined affect was not different than diabetic effect alone (HF-STZ=31.6±5.0, n=20). There was not a regional difference within groups; however, the high fat groups demonstrated significantly more lipid deposition in the outer wall, septum, and anterior wall (p<0.05). Lipid deposition increased in proportion to maternal TG levels and neonatal insulin levels. Clinically, lipid deposition resulted in cardiac hypertrophy, diminished systolic function and increased death rates. **Conclusions:** High-fat diet and gestational diabetes independently increase lipid deposition in neonatal heart tissue, suggesting that a low-fat diet during pregnancies complicated by diabetes or obesity may decrease the risk for cardiovascular disease in offspring.

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PEDIATRIC NONSYNDROMIC THORACIC AORTIC ANEURYSM: CLINICAL STRATIFICATION AND IMPACT OF EARLY MEDICAL THERAPY

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**Background:** Thoracic aortic aneurysm (TAA) is a subclinical disease associated with sudden cardiac death. Aortic dissections result in ~40,000 deaths per year in the US. Connective tissue disorders such as Marfan syndrome (MFS) are characterized by TAA, which has been shown to improve with beta blocker (BB) or angiotensin receptor blocker (ARB) therapy. The spectrum of phenotype that exists in pediatric nonsyndromic TAA, however, is not well described, and the impact of BB or ARB therapy is unknown. We hypothesized that: 1) BB or ARB therapy decreases TAA progression and 2) there are non-cardiovascular phenotypes associated with TAA severity in nonsyndromic TAA. **Methods:** This is an observational study of patients of age ≤21 years old with nonsyndromic TAA evaluated in cardiovascular genetics clinic from July 2010 to January 2013. TAA was defined as aortic root and/or ascending aorta z-score greater than +2 by echocardiography. Patients with clinical or molecular diagnosis of a genetic syndrome such as MFS were excluded. Longitudinal echocardiographic studies were reviewed. Repeated measures analyses were performed to evaluate the impact of medical therapy on TAA and phenotype associations with TAA severity. **Results:** A total of 69 patients with TAA were identified. The median age was 13.9 years (IQR 9.7 to 16.6), and 60 (87%) patients were male. There were 45 patients (60%) with aortic root z-score > +3. The mean z-score was lower in the no therapy group than in the group starting BB or ARB therapy (2.6 vs. 3.4, p<0.001). Patients on BB had significant reduction in the rate of aortic growth (p=0.05) while ARB did not have a significant impact (p=0.25). The majority of patients had at least one identified non-cardiovascular abnormality: skeletal (n=45, 69%), craniofacial (n=37, 54%), ocular (n=22, 34%), and cutaneous (n=13, 20%). Increased rate of aortic dilation was associated with presence of craniofacial (p<0.0001) and ocular (p=0.0012) abnormalities.
Conclusions: These results indicate that BB therapy reduces the rate of aortic dilation in a population of children with nonsyndromic TAA. Non-cardiovascular features were frequent with some features being associated with a more severe aortic phenotype. These findings suggest that timely diagnosis of TAA and early initiation of therapy may reduce disease progression and that comprehensive genetic evaluation may be useful for prognosis and medical therapy decisions.

17 MACROPHAGES AND REDUNDANTLY-ACTING Fc GAMMA RECEPTORS DRIVE AUTOIMMUNE VALVULAR CARDITIS
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Background: Arthritis and valvular carditis co-exist in several human rheumatic diseases, including systemic lupus erythematosus, rheumatic fever, and rheumatoid arthritis. The immune mechanisms by which these diseases provoke inflammation of the joints and cardiovascular system remain poorly understood. K/BxN T-cell receptor transgenic mice develop spontaneous, autoantibody-associated arthritis and valvular carditis. The common Fc receptor gamma signaling chain (FcγRγ) is required for carditis in K/BxN mice. FcγRγ pairs with numerous receptors in a variety of cells. Here we sought to identify the FcγRγ-associated receptors and FcγRγ-expressing cells that mediate valvular carditis in this model. Methods and Results: We bred K/BxN mice lacking the genes encoding the activating Fc gamma receptors (FcγRI, III, and IV) and assessed for valvular carditis via standard hematoxylin and eosin staining. Genetic deficiency of only one of the activating FcγRs did not prevent carditis, whereas deficiency of all three activating FcγRs did. Further analysis demonstrated that FcγRIII and FcγRIV were the key drivers of valve inflammation; FcγRI was dispensable. Complement component C3 was also not required. Reciprocal bone marrow transplantation studies revealed that Fcγ expression by radioresistant host cells was critical for valvular carditis to develop. Immunohistochemical analysis and cellular depletion studies pointed to macrophages as the key candidate FcγR-expressing effectors of carditis. Mice were bred and maintained under Institutional Animal Care and Use Committee-approved protocols at the University of Minnesota. Conclusions: FcγRIII and FcγRIV acted redundantly to promote valvular carditis in the K/BxN mouse model of systemic autoantibody-associated arthritis. Macrophage depletion reduced the severity of valve inflammation. These findings suggest that pathogenic autoantibodies engage FcγRs on macrophages to drive valvular carditis. These results provide new insight into the pathogenesis of cardiovascular inflammation in the setting of autoantibody-associated chronic inflammatory diseases as well as potential directions to pursue for rational therapeutic approaches.

18 MECHANOBIOLOGY OF NOTCH IN AORTIC VALVE DISEASE
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Background: Valvular heart disease affects 2% of the population, costing $1 billion annually. NOTCH1 mutations were identified as a cause of aortic valve disease (AVD), which results in hemodynamic perturbations in multiple valve and aorta cell types. Accordingly, we sought to examine the effects of NOTCH loss of function (LOF) and shear stress in order to better understand the mechanobiology of NOTCH in different cell types involved in AVD onset and progression. Methods: NOTCH LOF was achieved by treating human aortic valve interstitial cells (AVICs) and aortic root smooth muscle cells (SMCs) harvested from healthy human hearts (donors<40 years with normal cardiac structure/function) and human umbilical vein endothelial cells (HUVECs) for one week using 50μM DAPT. To approximate shear stress, an average fluidic shear stress of 10 dynes/cm² was periodically applied for 24 hours using an orbital shaker and electrical circuit interrupter. Results: Early control AVICs demonstrated calcific nodules upon NOTCH LOF using Alizarin Red (Figure 1), but did not morphologically respond to fluidic shear stress. However, HUVECs and SMCs uniquely aligned to fluidic shear stress (parallel & perpendicular, respectively) near the periphery where shear stress is the greatest (Figure 2). Moreover, HUVECs lost dynamic responsiveness upon NOTCH LOF (Figure 2). Conclusions: The three major cell types involved in AVD onset and...
progression respond differently to NOTCH LOF and/or shear stress. These results have broad implications, from congenital defects in the left ventricular outflow tract to enhanced leukocyte infiltration into AVICs during AVD, and warrant investigation into underlying molecular mechanisms.

**MWSPR PLENARY SESSION III**

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**LUMBAR PUNCTURE SIMULATION TRAINING: BRIDGING THE CLINICAL GAP.**
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**Background:** Lumbar puncture (LP) is a common procedure in the neonatal intensive care unit (NICU). Good procedural skills are required to conduct non-traumatic LPs. **Objective:** Following a performance audit at an academic Level 4 Neonatal Intensive Care Unit several areas of concern were identified. To address deficiencies we developed a novel, simulation-based educational curriculum. This study aimed to evaluate preliminary learning effects of this intervention. **Methods:** A total of 28 residents were assessed while rotating through the NICU from January to April 2013. In a pre-post design, we captured a variety of measures. Knowledge was assessed using a multiple-choice quiz, while self-rated surveys were used to capture learner self-efficacy. A validated OSATS-type instrument was utilized to assess LP procedural skill (Iyer, 2012) during live observation in a simulated setting. Pre-post comparison of quiz scores was performed using paired-student t-test, while differences in performance ratings were analyzed using a many-facet Rasch model. **Results:** Preliminary results indicate that this intervention resulted in an improvement among learners on procedural knowledge. The mean quiz score improved from 7.46/11 to 9.64/11, t(27) = 8.30, p < .001. There was a significant difference in proficiency, X²(3, N = 4) = 26.5, p < .001, across learners who perceived themselves as excellent (mean overall OSATS score = 2.7) and those who perceived themselves as lacking (mean overall OSTATS score = 2.0). When reviewing pre- and post-intervention OSATS LP scores, there were significant improvements in several of the 8 performance evaluation criteria (positioning, analgesia, lab management, sterile field and overall score). CSF return and laboratory management most frequently obtained high post-intervention scores. In addition, there was significant improvement between the pre- and post-intervention overall OSATS scores, X²(1,N=28 =167.5, p=0.001. Evaluation of rater differences across evaluation criteria indicated no rating differences, with the exception of the positioning component, with rater 2 being more lenient (Mean=2.18) than other raters (Mean=2.44). Although the difference was significant (p = .004), practical impact is relatively small. **Conclusion:** This educational intervention seemed to positively impact learner’s knowledge, self-efficacy and LP performance in a simulated setting. While intervention effects seem favorable, further analysis is needed. The ability of the task-trainer to replicate live LPs must be evaluated. **Implications:** We will continue to assess the success of this intervention with respect to clinical outcomes.

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**NEONATAL GROWTH RESTRICTION AND THE PROGRAMMING OF ADULT BEHAVIOR IN MICE**
*Lauritz Meyer, Vivian Zhu, Alise Miller, Robert Roghair, Department of Pediatrics, Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, IA*

**Background:** Associations have been made between prematurity or neonatal growth restriction (NGR) and Autism or ADHD risk. Leptin production is suppressed during periods of undernutrition, and we have previously shown neonatal leptin supplementation normalizes regional brain morphology of NGR mice. We hypothesized NGR programs adult behaviors that may be normalized by neonatal leptin administration. **Methods:** From postnatal day 4-14, C57BL/6 mice were randomized to daily injections of saline or murine leptin (80 ng/g). NGR mice were identified by a weanling weight below the tenth percentile, and control mice had weanling weights within one SD of the mean. Adult mice underwent social interaction testing within a tripartite chamber (N= 25-38), assessment of spatial learning by Barnes maze (N=17-32, and assessment of anxiety by elevated plus maze (N=11-26). Data were compared by ANOVA and Chi-square analysis. **Results:** Social Interaction: Compared to controls, mice within the NGR population were more likely to demonstrate social isolation (time interacting with a stranger >1 SD below the mean; NGR 23.5% vs control 7.4%, p=0.03). Spatial Learning: Baseline escape times on Barnes maze testing were significantly shorter for NGR-saline mice (65+/-.6 sec vs control 87+/-.7 sec, p=0.02), consistent with heightened activity and/or anxiety. Learning was delayed in NGR-saline mice on Day 3 (101% of baseline vs control 64%, P=0.01). Neonatal leptin supplementation corrected the delayed learning in NGR mice (50% of baseline). Anxiety: NGR-saline mice spent more time in the open arms of the plus maze than control-saline mice (9% vs 4%, p<0.001), and this was modulated by neonatal leptin. **Conclusion:** NGR increases the risk of Autism/ADHD type behavioral alterations in mice, and this may be partially mitigated by the neurotrophic hormone leptin. Further research is needed to better elucidate a possible mechanistic link between NGR and adult behavioral alterations.
INTESTINAL ALKALINE PHOSPHATASE IS PROTECTIVE TO THE PRETERM RAT PUP INTESTINE

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**Background:** Necrotizing Enterocolitis (NEC) is the most common surgical emergency in neonates with a mortality rate between 10 and 50%. Our prior research has shown that prematurity is associated with lower Intestinal Alkaline Phosphatase (IAP) expression but supplementation with enteral IAP can mitigate both the local and systemic effects of stressors leading to NEC. Thus, we hypothesize that supplemental, enteral IAP will inhibit intestinal inflammation and preserve barrier function in the preterm intestine. **Methods:** Sprague-Dawley rats were delivered one day prematurely via cesarean section and gavage fed three times daily. Control pups were fed formula and the IAP group was fed formula with 4 Units/kg IAP in each feed. On day of life 3, ileal segments were isolated and stimulated *ex vivo* with LPS. Utilizing a 4-Nitrophenyl phosphate (pNPP) assay, the total alkaline phosphatase activity was measured. Inhibitors were added to the pNPP assay to quantify specific IAP activity in the segments. RT-PCR was used to measure expression of IL-6, TNFa, TLR4 and iNOS in the terminal ileum. *Ex vivo* loops were filled with 10kD FITC-dextran (FD-10) with or without LPS. Translocation of FD-10 was measured in the bathing media to test intestinal permeability in response to LPS stimulation. **Results:** On day of life 3, despite exogenous, enteral IAP the total alkaline phosphatase activity and IAP specific activity in intestinal homogenates was unchanged between the two groups. However, the preterm pups fed formula with IAP had a two-fold reduction of expression of both iNOS and TNFa (p<0.03) when compared to unsupplemented formula-fed pups. There was no significant change in IL-6 or TLR4 expression. Enteral IAP improved intestinal barrier function as measured by FD-10 flux compared to controls (2 fold, p=0.1). Similarly, following stimulation with LPS *ex vivo*, pups fed formula containing IAP had a 50% reduction in expression of iNOS (p=0.02) and TNFa (p=0.02). Expression of IL-6 also fell but was not significant. Again, the addition of IAP augmented the intestinal barrier in LPS exposed loops as shown by a two-fold decrease in permeability compared to formula fed preterm rats (p=0.02). **Conclusion:** Premature pups exposed to enteral IAP do not have measurable increases in IAP activity. However, there is a significant reduction in both iNOS and TNFa expression in tissue taken from pups that received IAP. Moreover, exposure to IAP improved intestinal barrier function as measured by FD-10 flux when compared to *ex vivo* loops from control pups. Additionally, there was no significant increase in permeability when IAP supplemented loops were exposed to LPS. These data suggest that enteral IAP in the preterm intestine significantly reduces inflammation and permeability in response to enteral stressors such as LPS. Supplementation with IAP may be of benefit in the human preterm infant to prevent NEC.

METABOLOMICS ANALYSIS IDENTIFIES NOVEL PLASMA BIOMARKERS OF CF PULMONARY EXACERBATION

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**Background:** Metabolomics is an emerging field that studies metabolic substrates and products in biological samples. Metabolomic profiling provides an instantaneous snapshot of the physiology of an organism and can be a direct link to mechanism of disease. Cystic fibrosis (CF) patients exhibit a chronic decline in lung function accelerated by intermittent pulmonary exacerbations. The link between pulmonary exacerbation and the degree of obstructive lung disease remains unclear. Metabolomics analysis provides the unique opportunity to investigate how the metabolomic profile changes between different CF phenotypes to provide valuable insight into the mechanistic process. Our objective was to identify new biomarkers of lung injury in plasma from CF patients during pulmonary exacerbation. **Methods:** Plasma samples plus lung function data were collected from 45 CF patients at up to three time points during hospitalization for pulmonary exacerbation and during quarterly outpatient clinic visits for two years. A subset of 25 matched pair plasma samples from CF patients during exacerbation (SICK) and at baseline (WELL) were studied. In collaboration with Metabolon, Inc.®, plasma biochemical profiles were analyzed using both gas chromatography and liquid chromatography platforms coupled with mass spectrometry. Compounds were identified by comparison to libraries of purified standards. A matched pairs t-test was used to identify biochemicals that differed significantly (p≤0.05) between SICK and WELL. **Results:** Our population had a mean FEV1% predicted of 57% (18 – 105%). 398 named biochemicals were identified. Significant increases in SICK subjects were noted in metabolic pathways involving lipid peroxidation (13-HODE+9-HODE, sarcosine, glycine, lysolipids and glycerolphosphorylcholine) and fatty acid beta-oxidation (palmitoylcarnitine, stearoylcarnitine, 3-hydroxybutyrate and acetacacetate). Significant decreases in SICK subjects were noted in pathways involving liver (mannose, glucose, pyruvate and lactate) and kidney metabolism. Correlations with demographics, lung function, infection and inflammatory cytokines will be explored. **Conclusions:** Metabolic changes identified in SICK
individuals suggest lipid peroxidation, lipid membrane breakdown, changes in energy metabolism and altered liver function. Our findings will allow for hypothesis generation about the pathophysiology of pulmonary exacerbation and serve as potential targets for therapeutic intervention.

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DENDRITIC CELL MATURATION IS DELAYED IN NEONATES DURING RESPIRATORY VIRAL INFECTION

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**Background:** Respiratory Syncytial Virus (RSV) is a paramyxovirus and a leading cause of bronchiolitis in infants resulting in significant morbidity and mortality. A formalin-inactivated RSV vaccine was tested in the 1960s, but this vaccine failed because infants that received the vaccine developed enhanced respiratory disease during subsequent RSV infection. There is still no vaccine available, and the infant immune response is incompletely understood. During respiratory viral infection in adult lungs conventional dendritic cells (DCs) phagocytose viral antigen and undergo maturation. Activated adult DCs express increased levels of MHC class II molecules, costimulatory molecules (CD80 and CD86) and chemokine receptors (such as CCR7). Activated adult DCs migrate to draining lymph nodes where they present antigen to CD4⁺ helper cells and initiate the adaptive immune response. Our previous work has shown that during paramyxoviral infection neonates are able to clear viral infection in the absence of inflammation. Because inflammation is necessary to activate DC, we hypothesized that DC maturation and migration to the draining lymph nodes may be delayed or impaired in neonates. **Methods:** Adult and two-day old neonatal C57BL/6 mice were infected with the natural mouse pathogen Sendai virus (SeV). RSV and SeV are closely related paramyxoviruses, and SeV causes a neutrophilic bronchiolitis in mice that is similar to human RSV bronchiolitis. Mice were inoculated intranasally with 500 pfu SeV/g body weight. Tissues were harvested on days 1, 3, 5 and 7 post-infection. Thymic stromal lymphopoietin (TSLP) levels were assessed by ELISA and immunostaining. For flow cytometry, single cell suspensions were prepared from adult and neonatal lungs and cervical lymph nodes. **Results:** TSLP is a cytokine known to participate in DC activation; we observed significantly reduced expression of TSLP in neonatal mice during respiratory viral infection. Adult CD11c⁺ DC had increased expression of MHC Class II and CCR7 and had migrated to the lymph nodes on post-infection days 1 and 3. However, these events were delayed in neonates and did not reach adult levels until post-infection day 7. **Conclusion:** Neonatal DCs demonstrate delayed activation as evidence by decreased expression of MHC Class II and costimulatory molecules. Migration to the lymph nodes is also delayed, and this may be due to reduced expression of CCR7. The reduced activation of DC in neonates may be attributed, in part, to reduced levels of TSLP in the neonatal lung. Further studies will be needed to determine the mechanism for activation of the adaptive immune response and viral clearance in the neonatal lungs.

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IVH SCREENING BY CRANIAL ULTRASOUND FOR ALL PRETERM INFANTS ≥30 WEEKS IS NOT COST EFFECTIVE

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**Purpose:** Because intraventricular hemorrhage (IVH) is a common cause of morbidity and mortality in the preterm infant, it is routine practice to perform universal IVH screening by cranial ultrasound (CUS). Although it's well documented that the risk of IVH decreases as birth gestational age (GA) increases, uncertainty still exists on a GA limit for universal screening that is both safe and effective. Despite the American Academy of Neurology recommendation to perform CUS screening only for infants born <30 weeks GA, disparity exists among U.S. NICUs on the GA limit used (typically between 30–34 weeks). Objectives of this study are to: 1) Determine the incidence of significant IVH in infants born 30-33 6/7 weeks GA, and 2) Assess the necessity and cost-effectiveness of IVH screening in this age range. **Methods:** A retrospective, descriptive study design was implemented and CUS screening reports of infants born 30-33 6/7 weeks GA, inclusive, (our institution uniformly screens <34 weeks) admitted to our Level III NICU between Jan 2003 and Feb 2012 were evaluated. A significant bleed was defined as IVH ≥ Grade 3. **Results:** 1082/1138 infants met eligibility criteria and were screened by CUS on DOL 5–10. Only 6/1082 (0.55%) had significant IVH and all were <32 weeks GA.

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25
In the 30–31 6/7 group, 6/354 (1.69%) had significant IVH. Of these 6, only 1 was detected by screening CUS alone; 5 had CUS ordered earlier than routine screening because of clinical symptoms relating to IVH risk. No correlation between IVH and birth weight was detected. Using a 2012 CUS fee for service of $852, it cost $154,000 to detect significant IVH in 1 baby. Some infants had more than 1 CUS because of normal variants detected during routine screening, further raising the cost. **Conclusion:** CUS screening for infants >32 weeks GA is not cost effective. The incidence of significant IVH detected with routine screening in 30–31 6/7 week infants is very low (0.55%), and would have been identified clinically in almost all cases. Therefore, our study results demonstrate the validity of IVH screening only for those <30 weeks GA.

**25**

**BODY COMPOSITION AND PROCESSING SPEED OF VLBW INFANTS.**

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**Background:** Preterm infants are at risk for long-term neurodevelopmental delays as a function of postnatal nutritional status and growth. Very low birth weight (VLBW) infants are especially vulnerable given the developmental stage of their brains, and the length of nutritional derangements in the neonatal period. Even with adequate neonatal weight gain, preterm infants have lower fat-free mass (FFM) and increased adiposity at term corrected age (CA) compared to their term counterparts. **Objective:** The objective of this study was to assess the relationship between postnatal body composition and neurodevelopment as indexed by the visual evoked potential (VEP) in VLBW infants. **Methods:** Anthropometric measurements and body composition testing via air displacement plethysmography were performed on 24 appropriate for gestational age VLBW (mean birth weight = 1148 +/- 224 grams, mean gestational age = 28.8 +/- 1.8 weeks) infants at 4 months CA. Infant visual pathway development was assessed at 4 months CA using pattern-reversal VEP, with latency to the P100 wave used to index speed of neuronal processing. **Results:** Increased FFM (p = 0.04), fat mass (p = 0.04), weight (p = 0.007) and head circumference (p = 0.06) at 4 months CA were associated with faster latency to P100. **Conclusions:** Speed of neuronal processing in ELBW infants is associated with body composition at 4 months CA. Gross accumulation of both fat mass and fat free mass are associated with faster speed of processing. Fatty acid and protein accretion are integral to brain development. The peak of fetal fat deposition in the brain occurs during the last trimester. Brain fat is required for cell membranes, as well as myelin, which affects speed of transmission. FFM indexes protein accretion and organ growth, and protein status affects neuronal growth and differentiation. Rapid synaptogenesis occurs during the third trimester, which is largely driven by protein status. Body composition is an important biomarker to follow in VLBW infants, and nutritional adjustments to optimize fat mass and FFM may improve neurodevelopmental outcomes.

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**IRON MAY BE THE CRITICAL LINK BETWEEN MATERNAL OBESITY AND ASTHMA IN OFFSPRING**

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**Background:** Maternal pre-pregnancy obesity is associated with asthma diagnosis in offspring, however no clear mechanism for this association has been found. Our lab previously showed that obesity during pregnancy was linked to poorer iron status in offspring. Other studies have also linked iron deficiency at birth to wheezing in infancy. Together these studies suggest iron status plays a key role in this unknown mechanism. **Objective:** We analyzed newborn iron status and lymphocyte Th1/Th2 cytokine expression in obese vs. control pregnancies. Our hypothesis was that depleted newborn iron in obese pregnancy alters developmental inflammatory processes, predisposing to asthma. **Methods:** The University of Wisconsin and Meriter Hospital IRBs approved this study. Eligible subjects included mothers delivering healthy term newborns from routine scheduled caesarean sections. Umbilical cord blood samples from control and obese pregnancies were analyzed for iron status, including measures of hemoglobin (Hb), zinc protoporphyrin/heme ratio (ZnPP/H), and ferritin. Lymphocytes were isolated for cell culture, stimulated with phytohemagglutinin, and incubated for 24 hours in normal media or low iron media with deferoxamine (DFX). Cytokine expression profiles were examined using a multiple cytokine array. Statistical analysis included t-test and ANOVA. **Results:** Cord blood from 11 control and 12 obese pregnancies showed similar Hb and ZnPP/H, measures of erythrocyte iron, but a trend for lower ferritin in obese pregnancy. White blood cell counts did not differ between obese and controls; however, obese had higher cord Th2-associated eosinophil counts than control (p<0.05). Production of the Th1 cytokine, IFN-gamma, trended lower in obesity and was completely inhibited by low iron DFX media (p<0.05). The anti-inflammatory cytokine IL-10 was also inhibited by DFX (p<0.03). By contrast, the pro-inflammatory cytokine IL-8 was similar between groups and unaffected by low iron conditions. **Conclusion:** The combination of higher Th2-associated eosinophil counts and lower Th1-stimulated cytokine...
expression are consistent with a relative dysregulation of the balance between Th1 and Th2 cytokines in offspring of obese pregnancy. A predominance of Th2 cytokines can create an atopic phenotype that predisposes to asthma and allergies. Iron may be the critical link between obese pregnancy and future asthma development in offspring.

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PSEUDOTYPED ADENO-ASSOCIATED VIRUS 9 EXPRESSION OF GFP IN MICE USING A TRUNCATED NEPHRIN PROMOTER

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Background: Structural renal diseases such as nephrotic syndrome have no specific curative therapy and patients with these diseases often progress to end stage renal disease, requiring dialysis and kidney transplantation. Gene therapy offers the possibility of therapeutic intervention for diseases with single gene mutations. The kidneys have proven difficult to target with previous gene therapy vectors. Indeed, even when the kidneys have been effectively targeted, sustained, focused glomerular specific gene expression has proven difficult. Recently the pseudotyped adeno-associated virus 9 (AAV2/9) has been shown to have broad tissue tropism in mice including the kidneys. This vector has the ability to exert its effects through episome influence rather than that direct host DNA integration. A murine truncated 1.25kb promoter of NPHS1, the gene which encodes nephrin, a podocyte localized protein, has been shown to have renal specific expression. We developed a novel AAV2/9 with the truncated minimal nephrin promoter (MNP) to direct kidney specific gene expression and potential therapy. Objective: Characterization of green fluorescent protein (GFP) expression in mice after systemic tail vein injection with the pseudotyped AAV2/9-MNP-GFP vector. METHODS: We designed an AAV2/9-MNP-GFP vector with the 1.25kb NPHS1 promoter to drive GFP gene expression in mice. A cytomegalovirus (CMV) promoter driving global GFP expression (AAV2/9-CMV-GFP) was used as a positive control vector. Saline (vehicle) injected mice served as negative controls. Eight-week old female C57 mice were injected with 3x10^11 viral particles of each vector. Tissue was harvested 8 weeks after injection. Kidney, brain, liver and heart were analyzed for the presence of viral DNA copies, GFP RNA expression and GFP protein expression. Results: AAV2/9-MNP-GFP transfected kidneys showed 6 fold higher DNA viral copy numbers than CMV controls with similar viral copy numbers in liver, heart and brain. Renal GFP RNA expression was 5 fold higher in the AAV2/9-CMV-GFP transfected controls compared to the AAV2/9-MNP-GFP mice. Interestingly, AAV9-MNP-GFP RNA expression was also present in the liver. GFP RNA expression was minimal in brain and heart of MNP transfected mice. AAV2/9-MNP-GFP transfected mice demonstrated sustained glomerular GFP protein expression within the kidneys by immunofluorescence and no expression in the brain and heart. AAV2/9-MNP-GFP transfected mice showed no GFP protein expression in the liver by immunofluorescence which was confirmed by western blot. CMV transfected controls showed vast GFP protein expression throughout the kidney, liver, brain and heart. Conclusions: The AAV2/9 vector utilizing the 1.25kb NPHS1 promoter provides a safe, viable tool for renal directed gene therapy in mice. These experiments provide a novel method for the investigation and potential therapy for congenital renal diseases in mice.

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INTERROGATING THE MECHANISMS OF AFLATOXIN-ASSOCIATED CHILDHOOD STUNTING

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Background and Significance: Stunting affects ~200 million children in resource-poor settings worldwide, with stunted children at increased risk for impaired cognition, metabolic syndrome, and increased mortality. Epidemiological observations implicate chronic ingestion of aflatoxin B1 (AFB1), a fungal metabolite of Aspergillus species that contaminates some crops, as a contributor to childhood stunting. However, the specific causal role of dietary AFB1 exposure in human growth impairment has not been definitively established. The goal of this study was to develop a rodent model of dietary AFB1-induced stunting with which to establish such causality and interrogate the mechanisms responsible. Experimental Design: Three-week old rodents (C57BL6/J mice or Fischer rats; n=3 per experimental group) were maintained on AFB1-contaminated or vehicle-containing control rodent chow beginning at the time of weaning and continued throughout the experiment. Food intake and animal weight were monitored serially. Rodents were sacrificed 3-6 weeks after diet initiation. At that experimental endpoint, animals were injected with bromo-deoxyuridine (BrdU) prior to euthanasia and collection of serum, liver, small intestine, and tibia. Serum transaminases were determined by the St. Louis Children’s Hospital clinical laboratory. Hepatic gene expression was assessed by qRT-PCR using standard methodology. Liver and gut histology and hepatocellular BrdU incorporation (indicative of injury-induced liver regeneration) were assessed. Numerical data were compared between groups using the unpaired Student’s t-test with =0.05. Results: Adult mice are resistant to AFB1-induced toxicity; however neonatal mouse models of AFB1 exposure have proven useful for analyses of liver cancer. Therefore, we first evaluated growth in newly weaned C57BL6/J mice exposed to dietary AFB1. No suppression of weight gain or reduction in tibial length was seen in mice exposed to 1-10 parts
per million (ppm) AFB1 compared to control diet over 3 weeks. In contrast, juvenile Fischer rats exposed to a diet containing 5 ppm AFB1 showed significantly reduced weight gain compared to control animals within 3 weeks of diet initiation (p<0.05). Linear growth was also stunted by toxin in this model, with reduced tibial length observed in rats on the 5 ppm toxin-containing diet (p=0.05). The dose dependence of these effects was suggested by a trend towards reduced weight gain in rats exposed to 1 ppm toxin (p=0.07 vs. controls). Food consumption was not affected by toxin exposure. Examination of liver histology showed focal areas of increased hepatocellular vacuolization in animals exposed to AFB1 vs. controls. This finding is suggestive of hepatic steatosis, which occurs in response to aflatoxin exposure and other liver injuries; however, neither serum transaminases nor hepatocellular BrdU incorporation were increased in the AFB1-exposed rats. Because growth hormone (GH)-resistance occurs in association with growth impairment in various chronic pediatric liver diseases, we quantified hepatic mRNA expression of the GH-regulated genes insulin-like growth-factors (IGFs) 1 and 2. The results showed reduced IGF2 but not IGF1 expression in animals exposed to AFB1 compared to vehicle-controls (p=0.03). Summary, Conclusions, and Future Directions: Our data demonstrate dietary AFB1-induced stunting in newly weaned rats, establishing this as a robust model with which to investigate the specific mechanisms that mediate such stunting. Our data also suggest that dietary aflatoxin exposure might cause hepatic GH resistance. Studies are ongoing to evaluate the magnitude of AFB1-induced liver injury and determine whether toxin-induced gut injury occurs in this model. Future studies will examine whether the enteric microbiome is a modifier of AFB1-induced stunting in this model by employing the same strategy recently used to link enteric flora to Kwashiorkor (Smith et al., Science 2013). Together, these analyses will guide recent and emerging global public health interest in efforts to reduce human aflatoxin exposure and thereby improve childhood growth.

RECEPTION AND COMBINED POSTER SESSION

29 SEGMENTAL PROGERIA AS A MODEL OF CARDIAC AGING
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Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare genetic syndrome characterized by the rapid accumulation of progerin, a truncated form of lamin A that accumulates in the cell nucleus. Progerin accumulation causes structural and functional changes in the nucleus, and alters gene expression and the cellular response to DNA damage in a dominant negative, dose dependent manner. It has been hypothesized that the profound effect of HGPS on tissues with high cell turnover, including vascular tissue, is in part due to the depletion of mesenchymal stem cell populations in these tissues. Interestingly, progerin has been shown to accumulate slowly in vascular tissue during normal aging (M Olive, et al, 2010). This suggests that an understanding of the accelerated senescence that occurs in HGPS affected cells might provide insight into the reduction in cardiac and vascular regeneration that occurs with normal aging. We have used murine models of HGPS, with either G608G mutation or ZMPSTE24 deficiency, to characterize cardiac size and function by echocardiography. We show that infusion of mesenchymal stem cells can prolong life and reverse activation of the Notch pathway in HGPS mice. In order to further study the cellular impact of progerin accumulation on multiple cell types, induced pluripotent stem cells (iPSCs) were generated from individuals with HGPS. We show that cells differentiated from HGPS iPSCs accumulate progerin, and are useful tools to study cell proliferation, gene expression, and signaling in this segmental progeroid syndrome. Preliminary results show that proliferative capacity is reduced and that gene expression in progerin expressing cells including cardiomyocytes is abnormal. These results may lead to a new understanding of the normal cardiovascular aging process and identify targets for improving cardiac repair and regeneration.

30 DETERMINING THE ROLE OF PTPN12 IN CONGENITAL HEART DISEASE AND VASCULAR DEVELOPMENT
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Purpose: Congenital heart malformations, including defects of the great vessels, are among the most common birth defects in newborns. An infant patient at the University of Minnesota Amplatz Children’s Hospital was diagnosed with a Type A interrupted aortic arch and a ventricular septal defect (VSD). In order to identify the molecular basis of the disorder, the patient’s genomic DNA was analyzed by comparative genomic hybridization. This study identified a complete deletion of the gene PTPN12, a known downstream target of the Ras pathway, which is associated with cell proliferation, migration, and adhesion. Due to the co-occurrence of this single gene deletion and heart defect, a zebrafish model is being developed to further observe the effects of PTPN12 on cardiovascular development and the potential implications of its loss. Methods: Gene knockdown of ptpn12 was performed with
an antisense oligonucleotide (Morpholino) to establish phenotypes associated with the loss of \textit{ptpn12} expression in zebrafish. Initial experiments using brightfield and fluorescent imaging were used to determine observable effects of knockdown. Ongoing experiments utilizing vascular markers and histology will further examine heart structure and the surrounding vessels. \textbf{Results:} Dose dependent phenotypes were observed following Morpholino knockdown. Observable phenotypes include dorsalization and reduced head structures, although no vascular phenotype has been established. These phenotypes are consistent with published data demonstrating expression in the head structures and branchial arches. \textbf{Conclusions:} A patient was identified with a Type A interrupted aortic arch and VSD associated with the deletion of \textit{PTPN12}, a gene in the Ras signaling pathway. Due to this specific heart malformation, it is likely that this gene impacts smooth muscle development in the vasculature. Additional markers of vascular components, particularly smooth muscle and neural crest derivatives, will be utilized to further analyze the effects of \textit{ptpn12} knockdown on aortic arch development in zebrafish.

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\textbf{INTRAOPERATIVE TRANSESOPHAGEAL ECHOCARDIOGRAM ASSESSMENT OF LEFT VENTRICULAR TEI INDEX IN CONGENITAL HEART DEFECTS}
\textit{Shanthi Sivanandam, James St. Louis, University of Minnesota Amplatz Children’s Hospital, Minneapolis, MN.}

\textbf{Background:} Tei index has not been described during cardiac surgery in pediatric patients. We describe the change in left ventricular function before and after pulmonary valve placement and ASD closure in volume overloaded right heart defects. \textbf{Methods:} Prospective data on 55 patients who underwent cardiac surgery in the past 24 months for spectrum of congenital heart defects (CHD) were analyzed. Group 1 (n=15) (volume overload right heart cardiac defects), group 2 (n=40) (without volume overload, had significant CHD). We reviewed pre and postoperative left ventricular myocardial performance index (Tei index). Tei index was obtained from transesophageal Doppler echocardiogram. This study was designed to evaluate the LV function using the Tei index pre and post cardiopulmonary bypass after surgery and interest was focused in right ventricular volume overload patients. \textbf{Results:} A paired t-test was used to test the change in the LV Tei index pre and post bypass. In group 1 pre-operative mean LV Tei was 0.6 with a significant decrease of 0.207 post-operative Tei (p=0.014). In group 2 pre-operative mean LV Tei was 0.48 with no significant change of 0.01 post-operative Tei (p=0.82).Group 1 had a significant reduction of 0.207 in the Tei index implying better LV function. Group 2 had no change in LV function. \textbf{Conclusion:} Pre and post-operative TEE assessment provides an easy and quick way of evaluating global left ventricular function intra-operatively using LV Tei index. Tei index has been shown in transthoracic Echocardiogram studies to be a reliable indicator of ventricular performance. The effects of the right ventricular volume overload on the ventricular septal motion and the differential effect on the left ventricular function is still controversial and has not been well described in children’s. Our data demonstrates LV Tei Index in the right ventricular volume overload heart (group 1) pre-operative (value) was higher which indicates diminished LV global function and postoperative (value) had normal Tei Index. Left ventricular function recovered immediately after the placement of the pulmonary valve and ASD closure. In (group 2) consist of other cardiac defects without volume overload, demonstrated no changes in the pre and post-operative LV Tei.

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\textbf{SURGICAL REPAIR RESULTS OF ANOMALOUS AORTIC ORIGIN OF CORONARY ARTERY: A MULTI-INSTITUTIONAL PEDIATRIC CARDIAC CARE CONSORTIUM STUDY.}
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\textbf{Background:} Although the incident rate of anomalous aortic origin of coronary artery (AAOCA) has not changed significantly, the discovery of this anomaly has increased recently because of the improved techniques in diagnostic technology. The discussion remains whether the best course of action for these patients is continued observation or to correct the defect with surgical intervention. This is an important question because of the association between AAOCA and the onset of sudden death. The purpose of this study is to determine the characteristics and results of patients who had surgical intervention. \textbf{Materials and Methods:} The Pediatric Cardiac Care Consortium (PCCC) was queried and identified 3,305 patients with a diagnosis of AAOCA between the years of 1982 and 2007. We reviewed the characteristics of those who had surgical intervention and performed univariate analysis of these patients. \textbf{Results:} The cohort was comprised of 90 patients that underwent surgical correction of AAOCA (2.7%), with an in-hospital mortality rate of 2.2% (n=2). The majority of patients were male (61, 67.8%), while both deaths occurred in the female population (2/29, 6.9%). Fifty four patients (60.0%) had an anatomy of the right coronary artery off of the left coronary artery, although both deaths were from patients with the left coronary artery coming off of the right coronary artery (2/36, 5.6%). Eighty percent of patients had the anomalous coronary artery course above or at the commissures (n=72) and both of the deaths were within this group (2/72, 2.8%). Forty eight patients had a circular orifice between the aorta and coronary artery (53.3%), while both deaths came from patients who had
an oval orifice between these two structures (2/36, 5.6%). A majority of the cohort was under the age of 18 at the time of intervention (87, 96.7%). Fifty two patients (57.8%) were symptomatic prior to surgery and both deaths were in this group (2/57, 3.5%). Ten patients had a subsequent cardiac surgical procedure following AAOCA repair (11.1%), with 1 death occurring in this group (1/10, 10%). **Conclusions:** Mortality rates for surgical intervention of AAOCA remain low, although more detailed multivariable analysis is needed to better understand the best course of action for this defect. Further investigation and follow-up are also needed in patients who have had this defect but have not had surgical intervention to better correlate results between these two groups.

### 33
**RE-ACCESS OF THE LEFT ATRIUM VIA PRIOR TRANSEPTAL PUNCTURE SITE WITH USE OF THREE DIMENSIONAL NAVX.**

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**Background/Purpose:** Ablations requiring access to the left side of the heart place patients at an increased risk for stroke and bleeding due to associated clot and anticoagulation risks. Diminishing left atrial catheter dwelling time may decrease these risks. Three-dimensional NavX, though not previously used to assist transseptal procedures, can be used to facilitate re-access of transseptal puncture sites to allow catheter removal from the left atrium immediately after ablation, with re-access through the prior transseptal site if required. Here we describe the techniques employed, and our experience using 3-D NavX to facilitate re-access of the left atrium via the previously marked transseptal puncture site, a radiation free technique. **Methods:** With the use of 3-D NavX right atrial geometry is obtained. The transseptal puncture site is marked on this geometry using 3-D NavX via a unipolar electrode on the transseptal needle or at the time of catheter withdrawal from the left atrium. The catheter can then be removed immediately after the ablation, prior to the 30 minute monitoring time, to confirm a successful ablation. If repeat left atrial access is needed, the previously marked transseptal site is used to navigate the ablation catheter to re-access the left atrium. All patients <30 years who had undergone this technique over the past three years were evaluated. Data gathered included patient demographics, need for and success of transseptal re-access, left atrial catheter dwelling time, and complications. **Results:** The transseptal site was marked by 3-D NavX in 49 patients. We were able to successfully re-access the transeptal puncture site in all 6 patients where it was desired. The median procedure time was 117 min (range: 71-446 min), the median total fluoroscopic time for the entire procedure was 2.0 min (range: 0.0-30.8 min), and the median left sided catheter dwelling time was 27 min (range: 10-112 min). **Conclusions/Implications for Practice:** This is the first study describing this procedure. In our case series, re-access of transseptal puncture sites was reproducible and without complications. Our median left atrial dwelling time was reduced in comparison to a typical procedure and radiation exposure was minimal. Limiting left atrial catheter time has theoretical clinical advantages such as decreasing the risk of embolism which could cause stroke or heart attack as well as limiting the need for prolonged anticoagulation decreasing postoperative bleeding risk.

### 34
**INTRACRANIAL PATHOLOGY IN NEONATES WITH CONGENITAL HEART DISEASE: IS THERE A RISK TO DELAYING CARDIAC SURGERY?**

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**Background:** Studies have shown there is a high incidence of central nervous system (CNS) abnormalities in infants with congenital heart disease (CHD). An intracranial anomaly (ICA) or intracranial hemorrhage (IVH) can delay surgery and clear data on the impact of this delay is lacking. We evaluated the outcomes of neonates undergoing cardiac surgery with and without ICA or IVH. **Methods:** Retrospective review of 46 patients diagnosed prenatally with CHD was performed after IRB approval. Prenatal and postnatal courses and maternal and neonatal data were summarized. **Results:** The incidence of CNS abnormalities was 21.7% (6/46 had IVH and 4/46 had ICA). Cardiac surgery was delayed in 4 infants (8.7%) due to a CNS abnormality. Surgery was delayed in 3 neonates with Grade 2 or greater IVH until 2 weeks after resolution of IVH (cardiac defects: Aortic coarctation; Heterotaxy, atroventricular (AV) canal, pulmonary atresia (PA), total anomalous pulmonary venous return; Tetralogy of Fallot (TOF), PA). The fourth infant with delay in surgery had an ICA (thromboembolic CNS infarctions) and TOF and PA. The remaining neonates with ICA or IVH described below underwent surgery without delay. A neonate with grade 1 IVH and Hypoplastic Left Heart Syndrome underwent the Norwood procedure on day of life (DOL) 8. Another infant with Grade 1 IVH and double inlet left ventricle, L-TGA, aortic coarctation, and tricuspid atresia underwent surgery DOL 7 after resolution of the IVH. The third infant with grade 1 IVH, dilated cardiomyopathy and congenital complete heart block underwent pacemaker placement on DOL 2. One infant with an ICA (cysts in caudothalamic groove) and TOF and PA underwent a BT shunt. An infant with parietal periventricular leukomalacia underwent repair of an AV canal defect. The final infant had a severe ICA and AV canal and was offered palliative care. **Conclusions:** The results from this cohort demonstrate a delay in cardiac surgery if the IVH was Grade 2 or greater. These infants had resolution of IVH within 2 weeks and went on to have
successful cardiac surgery. The presence of Grade 2 IVH or significant CNS anomalies has a direct impact on the preoperative planning and timing of cardiac surgery. Knowledge of CNS abnormalities is important for appropriate planning by the cardiac team, and allows timely communication with the family. To our knowledge, this is the first report in the literature on the impact of CNS abnormalities on delaying surgery.

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FETAL TAPSE AND TRICUSPID ANNULAR PEAK SYSTOLIC VELOCITY IN FETAL HEARTS
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Background: TAPSE and Tricuspid annular peak systolic velocity (S’), as an echocardiographic index to assess right ventricular systolic function has not been, investigated in fetuses with normal and abnormal hearts. Methods: A prospective study was conducted in a group of 35 fetuses at 2nd trimester (14 to 27 weeks of gestation, group 1, n=25), 3rd trimester (28 to 40 weeks of gestation, group 2, n=10). M-mode application was applied to the tricuspid annulus, parallel to the ventricular septum and the amplitude of the resulting wave was measured for TAPSE values. Pulsed-waved Doppler tissue imaging was performed in the four-chamber view and a 5mm sample volume was placed at the lateral corner of the tricuspid annulus for (S’) values. Fetal echocardiograms were reviewed and the tricuspid annular plane systolic excursion (TAPSE) and the tricuspid annular peak systolic velocity (S’) were measured. TAPSE and S’ values in fetuses in group 1 were compared with those in group 2. Results: In group 1 mean TAPSE was 5.7 mm (standard deviation (SD) +1.5) and in group 2 mean TAPSE was 7.9 mm (SD +1.5). Tricuspid annular peak systolic velocity (S’) in group 1 mean was 4.8 cm/sec (SD +1.5). In Group 2 (S’) mean was 5.1 cm/sec, with SD of 2. Conclusions: TAPSE and tricuspid annular peak systolic velocities (S’) as an additional echocardiographic tool to analyse right ventricular (RV) systolic function in fetuses. Fetal TAPSE and S’ measurements in fetal hearts increase from the 2nd trimester to the 3rd trimester and correlate with normal right ventricular fetal growth patterns.

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USE OF HIGH FIDELITY SIMULATION TO IMPROVE MEDICAL STUDENT CONFIDENCE AND KNOWLEDGE OF PRE-ARREST PEDIATRIC PATIENT
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Background: Nationwide, medical student curriculums are shifting towards outpatient care. Subsequently, inpatient experiences are becoming more limited leading to students feeling unprepared in managing critically ill patients upon entering residency. High fidelity simulation fills a void in medical student education by improving exposure to the management of acutely ill children. Objectives: We hypothesize that confidence and medical knowledge in the recognition and management of acutely ill children will increase through the use of high fidelity simulation. Methods: We conducted a volunteer, prospective study of medical students during their third year pediatric rotation. Four simulations addressed children in pre-arrest situations due to asthma, bronchiolitis, anaphylactic shock, and hypovolemic shock. Scenarios were followed by debriefing sessions. A confidence survey and clinical knowledge exam were administered before and after simulation experiences. Institutional Review Board approval was obtained prior to the study. Results: Sample size to date is 36 students, with projected sample of 85. Currently, there are 16 males (52%) and 15 females (48%) with majority of students (94%) being between 25 to 34 years of age. Preliminary analysis revealed no significant change in clinical knowledge with pre- and post-test average scores of 15.77 and 16.17 respectively (p=0.25). All confidence questions demonstrated statistically significant improvement. Students felt more confident in caring for a pediatric patient (p=0.00), in talking with patients and families to gather information (p=0.02), in communicating patient’s condition to senior team members (p=0.01), in recognizing an acutely ill and/or decompensating child (p=0.00), and in activating rapid response/code blue or calling for assistance (p=0.00). Paired t-tests were conducted using STATA 11.2. Statistical significance set at p-values < 0.05. Conclusions: Preliminary results suggest that third year medical students have increased overall confidence in recognizing and responding to acutely ill children following simulation exercises. Knowledge tests have not shown significant increase following simulation, which may be secondary to debriefing sessions’ focus on teamwork, leadership and communication as opposed to illness specific medical knowledge. Implications: Simulation is a valuable tool in improving medical education for students on their pediatric rotation. Future studies are needed to develop validated assessment tools for measuring knowledge of medical students in simulation exercises.
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SHARING LIFE ALTERING INFORMATION: DEVELOPMENT OF PEDIATRIC HOSPITAL GUIDELINES AND TEAM TRAINING

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Background: Despite parent and physician reports of inadequate skill development, there are few guidelines for training pediatricians in sharing life-altering information (SLAI; i.e., “breaking bad news”). The necessary skills for SLAI differ between pediatric and adult medical environments. Methods: A multidisciplinary task force, which received feedback from parents of patients in multiple pediatric subspecialties, crafted children’s hospital-wide guidelines for SLAI. A one-hour training module on the guidelines was presented to several multidisciplinary pediatric team audiences; 159 voluntary pre- and post-presentation self-efficacy surveys were collected. Responses were analyzed by paired t-test (within groups) and ANOVA (between groups). Results: All evaluated groups of team members reported significant improvements in self-efficacy after the presentation along four objectives of effective SLAI. Medical trainees, newer physicians and non-physician (e.g., mid-level providers, nurses) team members reported the greatest improvements in self-efficacy, regardless of whether they had received previous training in SLAI. Conclusions: We recommend the implementation of children’s hospital-wide SLAI guidelines. Focus on patient- and family-centered, culturally-sensitive pediatric practices should be the basis for development of training that can be periodically reinforced. SLAI appears to require a skill set that benefits from life-long learning.

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COMPARISON OF MEDICAL STUDENT UNDERSTANDING AND RECALL OF ACUTE MANAGEMENT OF ASTHMA; TRADITIONAL LECTURE VS. INTERACTIVE TEACHING

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Purpose: In the past 50 years, many universities have focused on ways to improve medical student learning by making didactic teaching more interactive. While there has been much focus on problem-based learning, studies are showing equivocal improvement in test scores. In addition to problem based learning, there are other forms of active learning, and there has not been much focus on research looking at other forms of active learning. The purpose of this study is to compare medical student learning from a series of interactive “chalk-talk” lectures and learning from traditional PowerPoint lectures. Methods: During the third-year pediatric clinical rotation, student groups were alternately assigned to a PowerPoint lecture format or the chalk talk format. In the PowerPoint lecture, students watched a pre-prepared slideshow on the pathogenesis, physical exam, differential diagnosis, and treatment of asthma. For the chalk talk lecture, students were asked to talk through the same information about asthma; their answers were written on a white board and discussed during the lecture. Students received a multiple choice test on three occasions: one test given before the lecture, one given immediately after the lecture, and one given online 6 months after the lecture. Test scores were summarized in terms of means and standard deviations, specifically analyzing a change in test score from the pretest. A p value of < 0.05 was considered significant. Results: Analysis of the first 4 groups revealed no statistically significant difference in mean baseline scores in the PowerPoint and the "chalk talk" groups. There was no significant difference in the mean post-instruction scores, but both groups showed a statistically significant change from pretest to posttest. Conclusion: Preliminary data show that students in both groups learned from the PowerPoint lecture and the chalk-talk lecture. However, with the limited size of our study, we were not able to detect any difference in the amount of learning that was related to the lecture format.

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ADMINISTRATION OF LONG-ACTING INSULIN ANALOG IN PEDIATRIC PATIENTS ADMITTED FOR DIABETIC KETOACIDOSIS – DOES TIMING AFFECT OUTCOMES?

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Background: The standard of care for moderate to severe diabetic ketoacidosis (DKA) involves continuous insulin infusion and usually requires a stay in the intensive care unit (ICU). Long-acting insulin analogs provide basal insulin. It is unknown if early administration of subcutaneous long-acting insulin, simultaneously with insulin infusion, may have a role in the initial management of patients with DKA. Objective: This study was conducted to determine if patients admitted with DKA who receive long-acting insulin analogs on the same day of admission have better clinical outcomes compared to patients who receive standard DKA management. Methods: IRB approval was obtained prior to a retrospective review of the medical records for admissions from 5/30/2007 to
5/30/2012, ages 0-21 years old, with a diagnosis of diabetes mellitus (DM). Only admissions for DKA were included and were divided into two groups based on whether they received administration of long-acting insulin injection on the same day of admission or not. Severity of DKA at presentation was defined by previously established criteria. Statistical analysis was conducted using Student t-test and Fisher’s exact test. A p value less than 0.05 was considered statistically significant. **Results:** We identified 365 admissions for Diabetes Mellitus and 71 admissions met study criteria. Of those patients, 14 were in mild, 31 in moderate DKA, and 26 in severe DKA. The remaining 294 admissions were excluded for the following reasons: admission was not secondary to DKA, the patient did not require insulin infusion, or the patient had DM due to another underlying medical condition. When comparing all DKA admissions, we did not find a significant difference in hospital length of stay, length of ICU stay, time to resolution of acidosis, or complications. However, for severe DKA admissions, we found that those who received long-acting insulin on the same day of admission had a shorter ICU stay when compared to those that did not receive long-acting insulin on the same day (1.23 +/-0.44 days vs. 1.71 +/- 0.49; p = 0.0247). There were no other significant differences between the groups. **Conclusions:** Administration of long-acting insulin on the same day of admission in patients with severe DKA may lead to faster clinical improvement and to decreased ICU length of stay without increased complications.

**40 FEASIBILITY AND SUCCESSFUL USE OF A HOME COMPUTER SPREAD-SHEET PROGRAM DESIGNED TO HELP MAKE INSULIN DOSE CALCULATIONS AND ADJUSTMENTS TO INSULIN REGIMENS IN CHILDREN WITH TYPE 1 DIABETES.**

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**Objective:** This pilot study evaluated whether a computer spread-sheet program (CSSP) designed to make insulin dose (ID) calculations and adjustments in response to individualized dosing parameters and blood glucose (BG) patterns improves glycemic control (GC) in children with type 1 diabetes (T1DM), and assessed its feasibility and satisfactoriness to patients and parents. **Methods:** 7 children, 3-18 yrs with T1DM for >1yr participated. Subjects were required to check BG regularly and were on injection basal-bolus regimens. BG was entered before each meal. The CSSP calculated ID based on BG and carbohydrate to be eaten. 10% adjustments to basal or bolus ID were made based on BG patterns. Hemoglobin A1c (HbA1c) was before and after 1mo. Frequency of adjustments, hypoglycemia (hypo), ketones, emergency room (ER) visits, decisions to override the CSSP and average pre-meal BG were recorded. A 4 item survey (5 point scale) was completed to assess satisfaction and perceived benefit of the CSSP. **Results:** HbA1c before (8.49±0.89%, mean±SD) and after 1mo (8.47±1.03) did not differ. CSSP made dose adjustments for all subjects. Hypo occurred 4.4±2.3/mo with no severe hypo. No ketones or ER visits occurred. 4 of 7 subjects chose to override the CSSP at least once. Average pre-meal BG before (136±54mg/dL) and after 1mo (152±48) did not differ. Ease of use was (4.7±0.51). The CSSP aided in making more frequent ID adjustments (4.8±0.41). Subjects agreed with ID changes made by the CSSP (4.7±0.51). All but 1 subject reported they would use CSSP again. One subject used CSSP beyond 1 mo. **Conclusions:** This pilot study demonstrates successful use of a home CSSP designed to make individualized ID calculations and adjustments in patients with T1DM. Although there was no significant change in GC after 1mo, patients and parents found the CSSP to be a safe, easy tool for T1DM self-management. Follow up studies are indicated to determine if changes in GC are observed over longer periods of time.

**41 VITAMIN D DEFICIENCY IN CHILDREN EXPOSED TO PRENATAL ALCOHOL.**

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**Objective:** The objective of this study was to identify risk factors and determine the prevalence of vitamin D deficiency and insufficiency in an alcohol exposed pediatric population. **Methods:** A retrospective chart review study (N=62) was conducted using patients seen at the Fetal Substance Exposure Clinic at the University Of Minnesota. The chart review analyzed total 25-hydroxy vitamin D [25(OH)D] levels of pediatric patients at the initial clinical assessment between April 2012 and May 2013. Vitamin D sufficiency, insufficiency and deficiency were respectively defined as 25(OH)D≥30ng/ml (>12nmol/L), 20-29 ng/ml (<12nmol/L) and <20ng/ml (<8nmol/L). The study included 62 patients (58% female) aged 10 months to 23 years. Patients were excluded if they were currently being treated for known low levels of vitamin D at the time of evaluation. Data was analyzed with SPSS version 20 and One-Way ANOVA was used to evaluate cofounding variables. **Results:** Of those measured, 30% were deficient and 44% were insufficient, with a combined total of 74% of patients below target levels of vitamin D. There were no significant group differences for vitamin D levels by sex, ethnicity, region of birth, state of residence, or presence/absence of other prenatal drug exposure. **Conclusions:** Vitamin D insufficiency is highly prevalent in the alcohol exposed pediatric population and clinics evaluating children for Fetal
Alcohol Spectrum Disorder (FASD) should consider universal screening and treatment given the levels demonstrated in this study. Further studies are needed to determine if suboptimal levels of vitamin D may contribute to the growth failure, behavioral and cognitive issues seen in the alcohol exposed pediatric population.

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NATURAL LANGUAGE PROCESSING OF CLINICAL NOTES FOR PROBLEM LIST

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Background: A problem list facilitates electronic health record (EHR) operations such as templated notes, clinical decision support, ordering, billing and data analysis for research and outcomes measurement. Problem list use is an essential component of US Federal meaningful use (MU) of EHRs. Purpose: We hypothesize that principal cardiac diagnoses for problem lists can be generated from discharge summaries for children with heart disease using Natural Language Processing (NLP). Methods: We sought to use NLP tools of the Biomedical Information Collection and Understanding System (BioMedICUS) to identify a principal diagnosis from discharge summaries. The Metamap and weighted-phrases Stanford Parser methods were applied to discharge summaries We first trialed Metamap analysis for Concept Unique Identifiers (CUIs) for each diagnostic term using the Stanford parser and weighted each phrase by occurrence frequency and overlap with various cardiac diagnostic nomenclatures. The International Pediatric and Congenital Cardiac Code (IPCCC) was used as a lexicon in the Stanford parser, followed by the IPCCC short list of 168 terms (IPCCC-short) and then IPCCC-short augmented with common pediatric cardiac acronyms and lexical variants (IPCCC-short-acro). Finally the Pediatric Cardiac Care Consortium augmented diagnosis list (PCCC-acro) was used with the Stanford parser. A random sample of 100 records was manually analyzed to compare output of the weighted phrases methods to primary cardiac diagnosis. Results: The weighted phrases method using PCCC-acro found the primary cardiac diagnosis in the highest-weighted phrase (report line 1) in 88/100 subjects (88% sensitivity, see table). Although 10-20 phrases per patient were available, these added little to sensitivity beyond the first 5.

<table>
<thead>
<tr>
<th>Lexicon</th>
<th>IPCCC</th>
<th>IPCCC-short</th>
<th>IPCCC-short-acro</th>
<th>PCCC-acro</th>
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<tr>
<td>% sensitivity</td>
<td>76</td>
<td>82</td>
<td>80</td>
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Conclusion: Metamap was unhelpful for identification of pediatric cardiac principal diagnoses. Our Stanford parser NLP method using phrases weighted by frequency and overlap with several pediatric cardiac diagnostic terminologies allows BiomedICUS to accurately generate diagnostic phrases from discharge summaries. Implications: This early use of NLP in the pediatric cardiovascular domain offers promise to facilitate EHR implementation and MU for pediatric cardiac patients.

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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 disposition of neonates visiting ER during the first month of life. To document the main reasons for not contacting the primary MD (PMD) in a subset of self referred neonates. Materials and Methods: A retrospective chart review of all newborns (<1 month) who visited Mount Sinai Hospital ER between January 2010-December 2012 was conducted. The caregivers of a subset of newborns brought to ER during Jan-2012 to June-2012, were interviewed over the phone. Results: During the study period, 764/8442 (9%) of neonates born at Mount Sinai Hospital were evaluated in ER during the first month of life. The average age at visit was 13.8 days; 53% were males. Of the total visits, 77.1% were self-referred, 19.7% were physician referred and the remaining 3.2% were home births admitted through ER. 11.6% of neonates were admitted to the hospital. Of the 50 parents interviewed, all received written/verbal education at the time of discharge regarding the care of their newborn, 44 (88%) had the PMD name and F/U appointment made before discharge. Of the 44 who had F/U appointment made before discharge, 34 (77%) did not call PMD before ER visit. Conclusion: Majority of the newborn visits to the ER were for non-emergent conditions and were self-referred. Majority of parents interviewed did not call PMD before visit. Most common reasons were: the parent’s assessment of severity of symptoms and wish to be seen soon, events happening out of clinic hours, and parents wanted another doctors’ opinion. Improved discharge planning and education of parents during the post partum stay are needed to reduce the number of ER visits.
PRIMARY CARE PROVIDER PREFERENCES FOR CLINIC FOLLOW-UP AFTER EMERGENCY DEPARTMENT VISITS

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Background: Children discharged from Emergency Departments (EDs) are routinely advised to follow up with their primary care providers (PCPs), but little is known about how PCPs view these recommendations. Methods: This was an online survey of PCPs and Emergency Medicine Providers (EMPs) to assess their approach to ED follow-up recommendations for children seen in EDs for 15 common conditions. The survey assessed timing of follow-up and whether it should be definite or contingent on clinical status. Results: 124 PCPs and 39 EMPs completed the survey. In Acute Otitis Media, PCPs had 51% lower odds of choosing definite follow up than EMPs (p=0.009), and 77% higher odds of selecting follow-up ≥4 days after the ED visit (p=0.04). In simple upper respiratory infection, PCPs had 72% lower odds of choosing definite follow-up (p<0.0001) and 179% higher odds of selecting a lag of ≥4 days (p<0.0001). Most conditions had similar discrepancies. Conclusion: PCPs prefer significantly less conservative recommendations for clinic follow-up after ED visits than EMPs. This difference could result in perceived overuse of clinic resources.

TMEM35 (TUF1): A NOVEL FACTOR IN PAIN PATHWAYS?

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Chronic pain is a major health problem, affecting over 100 million adults in the USA, with considerable economic costs in healthcare and loss of productivity. Notable progress has been made in elucidating neural mechanisms underlying pain sensing and processing, leading to important insights into the maladaptive changes that produce persistent or chronic pain. Moreover, susceptibility to such maladaptive changes depends in part on the individual's genetic makeup as well as the interaction between genes and environment. There are on-going efforts to identify molecules or genes that mark specific neuronal cell types and their respective roles in pain behavior to better understand the molecular level the transition from acute to chronic pain and to provide essential tools for tailoring effective pain treatments. Here, we propose the novel TMEM35 (TUF1) is one such candidate. Our group investigates a 167-aa polypeptide (TMEM35/TUF1) that is strongly expressed in developing and adult neural and endocrine networks that mediate pain (i.e., skin, dorsal root ganglia, spinal cord, brain stem, amygdala, hippocampus, cortex, and HPA axis). The involvement of TUF1 in pain was indicated by evidence of thermal hyperalgesia and mechanical allodynia in the tuf1 KO mice. In addition, there is a strong link between chronic pain and anxiety. The tuf1 KO mice exhibit increased anxiety-like behavior accompanied by higher basal level of plasma corticosterone and adrenal hyperplasia, providing additional rationale for assessing TUF1's role in pain pathways.

AUTISM ON THE RISE: SURVEILLANCE OF PREVALENCE TRENDS BY SCHOOL NURSES

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Background: Current methods for estimating the incidence and prevalence of autism and its change over time are biased and may be invalid, as many rely on surveys of health care providers. Objectives: The purpose of this project was to analyze bi-annual school health record data reported by public school nurses to assess prevalence of autism in the metropolitan region of St. Louis, Missouri, a racially-diverse area with a population of 1.4 million people. Methods: Annual school health reports, including counts of school-age children with autism and other chronic conditions, were obtained from all public school districts in St. Louis City and County for 2005, 2007 and 2009. The counts include reports from divisions of public schools that specializes in special services for children (typically ages 5-18 years old) with developmental, cognitive and physical disabilities. Total school enrollments were also obtained. Prevalence (per 1000) was calculated for each year and statistical testing (z-test for proportions) assessed differences between the years. Results: School nurses reported there were 829, 1225 and 1129 students with autism enrolled in 25 school districts, in 2005, 2007 and 2009, respectively. The estimated prevalence (per 1000) for each year was: 4.3 per 1000 (2005), 6.4 per 1000 (2007) and 6.5 per 1000 (2009). A statistically significant increase in prevalence (+48%) was observed between 2005 and 2007, p < 0.002. The modest increase between 2007 and 2009 was not significant, p = 0.88. Conclusions: Data collection and reporting systems used by public school nurses provide another perspective on estimating prevalence of autism, especially among school-age children. Estimates drawn from this study are lower than national and regional figures reported by the Autism and Developmental Disabilities Monitoring (ADDM) Network. Such differences may be attributable to study methods.
regional variation or both. Regardless, schools may be able to provide localized estimates of prevalence to enhance public health planning and advocacy efforts in many communities.

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ARE RADIOLOGIC FINDINGS FOR BONE DISEASE ASSOCIATED WITH THE TIMING OF FRACTURES IN YOUNG CHILDREN?

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Background: Posterior rib fractures are highly specific for child abuse, though they can also occur in the setting of birth trauma and diseases associated with increased bone fragility. In older children, there is poor correlation between the radiographic diagnosis of osteopenia compared to the gold standard dual energy x-ray absorptiometry (DEXA). Objective: The objective is to determine if pediatric radiologists can consistently detect signs of metabolic bone disease on a skeletal survey in young children at a point when they are at risk for rib fracture.

Methods: We have collected complete skeletal surveys on 177 children 0 to 2 years old. There are four groups (A no bone disease and no fracture, B bone disease and no fracture, C no bone disease with fracture present, and D bone disease with fracture present). Each bone survey was read by two pediatric radiologists blinded to patient diagnosis. They answered “yes” or “no” for the presence of 8 bone characteristics consistent with bone fragility (osteopenia and 7 bone deformities) and if a rib fracture was present. The inter-rater agreement or Cohen’s kappa coefficient was calculated.

Results: Thirty-four bone surveys were analyzed; 18 with no bone disease and no fracture, 7 with bone disease and no fractures, 8 with fractures and no bone disease, 1 with bone disease and fractures. The electronic medical record confirmed the medical diagnosis. Of the 272 possible findings there were 24 findings noted in 13 patients with agreement for 2 patients with 3 separate findings. The inter-rater agreement was above 50% for 3 characteristics, 35-50% for 2 characteristics and 0% for 4. Only one posterior rib fracture was identified.

Conclusions: These preliminary data demonstrate that identification of bone disease by skeletal survey in children less than 2 years of age who have a disorder associated with metabolic bone disease is not reliable. There was poor to moderate inter-reader correlation among the 8 characteristics. We speculate that the presence of metabolic bone disease is not commonly present on skeletal surveys of young infants, and when present the findings are inconsistently identified.

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PECTUS CARINATUM TREATED WITH ORTHOTIC BRACING AS FIRST-LINE THERAPY

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Background: Pectus carinatum (PC) is a chest wall deformity that some surgeons continue to treat surgically. We hypothesized that all PC malformations in the skeletally immature patient can be treated with thoracic bracing as first-line therapy.

Methods: A retrospective review of 97 consecutive patients (2009 - 2011) with the diagnosis of PC was conducted.

Results: We report the outcomes of 23 patients that attempted full brace therapy; 16 patients were able to complete therapy. Mean duration of treatment was 13 ± 8 months. Seven patients were non-compliant. Fifteen patients (94% of patients completing therapy) had good-to-excellent correction of PC. Minimal-to-no correction of the PC was reported in 1 patient (4% of patients completing therapy) who required surgical correction of a protuberant rib.

Conclusions: Patients that use the thoracic brace have excellent outcomes. Thoracic bracing should be employed as first-line treatment in patients who have PC and have not reached skeletal maturity.

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EFFECT OF TOPIRAMATE ON BMI IN SEVERELY OBESE ADOLESCENTS

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Background: Adolescents with severe obesity respond marginally to lifestyle modification (LSM) alone, yet pharmacological options for use as an adjunct to LSM in this population are lacking. Topiramate, an antiepileptic medication, is associated with weight reduction in obese adults, yet no studies have examined the effect of topiramate on obesity in adolescents. The purpose of this study was to examine the effect of topiramate plus clinically-prescribed LSM on BMI reduction in adolescents with severe obesity.

Methods: Data for this retrospective chart review were collected from patients enrolled over the past 3 years in a tertiary care, multidisciplinary pediatric weight management program. Patients included were those who were treated with LSM plus topiramate (median dose 75 mg daily, range 25 to 125 mg daily) for a minimum of 3 months. Paired t-tests were used to compare baseline and follow-up characteristics.

Results: Twenty-eight patients (71.4% girls, mean
age 14.9±2.6 years) were identified for inclusion in this analysis. Baseline mean BMI was 45.3±10.4 kg/m². After a mean treatment time of 7.8±4.7 months, mean BMI decreased to 43.2±10.3 (P=0.0001). The mean BMI percent change from baseline was -4.8±5.2 %. A sub-analysis of patients (N=14) who were not concurrently taking any other weight-altering medications or specialized diets demonstrated a mean BMI percent change from baseline of -6.1±5.8 % after a mean treatment time of 9.0±5.5 months. Two of the 28 patients experienced paresthesias and one experienced hair thinning. Conclusions: Topiramate with concurrent LSM was associated with clinically-meaningful BMI reduction and acceptable tolerability in adolescents with severe obesity. Randomized controlled clinical trials examining the efficacy and safety of topiramate for the treatment of severe obesity in this population are needed.

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WHAT’S FOR LUNCH? AN ASSESSMENT OF SCHOOL NUTRITION IN INNER CITY MILWAUKEE
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Purpose: An estimated one in three U.S. children is overweight or obese, predicting an average of 112,000 deaths annually. Additionally, since the year 2000 it’s predicted that one in every three U.S. children is expected to develop diabetes, and live a shorter life than their parents. School meals, one facet of many that contributes to obesity rates, comprise a large portion of nutritional intake for many U.S. children. This is especially true in inner city children from low income families who rely primarily on free or reduced meals at school for their daily nutritional needs. This study was generated in response to rising obesity rates at the Bruce Guadalupe Community School (BGCS) in Milwaukee, WI. Methods: This study assessed the nutritional content of twenty meals — five breakfasts and five lunches from the 2011-2012 and 2012-2013 school years. The study analyzed changes made in response to stricter USDA nutrition standards implemented in 2012. Calorie, protein, fiber, sugar and sodium content were assessed using unpaired t-tests. Additionally, 459 students’ milk choices were observed during one lunch period, and a qualitative focus group regarding opinions of school food was performed with ten 6th grade students. Results: Differences between 2011-2012 and 2012-2013 values for the above parameters were not significantly improved except for increased lunch fiber, p<0.0001. Although not significant, sodium levels increased 350mg per lunch despite stricter restrictions. Regarding chocolate milk consumption, observed students consumed over 100lbs or 144,000 calories of excess sugar per week. Conclusions: These results represent the challenges faced by budget-constrained schools seeking to protect the health of their students as well as the bottom line. Though BGCS incorporated more whole grains and low fat condiments, further improvements can be made in beverage options, fresh produce offerings, meal planning, and greater involvement of students in nutritional referenda.

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GASTROINTESTINAL SYMPTOMS BEFORE AND AFTER TOTAL PANCREATECTOMY AND ISLET AUTOTRANSPLANTATION: IMPACT OF PANCREATIC ENZYME THERAPY
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Background/Objective: Total pancreatectomy with islet autotransplantation (TPIAT) can relieve the severe pain of chronic pancreatitis, but results in complete exocrine enzyme insufficiency. Little is known about management of pancreatic enzyme replacement therapy (PERT) and the prevalence and severity of GI symptoms in this population.

Methods: 362 pre and post-operative health questionnaires were collected from 184 pediatric and adult patients who underwent TPIAT for treatment of chronic pancreatitis at the University of Minnesota; including 70 questionnaires from 31 subjects ages 6-18 years (13.9±3.5 years, 17 female). Questionnaires were administered at baseline, and at 3 months, 6 months, and yearly after TPIAT. Self-reported frequency and severity of GI symptoms (diarrhea, steatorrhea, constipation, weight loss, and whether these GI symptoms interfered with their daily life), enzyme dose, and glycemic lability was collected. Results: All patients were prescribed pancreatic enzymes after TPIAT, while 79-94% reported consistent use of enzyme therapy with every meal. Diarrhea was common (47-87% across the two years within the pediatric cohort, 69-82% of adults), but was not affected by surgery. Surgery did not impact prevalence of weight loss. Two years after surgery, constipation had decreased. Steatorrhea increased significantly at 3-6 months after surgery (within the pediatric group, 28% at baseline vs 87% at 6 months, p=0.008), then declined. The interference of GI symptoms on daily activity was the same before and after surgery. Presence of GI symptoms did not vary with enzyme dose, although some subjects were receiving less than or greater than recommended doses. Glycemic lability was associated with steatorrhea. Conclusion: We have previously demonstrated improvement in abdominal pain after TPIAT; however, GI symptoms are common after surgery and are not related to pancreatic enzyme dose. Glycemic lability is associated with steatorrhea, suggesting that poor
response to enzyme replacement therapy may contribute to more difficult to manage diabetes in these patients. Patients often are on enzyme doses that are higher or lower than recommended.

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ABNORMAL CHROMOSOME 6 OR EZR GENE IS POSSIBLY RELATED TO INTESTINAL NECROSIS
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Necrotizing enterocolitis (NEC) is among the most common acute surgical emergencies associated with high morbidity and mortality in neonates. Many potential risk factors have been explored, including prematurity, acute illness and congenital heart disease. Bowel ischemia and intestinal necrosis in older infants is uncommon. There is no reported chromosomal abnormality that is associated with NEC or intestinal necrosis. We report two cases of non-neonatal intestinal necrosis which were associated with abnormal chromosome 6. The first patient was found to have 7.7 Mb deletion on the long arm of chromosome 6 with a karyotype of 46 XX, del 6(q25.3;q27). The deletion encompassed approximately 50 genes and transcripts, including EZR gene. The second patient was found to have 19.27 Mb deletion on the long arm of chromosome 6 with a karyotype of 46,XY,der(6) t (6;18) (q25.1;p11.23). EZR is a key component of microvilli cytoskeleton. Our hypothesis is that the loss of one copy of the EZR gene may have lead to the gut vulnerability in these patients, which then lead to intestinal necrosis. This hypothesis is based on mouse models with EZR expressed in microvilli epithelium, which regulates cell-cell adhesion in the gut.

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A CHILD WITH WORMS IN STOOL
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Introduction: Tapeworm infestation is a significant cause of morbidity worldwide, yet, infrequently encountered in the US. Taeniasis is the intestinal infection with the human tapeworms. The two species T.saginata and T.solium are often difficult to differentiate and require more laboratory techniques for species identification. T.solium infection can be serious as it has the potential of affecting the brain (neurocysticercosis). Case: A five year-old boy adoptee from Ethiopia presented to our Pediatric Infectious Diseases clinic with persistent visible worms in stool for the past 4 months since arrival to the US. He was evaluated by his pediatrician many times and received single-dose ivermectin several time without response. One of the worms was brought in a jar at the visit. Clinical examination was unremarkable and growth was appropriate. Stool microscopy was negative for ova and parasites (O&P). The worm was initially identified as Taenia proglottid but another sample was needed for speciation. Meanwhile the patient had a brain MRI which was normal. He was not started on anti-helminthic treatment until the species was identified by the laboratory as Taenia saginata on the second collected worm sample. The patient was prescribed a single dose of oral praziquantel. We recommended other family members’ stool to be tested for O&P and that the patient will have a follow up stool testing for O&P in 3 months. Discussion: Taeniasis infection is usually asymptomatic. The tapeworm proglottids are sometimes visible in stool and are mobile. Diagnosis can be difficult, often requiring testing 3 stool samples for ova or proglottids on different days to increase sensitivity. Speciation is often difficult as the ova look similar for both species T.saginata and T.solium look the same. Species differentiation is made based on the number of uterine branches of proglottids; with >15 branches/side observed in T.saginata versus T.solium which has <13 branches/side. Scolex appearance is also different between the two species, yet rarely seen on a stool sample. Praziquantel or niclozamide are anti-helminthics used for treatment of T.saginata. A stool test of cure is usually recommended. Conclusion: Taenia speciation is vital as each one has a different clinical course, treatment and complications. Serology is a promising area to aid in quick and accurate diagnosis and identification of Taenia.

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LONG-TERM SINGLE CENTER DONOR LYMPHOCYTE INFUSION OUTCOMES SHOW A ROLE FOR DURABLE RESPONSE IN HIGH-RISK PEDIATRIC LYMPHOID MALIGNANCIES.
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Background: Donor lymphocyte infusions (DLI) are a heterogeneous, peripheral blood stem cell product comprised of immune effector cells. They are widely used to treat relapsed disease after allogeneic hematopoietic cell transplantation (HCT) in adult centers. However, there is limited published evidence of their impact on overall survival (OS) in children with malignant diseases. Objectives: To determine whether DLI cellular content has any effect on the incidence of graft-versus-host disease (GVHD) and OS in pediatric patients with leukemia, the former being a surrogate clinical marker for graft-versus-leukemia (GVL) effects. Design/Method: An IRB-approved,
retrospective chart review investigating all consecutive pediatric DLIs from the CHW was performed. Data were input into a RedCap™ Database and survival was estimated using Kaplan-Meier. Mann-Whitney and Fisher’s Exact test were used to determine significance. Results: From 1991-2011, 30 patients with leukemia (myeloid,n=23; lymphoid,n=7) received 54 DLIs. Patients received their first DLI at a median age of 11.8 (range,0.6-21) years and at a median of 7.1 (range,1.3-69.5) months after transplant. The median infused CD3/kg, CD56/kg, CD19/kg, CD4/kg, and CD8/kg were 1(0.001-31.6)x10^7/kg, 1.6(0.0005-46.7)x10^6/kg, 2(0.001-92.0)x10^6/kg, 6.2(0.005-179.5)x10^6/kg, 3.8(0.003-140.0)x10^6/kg, respectively. DLI cellular content did not appear to have significant effects on GVHD and disease response (p=ns). With a median follow-up of 0.65 (range, .01-12.3) years, the OS at 5 years was low at an estimated 38%. Interestingly, the patients having lymphoid diseases clearly fared better with a 5 year survival at 71 ± 17% in comparison to 28± 10% survival for the myeloid patients although this was not statistically significant (p=.081). Conclusion: With a relatively long follow-up with single-center experience, our study is one of the first to characterize DLI outcomes in the pediatric population. We conclude that DLI has some benefit for promoting OS in a subset of high-risk pediatric malignancies, particularly lymphoid diseases. However, for most pediatric patients, DLI is ineffective at promoting disease remission and improving OS. Implications for Practice: Based on these results, we are developing a prospective clinical trial evaluating the role of augmented DLI and prophylactic timing to improve relapse rates and overall survival.

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**COAGULASE NEGATIVE STAPHYLOCOCCUS (CONS) AS A PATHGEN IN PEDIATRIC URINARY TRACT INFECTIONS (UTI).**

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**Background:** UTI is a common bacterial infection in children that may be associated with significant sequelae. CoNS have traditionally been identified as uropathogenic organisms in teenagers and young adults. Our goal was to explore the clinical significance of CoNS as uropathogens in the pediatric population presenting with greater than 50,000 colony forming units/mL (CFUs/mL) in urine culture (UCX) as per updated AAP guidelines. **Methods:** This is a retrospective chart review of patients 2 months to 21 years of age with CoNS identified on UCX at a large, pediatric, tertiary care center between Jan-Dec of 2011. Demographics, method of urine collection, clinical presentation, laboratory, imaging studies, management and follow-up plans were reviewed. Descriptive statistics using SPSS ver. 20 were used for data analysis. **Results:** A hundred and six patients were identified, of which only 94 had sufficient clinical and laboratory data available for review. Of the 94, 38 (40%) patients had a pure colony of CoNS with ≥50,000 CFUs/mL with no other source of infection. The following results describe these 38 cases. The mean age was 9.6 ± 5 years and 22 (58%) were females. The urine sample was collected by catheterization in 12 (32%) and by clean catch in 26 (68%) of the cases. Urinalysis revealed positive leukocyte esterase in 25 (67%), >5 WBC/HPF in 24 (63%) and bacteriuria in 13 (34%) of cases. Eleven (29%) had vesicoureteral reflux, 5 (13%) had urological abnormalities (megaureter, neurogenic bladder, posterior urethral valve) and 6 (16%) had voiding dysfunction. Dysuria was the most common presenting symptom reported in 16 (42%) of cases; only 8 (21%) reported fever. Seventeen (45%) were initially treated with antibiotics. Nearly half (47%) of patients required a change in antibiotic therapy based on susceptibility results. **Conclusions:** Our data suggests that CoNS can be a true urinary pathogen (≥50,000 CFUs/mL, pyuria and /or bacteriuria in a properly collected specimen as per AAP guidelines) and is more commonly isolated in patients with known urological abnormalities and voiding dysfunction. Clinically, dysuria may be an important diagnostic criterion. Fever in these patients is uncommon. Checking for susceptibilities is required as half of the patients might require change in antibiotic therapy.

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**THE KETOGENIC DIET AS AN ENERGY TREATMENT OF A COMPLEX I DEFICIENCY.**

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**Background:** The mechanistic action of the ketogenic diet, a century-old empiric therapy in the treatment of myoclonic epilepsy, has never been completely explained. Early theories suggested ketone bodies as the anticonvulsant-effective therapeutic agents of the ketogenic diet. However, no direct correlation between seizure cessation and ketone body levels has ever been confirmed. **Materials and Methods:** An individual diagnosed with a biopsy-proven severe OXPHOS complex I deficiency was observed to have acute and subsequent complete seizure cessation with the initiation of a 4:1 ketogenic diet 23 years ago. Based on this clinical result, energy calculations were performed in this report to demonstrate possible effectual differences of excess fats in individuals with and without complex I enzymatic activity. **Results:** With the preponderance of increased calculated energy production in increasing fat-to- carbohydrate-ratio ketogenic diets, increases in ATP production are calculated in all individuals that consume ketogenic diets. When comparing a ketogenic diet versus a normal diet (30% protein, 30% fat, 40% carbohydrate), complex I deficient individuals were calculated to have higher proportional increases in ATP.
were maintained with minimal fluctuation from baseline. Placement of the LMA device is feasible in neonates. Of patients in one attempt with an average total procedure time of approximately 2 minutes. Physiologic parameters decreased by 7% on average compared to baseline, heart rate increased 3 beats per minute on average.

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**Purpose:** Endotracheal intubation is the current standard of practice for surfactant administration in premature neonates with respiratory distress syndrome (RDS). However, endotracheal intubation is associated with adverse physiologic effects, including bradycardia and hypoxia. The laryngeal mask airway (LMA) is an device that may provide a more practical and less invasive alternative to endotracheal intubation for surfactant administration in this population. The objective of this study was to determine the feasibility of LMA placement in neonates by investigating the time, number of attempts and physiologic stability during placement of the device. **Methods:** This study is a component of a national, multi-center, randomized controlled trial investigating surfactant administration through an LMA in neonates. Infants ≥1250g, ≤36 hours old, with a clinical presentation of RDS requiring supplemental oxygen of 0.30-0.40 on nCPAP, and no prior surfactant or intubation were randomized to the LMA Group (surfactant delivery through the device) or Control Group (maintained on nCPAP with no surfactant administered). For this component, videotape of the LMA placement procedure was reviewed to determine total procedure time (define as duration from first insertion of the LMA until successful placement of the device; including placement attempts and recovery time) and duration of LMA time (sum of placement attempts alone). Heart rate and oxygen saturation were analyzed as change from baseline to determine physiologic stability during device placement. **Results:** Twenty-two infants were included in analysis. Mean total procedure time was 129 seconds (±187). Total LMA time was 59 seconds (±81). Successful placement was achieved on the first attempt in 73% of cases. Two attempts were required in 14% of cases and all procedures were successful in ≤3 attempts. As compared to baseline, heart rate increased 3 beats per minute on average (±4, range: -3 to 11) and oxygen saturation decreased by 7% on average (±8, range: -24 to 1). **Conclusions:** Successful placement was achieved in the majority of patients in one attempt with an average total procedure time of approximately 2 minutes. Physiologic parameters were maintained with minimal fluctuation from baseline. Placement of the LMA device is feasible in neonates.

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**Mast Cell-Derived Fas Ligand Promotes Enterocyte Apoptosis and Damages the Gut Mucosal Barrier During Extracorporeal Membrane Oxygenation (ECMO)**

**K. MohanKumar Krishnan,** Cheryl Killingsworth and Akhil Maheshwari

**Background:** ECMO-related systemic inflammatory response syndrome (SIRS) is characterized by mast cells activation, increased cytokine expression, and inflammatory tissue damage. We have shown recently that gut mucosal injury and bacterial translocation play a key role in ECMO-related SIRS. In this study, we used a porcine neonatal model of ECMO to investigate the mechanisms of enterocyte injury during ECMO. Objective: To elucidate the signaling mechanisms involved in enterocyte injury during ECMO/cardiopulmonary bypass. **Design/Methods:** 3-week-old healthy piglets were subjected to venoarterial ECMO for up to 8h. SIRS was assessed on histopathology and plasma cytokine concentrations. Enterocyte injury was measured by plasma I-FABP concentrations (ELISA), enumeration of apoptotic bodies, and by TUNEL staining. Mast cells were identified by immunostaining. Apoptotic pathways were investigated by immunostaining for cleaved caspase 8, cleaved caspase 9, fas and fas ligand (fasL) and qRT-PCR. FasL expression in c-kit+/FcgR1+ dual positive cells from piglet intestine was investigated by RT-qPCR and immunoblots. **Results:** Porcine neonatal ECMO was associated with SIRS similar to that seen in human ECMO. Increased I-FABP levels confirmed that enterocyte injury was an early event during ECMO. TUNEL staining showed increased enterocyte apoptosis. Immunoreactivity for cleaved caspase-8 but not caspase-9 showed that the extrinsic pathway was at work. PCR array for cytokine activators of apoptosis identified fasL as a major activator, which was immunolocalized to mast cells. In-vitro studies showed that LPS increased fasL expression in mast cells. **Conclusions:** We have identified mast cell-derived fasL as a therapeutic target in ECMO-related SIRS. These findings merit further investigation in pre-clinical and clinical models.
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SYSTEMIC MATERNAL INFLAMMATION PROMOTES INFLAMMATORY INNATE AND ADAPTIVE IMMUNE RESPONSES TO VIRAL LUNG INFECTION IN NEONATAL AND WEANLING MICE.
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Background: Subclinical (histologic) chorioamnionitis, a common antecedent of prematurity, is variably linked to chronic inflammatory disorders of infancy, particularly in the context of infection. Growing evidence supports a critical role of innate and adaptive immune interactions in the regulation of inflammation. However, whether exposure to chorioamnionitis disrupts these mechanisms to adversely affect the infant immune response is unclear. We hypothesized that antenatal inflammatory exposure modulates immunity and promotes inflammatory responses to infectious challenge in the postnatal period. Objective: To characterize the effects of antenatal inflammation on innate and adaptive immune responses, we utilized a combined murine model of maternal inflammation and postnatal ‘second hit’ lung infection with Sendai virus (SeV). Methods: Timed pregnant C57Bl/6 dams were injected (E18) with an LPS dose that preserved litter size and viability and caused no outward effects on the dams. D2 neonatal or D21 weanling mice were infected with i.n. SeV (or sham PBS), and sacrificed on post-infection D7, the peak of lung viral load. Blood and multiple organs were analyzed by flow cytometry, immunohistochemistry and real-time PCR to characterize innate and adaptive immune profiles and inflammatory responses. Results: Antenatal exposure followed by SeV challenge decreased body weight (a marker of systemic inflammation) and increased mortality in weanlings, but not neonates. While only LPS-exposed neonates had pronounced basal elevations of granulocytes, macrophages and immature dendritic cells in lungs and livers, SeV infection markedly altered these populations in exposed weanlings but not neonates. Exposure reduced CD4 lymphocytes in neonatal lymph nodes, but increased CD4 and CD8 populations in weanling mice. Basal lung Treg cell expression was increased in exposed neonates and weanlings, and SeV infection increased lung Th1, Th17 and Treg cell populations in exposed weanlings (p<0.001 vs. SeV-infected controls). Conclusion: Low-grade maternal inflammation altered postnatal innate and adaptive immune responses to viral lung infection and promoted an inflammatory phenotype in an age-specific manner. We speculate that antenatal modulation of the fetal immune system at critical developmental windows underlies the inflammatory co-morbidities observed in infected premature infants.

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ENDOGENOUS ERYTHROPOIETIN LEVELS AND BRAIN INJURY IN PRETERM INFANTS
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Background: Significant up-regulation of erythropoietin (Epo) and erythropoietin receptor has been observed in hypoxic-ischemic brain injury. The neuroprotective potential of Epo in newborn brain injury is currently being explored. Recent data suggest an association between cord blood Epo levels and the risk of intraventricular hemorrhage in preterm infants (PT). Objective: To describe Epo levels in the first month of life in PT infants <30 weeks gestation and investigate correlations between endogenous Epo levels and: (a) perinatal risk factors, and (b) cerebral injury defined by ultrasound (US) and magnetic resonance imaging (MRI). Design/Methods: In a prospective cohort study, PT infants with gestational age <30 weeks had Epo levels measured from cord blood and/or serum at < 24 hrs of life, at 1 week, 2 weeks, and 4 weeks of life. Perinatal data was collected. Cerebral injury was evaluated through serial cranial US and MRI close to 40 weeks corrected gestation. A modified scoring system was used to assess brain injury based on signal abnormalities detected on MRI in white matter, cortical and deep grey matter and cerebellum and on biometric studies. Results: 27 patients were included in the study, 14 females and 13 males, mean gestational age 27.5 ±1 and birthweight 1094 ±238 gm. Birth Epo levels showed wide variations with a mean level of 18.4 ±33.8 mU/ml (range 2.7 - 174). Epo levels on the first day of life were negatively correlated with birthweight and this trend became more evident and statistically significant by the end of the first (p=0.012) and second (p=0.007) weeks of life respectively. Elevated Epo levels trended with emergent cesarean deliveries (23.4 vs 6.5 mU/ml, p=0.08), and abnormalities detected on placental pathology (23.5 vs 9.7 mU/ml, p=0.2). There was also a negative correlation between Epo levels measured in the first two weeks of life and the biparietal diameter adjusted to term (p=0.027 and p=0.068 at the end of the first and second weeks of life respectively), otherwise there were no significant correlations between Epo levels at any time and cerebral injuries detected on US or MRI. Conclusions: These pilot data demonstrate variations in newborn Epo levels in PT infants. Epo levels in the first two weeks of life tended to be higher in the smallest and most immature infants. Epo levels at birth appear related to adverse perinatal factors and may act as a potential biomarker.
THE COMPONENT OF TRUST IN END OF LIFE DECISION MAKING IN THE NICU: PARENT PERPECTIVES.

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Purpose: Many families of infants in the NICU are faced with decisions concerning withdrawal of life-sustaining support for their infant. End of life decision making by parents in the NICU is facilitated by care providers who help families understand their infant’s health problems, treatment options, and prognosis, as well as the parent-physician relationship, communication and parents’ trust in their infant’s care providers. Trust is a multi-factorial concept and has been shown to impact decision making, and has not been well-studied in the NICU population. This study describes the role of parents’ trust in the physician when making decisions to continue or withdraw/withhold life prolonging treatments. Methods: This study consists of a series of semi-structured interviews of parents of infants cared for in the NICU, who had discussions and made decisions about withdrawal of life support for their infants. Also used is a quantitative tool, The Human Connection Scale, which measures aspects of the physician-patient relationship including patients’ trust in the physician when making end of life decisions. Analysis is via the grounded theory method and establishment of themes, as well as cumulative scoring of the trust scale. Results: All families interviewed report that they trust their physician and have high trust scores on the Human Connection Scale (mean score 60/64). Most families state that their trust in their physician played a role in helping them make their decision about withdrawal of life-sustaining support. Families describe many actions and traits that help build their trust in their physician including caring about the infant and the family, medical knowledge, competence, establishing a relationship, and frequent updates to the family. Conclusions: Families of NICU infants demonstrate high levels of trust in care providers when facing end of life decisions. Families rely heavily upon their care providers to guide them through the end of life decision making process, and report many specific physician behaviors and traits that improve the provider-parents relationship and build trust. This information gained from families could improve physicians’ actions and behavior during end of life discussions, and could also impact the way that physicians are trained in end of life care.

NURSES’ AND PARENTS’ PERCEPTIONS OF AN OPEN UNIT (OU) POLICY IN A NEONATAL INTENSIVE CARE UNIT (NICU).

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Background: Family centered care (FCC) is a philosophy often strived for in the NICU, but practice can often lag behind philosophy. The physical environment of a NICU is not conducive to FCC. Liberal visitation policies now are accepted as beneficial. Family presence is linked to reduced stress, better patient safety, and increased family education and satisfaction. Research has also shown it can increase nurses’ workload and make nurses feel uncomfortable. Finding a way to balance these concepts can be challenging. Objective: To determine nursing perceptions pre and post implementation of an OU. To compare parent satisfaction related to time allowed to be with infant pre and post OU. Design/Methods: An anonymous survey was given to nurses asking how they felt about an OU pre and post implementation. Responses were used to learn perceived barriers; focus groups were held to understand the concerns and develop solutions. Educational sessions on implementation were held. NRC Picker parent data pre and post OU were compared. Results: Initially, 87% (76/87) of nurses were not in favor of an OU. Most common concerns: HIPPA 71%, social issues 56%, and increased time for report 45%. Post OU 60% (32/59) were in favor and 22% were neutral. 54% expressed no major concerns. The most common concerns: interruptions 25%, limited space 22%, HIPPA 17%. 80% cited benefits for parents. Most common benefits: increased visiting 49% and improved parent emotional state (decreased stress and anxiety, increased satisfaction) 43%. Pre OU 78% (18/23) of parents felt they were allowed to be with their baby as much as they wanted compared to 92% (36/39) post. Conclusions: NICU nurses had skeptical beliefs and attitudes toward open visitation, over time most nurses favored the change and benefits for families were recognized. Parent satisfaction increased regarding time spent with infant. Change can be challenging. Soliciting staff attitudes, requesting involvement for solutions, and educating on the benefits for families can help initiate and sustain change.
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SMALL LEUCINE-RICH PROTEOGLYCANS BIND TGFβ2 IN HUMAN MILK AND LIMIT ITS BIOAVAILABILITY
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Background: We have previously shown that (1) enteral supplementation of transforming growth factor-beta (TGFβ2) can protect mouse pups against necrotizing enterocolitis (NEC)-like injury; and (2) preterm milk contains large amounts of latent TGF-β, which can be readily activated. Emerging evidence indicates that several small leucine-rich glycoproteins (SLRPs) such as decorin, biglycan, fibromodulin, and asporin can sequester TGF-β in the extracellular matrix and prevent its activation. Objective: Determine whether SLRPs (1) are expressed in human preterm milk, and (2) bind milk-borne TGF-β2. Design/Methods: Human milk samples were collected on days 0-3, 7-10, and 1 month (n=20 each) from mothers who delivered preterm and compared to term milk (n=20). TGF-β bioactivity was measured using reporter cells transfected with a luciferase reporter for the plasminogen activator inhibitor-1 promoter and with a smad-responsive element. SLRPs were sought in milk by western blots. SLRP-TGF-β binding was investigated using immunoprecipitation and non-denaturing gels. SLRP expression in human mammary tissue was confirmed by immunohistochemistry. Results: Preterm milk contained less TGF-β bioactivity than term milk (9±2 vs 20±4%, p<0.05), even though preterm milk contained a larger pool of TGF-β that could be activated. Measurement of TGF-β isoforms in the cellular and aqueous fractions of milk and by immunoprecipitation studies confirmed that TGFβ2 is the predominant isoform in milk. We detected decorin, fibromodulin, biglycan, and asporin in preterm milk, where fibromodulin and asporin were most abundant. All four SLRPs bound milk-borne latent TGF-β2, whereas biglycan bound both latent and active forms of TGF-β2. Immunohistochemistry localized decorin and fibromodulin in the interstitial cells, whereas biglycan and asporin were detected in mammary epithelial cells. High-magnification images showed that biglycan and asporin immunoreactivity was more prominent on the apical aspects of mammary epithelial cells, indicating a vectorial discharge pattern directed into the mammary glands. Conclusions: Preterm milk contains SLRPs such as fibromodulin and asporin, which bind latent TGF-β2. Further study is needed to determine the mechanisms by which SLRP-bound latent TGF-β2 could be activated for therapeutic purposes.

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THE GESTATIONAL AGE OF INDEPENDENT ORAL FEEDING IN PRETERM NEWBORNS
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Purpose: Preterm newborns (PN) are neurologically immature and the ability to suck, swallow, and breathe is not fully coordinated until they approach term gestation. The maturation of this innate reflex is often desired before PN can be safely discharged from the neonatal intensive care unit (NICU). The fetus has the ability to suck, swallow, and breath by 15 weeks gestational age (GA); postnatally the maturation of these skills varies considerably. There has been no large study examining at what GA PN achieve independent oral feeding. Investigations on this topic will enhance discharge planning for the parents and healthcare team. The study objective was to determine the mean GA when PN develop independent oral feeding skills and whether gender, ethnicity, or delivery route affects this reflex. Methods: We retrospectively evaluated 1603 PN ≤36 weeks GA over a 26-year period (1978-2004) in a single NICU. Exclusion criteria included: congenital anomalies, gavage feeding at discharge, APGAR score ≤4 at five minutes of life, and unknown GA at birth. Independent oral feeding was defined as the first 24 hour feedings period taken orally ad libitum (PO ad lib) with no regression to gavage feeding. The GA was calculated based on the EDC unless the Ballard Exam differed by ≥2 weeks. Results: The mean GA at birth was 31+3/7 weeks with a range of 23-36 weeks. In this study we had 53% males, 53% of PN delivered vaginally, and the ethnicity in this study approximated: 58% Caucasian, 26% African-American, and 16% Hispanic. The mean GA of independent oral feeding was achieved at 36+5/7 weeks (95% CI=±1 day) with a mean observation period of four days before discharge. There was no statistical significance in GA of independent oral feeding based on ethnicity. PN delivered by c-section had a significant delay (3 days) in achieving independent oral feeding (p-value 0.002) and female PN achieved independent oral feeding one day earlier (p-value 0.039). Conclusion: We found the mean GA for the maturation of independent oral feeding was 36+5/7 weeks. Studies have shown females have a distinct advantage in prematurity. Females achieved independent oral feeding one day sooner. The ethnicity did not impact maturation of independent oral feeding in our study. We found PN delivered by c-section had a significant delay in maturation of this reflex. PN delivered by c-section could represent a more critically ill population or the process of parturition could influence the maturation of the feeding reflex.
PULMONARY NITRIC OXIDE EXCRETION IN TRACHEOSTOMIZED AND VENTILATOR-DEPENDENT CHILDREN: A PILOT STUDY

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PURPOSE OF STUDY: Nitric oxide (NO) plays a key role in preterm infants with bronchopulmonary dysplasia (BPD) as well as in term infants broadly categorized to have chronic lung disease of infancy (CLDI). Our aim is to measure exhaled NO (eNO) in tracheostomized and ventilator-dependent infants with BPD and CLDI and to compare with values measured from face mask reported in the literature. We also calculated pulmonary NO excretion (V̇NO = eNO (plateau) X minute ventilation in L/minute/kg). METHODS: This is a pilot study to measure eNO from the trachea in a cohort of tracheostomized and ventilator-dependent infants with BPD/CLDI. Average of two measurements of eNO levels were taken (assuming less than 10% discrepancy) using Nitric Oxide Analyzer (Sievers NOA280i). The eNO (plateau) and V̇NO were calculated. RESULTS: Preliminary data (n=14): There were 8 patients with BPD, 6 with CLDI. In BPD patients: mean gestational age (GA): 25 weeks (23-29); mean birth weight (BW): 0.75 kg. Mean age at eNO measurement: 13 months (range 7-25); For CLDI patients, mean GA: 37 weeks (31-39); mean BW: 2.6 kg. Mean age at eNO measurement: 21 months (range 7-35). The mean eNO (max) for BPD patients was 3.23 ppb (range 1.32-5.58) compared to 4.35 ppb (range 1-12ppb) in CLDI patients. The mean V̇NO for BPD infants: 0.83nl/kg/min (range 0.30-1.79) compared to 0.73nl/kg/min (range 0.16-1.46) in CLDI infants. There was no statistically significant difference between the BPD and CLDI groups for eNO and V̇NO values. The published reports by Gabrielle, et al., and Leipala, et al. showed eNO levels measured from face mask in infants with BPD: 11.8ppb (8.2-16.8) and 12.2 ppb (4.6-34.5) respectively. CONCLUSION: The eNO levels directly measured from the trachea of tracheostomized and ventilator-dependent infants with severe BPD/CLDI are significantly lower than what is reported in the literature measured from a face mask. Our measurements represent reliable endogenous quantified selective lower airway eNO output, eliminating upper airway NO contribution.

NEONATAL LENTICULOSTRUATE VASCULOPATHY: CHARACTERIZATION OF 42 CASES.


Background: Lenticulostriate vasculopathy (LSV) is an incidental finding in neonatal ultrasound of the head with varied and unspecified etiology. It is characterized by linear echogenicity in the areas of the thalamus and basal ganglia. Purpose: To provide some clinical evidence relevant to etiology by analysis of a large series. Methods: The digital medical records of neonates admitted to the NICU at our tertiary care center were reviewed for any consistency with “LSV” or “linear echogenicity” spanning a 16-year period, dating from July of 1996 to July of 2011. The ultrasound images associated with these reports were then verified by a pediatric radiologist for being consistent with LSV. Then, 120 age-matched controls born less than 32 weeks gestation and admitted to the NICU were chosen by random selection, and compared across a number of independent variables using the two sample t-test for normal data, and the Wilcoxon test for all other, non-normal data. In comparing categorical variables, Fisher’s Exact test was used. p < 0.05 was considered significant. Results: We found statistically significant differences between LSV and control infants in a number of areas including: lower APGAR scores at 1 and 5 minutes, smaller head circumference and length, lower first magnesium levels, higher levels of broncho pulmonary dysplasia, hydrops fetalis, patent ductus arteriosus, necrotizing enterocolitis, and sickle cell train, greater instances of blood and trachea cultures positive for infection, higher use of antibiotics, greater instances of sepsis, higher rates of mechanical ventilation, more likely to require transfusion, and mothers were more likely to suffer from vaginal bleeding and have had general anesthesia during delivery. Conclusions: An overarching theme or themes can be drawn from our data suggesting that LSV might be a result of hypoxic insults suffered in utero or shortly after birth, and/or an inflammatory response. Our data refutes previous studies suggesting that LSV is the result of chromosomal abnormalities, fetal alcohol syndrome, drugs, or twin-twin transfusion syndrome.

A NORMATIVE URINARY METABOLOMIC PROFILE OF CARNITINE IN PREMATURE INFANTS

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Background: Carnitine is an essential metabolite in fatty acid beta-oxidation required for energy production. Carnitine deficiency can have severe consequences, particularly in times of illness and stress. Serum carnitine levels in preterm infants are decreased when compared to term infants. The clinical relevance is uncertain. Urinary
Carnitine levels are thought to be representative of plasma levels. Serum in preterm infants is a less desirable medium for study given the difficulty associated with collection and the small whole-body blood volumes. Urine provides a non-invasive, easily collected specimen for study. **Objective:** Identify a normative metabolomic urinary profile of the developing kidney. **Methods:** 30 preterm infants were divided into 3 groups of 10 based on weight: 500-1000g, 1000-1500g and 1500-2000g. Infants were excluded if there were major congenital anomalies, anomalies of the genitourinary tract or abnormal maternal conditions during pregnancy. Urine was collected on days 1, 3, 7, 14 and 30. Samples were sent to Metabolon (Durham, NC) for analysis using mass spectrometry (GC/MS and LC/MS/MS). **Results:** Urinary carnitine levels in the lowest birthweight infants were significantly decreased over the 30 day time course compared with larger infants. Urinary pivaloylcarnitine levels were significantly increased during this time. **Conclusion:** The smallest preterm infants had reduced urinary carnitine, consistent with previous studies demonstrating low plasma levels in these infants. Increased excretion of carnitine may contribute to carnitine deficiency in the most preterm infants. Carnitine deficiency may lead to defects in fatty acid beta-oxidation and energy production, particularly in the renal tubules, which depend on this source of energy. Such a state may predispose to renal injury in their most formative stages. Carnitine supplementation may therefore be warranted in the most preterm neonates.

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**TRAINING AND DECISIONS REGARDING RESUSCITATION OF EXTREMELY PREMATURE INFANTS AMONG U.S. PEDIATRIC RESIDENTS AND FELLOWS.**

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**Purpose:** To determine whether variability exists among US training programs with regard to resuscitation of premature infants born between 22-27 weeks gestational age and to categorize the decisions trainees would make if they were the attending neonatologists. **Methods:** A survey asked US pediatric residents and neonatal-perinatal medicine fellows how they had been trained with regard to resuscitation of premature infants born at each gestational age, 22-27 weeks. Participants were then provided national survival rate data for each age and responded with how they would choose to proceed if they were the attending neonatologists. For both series of questions, four response options ranged from choosing to always resuscitate to never resuscitate. For the first series of questions respondents could also answer that they had not learned a consistent approach with regard to resuscitation at each gestational age. **Results:** The majority reported learning a consistent approach at each age. The percent that had not learned a consistent approach increased with younger gestational ages. The majority would choose to resuscitate infants born at 24 weeks whereas the majority would choose not to resuscitate infants born at 22 weeks. At 23 weeks, respondents were split approximately one-third to two-thirds between those who would choose to resuscitate always or most of the time and those who would choose to resuscitate never or rarely, respectively, though this was closer to half and half among third year fellows. **Conclusions:** Substantial variability exists among individuals’ decisions concerning infants born at 23 weeks gestational age. Future research should investigate how pre-determined actions regarding resuscitation affect clinical practice and how to best enable parents to participate in shared decision making when faced with conditions under which physicians are divided.

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**UPREGULATION OF HEPCIDIN EXPRESSION BY LACTOFERRIN ADMINISTRATION TO PRE-WEANLING MICE**

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**Background:** Hepcidin is a peptide hormone produced in hepatocytes which regulates dietary iron absorption and systemic iron distribution. Liver hepcidin gene expression is upregulated in association with body iron status. This regulation includes a signal from the circulating iron-binding protein transferrin via transferrin receptor 2. Lactoferrin (Lf) is a related iron-binding protein found in high concentrations in human milk, where it contributes to newborn host defense. While the contribution of lactoferrin to systemic iron metabolism is unclear, lactoferrin is capable of delivering iron to hepatocytes. Lactoferrin, however, does not interact with transferrin receptor 2.

**Purpose:** To determine whether delivery of iron to hepatocytes in a form other than transferrin could signal to hepcidin we tested the effect of iron-replete lactoferrin administration to mice on liver hepcidin mRNA expression. **Methods:** Mice at 12-14d (pre-weanling) were administered human Lf (equivalent to 2 mg/kg iron) or carrier intraperitoneally (IP) and sacrificed 6 h later. Other mice were administered a comparable IP dose of iron as transferrin. Another group of mice were delivered Lf or carrier enterally (by orogastric tube), and the sacrificed 6h or 24h later. Liver hepcidin (Hamp1) mRNA was measured by real-time RT-PCR. **Results:** Parenteral administration of Lf in pre-weanling mice was associated with a ~70-fold increase in liver Hamp1 expression after 6 hours (P=0.002). This compares with an only 4.5 fold increase in Hamp1 expression 6h after a comparable dose of
transferrin. Enteral Lf resulted in a ~45-fold increase in Hamp1 expression (P<0.001) after 24 hours. **Conclusions:** Exogenously administered Lf increases liver Hamp1 expression in pre-weanling mice. Iron delivery to the liver in a form other than transferrin can therefore upregulate hepcidin expression. Lactoferrin-mediated changes in hepcidin expression may contribute to reported benefits of supplemental Lf on host defense.

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**PARENTAL NICU VISITATION IN LOW BIRTH WEIGHT INFANTS DURING THE FIRST 28 DAYS OF LIFE IN AN INNER CITY HOSPITAL.**


**Background:** Early, frequent and prolonged parent-infant contact has been shown to enhance maternal bonding, stabilize thermal status in preterms and support / encourage breastfeeding. **Aim:** To study the patterns of NICU visitation in preterm infants during the first 28 days of life and identify time frames when parental presence can be enhanced and education can be maximized. **Methods:** Data was collected prospectively on preterm infants admitted to Sinai Children’s Hospital’s NICU between November 2012 and April 2013. Infants < 2500 g and 36 6/7 weeks were included in the study. Frequency and duration of visits by mother, father and grandparents were recorded on a daily basis for the duration of the patients hospitalization using the visitor log book. To ensure accurate data only patients born from Monday to Friday were enrolled. **Results:** A total 159 neonates were admitted to the NICU during the study period. Data was available for the first 100 (62.8%) patients that fulfilled the criteria. Of the infants studied, 62% were males, 62% were African American, 33% were Hispanic and 5% were a mixed group. Average gestational age and birth weights were 32.63 weeks and 1843 g for male infants and 32.32 weeks and 1665g for female infants. Average length of stay was 25.3 days. A total of 82% of parents visited by DOL 4, 87% on DOL 4 and 97% on DOL 10. Grandparents visited in 51% of patients.

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<th>Paternal Length of Visit (hrs)/day</th>
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Moms show a significant increase in frequency of visitation compared to fathers all throughout the patients hospital stay. While each parent showed a decreasing visitation trend, this did not approach significance. Only 14% of fathers were present during discharge, hence 86% of Moms go through the discharge process and take baby home without paternal support. **Conclusions:** Mothers significantly displayed an increase in frequency and duration throughout the patients hospital stay. DOL 4-5 and 9-10 were the peak visitation periods in the cohort. Paternal presence needs to be supported during the peak visitation days and strategies need to be developed to increase involvement of both parents as infants stay in the NICU goes beyond week 2 of life.

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**USING CBC AS A MARKER FOR CLABSI IN THE NICU**

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**Introduction:** Central line-associated blood stream infections (CLABSI) increase length of stay and mortality risk among infants in the intensive care units. The purpose of this study is to investigate markers of such infections through the use of the complete blood count (CBC) prior to the positive blood culture. **Methods:** This is a retrospective chart review and analysis of infants with CLABSI admitted to our neonatal intensive care unit (NICU) between January 2007 and January 2013. Updated guidelines to prevent CLABSI during insertion and maintenance of central lines were followed throughout this period. The CBC closest to time of central line insertion, the last before blood culture, and the closest to time of positive blood culture was recorded. White blood cells (WBC), immature to total (IT) neutrophil ratio, and platelet count results were compared among the three sets. **Results:** Eighty six patients were included, 28 of which (33%) had more than one line infected, and 15 patients (17%) had more than one organism. Coagulase Negative Staphylococci (CoNS) was the most common organism (54%). The average number of days since line insertion to infection was 14 days. The platelet count was significantly higher in the second set compared with either the first or third sets. The IT ratio was significantly different among the three sets, with set three being the highest at a mean of 0.25. There was no significant difference in WBC count among the three sets. **Conclusion:** The distribution of the most common organisms is consistent with previous studies. This study demonstrates that infection indicators are only observed in the CBC closest to the positive blood culture.
HYPOCALVARIA AS AN ISOLATED SKELETAL DYSOSTOSIS

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Acalvaria/hypocalvaria is an extremely rare condition (estimated to occur 1 in every 100,000 births) that presents as a spectrum of hypoplasia or partial to complete absence of flat bones of the cranial vault. The recognized etiologies demonstrate a diverse pathogenesis including neural tube or post-neurulation defects, amniotic banding sequence, and ACE-inhibitor embryopathy. Many cases reported are idiopathic. Most reported cases also have underlying brain anomalies, including severe anomalies responsible for early neonatal death, and myriad other major congenital anomalies. Given the diversity of pathophysiology and associated anomalies, it is both a heterogeneous and poorly understood condition. We report a term female infant born by planned Caesarean section following an uncomplicated pregnancy. Family history was remarkable only for a sibling born small for gestational age. At delivery the infant had no palpable bones above the level of the forehead. Upon transfer to neonatal intensive care, exam was significant for symmetric growth restriction, with all parameters below the 3rd percentile, and a soft cranium with minimally palpable bones between the forehead and occiput. Face exam had blue sclera, hypertelorism, exotropia, broad nasal bridge, upturned nasal tip, high-arched palate, and low set ears. Left hand had a single palmar crease. Remainder of the detailed physical exam was normal. A full skeletal survey only showed wormian bones of the calvaria. Computerized tomography of the head with 3D skull reconstruction showed marked deficiency of the frontal, parietal, and squamous temporal bones. Brain MRI was normal. Echocardiogram and renal ultrasounds were without major anomalies. Laboratory studies ruled out hypophosphatasia, cytomegalovirus, and the most common genetic causes of osteogenesis imperfecta. Routine chromosome studies and comparative genomic hybridization were normal. The infant’s neonatal course was uncomplicated. Follow-up at 7 months of age revealed that the infant has had moderate development of the bones of the calvaria. We report this case of hypocalvaria isolated from other major anomalies or a known cause. The infant’s significant growth restriction leads one to consider a proposed mechanism of chronic intrauterine hypotension and possible hypoxia, the same mechanism implicated in cases of ACE-inhibitor embryopathy with acalvaria/hypocalvari a and renal agenesis. This patient suggests the clinical spectrum of hypocalvaria is broader than reported in current literature and may present without other major congenital anomalies.

ACUTE DOXORUBICIN EXPOSURE IN NEONATAL RAT ENGINEREED CARDIAC TISSUE RESULTS IN CELL DEATH

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Doxorubicin (DOX) is a highly effective chemotherapeutic agent in treatment of pediatric and adult cancers. Cardiotoxicity limits the therapeutic dose and presents a long-term source of significant morbidity which may be more severe when exposure occurs very early in life. We hypothesized that the neonatal rat engineered cardiac tissue model (ECT) would demonstrate altered contractility after short-term exposure to therapeutic doxorubicin. Isolated cardiac cells from one day old rat ventricles were either plated in 12-well dishes for monolayer cultures, or were mixed with collagen and Matrigel™ in 6-well FlexCell culture plates that polymerized to form ECTs. Monolayer cultures were treated for 48 hrs with either 0.1, 0.5, 1, 2 or 5μM DOX, followed by assessment of cell survival by MTT assay. Based on the observed toxicity, ECT were treated with either 0.1 μM DOX or vehicle for 24 hours followed by measurement of twitch force amplitude and contraction kinetics. RNA were isolated and GAPDH and MYBPC3 gene expression quantified. Comparisons between DOX and vehicle treated ECTs were made using Students t-test. Cell viability by MTT assay was markedly decreased even at the lowest DOX concentration (1.80±0.16AU vs. 0.79±0.09AU; p=0.01). 0.1 μM DOX treated ECTs had a 21.3±3.3% reduction in twitch force amplitude with no change in contractile kinetics compared to vehicle-alone ECT. Furthermore, a decrease in the cMyBP-C/GAPDH mRNA ratio in cardiac cells treated with 0.5μM DOX (1.22±0.11AU vs. 0.46±0.03AU; p<0.001) indicates disproportionate loss of cardiomyocytes vs. non-myocytes. We conclude that DOX decreases neonatal cardiac force amplitude without affecting contraction kinetics. Our data suggest a mechanism of preferential cardiomyocyte death after exposure to DOX and may indicate that the immature heart is more at risk for the long-term cardiotoxic effects of this class of agents.
DISTINCT GROUP EXPRESSION PROFILE OF ENDOTHELIAL PROGENITORS EXPOSED IN UTERO TO GESTATIONAL DIABETES

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Gestational diabetes mellitus (GDM) is common, complicating ~5-9% of all pregnancies. Children exposed to GDM in utero are at an increased risk to develop endothelial dysfunction and hypertension. Previous studies in the lab showed that cord blood endothelial progenitors, or endothelial colony forming cells (ECFCs), from diabetic pregnancies exhibit reduced colony formation and decreased vessel forming ability as well as increased senescence. The objective of the current study was to identify novel molecular targets responsible for ECFC functional deficits. We hypothesized that prenatal exposure to GDM induces epigenetic changes resulting in altered gene expression of ECFCs. Using an Affymetrix microarray that screens a total of 36,079 transcripts, cord blood ECFC lines from healthy controls and from pregnancies complicated by GDM requiring insulin therapy were screened for changes in mRNA abundance. Of the 36,079 transcripts on the microarray, only 32,020 were coding transcripts. The 32,020 molecular targets from the microarray were then prioritized, examining for a p value ≤ 0.05 and a ±2 fold change in gene expression. After evaluating for a p value ≤ 0.05, 2,056 molecular targets remained and were reduced to 36 molecular targets after assessing for a ±2 fold change in gene expression at the RNA and protein levels, respectively. Of the 20 molecular targets, 5 confirmed the results of the microarray at the RNA level, however only 3 were confirmed at the protein level. ECFCs from pregnancies complicated by GDM requiring insulin therapy had decreased FERMT3 RNA and protein levels compared to healthy controls, while ECFCs from pregnancies complicated by GDM requiring insulin treatment had increased PLAC8 and SM22 RNA and protein levels compared to healthy controls. The analysis determined three novel molecular targets for further study in endothelial cell dysfunction, FERMT3, PLAC8, and SM22. Future knock down studies are needed to investigate each molecular target’s potential contribution to ECFC functional deficits.

THE ROLE OF ALTERED GENE EXPRESSION IN ENDOTHELIAL COLONY FORMING CELLS FROM INFANTS OF DIABETIC MOTHERS.

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Background: Diabetes complicates ~18% of pregnancies. Long term complications for infants of diabetic mothers (IDMs) include type 2 diabetes (T2DM), hypertension, obesity, and metabolic syndrome. The mechanism for this increased risk is unknown. Endothelial colony forming cells (ECFCs) are highly proliferative progenitor cells with vasculogenic potential. Our previous studies show a reduction in cord blood ECFCs from pregnancies complicated by pre-gestational diabetes as well as alterations in ECFC function including reduced proliferation, decreased vasculogenesis, and increased senescence. Conversely, our unpublished studies show that ECFCs from gestational diabetes (GDM) pregnancies have increased proliferation and reduced senescence. An unbiased microarray screening study evaluated for changes in ECFC gene expression between control, GDM, and T2DM pregnancies by examining >28,000 gene transcripts. Preliminary data revealed significant differences in gene expression between control, GDM, and T2DM cells. Two transcripts with the greatest differences in expression were MEOX2 and PLAC8. MEOX2 is a transcription factor that increases senescence in other cells, and PLAC8 is a transcription factor associated with increased proliferation. Objective: The goals of this study are to confirm MEOX2 and PLAC8 overexpression in ECFCs from diabetic pregnancies, to examine MEOX2 and PLAC8 subcellular localization, and to evaluate if MEOX2 or PLAC8 overexpression contributes to ECFC dysfunction. Method: Cord blood ECFCs from control, GDM, and T2DM pregnancies were used for all studies. Western blotting was conducted to quantify protein expression and to examine subcellular localization. Transfection of short interfering-RNAs (siRNAs) into ECFCs was conducted to decrease protein expression followed by Western blotting. Preliminary data show increased nuclear localization of MEOX2 in T2DM cells versus controls while PLAC8 is primarily in the membrane of T2DM and GDM cells. Initial siRNA data revealed reduced expression of PLAC8 on Western blot. Conclusion: Our preliminary data confirm overexpression and altered subcellular localization of MEOX2 and PLAC8 in ECFCs from IDMs. Immunofluorescence to confirm cellular localization is pending and functional studies after siRNA knockdown are ongoing, which include proliferation and cell cycle analyses.
25-HYDROXY VITAMIN D LEVELS AND IMMUNE FUNCTION IN PRETERM INFANTS.
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Purpose: The primary objective of this study is to assess the relationship between 25-hydroxy vitamin D (25OHD) levels and immune function in 50 preterm (≤ 32 6/7 weeks gestational age) infants. The secondary objective is to assess the adequacy of our current vitamin D supplementation practice in supporting sufficient 25OHD levels for this population. Methods: This is an IRB approved, prospective, observational study conducted in a level III neonatal intensive care unit. After obtaining parental consent, 25 OHD, IL-6, IL-10 and TNF-alpha levels are analyzed from umbilical cord blood, infant blood samples at 3rd week of life and prior to hospital discharge. T-cell subset analyses are performed on all subjects at 34 weeks postmenstrual age. Maternal and infant demographics, medical diagnoses and nutritional intake data are collected. The relationships between 25OHD levels, cytokines, and T-cell subsets are assessed using correlation statistics. Results: To date, 34 subjects have been enrolled. Preliminary analyses on a subset of data (20 subjects) revealed a significant correlation between 25OHD and TNF alpha in cord blood (r=0.56; p= 0.02), as well as cord blood and 3rd week 25OHD levels (r=0.65; p<0.01). However, correlation between cord blood 25OHD levels and gestational age or T-cell subsets; 3rd week 25OHD levels and T-cell subsets are not significant. Despite all mothers reporting prenatal vitamin supplementation during pregnancy, none of 28 (32%) cord blood 25OHD levels were < 20ng/mL indicating deficiency. Mean cord blood level was 24.7ng/mL ± 7.2 (range: 10.3 – 50.1ng/mL). By the 3rd week of life, 25OHD levels significantly increased (p<0.01): mean = 40.2ng/mL ± 12.7 (range: 24.0 – 73.0ng/mL). Enrollment continues and final analyses are pending. Conclusion: Based on preliminary analysis, TNF alpha, a proinflammatory cytokine, is the only immune function marker found to correlate with cord 25OHD levels. The current level of vitamin D supplementation administered in our NICU appears to support achievement of adequate serum levels (based on reference goal of ≥ 20ng/mL) in preterm infants – including those born with deficient stores. Additional analyses will include clinical indices of immune function (i.e., septic evaluations, respiratory outcomes, etc). Study enrollment continues.

CORD BLOOD VITAMIN D STATUS IN PRETERM INFANTS
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Background: Vitamin D is an essential nutrient for neonates, particularly with regards to bone health. Increasing evidence also suggests an association between vitamin D, innate immunity, and lung health. The optimal dosage of vitamin D supplementation in pregnant women and neonates is still under debate. A lack of information exists about vitamin D status in preterm neonates, particularly the moderate and late preterm population. Objectives: We hypothesized that preterm infants born smaller and at earlier gestational ages have lower cord blood vitamin D concentrations due to a lack of third trimester nutrient accretion. Methods: Following parental written consent, we obtained cord blood serum 25-hydroxyvitamin D (25OHD) concentrations on infants born between 30 0/7 and 36 6/7 weeks’ gestational age (n=41). We defined 25OHD concentrations less than 25 ng/ml as deficient, 25-32 ng/ml as insufficient, and greater than 32 ng/ml as sufficient or normal. Results: The mean gestational age was 34.4 ± 2.0 (SD) weeks and mean birth weight was 2194.5 ± 691.0 grams. The mean cord blood 25OHD concentration was 27.5 ± 13.6 ng/ml. Vitamin D deficiency was present in 21/41 (51%) of infants and insufficiency was present in 8/41 (20%); normal levels were present in 12/41 (29%). There was no correlation between gestational age or birth weight percentile and 25OHD levels. Infants with Medicaid insurance had lower vitamin D concentrations than those with commercial insurance [19.2 ± 6.1 ng/ml (n=9) and 29.9 ± 14.2 ng/ml (n=32), p=0.03]. Conclusions: Vitamin D deficiency or insufficiency exists in a majority of moderate and late preterm infants at birth. Maternal socioeconomic status but not gestational age or birth weight percentile seems to affect vitamin D status. We are now conducting phone interviews at 3, 6, and 12 months of age to test the hypothesis that preterm infants with vitamin D deficiency or insufficiency at birth are at increased risk for respiratory morbidity during the first year of life. Implications for Practice: Additional monitoring and supplementation of vitamin D may be required for at risk pregnant women and neonates with vitamin D deficiency or insufficiency, particularly if further research demonstrates a significant association between vitamin D status at birth and the future respiratory health of preterm infants.
INTESTINAL ALKALINE PHOSPHATASE ADMINISTRATION DECREASES INTESTINAL PERMEABILITY AND BARRIER DYSFUNCTION THROUGH THE ALTERATION OF TIGHT JUNCTION PROTEINS

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Background: Recent studies have shown an increase in intestinal permeability precedes necrotizing enterocolitis (NEC). Prior research has shown supplemental enteral Intestinal Alkaline Phosphatase (IAP), an endogenous protein in the intestines, was shown to decrease intestinal permeability and the severity NEC in a rodent model. We hypothesize that IAP decreases intestinal permeability prior to the development NEC through modification of tight junction proteins.

Materials and Methods: One day preterm Sprague Dawley rat pups where delivered via cesarean section and fed formula. Select pups received 4 units/kg of IAP in their formula. All pups were sacrificed on day of life 3 and the terminal ileum was harvested. Intestinal permeability was measured by filling loops of intestine with a fluorescein isothiocyanate-dextran (FITC-dextran) solution and measuring flux into the incubating media. Select loops had lipopolysaccharide added to the FITC-dextran solution. Expression of the gap junction proteins ZO-1, occludin, and claudin-1, 2 and 3 were measured by RT-PCR and Western-blot on ileal intestinal homogenates. Messenger RNA expression was compared to the housekeeping gene GAPDH. Statistical analysis was performed using a paired t-test and a p<0.05 considered significant.

Results: Supplemental IAP decreases intestinal permeability compared to formula fed preterm rats measured by FITC-dextran flux. Intestine loops exposed to lipopolysaccharide and FITC-dextran had a statistically significant increase in flux. Preliminary data showed a decrease in protein expression and messenger RNA levels of claudin-2 in IAP fed rats. ZO-1 showed an increase in protein expression in IAP fed rats.

Conclusions: Early supplemental IAP may reduce LPS induced permeability by preventing altered expression of tight junction proteins. Claudin-2 has been shown to increase paracellular permeability of small ions and molecules and is increased in NEC. A decrease in claudin-2 expression would therefore provide a potentially beneficial effect. Increase in protein levels of ZO-1, which functions as an adaptor between the transmembrane proteins and the cell cytoskeleton, would promote membrane stability. Enteral IAP may be useful in preventing NEC related injury.

INTESTINAL ALKALINE PHOSPHATASE ACTIVITY IS DECREASED IN NECROTIZING ENTEROCOLITIS

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Background: In a neonatal rat model of necrotizing enterocolitis (NEC), alkaline phosphatase (AP) activity is attenuated. Contributions of two forms of AP, intestinal alkaline phosphatase (IAP) and tissue-nonspecific alkaline phosphatase (TNAP) are unknown. L-phenylalanine (L-Phe) and CID-2931238 inhibit IAP and TNAP respectively, and are useful to assess which AP isoform is present. Methods: Sprague-Dawley control pups were vaginally delivered at term and dam fed. NEC pups were delivered one day premature, exposed to hypoxia, and fed formula containing lipopolysaccharide. Small intestinal tissue was harvested on day 4 and analyzed for AP activity using a colorimetric assay, with and without L-Phe and CID-2931238 in order to identify the active isoform in the tissue. Purified IAP and TNAP activity was assessed with L-Phe and CID-2931238 to confirm specificity of inhibitors.

Results: L-Phe specifically inhibited purified IAP, and CID-2931238 specifically inhibited purified TNAP. Total small intestinal AP activity was significantly decreased in NEC pups compared to controls (p<0.001). 50 mM L-Phe nearly completely inhibited control AP activity (p<0.001). CID-2931238 did not inhibit control AP activity. NEC samples were inhibited by L-Phe (p<0.001) and CID-2931238 (p<0.01). The combination of 50mM L-Phe and 10uM CID-2931238 resulted in near complete inhibition of NEC samples (p<0.001).

Conclusion: IAP is the predominant AP isoform in neonatal rat small intestine as indicated by robust inhibition by L-Phe and no inhibition by CID-2931238. Additionally, IAP activity is decreased in this model of NEC. CID-2931238 inhibition in NEC suggests TNAP contribution increases in NEC. Further research is needed to determine if the inhibition of IAP and TNAP in vivo contributes to the onset or severity of NEC.
ASSOCIATION OF NIL PER ORAL (NPO) DAYS AND ANTIBIOTIC USE WITH THE DEVELOPMENT OF NECROTIZING ENTEROCOLITIS (NEC) IN LOW BIRTH WEIGHT (LBW) INFANTS.
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Background: NEC is the most common gastrointestinal emergency in neonates and has a multifactorial etiology. Objective: To evaluate association between NPO days and initial antibiotic use for presumed sepsis in neonates. Methods: Retrospective review of the medical records of all neonates admitted to the neonatal intensive care unit of Sinai Children's Hospital between January 2010 to December 2012. All cases of stage II and stage III NEC were identified. Results: During the study period, 17 neonates with stage II or greater NEC were identified. The mean gestational age was 28.4 weeks (range 24-34) and mean birth weight 1055.8 grams (range 580-1905). The mean day of life when these patients developed NEC was 15.2 days (range 4-37). 9 infants (53%) were treated surgically and 8 infants (47%) were medically managed. 6 infants (35.2%) expired. The mean duration of initial NPO days was 5.4 days (range 1-28). The mean duration of initial antibiotic use for presumed sepsis was 5.3 days (range 2-10). 10 (58.8%) infants received blood transfusion within 48 hours prior to diagnosis of NEC. 8 (47%) infants received famotidine in the hyperalimentation. Conclusion: This is a single center experience with NEC over a 3 year period. The various clinical risk factors need to be studied in a larger multicenter cohort to ascertain statistical significance.

INFLAMMATORY NEONATAL NEUTROPHILS ATTRACT T REGULATORY CELLS THROUGH UNIQUE CHEMOKINE PROFILES.
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Background: Neonates infected with the common pathogen, Group B Streptococcus (GBS), exhibit exaggerated systemic inflammatory reactions that can increase morbidity and mortality. Recent evidence indicates unique innate-adaptive immune interactions that regulate inflammation, although the underlying cross-talk mechanisms are not well defined. We have shown that neonatal T regulatory cells (Tregs) migrate in response to mediators released by GBS-stimulated neutrophils (PMNs) more readily than those of adults (Heithaus, 2011). However, the chemokines and the cognate receptors mediating this chemotaxis are unknown. Objective: We hypothesized that GBS promotes release of PMN-derived chemokines that attract Tregs to inflammatory sites, and that PMN chemokine release and Treg receptor expression differ between neonates and adults. To test this, we characterized PMN-Treg cell interactions by comparing Treg chemokine receptor expression and PMN chemokines induced by GBS stimulation in neonates and adults. Design/Methods: Target cells were isolated from adult donors (AD) and term umbilical cord blood (CB); Tregs were further purified by immunomagnetic separation. Chemokine receptor expression on CD4+CD25+CD127lo Tregs was analyzed by multicolor flow cytometry. In complementary studies, supernatants of GBS-stimulated PMN cultures were analyzed for chemokines by Cytometric Bead Assay and ELISAs.

Results: Profiling of PMN-derived chemokines in GBS-PMN supernatants revealed greater expression of macrophage migration inhibitory factor (MIF), IL-8, CCL4 and CCL20 in CB vs. AD supernatants. CB Tregs had greater expression of the MIF receptor [CD74/CD184 complex] and CCR7, the CCR2, CCR4, CCR5, and CCR6 compared to CB Tregs, but similar expression of CXCR1, the IL-8 receptor. Conclusions: Our data suggest that neonatal neutrophils exhibit a unique chemokine profile that can promote Treg cell attraction to inflammatory sites. Studies are underway to more fully characterize the receptor-ligand interactions involved in this process.

THE PREDICTIVE VALUE OF ZINC PROTOPORPHYRIN/HEME FOR IRON DEFICIENCY SCREENING OFF OF FILTER PAPER

Background: Iron deficiency is common in newborns and can lead to impaired neurodevelopment. With early identification in newborns, long-term neurocognitive deficits can be prevented. The zinc protoporphyrin/HEME (ZnPP/H) biomarker is a sensitive and efficient test of iron status measured on washed whole blood of newborns. Iron deficiency and its identification via ZnPP/H are a condition and test, respectively, that meet criteria for inclusion in the newborn screening panel. This is a single center experience with NEC over a 3 year period. The various clinical risk factors need to be studied in a larger multicenter cohort to ascertain statistical significance.
removed during blood washing, interferes with ZnPP/H readings in the eluted blood samples. However, treatment of the eluted samples with Bilirubin Oxidase (BO) reduces this interference. **Objective:** To examine whether ZnPP/H from dried blood spots on filter paper holds promise as a potential screening test. **Methods:** De-identified cord blood was collected and washed. ZnPP/H ratios were measured by hematofluorometry. Unwashed blood was spotted onto Whatman 903 filter paper. Specimens were dried for 24 hour and eluted from the paper using PBS. The experimental group of eluted samples then received a BO treatment, while the control group received no treatment. The trials were repeated on day 2 and day 3 to measure stability of the ratio over time. **Results:** Filter paper ZnPP/H ratios were higher when eluted, compared to washed blood ($p<0.0001$). Elution with PBS was highly correlated with rinsed blood on day 1 ($R^2=0.76$, $p<0.0001$), day 2 ($R^2=0.50$, $p<0.0001$), and day 3 ($R^2=0.40$, $p<0.0002$), with slight improvement from BO treatment at day 2 ($R^2=0.56$, $p<0.0001$) and day 3 ($R^2=0.55$, $p<0.0001$). Strength of correlations were reduced, values rose, and lines of identity shifted in response to the aging of the blood spots over the 3-day period; however, identification of a correction factor could correct for these shifts. Even without correction, the highest (most iron deficient) 5% of washed samples remained in the highest quartile of eluted samples over the 3-day study. Importantly, the negative predictive value remained at 100% although the positive predictive value fell over the 3-day period. **Conclusions:** In regards to application for newborn screening, it is possible for the highest quartile of samples to be re-assayed using a more definitive and time intensive HPLC method, which will exclude samples that are false positives. Despite the changes in ZnPP/H readings over the time course, a plausible adaption of the ZnPP/H test to the newborn screening program still exists, particularly when combined with HPLC as a second tier method reserved for testing the highest quartile.

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**ROLE OF TLR4 IN REGULATING SELF-RENEWAL AND DIFFERENTIATION OF CORD BLOOD HEMATOPOIETIC STEM CELLS DURING RESPONSE TO LPS**

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**Background/Purpose:** The TLR4 receptor is necessary for lipopolysaccharide (LPS) recognition and critical for immune response in sepsis. By using a murine model of sepsis, previous work in our lab demonstrated that LPS induced a significant expansion of bone marrow (BM) hematopoietic stem cells (HSC). However, “septic” HSC were not able to differentiate myeloid progenitors and had lower short- and long-term engraftment when transplanted in healthy animals, suggesting an effect on HSC self-renewal. All these changes were rescued by the loss of TLR4 in the TLR4 knockout mice. To determine whether the effects observed in the murine model were conserved in human cells, we optimized a model of LPS-induced response using cord blood (CB) derived CD34+ cells. **Methods:** Mononuclear cells were collected from CB via Ficoll-Paque gradient followed by CD34+ isolation (Miltenyi microbead system). CD34+ cells were cultured with X-Vivo synthetic media (Lonza) with Stem Cell Factor (50ng/mL) IL-3, FLT-3, GMCSF (20ng/mL) and GCSF (10ng/mL) in the presence of 10ug/mL LPS from E. Coli or PBS. Analysis of differentiation was performed at day 4, 7, 10 and 14 by FACS staining. RNA was extracted for qPCR analysis. **Results:** LPS stimulation did not affect survival and proliferation of CB-CD34+ cells. No significant differences were found in the kinetic of differentiation during in vitro culture between the two groups: percentage of CD34+ cells declined similarly in LPS and PBS stimulated cells, and there were not substantial differences in the acquisition of myeloid markers CD11b and CD14. However, LPS stimulation induced a significant increase of the CD34-/CD33+/c-Kit+ cell phenotype starting at day 10 ($P<0.05$), associated to a marked upregulation of TLR4 and MyD88 expression. **Conclusions:** LPS stimulation of CD34+ cells did not lead to expansion of CD34+ progenitors or decreased of myeloid cells in vitro, but resulted in the expansion of a CD34-/c-Kit+ population expressing high TLR4, which significance needs to be further investigated. Future studies will include the optimization of a xenotransplantation model in NOD/SCID mice for the investigation of the LPS impact on human CD34+ cells in vivo.

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**HUMAN MILK OLIGOSACCHARIDES (HMOs) INHIBIT CANDIDA ALBICANS INVASION OF PREMATURE HUMAN ENTEROCYTES**

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**Candida albicans** causes the overwhelming majority of invasive fungal disease in premature infants. *C. albicans* colonizes the infant intestine and is highly associated with concurrent diagnoses of necrotizing enterocolitis and focal intestinal perforation, indicating that the intestine is a primary site for invasion by this organism. In support of this idea, we previously showed that *C. albicans* invades, injures, and causes pro-inflammatory cytokine release from cultured premature human enterocytes. Human Milk Oligosaccharides (HMOs) are a highly abundant, diverse group of unique glycans, postulated to promote the development of “protective” bacterial microbiomes and prevent adhesive and invasive interactions of pathogenic bacteria with the neonatal gut. The goal of the current study was to
explore the impact of HMOs on fungal interactions with the premature infant intestine. We hypothesized that the addition of HMOs to premature enterocytes would protect them from invasion by *C. albicans*. To model the premature intestine, we used H4 cells, a primary human fetal enterocyte line obtained from the laboratory of W. A. Walker (Harvard). To investigate the effect of HMO addition on *C. albicans* invasion of H4 cells, we used an immunohistochemical assay that distinguishes invading from non-invading *C. albicans* cells and compared fungal invasion of enterocytes with, or without, physiologic concentrations of HMOs present. We found that treatment with HMOs resulted in an ~60% reduction in the ability of *C. albicans* to invade H4 cells (p<0.05). *C. albicans* invasion of epithelial cells has previously been shown to be associated with its ability to form the filamentous hyphal morphology. Thus, to investigate the possibility that HMOs reduce H4 invasion by inhibiting *C. albicans* growth and/or morphogenesis, we performed morphometric analyses of fungal cells after incubation with H4 cells. We observed that HMO treatment was associated with shorter hyphae of abnormal morphology (p<0.05). In conclusion, our results indicate that HMOs decrease the ability of *C. albicans* to invade premature human enterocytes, supporting a protective role for HMOs in the premature infant intestine. We speculate that this function of HMOs is partially attributed to their negative effect on *C. albicans* hyphal growth and morphogenesis. Studies are currently underway to investigate further how HMOs modulate interactions between *C. albicans* and the premature intestine with a long-term goal to develop therapies that prevent fungal-associated disease.

85 ROLE OF TRX1 COMPARTMENTALIZATION DURING HYPEROXIC LUNG INJURY
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**Background:** Bronchopulmonary dysplasia (BPD), a chronic lung disease of extremely premature infants, is characterized clinically by prolonged respiratory distress and oxygen dependence; tissue histology demonstrates alveolar simplification and decreased pulmonary microvasculature, consistent with developmental arrest. Alterations in lung development result from oxidative injury associated with hyperoxia, mechanical ventilation, and infection; this is aggravated by immature antioxidant systems of the premature infant. Thioredoxin-1 (Trx1) is an endogenous thiol oxidoreductase necessary for normal cell proliferation, redox homeostasis, and antioxidant induction; but little is known about its role in response and injury of type II pneumocytes during hyperoxic exposure leading to BPD.

**Objective:** To examine the role of nuclear Trx1 during hyperoxic (95% oxygen) injury in type II pulmonary epithelial cells, and define compartmentalized Trx1 protein interactions. **Design and Methods:** Human adenocarcinoma H1299 and A549 cells were utilized as a model of type II pneumocytes to investigate Trx1 expression and localization during hyperoxic injury (95% oxygen). Outcomes of cell viability and Trx1 localization were analyzed. Additional studies are directed to examine these outcomes in cells transfected with nuclear targeted Trx1 constructs with and without redox active site mutations. Trx1 redox mutants were subsequently utilized for immunoprecipitation of proteins interacting specifically with the redox active site of Trx1 and a nuclear targeted Trx1 localization mutant. **Results:** Trx1 protects cells from hyperoxia induced cell death. Immunoblotting of nuclear and cytosolic enrichments under room air conditions reveal 19- and 8-fold more Trx1 in the cytosolic compartment of H1299 and A549 cells respectively; following 3 days of hyperoxia, a 4-fold increase in nuclear Trx1 was observed for both cell lines. Targeting of Trx1 localization and redox targets was verified by immunoblot and immunocytochemistry. Immunoprecipitations (IP) were performed with total and nuclear lysates; elutions were analyzed by mass spectrometry. Targets were confirmed by immunoblot of lysates and IP eluates. **Conclusion:** Trx1 attenuates hyperoxia mediated cell death of type II pneumocytes; IP of Trx1 redox and localization mutants have identified different protein interaction profiles under room air conditions.

86 IMPACT OF INTERCURRENT RESPIRATORY INFECTIONS ON LUNG HEALTH IN INFANTS BORN < 29 WEEKS GESTATION WITH BRONCHOPULMONARY DYSPLASIA
JB Taylor1,2, M Nyp1,2, M Norberg1,2, H Dai3, H Escobar1,2, 1Center for Infant Pulmonary Disorders, Children’s Mercy Hospitals and Clinics, Kansas City, Missouri, 2Department of Pediatrics, University of Missouri-Kansas City School of Medicine, Kansas City, Missouri, 3Department of Preventative Medicine, University of Kansas Medical Center, Kansas City, Kansas

**Objective:** To assess the impact of intercurrent respiratory infections in infants <29 weeks gestational age (GA) with bronchopulmonary dysplasia (BPD) thru oxygen, diuretic and inhaled steroid use over the first year of life in one academic center with close outpatient follow-up. **Study Design:** A retrospective cohort study on 111 infants born <29 weeks GA with BPD transferred to one academic center within 24 hours of birth from 2008-2010. **Results:** Backward stepwise logistic regression showed viral infections significantly increased oxygen use (OR of 15.5 [CI 3.4, 71.3]). Stratified Cochrane-Mantel-Hansel chi-square analysis showed both viral and bacterial infections affected oxygen use when compared to infants without infections (9% vs. 47%, p<0.0002 and 8% vs. 15.5 [CI 3.4, 71.3]).
24%, p =0.02). The Cochran-Armitage trend test showed an increasing number of viral infections was associated with increased oxygen (OR [95% CI] = 6.4 [2.3-17.4], p=0.0003), diuretic (OR [95% CI] = 2.4 [1.1 – 5.2], p=0.02) and inhaled steroid use (OR [95% CI] = 2.2[1.003 – 5.2], p=0.049). The same trend was not appreciated in bacterial infections. A secondary outcome variable of death after NICU discharge was evaluated. 6/7 infants had recent or ongoing viral infections at the time of their death (p<0.0001). **Conclusions:** Viral infections caused more long term pulmonary morbidity/mortality than bacterial infections on premature lung health, even in the no/mild BPD group. Infant mortality did not appear to correlate with the 36 week BPD severity assessment.

87 CLOSING THE GAP: DEVELOPMENT OF A NOVEL ZEBRAFISH-BASED TOOL TO ASSESS OPTIC FISSURE CLOSURE DEFECTS AND COLOBOMA.

**Purpose:** Proper closure of the optic fissure during early embryogenesis is critical for normal eye formation. Failure of optic fissure closure results in coloboma and related ocular defects. Mutations in several developmentally important genes are known to cause colobomas; however, the genetic etiology for most patients remains unknown. As a means to characterize novel genes and pathways that contribute to coloboma formation, we developed a method to evaluate optic fissure closure in zebrafish. **Methods:** The genetic and developmental similarities to the mammalian eye make zebrafish (Danio rerio) an ideal model to study early vertebrate eye development. To evaluate optic fissure closure, we assayed for changes in pax2a expression, a gene transiently expressed in the ventral optic cup prior to optic fissure closure. The quantity of green fluorescent protein (GFP) in the enhancer trap mp204a:GFP transgenic zebrafish line was used as a proxy for pax2a expression. As proof of principle, we tested whether sema3e, a gene expressed in ventral mesenchyme that exists between the edges of the optic fissure, affected GFP levels in the enhancer trap mp204a:GFP transgenic line. As a second test of optic fissure closure, we evaluated basement membrane dissolution by observing changes in laminin expression at the edges of the closing optic fissure. **Results:** Transgenic expression of GFP in the mp204a:GFP enhancer trap line recapitulates endogenous pax2a expression in the eye field, midbrain-hindbrain boundary, otic placode and pronephric mesoderm. Quantitative three-dimensional analysis using ImageJ software revealed increased expression of pax2a in sema3e knockdown embryos compared to uninjected controls at 48 hours post fertilization (hpf), indicating delayed optic fissure closure. Moreover, a reduction in overall eye size was observed at 48 hpf. We also observed that in sema3e knockdown zebrafish, laminin expression in the basement membrane appeared thickened and less organized compared to uninjected wild-type at 24 hpf. **Conclusions:** We demonstrate that quantitative three-dimensional analysis of the enhancer trap mp204a:GFP transgenic zebrafish line can facilitate the identification and screening of candidate genes that would be biologically relevant for disorders characterized by coloboma.

88 INCREASED SMAD7 EXPRESSION IN GUT MACROPHAGES CAN EXPLAIN THE INFLAMMATORY ACTIVATION OF THESE CELLS DURING NEC

**K. MohanKumar Krishnan,** K. Namachivayam, R. Jagadeeswaran, Gauthaman V., Sanjana Srinivasan, Anoop Kumar, Steven A. Garzon, Akhil Maheshwari

**Background:** We have previously shown that transforming growth factor-β2 (TGF-β2) suppresses macrophage inflammatory responses in the preterm intestine and prevents necrotizing enterocolitis (NEC). To explain the inflammatory activation of macrophages during NEC, we hypothesized that macrophage precursors newly recruited to the intestine fail to undergo TGF-β2-mediated inflammatory downregulation during NEC because of increased expression of Smad7, which is a negative regulator of TGF-β signaling, in these cells. **Objective:** Determine (1) whether NEC is associated with increased Smad7 expression in macrophages, and (2) the mechanism(s) for increased Smad7 expression in these cells. **Design/Methods:** NEC-like inflammatory mucosal injury was induced in 10-day-old mouse pups by administering trinitrobenezene sulfonic (TNBS) acid by gavage and enema. Inflammatory cytokines, TGF-β(2), Smad7, Ski, and strawberry notch N (SnoN)/Ski-like oncoprotein (SKIL) was measured using quantitative reverse transcriptase-polymerase chain reaction, immunoblots, and immunohistochemistry. Smad7 effects were examined in transfected RAW264.7 mouse macrophages in vitro. Findings were confirmed in archived human tissue sections of NEC. **Results:** TNBS-entereocolitis resulted in macrophage infiltration and necrosis in the intestine. We detected increased Smad7 expression in the intestine, which was immunolocalized to F4/80+ macrophages. Because bacterial translocation is a key finding in NEC, we treated RAW264.7 murine macrophages with E. coli LPS and detected increased Smad7 expression. These findings were explained by decreased expression of SnoN/SKIL, which is a transcriptional repressor of Smad7. Transfection of RAW264.7 cells to overexpress Smad7 increased cytokine production and NF-κB activation, indicating
inflammatory activation of these macrophages similar to that seen in NEC. We also detected increased Smad7 expression in human NEC macrophages, indicating that a similar pathway is at work in NEC. **Conclusions:** Inflammatory activation of gut macrophages during NEC can be explained, at least in part, by increased Smad7 expression in these cells.
The James Sutherland Award

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

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

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

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

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

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

1989  Michael S. (Mickey) Caplan, MD
1996  Brenda B. Poindexter, MD
2001  J. Carter Ralphe, MD
2002  Indra D. Chandrasekar, MD
2003  Heather Bartlett, MD
2004  Eyal Shteyer, MD
2005  Peter DeYoung, MD
2006  Rinku Mehra, MD
2007  Wendy Luce, MD
2008  Melissa Agoudemous, MD
2009  Suzanne Kingery, MD
2010  Misty Good, MD
2011  Andrew Harris, MD
2012  Brian Becknell, MD
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  
2012  Brian Stansfield, MD
The William Segar Award

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

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

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

2012 Carl Backes, MD
Cleveland Clinic Award

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

2001  Anthony Ratanproeksa
2002  Liza Cadnapaphornchai
2003  Karen Wiseman
2004  Emily Segar
2005  Amy Hurst
2006  Christopher Lux
2007  Keri Drake
2008  Christa Pittner
2009  Katie Meyer
2010  Emily Peterson
2011  Jeremy Sandgren
2012  Brandon Downing
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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<th>Year</th>
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<td>1986</td>
<td>Samuel J. Fomon, MD</td>
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<td>William E. Segar, MD</td>
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<td>1988</td>
<td>Orville C. Green, MD</td>
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<td>Ira M. Rosenthal, MD</td>
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<td>1990</td>
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<td>1991</td>
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<td>Reginald D. Tsang, MD</td>
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<td>Rosita Pildes, MD</td>
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<td>Dharmapuir Vidyasagar, MD</td>
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<td>Fred G. Smith, MD</td>
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<td>Gunner B. Stickler, MD</td>
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<td>Dorothy J. Becker, M.B.B.Ch.</td>
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<td>Laurence A. Boxer, MD</td>
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<td>Edward S. Ogata, MD</td>
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<td>Frank R. Greer, MD</td>
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<td>James E. Heubi, MD</td>
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<td>Edward F. Bell, MD</td>
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<td>William E. Truog, MD</td>
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<td>Avory A. Fanaroff, MD</td>
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<td>Michael K. Georgieff, MD</td>
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<td>Juan F. Sotos, MD</td>
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<td>Alan H. Jobe, MD, PhD</td>
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Ohio State University

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Conference Map, University of Minnesota Twin Cities Campus

Legend
- Cancer and Cardiovascular Research Building
- McNamara Alumni Center
- Commons Hotel
- McGuire Translational Research Facility/Lions Research Building

Your walking route