Program Guide

March 28–30, 2008 • Crowne Plaza Philadelphia • Philadelphia, PA





THE EASTERN SOCIETY FOR PEDIATRIC RESEARCH

20th Annual Meeting

In cooperation with:
The Center for Continuing Education,
Tulane University Health Sciences Center

Eastern SPR
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Bruce D. Gelb, MD
Department of Pediatrics
Mount Sinai School of Medicine
One Gustave Levy Pl, Box 1040
New York, NY 10029
Email: bruce.gelb@mssm.edu
Phone: (212) 241-3303

Secretary 2006-2011

Edmund F. La Gamma, MD, FAAP
Chief, Division of Newborn Medicine
Director, Neonatal-Perinatal Fellowship Program
Professor of Pediatrics, Biochemistry & Molecular Biology
The Regional Neonatal Center
The Maria Fareri Children's Hospital at Westchester Medical Center
New York Medical College
Valhalla, NY 10595
Email: edmund_lagamma@nymc.edu
Phone: (914) 493 - 8558

Treasurer 2006-2011

Michael Posencheg, MD
Division of Neonatology and Newborn Services
Hospital of the University of Pennsylvania
3400 Spruce Street, Ravdin Building, 8th floor
Philadelphia, PA 19104
Email: posencheg@email.chop.edu
Phone: (215) 615 - 4376

Chairperson, Planning Committee

Vineet Bhandari, MD
Yale Unversity School of Medicine
333 Cedar Street
New Haven, CT 06510
Email: vineet.bhandari@yale.edu
Phone: (203) 688-4661

Director of Sponsorship 2004-2008

Ian R. Holzman, MD
Professor of Pediatrics, Obstetrics and Reproductive Science
Mount Sinai School of Medicine
One Gustave Levy Place, Box 1508
New York, NY 10029
Email: ian.holzman@mssm.edu
Phone: (212) 241-6186

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Vineet Bhandari, MD *(Chair)*
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Heber Nielsen, MD
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Contents

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Chairman, Department of Pediatrics
Stonybrook University School of Medicine
Stonybrook, NY

Dear Colleagues,

Welcome to the 20th Annual Meeting of the Eastern Society for Pediatric Research (Eastern SPR) and to our host city of Philadelphia, the Cradle of Liberty!

The Eastern SPR Council and Planning Committee are confident that you will enjoy our exciting offerings of State-of-the-Art Plenary Talks plus Subspecialty Sessions featuring leading clinical and scientific authorities moderating the many high-quality original research abstracts as well as the highly popular Lunch with the Professor educational program for trainees.

The goals of the Eastern SPR Annual Meeting are to create a forum: i) in which young investigators can present their research in a structured yet relaxed atmosphere, ii) where regional clinicians can be exposed to cutting edge clinical and basic science, iii), to enable timely educational programs addressing important topics in Pediatrics and iv) providing opportunities for trainees to network with senior investigators/researchers in an informal setting.

The continued successes of our previous meetings has enabled an entirely web-based system for membership, registration and payments, in making timely announcements, in enhanced room booking services, and for the improvement in the overall ease of running the meeting. In addition, we will again have centralized informatics enabling presenters to load their slide-show in advance at a speaker-ready station.

ACKNOWLEDGEMENTS: The organization of this meeting would not have been possible without the help of the administrative offices of the American Pediatric Society (APS) and the Society for Pediatric Research (SPR). We are especially grateful to: Debbie Anagnostelis, Executive Director, Kathy Cannon, Belinda Thomas, Jesse Osman and Lisa Thompson. We also recognize the energetic efforts of the Eastern SPR Planning Committee and Council Members for their guidance and vision in selecting this new venue and the efforts of Tulane University in New Orleans as our 2008 sponsor for CME program. Lastly, our corporate and leading academic sponsors were instrumental in making this meeting possible.

Most of all, we want to thank you for attending and for contributing your wisdom in the pursuit of excellence. We look forward to seeing you in Philadelphia!

Bruce D. Gelb, MD
President

Edmond F. LaGamma, MD, FAAP
Secretary

Vineet Bhandari, MD
Chair, Planning Committee

Meeting Services & CME Accreditation

Registration and CME Desk Hours

Registration will be held in the Liberty Ballroom Foyer. Registration hours are as follows:

Friday, March 28	4:00pm – 7:00pm
Saturday, March 29	7:30am – 7:30pm
Sunday, March 30	7:30am – 1:00pm

Abstract Publication

All abstracts being presented at the 2008 Eastern SPR Annual Meeting are printed in this Program Guide, beginning on page 14.

Audio/Visual Information

All oral presentations must be made using PowerPoint. Computers and LCD projectors will be provided. Slide projectors will not be provided. Presenters should have submitted their presentations in advance, but still are required to check in at Speaker Ready.

Speaker Ready (Board Room-2nd floor)

Presentations will be loaded onto a central computer during the session prior to the session in which the presentation is to be made (i.e., Friday evening for Saturday morning presentations, Saturday morning for Saturday afternoon presentations, and Saturday afternoon for Sunday morning presentations). Please also bring your CD-ROM, ZIP drive or flash memory.

Business Center

The Business Center at the Crowne Plaza Philadelphia Center is located on the 2nd floor, adjacent to the Constitution Room.

CME Accreditation

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Tulane University Health Sciences Center and the Eastern Society for Pediatric Research. Tulane University Health Sciences Center is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation Statement

Tulane University Health Sciences Center designates this educational activity for a maximum of **11.5** AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Tulane University Health Sciences Center presents this activity for educational purposes only and does not endorse any product, content of presentation, or exhibit. Participants are expected to utilize their own expertise and judgment while engaged in the practice of medicine. The content of the presentations is provided solely by presenters who have been selected because of their recognized expertise.

Disclosure Policy

It is the policy of the Center for Continuing Education at Tulane University Health Sciences Center to plan and implement all of its educational activities in accordance with the ACCME's Essential Areas and Policies to ensure balance, independence, objectivity and scientific rigor. In accordance with the ACCME's 2004 Standards for Commercial Support, everyone who is in a position to control the content of an educational activity certified for *AMA PRA Category 1 Credit™* is required to disclose all relevant financial relationships with any commercial interests within the past 12 months that creates a real or apparent conflict of interest. Individuals who do not disclose are disqualified from participating in a CME activity. Individuals with potential for influence or control of CME content include planners and planning committee members, authors, teachers, educational activity directors, educational partners, and others who participate, e.g. facilitators and moderators. This disclosure pertains to relationships with pharmaceutical companies, biomedical device manufacturers, or other corporations whose products or services are related to the subject matter of the presentation topic. Any real or apparent conflicts of interest related to the content of the presentations must be resolved prior to the educational activity. Disclosure of off-label, experimental or investigational use of drugs or devices must also be made known to the audience.

Procedures for CME Credit

To receive the appropriate number of CME credits, it is important to do the following:

- Locate your verification form included with your registration packet or pick one up at the Registration Desk.
- Complete your verification form as you attend each activity.
- On your departure date, turn in your completed verification form at the Registration desk.

Faculty

Maida Galvez
Mount Sinai School of Medicine
New York, NY

Jonathan D. Gitlin
Washington University
St. Louis, MO

Sandra Hassink
Al Dupont Hospital for Children
Wilmington, DE

Matilde Irigoyen
Albert Einstein Medical Center
Philadelphia, PA

Haresh Kirpalani
The Children's Hospital of Philadelphia
Philadelphia, PA

Ian D. Krantz
The Children's Hospital of Philadelphia
Philadelphia, PA

Satyan Lakshminrusimha
Women & Children's Hospital of Buffalo
Buffalo, NY

Raemma P. Luck
Temple University School of Medicine
Philadelphia, PA

Jane McGowan
St. Christopher's Hospital for Children;
Drexel University, Philadelphia, PA

Sharon McGrath-Morrow
The Johns Hopkins Medical Institution
Baltimore, MD

Jane W. Newburger
Children's Hospital Boston, MA

Suzette Oyeku
Children's Hospital at Montefiore/Family
Care Center, Bronx, NY

Jim F. Padbury
Women and Infants Hospital
Providence, RI

Richard A. Polin
Babies and Children's Hospital of NY
New York, NY

Andrew D. Racine
AECOM / Montefiore Children's
Bronx, NY

Frederick J. Suchy
Mt. Sinai Medical Center, New York, NY

Marietta Vasquez
Yale University School of Medicine
New Haven, CT

Steven M. Willi
The Children's Hospital of Philadelphia
Philadelphia, PA

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Eastern SPR Schedule-at-a Glance

Crowne Plaza Philadelphia
March 28-30, 2008

Friday, March 28

6:00pm–7:30pm

Poster Session I & Reception
— Independence Ballroom —

Saturday, March 29

7:00am–8:15am

Continental Breakfast
— Liberty Foyer —

8:15am–10:30am

Cardiopulmonary
— Constitution Room —

Emergency Medicine (begins at 8:00am)
— Declaration Room —

General Pediatrics I
— Liberty Ballroom A —

GI/Nutrition/Growth
— Liberty Ballroom B —

Infectious Diseases
—Freedom Room —

Neonatology I: Neonatal Pulmonology
— Liberty Ballroom C—

10:30am–10:45am

Coffee Break
— Liberty Foyer —

10:45am–11:45am

Plenary Session I

MENTOR OF THE YEAR PRESENTATION
Jane Newburger, MD, Children's Hospital Boston
— Liberty Ballroom C —

12:00pm–1:00pm

Meet the Professor Lunch
Iman Sharif, MD, Children's Hospital of Montefiore
Nuts and Bolts of Writing an IRB Proposal
— Congress Room —

Eastern SPR Business Meeting
— Liberty Ballroom A —

1:10pm–4:00pm

Plenary Session II

PLENARY LECTURE
Frederick J. Suchy, MD, Mount Sinai School of Medicine
Recent Advances in Inherited Cholestatic Liver Disease
— Liberty Ballroom C —

YOUNG INVESTIGATOR PRESENTATIONS: (2:00pm–4:00pm)

4:00pm–4:15pm

Coffee Break
— Liberty Foyer —

4:15pm–5:45pm

Adolescent Medicine
—Freedom Room —

Developmental Biology
— Liberty Ballroom B —

General Pediatrics II
— Liberty Ballroom A —

Metabolism/Obesity
— Declaration Room —

Neonatology 2 - Epidemiology and Follow-Up
— Liberty Ballroom C —

Pulmonary and Asthma
— Constitution Room —

6:00pm-7:30pm

Poster Session II & Reception
— Independence Ballroom —

Sunday, March 30

7:00am–8:30am

Continental Breakfast
— Liberty Foyer —

8:30am–9:30am

Plenary Session III

PRESENTATION OF THE YOUNG INVESTIGATOR AWARDS

PLENARY LECTURE
Jonathan D. Gitlin, MD, Washington University School of Medicine
The Inorganic Chemistry of Life: Lessons from Genetics
— Liberty Ballroom C—

9:30am–9:45am

Coffee Break
— Liberty Foyer —

9:45am–12:00pm

Endocrinology/Metabolism
— Declaration Room —

General Pediatrics III
— Liberty Ballroom A —

Genetic Basis of Disease
— Freedom Room —

Neonatology III: Clinical Studies
— Liberty Ballroom C —

Neurobiology
— Liberty Ballroom B —

Pulmonary Development & Injury
— Constitution Room —

• • •Friday, March 28, 2008 • • •

Poster Session I

6:00 PM-7:30 PM **Independence Ballroom**

1 **Maternal Satisfaction with Prenatal Care: Are We Educating Enough?**
Vivien Carrion, Karola Long, James Shelton. – Abstract 1

2 **Nursing Staff Education Can Improve Adherence with Central Line Hub Care Protocol**
Sulaiman Sannoh, Hassan Khan, Maria Khan, Barbara Clones, Boriana Parvez. – Abstract 2

3 **Educating Neonatal Intensive Care Unit (NICU) Parents About Sudden Infant Death Syndrome (SIDS) Risk Reduction: Promoting a Consistent Message by NICU Nurses**
Nilay Baxi, Barbara M. Ostfeld, Thomas Hegyi. – Abstract 3

4 **Animal Origins of Surfactant: Physician Practice and Parental Information Sharing**
Sean M. Bailey, George E. Fryer, Karen Hendricks-Munoz, Pradeep Mally. – Abstract 4

5 **Incidence of Late Preterm Birth and Associated Respiratory Morbidities**
Sean M. Bailey, Shaveta Malik, Nicholas Paik, Annika Brown, George E. Fryer, Karen Hendricks-Munoz, Pradeep Mally. – Abstract 5

6 **Effect of Surfactant Type on the Pro-Inflammatory Response of ELBW Infants**
Vanessa V. Mercado, Mitashi Singh, Hima Maramreddy, Joie Fisher, Lance A. Parton. – Abstract 6

7 **Epidemiology of Neonatal Bacteremia in a South Bronx Hospital**
Deepthi Alapati, Dinabel Peralta-Reich, Ginaida Cirilo, Benamanahalli K. Rajegowda, Robert J. Leggiadro. – Abstract 7

8 **G6PD Deficiency – A Risk Factor for Increased Mortality in Septic Newborns?**
Anja Mowes, David L. Schutzman, Lisa Duffy, Rachel Porat. – Abstract 8

9 **Utilization of a Rapid Detection Blood Culture System To Decrease Length of Stay in the Neonatal Intensive Care Unit**
Karen D. Lidoshore-Fuld, Rishara Maharaj, Monica Zarate, Karen Hendricks-Munoz, Yang Kim. – Abstract 9

10 **Blood Lactate as a Marker for Late-Onset Neonatal Sepsis**
Rebecca J. Eick, Kabir M. Abubakar, Martin Keszler. – Abstract 10

11 **Timely Administration of Antibiotics for Infants at Risk for Sepsis in the Neonatal ICU**
Misha Bhat, Susan Southee, Rebecca Q. Beck, Claire Pagano, Ann Cherry, Jason Corcoran, Jefferson Pickard, John M. North. – Abstract 11

12 **Are the Trends in Incidence of Fungal Sepsis in VLBW Neonates Related to Postnatal Steroids?**
Oluwatoyin A. Abiodun, Joaquim M.B. Pinheiro, Martha Lepow. – Abstract 12

13 **Surveillance Cultures in Babies Less 1500 Grams May Decrease Incidence of Fungemia**
Sujana Reddy, Santosh Parab, Anthony Barone, Anantham Harin. – Abstract 13

14 **Single Cell Sorting To Decipher the Checkpoints for B Cell Selection in Neonatal Cord Blood**
Kavita Kasat, Jie Xu, Karen Hendricks-Munoz, Amy Reichlin. – Abstract 14

15 **Effects of Prenatal Tobacco Exposure on Gene Expression Profiling in Umbilical Cord Tissue**
Naveed Hussain, Winfried Krueger, Steve Walsh, Jonathan Covault, Henry Kranzler, Cheryl Oncken. – Abstract 15

16 **Nitric Oxide Production in Peripheral Blood Mononuclear Cells (PBMC) Measured in Prepubertal and Pubertal Children**
Andrey Mamkin, Andrey Kolesnikov, Theresa Jacob, Svetlana Ten. – Abstract 16

17 **Oral Glyburide for the Treatment of Gestational Diabetes and Its Effects on the Fetus**
Sara D. Sibley, Randi Wasserman, Pradeep Mally, Karen Hendricks-Munoz. – Abstract 17

18 **Development of Sleep Wake Cycling and Presence of Seizures on aEEG During Whole Body Hypothermia**
Mohamed El-Dib, Tammy Tsuchida, Tamara John, Raquel Bernier, An Massaro, Stephen Baumgart, Billie Short, Taeun Chang. – Abstract 18

19 **Continuous Amplitude-Integrated EEG (aEEG) Monitoring During Selective Head Cooling (HC)**
Susan Adeniyi-Jones, Zachary Cohn, Vidula Damle, Dorothy McElwee. – Abstract 19

20 **Utility of Performing Routine Head Ultrasounds in Preterm Infants with Gestational Age 30-34 Weeks**
Michelle Karam, Judy G. Saslow, Heidi Taylor, Barbara Amendolia, Gary Stahl, Kee Pyon, Nosrat Razi, Nicole Kemble, Zubair H. Aghai. – Abstract 20

21 **Endogenous Cannabinoid System Activation in Neonatal Focal Cerebral Ischemic Injury in Rat Pups**
Marta R. Rogido, Jose A. Martinez Orgado, Ruth Pazos, Tong C. Wen, Augusto Sola, Julian Romero. – Abstract 21

22 **Maternal Methadone Dose Does Not Predict Frequency of Treatment for Neonatal Abstinence Syndrome**
Neil Seligman, Kevin Dysart, Nicole Salva, Edward Hayes, Marie O'Neill, Benjamin Leiby, Jennifer Kern, Jason Baxter. – Abstract 22

23 **High PaO_2 Is Directly Proportional to SpO_2 Levels 94%-100% in Newborns Receiving Oxygen in the Neonatal Intensive Care Unit**
Armando R. Castillo, Hernando Baquero, Freddy Neira, Ramiro Alvis, Ann Critz, Richard Deulofeut, Augusto Sola. – Abstract 23

24 **T-Lymphocytes in Human Infants with Bronchopulmonary Dysplasia (BPD)**
Rita M. Ryan, Qadeer Ahmed, Christopher A. D'Angelis, Vasanth H. Kumar, Satyan Lakshminrusimha, Leon A. Metlay, Huamei Wang, Gloria S. Pryhuber. – Abstract 24

25 **Quantified Impulse of Helicopter Versus Ground Transport as Measured by Biophysical Accelerometery**
Shetal Shah, Andrew Dylag, Joseph Hudak. – Abstract 25

26 **Transport-Induced Biophysical Impulse Alters Respiratory Finction in Neonatal Sprague-Dawley Rats in an Dose-Dependent Manner**
Joseph J. Hudak, Andrew Dylag, Shetal I. Shah. – Abstract 26

27 **Desaturation (Desats) Events Are Related to Threshold Retinopathy of Prematurity (TROP) and Laser Therapy (LT) in Extremely Low Birth Weight Infants (ELBWI) < 750g**
Michelle Weissman, Tammy Rousseau, Jeffrey Perlman. – Abstract 27

28 **Marked Elevation of Cardiac Troponin I (cTnI) Is Associated with Increased Ventilator Days and Length of Hospital Stay for Infants with Perinatal Asphyxia**
Constance G. Andrejko, Vidula Damle, Susan C. Adeniyi-Jones. – Abstract 28

29 **Predictors of Prevalent Medical Issues of Former Preterm Infants up to Two Years of Age**
Jordan S. Kase, Paul Visintainer. – Abstract 29

30 **Cognitive Scores in Very Low Birth Weight Infants (VLBWI) <1000g ↑ Significantly with Time Suggestive of Brain Plasticity**
Vivien L. Yap, Jeffrey M. Perlman, Gail Ross. – Abstract 30

31 **Anaphylaxis Treatment in an Urban Academic Hospital**
Alison Miles, Cortney Foster, Adam Friedlander, Amy Kryder, Mary B. Bollinger. – Abstract 31

32 **Community-Associated Staphylococcal Infection in a South Bronx Pediatric Inpatient Population**
Majda Behani, Elizabeth Tejeda-Ramirez, Robert J. Leggiadro. – Abstract 32

33 **Variability in Clearances, Electrolytes and Anemia in Children Receiving Hemodialysis – When Should Labs Be Drawn?**
Christina R. Nguyen, Dale Bednarz, Jim Flanagan, Abubakr Imam, Deepa Chand. – Abstract 33

34 **Recurrent Focal Segmental Glomerulosclerosis (rFSGS) in Renal Allograft Recipients: Role of Donor-Specific Circulating Antibodies (PRA) and HLA Mismatching**
Shimi Sharief, Shefali Mahesh, Vivian Tellis, Marcela Del Rio, Fredrick J. Kaskel, Robert P. Woroniecki. – Abstract 34

35 **Obesity as a Risk Factor for Microalbuminuria in Hypertensive Children**
Gunjeet Kala, Sudha Garimella, James Springate. – Abstract 35

• • •Saturday, March 29, 2008• • •

Cardiopulmonary Platform Session

8:15 AM-10:30 AM **Constitution**

Moderators: Jane Newburger and Heber Nielsen

8:15 AM **Myocardial Regeneration Therapy with Adeno-Thioredoxin Gene Delivery Attenuates Ischemic Cardiomyopathy in Diabetic Rats**
Ramesh Vidavalur, Srikanth Koneru, Mahesh Thirunavukkarusu, Suresh Varma Penumathsa, Maulik Nilanjana. – Abstract 36

8:30 AM **Sildenafil Augments Early Protective Transcriptional Changes After Ischemia in Mouse Myocardium – cDNA Microarray Analysis**
Ramesh Vidavalur, Srikanth Koneru, Suresh Varma Penumathsa, Maulik Nilanjana, Winifried Kruger. – Abstract 37

8:45 AM **Echocardiographic Predictors of Mortality in Congenital Diaphragmatic Hernia (CDH)**
Monisha Bahri, Matthew Eig, Robin Doroshow, Stephen Baumgart, Martin Keszler. – Abstract 38

9:00 AM **Heme Oxygenase-1 Is Required for Lung Vascular and Alveolar Development**
Sara Q. Lin, Tiangang Zhuang, Guang Yang, Phyllis A. Dennery. – Abstract 39

9:15 AM **Effects of Moderate Hyperoxia with Intermittent Hypoxia on Neonatal Lung PECAM-1 Expression and Endothelial Cell Function**
Huayan Zhang, Bo Han, Horace M. DeLisser. – Abstract 40

9:30 AM **BMP2 Preventes Hypoxia Induced PY-STAT3 Activation in Pulmonary Artery Endothelial Cells**
X.L. Li, L.A. Parton, R. Mathews, J. Wang, S.C. Olson. – Abstract 41

9:45 AM **ErbB Ligand-Specific Induction of Proliferation and Differentiation in MEK-Inhibited Fetal Mouse Lung Type II Cells**
Sujatha M. Ramadurai, Lucia Pham, Karen T. Wang, Heber C. Nielsen. – Abstract 42

10:00 AM **Pigment Epithelium Derived Factor (PEDF) in a Mouse Model of BPD**
Anne Chetty, Cao Gong-jee, Heber C. Nielsen. – Abstract 43

10:15 AM **Effect of NADPH Oxidase Inhibition in Lambs with Persistent Pulmonary Hypertension of the Newborn (PPHN)**
Fernando A. Soares, Satyan Lakshminrusimha, Kathryn N. Farrow, Stephen Wedgwood, Sylvia F. Gugino, Lyuba Czech, James A. Russell, Robin H. Steinhorn. – Abstract 44

Emergency Medicine Platform Session

8:00 AM-10:30 AM **Declaration**

Moderator: Raemma Luck

8:00 AM **Ketamine versus Etomidate: Procedural Sedation for Pediatric Orthopedic Reductions**
Jannet J. Lee-Jayaram, Adam Green, Joshua Siembieda, Edward J. Gracely, Colette C. Mull, Eileen Quintana, Terry Adirim. – Abstract 44A

8:15 AM **Accuracy of Point-of-Care Ultrasound for the Diagnosis of Fractures in the Pediatric Emergency Department**
E.R. Weinberg, J.W. Tsung, M.G. Tunik. – Abstract 45

8:30 AM **First Responder Performance in Pediatric Versus Adult Trauma**
Sunday Bankole, Arsenia Asuncion, Gary Stahl, Zubair Aghai, Shonola Da-Silva. – Abstract 46

8:45 AM **Utility of Bedside Ultrasound vs CT Scan in Detecting Neck Abscesses: A Case Series**
Raemma P. Luck, Michael Cohen, Thomas Costantino. – Abstract 47

9:00 AM **What Do Pediatric Residents Know About Medical Malpractice?**
Amy D. Roy, Karen A. Santucci, Lei Chen. – Abstract 48

9:15 AM **Improving Emergency Department Efficiency: An Integrated Patient-Centered System**
Johnathon C. LeBaron, James F. Wiley II, Marvin C. Culbertson III, Sharon R. Smith. – Abstract 49

9:30 AM **Communication About Interfacility Patient Transfers to Pediatric Emergency Departments**
Amy D. Roy, Karen A. Santucci. – Abstract 50

9:45 AM **Abdominal Trauma in Children as a Result of Snowboarding**
Alison B. McCrone, Kathleen Lillis, Steven Shaha. – Abstract 51

10:00 AM **Emergency Preparedness in the Outpatient Setting**
Thuy L. Ngo, Kathleen Donnelly. – Abstract 52

10:15 AM **Optimal Empiric Antimicrobial Therapy for Non-Drained Skin and Soft-Tissue Infections (SSTI) in the Era of Methicillin-Resistant *Staphylococcus aureus* (MRSA)**
Daniel J. Elliott, Theoklis E. Zaoutis, Andrea B. Troxel, Andrew J. Loh, Ron Keren. – Abstract 53

General Pediatrics I Platform Session

8:15 AM-10:30 AM **Liberty A**

Moderator: Maida Galvez

8:15 AM **Effect of Massage for Methadone Exposed Infants**
Yun J. Lee, Jing Liu, Barry M. Lester, Joseph M. McNamara, Pauline Wright. – Abstract 54

8:30 AM **Communication Between Pediatric Hospitalists and Referring Physicians**
Riva Kamat, John Jones, Michael Sheridan. – Abstract 55

8:45 AM **Factors Affecting the Age of Diagnosis of Autism Spectrum Disorders at a New York City Early Intervention Center**
Ginger L. Janow, Leonardo Trasande. – Abstract 56

9:00 AM **Clinical Vignette Tool To Assess Resident Needs in Communication and Interpersonal Skills**
Alexis S. Lieberman, Krissa George, Yolandee Bell-Cheddar, Mario Cruz, Cindy DeLago, Matilde Irigoyen. – Abstract 57

9:15 AM **Performance in Digit Span Test for Short Term Memory in Children with Attention Deficit Hyperactivity Disorder (ADHD) as Compared to Control Group**
Lysette Iglesias, Kanchana Roychoudhury, Barbara Cicero, Salimah Walia. – Abstract 58

9:30 AM **Predictors of Maternal Subjective Socioeconomic Status (SSES) Rankings**
Erika F. Dennis, Scott Lorch, Leny Mathew, Jennifer Culhane. – Abstract 59

9:45 AM **An Education Program To Increase Knowledge of and Immunization with Adult Pertussis Vaccination Among Parents of Newborns**
Pui-Ying Iroh Tam, Benjamin Smith, Donna Fisher. – Abstract 60

10:00 AM **Girls Who Disclose Sexual Abuse: What Do They Tell Us?**
Cindy W. DeLago, Martin A. Finkel. – Abstract 61

10:15 AM **Prenatal Consultation for Congenital Anomalies: Parental Expectations and Perceptions**
Franscesca Miquel-Verges, S. Lee Woods, Susan W. Aucott, Renee D. Boss, Leslie J. Sulpar, Pamela K. Donohue. – Abstract 62

GI/Nutrition/Growth Platform Session

8:15 AM-10:30 AM **Liberty B**

Moderator: Fred Suchy

8:15 AM **In Utero High Fat Diet and Maternal Genotype Program Fetal Growth**
Harpreet Kaur, Kirsten Hartil, Michael Kruse, Ariana Fiallo, Maureen J. Charron, Patricia Vuguin. – Abstract 63

8:30 AM **Periconceptional Multivitamin Use and Its Association with Infant Birth Weight Disparities**
Heather H. Burris, Martha M. Werler, Allen A. Mitchell. – Abstract 64

8:45 AM **Circulating Levels of Hepatocyte Growth Factor Activator Inhibitor-1 (HAI-1) May Predict Fetal Intrauterine Growth Restriction**
Alice Wang, Alejandro Rauh-hain, Hector Tamez, Ananth Karumanchi, Ravi Thadhani. – Abstract 65

9:00 AM **Maternal Intrapartum Antibiotic Prophylaxis and Gut Microbiotic Composition in Newborn**
GianVincenzo Zuccotti, Laura Pogliani, Dario Dilillo, Elena Bessi, Belinda Benenati, Lorenzo Morelli, Marcello Giovannini, Giacomo Biasucci. – Abstract 66

9:15 AM **Niroscopic Tissue Oxygenation Changes of the Splanchnic Region in Preterm Neonates After Feeds**
Viral Dave, Luc P. Brion, Deborah E. Campbell, Melissa Scheiner, Carolyn Raab, Suhas M. Nafday. – Abstract 67

9:30 AM **Nutritional Practices in Extremely Low Birth Weight Infants (ELBW, <1000g): 2002 vs. 2006**
Rita M. Ryan, Jennifer A. Clark, Nancy Garrison, Alyssa Hermann, Anne Marie Reynolds. – Abstract 68

9:45 AM **Growth Velocity in the Extremely Low Gestational Age Newborn**
Yolanda F. Brown, Camilia R. Martin, Elizabeth N. Allred, Richard A. Ehrenkranz, Michael O'Shea, Mandy B. Belfort, Marie C. McCormick, Alan Leviton, ELGAN Study Investigators. – Abstract 69

10:00 AM **Home Environment Independently Influences Growth of Very Low Birth Weight (VLBW < 1500g) Former Preterm Infants**
Vincent C. Smith, Gareth Parry, Marie C. McCormick. – Abstract 70

10:15 AM **Changing Epidemiology of Cholecystitis and Cholelithiasis in the Pediatric Population**
Fadel Balawi, Robert Lee, Warren Rosenfeld. – Abstract 71

Infectious Disease Platform Session

8:15 AM-10:30 AM **Freedom**

Moderator: Marietta Vazquez

8:15 AM **Rhinovirus Epidemiology, Disease Spectrum, and Association with Serious Bacterial Infections in Febrile Young Infants**
Mark X. Cicero, Lei Chen, Carla Weibel, Caleb Korngold, Jeffrey Kahn. – Abstract 72

8:30 AM **Individual Differences in the Concentration of Intracellular Metabolites of Anti-HIV Nucleoside Analogs**
Elijah Paintsil, Rong Hu, Yung-Chi Cheng. – Abstract 73

8:45 AM **Variability in the Presence of CSF Pleocytosis Among Young Infants with Enterovirus Infections of the Central Nervous System**
Jeffrey A. Seiden, Joseph J. Zorc, Richard L. Hodinka, Samir S. Shah. – Abstract 74

9:00 AM **Sequential Evidence-Based Central Line Care Interventions Can Decrease Line Associated Sepsis**
Sulaiman Sannoh, Barbara Clones, Jose Munoz, Boriana Parvez. – Abstract 75

9:15 AM **Prevalence and Characterization of HIV-Associated Nephropathy and Other Renal Disorders in a Cohort of Perinatally HIV-1 Infected Children**
Murli U. Purswani, Charles Mitchell, James Oleske, Kathleen Kaiser, Miriam C. Chernoff, Hans Spiegel, Warren A. Andiman, George Seage. – Abstract 76

9:30 AM **Human Papillomavirus Antibodies from Natural Infection Are Protective Against Subsequent HPV Species-Related Infections**
Zainab A. Malik, Susan M. Hailpern, Robert D. Burk. – Abstract 77

9:45 AM **Phagocytosis and Oxidative Burst of Neonatal Neutrophils Confronted with *Candida albicans* and *Candida parapsilosis***
Kisha G. Destin, Matthew A. Maccani, Sonia S. Laforce-Nesbitt, Joseph M. Bliss. – Abstract 78

10:00 AM **Pro- and Anti-Inflammatory Cytokine Release by Circulating Monocytes in the Newborn: Control by Endogenous Interleukin-10 and Effects of Exogenous Interleukin-10 Versus Dexamethasone**
Lina Elbash, Lucy Pereira-Argenziano, Veronika Miskolci, Ivana Vancurova, Dennis Davidson. – Abstract 79

10:15 AM **Use of Umbilical Cord Blood Cultures for the Diagnosis of Early-Onset Sepsis**
Secelela Malecela, Judith Palafoutas, Michelle Peterson, Zacharia Cherian, Jayashree Ramasethu. – Abstract 80

Neonatology I - Neonatal Pulmonology Platform Session

8:15 AM-10:30 AM **Liberty C**

Moderator: Satyan Lakshminrusimha

8:15 AM **Carcinoembryonic Cell Adhesion Molecule 6: A New Human Surfactant Associated Protein**
Philip L. Ballard, Cheryl J. Chapin, Linda W. Gonzales, Nicole Bailey, Jeffrey D. Merrill, Marye Godinez, Roberta A. Ballard. – Abstract 81

8:30 AM **Simulated Medical Transport Is Associated with Decreased mRNA Expression of Surfactant Proteins A, B & C and Higher Active Phospholipid Content in Neonatal Sprague-Dawley Rats**
Ashraf Gad, J. Craig Cohen, Avinash Chander, Shetal Shah. – Abstract 82

8:45 AM **ErbB4 Regulation of Type II Cell Maturation in Murine Lung**
Lucia D. Pham, Sujatha M. Ramadurai, Washa Liu, Christiane E.L. Dammann, Heber C. Nielsen. – Abstract 83

9:00 AM **Nitrolinoleate Acts as a Signaling Molecule in Pulmonary Cells Via Modification of Membrane Proteins**
Jayshree Savla, ChangJiang Guo, Bruce Freeman, Andrew Gow. – Abstract 84

9:15 AM **The Role of Reactive Oxygen Species (ROS) in A549 Respiratory Epithelial Cell Infection by Adenovirus Type 21 (ADV-21) and Parainfluenza Virus Type 3 (PIV-3)**
Khalid S. Ahmad, Ansamma Joseph, Melodi B. Pirzada, Byung-Min Choi, Jeffrey A. Kazzaz, Leonard R. Krilov. – Abstract 85

9:30 AM **Angiopoietin 2 Release by Tracheal Aspirate Cells from Ventilated Premature Infants Is Not Regulated by Nuclear Factor-KappaB**
Zubair H. Aghai, Judy G. Saslow, Tarek Nakhla, Gary Stahl, Riva Eydelman, Louise Strande, Vineet Bhandari. – Abstract 86

9:45 AM **Nasal Continuous Positive Airway Pressure (NCPAP) vs Bi-Level NCPAP (SiPAP) in Preterm Infants: A Comparison of Work of Breathing (WOB) and Respiratory Function**
Vita M. Boyar, Sherry E. Courtney, Jennifer Beck, Christer Sinderby, Robert H. Habib. – Abstract 87

10:00 AM **High Flow Nasal Cannula in Preterm Infants: Effects of High Flow Rates on Work of Breathing**
Kee H. Pyon, Zubair H. Aghai, Tarek A. Nakhla, Gary E. Stahl, Judy G. Saslow. – Abstract 88

10:15 AM **Is There a Relationship Between the Initial (I) FiO_2 in the Delivery Room (DR) and Bronchopulmonary Dysplasia (BPD)?**
Anita Stola, Jeffrey Perlman, Joseph Schulman. – Abstract 89

Plenary Session I

10:45 PM-11:45 PM **Liberty C**

10:45 AM **Mentor of the Year Presentation**
Jane Newburger, Children's Hospital, Boston, MA

Meet the Professor Lunch

12:00 PM-1:00PM **Congress**

10:15 AM **Nuts and Bolts of Writing an IRB Proposal**
Iman Sharif, Children's Hospital of Montefiore, Bronx, NY

Eastern ESPR Business Meeting

12:00 PM-1:00PM **LIberty A**

Plenary Session II & Young Investigator Presentations

1:10 PM-4:00 PM **Liberty C**

1:10 PM **Plenary Lecture - Recent Advances in Inherited Cholestatic Liver Disease**
Frederick J. Suchy, Mount Sinai School of Medicine

2:00 PM **Resuscitation of Neonatal Lambs with Pulmonary Hypertension with 21% and 100% Oxygen – Effect on Pulmonary Hemodynamics**
Satyan Lakshminrusimha, Daniel D. Swartz, Sylvia F. Gugino, Karen Wynn, Robin H. Steinhorn, James A. Russell. – Abstract 90

2:15 PM **Missense LEOPARD Syndrome Mutations in *PTPN11* Have Gain of Function Effects During Development**
Kimihiko Oishi, Cindy J. Wang, Tabassum Rahman, Natalie Pica, Bruce D. Gelb. – Abstract 91

2:30 PM **Hospital Stays for Ambulatory Care Sensitive Conditions in Children with Sickle Cell Disease: 1997 to 2003**
Suzette O. Oyeku, Ryan Conrad, Andrew D. Racine. – Abstract 92

3:00 PM **Oxidative Stress Disrupts Oligodendrocyte Maturation**
Heather M. French, Polina Mamontov, Mary Reid, Judith Grinspan, Rebecca A. Simmons. – Abstract 93

3:15 PM **Enhanced Lung Maturation Using Intrauterine Gene Therapy**
Gabriela I. Mihalache, Erin C. Killeen, Delon Callender, Janet E. Larson, J.C. Cohen, Manoj A. Biniwale. – Abstract 94

3:30 PM **Oligodendrocyte Maturation in a Rabbit Model of Intraventricular Hemorrhage**
Caroline O. Chua, Furong Hu, Hongmin Xu, Praveen Ballabh. – Abstract 95

3:45 PM **Transcription Factor Ap2δ Associates with Ash2l and ALR, a Histone Methyltransferase, To Activate *Hoxc8* Transcription During Development**
Cheryl C. Tan, K.V. Sindhu, SiDe Li, Hitomi Nishio, Jason Z. Stoller, Kimihiko Oishi, Sahitya Puttreddy, Tamara J. Lee, Jonathan A. Epstein, Martin J. Walsh, Bruce D. Gelb. – Abstract 96

Adolescent Medicine Platform Session

4:15 PM-5:45 PM **Freedom**

Moderator: Matilde Irigoyen

4:15 PM **Are There Neurocognitive Correlates of Risk Behaviors in Preadolescents?**
Daniel Romer, Laura M. Betancourt, Joan M. Giannetta, Nancy L. Brodsky, Martha Farah, David Shera, Hallam Hurt. – Abstract 97

4:30 PM **Predictors of Unstable Housing Among Adolescents with HIV**
Jeffrey M. Birnbaum, Elizabeth A. Eastwood. – Abstract 98

4:45 PM **Low Literacy in Adolescents and Health Outcomes**
Alexis Lieberman, Jennifer Cromley, Lauren Charles, Oscar Rodriguez, Maria Lopez-Marti, Srikanth Das, Diego Moguillansky. – Abstract 99

5:00 PM **Teen High-Risk Behaviors Improved by Patient-Centered Counseling Intervention**
Kedron Horvath, Alexis S. Lieberman, Rebecca Merkh, Paul G. Whittaker. – Abstract 100

5:15 PM **Internet Usage To Obtain Health Information Among Adolescents in an Urban Healthcare Network**
Adeleye Afolayan, Cesar Mella, Zarlasht Manzoor, Cynthia Lewis, Ayoade Adeniyi, Ronald Bainbridge, Richard Neugebauer. – Abstract 101

5:30 PM **Outpatient (O) Directly Observed Therapy (DOT) for Children/Youth with Perinatally-Acquired HIV Infection (CYPAHIV) with Antiretroviral (ARV) Treatment Failure (TF) Due to Chronic Non-Adherence (CNA)**
Eberechi I. Nwaobasi, Barry Dashefsky. – Abstract 102

Developmental Biology Platform Session

4:15 PM-5:45 PM **Liberty B**

Moderator: Jonathan Gitlin

4:15 PM **The Cardiac L-Type Calcium Channel Is Required for Normal Cardiogenesis and Embryonic Survival**
George A. Porter. – Abstract 103

4:30 PM **Neonatal Ex4 Administration Normalizes Epigenetic Modifications at the Proximal Promoter of Pdx-1**
Sara E. Pinney, HongShun Niu, Fenglen Li, Rebecca A. Simmons. – Abstract 104

4:45 PM **A Novel Cre Reporter Mouse Reveals New Derivatives of Pax3-Expressing Precursors**
Jason Z. Stoller, Karl R. Degenhardt, Li Huang, Min Min Lu, Jonathan A. Epstein. – Abstract 105

5:00 PM **Identification of Progenitor Cell Characteristics in Naive Human Fetal Lung Epithelium**
Kristen Glass, Linda Varghese, Linda Gonzales, Michael Beers, Cherie Foster. – Abstract 106

5:15 PM **Hypoxia Inducible Factor-1α Activity Is Increased in Neonatal Neutrophils**
Anna Vetrano, Faith Archer, William Hoffman, Barry Weinberger. – Abstract 107

5:30 PM **Static Stretch of Differentiated Human Fetal Type II Cells Promotes Transition to a Type I Phenotype**
Cherie Foster, Linda Varghese, Linda Gonzales, Susan Margulies. – Abstract 108

General Pediatrics II Platform Session

4:15 PM-5:45 PM **Liberty A**

Moderator: Andrew Racine

4:15 PM **The Efficacy of EMLA Versus Synera for Venipuncture in Children**
Ting A. Lee, C. Anthoney E. Lim, Kathy Freeman, Catherine C. Skae. – Abstract 109

4:30 PM **Nutritional Status of Children After a Food Supplementation Program Integrated with Routine Health Care in Migrant Communities of the Dominican Republic**
Kavita Parikh, Gabriela Marein-Efron, Shirley Huang, Samir S. Shah, Geraldine O'Hare, Rodney Finalle. – Abstract 110

4:45 PM **Maternal Ethnicity, Education and Observation of Infant Sleeping Position in the Hospital Nursery as Correlates of Back-to-Sleep Practices**
Irfan Ali, Gracia Marte, Gawin Tsai, Ram Kairam, Richard Neugebauer, Gerrad Augustine, Anantha Harijith, Ronald Bainbridge, Ayoade Adeniyi. – Abstract 111

5:00 PM **Under-Representation of Minority Children in Pediatric Statin Trials**
Brook Belay, Andrew Racine, Peter F. Belamarich. – Abstract 112

5:15 PM **Acute HIV Syndrome in a General Pediatric Practice: Missed Opportunities**
Andres F. Camacho-Gonzalez, Natasa Milosavljevic, Barbara Kelly. – Abstract 113

5:30 PM **Improving Tuberculosis Case-Finding in an Inner City Pediatric Clinic**
Gina Montealegre, Guadaloupe Lopez-Marti, Krissa George, Erika Mendoza, Ryan Kotton, Barbara Black, Alan Schindler, Barbara Kelly. – Abstract 114

Metabolism/Obesity Platform Session

4:15 PM-5:45 PM **Declaration**

Moderator: Sandra Hassink

4:15 PM **Correlation of Weight Gain in First Ten Days of Life and Childhood Obesity**
Riti S. Dayal, Fernanda E. Kupferman, Fernando Llopiz, Salimah Walani, Kanchana Roychowdhury. – Abstract 115

4:30 PM **The Effect of an Intervention Program on Overweight Second and Third Grade Students in an Inner City Elementary School: A Pilot Study**
Sister Melinda Lando, K. Nicole Jalandoni, Haydee Larralde, Nicholas Obiri, Ronald Bainbridge, Ayoade O. Adeniyi, Richard Neugebauer. – Abstract 116

4:45 PM **Effect of Caloric Information on Menu Selection by Caregivers in an Inner City, Minority Population**
Wipanee Phupakdi, Jeremy Aiss, Stanley Cho. – Abstract 117

5:00 PM **Acceptance of Referrals to an Obesity Management Program at an Inner-City Health Center**
Maya Ilowite, Iman Sharif. – Abstract 118

5:15 PM **The Relationship Between the Density of Food Sources in the Built Environment and Obesity Among Inner City School Children**
James J. Burns, Jane Garb, Coleen Walsh, Thomas Yarsley. – Abstract 119

5:30 PM **Effects of a Lifestyle Plus Exercise Intervention on Metabolic Parameters in 7th Grade School Children: A Randomized Controlled Trial**
Radhika Purushothaman, Amrit Bhangoo, Sunil Sinha, Viral Gala, Margarita Smotkin-Tangorra, Irina Kazachkova, Jessica Hileman, Neesha Ramchandani, Joyce Munga, Debbie Perez, Kate Pavlovich, Michael Rosenbaum, Svetlana Ten, Deborah DeSantis, Lisa Altshuler, Steven Shelov. – Abstract 120

Neonatology II - Epidemiology and F/U Platform Session

4:15 PM-5:45 PM **Liberty C**

Moderator: Haresh Kirpalani

4:15 PM **Do Predischarge Bilirubin (BR) Measurements Predict Risk for Significant Hyperbilirubinemia Following Discharge?**
Fadel Balawi, Amy Urban, Lynda Adrouche-Amrani, Warren Rosenfeld. – Abstract 121

4:30 PM **Early Medical and Behavioral Characteristics of NICU Infants Later Diagnosed or Suspected with Autism Spectrum Disorder (ASD)**
Bernard Z. Karmel, Judith M. Gardner, Lauren D. Swensen, Ira L. Cohen, Eric London, Elizabeth M. Lennon, Michael J. Flory, Santosh M. Parab, Anthony Barone. – Abstract 122

4:45 PM **Executive Function in Former Preterm Children at Preschool Age**
Elise M. Lavery, Soraya Abbasi, Nancy L. Brodsky, Laura M. Betancourt, Hallam Hurt. – Abstract 123

5:00 PM **Shifts in the Relative Influence of Biological and Environmental Risk Factors on Developmental Outcome of High-Risk Infants**
Judith M. Gardner, Bernard Z. Karmel, Elizabeth M. Lennon, Phyllis M. Kittler, Michael J. Flory. – Abstract 124

5:15 PM **Neurodevelopmental (ND) Outcomes of Moderately Low Birth Weight (MLBW) Infants**
Melissa A. Woythaler, Marie C. McCormick, Vincent C. Smith. – Abstract 125

5:30 PM **Do Premature Females Really Do Better Than Their Male Counterparts?**
Jody L. Kohut, Linda H. Green, Sharon Kirkby, David Webb, Kevin Dysart. – Abstract 126

Pulmonary and Asthma Platform Session

4:15 PM-5:45 PM **Constitution**

Moderator: Sharon McGrath-Morrow

4:15 PM **Perfluorochemical (PFC) Liquids Decrease Diaphragm Stress in Hyperoxic Lung Injury**
Daniel J. Malone, Jichuan Wu, Mary F. Barbe, Thomas H. Shaffer, Marla R. Wolfson. – Abstract 127

4:30 PM **Transport-Induced Biophysical Impulse Results in Long-Term Alterations of Respiratory Function in Neonatal Sprague-Dawley Rats**
Joseph J. Hudak, Andrew Dylag, Shetal Shah. – Abstract 128

4:45 PM **Discordance Between Reported Compliance and Knowledge Regarding Appropriate Home Management of Childhood Asthma in an Underserved Population**
Cathleen Ballance, GianeCarla Montero, Anna Petrova. – Abstract 129

5:00 PM **Improved Documentation of ED Asthma Severity**
Michael A. Colon, John M. Corsi, James F. Wiley II, Sharon R. Smith. – Abstract 130

5:15 PM **Association of Obesity and Asthma in Inner City Minority Children**
Nita Vangeepuram, John Doucette, Julie A. Britton, Maida Galvez, Barbara Brenner, Susan L. Teitelbaum, Mary S. Wolff. – Abstract 131

5:30 PM **Chitinase Activity in Bronchoalveolar Lavage Fluid from Children with Asthma and Other Allergic Lung Diseases**
Alfin G. Vicencio, Zhongfang Du, Wang Yong Zeng, Mark Suhrland, Stacy Kipperman, David L. Goldman. – Abstract 132

Poster Session II

6:00 PM-7:30 PM **Independence Ballroom**

1 **Comparative Readability of Spanish and English Patient Education Materials**
Maya Ilowite, Iman Sharif. – Abstract 133

2 **Communication and the Pediatric Residency Match**
Catherine C. Skae, Marina Reznik, Philip O. Ozuah. – Abstract 134

3 **The Effectiveness of Web-Based Learning During Pediatric Residency Training**
Honey E. Sward, Carol P. Carraccio, Alison Falck. – Abstract 135

4 **Documenting Resident Education in Systems-Based Practice**
Sandra F. Braganza, Iman Sharif. – Abstract 136

5 **Resident as Teacher: Evaluation of a Teaching Curriculum for Pediatric Housestaff**
Czer Anthoney E. Lim, Cristina E. Farrell, Catherine C. Skae. – Abstract 137

6 **An Intervention To Improve Neonatal Endotracheal Intubation Skills of Pediatric Residents**
Colleen A. Hughes, Rose M. Viscardi, Alison J. Falck. – Abstract 138

7 **Education and Monitoring of Residents' Proficiency in Neonatal Resuscitation**
Matthew A. Rainaldi, Yang S. Kim, Karen D. Hendricks-Munoz. – Abstract 139

8 **Neonatal Resuscitation Simulation Measurement Tool Development**
Jesse Bender, Karen Kennally, Sheree Lindgard, Jean Salera, Richard Tucker. – Abstract 140

9 **Antenatal Corticosteroids Are Associated with Decreased Odds of Death in Neonates Born at 23 Weeks**
Edward J. Hayes, David A. Paul, Gary E. Stahl, Jolene Seibel-Seamon, Kevin Dysart, Benjamin E. Leiby, Amy B. Mackley, Vincenzo Berghella. – Abstract 141

10 **Antenatal Smoking Does Not Affect the Severity of Apnea in Premature Infants**
Zlatka Jeliazkova, Nosrat Razi, Judy G. Saslow, Barbara Amendolia, Gary Stahl, Kee Pyon, Nicole Kemble, Zubair H. Aghai. – Abstract 142

11 **Analysis of Cesarean Section Trends in Very Low Birth Weight Infants (VLBW) over Time and Impact on Birth Outcome (1994-2006)**
Hashini R. Seneviratne, Charlan Kroelinger, David A. Paul. – Abstract 143

12 **Duration of Caffeine Citrate Therapy Is Associated with Increasing Postnatal Growth Restriction in Very Preterm and Low Birth Weight Infants**
Jennifer L. Lefner, Richard Tucker, Leslie McKinley, William Oh. – Abstract 144

13 **Patent Ductus Arteriosus Ligation in the Neonatal Intensive Care Unit Versus the Operating Room: Short Term Morbidities**
Sara D. Sibley, Martha C. Caprio, Pradeep V. Mally, Karen D. Hendricks-Munoz. – Abstract 145

14 **Decrease in Number of PRBC Transfusions but Not Exposure in Very Low Birth Weight Infants Between 1994 and 2006**
Celina C. Sindall, Robert G. Locke, Amy Mackley, David A. Paul. – Abstract 146

15 **Packed Red Blood Cell Transfusions Are Strongly Associated with Necrotizing Enterocolitis in the Very Low Birthweight Infant**
Kelly J. Zook, Alexandra Remakus, Amy Mackley, Deborah Tuttle, Robert Locke, David A. Paul. – Abstract 147

16 **Amplitude Integrated EEG (aEEG) Monitoring During Selective Hypothermia Has Potential Important Clinical and Prognostic Implications**
Vivien L. Yap, Jeffrey M. Perlman, Murray Engel. – Abstract 148

17 **Indicators of Compliance for Neonatal Follow-Up**
Vedika Nehra, Paul Visintainer, Jordan S. Kase. – Abstract 149

18 **Benign Extra-Axial Fluid Collections in Ex-Preterm Children**
Noah Cook, Nancy Brodsky, Jo Ann D'Agostino, Frances Orlando, Judith Bernbaum, Hallam Hurt, Robert Zimmerman. – Abstract 150

19 **Dermoid Cysts Following Fetal Myelomeningocele Closure: Clinical Implication and Follow-Up**
Enrico Danzer, N. Scott Adzick, Natalie E. Rintoul, Deborah M. Zarnow, Erin M. Simon Schwartz, Jeanne Melchionni, Leslie N. Sutton, Alan W. Flake, Mark P. Johnson. – Abstract 151

20 **Pressure-Flow Relationship: Relevance to Bidirectional Glenn Shunt To Reduce Flow Across Pulmonary Outflow Obstruction**
Joshua Wiesman, Nancy Ross-Ascuitto, Robert Ascuitto. – Abstract 152

21 **A Prospective Cohort Study of Arrhythmias in the Neonatal Intensive Care Unit**
Nadia Badrawi, Ranya Hegazi, Edisa Tokovic, Wael Lotfy, Fadya Mahmoud, Hany Aly. – Abstract 153

22 **Clinical Significance of Neutropenia (N) in HIV Infected Children (HIVIC)**
Tong Wei Ch'ng, Barry Dashefsky, Arry Dieudonne, James Oleske, J. Flyer, S. Keller. – Abstract 154

23 **Natural History of Progression of Metabolic Risk Factors in Uncomplicated Obesity in Urban, Inner City Children with Diet and Exercise Recommendations Alone**
Minu M. George, Radhika Purushothaman, Shahid Malik, Arlene B. Mercado, Salvador Castells, Svetlana Ten. – Abstract 155

24 **The Relationship Between Healthy Land Use in the Built Environment and Body Mass Index (BMI) Percentiles Among Inner City School Children**
James J. Burns, Jane Garb, Coleen Walsh, Thomas Yarsley. – Abstract 156

25 **Childhood Obesity and Neighborhood Food Store Availability in an Inner City Community: The Growing up Healthy in East Harlem Study**
Maida P. Galvez, Kimberly Morland, Laura Liao, Cherita Raines, Jessica Kobil, Nita Vangeepuram, James Godbold, Barbara Brenner, Mary S. Wolff. – Abstract 157

26 **Clinical Manifestations of Obesity in a Sample of Urban Minority Children**
Nita Vangeepuram, Allison Gault, Ellen Schranz, Danielle Laraque. – Abstract 158

27 **Parent and Pediatrician Input in the Development of an Obesity Program**
Nita Vangeepuram, Allison Gault, Ellen Schranz, Danielle Laraque. – Abstract 159

28 **Congenital Lead Poisoning Discovered by Routine Screening of a "High Risk" Pregnant Woman**
Nachammai R. Chinnakaruppan, Allison K. Wawer, Eugene Shapiro, Eduardo Bautista, Steven Marcus. – Abstract 160

29 **Do Orphanage Children Exhibit Better Growth Than Those in Communities in Honduras?**
Gilma Marimon, Erin Dahlinghaus, Christine Narad, Annie Kautza, Patrick Mason. – Abstract 161

30 **Infant Growth and Child Cognition at 3 Years of Age**
Mandy B. Belfort, Sheryl L. Rifas-Shiman, Janet W. Rich-Edwards, Emily Oken, Ken P. Kleinman, Matthew W. Gillman. – Abstract 162

31 **Adverse Asthma Outcomes in Pediatrics**
Alan S. Weller, Kitaw Demissie. – Abstract 163

32 **Breastfeeding Initiation and Weaning in a South Bronx Hospital: Influence of Knowledge, Attitude and Practices**
Irfan Ali, Anthony Ani, Harleen Bhandhal, Priya Bhate, Ronald Bainbridge, Ayoade Adeniyi, Richard Neugebauer. – Abstract 164

33 **Referral Patterns for Victims of Intimate Partner Violence Identified in a Pediatric Hospital**
Maria McColgan, Patricia Barry, Mario Cruz. – Abstract 165

34 **Pubertal Assessment Methodology and Baseline Characteristics in a National Cohort of 6-8 Year Old Girls: The Breast Cancer and the Environment Research Center Cohort**
Frank M. Biro, Maida P. Galvez, Louise C. Greenspan, Nita Vangeepuram, Larry Kushi, Susan Pinney, Mary S. Wolff. – Abstract 166

35 **Administration of Tetanus, Diptheria, & Acellular Pertussis (Tdap) Vaccine to Parents of High-Risk Infants in the Neonatal Intensive Care Unit (NICU)**
Andrew Dylag, Shetal Shah. – Abstract 167

• • •Sunday, March 30, 2008• • •

Plenary Session III & Presentation of The Young Invesigator Awards

8:30 AM-9:30 AM **Liberty C**

8:30 AM **Presentation of The Young Investigator Awards**

8:40 AM **Plenary Lecture - The Inorganic Chemistry of Life: Lessons from Genetics**
Jonathan D. Gitlin, Washington University School of Medicine

General Pediatrics III Platform Session

9:45 AM-12:00 PM **Liberty A**

Moderator: Suzette Oyeku

9:45 AM **PIC'M Study: Parental Influence in Clinical Management**
Sean M. Bailey, George E. Fryer, Karen Hendricks-Munoz, Pradeep Mally. – Abstract 168

10:00 AM **Availability and Accuracy of Spanish Language Medication Labels**
Iman Sharif, Julia Tse. – Abstract 169

10:15 AM **Mental Health Care Needs of Latino Families in the South Bronx: Perspectives of Parents and Pediatricians**
Anagha Loharikar, Iman Sharif, Sandra Braganza. – Abstract 170

10:30 AM **Integration of a Mandatory, Web-Based Neonatology Curriculum into Pediatric Residency Training**
Priya Garg, Jamelah Tucker, Carol Carraccio, Alison Falck. – Abstract 171

10:45 AM **Experience with a Pediatric and Surgical Co-Management Model in Pediatric Residency Training**
Anna M. Carr, Allan M. Arbeter, Matilde Irigoyen, Robert S. Wimmer. – Abstract 172

11:00 AM **Growth Assessment of Children Living in a Honduran Orphanage**
Jillian Kunar, Christine Narad, Annie Kautza, Patrick Mason. – Abstract 173

11:15 AM **Communication of Care: Results of the District of Columbia American Academy of Pediatrics, Fetus and Newborn Committee Hepatitis B (HepB) Survey**
Mary Revenis, Inez Reeves. – Abstract 174

11:30 AM **A Comprehensive Intimate Partner Violence Intervention Results in Sustained Improvement in Screening Rates by Pediatric Residents**
Maria McColgan, Patricia Barry, Angelo P. Giardino, Mario Cruz, Sandra Dempsey, Martha Davis, Jessica McKee, Ana Lisa Yoder, Coleen Fitzpatrick, Dalvi Monique. – Abstract 175

11:45 AM **Infant Safe Sleeping in Homeless Family Shelters**
Sonia Chaudhry, Nancy Miller. – Abstract 176

Genetic Basis of Disease Platform Session

9:45 AM-12:00 PM **Freedom**

Moderator: Ian Krantz

9:45 AM **Single Nucleotide Polymorphisms (SNPs) of Interleukin-8 (IL8) and IL8 Receptors and BPD in ELBW Infants**
J. Fisher, M. Brown, E. Kaoi, M. Singh, C. Pham, N. Ali, H. Maramreddy, S. Strassberg, L.A. Parton. – Abstract 177

10:00 AM **Single Nucleotide Polymorphisms of Fas, Fas Ligand, and the Caspases and Bronchopulmonary Dysplasia in ELBW Infants**
Hima Maramreddy, A. Yao, C. Pham, N. Ali, J. Fisher, S. Strassberg, L.A. Parton. – Abstract 178

10:15 AM **Role of Epigenetic Modifications in the Maturational Regulation of Lung HO-1**
Sacha Kassovska-Bratinova, Phyllis A. Dennery. – Abstract 179

10:30 AM **Familial Turner Syndrome Due to a Heritable Xp Deletion**
Sreenivas Dutt Gunturu, Radhika Purushothaman, Henry Anhalt, Svetlana Ten, Harry Ostrer. – Abstract 180

10:45 AM ***SHOX* Gene Analysis in Families of Children with Short Stature**
Genna W. Klein, Yeray Novoa, Sofia Shapiro, Elizabeth Wallach, Robert Rapaport. – Abstract 181

11:00 AM **Hemoglobin Fast Variant/Possible Bart's in Newborns: Correlation with DNA alpha-Thalassemia Testing**
Fariha Kamran, Dominick Sabatino, Sujatha Kosuri, Stephen P. Katz, Harvey Aiges. – Abstract 182

11:15 AM **Effect of GH and IGF-1 Therapy in 3 Patients with Growth Hormone Insensitivity (GHI) Due to Mutation of the GH Receptor Gene**
Nauman Basit, Sunil K. Sinha, Amrit Bhangoo, Svetlana Ten. – Abstract 183

11:30 AM **Anti-Mullerian Hormone as a Marker of Ovarian Reserve in Young Girls with Turner's Syndrome**
Radhika Purushothaman, Oksana Lazareva, Munazza Basit, Svetlana Ten. – Abstract 184

11:45 AM **Interfamily Phenotypic Difference in Familial Isolated Growth Hormone Deficiency Due to a Novel Homozygous Mutation of Growth Hormone Releasing Hormone Receptor (*GHRHR*) Gene**
Sunil K. Sinha, Kyriaki S. Alatzoglou, Amrit Bhangoo, Svetlana Ten, Mehul T. Dattani. – Abstract 185

Neonatology III - Clinical Studies Platform Session

9:45 AM-12:00 PM **Liberty C**

Moderator: Richard Polin

9:45 AM **Utility of Measuring Direct Bilirubin at 12-24 Hours of Age in Neonates Admitted to the Neonatal Intensive Care Unit**
Sukesh Sukumaran, Ronald Sutsko, Barbara Amendolia, Judy G. Saslow, Tarek Nakhla, Nicole Kemble, Nosrat Razi, Gary Stahl, Kee Pyon, Zubair H. Aghai. – Abstract 186

10:00 AM **Effect of a High Fidelity Simulation Curriculum on Pediatric Resident Competency in Neonatal Airway Management Skills**
J. Arnold, M. Fiedor Hamilton, J. Kloesz, R. Clark, S. Kanter, B. Lowmaster, S. Wisneiski, D. Hofkosh, P. Kochanek. – Abstract 187

10:15 AM **Impact of Instrumental Dead Space on Pressure Support Volume Guarantee (PS-VG) Mode of Ventilation in Extremely Low Birth Weight (ELBW) Infants**
Rebecca J. Eick, Sepideh Montazami, Kabir M. Abubakar, Martin Keszler. – Abstract 188

10:30 AM **Predictors of Morbidity and Mortality in Infants with Congenital Diaphragmatic Hernia: A National Database Review**
Hany Aly, Maria D. Bianco-Batlles, Anthony Sandler, Mohamed H. Mohamed. – Abstract 189

10:45 AM **An Evaluation of an ROP Screening Program**
Rachel Porat, Dafna Ofer, Dana Toib, Ahashta Johnson, David L. Schutzman. – Abstract 190

11:00 AM **Amplitude Integrated Electroencephalography (aEEG) in Premature Infants (PREMS): Frequent Artifacts (ARTs) Limit a Role in Assessing Cerebral Function?**
Debbie Suk, Alfred N. Krauss, Murray Engel, Jeffrey M. Perlman. – Abstract 191

11:15 AM **Ascorbic Acid Combined with Ibuprofen in Hypoxic Ischemic Encephalopathy: A Randomized Controlled Trial**
Hany Aly, Mohamed El-Dib, Laila Abd-Rabboh, Fathy Nawwar, Hassan Hassan, Mohamed Aaref, Ahmad Elsayed. – Abstract 192

11:30 AM **Vinyl Bag vs. Thermal Mattress To Prevent Hypothermia in Extremely Low Birth Weight (ELBW) Infants**
Bobby Mathew, Satyan Lakshminrusimha, Vivien Carrion. – Abstract 193

11:45 AM **Use of Chemical Warming Packs During Delivery Room Resuscitation and Admission Temperatures in Very Low Birth Weight Neonates**
Joaquim M. Pinheiro, Susan Boynton, Susan A. Furdon, Robin Dugan, Sharon Jensen, Christine Reu-Donlon, Mary A. Miller, Andrea Degnan. – Abstract 194

Neurobiology Platform Session

9:45 AM-12:00 PM **Liberty B**

Moderator: Jane McGowan

9:45 AM **Cardiac Troponin I (cTnI) Levels in Asphyxiated Infants Undergoing Selective Head Cooling Correlate with Mortality and Neurodevelopmental Outcome**
Constance G. Andrejko, Vidula Damle, Susan C. Adeniyi-Jones. – Abstract 195

10:00 AM **Altered Fractional Anisotropy Caused by Neonatal Hypoxia Ischemia Is a Result of Increased Radial Diffusivity in Injured White Matter**
Brian S. Stone, Jiangyang Zhang, Susumu Mori, Frances J. Northington. – Abstract 196

10:15 AM **A Randomized Controlled Trial To Determine the Lowest Effective Dose for Adequate Mydriasis in Premature Infants**
Monisha Bahri, Gonzalo C. Vicente, Judith J. Palafoutas, Nitin R. Mehta. – Abstract 197

10:30 AM **A Comprehensive Analysis of Protein Secretion by Neonatal Murine Astrocytes After Inflammatory Stimulation**
Sarah D. Keene, Todd Greco, Harry Ischiropoulos. – Abstract 198

10:45 AM **Regional Tissue Oxygenation in Association with Alterations in the Physiologic Parameters in Preterm Infants**
Anna Petrova, John Chuo, Uday Nadgir, Mayoor Bhatt, Rajeev Mehta. – Abstract 199

11:00 AM **Blood Glucose Levels and ROP in ELBW Infants**
Raul Chavez-Valdez, Christoph U. Lehmann, Elizabeth A. Cristofalo, Jane E. McGowan. – Abstract 200

11:15 AM **Childhood Syncope**
Cristina S. Wheeler Castillo, Francis J. DiMario. – Abstract 201

11:30 AM **Peak-To-Peak Amplitude in Neonatal Brain Monitoring of Premature Infants**
Deirdre O'Reilly, Michael Navakatikyan, Marcia Filip, Deirdre Greene, Linda J. Van Marter. – Abstract 202

11:45 AM **Effect of Relative Intrauterine Growth Restriction (RIUG) and Relative Discordancy (RDIS) on Auditory Brainstem Evoked Responses (ABRs) in Newborn Twins**
Ha T.T Phan, Bernard Z. Karmel, Judith M. Gardner, Phyllis Kittler, Inna Miroshnichenko, Anthony Barone, Anantham Harin, Santosh Parab.

Pulmonary Development and Injury Platform Session

9:45 AM-12:00 PM **Constitution**

Moderator: James Padbury

9:45 AM **Role of the NF-κB Subunit p50 in Postnatal Lung Development**
Guang Yang, Maurice Hinson, Jessica Bordner, Tiangang Zhuang, Clyde Wright, Phyllis A. Dennery. – Abstract 204

10:00 AM **Inhibition of NF-κB Activation by Preventing IκB-β Degradation Improves Neonatal Survival in Hyperoxia and Preserves Lung Architecture**
Clyde J. Wright, Guang Yang, Phyllis A. Dennery. – Abstract 205

10:15 AM **ErbB Signaling in Hypoxia- and Hyperoxia-Induced Lung Epithelial Cell Injury**
Washa Liu, Hshi-chi Koo, Jonathan M. Davis, Heber C. Nielsen, Christiane E.L. Dammann. – Abstract 206

10:30 AM **Bach-1 Modulates Heme Oxygenase-1 (HO-1) Transcription in the Newborn in Hyperoxia**
Sacha Kassovska-Bratinova, Guang Yang, Kazuhiko Igarashi, Phyllis A. Dennery. – Abstract 207

10:45 AM **Heparin-Binding VEGF Isoforms Attenuate Hyperoxic Lung Injury in Explanted Mouse Embryonic Lung**
Americo E. Esquibies, Alia Bazzy-Asaad, Lloyd G. Cantley. – Abstract 208

11:00 AM **Lung Contusion Alters Pulmonary Vasoreactivity in Rats**
Satyan Lakshminrusimha, Bruce A. Davidson, Rita M. Ryan, Jadwiga D. Helinski, Krishnan Raghavendran. – Abstract 209

11:15 AM **Surfactant Administration Does Not Normalize Respiratory Function Changes Associated with Transient *In Utero* Knockout (TIUKO) of the CFTR Gene in Sprague-Dawley Rats**
Andrew Dylag, Joseph Hudak, Shetal Shah, J. Craig Cohen. – Abstract 210

11:30 AM **Transient In-Utero Exposure to Nicotine Directly Stimulates Expression of Proteins Necessary for Mechanico-Sensory Dependent Lung Development**
Shruti Gupta, Shanthy Sridhar, Craig J. Cohen, Janet E. Larson. – Abstract 211

11:45 AM **Airway Injury Resulting from Repeated Endotracheal Intubation: Possible Prevention Strategies**
Adebayo A. Oshodi, Kevin Dysart, Alison Cook, Elena Rodriguez, Yan Zhu, Thomas H. Shaffer, Thomas L. Miller. – Abstract 212

Endocrinology/Metabolism Platform Session

9:45 AM-12:00 PM **Declaration**

Moderator: Steven Willi

9:45 AM **A Short Version GHRH Stimulation Test as a Novel and Effective Tool in Children with Idiopathic Short Stature**
Amrit Bhangoo, Nauman Basit, Vijay Chickajaju, Svetlana Ten. – Abstract 213

10:00 AM **Markers of Insulin Reserve in Pediatric Type 2 Diabetes (T2DM)**
Lorraine E. Levitt Katz, Marcia Hernandez, Heather M. McKnight, Paul R. Gallagher, Kathryn M. Murphy. – Abstract 214

10:15 AM **HbA1c as a Screening Tool for Pediatric Type 2 Diabetes**
Alisa B. Schiffman, Kristen T. Sonnek-Schmelz, Sarah J. Ratcliffe, Lorraine Levitt-Katz, Steven M. Willi. – Abstract 215

10:30 AM **Hypoglycemia in Critically Ill Children**
E. Vincent Faustino, Clifford Bogue. – Abstract 216

10:45 AM **Hypoglycemia Associated Autonomic Failure: Are Free Fatty Acids (FFA) Responsible?**
A.S. Nayak, B.B. Nankova, E.F. LaGamma. – Abstract 217

11:00 AM **Does One Enteral Feeding Correct Asymptomatic Hypoglycemia in the Newborn?**
Yesenia Morales, Debra Potak, Richard J. Schanler. – Abstract 218

11:15 AM **Disruption of Late Rat Intestinal Organogenesis Leads to Adult Onset Obesity and Insulin Resistance**
Malgosia Skowron, Janet E. Larson, Haihong Zong, Jeffery E. Pessin, J. Craig Cohen. – Abstract 219

11:30 AM **Effects of Maternal Depression or SSRI Use on Placental NET and SERT Gene Expression**
Kathryn L. Ponder, Bethany McGonnigal, Jennifer Bauer, Alyse Laliberte, Amy Salisbury, James Padbury. – Abstract 220

11:45 AM **Vitamin D Responsiveness Is Impaired in Neonatal Neutrophils**
Daniel Hirsch, Faith Archer, Barry Weinberger, Anna Vetrano. – Abstract 221



2008 ESPR Abstracts

Poster Session I

Friday, March 9, 2007 6:00 PM-7:30 PM

1

Maternal Satisfaction with Prenatal Care: Are We Educating Enough?

Vivien Carrion, Karola Long, James Shelton. Neonatology/Pediatrics, Women and Children's Hosp. of Buffalo, Buffalo, NY.

BACKGROUND: Maternal satisfaction with prenatal care has been associated with patient education, quality of prenatal visits and availability of services.

OBJECTIVE: To evaluate the education provided to pregnant patients during their prenatal visits as well as patient satisfaction with their prenatal care.

DESIGN/METHODS: A cross-sectional, self-administered survey was given to post-partum mothers ≥ 18 years of age after delivering a live birth in the 8 county region of western New York. Respondents completed an anonymous survey of 23 questions including: Insurance type, infant birth weight, gestational age (GA), site of prenatal care, number of prenatal visits, education provided at visits, and patient satisfaction. Statistical analysis was conducted using the chi-square test.

RESULTS: Study population included 470 women age 18 - 44 (mean of 27 years), who received prenatal care during pregnancy. Mean birth weight of infants was 3343 g with 7.2% < 2500g and mean GA was 39 weeks with 7.7% < 37 weeks. Women received prenatal care at private offices (69%), in-hospital clinics (12%) and out of hospital clinics (18%). Medicaid (MA) was the primary insurance for 48% of the women, private insurance for 50% and other/no insurance for 2%. The majority of women had 10 or more prenatal visits(88%). Patient education during prenatal visits varied by topic.[table1]Education regarding folic acid use was more often discussed in the private setting ($p<.05$). MA patients were less likely to be educated regarding folic acid use and diet and more often received questions on family concerns/domestic violence. They were also significantly less likely to be satisfied with quality of prenatal visit.

CONCLUSIONS: Important factors that providers need to address during prenatal visits were not always discussed. Discussion of folic acid use, diet, safety/domestic violence or family concerns may be influeneced by insurance type or provider care site.

Percent factor discussed

		Type of insurance		Clinical setting
	All women	private	medicaid	private
Factor	n=470	n=233	n=222	n=325
signs of preterm labor	96%	96%	96%	97%
diet	89%	93%	86%*	91%
alcohol / drugs	83%	85%	81%	83%
exercise	82%	83%	83%	82%
stress	76%	75%	78%	77%
STDs	74%	73%	77%	74%
birth control	74%	70%	78%	74%
folic acid	73%	78%	69%*	77%
safety / domestic violence	61%	57%	66%*	60%

*P<0.05

2 Fellow in Training

Nursing Staff Education Can Improve Adherence with Central Line Hub Care Protocol

Sulaiman Sannoh, Hassan Khan, Maria Khan, Barbara Clones, Boriana Parvez. RNICU, MFCH WMC, Valhalla, NY; SUNY, Binghampton, NY.

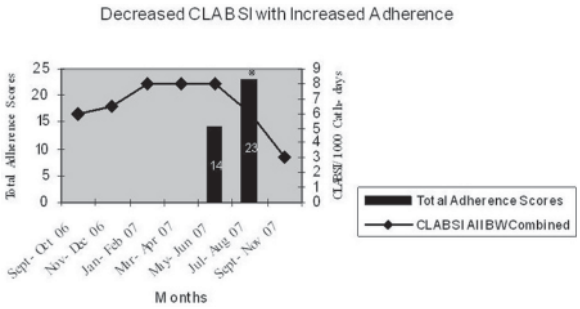
BACKGROUND: Central Line-associated bloodstream infections (CLABSI) increase morbidity, mortality, LOS and healthcare costs. Educational programs to promote best practices for central line (CL) care can reduce sepsis. Adherence to healthcare protocols declines over time, which may increase infections. We have previously shown sustained decrease in CLABSI 9 months after introduction of new CL hub care protocol (2/06). But infection rates increased after the 9 months. We hypothesized that there was decline in adherence with CL hub care protocol.

OBJECTIVE: To assess adherence with CL hub care protocol and effectiveness of education.

DESIGN/METHODS: CL hub care protocol has 9 distinct steps which focus on establishing sterile fields and disinfection with chlorhexidine. Nursing adherence with CL hub care protocol was observed by blinded observers three days/week and scored using Observer Check List. Education was conducted with DVD presentation. Adherence with each of 9 the steps of protocol was marked as Yes or No and given a score of 1 or 0 respectively. Observations for each step were expressed as % Yes of total observations. Overall total adherence score was generated, summing all Yes scores. Adherence differences before and after education were analyzed using X^2 for each protocol step and unpaired t-test for the total score.($p<0.05$).

RESULTS: 24 and 26 nurses were randomly observed during CL hub care before and after education respectively. Significant improvement in adherence was noted post- education in 6 out of the 9 protocol steps ($p<0.05$). The total adherence score was significantly improved, 14 ± 7 vs 23 ± 3 *(Mean±SD)*($p<0.05$). CLABSI rate decreased after education by 55% from 8 to 3.6/1000.

CONCLUSIONS: DVD education had significant impact on nurses' adherence with CL hub care protocol, but periodic re-education campaigns may be necessary to maintain adherence and to promote improvement. In order to achieve complete compliance with each step of protocol, the reasons for non-compliance should be investigated.



3

Educating Neonatal Intensive Care Unit (NICU) Parents About Sudden Infant Death Syndrome (SIDS) Risk Reduction: Promoting a Consistent Message by NICU Nurses

Nilay Baxi, Barbara M. Ostfeld, Thomas Hegyi. Pediatrics, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

BACKGROUND: Since 1990 there has been a 16% rise in the US in the rate of premature births, a risk factor for SIDS. In New Jersey, 27% of SIDS cases compared to 9% of all births are premature. The greater vulnerability of this growing population underscores the need for effective NICU parent education on risk reduction. The American Academy of Pediatrics' (AAP) Task Force on SIDS has encouraged greater participation by NICU nurses in parent education, yet, compared to physicians, there appear to be fewer opportunities for nurses to receive relevant information (Esposito, Ostfeld, Hegyi, Journal of Perinatal & Neonatal Nursing, 2007).

OBJECTIVE: To determine a baseline for spontaneous bedside education on SIDS risk reduction by nurses practicing in NICUs, in anticipation of regional educational interventions.

DESIGN/METHODS: Anonymous surveys were distributed to NICU nurses in an urban community and returned by direct mail or by placement in sealed drop boxes distributed for that purpose. The study met standards for exempt review.

RESULTS: Of 90 surveys distributed, 46 (51%) were completed; 70% had 10 or more years of experience. Examples of NICU nurse bedside guidance to parents concerning SIDS risk reduction initiatives are presented in Table 1. Supine sleep was the topic most frequently offered, and 22% of respondents noted in qualitative comments that they also addressed related parental concerns regarding aspiration. Least likely to be discussed were pacifier use, avoidance of bed sharing and benefits of room sharing.

NICU Nurse Bedside SIDS Risk Reduction Commentary

Topic Discussed	% Always	% Sometimes	% Never
Back to Sleep	78.3	21.7	0
No side sleep	54.3	34.8	10.9
No pillows or soft objects in crib	78.3	15.2	6.5
No second hand smoke	84.4	10.9	4.3
Remind all caregivers	63.6	27.3	9.1
Offer pacifier at sleep	17.4	28.3	54.3
Tummy time when awake	80.4	13.0	6.5
No overheating	84.8	13.4	2.2
No bed sharing	56.5	28.3	15.2
Room sharing reduces risk	21.4	26.2	52.4
Safety and efficacy of devices not known	20.5	25.0	54.4

CONCLUSIONS: NICU nurses are less likely to discuss newer risk factors for SIDS from the revised 2005 AAP guidelines, such as pacifier use, than they are to discuss those that were part of the Back to Sleep Campaign since 2000 or earlier. Educational programs for NICU nurses should raise awareness and address any discrepancies between guidance and belief systems.

4 Fellow in Training

Animal Origins of Surfactant: Physician Practice and Parental Information Sharing

Sean M. Bailey, George E. Fryer, Karen Hendricks-Munoz, Pradeep Mally. Pediatrics, New York University School of Medicine, New York, NY.

BACKGROUND: There is no consensus amongst US physicians regarding natural surfactants.Clinicians care for increasingly diverse patients.Many practice Islam,Judaism;teachings of the Seventh Day Adventist Church in which pork is forbidden.Others practice religions in which cow is sacred,or where vegetarianism is a sign of spirituality, Hinduism and Buddhism.

OBJECTIVE: To determine a)if neonatologists discuss the animal origins of surfactant with parents.b)If parental preference would influence practice.c)barriers to information sharing.

DESIGN/METHODS: We conducted an anonymous web-based survey of 2,187 physicians self identified as members of the American Academy of Pediatrics section on perinatal pediatrics.Practicing US neonatologists with active e-mail accounts were eligible and allowed to answer once.

RESULTS: 1000 surveys were returned,a response rate of 46%;978 were eligible.Surfactant use:63% bovine,15%,porcine,22% combination.67% have access to one type.

Table1.Opinions Regarding Surfactant

	Always	Sometimes(S)/ Maybe(M)	Never
Do you discuss surfactant in NICU consults?	74%(695/936)	24%(S)(226/936)	2%(15/936)
Do you discuss animal origins with parents?	2%(22/915)	26%(S)(236/915)	72%(657/915)
Do you personally feel this information should be discussed?	12%(112/928)	30%(M)(276/928)	58%(540/928)
Would knowledge of parent religious preference impact your choice?	21%(193/937)	32%(M)(302/937)	47%(442/937)

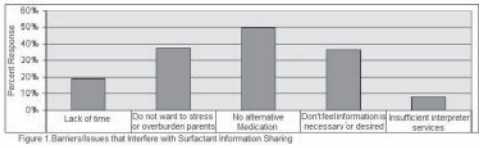


Figure 1.Barriers/Issues that Interfere with Surfactant Information Sharing

CONCLUSIONS: Most neonatologists discuss surfactant,but rarely its origins.Lack of available alternative preparations is the most common communication barrier.With access to alternatives,a majority would consider parental preference.Most religions that do not allow pork/cow products make exceptions in life-saving situations.However,with equally efficacious forms,we surmise that parents likely have a preference. Parents have a right to the highest standard of care,including recognition of their cultural needs.Hospitals should provide alternative surfactants to allow physicians freedom to respect these needs.

5 Fellow in Training

Incidence of Late Preterm Birth and Associated Respiratory Morbidities

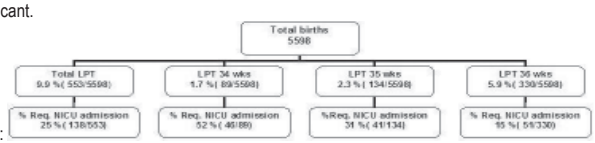
Sean M. Bailey, Shaveta Malik, Nicholas Paik, Annika Brown, George E. Fryer, Karen Hendricks-Munoz, Pradeep Mally. Pediatrics, New York University School of Medicine, New York, NY.

BACKGROUND: Late preterm (LPT) neonates are often admitted to the Newbown Nursery.The perception is that these infants are low-risk,requiring little evaluation and monitoring.

OBJECTIVE: To determine:a)the incidence of LPT births.b)the etiology and treatment of respiratory distress associated with LPT neonates.

DESIGN/METHODS: Retrospective chart review of inborn neonates $34^{0/7}$-$36^{6/7}$ wks GA admitted to NICU at NYU from Jan 2006 to June 2007.Neonates with CHD,surgical conditions,genetic disorders; birth asphyxia were excluded.Data were analyzed using student-t test,chi-square test;one-way ANOVA test.P-value≤.05 was significant.

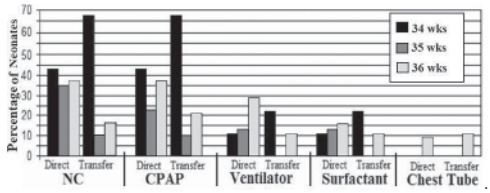
RESULTS:



Incidence of LPT Births & NICU Admissions.

Table 1.Respiratory Diagnoses & Interventions

	34 wks	35 wks	36 wks	P value
RDS	17% (8/46)	12% (5/41)	18% (9/51)	NS
TTN	22% (10/46)	15% (6/41)	22% (11/51)	NS
PTX	0	2% (1/41)	14% (7/51)	0.01*
NC	48% (22/46)	29% (12/41)	30% (15/51)	NS
CPAP	48% (22/46)	22% (9/41)	33% (17/51)	0.03*
Ventilator	13% (6/46)	10% (4/41)	16% (8/51)	NS
Surfactant	13% (6/46)	10% (4/41)	14% (7/51)	NS
Chest Tube	0	0	10% (5/51)	0.05*
Antenatal Steroids	44% (18/41)	14% (5/37)	8% (4/48)	<0.01*



Respiratory Interventions by GA/Location Prior to NICU.

CONCLUSIONS: A majority of 34wk GA neonates were admitted to the NICU;those not directly admitted had increased need of respiratory intervention.36 wk GA neonates with respiratory symptoms had significantly increased rates of pneumothorax and decreased exposure to antenatal steroids.

6

Effect of Surfactant Type on the Pro-Inflammatory Response of ELBW Infants

Vanessa V. Mercado, Mitashi Singh, Hima Maramreddy, Joie Fisher, Lance A. Parton. Division of Newborn Medicine, Maria Fareri Children's Hospital, Westchester Med, Valhalla, NY; New York Medical College, Valhalla, NY.

BACKGROUND: While *in vitro* and *in vivo* studies have identified surfactant apoproteins (SP)-A and -D as important immune mediators, natural surfactant preparations such as Survanta® and Curosurf® have variable concentrations of SP-A and SP-D. The role of these SPs in inflammatory or infectious lung disease has not been extensiveley investigated in preterm newborns. *In vitro* studies have shown that Curosurf® suppresses secretion of inflammatory cytokines in a dose-dependent manner. In our pilot study, there was no difference in the expression of pro-inflammatory mediators between preterm infants who received either of 2 surfactants, perhaps because we excluded patients at risk for a perinatal inflammatory exposure (e.g., PPROM, choriamnionitis). In this subsequent phase of the study, we include patients who may have been perinatally exposed to inflammation and/or infection.

OBJECTIVE: We hypothesize that a differential surfactant-mediated suppression of airway inflammation may be appreciated from preterm infants <30 wks weighing <1 kg requiring mechanical ventilation for RDS.

DESIGN/METHODS: Infants <30 weeks gestational age (GA) and weighing <1 kg at birth were randomly assigned to receive either Curosurf® (N=7) or Survanta® (N=8) following parental consent. Airway secretions (TA) were collected and analyzed for IL8 and IL6 on days 1,3,5, and 7. We excluded patients with multiple congenital anomalies and those exposed to maternal anti-inflammatory medications.

RESULTS: There were no significant differences in birth wt (Curosurf® 716±92g; Survanta® 787±137g; mean±SD) or GA (Curosurf: 26±2; Survanta: 26±1 weeks). No differences were seen between or within the 2 groups when levels of TA IL-6 and IL-8 were compared.

TA Il-8 (pg/ml)

	Day 1	Day 3	Day 5	Day 7
Curosurf®	50(20,107)	271(100,484)	66(28,104)	753(588,920)
Survanta®	112(54,178)	282(137,704)	143(63,690)	933(933,933)

Median (25%,75%)

TA Il-6 (pg/ml)

	Day 1	Day 3	Day 5	Day 7
Curosurf®	2 (1,7)	3(2,5)	3(1,4)	2(2,2)
Survanta®	2(1,3)	2(1,4)	1(1,4)	0.1(0.1,0.1)

Median(25%,75%)

CONCLUSIONS: There were no differences in the pulmonary pro-inflammatory responses within the first week of life in neonates <1kg with RDS given either Curosurf® or Survanta®, even when stratified for indication of increased inflammation (maternal chorioamnionitis, need for DR resuscitation).

7 House Officer

Epidemiology of Neonatal Bacteremia in a South Bronx Hospital

Deepthi Alapati, Dinabel Peralta-Reich, Ginaida Cirilo, Benamanahalli K. Rajegowda, Robert J. Leggiadro. Pediatrics, Lincoln Medical and Mental Health Center, Bronx, NY; Pediatrics, Weill Medical College of Cornell University, New York, NY.

BACKGROUND: Bacteremia in neonates increases risk for morbidity and mortality. It occurs in two forms, early onset (perinatally acquired) and late onset (hospital acquired, late manifestation of perinatally acquired or community acquired).

OBJECTIVE: To evaluate the incidence of neonatal bacteremia and identify any trends between early vs late onset.

DESIGN/METHODS: Medical records of neonates age <28 days with positive blood and / or cerebrospinal fluid cultures admitted to nurseries (normal newborn and intensive care), pediatric inpatient and intensive care units between Jan 2000 and Dec 2006 were reviewed retrospectively using data obtained from nursery log, infection control and microbiology laboratory records.

RESULTS: 136 positive blood cultures were identified, out of 18307 births. 72 (53%) of 136 were considered contaminants and the remaining 64 (47%) represented true bacteremia. The incidence of early and late bacteremia was 3.4 per 1000 live births. Our study showed an early onset group B streptococcus bacteremia incidence of 0.76 per 1000 live births. Nearly half (46%) of early onset bacteremia was due to non-GBS organisms. 84% of late onset bacteremia occurred in low birth weight premature infants who required invasive procedures and prolonged hospital stay. They were caused by commensal species.

CONCLUSIONS: Bacteremia due to GBS in our population is 2-3 times higher than nationally reported rates. Racial differences continue to exist. The population served by our hospital is primarily Hispanic and Black of low socioeconomic status. Most episodes of neonatal bacteremia occurred in very-low-birth-weight premature infants with prolonged NICU stay with or without invasive procedures. Close monitoring of maternal infection and treatment, strict hand washing, aseptic precautions for all invasive procedures and avoidance of overcrowding are essential preventive measures. Continued surveillance is warranted to identify the changing trends in the epidemiology of neonatal bacteremia to assist in strategy formulation to decrease the morbidity and mortality.

8 House Officer

G6PD Deficiency – A Risk Factor for Increased Mortality in Septic Newborns?

Anja Mowes, David L. Schutzman, Lisa Duffy, Rachel Porat. Pediatrics, Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: Known risk factors for neonatal sepsis include prematurity, low birth weight, perinatal asphyxia and PROM. Whether G6PD deficiency is a risk factor for sepsis in term babies remains controversial and is not well studied in preterm babies. To our knowledge late onset sepsis was mainly described among those with the more severe Mediterranean mutation.

OBJECTIVE: To assess whether G6PD deficiency is an additional risk factor for sepsis in term and preterm infants.

DESIGN/METHODS: This study was a retrospective chart review of all infants in our level 3 NICU with sepsis over a three year period, 07/2004- 06/2007. Data collected included known risk factors for sepsis, clinical findings, and G6PD status. An episode of sepsis was defined as a positive blood culture for bacteria or a negative blood culture with positive neonatal sepsis score with the presence of infectious markers (Gerdes JS, 2004).

RESULTS: All 1186 admissions to the NICU from this period were studied. 137 infants met inclusion criteria. Of them 8 (5.8%) were G6PD deficient, a prevalence similar to our delivery population as a whole. All 8 patients had the G202A-A376G mutation, the most common mutation among African-Americans. Septic babies with G6PD deficiency were more likely to weigh less and to be more premature (BW 1.4 ± 0.8 kg, GA 30 ± 4.6 wks) than those without G6PD deficiency (BW 2.2 ± 1.2 kg; p= 0.14 GA 33 ± 6 wks; p=0.1), but this was not significant. There was no significant difference among the groups regarding maternal fever or length of ROM. In addition levels of CRP, WBC, IT ratio, incidence of hypotension, incidence of NEC and ventilatory requirements did not differ between the groups.

Significantly more babies with G6PD deficiency had late-onset sepsis compared to the group with normal G6PD levels (62.5% vs. 27.9%; p=0.04; OR 4.3))

Incidence of death was significantly higher among septic infants with G6PD deficiency. 3 of 8 compared to 5 of 129 septic infants with normal G6PD status died (p= 0.006; OR 14.8).

CONCLUSIONS: G6PD deficiency appears to be a risk factor for late onset sepsis in our mostly African-American neonates.

Mortality was higher among G6PD deficient infants with sepsis.

G6PD deficiency may be a marker for an unfavorable outcome in septic infants.

9 Fellow in Training

Utilization of a Rapid Detection Blood Culture System To Decrease Length of Stay in the Neonatal Intensive Care Unit

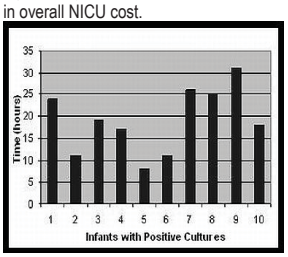
Karen D. Lidoshore-Fuld, Rishara Maharaj, Monica Zarate, Karen Hendricks-Munoz, Yang Kim. Pediatrics, Division of Neonatology, New York University Medical Center, New York, NY.

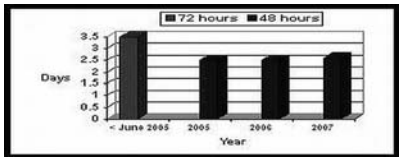
BACKGROUND: In the US, neonatal sepsis remains a major cause of infant morbidity. Traditional sepsis evaluations utilize a 72 hour assessment. We hypothesized that implementation of a multidisciplinary rapid microbiology detection system would be associated with 1) a return of positive cultures prior to 48 hours at Bellevue Hospital Regional Perinatal Center (RPC) and 2) a reduction in length of Neonatal Intensive Care Unit (NICU) stay and NICU hospitalization cost.

OBJECTIVE: To review charts of infants with blood cultures as part of their sepsis evaluation; number of positive cultures, rapidity of reporting positive cultures, and bacteria present in positive cultures. To compare the length of NICU stay and cost associated with a 48 versus 72 hour protocol.

DESIGN/METHODS: A retrospective chart review was performed from June 1, 2004 through May 31, 2007 to identify all neonates who underwent sepsis evaluations at Bellevue Hospital RPC.

RESULTS: All positive blood cultures were reported at less than 48 hours. Organisms were consistent with those in the common spectrum of known neonatal bacteria. The length of stay for the 48 hour cohort was significantly less than in the 72 hour cohort with regard to vaginal deliveries only. There was also a decrease in overall NICU cost.





CONCLUSIONS: A multidisciplinary rapid detection system was associated with positive blood culture reports within 48 hours. Utilization of this system was associated with a decrease in NICU hospitalization days and overall cost within the cohort of vaginal deliveries.

10 Fellow in Training

Blood Lactate as a Marker for Late-Onset Neonatal Sepsis

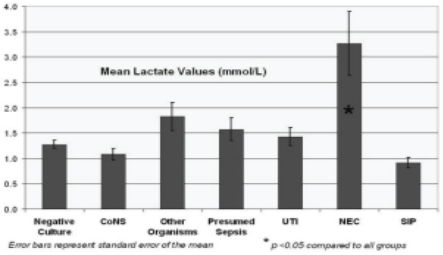
Rebecca J. Eick, Kabir M. Abubakar, Martin Keszler. Neonatology, Georgetown University Hospital, Washington, DC.

BACKGROUND: Late-onset neonatal sepsis is associated with high morbidity and mortality. In pediatric and adult studies blood lactate is a marker of the degree of circulatory disturbance due to sepsis and an indicator of tissue oxygen debt. Elevated lactate has been shown to be an early marker of neonatal sepsis in the first 48 hours of life, but studies to date have not reported a correlation between lactate and late-onset sepsis.

OBJECTIVE: To determine if blood lactate level may be a useful indicator of late-onset neonatal sepsis.

DESIGN/METHODS: From existing medical records, we collected blood gas, lactate, blood count and culture results in infants who were evaluated for late-onset sepsis in our NICU. Lactate levels were available as part of routine blood gas analysis. Mean lactate levels from 24 hours before to the time of sepsis evaluation were correlated with culture results. Lactate levels 72 to 48 hours before sepsis evaluation served as baseline. Cases were categorized as suspected sepsis (culture negative), coagulase negative staph (CoNS), other organism culture positive, presumed sepsis (culture negative but fully treated), urinary tract infection (UTI), necrotizing enterocolitis (NEC) and spontaneous intestinal perforation (SIP). Data were analyzed using one-way ANOVA with post-hoc analysis using Scheffe contrasts among pairs of means.

RESULTS: A total of 173 sepsis evaluations were examined from 86 infants. Mean lactate levels in infants with negative cultures, positive cultures, or presumed sepsis were similar, but lactate values in infants with NEC were significantly higher, compared to all other groups ($p<0.05$).



There was no correlation between blood lactate and pH or base deficit. Only infants with UTI (108%) and NEC (272%) had a significant increase in lactate levels within 24 hours of sepsis evaluation, compared to baseline.

CONCLUSIONS: Blood lactate measurements in the 24 hours preceding and during sepsis evaluation are not a reliable predictor of blood culture results but may differentiate infants with NEC from those with SIP and other infections.

11 House Officer

Timely Administration of Antibiotics for Infants at Risk for Sepsis in the Neonatal ICU

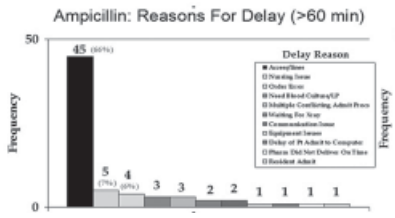
Misha Bhat, Susan Southee, Rebecca Q. Beck, Claire Pagano, Ann Cherry, Jason Corcoran, Jefferson Pickard, John M. North. Neonatal ICU, Inova Fairfax Hospital for Children, Falls Church, VA; Department of Pediatrics, Inova Fairfax Hospital for Children, Falls Church, VA; Quality Improvement, Inova Fairfax Hospital, Falls Church, VA; Pharmacy, Inova Fairfax Hospital, Falls Church, VA.

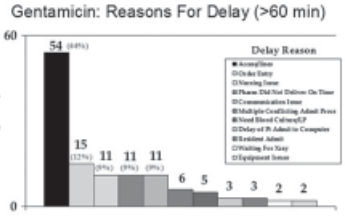
BACKGROUND: It has been shown in adult studies that timeliness of antibiotics can improve survival rates in community acquired pneumonia as well as sepsis in the ICU.

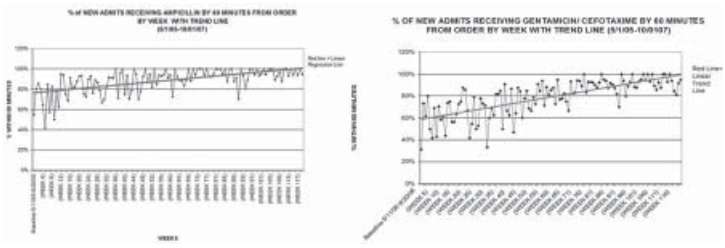
OBJECTIVE: To identify and manage barriers to achieve a 95% compliance rate of administering antibiotics within one hour of ordering in a high volume level three NICU.

DESIGN/METHODS: FAST PDCA was used to flow process and identify barriers in the process from order to administration of gentamicin and ampicillin in the NICU at Inova Fairfax Hospital for Children. These were subsequently targeted and measures instituted to overcome these barriers were instituted.

RESULTS: The major barriers that were targeted for further intervention were line access (50%), pharmacy deliver (11%) and order writing practice (10%). Compliance for the one hour to antibiotics policy improved from 31.3% and 54.7% at baseline to greater than 90% in Q3 07. These results can be viewed in figures 1 and 2.







CONCLUSIONS: It is possible to achieve timeliness of antibiotic administration in the setting of a high volume level three NICU.

12

Are the Trends in Incidence of Fungal Sepsis in VLBW Neonates Related to Postnatal Steroids?

Oluwatoyin A. Abiodun, Joaquim M.B. Pinheiro, Martha Lepow. Department of Pediatrics, Albany Medical Center, Albany, NY.

BACKGROUND: We have noted a recent and unexpected decline in the frequency of systemic fungal infection (SFI) in our NICU and postulate that this is related to changes in use of postnatal steroids for bronchopulmonary dysplasia (BPD).

OBJECTIVE: To describe temporal trends in the incidence of SFI in VLBW neonates and to evaluate the hypothesis that postnatal systemic steroids are an independent risk factor for SFI.

DESIGN/METHODS: Cases were identified retrospectively from the NICU and Vermont Oxford Network databases at Albany Medical Center, between January 1, 1993 and December 31, 2006. The main outcome measure was SFI in neonates 501-1500 grams. Incidence (number of SFIs per 100 patients) was plotted on a p-control chart against 4 prospectively identified eras using 2-sigma control limits. Characteristics and outcomes of infected and non-infected patients were compared using unpaired t-test, chi-square statistics and logistic regression.

RESULTS: 77 fungal infections were identified in 1706 VLBW babies surviving > 3 days in NICU. Incidence of SFI increased progressively between 1993 and 2002, then declined abruptly. SFI had strong independent associations with antibiotic treatment (OR 3.0, [95%CI 2.0-4.6]), era of birth (Era 3, OR 3.4, [2.5-4.4]), birth weight, gestational age, male sex and vaginal delivery. Steroids for BPD were associated with SFI on univariate analysis, but not independently (OR from logistic regression 1.5, [0.75-2.84]). However, an interaction between era of birth and steroids was observed (Era 3*SterBPD, OR 0.25, [0.18-0.35]).

CONCLUSIONS: Measures of immaturity, male sex, full courses of antibiotics, and era of birth were associated with SFI in this cohort of VLBW neonates. Steroids for BPD were not independently associated with SFI, except for an interaction with era of birth, wherein steroids appear to decrease the risk of SFI. This likely indicates an unmeasured change in the mode of usage of steroids in different eras (timing, dose, route), or other unobserved obstetrical or neonatal factors.

13 Resident

Surveillance Cultures in Babies Less 1500 Grams May Decrease Incidence of Fungemia

Sujana Reddy, Santosh Parab, Anthony Barone, Anantham Harin. Pediatrics, Richmond University Medical Center, Staten Island, NY.

BACKGROUND: Systemic fungemia is a know cause of mortality and morbidity in the VLBW neonatal population. Risk factors for fungal infection include multiple courses of IV antibiotics, central lines and extensive areas of skin breakdown.

OBJECTIVE: The purpose of this study was to determine if weekly urine mycology cultures and treating positive cultures would prevent systemic fungal infection.

DESIGN/METHODS: Retrospective chart review of babies <1500 g from 1/1/99-12/31/06. From 1/1/99-12/31/02 diagnosis of systemic fungemia was based on clinical and positive blood cultures for fungus. From 1/1/03-12/31/06 we increased our surveillance of infections by obtaining blood for bacterial/fungal and urine specimens for fungus, from two weeks of age irrespective of clinical status and at weekly intervals there after (or if suspected sepsis was entertained after the initial antibiotic course.) Urine was sent in a sterile container to the microbiology lab. Blood cultures were sent in standard aerobic bottles. Any positive urine cultures were repeated with a catheterized sample along with a blood culture.

RESULTS: From 1/1/03-12/31/06 (N=196) there were 3 cases (1.53 per 100) of fungemia in babies <1500 grams. In the 4 years prior (N=242) we had 12 cases (4.96 per 100) of fungemia. The >3 fold decrease in odds ratio was statistically significant ($Chi^2=.28$, $p<.04$). For babies <1500 g born 1/1/03-12/31/06 increased surveillance consisted of blood and urine mycology cultures weekly starting second week of life unless sepsis was suspected. Of 196 babies <1500 g, 27 (13.7 %) had positive urine surveillance cultures for fungus. Of these 27 positive culture 64% C albicans 23% C parapsilosis 5.8% C tropicalis 5.8 % saccharomyces cenevisiae. Mean chronological age at the time of positive urine cultures was 22.8 days with a range of 5 days being earliest, 46 days latest and mean weight 823 g. Central line (UA/UV/PICC) were present in 85 % of the babies and 95 % had ventilator support at the time of positive cultures. 3 out of 196 had positive blood cultures for fungus that grew C albicans and parapsilosis (two organisms found in blood). These risk factors were also present for the time period 1/1/99-12/31/02.

CONCLUSIONS: Treatment of asymptomatic/symptomatic positive urine mycology cultures from babies <= to 1500 g has decreased the incidence of systemic fungal infection over 3 fold in our unit. Close surveillance by all health care workers to minimize fungal infection is the key.

14 Fellow in Training

Single Cell Sorting To Decipher the Checkpoints for B Cell Selection in Neonatal Cord Blood

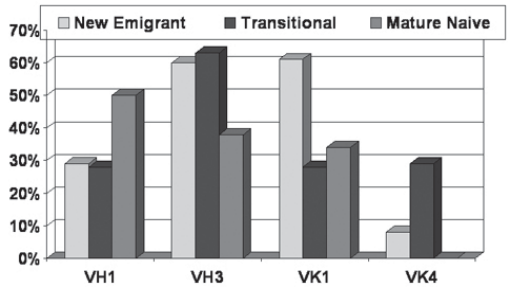
Kavita Kasat, Jie Xu, Karen Hendricks-Munoz, Amy Reichlin. Pediatrics, Division of Neonatology, New York University Medical Center, New York, NY.

BACKGROUND: Autoimmune diseases are caused by dysfunction in the immune system leading to the production of self-reactive antibodies. In healthy adults, polyreactive and self reactive antibodies are removed at two "checkpoints." In the neonate, studies have shown that polyreactive B cells are a major constituent of cord blood B cells, and the neonate is reactive to more antigens than adults. Our initial data on B cell phenotyping shows that the predominant B cells in neonatal cord blood include transitional cells, new emigrant cells, and mature naïve cells. The checkpoints at which polyreactive cells are removed from the neonatal repertoire have not been evaluated. The role of polyreactive antibodies in the neonatal immune defense is unclear.

OBJECTIVE: To determine the checkpoints for B cell selection in the neonate.

DESIGN/METHODS: Single cell sorting of cord blood B cell subsets was performed using flow cytometry. RT-PCR was done on all cells, followed by two rounds of PCR to amplify the immunoglobulin heavy chain and light chain. DNA sequencing was used to identifiy gene usage by NCBI Blast analysis.

RESULTS: Single cell sorting was done on 3 cord blood samples, followed by RT-PCR and PCR on 1440 cells. Seven percent contained PCR product. Results of DNA sequencing of selected genes is shown below:



CONCLUSIONS: Cord blood immature B cells, such as transitional and new emigrant cells, more frequently express V_H3, V_K1,V_K4, and longer CDR3s, when compared to mature naive cells. These immunoglobulin gene segments have been associated with self reactivity in previous studies. Thus, these immature cells may be responsible for the polyreactivity seen in neonates. The checkpoints for B cell selection in neonates could exist at the new emigrant and transitional B cell stage. The predominance of polyreactive, low affinity B cells in neonatal cord blood, with fewer specific antibody secreting cells, partially accounts for the poor initial response to infection leading to impaired adaptive immunity in the neonate.

15

Effects of Prenatal Tobacco Exposure on Gene Expression Profiling in Umbilical Cord Tissue

Naveed Hussain, Winfried Krueger, Steve Walsh, Jonathan Covault, Henry Kranzler, Cheryl Oncken. Depts. of Pediatrics, Genetics, Community Medicine, Psychiatry and Obstetrics and Gynecology, University of Connecticut Health Center, Farmington, CT.

BACKGROUND: Smoking during pregnancy has significant effects on the fetus, especially its association with low birth weight (LBW). LBW is associated with many adult-onset diseases. Although the exact mechanism is unknown, it is postulated that prenatal factor(s) (e.g. tobacco smoke) may result in fetal reprogramming or alterated gene expression.

OBJECTIVE: The purpose of the present study was to examine the effects of prenatal tobacco exposure on mRNA expression in infant umbilical cord tissue.

DESIGN/METHODS: Pregnant women (N=30) who reported no smoking (less than 100 cigarettes in their lifetime and none during the current pregnancy) or who smoked at least 1 cigarette per day in their third trimester of pregnancy were enrolled in the study. Umbilical cord tissue was collected at the time of delivery, snap frozen, and RNA was isolated. Microarray analyses was performed using Affymetrix GeneChip Scanner 3000. Statistical analysis was performed on RMA-normalized data using R/MAANOVA with a fixed effect permutation ANOVA model consisting of the independent variable, smoking status (smoker versus non-smoker), and the covariables gender and tissue blood content (low, intermediate and high).

RESULTS: There were 678 probes that demonstrated differential expression with an intensity ratio that exceeded +/-1.3 and a false discovery rate corrected significance value < 0.005 for smokers versus non-smokers. The most highly up-regulated gene was *CSMH1* which was elevated at approximately 2.49 fold compared with nonsmokers. Other sommatomamotropin genes were also up-regulated (*CSMH2* and *CSH-Like1*). The most highly down-regulated gene was Apolipoprotein B as well as other genes that may be important in immune function (*MAL, MAL 2, SERPIN B2, SPINK5, TCN1, CEACAM1, SERPIN B7*). PCR validation was performed only on the somatomammotropin genes. There was a high correlation between qPCR *CSMH1, CSMH2,* and *CSH-Like1* and corresponding Microarray expression values.

CONCLUSIONS: Maternal smoking is associated altered gene expression findings in the offspring. The up-regulation of growth related genes in fetal tissue of smokers may be an adaptive response to limited nutritive supply. The consequences of this finding in fetal programming of adult disease may be important. Further studies are needed to validate these findings, examine mechanisms of these effects, and correlate them with other medical consequences.

16 House Officer

Nitric Oxide Production in Peripheral Blood Mononuclear Cells (PBMC) Measured in Prepubertal and Pubertal Children

Andrey Mamkin, Andrey Kolesnikov, Theresa Jacob, Svetlana Ten. Department of Pediatrics, Maimonides Infants and Children's Hospital, Brooklyn, NY; Department of Surgery, Vascular Surgery Division, Maimonides Infants and Children's Hospital, Brooklyn, NY; Department of Pediatrics, Endocrine Division, Maimonides Infants and Children's Hospital and SUNY Downstate, Brooklyn, NY.

BACKGROUND: Nitric oxide (NO) produced from amino acid L-arginine by the endothelial NO synthase is a potent vasodilator. Previous study showed that endothelial vasodilation was better in pubertal children compared with prepubertal. Based on that data we hypothesized that we can find a difference in NO production between pre-and pubertal children.

OBJECTIVE: This study was design to examine the relationship btw. NO production in PBMC in pre- and pubertal children by measuring Nitrate NO_3^- and Nitrite NO_2^-byproducts using Griess reagent method.

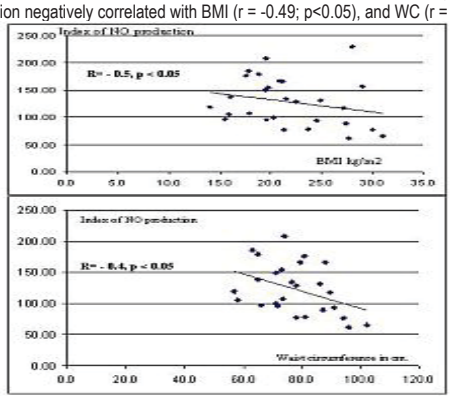
DESIGN/METHODS: 2 groups were established: prepubertal (ave. age 11.29; n=9, 3f ,6m) and pubertal (ave. age 13.15; n=20, 9f, 11m).

PBMC were extracted from blood and purified with phosphate buffer. Index of NO was predicted by measuring final byproducts: NO_2^- and NO_3^-. We converted NO_3^- to NO_2^- by nitrate reductase. Conversion reaction of NO_2^- and Griess reagents produces stable purple color azo end product, which was quantified by colorimetric analytical techniques. Ht, Wt, waist circ.(WC), BMI, fasting lipid profile, glucose, insulin and DHEAS levels were measured.

RESULTS: There were no differences in age, BMI, WC, cholesterol, HDL, LDL, glucose and insulin within the groups.

There were no sign. differences in index of NO production between pre- and pubertal groups.

Index of NO production negatively correlated with BMI (r = -0.49; p<0.05), and WC (r = -0.40; p<0.05)



CONCLUSIONS: No difference in NO production between 2 groups in our study can be secondary to the fact that PBMC were extracted and washed out before experiment that could eliminate the influence of pubertal sex steroids on NO production in these cells.

Risk factors for atherosclerosis like obesity and visceral obesity are associated with endothelial dysfunction in adults. In our study we are for the first time found significant negative correlation between index of NO production in PBMC and risk factors for endothelial dysfunction, as obesity and specifically visceral obesity, measured by WC.

17 Fellow in Training

Oral Glyburide for the Treatment of Gestational Diabetes and Its Effects on the Fetus

Sara D. Sibley, Randi Wasserman, Pradeep Mally, Karen Hendricks-Munoz. Pediatrics, New York University School of Medicine, New York, NY.

BACKGROUND: The use of oral sulfonylureas (SU) for treatment of gestational diabetes mellitus (GDM) is currently increasing, although it was previously thought to increase the risk of fetal adverse effects, such as hypoglycemia and congenital anomalies. Glyburide is a SU thought to offer clinical benefit without additional fetal risk.

OBJECTIVE: To assess the morbidities of infants whose mothers were treated with glyburide for GDM, and compare them to infants whose mothers were treated with insulin.

DESIGN/METHODS: We conducted a retrospective chart review of all mothers and their infants at Bellevue Hospital with abnormal glucose tolerance tests who delivered between 1/1/05 and 3/26/06. There were 202 mother/baby pairs. 128 (63%) were treated with diet alone, and excluded from the study. Infants were divided into 2 groups: Infants of mothers who were treated with glyburide, and infants of mothers who were treated with insulin. Groups were then divided into well-controlled and poorly-controlled based on compliance and glucose levels. Outcomes compared included hypoglycemia, congenital anomalies, clinical sepsis, macrosomia, RDS, and hyperbilirubinemia requiring phototherapy.

RESULTS: The study included 74 mother/baby pairs. 36 (49%) of the mothers were treated with glyburide and 38 (51%) were treated with insulin. Infants in the glyburide group fared better with regards to gestational age at birth, congenital anomalies, RDS, IV glucose and phototherapy requirement. Glyburide infants were also larger than the insulin infants (see table). There was no significant difference in length of stay(5.2±10 days for glyburide vs 6.1±7.5 days, p=0.67). On comparison of infants of poorly-controlled to well-controlled GDM, there was an increased IV glucose requirement in the poorly controlled insulin group [50% (7/24) vs 0% (p=0.03)].

Infant Outcomes

	Glyburide (n=36)	Insulin(n=38)	P Value
Cong Anomalies	6%	21%	.04*
RDS	3%	16%	.02*
IV Glucose	14%	37%	.02*
Phototherapy	3%	16%	.05*
Mean GA (wks)	39±1.2	38±2	.02*
Mean BW	3600±500	3200±800	.006*

mean±SD, *=significant

CONCLUSIONS: Maternal treatment with glyburide for GDM results in larger infants, later births, and fewer short term morbidities when compared to infants of insulin treated mothers. Glyburide treatment was not associated with greater fetal anomalies or hypoglycemia and may be a therapeutic choice in selected diabetic mothers.

18 Fellow in Training

Development of Sleep Wake Cycling and Presence of Seizures on aEEG During Whole Body Hypothermia

Mohamed El-Dib, Tammy Tsuchida, Tamara John, Raquel Bernier, An Massaro, Stephen Baumgart, Billie Short, Taeun Chang. Department of Neonatology, Children's National Medical Center, Washington, DC; Department of Neurology, Children's National Medical Center, Washington, DC.

BACKGROUND: Though amplitude-integrated EEG (aEEG) has been used as an inclusion criterion in therapeutic hypothermia, continuous EEG monitoring during hypothermia has not been examined.

OBJECTIVE: To evaluate the progression of aEEG background changes, sleep wake cycling (SWC) and seizures in newborns with neonatal encephalopathy receiving whole-body therapeutic hypothermia.

DESIGN/METHODS: Therapeutic whole body cooling for 72 hours was performed in 44 infants with moderate or severe hypoxic ischemic encephalopathy. Continuous video EEG was monitored with the electrodes placed in a modified International 10-20 system. To date, background, SWC and seizures were blindly evaluated in 232 segments of two-channel aEEG from 34/44 treated infants.

RESULTS: 44 neonates (mean weight 3.41±0.72 kg, gestation 38.6±1.7 wks) were admitted at age of 4.4±1 hours of life for hypothermia. 4 patients required ECMO. 15 infants had clinical seizures (34%). Six deaths occurred (14%). EEG monitoring was initiated between 0-26 hours (mean=13) after initiation of hypothermia.

Background analysis of the 1st hour of recording (n=34) showed flat tracing (FT) in 15%, burst suppression (BS) in 21%, low voltage (LV) in 15%, discontinuity (D) in 9% and borderline normal (BLN) to normal (N) tracing in 27%. Background could not be evaluated in 2 patients due to poor quality of recordings and 3 patients had status epilepticus. With rewarming (72-79 hrs of cooling)(n=27),background was FT in 7%, BS in 7%, LV in 59%, D in 11 % and BLN to N in 15%. After rewarming (80-92 hrs of cooling)(n=25),background was FT in none of the segments, BS in 16%, LV in 48%, D in 20 % and BLN to N in 16%.

SWC showed progressive improvement during the course of cooling. SWC were definitely identified in 3.4% in day of life 1 (DOL1), 20.7% in DOL2, 35.5% in DOL3 and 55.6% while rewarming.

EEG-confirmed seizures were detected in 6/34 (18%). Only one patient with seizures detected by full EEG was not picked up by aEEG. No patients who completed hypothermia had seizures and no new seizures developed with rewarming.

CONCLUSIONS: Development of sleep wake cycling and seizures can be observed in aEEG recordings. aEEG appears to be a helpful tool in monitoring patients during hypothermia and rewarming. It does not appear that hypothermia itself makes a significant impact on background aEEG activity.

19

Continuous Amplitude-Integrated EEG (aEEG) Monitoring During Selective Head Cooling (HC)

Susan Adeniyi-Jones, Zachary Cohn, Vidula Damle, Dorothy McElwee. Pediatrics, Thomas Jefferson University/duPont Hosp for Children, Philadelphia, PA; Undergraduate Office-(Student), Connecticut College, New London, CT.

BACKGROUND: In term newborns with hypoxic ischemic encephalopathy (HIE), the evolution of the aEEG pattern predicts recovery and neurodevelopmental outcome. No information is available about the evolution of the aEEG during HC. The aEEG is routinely monitored via biparietal electrodes however placement of scalp electrodes under the CoolCap™ is contraindicated. Bi-frontal placement of electrodes generates an aEEG tracing that detects trends in background cerebral activity and seizures and permits continuous brain function monitoring during HC with the CoolCap™.

OBJECTIVE: To examine evolution of the aEEG background and seizures in infants with HIE during treatment with HC.

DESIGN/METHODS: Continuous aEEG monitoring was perfomed during HC in 56 infants with HIE. After skin cleansing, needle electrodes were inserted at the hair line and directed posteriorly . A Lead was placed in the midline and at each temple, 7 cm apart (3.75 cm from the midline). The leads were secured with clear bio-occlusive dressing. After placing the CoolCap™, Infants were cooled to a target rectal temperature of 34.5ºC (± 5ºC) for 72 hours and then rewarmed at 0.3 ºC/hr to 36.5 ºC. Skin integrity at the electrode sites was checked ~ 8 hourly. Changes in the aEEG were analyzed. An EEG was performed 0 to 4 days after HC. Neurodevelopmental testing is ongoing.

RESULTS: aEEG monitoring was initiated between 2.6-6.2 hrs of age (mean 4.8 hrs). CFM was discontinued after < 48 hours in 3 infants that died. Electrodes remained in place for ≥72 hrs (max. 159 hours) in 56 infants. No skin complications occured at any of the electrode sites. The initial aEEG background pattern was continuous normal voltage(CNV) with seizures in 26(46%); discontinuous normal voltage(DNV) in 13(23%); burst suppression (BS) in 3(5%); continuous low voltage(CLV) in 5(9%); flat trace (FT) in 9(16%) infants. After 72 hours of HC, the background pattern remained normal or improved as follows: CNV 18/26; DNV 5/12; BS 1/3; CLV 2/5 and FT 2/9 and SWC was present in 26(64%). Seizures were seen in up to 73% of tracings and recurred during rewarming in 4 infants. Analysis of post-HC EEGs and early neurodevelopmental evaluation at 3 to 5 months are planned.

CONCLUSIONS: Continuous aEEG monitoring during HC is feasible and safe. aEEG changes including seizures occur during HC. Recovery is least likely to occur when the initial background is severely abnormal.

20 House Officer

Utility of Performing Routine Head Ultrasounds in Preterm Infants with Gestational Age 30-34 Weeks

Michelle Karam, Judy G. Saslow, Heidi Taylor, Barbara Amendolia, Gary Stahl, Kee Pyon, Nosrat Razi, Nicole Kemble, Zubair H. Aghai. Pediatrics/Neonatology, Cooper University Hospital-Robert Wood Johnson Medical School, Camden, NJ.

BACKGROUND: The American Academy of Neurology and Child Neurology Society recommends performing routine screening head ultrasounds (HUS) on preterm infants of less than 30 weeks gestation. This recommendation is based on studies that suggest only severe IVH (Grades III/IV) is associated with an adverse neonatal outcome; and that the incidence of severe abnormality on HUS is less frequent in premature infants with gestational age (GA) of 30 weeks or higher. However, more recent studies demonstrate that even milder IVH (Grades I and II) can be associated with adverse neurodevelopment outcomes in very low birth weight infants.

OBJECTIVE: To study the incidence of IVH and evaluate the need for screening HUS in preterm infants with GA of 30-34 weeks.

DESIGN/METHODS: Preterm infants (GA; 30-34 w) admitted to the neonatal intensive care unit (NICU) between January 1997 and September 2007 were included in this study. Grades of IVH were defined as per the Papile classification. Relevant clinical data were collected from the infants' medical records.

RESULTS: Screening HUS were performed on 463 infants with GA of 30-34 weeks. Twentyseven infants (5.8 %) had abnormal cranial US (IVH or PVL). The incidence of IVH ranges between 3.3% to 6.3% at various GA. There was no significant decrease in the incidence of IVH with increasing GA. Seven (1.5%) infants had severe abnormality on HUS (Grades III/IV or PVL).

Incidence of IVH

GA (n)	IVH (Grade I-II) (%)	IVH (III-IV/PVL) (%)	Any IVH/PVL (%)
30 W (140)	4 (2.8)	2 (1.4)	6 (4.3)
31 W (159)	8 (5.0)	2 (1.3)	10 (6.3)
32 W (146)	4 (2.7)	1 (0.7)	5 (3.4)
33 W (90)	4 (4.4)	1 (1.1)	3 (3.3)
34 W (68)	4 (5.9)	1 (1.5)	3 (4.4)
30-34 W (463)	20 (4.3)	7 (1.5)	27 (5.8)

CONCLUSIONS: A significant number of infants born between 30 to 34 weeks of gestation have abnormalities on screening cranial US. Additional studies are needed to examine the adverse neurodevelopmental outcomes in this group of preterm infants with mild abnormality (IVH Grades I or II) on cranial US before recommending routine screenings for IVH.

21

Endogenous Cannabinoid System Activation in Neonatal Focal Cerebral Ischemic Injury in Rat Pups

Marta R. Rogido, Jose A. Martinez Orgado, Ruth Pazos, Tong C. Wen, Augusto Sola, Julian Romero. Neonatology, Atlantic Neonatal Research Institute MANA, Morristown, NJ; Laboratorio de Apoyo a la Investigación, Fundación Hospital Alcorcón, Madrid, Spain.

BACKGROUND: The endogenous cannabinoid system has been found to provide neuroprotective effects both *in vitro* and *in vivo* in the adult animal. It could be speculated that the antioxidant and immunomodulatory effects could also be protective to the developing brain. However, the role of the endogenous cannabinoid system has not been determined in perinatal ischemia.

OBJECTIVE: To study the expression of cannabinoid receptors CB1 and CB2 and the enzyme Fatty Acid Amide Hydrolase (FAAH) of the cannabinoid system in a model of perinatal stroke.

DESIGN/METHODS: P7 Wistar rat pups were subjected to permanent focal cerebral ischemia (FCI) as previously described (Wen, 2003). This procedure results in a highly reproducible ipsilateral stroke. Pups were sacrificed at 1, 3 or 7 days alter FCI. The brains were fixed and cryoprotected. We performed Nissl staining for neurons and immunohistochemistry for astrocytes (GFAP). CB1, CB2 and FAAH expression were determined using a polyclonal rabbit antibody and an anti-rabbit goat antibody and Alexa 488 or 546. Statistical analysis was with Student's t-test and statistical significance defined as $p<0.01$.

RESULTS: We included 4 pups for each time period. FCI caused a well defined ipsilateral injury with an almost absence of neurons and an intense glial reaction. We also observed an increase in neuronal population in the penumbra starting on day 3 post FCI. The expression of CB1 in neurons increased significantly very early, starting 24 hours post FCI. The reactive astrocytes showed an increase in the expression of FAAH, and this occurred 7 days after FCI. The expression of CB2 was also significantly increased in the reactive astrocytes in the penumbra at that time.

CONCLUSIONS: An ischemic episode to the developing brain causes early and sustained increase in the expression of CB1 and a later increase in the expression of CB2 and FAAH associated with the glial response. These findings suggest a relevant role of the endogenous cannabinoid system in general and of the CB2 receptors in particular, in the natural response to an ischemic lesion. Modulation of the cannabinoid system needs to be explored as a neuroprotective strategy for the developing brain.

22 House Officer

Maternal Methadone Dose Does Not Predict Frequency of Treatment for Neonatal Abstinence Syndrome

Neil Seligman, Kevin Dysart, Nicole Salva, Edward Hayes, Marie O'Neill, Benjamin Leiby, Jennifer Kern, Jason Baxter. Obstetrics and Gynecology, Thomas Jefferson University Hospital, Philadelphia, PA; Pediatrics, Thomas Jefferson University Hospital, Philadelphia, PA; Division of Biostatistics, Thomas Jefferson University Hospital, Philadelphia, PA.

BACKGROUND: Treatment of opioid dependence in pregnancy is recommended to decrease illicit opioid use, criminal activity, and mortality but the appropriate daily methadone dose is controversial.

OBJECTIVE: Our objective was to determine whether the daily maternal methadone dose is related to the incidence of neonatal abstinence syndrome (NAS).

DESIGN/METHODS: Retrospective cohort study of neonates born to mothers treated with methadone for opiate addiction between 2000-2006 (n=317). Inclusion criteria included urine drug screen positive for methadone within 2 weeks of delivery. Infants were scored by the Finnegan scoring system and treatment was initiated when the sum of the last 3 scores exceeded 24. Logistic regression was used to model the association between neonatal treatment and dose at delivery. Multivariate logistic regression was performed to adjust for confounding factors. The analysis was repeated for infants ≥32 weeks because prematurity is known to complicate NAS.

RESULTS: Overall, 180 (56%) infants recieved treatment for NAS. Dose at delivery was associated with trimester of initial exposure (p=0.002), length of exposure (p=0.005), and maternal race (p=0.003). Information was incomplete in 22 patients. After adjusting for these possible confounders (n=295), there was a non-significant trend toward increased frequency of treatment for NAS with higher maternal methadone doses at delivery (p=0.683). This non-significant trend was also present after excluding neonates born at less than 32 weeks gestational age (n=273; p=0.524).

CONCLUSIONS: Despite the appearace of a trend, there is no relationship between the maternal dosage of methadone at delivery and the incidence of NAS in a large inner city population. The findings are consistent with previously published data by V. Berghella (Am J Obstet Gynecol; 2003) in the same population. Our practice is titration of maternal methadone dosage in relation to symptoms of withdrawal.

Frequency of Treatment for NAS

	Adjusted Odds Ratio All Births (n=295) p = 0.683			Adjusted Odds Ratio GA at Delivery ≥32 wks (n=273)* p = 0.524		
Dose (mg)	n	% treated	OR (95% CI)	n	% treated	OR (95% CI)
<50	21	52.4	1.0	20	55.0	1.0
50-99	87	54.0	1.15 (0.45-2.94)	81	56.8	1.11 (0.43-2.91)
100-149	112	55.4	1.22 (0.49-3.05)	100	57.0	1.12 (0.43-2.92)
150-199	52	59.6	1.46 (0.53-4.02)	52	59.6	1.31 (0.46-3.72)
≥200	23	69.6	2.18 (0.65-7.35)	20	75.0	2.60 (0.69-9.81)

*Data for length of treatment, trimester first exposed, and maternal race was incomplete in 22 patients.

23 Fellow in Training

High PaO_2 Is Directly Proportional to SpO_2 Levels 94%-100% in Newborns Receiving Oxygen in the Neonatal Intensive Care Unit

Armando R. Castillo, Hernando Baquero, Freddy Neira, Ramiro Alvis, Ann Critz, Richard Deulofeut, Augusto Sola. Neonatal-Perinatal Medicine, Emory University, Atlanta, GA; Neonatology, Universidad del Norte, Barranquilla, Atlantico, Colombia; Neonatology, Pediatrix Medical Group, Dallas, TX; Neonatology, Atlantic Neonatal Research Institute and MANA, Morristown, NJ.

BACKGROUND: As described by our group and others, newborns (NB) breathing FiO_2>0.21 with SpO_2>93% are exposed to persistent or intermittent hyperoxemia, which is associated with a higher morbidity. No description in human infants exists of PaO_2 values at varying SpO_2 of 94% and above.

OBJECTIVE: To evaluate the PaO_2 at different SpO_2 levels above 93% in NB with arterial catheters.

DESIGN/METHODS: Prospective comparison of PaO_2 and SpO_2 in NB in 6 NICU's located at or near sea level in 2 countries. PaO_2 obtained for clinical indications; simultaneous SpO_2 was recorded at the time of the arterial gas. Comparisons were made if the SpO_2 changed <1% before, during and after the collection of the sample. Statistics: Chi square, ANOVA.

RESULTS: A total of 530 SpO_2 values were>93% in 122 NB; 80% of these samples where in NB with FiO2>0.21. GA and BW: 29.2±5.2w and 1338±871g. For NB in RA, mean (±SD) and median PaO_2 at different SpO_2 intervals were: A) SpO_2 94-95%: 61.3±12.6 and 59.5(43-94); B) SpO_2 96-97%: 69.8±14.6 and 66.5(45-108) & C) SpO_2 98-100%: 72±18.4 and 70(34-120). In NB breathing FiO_2>0.21 the PaO_2 were: 1) SpO_2 94-95%: PaO_2 71.03±26.7 and 62(34-150); 2) SpO_2 96-97%: 92.3±38.1 and 84(38-256) ($p \leq 0.05$ vs 1) & 3) SpO_2 98-100%: 143±66.5 and 131(48-438) ($p \leq 0.05$ vs 1 and 2). At the three SpO_2 intervals, the PaO_2 of NB with FiO_2>0.21 was significantly higher ($p \leq 0.001$) than in NB in RA.

CONCLUSIONS: In NB breathing supplemental oxygen there is potential increase in risk for oxidant damage as the SpO_2 increases between 94% and 100%, since in these ranges PaO_2 values increase in a linear relation to SpO_2. These findings add to the growing evidence that SpO_2 must be kept at or below 93% in an effort to avoid potential morbidity associated with hyperoxemia.

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T-Lymphocytes in Human Infants with Bronchopulmonary Dysplasia (BPD)

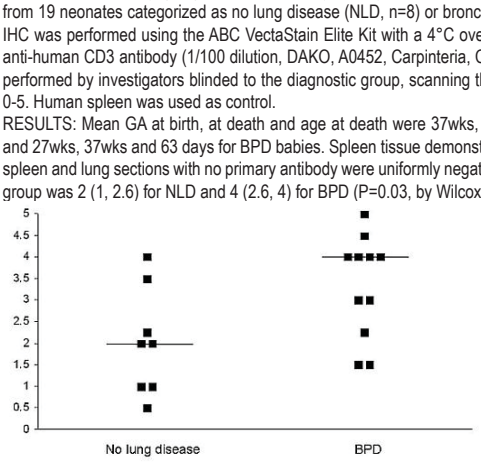
Rita M. Ryan, Qadeer Ahmed, Christopher A. D'Angelis, Vasanth H. Kumar, Satyan Lakshminrusimha, Leon A. Metlay, Huamei Wang, Gloria S. Pryhuber. Pediatrics (Neonatology) and Pathology, Univ Buffalo, Buffalo, NY; Pediatrics (Neonatology), Environmental Medicine and Pathology, Univ Rochester, Rochester, NY.

BACKGROUND: Previous studies have examined the roles of inflammatory cells such as macrophages and neutrophils in the early phases of bronchopulmonary dysplasia. In other chronic lung diseases, for example idiopathic pulmonary fibrosis, it appears the lymphocyte is an important contributor to disease. The role of the lymphocyte in the development of bronchopulmonary dysplasia has not been studied.

OBJECTIVE: To examine human infant autopsy samples for the presence of T-lymphocytes.

DESIGN/METHODS: The right middle or lower lobe of human neonatal lung was preserved within 6 hours of death by inflation fixation with 10% buffered formalin at 20-25 cm H_20 for 20h and paraffin embedded. Immunohistochemistry (IHC) for the broad T-lymphocyte marker, CD3, was performed on lung sections from 19 neonates categorized as no lung disease (NLD, n=8) or bronchopulmonary dysplasia (BPD, n=11). IHC was performed using the ABC VectaStain Elite Kit with a 4°C overnight incubation in polyclonal rabbit anti-human CD3 antibody (1/100 dilution, DAKO, A0452, Carpinteria, CA). A semi-quantitative analysis was performed by investigators blinded to the diagnostic group, scanning the entire section, scoring slides from 0-5. Human spleen was used as control.

RESULTS: Mean GA at birth, at death and age at death were 37wks, 38wks and 2.5 days for NLD babies and 27wks, 37wks and 63 days for BPD babies. Spleen tissue demonstrated expected positive staining, and spleen and lung sections with no primary antibody were uniformly negative. The median score (IQR) for each group was 2 (1, 2.6) for NLD and 4 (2.6, 4) for BPD (P=0.03, by Wilcoxon rank-sum test).



CONCLUSIONS: T-lymphocytes were found more frequently in the lung parenchyma of babies who died with BPD compared with those of similar corrected gestational age without lung disease. Further investigation into the role of lymphocytes and lymphocyte subsets may provide important information about the pathogenesis of the chronic phase of BPD.

25 Medical Student

Quantified Impulse of Helicopter Versus Ground Transport as Measured by Biophysical Accelerometery

Shetal Shah, Andrew Dylag, Joseph Hudak. Department of Pediatrics, Division of Neonatology, Stony Brook University Medical Center, Stony Brook, NY.

BACKGROUND: Impulse (force per unit time) transmission to the neonate as a consequence of accelerations during transport has been implicated in the increased morbidity of this population. Currently, impulses experienced by infants compared to mode of transport (helicopter vs. ground) have not been well characterized.

OBJECTIVE: To mathematically model the magnitude & direction of impulses experienced by neonates during air & ground transport using biophysical accelerometry. We further examined the effect of airfoam on impulse measurements.

DESIGN/METHODS: Ten ground transport trials (randomized as to use of airfoam) were conducted using a common route (mean distance 4 miles) for a transferred neonate using a standard medical ambulance & transport isolette. Two air transport trials were conducted on a military-outfitted Blackhawk transport helicopter. During the trials, acceleration measurements in the X (front-to-back), Y (side-to-side), & Z (up-&-down) planes were sampled at 5 Hz using a computerized accelerometer attached to a neonatal resuscitation mannequin.

We characterized impulse transmission by mathematically integrating acceleration measurements in each plane. Accelerometry data underwent curve-fitting analysis using a model sinusoidal pattern to determine the amplitude, frequency, phase, & offset of movements. Total trial impulse, defined as the vector summation of each integral, were subjected to 2x2 factorial ANOVA.

RESULTS: Overall, ambulance transport with airfoam resulted in significantly less total trial impulse compared with helicopter or ambulance without airfoam (p< 0.0001, ANOVA).

Between the helicopter trials, use of the airfoam mattress resulted in less overall impulse (50.3±4.5 vs. 70.2±5.8 m/sec^2/min; p<0.001, Student's T-test) despite an increase in Y-plane accelerations (45.14 ±1.23 vs 30.79±1.57 m/sec^2/min; p< 0.0001).

Using best-fit-curve analysis, helicopter transport was associated with greater amplitude (3.2 vs 1.1 m/sec,^{2} p< 0.001) & frequency (261 vs 2.8 Hz, p< 0.001) of acceleration changes during transport.

CONCLUSIONS: In this model, neonates transported via air experienced significantly greater impulse than those transported via ground. Ground transport with airfoam imparted the least overall impulse of all trials conducted & should be considered if practical. Attention must be paid to the biophysical stress created during transport, which may decrease transport-related morbidity for these infants.

26 Fellow in Training

Transport-Induced Biophysical Impulse Alters Respiratory Finction in Neonatal Sprague-Dawley Rats in an Dose-Dependent Manner

Joseph J. Hudak, Andrew Dylag, Shetal I. Shah. Pediatrics, Stony Brook University Hospital, Stony Brook, NY.

BACKGROUND: Forces experienced by neonates due to accelerations during transport are associated with adverse neonatal outcomes. These accelerations measured per unit time (impulse) were shown previously to alter respiratory function in rats. Dose-response changes in respiratory function as a result of increasing transport time are not well characterized.

OBJECTIVE: To examine changes in respiratory function resulting from different cumulative impulse levels using a neonatal rat model.

DESIGN/METHODS: 4 groups of Sprague-Dawley rat pups underwent simulated transport on day of life 11 or 12. During the simulation each group was exposed to an average impulse of 27.4 m/sec^2-min for 0, 30, 60 or 90 minutes. Average impulse magnitude was chosen from a previously published study and closely simulates ambulance transport. During the trials, acceleration measurements in the X, Y, and Z planes were sampled at using a computerized accelerometer.

Post intervention, the rats were paralyzed and ventilated on a SCIREQ small mammal ventilator. Using a forced-oscillation technique, measurements of elastance, tissue damping, airway resistance, and ratio of damping to elastance (eta), were obtained at PEEP of 0, 3 and 6 cm of H_2O. Running averages or each respiratory parameter were compared among groups by 2x2 factorial ANOVA.

RESULTS: A total of 81,006 data points were analyzed in the trials. Increased transport time resulted in a step-wise increase in conducting airway resistance at all levels of PEEP (p<0.01). Static compliance decreased after 60 minutes at PEEP of 3 and 6 cm H_2O (p<0.05). Eta decreased with greater transport time at a PEEP of 6 cm H_2O (p<0.05). Tissue damping increased with duration of transport time across all PEEP levels, but only exhibited statistical significance at a PEEP of 0 cm H_2O (p<0.05). No statistically significant differences were seen in hysterisivity. PV curves were altered at all levels of peep in a dose-dependant manner, (p<0.0001).

CONCLUSIONS: In this model transported neonatal rats experienced significant deterioration of respiratory function with increasing duration of simulated transport. Taken together, decreases in static compliance and increases in tissue damping are consistent with an inflammatory response. Further studies are needed to fully understand the response of the preterm neonate to transport-mediated stress.

27 Fellow in Training

Desaturation (Desats) Events Are Related to Threshold Retinopathy of Prematurity (TROP) and Laser Therapy (LT) in Extremely Low Birth Weight Infants (ELBWI) < 750g

Michelle Weissman, Tammy Rousseau, Jeffrey Perlman. Newborn Medicine, New York Presbyterian-Weill Cornell, New York, NY.

BACKGROUND: ROP remains a major morbidity in the ELBWI with threshold ROP extremely common in those <750g. Known risk factors include ↓ gestational age (GA), birthweight (BW), severity of illness and supplemental O_2. Experimental evidence suggests that a paradigm of hypoxia/ hyperoxia versus hypoxia alone ↑ the risk for TROP. We hypothesized that ELBWI who develop TROP would exhibit more episodes of Desats suggesting a hypoxia/hyperoxia scenario than those without TROP.

OBJECTIVE: The study objectives were to determine weekly episodes of apnea (A), bradycardia (B) and Desats in ELBWI and the relationship of these events to the development of TROP.

DESIGN/METHODS: A retrospective chart review 2003-2007 of ELBWI < 750g (n= 44) who survived to discharge was done. Weekly events recorded for each incremental ↑ in GA. Apnea was defined as absent

breathing for ≥ 20 seconds, bradycardia as heart rate < 100 BPM, Desats as SaO2 < 85%. Saturations (SATS) are managed by ↑ baseline FiO2 by 10% until the SATS are > 90%. The number of weekly events between those who developed TROP requiring LT (n= 9) vs with those with ROP ≤ stage 3 (n=35) were compared using student and paired t tests.
RESULTS: Infants who developed TROP vs No threshold were of a ↓ GA i.e.24±0.6 vs 26±1.88 wks (P=0.001). No differences were noted related to BW (669±32 vs. 662±80), gender, and days requiring respiratory support. Infants that developed TROP vs. No threshold disease exhibited significantly ↑ Desat (p=0.003), during weeks 26-34. The number of apneas and bradycardic events however was not different between groups during the comparable weeks.
CONCLUSIONS: ELBW infants who develop threshold disease requiring LT exhibited significantly more Desat episodes than those who did not progress in severity. No differences in the number of apneic or bradycardic episodes were noted. We speculate that the therapeutic intervention of providing O_2 with an ↑ in sats is consistent with the experimental data that hypoxia/hyperoxia is a major pathway for the development of severe ROP. The mechanisms accounting for the Desat episodes remain unclear but critical to determine. Maintaining sat values in a tight range and avoiding wide fluctuations should be a clinical goal.

28 Fellow in Training

Marked Elevation of Cardiac Troponin I (cTnI) Is Associated with Increased Ventilator Days and Length of Hospital Stay for Infants with Perinatal Asphyxia

Constance G. Andrejko, Vidula Damle, Susan C. Adeniyi-Jones. Pediatrics, Thomas Jefferson University Hospital, Philadelphia, PA.

BACKGROUND: Infants experiencing perinatal asphyxia are at increased risk for morbidity and prolonged hospital stay. Ischemic myocardial injury may worsen end organ damage and morbidity. Serum levels of cTnI provide a marker of cardiac muscle ischemia/injury. Adult studies have shown elevated cTnI levels are associated with more severe disability and longer recovery in acute ischemic stroke. In newborns, elevated cTnI levels are associated with RDS and perinatal asphyxia. The role of cTnI levels is unknown in predicting short term outcomes in asphyxiated infants treated with head cooling.
OBJECTIVE: To determine if elevated cTnI levels are associated with increased ventilator days and increased length of stay among asphyxiated infants undergoing head cooling.
DESIGN/METHODS: A retrospective chart review of 86 asphyxiated infants ≥36 weeks gestation and≥1.8 kg undergoing head cooling at Thomas Jefferson University Hospital, Philadelphia, Pennsylvania was performed. Infants studied had a cord pH or serum pH within one hour of life of <7.0 or a base deficit of >-16 or a 10 minute Apgar score of ≤ 5 or ongoing need for mechanical ventilation, and signs of encephalopathy. cTnI levels were measured at least once following admission. Surviving patients were grouped by cTnI levels. Group I, ≥0.3 ng/mL (n = 35) and Group II, TnI <0.3 ng/mL (n = 40). Ventilator days and length of stay for groups I and II were compared using Mann-Whitney U statistical test.
RESULTS: Of 86 infants undergoing head cooling that had available cTnI levels, 75 (87%) survived. The mean gestational age for survivors, was 39.0 weeks, mean birth weight was 3228 grams, and median 5 minute Apgar score was 3. Ventilator days were greater for neonates with highly elevated cTnI levels (n=35, median=8, interquartile range=4.5-13) compared to those with lower cTnI levels (n=40, median=4, interquartile range=1-8, p = 0.01). Also, length of stay was increased for patients whose cTnI levels were ≥ 0.3 (n=35, median=23.5, interquartile range=15-37) compared to those whose cTnI levels were <0.3 (n=40, median=15, interquartile range=10-23, p = 0.02).
CONCLUSIONS: In asphyxiated infants, a serum cTnI level ≥ 0.3 ng/dl in the immediate newborn period is associated with a longer duration of respiratory morbidity and prolonged hospitalization.

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Predictors of Prevalent Medical Issues of Former Preterm Infants up to Two Years of Age

Jordan S. Kase, Paul Visintainer. Pediatrics, The Regional Neonatal Center Maria Fareri Children's Hospital Westchester Medical Center-New York Medical College, Valhalla, NY; School of Public Health, New York Medical College, Valhalla, NY.

BACKGROUND: Preterm (PT) infants often encounter medical problems at a more profound rate in the toddler years than those born at term. This is supported by the fact that they have higher rates of ER visits and hospitalizations.
OBJECTIVE: To identify associations between 3 common medical conditions (reactive airway disease: RAD, eczema, and gastroesophageal reflux: GERD) and antenatal/neonatal co-morbidities in former PT children during their toddler years.
DESIGN/METHODS: Retrospective observational cohort study of former PT infants seen at the Regional Neonatal Follow-up Program of the Lower Hudson Valley Region, NY. Subjects evaluated up to 2 years of age from January 2005 through November 2007 were included. 19 co-morbidities were compared between those with each medical condition and those without. Comparison of categorical variables was done with χ^2 analysis. Mann Whitney U Rank sum test compared ordinal variables. Rank sum results are reported as [median (min-max)]. Significance defined as p<0.05.
RESULTS: 755 PT infants were included. 9.4% RAD, 10% had eczema; and 22% GERD. RAD correlated significantly with: ↓ GA: moderately preterm 6.3% vs. very preterm 14%; length of stay in weeks (LOS): [6.6(0.4-37.6) vs. 3.1(0.1-54.9)] ; vent days: [2(0-74) vs. 0(0-210)]; CPAP days: [3(0-49) vs. 1(0-75)]; nasal cannula days (NC): [5(0-120) vs. 0(0-508)]. BPD: 20.6% vs. 8.1%; apnea of prematurity (AOP): 15.1% vs. 6.2%; RDS: 11.2% vs. 6.6%; oxygen at d/c: 26% vs. 8.2%. Eczema was not significantly correlated with any of the co-morbidities analyzed.
GERD was significantly associated with BPD: 39.7% vs. 20.6%; AOP: 28.4% vs. 19%. LOS: [4.1(0.1-54) vs. 3(0.3-54.9)]; vent days: [0(0-210) vs. 0(0-96)]; cpap days: [1(0-60) vs. 1(0-75)]; NC days [1(0-294) vs. 0(0-508)].
RAD was significantly associated with both eczema: (20.5% vs. 8.2%), and GERD: (14.3% vs. 8%). There was no association between GERD and eczema.
CONCLUSIONS: RAD is correlated with co-morbidities associated with respiratory support. Results of these analyses cannot determine whether RAD experienced in these children is due to direct damage to the lungs or the primary morbidity of the lungs which required prolonged respiratory support. GERD is similarly associated with these co-morbidities, this may be due to distortion of the upper GI anatomy from positive pressure pulmonary support. These results should alert pediatricians caring for former preterm infants of such potential medical issues.

30 Fellow in Training

Cognitive Scores in Very Low Birth Weight Infants (VLBWI) <1000g ↑ Significantly with Time Suggestive of Brain Plasticity

Vivien L. Yap, Jeffrey M. Perlman, Gail Ross. Pediatrics, New York Presbyterian Hospital-Weill Cornell Medical Center, New York, NY; Psychology, New York Presbyterian Hospital-Weill Cornell Medical Center, New York, NY.

BACKGROUND: The VLBW infant is at high risk for cognitive deficits and a mental development index (MDI) <70 reflective of moderate to severe mental retardation (MR) has been observed in ~30% when evaluated at 18mo. Associated contributing factors include white matter injury (WMI) ± intraventricular hemorrhage (IVH), bronchopulmonary disease (BPD), nosocomial sepsis. There are limited data regarding the potential for improvement with time, i.e. plasticity. VLBWI in our follow up are enrolled in a rigorous early childhood intervention (ECI) program that includes frequent OT/PT, speech therapy, & sensory stimulation.
OBJECTIVE: To determine whether the neurocognitive scores of VLBWI <1000g at 18mo have the potential for improvement as early as at 36mo.
DESIGN/METHODS: VLBWI were evaluated at 18±2mo with a Bayley II and at 36±1mo with WPPSI-3 IQ. Data on associated factors included IVH, WMI by MRI, BPD (O_2 requirement at 36wks PCA), sepsis (+ blood culture), inborn (I) vs outborn (O), duration of hospitalization (DOH). Data were analyzed with student & paired t-tests.
RESULTS: The 20 VLBWI were of BW 754±163g, GA 26±1.6wk; I=15, O=5. Complications included IVH+WMI (n=3), WMI (n=1), BPD (n=11), sepsis (n=9), DOH 116±48d. At 18 vs 36mo, the group scores were 79±21 vs 94±22 (p=0.02). At 18 vs 36mo, 7/20 vs 2/20 had an MDI<70 (NS). Conversely, at 18 vs 36mo 4/20 vs 11/20 had an MDI>96 (p=0.04). At 18mo for infants with WMI±IVH vs none, MDI=70±17 vs 81±22 (NS); at 36mo, 78±21 vs 98±21(p=0.05). The ↑ from 70 to 78 at 18 vs 36mo with WMI was NS. For BPD vs none, the MDI at 18mo=70±19 vs 90±20 (p=0.02); at 36mo, 86±22 vs 104±18 (p=0.03); the ↑ from 70 to 86 (BPD) and 90 to 104 (none) at 18 vs 36m was SIG (p<0.05). MDI at 18mo for O vs I was 57±18 vs 86±17(p=0.007); at 36mo, 82±21 vs 98±22 (NS); the ↑ from 57 to 82 for O was SIG (p=0.01) and for I (p=0.002). For sepsis vs. none at 18mo, the MDI was 79±19 vs 79± 22 (NS); at 36mo, 86±22 vs 99±18 (p=0.01). The ↑ for sepsis at 18 vs 36m (79 vs 86) was NS (p=0.07).
CONCLUSIONS: These data demonstrate both a significant ↑ in cognitive scores for the group, with ↓ in number of VLBWI who exhibit mod/severe MR with time. Specifically, the scores for VLBWI with BPD & O significantly ↑ with time as compared to those with WMI±IVH and sepsis. The significant ↑ in cognitive scores, in part, likely reflect the rigorous ECI program and suggest potential for brain plasticity particularly in the absence of overt WMI.

31 House Officer

Anaphylaxis Treatment in an Urban Academic Hospital

Alison Miles, Cortney Foster, Adam Friedlander, Amy Kryder, Mary B. Bollinger. Pediatrics, University of Maryland Medical Center, Baltimore, MD; Pediatric Allergy and Immunology, University of Maryland Medical Center, Baltimore, MD.

BACKGROUND: Although a recent NIH symposium standardized the definition and management of anaphylaxis, current medical literature reveals that recognition and management of anaphylaxis in the emergency setting is variable.
OBJECTIVE: To evaluate adherence to the current guidelines for the management of anaphylaxis in an urban, academic emergency department.
DESIGN/METHODS: We conducted a retrospective chart review of patients presenting to the University of Maryland Medical System emergency department with food allergy induced anaphylaxis or angioedema between July and December 2006. We focused on the recognition of anaphylaxis by the physician, epinephrine administration including timing and route, observation period in the ED, and disposition. For patients discharged from the ED, we investigated discharge planning, specifically, education about allergen avoidance, self injectable epinephrine prescriptions (Epi-Pen,) and allergist referral.
RESULTS: Ten patients met our evaluation criteria, with ages ranging 4 months to 59 years. Five patients were seen in the pediatric ED, and five in the adult ED. Nine of the ten had mouth, upper respiratory, or GI symptoms at presentation, and seven of ten received epinephrine in the ED. Of these, six received epinephrine subcutaneously and one received it IM. Average time to epinephrine administration was within 7.5 minutes of arrival. Five patients were admitted to the hospital, and five were discharged from the ED. Of the patients discharged, three were observed in the ED for less than four hours. Four of the ten patients were discharged with a prescription for an Epi-Pen. We were unable to determine if any were referred to an allergist for follow-up.

Use of Epinephrine

Home Epi-Pen	1
Used home Epi-Pen	0
Mouth/throat/respiratory/GI symptoms	9
ED epinephrine	7
Time to ED epinephrine	7.5 minutes
Home with Epi-Pen prescription	4

n=10

CONCLUSIONS: More patients received epinephrine in the ED than we had expected, but only one by the recommended route. Less than half received a prescription for an Epi-Pen. The majority of patients discharged from the ED were observed for less than the recommended amount of time. Development of an anaphylaxis pathway for appropriate ER management may facilitate adherence to recommended guidelines. The next step in our study will be to evaluate a larger data set including all patients presenting to the ED with anaphylaxis, urticaria, or angioedema between 9/2000 and 10/2007.

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Community-Associated Staphylococcal Infection in a South Bronx Pediatric Inpatient Population

Majda Behani, Elizabeth Tejeda-Ramirez, Robert J. Leggiadro. Pediatrics, Lincoln Medical and Mental Health Center, Bronx, NY.

BACKGROUND: Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as a serious problem in the community setting in the past decade, primarily as a cause of skin and soft tissue infections.
OBJECTIVE: To determine the frequency, epidemiology, clinical features, management and outcome of staphylococcal infection in a South Bronx inpatient pediatric population in order to assess the burden of this infection acquired in the community.

DESIGN/METHODS: This is a retrospective study based on review of pediatric inpatients admitted at Lincoln Medical and Mental Health Center from March 2006 to February 2007. Demographic information, underlying conditions, risk factors, microbiology, management, and outcome of patients were assessed from medical records.

RESULTS: Eighteen (55%) of thirty-three patients identified were infected with community-associated (CA) MRSA. All patients had skin and soft tissue infections. The majority (56%) of patients infected with MRSA did not have a predisposing factor or underlying condition. Seventeen (94%) of eighteen CA-MRSA isolates were susceptible to trimethoprin-sulfamethoxazole (TMP-SMZ) and tetracycline, respectively, eleven (61%) were susceptible to levofloxacin, and three (17%) were susceptible to erythromycin that were also clindamycin susceptible (Table). Only five (28%) of eighteen MRSA patients, and one (7%) of fifteen MSSA patients were treated empirically for MRSA on admission. One-third of MSSA and MRSA patients, respectively, had surgical intervention, and one patient with MRSA infection had a relapse.

CONCLUSIONS: Skin and soft tissue infections are the most common clinical manifestations of CA-MRSA in our pediatric population. The 55% prevalence of MRSA in our community-associated staphylococcal infections suggests a need to reconsider empirical antimicrobial choices in these cases. Surgical intervention is important in the management of these infections, and clindamycin resistance among CA-MRSA isolates should be monitored locally to determine if empiric therapy with this drug is appropriate.

Frequency of susceptible antibiogram results in CA-MRSA isolates

Antibiotics	Frequency	Percentage
Tetracycline	17	94%
TMP/ SMZ	17	94%
Levofloxacin	11	61%
Erythromycin	3	17%

33 House Officer

Variability in Clearances, Electrolytes and Anemia in Children Receiving Hemodialysis – When Should Labs Be Drawn?

Christina R. Nguyen, Dale Bednarz, Jim Flanagan, Abubakr Imam, Deepa Chand. Pediatric Nephrology, Cleveland Clinic Childrens Hospital, Cleveland, OH; Pediatric Nephrology, Akron Childrens Hospital, Akron, OH.

BACKGROUND: The National Kidney Foundation guidelines recommend the delivered dose of hemodialysis (HD) be measured no less than monthly by checking clearances (Kt/V and urea reduction rates). Studies demonstrate correlation between delivered dose of HD and patient morbidity/mortality. Nephrologists vary in the clinical practice of determining Kt/V based on theory that the patient should be in a steady state and without variability. Pediatric patients have more metabolic variability and growth velocity than their adult counterparts. Furthermore, it is unknown whether other parameters evaluated during dialysis vary depending on the day of monitoring. Dialysis prescriptions are based on clearances calculated monthly, but no guidelines exist as to when labs should be obtained.

OBJECTIVE: The purpose of this study is to determine variability of electrolytes, clearances, and hemoglobin levels in children based on samples obtained at two different days of the week.

DESIGN/METHODS: Prospective data collection was performed at 2 independent pediatric hemodialysis centers in a total of 17 patients under 21 years of age receiving HD M-W-F over six consecutive months. Data obtained at each timepoint (Mondays and Wednesdays) included age, race, gender, dialysis vintage, renal disorder, ultrafiltration volume, serum electrolytes, and hemoglobin. Dialysis prescriptions remained constant between the two timepoints. Clearances were calculated on each occasion. Data was analyzed using SPSS® software using analysis of variance.

RESULTS: Preliminary analysis shows mean difference in Kt/V of -0.21 between Monday and Wednesday. Hemoglobin levels varied between the two timepoints each month with a mean difference of 0.28. Serum potassium levels had a mean difference of 0.1. Results are illustrated in Table 1.

Monthly Average Values

	Mean Difference Kt/V	Mean Difference Potassium	Mean Difference Hemoglobin
Month 1	-0.196	-0.08	0.57
Month 2	0.426	0.109	0.136
Month 3	-0.048	0.06	0.226
Month 4	-0.17	0.31	0.16
AVERAGES	-0.21	0.1	0.28

CONCLUSIONS: This study is the first to demonstrate variability in clearances, potassium levels, and hemoglobin levels in children receiving hemodialysis based on the day of laboratory collection. This factor is important in dialysis dosing in children who require precise monitoring to decrease morbidity and mortality.

34 Medical Student

Recurrent Focal Segmental Glomerulosclerosis (rFSGS) in Renal Allograft Recipients: Role of Donor-Specific Circulating Antibodies (PRA) and HLA Mismatching

Shimi Sharief, Shefali Mahesh, Vivian Tellis, Marcela Del Rio, Fredrick J. Kaskel, Robert P. Woroniecki. College of Medicine, Albert Einstein College of Medicine, Bronx, NY; Pediatric Nephrology, Montefiore Medical Center, Bronx, NY; Transplant Surgery, Montefiore Medical Center, Bronx, NY.

BACKGROUND: Incidence of pediatric rFSGS is 30-50%. The effectivness of therapeutic plasma exchange (TPE) suggests that a humoral mechanism underlies rFSGS. We hypothesized that peak PRA levels (pPRA) and HLA mismatching could be used as surrogate markers of rFSGS.

OBJECTIVE: To examine a relationship between pPRA and HLA mismatching and rFSGS.

DESIGN/METHODS: In a cross-sectional study of primary FSGS subjects transplanted from 1990-2007 at a single pediatric center, we analyzed the relationship between rFSGS and pPRA and HLA matches. Relationship between rFSGS, pPRA, and number of HLA mismatches (A, B, DR) was analyzed by logistic regression.

RESULTS: 42 subjects received 52 allografts (9 had 2nd, and 1 had 3rd allograft). 15 had rFSGS in 1st, 2 in the 2nd, and none in 3rd allograft. There were 18(43%) black, 15(36%) white, 6(13%) latino, and 3(7%) other race subjects. rFSGS and control (CT) groups were not different for: age at transplant, gender, donor source, number of acute rejection episodes (AR), chronic rejections, HLA matches, (Table), and immunosuppressive regimen (IR) of prednisone, calcineurin and purine inhibitors, and rapamycin. pPRA after adjusting for AR were not significantly different between the two groups. rFSGS was not associated with high pPRA and HLA mismatches, power = 0.41. Kaplan-Meier analysis showed rFSGS free survival time was similar in subjects with PRA<30 and PRA≥30, p=0.88. IR had no effect on rFSGS, p=0.22. pPRA was associated with AR, p=0.008. 3/9 (33.3%) subjects with rFSGS and 0/14 CT had humoral AR.

	All (N=52)	rFSGS (N=17)	CT (N=35)	P
Male	27 (52%)	8 (47%)	19 (54%)	0.57†
Age (years)	15.8±5.2	14.2±4.2	16.7±5.6	0.10‡
Living Donor	22 (42%)	7 (41%)	15 (43%)	0.77†
Number of HLA matches	1.4±1.4	1.3±1.3	1.5±1.5	0.62⊥
PRA levels	17.8±3.4SEM	12.3±4.2SEM	20.7±4.6SEM	0.39⊥
Pre Tx TPE	8 (15%)	2 (12%)	6 (17%)	0.70†
Post Tx TPE	20 (38%)	16 (94%)	4 (11%)	0.0001†
AR	23 (44%)	6 (35%)	17 (49%)	0.40†
Chronic Rejection	21 (40%)	9 (53%)	12 (34%)	0.40†
Hypertension	28 (54%)	12 (71%)	16 (46%)	0.25†

† Fisher exact, ‡ t-test, ⊥ Mann-Whitney, ± SD, Tx transplant

CONCLUSIONS: pPRA levels are associated with AR. We found no association between pPRA and HLA mismatching and rFSGS. In our experience rFSGS is associated with humoral AR.

35 Fellow in Training

Obesity as a Risk Factor for Microalbuminuria in Hypertensive Children

Gunjeet Kala, Sudha Garimella, James Springate. Pediatrics, SUNY at Buffalo, Buffalo, NY.

BACKGROUND: Microalbuminuria, defined as a urine albumin to creatinine ratio of 30-300mg/gm, is a well-known marker for kidney end-organ damage in diabetics. More recently adult studies have shown that microalbuminuria can serve as a strong indicator of renal damage and poor cardiovascular outcomes in hypertensive patient populations. There have not been many studies documenting microalbuminuria in hypertensive children. Garimella et al. (PAS2005:57:467) had completed a study which concluded that proteinuria was more prevalent amongst hypertensive children than in the general pediatric population. However it was found that obesity may have been a confounding factor for the study and that a larger study group was required.

OBJECTIVE: Our objective in this study is to calculate and statistically analyze the prevalence of microalbuminuria in normal, hypertensive, and/or obese children in pediatric clinics.

DESIGN/METHODS: The study was approved by the IRB at the Women and Children's Hospital of Buffalo. Patients were excluded from the study if they had pre-existing renal disease, secondary hypertension, diabetes, blood pressure-altering medications, illness, fever or recent excessive exercise. Parameters and definitions for hypertension and BMI/obesity were based on current accepted guidelines by the AAP. Urine samples were collected with consent from children who met inclusion criteria between the ages of 3 to 18. The subjects were allotted into one of four groups: normotensive/normal BMI, hypertensive/normal BMI, normotensive/obese, and hypertensive/obese. The priniciple investigator collected samples and tested each sample using Immunodip©.

RESULTS: In total, 95 patients were enrolled in the study: 19 were hypertensive, 20 were obese, 39 were both hypertensive and obese, and 17 were normotensive/normal BMI. The prevalence/p-values of microalbuminuria in the hypertensive population was 52.6% (p=0.01); the obese population was 30%(p=0.17); the hypertensive and obese population was 20.5%(p=0.35); and the normal population was 11.8%.

Study Results

	MA +	MA -	Total
Hypertensive	10	9	19
Obese	6	14	20
Hypertensive/Obese	8	31	39
Normal	2	15	17

CONCLUSIONS: From this study we can conclude that there is a statistically significant prevalence of microalbuminuria in the pediatric hypertensive population. We can also conclude that obesity alone is not a confounding variable when testing for microalbuminuria in children.

Cardiopulmonary Platform Session

Saturday, March 29, 2008 8:15 AM-10:30 AM

36 8:15 AM House Officer

Myocardial Regeneration Therapy with Adeno-Thioredoxin Gene Delivery Attenuates Ischemic Cardiomyopathy in Diabetic Rats

Ramesh Vidavalur, Srikanth Koneru, Mahesh Thirunavukkarusu, Suresh Varma Penumathsa, Maulik Nilanjana. Pediatrics, Connecticut Children's Medical Center, Hartford, CT; Surgery, University of Connecticut Health Center, Farmington, CT.

BACKGROUND: The prevalence of childhood diabetes has increased by 33% in the past 15 years resulting an increase in morbidity and mortality with higher incidence of cardiovascular complications. Decreased collateral vessel formation and impaired functional recovery play a significant role in diabetes induced cardiomyopathy.

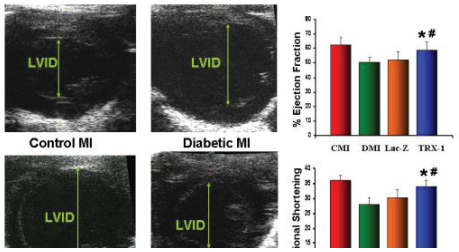
OBJECTIVE: We aimed to examine the ability to augment angiogenesis and to prevent heart failure by inducing over expression of redox-regulating protein thioredoxin (Trx-1) in diabetic rat MI model.

DESIGN/METHODS: Streptozotocin induced diabetic rats in experimental group underwent left anterior descending coronary artery ligation followed by intramyocardial delivery of either Trx adenoviral vector (Ad-Trx) or LacZ adeno vector (Ad-LacZ). Hearts were explanted for infarct size, measurement of apoptosis, immunohistochemistry, arteriolar and capillary density and immunoblotting. In vivo myocardial function was analyzed by echocardiography after 4 weeks.

RESULTS: Trx1 hearts exhibited reduced infarct size (42% vs 53%) as compared with Lac Z controls along with increased capillary and arteriolar density (2.68 vs 1.69 counts/mm^2) and significant reduction in endothelial (158 vs 375) and cardiomyocyte (375 vs 550) apoptosis. Immunohistochemical analysis demonstrated local myocardial overexpression of VEGF, heme oxygenase and thioredoxin in Trx treated animals. Echocardiographic analysis revealed significant increase in ejection fraction (58% vs 52%), improved fractional shortening (35% vs 30%), decreased E/A ratio (2.72 vs 4.26) in the group that received Trx-1.

CONCLUSIONS: In failing diabetic hearts, targeted delivery of Trx-1 decreases infarct size, induces angiogenesis and improves hemodynamic function, as measured by echocardiography. Altogether, our results indicate dual effectiveness of Trx in diabetic animals in promoting neovascularization and augmenting protective as well as regenerative response in ischemic rat myocardium.

PARASTERNAL SHORTAXIS VIEW



37 8:30 AM House Officer

Sildenafil Augments Early Protective Transcriptional Changes After Ischemia in Mouse Myocardium – cDNA Microarray Analysis

Ramesh Vidavalur, Srikanth Koneru, Suresh Varma Penumathsa, Maulik Nilanjana, Winifried Kruger. Pediatrics, Connecticut Children's Medical Center, Hartford, CT; Surgery, Molecular Cardiology Laboratory, University of Connecticut Health Center, Farmington, CT; Microarray Laboratory, University of Connecticut Health Center, Farmington, CT.

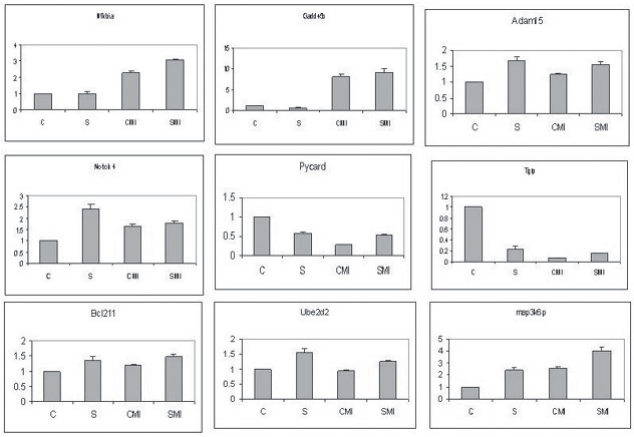
BACKGROUND: Targeting cyclic-GMP specific phosphodiesterase-5 (PDE5) has attracted interest in several cardiopulmonary diseases, in particular low flow states associated with surgical repair of congenital heart disease in children. Although multiple mechanisms were postulated for beneficial effects at cellular level, early transcriptional changes were unknown.

OBJECTIVE: To examine differential gene expression profiles in response to MI after 24 hours of ischemia in murine model and compare transcriptional modulation by sildenafil, a popular PDE5 inhibitor.

DESIGN/METHODS: Mice were divided into four groups. Control sham (C), Sildenafil sham (S), Control MI (CMI) and Sildenafil MI (SMI). Sildenafil was given at a dose of 0.7 mg/kg intraperitoneally 30 minutes before LAD occlusion. cDNA microarray analysis of peri-infarct tissue was done using a custom cloneset and employing a looped dye swap design. Replicate signals were median averaged and normalized using LOWESS algorithm. R/MAANOVA analysis was used and false discovery rate corrected, permutation p-values < 0.005 were employed as significance thresholds. RT-PCR was done to validate microarray results.

RESULTS: 156 genes were identified as significantly regulated demonstrating fold difference >1.5 in atleast one of the four groups. 52 genes were differentially expressed in SMI compared to CMI. For a subset of 9 genes, microarray data were confirmed through QRT-PCR. Infarct size measurement showed 48% reduction in SMI compared to CMI. The differentially expressed genes were grouped into following groups: Phosphorylation (e.g. map3k6, ; kcnh2), Apoptosis (e.g bcl2l1; Gadd45g, Pycard), differentiation (e.g. gata2; foxg1), ATP binding (Hsp1a; Tap2).

CONCLUSIONS: These data suggest that sildenafil, within the peri-ischemic myocardium, may regulate early genetic reprogramming conferring cardioprotection which may represent the balance between the control and sildenafil-induced molecular mechanisms.



38 8:45 AM Fellow in Training

Echocardiographic Predictors of Mortality in Congenital Diaphragmatic Hernia (CDH)

Monisha Bahri, Matthew Eig, Robin Doroshow, Stephen Baumgart, Martin Keszler. Neonatology, Georgetown University Hospital, Washington, DC; Neonatology, Children's National Medical Center, Washington, DC; Cardiology, Children's National Medical Center, Washington, DC.

BACKGROUND: Reliable prediction of outcome in patients with CDH is important to identify those who may benefit from maximal therapies and to counsel parents. A mathematical model based on measures of left heart hypoplasia (LV mass x fractional shortening)^{½} was previously shown to predict death in a small case series.

OBJECTIVE: To evaluate the ability of the left ventricular mass index to predict outcome in infants with CDH in a large multi-center series.

DESIGN/METHODS: We retrospectively reviewed echocardiograms, hospital course, need for ECMO and survival of CDH patients treated at our two institutions from Jan 1993 to Jun 2007. Infants with GA <36 weeks or major anomalies were excluded. Each infant's first available echocardiogram was de-identified and independently reviewed by a cardiologist masked to the patient's outcome. LV mass (LVM) using area-length method of Wyatt et al, fractional shortening (FS) and LVM index (LVM x FS)^{½} were calculated. Descriptive statistics and t-test were used. Sensitivity, specificity and +/- predictive values were calculated.

RESULTS: 59 of 114 eligible patients had digital echocardiograms available for analysis. Eleven patients with poor echo quality, 1 with incomplete data and 2 who died acutely of other causes were excluded. 34 (75%) infants survived and 11 (25%) died with no difference in GA (38.3 ± 2.1 v. 38.2 ± 2.0 wks) and BW (3.11 ± 0.6 v. 3.0 ± 0.4 kg) between groups. LVM/kg, FS and LVM index were significantly lower in the nonsurvivors. Data are mean±SD.

	Survivors(n=34)	Nonsurvivors(n=11)	p value
LV Mass/kg	1.52±0.47	1.15±0.18	0.01
FS	0.90±0.21	0.57±0.16	0.001
(LVM X FS)^{½}	2.03±0.50	1.39±0.32	0.0003
(LVM/kg X FS)^{½}	1.18±0.26	0.93±0.26	0.0029

A modified index using LVM/kg instead of total LVM i.e (LVM/kg x FS)^{½} resulted in the best separation of survivors/non-survivors (sensitivity 91%, specificity 76%, negative predictive value 96%) using a cutoff value of 0.95. Infants who needed ECMO (22/45) had lower LVM/kg (1.27 ± 0.35 gm/kg) compared to those who survived without ECMO (1.68 ± 0.48 gm/kg, p=0.003).

CONCLUSIONS: Infants who require ECMO have lower LVM/kg compared to infants surviving without ECMO. Indexes of LV mass are reduced significantly in nonsurvivors with CDH. The modified LV mass index predicts non survival with a high sensitivity and specificity.

39 9:00 AM

Heme Oxygenase-1 Is Required for Lung Vascular and Alveolar Development

Sara Q. Lin, Tiangang Zhuang, Guang Yang, Phyllis A. Dennery. Pediatrics, University of Pennsylvania, Philadelphia, PA; Pediatrics/Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Heme oxygenase (HO)-1 is a cytoprotective molecule that degrades cellular heme to CO, iron, and bilirubin. HO-1 can up-regulate VEGF and VEGF receptors, increase endothelial cell proliferation, and promote angiogenesis. Lung specific overexpression of HO-1 in transgenic mice protects the animals from hypoxia-induced vasoconstriction and pulmonary hypertension. HO-1 knockout mice show reduced viability, growth retardation and deficiency in iron metabolism.

OBJECTIVE: To determine the in vivo roles of HO-1 in mouse vascular and postnatal alveolar development with molecular and genetic approaches.

DESIGN/METHODS: Mouse embryos from heterozygous HO-1 breeding were harvested between E14.5 and E18.5, fixed for histological study, or homogenized for protein and mRNA analysis. To determine the HO-1 function in lung development, newborn pups from heterozygous HO-1 breeding were injected with Dexamethasone (Dex, 0.25ug/pup per day) for 14 days. Wildtype and HO-1 mutant lungs were inflated and fixed for histology study, or homogenized for gene expression analysis. Protein expressions were determined by Western blot analysis. mRNA levels were determined by real-time RT-PCR analysis.

RESULTS: HO-1 mutant embryos displayed general growth retardation and severe hemorrhage in the brain, lung, muscle and other organs, indicating disrupted vascular integrity. Histological analysis of E17.5 mutant embryos showed dilated blood vessels with rupture and thinning of the smooth muscle layers. Real time RT-PCR analysis demonstrated that in E14.5 HO-1 mutants, mRNA levels of two endothelial cell (EC) specific genes, KDR/flk-1 and Tie-1, were decreased 35% and 19.8%, respectively.

HO-1 mutants have reduced viability at birth. At postnatal day 10, HO-1 mutant lung displayed disorganized and simplified alveolar structure. In wildtype, Dex treatment inhibits postnatal alveolar development and causes reduction of EC markers (KDR/flk-1 and Tie-1) expression. HO-1 expression was also decreased in DEX treated wildtype animals. Furthermore, postnatal treatment of the HO-1 mutants with Dex resulted in more severely affected alveolarization. mRNA expression level of KDR/flk-1 and Tie-1, further decreased to 7% and 34% of the wildtype value. All four surfactant mRNAs decreased significantly in the mutant lung as well.

CONCLUSIONS: HO-1 is critical to vascular and postnatal alveolar development and it has a protective role against lung injury through its contribution to vascular function.

40 9:15 AM

Effects of Moderate Hyperoxia with Intermittent Hypoxia on Neonatal Lung PECAM-1 Expression and Endothelial Cell Function

Huayan Zhang, Bo Han, Horace M. DeLisser. Divison of Neonatology, Dept. of Pediatrics, Children's Hospital of Philadelphia- Univerisity of Pennsylvania Medical School, Philadelphia, PA; Pulmonary, Allergy and Critical Care Division, University of Pennsylvania Medical School, Philadelphia, PA.

BACKGROUND: Bronchopulmonary dysplasia (BPD) is a chronic lung disease that occurs in very premature infants and is characterized by an arrest of lung vascular and alveolar development. Previous stuides have suggested that appropriate lung vascular development is crucial to normal lung development. Exposure to hyperoxia or hypoxia causes similar changes in lung structure as seen in BPD. However, the effects of oxygen exposure on lung vascular development are not well understood.

OBJECTIVE: The objective of this study was to evaluate the effect of moderate hyperoixa with intermittent hypoxia on neonatal lung PECAM-1 expression and endothelial cell function *in vivo* and *in vitro*.

DESIGN/METHODS: Newborn GFP-TGFβ reporter mice were placed in room air or 60% O_2 with 10 minutes of 12% O_2 per day from postnatal day 3 for up to 21 days. Alveolar development, lung endothelial content and PECAM-1 expression were assessed at postnatal day 7, 14 and 21. Human Umbilical Vein Endothelial Cells (HUVEC) were cultured under room air or 60% O_2 with 10 minutes of 12% O_2 twice a day for up to 3 days. EC proliferation, apoptosis and migration were evaluated.

RESULTS: Mice exposed to oxygen showed inhibition of alveolarization as compared to room air controls at 14 and 21 days. Exposure to moderate hyperoxia/intermittent hypoxia did not appear to induce increased apoptosis or inflammatory response in the lung. However, the expression of PECAM-1 was decreased at both postnatal day 7 and 14 in the oxygen-exposed animals without significant changes in endothelial content. Active TGFβ and phospho-smad2 were increased in the hyperoxia/hypoxia group at each time point as shown by GFP staining and western blot. No differenence in EC proliferation or apoptosis was seen between the normaoxia and hyperoixa/hypoxia group in the cultured HUVEC. Exposure to moderated hyperoxia with intermittent hypoxia, however, induced delay in EC migration.

CONCLUSIONS: This observation suggests that moderate hyperxoia with intermittent hypoxia may directly affect the expression of PECAM-1 and induces endothelial dysfunction in the neonatal lung that might contibute to delayed alveolarization. The relationship between TGFβ activation and PECAM-1 expression needs to be further investigated.

41 9:30 AM Fellow in Training

BMP2 Preventes Hypoxia Induced PY-STAT3 Activation in Pulmonary Artery Endothelial Cells

X.L. Li, L.A. Parton, R. Mathews, J. Wang, S.C. Olson. RNICU, Maria Fareri Child's Hosp, Westchest Med Ctr, Valhalla, NY; Biochemistry & Molecular Biology, New York Medical College, Valhalla, NY; Pediatrics, New York Medical College, Valhalla, NY.

BACKGROUND: Pulmonary arterial hypertension (PAH), resulting from increased pulmonary pressure and narrowing of the arteries, leads to cardiac arrest. The pathology of PAH results from a combination of environmental and genetic hits, and the prognosis remains poor.

One of the key biologic events in the pathogenesis of PAH is dysfunction of endothelial cells. STATs are a family of proteins that mediate signals from the extracellular milieu of cells to the nucleus. Then they regulate the activity of many genes that play diverse roles in cellular functions, including cell growth, apoptosis, and differentiation.

Our preliminary data suggest that hypoxia, and bone morphogenetic proteins (BMP2) regulate the activity of signal transducer and activator of transcription 3 (STAT3) in pulmonary artery endothelial cells (PAEC).

OBJECTIVE: BMP2 preventes hypoxia induced PY-STAT3 activation in PAEC.

DESIGN/METHODS: PAEC were subjected to hypoxia (5% O_2) for 0-8 hours with/w/o BMP2 treatment. Cell lysates prepared and proteins separated by SDS gel.

PY-STAT3 level determined by western blot analysis and immunofluorescence stain.

Pooled data were from 3 independent experiments.

RESULTS:

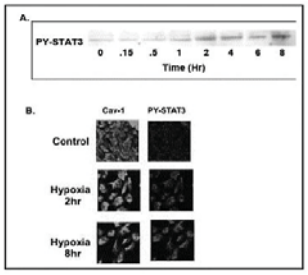


Fig 1: *Hypoxia activates STAT3 in PAECs.*

Fig 1 showed hypoxia caused time dependent PY-STA3 activation in PAEC.

Interestingly, BMP2 (100ng/ml) prevented this activation to 60% of base level vs. unchanged total STAT3 at 1 hour.

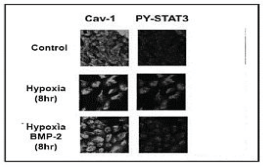


Fig2 BMP2 prevents hypoxia induced PY-STAT3 activation

Fig2 showed the prevention was maintained up to 8 hours.

Anti Caveolin-1 data shown to rule out nonspecific effect of hypoxia.

CONCLUSIONS: Hypoxia, and bone morphogenetic proteins (BMP2) regulate the activity of STAT3 in pulmonary artery endothelial cells.

42 9:45 AM

ErbB Ligand-Specific Induction of Proliferation and Differentiation in MEK-Inhibited Fetal Mouse Lung Type II Cells

Sujatha M. Ramadurai, Lucia Pham, Karen T. Wang, Heber C. Nielsen. Pediatrics, Tufts-New England Medical Center, Boston, MA.

BACKGROUND: Cell proliferation and differentiation are often in tension, a phenomenon we have reported in lung development. The ErbB1 ligands EGF and TGFα, and the ErbB4 ligand neuregulin (NRG) are important in lung development. We recently reported that EGF, TGFα, and NRG have ligand- and gestation-specific effects on fetal lung type II cell proliferation and differentiation, with no apparent tension between proliferation and differentiation. Further, MAP kinase inhibition using the MEK inhibitor PD98059 inhibited ligand-stimulated proliferation.

OBJECTIVE: We hypothesized that inhibition of MAPK-controlled proliferation would enhance effects of EGF, TGFα, and NRG on type II cell differentiation.

DESIGN/METHODS: Primary cultures of d16, d17, and d18 gestation fetal mouse lung type II cells were grown in DMEM+20% stripped fetal calf serum to 80% confluence, serum starved for 3 hrs, treated with 20 uM PD98059 for 1 hr, then EGF (10ng/ml), TGFα (10ng/ml), or NRG (33nM) added for 24 hrs. We studied surfactant protein B and C (SP-B, SP-C) gene expression by QRT-PCR, DSPC synthesis (using ^{3}H-choline) and proliferation (using ^{3}H-thymidine).

RESULTS: PD98059 decreased both baseline and ligand-stimulated proliferation on all three gestations. Choline incorporation into DSPC showed gestational differences. On d16, PD98059 ± EGF, TGFα or NRG did not affect DSPC synthesis compared to control. On d17 and d18 DSPC synthesis increased to 150% after PD98059, but EGF, TGFα or NRG did not furthur stimulate this. In control d16 cells, SP-B and SP-C expression were not stimulated by EGF, TGFα or NRG. But after exposure to PD98059 NRG stimulated SP-C gene expression 6-fold. On d17, EGF, TGF, and NRG each stimulated SP-B and SP-C gene expression. PD98059 increased SP-C but not SP-B gene expression. In d18 cells SP-B and SP-C were not stimulated by EGF, TGFα or NRG but after PD98059 EGF and NRG each caused a 2-4 fold increase in SP-B and a 200 fold increase in SP-C gene expression.

CONCLUSIONS: MAPK inhibition blocked stimulation of type II cell proliferation by EGF, TGFα, and NRG. MAPK inhibition allowed gestation dependent stimulation of DSPC synthesis and SP-B and SP-C gene expression, suggesting a release in the tension between proliferation and differentiation.We speculate that ErbB ligands promote type II cell differentiation while other factors simultaneously reduce proliferation. (NIH 37930, Peabody and Gerber Foundations).

43 10:00 AM

Pigment Epithelium Derived Factor (PEDF) in a Mouse Model of BPD

Anne Chetty, Cao Gong-jee, Heber C. Nielsen. Pediatric Pulmonology, Floating Hospital for Children, Tufts-New England Medical Center, Boston, MA; Newborn Medicine, Floating Hospital for Children, Tufts-New England Medical Center, Boston, MA.

BACKGROUND: The lung pathology in bronchopulmonary dysplasia (BPD) is characterized by impaired development of the alveolar unit (alveolar epithelium and the underlying capillary bed). Vascular remodeling is an important component of the injury/repair process of the alveolar unit in BPD. Vascular endothelial growth factor (VEGF), an angiogenic growth factor, is important in vascular development. Studies suggest that VEGF activity and vascular remodeling participate mechanistically in the alveolarization process. PEDF, an angiostatic cytokine, inhibits VEGF, creating a necessary control of angiogenesis. Matrix metalloprotease-9 (MMP-9) is involved in hyperoxic lung injury, where it can degrade extracellular matrix. MMP-9 also regulates proangiogenic and angiostatic molecules.

OBJECTIVE: PEDF is an important mediator of injury to the components of alveolar unit in oxygen mediated injury in developing lung leading to impaired vascular development in BPD.

DESIGN/METHODS: Eight -day-old WT (CD1) and MMP-9 (-/-) mice were exposed to hyperoxia or room air for five days. Western blot analyses for PEDF, VEGF and MMP-9 were done in lung lysates. 5 micron lung sections from paraffin embedded lungs were examined by immunohistochemistry for PEDF and co-stained for PECAM to show the endothelial localization of PEDF.

RESULTS: PEDF was higher in the lungs of WT and MMP-9 (-/-) oxygen-exposed mice compared to room air-exposed WT and MMP-9 (-/-) mice. The increase with hyperoxia was much smaller in MMP-9 (-/-) (1.9 fold increase compared to room air MMP-9 (-/-)) than in WT (7.2 fold increase vs room air WT, P = 0.0001). VEGF in the lungs from oxygen-exposed WT mice was significantly reduced compared to room air-exposed (N=3; P = 0.014). This reduction was not seen in MMP-9 (-/-) mice after hyperoxia compared to room air-exposed MMP-9 (-/-) (P = 0.07). In addition, MMP-9 expression was increased after hyperoxia in WT mice (P = <0.05). Immunohistochemistry for PEDF revealed expression was strongly increased in the enlarged alveolar regions after exposure to hyperoxia.

CONCLUSIONS: PEDF, an angiostatic cytokine, is upregulated in developing lung following hyperoxic exposure in association with decreased VEGF and abnormal alveolar unit development. Increased MMP-9 may increase PEDF activity. Altered PEDF and VEGF may contribute to the arrested alveolarization seen in BPD by inhibiting normal vascular remodeling in the developing alveolar unit. (Support by NIH HL37930).

44 10:15 AM Fellow in Training

Effect of NADPH Oxidase Inhibition in Lambs with Persistent Pulmonary Hypertension of the Newborn (PPHN)

Fernando A. Soares, Satyan Lakshminrusimha, Kathryn N. Farrow, Stephen Wedgwood, Sylvia F. Gugino, Lyuba Czech, James A. Russell, Robin H. Steinhorn. Pediatrics, SUNY, Buffalo, NY; Pediatrics, Northwestern Univ, Chicago, IL.

BACKGROUND: Pulmonary arteries (PA) from PPHN lambs have low levels of endothelial nitric oxide synthase (eNOS) and relax poorly to exogenous NO. We previously reported that NADPH oxidase-derived reactive oxygen species (ROS) are elevated in PA from lambs with PPHN, which may explain these findings (Brennan et al, Circ Res 2003).

OBJECTIVE: To study the effect of inhibiting NADPH oxidase activity with intratracheal (IT) apocynin on lambs with PPHN.

DESIGN/METHODS: Fetal lambs had PPHN induced by ductal ligation 9d prior to delivery, followed by delivery and ventilation with 100% O_2 for 24h. At birth, 5 lambs received IT apocynin (3mg/kg) mixed with calfactant and 8 lambs received calfactant only. After sacrifice at 24h, ROS were assayed by DHE fluorescence; eNOS, PDE5, and NADPH oxidase expression were assayed by Western blot.

RESULTS: Three lambs in the 100%O_2 group died and survivors remained hypoxic throughout the 24h period (table). All lambs in the apocynin group survived and had oxygenation significantly higher than O_2-only lambs for the first 10h of life. However, by 24h, oxygenation in the apocynin group was similar to the survivors in the 100%O_2 alone group. PA eNOS levels were significantly higher in the apocynin group compared to O_2 alone. However, ROS increased similarly in both the apocynin and O_2 groups. Further, PDE5 expression was higher in apocynin-treated lambs relative to O_2-treated animals.

Group	a/A ratio at 6h	a/A ratio at 10h	a/A ratio at 24h	ROS (fold fetal)	eNOS (fold fetal)	PDE5 (fold fetal)
100% O_2 (n=8)	0.05±0.01	0.06±0.02	0.16±0.06†	3±0.6	1±0.1	1.2±0.2
100% O_2+Apocynin (n=5)	0.23±0.06*	0.18±0.05*	0.3±0.12	4.3±0.5	23±8*	3.7±0.9*

* $p < 0.05$ compared to 100% O_2 only group; † mean of 5 survivors

CONCLUSIONS: NADPH oxidase inhibition with apocynin at birth improved short-term oxygenation in lambs with PPHN, and increased PA eNOS levels. However, PDE5 levels also increased, likely due to the accumulation of ROS (Farrow et al, Circ Res 2007). It is possible that apocynin activity is short-lived, or that eNOS functioned in the "uncoupled" state and generated superoxide. We speculate that NADPH oxidase inhibition alone is not sufficient to reduce ROS and correct the abnormalities of PPHN.

Emergency Medicine Platform Session

Saturday, March 29, 2008 8:15 AM-10:30 AM

44A 8:00 AM

Ketamine Versus Etomidate: Procedural Sedation for Pediatric Orthopedic Reductions

Jannet J. Lee-Jayaram, Adam Green, Joshua Siembieda, Edward J. Gracely, Colette C. Mull, Eileen Quintana, Terry Adirim. Pediatric Emergency Medicine, St. Christopher's Hospital for Children, Philadelphia, PA, College of Medicine, Drexel University College of Medicine, Philadelphia, PA, Family, Community, and Preventive Medicine, Drexel University College of Medicine, Philadelphia, PA , Office of Health Affairs, Department of Homeland Security, Washington, DC.

BACKGROUND: Orthopedic reductions are commonly performed procedures requiring sedation in the pediatric emergency department (PED). Etomidate is a commonly used induction agent for rapid sequence intubation in the PED. Several retrospective studies support etomidate's safety and efficacy in pediatric procedural sedation.

OBJECTIVE: To compare etomidate/fentanyl (E/F) with ketamine/midazolam (K/M), for procedural sedation during orthopedic reductions in the PED.

DESIGN/METHODS: Prospective, blinded, randomized-controlled study comparing IV K/M with IV E/M. A convenience sample of patients, ages 5 to 18 years, presenting to an urban PED with fracture requiring reduction were enrolled. The procedure was videotaped from initial medication administration until cast application. Outcome measures included: visual analog scale (VAS) of pain, Likert scales for satisfaction of sedation and OSBD-r (observational scale of behavioral distress-revised). Phone follow-up to the family was done to track late side effects and satisfaction with sedation medication. Descriptive tracking of side effects, adverse events and interventions were recorded at the sedation and during phone follow-up.

RESULTS: Twenty patients were enrolled, 10 in each group. The K/M group had significantly lower mean OSBD-r scores compared to the E/F group (0.079 vs 0.703, p = .003). Spearman's rho correlation coefficient at 0.789 showed good correlation between the two blinded scorers. Parents rated lower VAS scores with K/M than with E/F (12.75 vs 48.22, p = .006) and favored K/M on a 5-point satisfaction scale (p = .015). E/F had significantly shorter total sedation times (49.4 vs 79.7 minutes, p = .007) and recovery times (23.4 vs 61.5 minutes, p = .001). There were no significant differences with respect to procedural amnesia and orthopedist satisfaction. Side effects noted in the K/M group included dysphoric emergence reaction (10%) and vomiting (10%). Vomiting (10%), injection site pain (10%), myoclonus (20%), airway readjustment (20%) and supplemental oxygen use (10%) were observed in the E/F group.

CONCLUSIONS: For pediatric orthopedic reductions, K/M appears to be more effective at reducing observed distress than E/F, although both provide equal procedural amnesia. With its significantly shorter sedation and recovery times, E/F may be more applicable for procedural sedation for shorter painful procedures in the PED.

45 8:15 AM Fellow in Training

Accuracy of Point-of-Care Ultrasound for the Diagnosis of Fractures in the Pediatric Emergency Department

E.R. Weinberg, J.W. Tsung, M.G. Tunik. Pediatric Emergency Medicine, NYU School of Medicine/Bellevue Hospital Center, NY, NY.

BACKGROUND: Previous studies support Point-of-Care Ultrasound (PoCUS) for fracture (Fx) diagnosis in adults, but studies in pediatrics are limited. PoCUS screening for Fx can benefit patients in: pre-hospital care, triage, developing countries, and remote locations without access to Xray or CT scan (XR/CT). Previous PoCUS studies had a higher Fx rate (35-65%) than commonly observed in a Pediatric Emergency Department (PED). There are no existing pediatric PoCUS studies that: 1) include a high proportion of non-long bones; 2) assess accuracy of PoCUS performed by sonologists with limited ultrasound training.

OBJECTIVE: To determine the test performance characteristics of PoCUS compared to XR/CT for the diagnosis of Fx in patients presenting to the PED.

DESIGN/METHODS: Prospective cohort, convenience sample of patients. Pediatric Emergency Medicine physicians (PEM MDs) initially underwent 1 hour of PoCUS training, then performed PoCUS on eligible patients. Eligible patients were 0-25 years of age presenting to the PED with a musculoskeletal injury requiring XR/CT. Eligible bones had an identifiable linear cortex on PoCUS (Skull, Mandible, Clavicle, Rib, Humerus, Elbow/Fat Pad, Radius, Ulna, Metacarpal, Phalange, Femur, Patella, Tibia, Fibula, Metatarsal). Grossly angulated deformities were excluded to maintain diagnostic uncertainty. Bones were identified as positive or negative for Fx based on PoCUS. Results of the PoCUS were compared to radiologist readings of XR (or CT for skull fracture). Pediatric Emergency Medicine physicians were blinded to XR/CT results during PoCUS screening.

RESULTS: PoCUS was performed on 117 children/young adults with 192 suspected fractures. Median age was 14 years (IQR 12), 56% were male. Median time to perform PoCUS was 4 minutes (IQR 5). A high proportion of included bones were non-long bones (31%). Fx rate based on XR/CT was 24%. PoCUS test characteristics are listed in the Table (see below).

Table: Test Characteristics for Point-of-Care Ultrasound Screening for Fractures

Sensitivity	72%	CI 57-84%
Specificity	91%	CI 85-95%
PPV	72%	CI 57-84%
NPV	91%	CI 85-95%
LR +	8.1	CI 4.7-14
LR -	0.3	CI 0.2-0.5

CONCLUSIONS: Pediatric Emergency Medicine physicians, with limited Point-of-Care Ultrasound training, accurately identified fractures in children and young adults. The observed study fracture rate and bone distribution are representative of the typical injury spectrum seen in a Pediatric Emergency Department.

46 8:30 AM Fellow in Training

First Responder Performance in Pediatric Versus Adult Trauma

Sunday Bankole, Arsenia Asuncion, Gary Stahl, Zubair Aghai, Shonola Da-Silva. Pediatrics, Cooper University Hospital/UMDNJ-Robert Wood Johnson Medical School, Camden, NJ.

BACKGROUND: Management of the injured child in the prehospital setting by EMS providers continues to be a subject of ongoing debate. Majority of reports in the literature point to inadequate care of pediatric patients compared with the adult population.

OBJECTIVE: To evaluate the prehospital care provided by first responders to pediatric patients (<12yrs) compared with the adult group (>12yrs) in order to determine if the EMS providers are able to adequately assess and provide emergency services to children consistent with adult standards.

DESIGN/METHODS: Retrospective descriptive study of pediatric (0-12yrs) and adult patients (>12yrs), with head injury (GCS <15) who were treated at Cooper University Hospital between Jan.2003- Dec.2006.

EMS interventions such as peripheral access, endotracheal intubation, spine immobilization and vital signs documentation were reviewed.Patients that required further intervention on arrival at the trauma center either from non performance of a required procedure or complications arising from such procedure were evaluated.

RESULTS: A total of 201 subjects were included,102 pediatric patients and 99 adults.94 subjects required endotracheal intubation at the scene, 55 adults (55.6%) and 39 children (38.2%). Significantly more pediatric subjects had problems with intubation, 27 children (69.2%) versus 14 adults (25.5%) p<0.001.

More peripheral access were established at the scene in adults compared with children,85 adults (85.9%) versus 67 children(65.7%) with p = 0.001. Conversely at the trauma center, more children required establishment of peripheral access, 82(80.4%) compared with 63 adults(63.6%) with p = 0.011. More children required fluid bolus compared with adults at the trauma center,26 children(25.5%) versus 9 adults (9.1%), p = 0.003.

Pediatric versus Adult interventions

	Total	Adult	Adult%	Peds	Peds%	P-values
Sample size	201	99	49.3%	102	50.7%	
Needed intubation at scene	94	55	55.6%	39	38.2%	0.016
Received intubation	73	43	78.2%	30	76.9%	Not significant
Problems with scene intubation	41	14	25.5%	27	69.2%	<0.001
Peripheral IV (scene)	152	85	85.9%	67	65.7%	0.001
Peripheral IV (trauma center)	145	63	63.6%	82	80.4%	0.011
Fluid bolus (trauma center)	35	9	9.1%	26	25.5%	0.003

CONCLUSIONS: Prehospital care of children is suboptimal compared with adults in areas of endotracheal intubation, establishment of peripheral access and fluid bolus.

47 8:45 AM

Utility of Bedside Ultrasound vs CT Scan in Detecting Neck Abscesses: A Case Series

Raemma P. Luck, Michael Cohen, Thomas Costantino. Pediatrics, Temple University School of Medicine, Philadelphia, PA; Otolaryngology, Temple University School of Medicine, Philadelphia, PA; Emergency Medicine, Temple University School of Medicine, Philadelphia, PA.

BACKGROUND: CT Scan with contrast (CTSC) is often utilized to delineate superficial neck masses such as abscesses or cysts. In recent years, use and mastery of bedside ultrasound (BUS) by emergency physicians has been increasing. There are no studies to date comparing CTSC and BUS in detecting neck abscesses. If it can be shown that BUS is just as good as CTSC in this condition, it may obviate the need for a CTSC and thus decrease radiation exposure in these patients.

OBJECTIVE: To compare the ability of BUS with that of a CTSC in detecting neck abscesses in children.

DESIGN/METHODS: This is a descriptive case series of 7 patients with neck masses undergoing both CTSC and BUS to compare their abilities to rule out an abscess. Demographic data such as age, race and sex was collected as well as WBC results, disposition and antibiotics used. BUS images were interpreted by one of the authors and findings compared to final CT reports.

RESULTS: The median age was 25 months and 85.7% were black and male. The median duration of neck swelling was 1 day with fever present in 57.1%. Of the 7 patients, 3 (42.9%) had CTSC and 4 (57.1%) had BUS findings consistent with an abscess. Compared to CTSC, BUS has a sensitivity of 67%, specificity of 50%, a positive predictive value of 50% and a negative predictive value 67% in detecting an abcess. In those 3 patients with a final diagnosis of an abscess, both CTSC and BUS have similar sensitivities of 66.7% although CTSC has a higher specificity (75% vs 50%), positive predictive value (67% vs 50%) and negative predictive value (75% vs 67%) than BUS. Patients with abscesses have higher WBC than those without (20.1 vs 17.4) but no more likely to be admitted (33.3% vs 50%). Clindamycin is the drug of choice (71.4%) in neck masses needing antibiotics.

CONCLUSIONS: In this small case series, both CTSC and BUS have similar abilities in detecting a neck abscess. Large prospective studies are needed to confirm this preliminary finding.

48 9:00 AM Fellow in Training

What Do Pediatric Residents Know About Medical Malpractice?

Amy D. Roy, Karen A. Santucci, Lei Chen. Pediatrics, Section of Pediatric Emergency Medicine, Yale-New Haven Children's Hospital, New Haven, CT.

BACKGROUND: There is little literature about either pediatric residents' attitudes towards or understanding of medical malpractice.

OBJECTIVE: To assess pediatric residents' attitudes towards and knowledge about medical malpractice.

DESIGN/METHODS: Three pediatric chief residents were interviewed about their attitudes towards and experience with medical malpractice. Their responses were used to develop a survey that was offered to all the pediatric, internal medicine/pediatric and psychiatry/pediatric residents at our academic, tertiary care center.

RESULTS: Surveys were completed by 46 of 71 eligible residents (65%). Only 1 resident (2%) had been involved in a claim. Of the respondents, 87% thought medical malpractice was an important topic to learn about during residency, 67% reported one hour or less of malpractice education (30% reported none at all) and 63% felt uncomfortable with their knowledge of malpractice. Only 43% felt that fear of being involved in a claim affected their current practice, though an additional 9% thought it would affect their practice in the future. When asked to identify factors that prompt families to file lawsuits, 67% of the respondents selected the need to find out what happened to the child, followed by the need for financial compensation to support the injured child (56%) and the desire to prevent the same mistake in the future (48%). Most respondents

(80%) had never heard of the National Practitioner Database (NPDB), a database of physicians with claims or judgments against them or other disciplinary actions. Likewise, 80% estimated the risk of being involved in a claim during residency at ≤ 1:100 (actual risk is 1:10). The majority of respondents (91%) estimated that a pediatrician would be notified of a claim within 6 to 18 months of the adverse event when the actual mean delay is > 2 years.

CONCLUSIONS: Most pediatric residents are uncomfortable with their knowledge of medical malpractice and think it should be taught during residency. Unfamiliarity with the NPDB and underestimates of both the likelihood of being sued as a resident and delay in notification of a claim are examples of this lack of knowledge and support the need for malpractice education in residency.

49 9:15 AM Undergraduate Student

Improving Emergency Department Efficiency: An Integrated Patient-Centered System

Johnathon C. LeBaron, James F. Wiley II, Marvin C. Culbertson III, Sharon R. Smith.
Pediatrics, Connecticut Children's Medical Center, Hartford, CT.

BACKGROUND: Families to the Emergency Department (ED) are often asked to accomplish several tasks prior to evaluation that increases the length of time before seeing a medical provider and the overall length of stay (LOS). Waiting for in-patient beds also increases LOS.

OBJECTIVE: To study the effects of an integrated system on time to medical provider, LOS, and left without being seen rates (LWBS).

DESIGN/METHODS: Small workgroups composed of ED staff evaluated areas for possible improvement in efficiency, and developed BEQK (Be Quick):

B: bedside registration- information entered at bedside

B: bed ahead program-Inpatient beds designated and staff assigned before known ED admissions

E: electronic medical record-transition to "paperless" ED

Q: quick triage-the traditional system was replaced by a brief simple method

K: kids express- four bed, separate clinic-like area, staffed by a nurse and general pediatrician

All of these changes were implemented over a 6-month period. Medical charts were reviewed for patients presenting to the ED from June to November 2005, before the changes were implemented (before BEQK). Electronic data was reviewed on all patients presenting to the ED from June to November 2006 (after BEQK).

RESULTS: A total of 18,696 children were evaluated before BEQK and 19,932 were evaluated after BEQK. Demographics were not similar, after BEQK children were often younger, African-American, publically insured, and admitted more frequently (Table 1). Signficant decreases were found in LWBS, LOS, and improved parental satisfaction (Table 1).

Before and Afer BEQK

	Before BEQK	After BEQK	Statistics
N	18,696	19,932	n/a
Age (mean/SD)	7.3 (5.8)	6.4 (5.4)	t-test: p < 0.0001
Girls (%)	45.6	45.4	NS
Hispanic (%)	45.6	45.7	NS
African-Am (%)	16.8	20.1	X2: p < 0.0001
Admitted (%)	7.2	7.9	X2: p < 0.01
Public insurance (%)	54.5	57.3	X2: p < 0.0001
LWBS (number/%)	606 / 3.2%	103 / 0.5%	OR 0.22 (95%CI 0.19, 0.26)
Press Ganey (Free standing rank)	25th	79th	n/a
Press Ganey (Overall mean, %)	79.3%	85.6%	n/a
Time to provider (min)	74.2	67.7	X2: p<0.0001
LOS (min)	152.7	135.2	X2: p<0.0001

CONCLUSIONS: BEQK appeared to decrease LWBS rates, time to medical provider, and LOS in the pediatric ED. We also found much improved Press Ganey scores implying improved parental satisfaction with ED visits.

50 9:30 AM Fellow in Training

Communication About Interfacility Patient Transfers to Pediatric Emergency Departments

Amy D. Roy, Karen A. Santucci. Pediatrics, Section of Pediatric Emergency Medicine, Yale-New Haven Children's Hospital, New Haven, CT.

BACKGROUND: Despite considerable recent attention to inter-physician communication, particularly regarding patient handoffs, there is little information about what happens with patient transfers between facilities. This is an opportunity for information loss and poor communication, factors frequently cited as contributing to medical errors and malpractice suits.

OBJECTIVE: To describe the practices Pediatric Emergency Medicine (PEM) physicians follow when accepting interfacility transfers.

DESIGN/METHODS: A self-administered survey was mailed to the directors of all accredited US and Canadian PEM fellowship training programs. Participants were asked to assess their practice patterns in a number of areas, including whether PEM physicians routinely clarify and record the goals of transfer with the transferring physician when accepting patients from another facility, whether accepted transfers were routinely signed out at change of shift and whether criteria were in place for activation of a formal transport team.

RESULTS: Responses were received from 51 of the 64 fellowship directors (79%). Of the respondents, 75% reported that their facility received more than 200 transfers from other facilities each year and 86% indicated that the attending physician was always notified of the transfer, regardless of who accepted the call from the transferring facility. Of the respondents, 80% reported that incoming transfers were routinely signed out at the change of shift, but only 66% reported that the transferring physician was asked to identify the goal of transfer. Of the 38 facilities with ≥200 transfers per year, 21 (55%) had explicit criteria for activation of a formal transport team while only 2 of the 12 facilities with <200 transfers per year (12%) had similar criteria (p = 0.02). 1 respondent did not indicate the number of transfers received.

CONCLUSIONS: A majority of PEM fellowship directors report that PEM physicians sign out transfers at change of shift, although substantially fewer report that they attempt to clarify the goals of transfer with the transferring physician. Many programs do not have explicit criteria for activation of a transport team. Additional research is needed to explore ways to improve physician communication at this important transition of patient care.

51 9:45 AM

Abdominal Trauma in Children as a Result of Snowboarding

Alison B. McCrone, Kathleen Lillis, Steven Shaha. Pediatric Emergency Medicine, Women and Children's Hospital of Buffalo, Buffalo, NY; Center for Policy and Public Administration, University of Utah, Salt Lake City, UT.

BACKGROUND: Snowboarding has become a popular winter sport among children and adolescents in recent years.

OBJECTIVE: Our aim was to identify the demographics, mechanism and patterns of injury in children presenting with snowboarding injuries.

DESIGN/METHODS: We conducted a retrospective chart review on children age 6-21 years that presented to our Level I pediatric trauma center between January 2000 and March 2007 with injuries related to snowboarding. Ecodes for snowboarding injuries identified patients. Statistical analyses included Chi-squares and t-tests.

RESULTS: Our study identified 213 patients of whom 79% were male, 55% were in the 12-14 year age group, and 82% were injured during a fall. Presenting injuries included those to the head/neck (27%), trunk (19%), upper extremity (58%), or lower extremity (10%). Wrist and forearm fractures accounted for 56% of all injuries, most of these (68%) requiring closed reduction. Males were more likely to have fractures (p< .01), less likely to have a head injury (p< .05) and more likely to wear a helmet (p<.01). Of 213 patients enrolled in our study, 39 (18%) presented with trunk (chest, back, abdomen, or pelvis) injuries of which 19 involved the abdomen and 8 involved the pelvis. Of the 19 children with abdominal trauma, 14 (74%) involved lacerations or contusions of abdominal organs. The most common organ injury was laceration of the spleen (n=11). Falls were associated with abdominal or pelvic trauma (p<.05) more than with back or chest trauma. Falls from a significant elevation >3ft were not significantly associated with organ injury. Females were more likely to have pelvic injury (p<.001) and males were more likely to have abdominal injury (p<.001). Younger children ages 6-14yrs were more likely to have abdominal injury (p<.05) whereas pelvic injury was significantly higher among older children ages 15yrs and older (p<.05). There is a significant relationship between fractures or dislocations of the upper extremity and associated abdominal or pelvic trauma (p=.003).

CONCLUSIONS: Young male snowboarders with abdominal trauma are at risk of having splenic lacerations or other abdominal organ injury. There is a high incidence of children presenting with both upper extremity and abdominal trauma following a fall while snowboarding. We must maintain a high level of suspicion for abdominal trauma in children presenting with distracting upper extremity injuries.

52 10:00 AM House Officer

Emergency Preparedness in the Outpatient Setting

Thuy L. Ngo, Kathleen Donnelly. Pediatrics, Inova Fairfax Hospital for Children, Falls Church, VA.

BACKGROUND: Recent literature has shown that children with potentially life-threatening illnesses and injuries often present to primary care offices. Caregivers trust their primary care providers and are adverse to the atmosphere in the emergency department. Primary care physicians, however, encounter emergencies infrequently. In one study, 82% of surveyed pediatric offices encountered, on average, one emergency per month. The AAP policy statement, *Preparation for Emergencies in the Offices of Pediatricians and Pediatric Primary Care Providers*, July 2007 recommends outpatient offices to self-assess their readiness from emergencies: organized plans, emergency equipment, medications, staff and patient education to recognize emergent situations, and practice mock codes. To date, there have been no reports of a GME initiative to assess the level of preparedness in the outpatient setting.

OBJECTIVE: To compare level of emergency preparedness at referral clinics based on 1) office location and proximity to an emergency department / urgent care facility and 2) general versus subspecialty pediatric offices.

DESIGN/METHODS: A questionnaire including an equipment checklist was distributed by residents to community and subspecialty pediatricians. The survey results were tabulated into a spreadsheet to evaluate trends. Comparisons were made to published recommendations of office emergency resources.

RESULTS: Nineteen local practices (10 general pediatric and 9 subspecialty offices) were surveyed. Data was received from 10 of 19 practices. Of the total number of hospitalizations or patients requiring urgent stabilizations, general pediatric offices reported 90% (190/210) and subspecialty offices reported 10% (20/210). Despite this, a significant difference was not found between practice types and equipment maintained. Overall, this referral base was compliant with AAP recommendations for equipment and supplies at 75% for general pediatric practices and 72% for subspecialty practices. Interestingly enough, when comparing practices based on distance from an emergency room / urgent care facility, practices located 1 mile or less were compliant at 80% and those located more than a mile away were at 65%.

CONCLUSIONS: All outpatient offices should develop and maintain an active plan for emergencies. In the next phase of this project, residents will participate in office site reviews to assess the adequacy of office emergency plans and to perform simulated patient emergencies.

53 10:15 AM Fellow in Training

Optimal Empiric Antimicrobial Therapy for Non-Drained Skin and Soft-Tissue Infections (SSTI) in the Era of Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Daniel J. Elliott, Theoklis E. Zaoutis, Andrea B. Troxel, Andrew J. Loh, Ron Keren.
University of Pennsylvania School of Medicine, Philadelphia, PA; Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: MRSA has emerged as a major pathogen in community-onset SSTI. Primarily associated with localized abscesses, the role of MRSA in cellulitis and SSTIs that do not require drainage is less clear. The need for empiric MRSA-coverage in these clinical situations therefore remains unknown.

OBJECTIVE: To determine the most effective empiric antimicrobial mono-therapy for the outpatient management of non-drained SSTI in a MRSA-endemic region (community prevalence among drained SSTI = 45%).

DESIGN/METHODS: We used a retrospective, nested, case-control design to investigate the association of treatment failure and mono-therapy with a beta-lactam, clindamycin, or trimethoprim-sulfamethoxazole (TMP-SMX). We identified all patients aged 0-21 treated with mono-therapy for SSTI from January 2004 to March 2007 in five pediatric practices. Exclusion criteria included incision and drainage (I&D) or hospitalization on the day of the initial visit. The primary outcome was treatment failure defined by subsequent I&D or hospitalization, or a second antibiotic prescription due to inadequate response. We chose four controls matched on calendar quarter for each case and used conditional logistic regression to identify factors

associated with treatment failure.
RESULTS: Of 3887 children with SSTI, we identified 132 treatment failures and matched 528 controls. Compared to beta-lactam therapy, clindamycin was equally effective (OR 1.20, [0.67-2.13]) but TMP-SMZ was associated with an increased risk of failure (OR 2.1, [1.20-3.7]). Other factors independently associated with failure included prior history of Group A Streptococcus (GAS) infection (OR 2.43, [1.18-5.05]); initial treatment in the Emergency Department (OR 2.86,[1.29-6.37]); age less than 1 year (OR 1.78 [0.99-3.23]); presence or history of fever (OR=2.18, [1.31-3.66]); and the presence of either induration, abscess ≥1cm, or erythema greater than 3cm (OR 1.88, [1.24-2.84]). Infections on the head were associated with a lower risk of failure (OR 0.57, [0.34-0.94]).
CONCLUSIONS: Among children with SSTI who did not receive I&D as part of initial management, TMP-SMZ was associated with a higher risk of treatment failure than beta-lactams or clindamycin, likely because of poor GAS-activity. Even in communities with high MRSA endemicity, beta-lactams may still be the optimal empiric treatment for children with non-drained SSTI.

General Pediatrics I
Platform Session

Saturday, March 29, 2008 8:15 AM-10:30 AM

54 8:15 AM

Effect of Massage for Methadone Exposed Infants

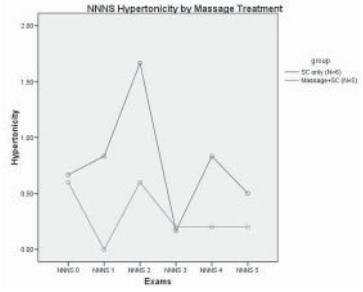
Yun J. Lee, Jing Liu, Barry M. Lester, Joseph M. McNamara, Pauline Wright. Pediatrics, Women & Infants Hospital, Providence, RI.

BACKGROUND: Infant massage (M) relaxes infants using deep pressure strokes along the length of the muscles. Massage in term infants results in decreased agitated behavior and improved orientation and excitability. The effects of massage has not been studied in methadone exposed infants.
OBJECTIVE: To determine the effect of massage on methadone exposed neonates receiving phamacological treatment for neonatal abstinence syndrome(NAS) on lenght of stay, weight gain, NAS scores, amount of morphine and neurobehavior.
DESIGN/METHODS: Methadone exposed infants born at ≥35 weeks GA requiring drug treatment were randomized to the the SC or M/SC group. Hospital staff was blinded to SC of M/SC treatment. Treatments were given five days a week for 40-45 minutes per session. NNNS, a neurobehavioral exam, was given before randomization then, after 3, 5, 7, 10, 15, 21 and 28 treatments(or at discharge).
RESULTS:

Demographics of infants

	Standard Care	Massag+SC	P value
Methadone dose, mg	99±59	97±50	ns
Birth weight, gm	2995±427	2852±546	ns
Head Circumference, cm	33±1	33±1	ns
Sex, male	5	6	--
Sex, female	6	4	--

Demographics were comparable at the 2 sites. Daily mean NS, weight gain and head growth and total amount of morphine/kg did not differ significantly. Morphine dosing after treatment was initiated were 2.29±1.51 mg/kg for SC and 1.11±1.07mg/kg for M/SC group. Infants in the M/SC group were discharged 4 days earlier than infants in the SC group. Infants in the M/SC group showed less hypertonicity on the neurobehavioral exam than infants in the SC group. Infants in the M/SC group showed better scores on quality of movements, regulation and excitibility after 10 treatments.
CONCLUSIONS: Preliminary results suggest that massage could facilitate the methadone-exposed infant's recovery from NAS.



55 8:30 AM

Communication Between Pediatric Hospitalists and Referring Physicians

Riva Kamat, John Jones, Michael Sheridan. Department of Pediatrics, Inova Fairfax Hospital for Children, Falls Church, VA.

BACKGROUND: As pediatric hospitalists assume greater responsibility for the in-hospital care of patients, it is vitally important that clear communication occurs between the hospitalist, emergency room physicians and the primary care physicians. Despite the belief that clear communication is important to patient care, no studies to date have confirmed a preferred method of communication between pediatric hospitalists and the doctors who refer to them.
OBJECTIVE: The objective of this study was to evaluate the content and the preferred method of receiving follow-up information by physicians referring patients to a large suburban tertiary pediatric hospital. We sought to answer this question by comparing the various methods of communication between pediatric hospitalists, emergency room physicians and primary care physicians.
DESIGN/METHODS: The study design was a cross-sectional survey available by internet, phone, email or fax to 37 pediatric practices and 10 emergency departments within a 50-mile radius, that refer patients to our hospital. Seventy-nine responses were returned, (44 primary care physicians and 21 emergency physicians and 13 did not provide identifiing data) representing all of the pediatric practices and emergency departments. The survey queried the referral base for demographic, impact on clinical care, preferred method of commucation and preferred content method.
RESULTS: Ninety-four percent of our respondents felt that follow-up, impacted clinical care and 65% preferred to be contacted by email/fax. The characteristics of the follow-up were rated similarly (72%), with very minor differences among direct, accurate, ease, and timely. The content of the follow-up was rated similarly (96-98%), with very minor differences among diagnosis, consultation, hospital course, and lab/radiology data. There was no difference in preference of communication method by gender, years since graduation from medical school (≤1989 or >1989), type of practice (group or solo) or specialty (pediatric or pediatric emergency medicine).
CONCLUSIONS: Referring physicians want faxed and emailed communication. Phone call communication is no longer the preferred method of communication. In an era of information technology, physicians should be able to communciate information about their patients in an efficient manner so as to improve patient care.

What is the best method to communciate with you?

Email/Fax	51	64.6%
Mixed	15	19%
Letter	6	7.6%
Phone	6	7.6%
Missing	1	1.3%

56 8:45 AM House Officer

Factors Affecting the Age of Diagnosis of Autism Spectrum Disorders at a New York City Early Intervention Center

Ginger L. Janow, Leonardo Trasande, Pediatrics, The Children's Hospital at Montefiore, Bronx, NY, Mount Sinai School of Medicine.

BACKGROUND: Effectiveness of behavioral interventions in improving long-term outcomes for children with autism spectrum disorders (ASD) is directly related to the age at which the interventions are initiated. While early diagnosis is critical, it is often delayed until school age.
OBJECTIVE: The purpose of this study is to identify factors associated with age of diagnosis in New York City among children seen at the Mt. Sinai Early Intervention Center (MSEIC). The secondary purpose is to assess trends in diagnosis over time.
DESIGN/METHODS: A retrospective chart review of the charts of 116 children diagnosed with ASD at the MSEIC between 1995 and 2005 was conducted, and demographic and clinical data was abstracted. Frequencies and means with standard deviations were calculated for all variables of interest. Data were analyzed using independent sample two-tailed t-tests for binary categories (sex, diagnosis, initial vs. supplemental evaluation). Scatter plots and bivariate correlations were created to assess continuous variables (percent delay, year of diagnosis, time from referral to evaluation). Estimated income was imputed based on zip-code using census data. One-way ANOVAs were performed on variables with more than two categories.
RESULTS: The average age of diagnosis for the sample was 26.6 months (SD 4.9 months) with a range from sixteen months to forty months. Patients diagnosed at the initial evaluation were diagnosed 2.3 months younger than those diagnosed at supplemental evaluations ($p<0.01$). Decreased age at diagnosis correlated directly with decreased time from referral to the Early Intervention Program to evaluation ($p<0.05$, $R^2=0.1$) and increased severity of adaptive ($p<0.001$, $R^2=-0.4$) and fine motor ($p<0.01$, $R^2=-0.3$) delays. Estimated income and neighborhood failed to show an independent relationship with age of diagnosis ($p=0.067$ and $p=0.891$, respectively). Age of diagnosis did not change significantly over the ten year period ($p= 0.3$), but prevalence increased significantly.
CONCLUSIONS: The most significant predictors of a younger age of diagnosis were diagnosis at initial evaluation (vs. supplemental), shorter interval from referral to evaluation, and increased fine-motor and adaptive delays. These data suggest the need for interventions to improve clinician identification of domain-specific developmental delays. Policy interventions could reduce delays in referral, reduce age of diagnosis, and improve long-term neurodevelopmental outcome for children with ASD.

57 9:00 AM House Officer

Clinical Vignette Tool To Assess Resident Needs in Communication and Interpersonal Skills

Alexis S. Lieberman, Krissa George, Yolandee Bell-Cheddar, Mario Cruz, Cindy DeLago, Matilde Irigoyen. Department of Pediatrics, Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: The ACGME requires programs to train residents in the competencies of interpersonal and communication skills. Towards this end, medical educators require useful methods to assess resident learners' needs.
OBJECTIVE: To pilot an assessment tool to measure residents' level of confidence and preparedness and desire for further training in the area of communication skills.
DESIGN/METHODS: We developed on line anonymous survey consisting of challenging clinical vignettes requiring high-level communication and interpersonal skills. Topics included psychosocial issues (ie giving bad news, domestic violence, mental illness, poverty, sexuality) and more biomedical topics (refusal of care, chronic illness, non-compliance). Example: 1) *You enter a room to do a well-check for a 4 month old, and see that the mother has a black eye.* 2) *You are interviewing a 15 year old boy at a well-check. He reveals to you that he has had sex. When you ask if his partners are male or female, he looks away and seems uncomfortable.* 3) *You are conducting a first well-check for a newborn baby. The mother has a flat affect, and does not look at or hold the baby.*
Outcome measures were level of confidence and preparedness and desire for further training, each rated on a 5-point Likert scale (for example, 1-2 unprepared, 3 ambivalent, 4-5 prepared).
RESULTS: All residents (n=39) completed the survey: 58 % were female, 44% had post-medical school training prior to residency, 25% PL1. Only a third of residents felt prepared to communicate with parents around psychosocial issues, ie giving bad news 27%, domestic violence 29%, mental illness, poverty, and sexuality, each 39%. Conversely, most residents felt prepared to communicate with parents around biomedical topics: refusal of care 54%; chronic illness 59%; non-compliance 76%. Less than 5% of the residents felt unprepared to address each of the latter topics.
CONCLUSIONS: An assessment tool including challenging clinical vignettes was useful in measuring residents' level of confidence and preparedness in the area of communication skills.

58 9:15 AM Fellow in Training

Performance in Digit Span Test for Short Term Memory in Children with Attention Deficit Hyperactivity Disorder (ADHD) as Compared to Control Group

Lysette Iglesias, Kanchana Roychoudhury, Barbara Cicero, Salimah Walia. Pediatric, Flushing Hospital Medical Center, Flushing, NY.

BACKGROUND: The prevalence of ADHD is high in children being 6-9% in some studies and attention issues affect memory causing academic under-achievement. Six major tasks of executive functioning are affected including working memory (receiving, storing then retrieving information within short-term memory). Digit Span Test (DS) is a common measure of short-term memory comprising of Digit Span Forward (DSF) and Digit Span Backward (DSB). DSF relies on simple short-term auditory memory with sequencing and verbal expression ,while DSB requires more attentional demands including working memory.

Survey of literature revealed in one study weak association of DS in measuring everyday attention compared to other tests like picture completion. In another study ADHD inattentive group did better in DSB than ADHD combined type.Other studies also failed to reveal clear results but questions about diagnostic implication of DS, Diagnostic utility of DSF and DSB, and effect of IQ on executive function including DS in ADHD children were raised.

OBJECTIVE: The objective of this study was to explore relationship between DSF and DSB and ADHD and compare this with the control group including total DS scores also.

DESIGN/METHODS: This is a prospective, cross-sectional study with 64 children between 7-12 years of age of both sexes with IQ more than 85 as tested by Kaufman Brief Intelligence Test, and academics being at age/grade level as tested by Einstein Evaluation of school related skills. Of these 29 were control group with no significant neurological or developmental disorders and 35 were established ADHD children with scores on Continuous PerformanceTest in clinical range while the control group had scores in non-clinical range.

All children did the DSF and DSB subtests of WISC IV and total DS scores were also calculated. Statistical analysis was done by using T-test, ANOVA,CHi-square And correlation coefficient.

RESULTS: In total DS score, control group did better than ADHD($p=0.0002$), in DSF there was no difference, and in DSB the control group did better than ADHD group($p=0.00$).

The ADHD group did better in DSF than DSB ($p=0.015$), while in the control group there was no difference.

CONCLUSIONS: The performance of children with ADHD in tests of short-term memory was poor in comparision with typically functioning children. In addition they had differential performance doing better in DSF than DSB.

59 9:30 AM Fellow in Training

Predictors of Maternal Subjective Socioeconomic Status (SSES) Rankings

Erika F. Dennis, Scott Lorch, Leny Mathew, Jennifer Culhane. Pediatrics/Division of Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Department of Obstetrics and Gynecology, Drexel University College of Medicine, Philadelphia, PA.

BACKGROUND: There is a clear association between objective measures of SES and health status, specifically, as SES increases so does health. This relationship holds true for reproductive outcomes. The association between subjective SES (SSES) and health status is less clear, particularly in the area of reproduction.

OBJECTIVE: To compare the association between traditional objective measures of SES and subjective measures of SES in a cohort of low-income childbearing age women in Philadelphia, PA.

DESIGN/METHODS: Face-to-face interviews were used to obtain financial and lifestyle information on pregnant women, who were recruited at their first prenatal visit between 1999-2004 and subsequently interviewed three additional times in the two years after delivery (N= 1143). A 10 rung self-anchoring scale previously used in the London-based Whitehall II study was used to determine SSES. Ordinal logistic regression models were constructed to determine factors associated with higher SSES rankings.

RESULTS: While higher SSES rankings were associated with traditional SES measures such as income (OR=1.34, 95% CI 1.03-1.76), there was no association between SSES rankings and education or marital status. Women under the age of 21 ranked themselves higher than older women (OR= 1.58, 95% CI 1.20-2.09), and African-American women ranked themselves higher than their White counterparts (OR=1.49, 95% CI 1.03-2.16). Having assets such as access to a car (OR=1.29, CI 95% 1.01-1.64) and a functional dishwasher were strongly linked to a higher SSES ranking (OR=1.73, 95% CI 1.26-2.37). Women who were somewhat worried (OR=1.68, 95% CI 1.11-2.53) or not worried (OR=1.90, 95% CI 1.31-2.77) about having an adequate income over the next 5 years ranked themselves higher compared to those who were very or extremely worried about their future income. Inability to afford food (OR=0.64, 95% CI 0.42 -0.95), leisure activities (OR=0.67, 95%CI 0.46-0.97), and children's clothing (OR=0.49, 95% 0.26-0.91) were associated with a lower SSES ranking. The inability to afford medical care or formula was not associated with SSES perceptions.

CONCLUSIONS: Typical SES measures do not provide a complete picture of a woman's perception of her socioeconomic status. While a feeling of financial security and certain assets, such as access to a car and having a dishwasher are associated with higher SSES perceptions. Essentials that are provided by society such as medical care and formula have no affect on SSES rankings.

60 9:45 AM House Officer

An Education Program To Increase Knowledge of and Immunization with Adult Pertussis Vaccination Among Parents of Newborns

Pui-Ying Iroh Tam, Benjamin Smith, Donna Fisher. Department of Pediatrics, Baystate Children's Hospital, Springfield, MA; Pediatric Infectious Diseases, Baystate Children's Hospital, Springfield, MA.

BACKGROUND: Pertussis is a cause of significant morbidity and mortality among children. The Advisory Committee on Immunization Practices (ACIP) recommends pertussis vaccine for adults having close contact with infants. Household members and parents are responsible for a large proportion of transmission to infants, thus vaccination of parents is of primary importance for the control of infant pertussis.

OBJECTIVE: To increase awareness and knowledge of pertussis among parents of newborns, and to assess the effect of this program on parental acceptance and uptake of vaccination from their providers.

DESIGN/METHODS: Prospective study carried out in our Neonatal Intensive Care Unit (NICU)/Continuing Care Nursery (CCN) and newborn nursery (NN) units. From June - September 2007, parents and grandparents were invited to participate in our education program to learn about the risks and transmission of pertussis, as well as the benefits and side effects of pertussis vaccination. We evaluated their knowledge and feelings about vaccination before and after our intervention using chi-square testing. Callbacks were done at least 6 weeks later to document uptake.

RESULTS: Of 195 people approached, 150 parents/grandparents (77%) were surveyed. 63 participants were from the NICU/CCN and 87 from the NN. Demographics between the 2 groups were similar. Only 25% of NICU/CCN parents and 40% of NN parents knew that pertussis immunization is subject to waning immunity ($p=0.06$). 52% knew pertussis is transmitted through air droplets and coughing. 85% of parents were not aware of ACIP recommendations. 78% felt the educational intervention was very helpful. Parental knowledge significantly increased after our education program ($p<0.01$). Parents of all newborns considered their baby significantly more at risk for infection, and were more willing to receive the vaccine after our education program (all p values<0.05). 21% were still unsure/unwilling to receive the vaccination afterwards. Of 138 parents who agreed to callbacks, 56% were successfully contacted and 8% were immunized.

CONCLUSIONS: Our educational program was effective in increasing parental knowledge of pertussis and willingness to receive the vaccine. Some parents were still unsure or unwilling to receive the vaccine even after our educational intervention, and immunization uptake was low. Further research needs to be done to identify and reduce barriers for parental vaccination.

61 10:00 AM

Girls Who Disclose Sexual Abuse: What Do They Tell Us?

Cindy W. DeLago, Martin A. Finkel. Pediatrics, Albert Einstein Medical Center, Philadelphia, PA; Pediatrics, University of Medicine and Dentistry School of Osteopathic Medicine, Stratford, NJ.

BACKGROUND: Idiosyncratic historical details provided by sexually abused girls help the physician diagnose abuse, yet little information is available about these.

OBJECTIVE: Describe the type and frequency of urogenital signs/symptoms reported by girls who disclosed direct genital contact and explore what factors are associated with this reporting.

DESIGN/METHODS: We reviewed the medical records of 161 girls, ages 3 to 18 years old, who were examined at a regional child abuse center after they disclosed direct genital contact for urogenital symptoms/signs, type of genital contact (oral or object, digital, genital or multiple types), genital findings, medical diagnoses, time interval between last contact with the perpetrator and physical exam, age and sexual maturity. Regression analyses were performed to determine factors most predictive of symptom or sign.

RESULTS: The mean age of girls was 10.4 years (SD 3.9 years); 41% white, 28% AA, 25% Hispanic. Contact with genitalia was oral or with an object (4%), digital (35%), genital (21%), multiple ways (40%). The majority of girls (60%) reported 1+ symptoms/sign; of these 53% had genital pain, 37% dysuria, 11% genital bleeding. Seventeen parents (11%) sought medical help for their child's symptoms prior to or at the time of disclosure: 5 were diagnosed UTI, 1 yeast infection, 7 suspected sexual abuse, 2 STI, 1 strep vaginitis. Only 9 (5.6%) girls had positive genital exams consistent with a history of sexual abuse (lacerations, abrasions, acute or healed hymen transections) and of these, 6 reported bleeding. Genital–genital contact was described by 70% of girls reporting dysuria, 73% reporting genital pain and 82% reporting genital bleeding when the abuse occurred. Digital-genital contact was described by 40% of girls reporting dysuria, 40% with genital pain and 35% reporting genital bleeding. Using regression analysis, the strongest factor predictive of symptom/sign reporting by girls was genital-genital contact during the abuse.

CONCLUSIONS: Sexually abused girls who experienced direct genital contact frequently reported symptoms related to the abusive episode and these symptoms were most frequently reported if the girl experienced genital-to-genital contact. Physicians evaluating sexually abused girls who report these temporally related symptoms should primarily suspect genital-genital contact even if this was not explicitly stated.

62 10:15 AM Fellow in Training

Prenatal Consultation for Congenital Anomalies: Parental Expectations and Perceptions

Franscesca Miquel-Verges, S. Lee Woods, Susan W. Aucott, Renee D. Boss, Leslie J. Sulpar, Pamela K. Donohue. Pediatrics/Neonatology, Johns Hopkins University, Baltimore, MD.

BACKGROUND: Screening advances have increased the number of prenatally diagnosed congenital anomalies. As a result, more families are referred to neonatologists for prenatal consultation. Limited data exist regarding parental views and preferences about these interactions.

OBJECTIVE: Investigate parental expectations and perceptions of a prenatal consultation with a neonatolgist for a prenatally diagnosed congenital anomaly, and to solicit recommendations for improving physician – parent communication.

DESIGN/METHODS: Qualitative interviews conducted with the mother one week after a consultation with a neonatologist and one week after delivery. Transcribed interviews were analyzed for themes.

RESULTS: Thematic saturation was achieved after 42 interviews (22 women). Themes were similar in the prenatal and postnatal interviews. Maternal age ranged from 18-40 years, 63% were white, 32% black, 50% had a high school education or less. Most mothers either had no expectations for the consultation, or thought it was only a NICU tour. Mothers wanted information specific to their situation and tailored to their knowledge base. They wished to know the management plan and all possible outcomes. Receiving conflicting information from physicians about the anomaly or management plan increased anxiety and eroded confidence in hospital care. A NICU tour was valuable but emotionally difficult. During the tour, mothers were comforted by the perception that NICU staff provides a safe, caring environment. Mothers wanted realistic information regardless of how grim, yet wanted to retain hope. Physicians who acknowledged parents' hope were perceived to be empathetic and compassionate. Mothers were surprised and comforted by the time and support they got from the neonatologist. All mothers would recommend a prenatal consultation with a neonatologist.

CONCLUSIONS: Mothers perceived that a consultation with a neonatologist, which included a NICU tour, decreased anxiety and prepared them for the perinatal course. Parents expect realistic medical information provided in an empathetic way. Future research should investigate the meaning of hope for parents and the qualities of physician communication parents find supportive.

Saturday, March 29, 2008 8:15 AM-10:30 AM

63 8:15 AM Fellow in Training

In Utero High Fat Diet and Maternal Genotype Program Fetal Growth

Harpreet Kaur, Kirsten Hartil, Michael Kruse, Ariana Fiallo, Maureen J. Charron, Patricia Vuguin. Department of Pediatrics, Albert Einstein College of Medicine, Bronx, NY; Department of Biochemistry, Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: To determine the effects of in utero high fat diet (HF) and maternal insulin resistance on fetal growth.

DESIGN/METHODS: Female CD1 mice (10-12wks) wild type (WT) or glucose transporter-4 (GLUT-4) heterozygous knockout (G4; model of prediabetes), were fed a HF (36% fat) or control chow (C, 10% fat) for 2 wks prior to mating and throughout pregancy. Maternal body weight (BW), glucose and lipid levels were assessed (n=8-15/group). Mothers were sacrified at embryonic day (e) 18.5, GLUT 4 and hexokinase (HK) protein expression in gonadal fat were assesed by Western blot analysis. Fetal BW, crown-rump length (CRL), placental weight (PW), and glucose levels were analyzed (n=30-51/group).

RESULTS: HF was associated with decreased BW and increased non essential fatty acid (NEFA) and triglyceride (TG) levels in WT compared to WT-C and G4 mothers (Table 1). G4 females had higher glucose levels compared to WT. HF decreased GLUT4 (4.1±1.5 vs 1.9±0.46, WT-C vs WT-HF p<0.01) and HK expression (0.46±0.22 vs 0.19±0.06, WT-C vs.WT-HF, p<0.05) in gonadal fat in WT mothers. HF did not alter GLUT4 and HK expression in G4 mothers. Fetuses did not have any macroscopic abnormalities and were present at the expected Mendelian frequencies (49 vs 51% WT vs G4, n=306). Maternal G4 genotype was associated with decreased fetal BW, CRL, PW and increased fetal glucose levels compared to WT mothers. HF resulted in a decreased fetal BW, CRL and PW independently of maternal genotype (Table 2). *p<0.05 vs WT-C, **p<0.05 vs G4-C, #p<0.05 vs WT-C, ## p<0.05 vs WT-HF.

Table 1	BW (g)	NEFA (uEq/l)	TG (mg/dl)	Glucose (mg/dl)
WT-HF	52± 8*	3.1± 0.75*	52±46 *	127± 22
WT-C	63±12	2.4± 0.7	86± 65	127± 11
G4-HF	59 ±9##	2.2± 0.9	39± 31**	141±25##
G4-C	57± 15	2.1± 0.9	76± 64	137± 14#

Table 2	BW (g)	PW (g)	CRL (cm)	Glucose (mg/dl)
WT-HF	1.28± 0.02*	0.11±0.003	2.46 ± 0.04*	59 ±3
WT-C	1.46±0.02	0.12±0.003	2.64 ± 0.03	55 ±2
G4-HF	1.2± 0.02**#	0.10±0.003**#	2.31 ± 0.02**#	92 ±5**##
G4-C	1.51± 0.02	0.13 ±0.003	2.48 ±0.03	63 ±3*

CONCLUSIONS: HF causes fetal growth restriction independently of maternal genotype. Despite that G4 mothers do not exhibit alteration in protein expression; HF does impact fetal growth, suggesting that maternal GLUT4 is not the major determinant for fetal growth.

64 8:30 AM Fellow in Training

Periconceptional Multivitamin Use and Its Association with Infant Birth Weight Disparities

Heather H. Burris, Martha M. Werler, Allen A. Mitchell. Division of Newborn Medicine, Harvard Medical School, Boston, MA; Slone Epidemiology Center, Boston University, Boston, MA.

BACKGROUND: Black women deliver preterm and low birth weight infants 2-3 times more often than white women. Black women take multivitamins less often than white women. Identification of modifiable risk factors like nutritional interventions may represent an important area for narrowing disparities in low birth weight.

OBJECTIVE: Our aim was to determine whether maternal periconceptional multivitamin use was associated with birth weight and gestational age and whether this association was different in black women versus white women.

DESIGN/METHODS: This retrospective cohort study included 2374 Non-Hispanic white and 135 Non-Hispanic black mother/infant pairs who served as controls in the Boston University Slone Epidemiology Center Birth Defects Study, 1998-2007. Mothers were interviewed by telephone within six months after delivery about their use of multivitamins (MVIs) prior to and during pregnancy, including start and stop dates and frequency of use. Stratified by race, two linear regression models were built controlling for smoking, maternal age, pre-pregnancy BMI, parity, education, marital status and income to determine associations of periconceptional MVIs with birth weight and gestational age.

RESULTS: In white subjects exposed to periconceptional MVIs, mean gestational age did not differ significantly from subjects not exposed (0.95 days shorter gestation; p=0.06). An increased gestational age by 3.38 days in black women exposed to MVIs compared to unexposed black women failed to reach statistical significance (p=0.34). Mean birth weight among white subjects did not differ significantly (-3.4 grams, p=0.8773). However, black women who took periconceptional MVIs had infants weighing an average of 454 grams more than infants born to black women who did not take periconceptional MVIs (p=0.0017). When we controlled for gestational age, the effect persisted with black mothers exposed to periconceptional MVIs having infants who weighed 365 grams (95% CI 155-575) more than infants born to black mothers who were not exposed (p=0.0008).

CONCLUSIONS: We found an association, in terms of increased birth weight and possibly increased gestational age, for black, but not white, women who took MVIs in the periconceptional period. Our results suggest that there may be nutritional interventions that could help narrow racial disparities in rates of preterm birth and low birth weight.

65 8:45 AM Fellow in Training

Circulating Levels of Hepatocyte Growth Factor Activator Inhibitor-1 (HAI-1) May Predict Fetal Intrauterine Growth Restriction

Alice Wang, Alejandro Rauh-hain, Hector Tamez, Ananth Karumanchi, Ravi Thadhani. Vascular Medicine, Beth Israel Deaconess Medical Center, Boston, MA; Nephrology, Massachusetts General Hospital, Boston, MA; Newborn Medicine, Children's Hospital Boston, Boston, MA.

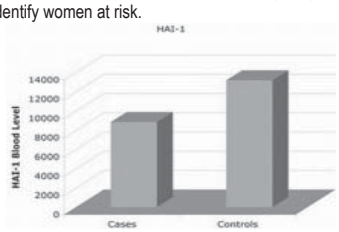
BACKGROUND: Intrauterine growth restriction (IUGR) secondary to placental insufficiency can cause significant neonatal morbidity and mortality. Like preeclampsia where there is dysregulated placental angiogenesis and increased levels of circulating anti-angiogenesis factors, alterations in specific growth factors and angiogenesis factors may lead to fetal growth restriction. A candidate factor, hepatocyte growth factor activator inhibitor-1 (HAI-1) was identified because HAI-1 is a protease inhibitor that regulates cell surface and extracellular proteases involved in tissue remodeling and tumorigenesis and because HAI-1 deficient mouse embryos show growth retardation due to failed placental vascular development and function.

OBJECTIVE: We tested whether decreased circulating HAI-1 levels early in pregnancy is associated with subsequent IUGR.

DESIGN/METHODS: We performed a prospective nested case-control study of patients who had enrolled in the Massachusetts General Hospital Obstetrical Maternal Study (MOMs) and who were nulliparous prior to enrollment. A total of 12 women who delivered an IUGR infant (<5th% for weight) and 135 contemporaneous and consecutive controls (BW>10th%) who delivered at the same time were included. Samples were collected between 16-18 weeks of pregnancy. Serum levels of HAI-1 were assayed in duplicate using a sandwich ELISA. Statistical analysis was performed.

RESULTS: No statistically significant differences in baseline characteristics between the two groups were noted. There was no difference in maternal age, BMI, smoking status, blood pressure or level of proteinuria between groups. Levels of HAI-1 were 8847 pg/ml vs 13189 pg/ml , p = 0. 0 4 . The odds ratio for severe IUGR comparing low vs. high HAI-1 blood levels (divided by median level in the controls) was 4.9 (95% CI 1.02, 23.46).

CONCLUSIONS: HAI-1 may serve as an early marker of IUGR during pregnancy, and low second trimester serum levels of HAI-1 may identify women at risk.



66 9:00 AM

Maternal Intrapartum Antibiotic Prophylaxis and Gut Microbiotic Composition in Newborn

GianVincenzo Zuccotti, Laura Pogliani, Dario Dilillo, Elena Bessi, Belinda Benenati, Lorenzo Morelli, Marcello Giovannini, Giacomo Biasucci. Department of Pediatrics, University of Milan, L Sacco Hospital, Milan, Italy; Advanced Analytical Technologies Srl, Piacenza, Italy; Department of Pediatrics and Neonatology, Piacenza, Italy; Institute of Microbiology, Sacred Heart Catholic University, Piacenza, Italy; Department of Pediatrics and Neonatology, University of Milan, San Paolo Hospital, Milan, Italy.

BACKGROUND: Many factors can affect intestinal colonization of newborns. Antibiotics are increasingly prescribed in the peripartum period and may affect the newborn outcome.

OBJECTIVE: To examine whether the maternal intra-partum antibiotic prophylaxis (IAP) may modify gut microbiotic composition in newborn during the first days of life.

DESIGN/METHODS: Thirty term vaginally-delivered newborns, exclusively breastfed at birth were enrolled. Fifteen infants were born to mothers with IAP and fifteen infants to mothers without IAP. Stool samples were collected on day 3 and day 10 after birth. Fresh faecal samples were plated on Rogosa Agar, TPY Agar and VRBA plus MUG media to select and count the faecal amount of bifidobacteria and lactobacilli.

RESULTS: In newborns to IAP vs non-IAP mothers, the prevalence of bifidobacteria was lower both at 3 days (13.3% vs 66.7% P=0.008) and 10 days (40.0% vs 86.7%, P=0.021) after birth, while the prevalence of lactobacilli was lower at 3 days (6.7% vs 66.7%, P=0.002 but not at 10 days (46.7% vs 53.3%, P=1.00) . The amount of bifidobacteria (10^8 cfu/g) did not change in IAP group (median [range], day 3, 0 [0-250] vs 0 [0-520], day 10, P=0.069) but increased in non-IAP group (day 3, 0.1 [0-370] vs 30 [0-830], day 10, P=0.018). The amount of lactobacilli did not change both in IAP (day 3, 0 [0-17] vs 0 [0-310], day 10, P=0.878) and non-IAP (day 3, 0.7 [0-270] vs 0.2 [0-190], day 10, P=0.318) group.

CONCLUSIONS: In the early days of life, gut microbiotic composition may differ between newborns exclusively breastfed and born to IAP vs non-IAP mothers.

67 9:15 AM

Niroscopic Tissue Oxygenation Changes of the Splanchnic Region in Preterm Neonates After Feeds

Viral Dave, Luc P. Brion, Deborah E. Campbell, Melissa Scheiner, Carolyn Raab, Suhas M. Nafday. Pediatrics - Division of Neonatology, Children's Hospital at Montefiore, Bronx, NY; Division of Neonatal-Perinatal Medicine, University of Texas Southwestern Medical Center at Dallas, Dallas, TX.

BACKGROUND: Several reports have shown that enteral feeding induces a significant increase in blood flow velocity in the superior mesenteric artery. Doppler ultrasonography is the method currently used for the clinical assessment of velocity of superior mesenteric artery blood flow. Near infrared spectroscopy (NIRS) is frequently used to monitor oxygenation of the brain in neonates by measuring the ratio of oxygenated to de-oxygenated hemoglobin (termed "tissue oxygenation index"[TOI]). Regional tissue oxygenation of other vascular beds such as the splanchnic area can be followed compared with brain oxygenation as a reference since cerebral blood flow autoregulation minimizes changes in brain oxygenation during events affecting splanchnic circulation. NIRS has been reported to be useful in detecting changes in splanchnic oxygen delivery during apneic episodes and in predicting splanchnic ischemia in neonates by measuring cerebro-splanchnic oxygenation ratio (CSOR). NIRS has also been utilized to measure known physiologic changes in tissue oxygenation of the liver in newborn infants during and after feeding via a naso-gastric tube.

OBJECTIVE: The objective of this prospective, observational study was to test the hypothesis that tissue oxygenation in the splanchnic bed changes after feeding in preterm neonates.

DESIGN/METHODS: Clinically stable premature neonates with post menstrual age between 32 and 35 6/7 weeks who were tolerating full bolus feedings were studied by near infrared spectroscopy before feeding and one hour after feeding. The ratio of oxygenated to reduced hemoglobin (TOI) in the cerebral circulation bed was divided by the ratio of the TOI in the splanchnic circulation, thereby yielding cerebro-splanchnic oxygenation ratio (CSOR). We compared CSOR before and after feeding.

RESULTS: Among 32 infants with reliable (with out variation >15%) tracings, CSOR significantly increased by 0.09±0.24 units one hour after feeding (p=0.032), whereas pulse oximetry did not change (p=0.600). The change in CSOR with feeding was inversely related to baseline value (r=-0.737, p < 0.001), thus CSOR increased most in those infants with a low baseline value.
CONCLUSIONS: This study indicates that tissue oxygenation of the splanchnic region decreases relative to the cerebral circulation after feeding in preterm infants, thereby suggesting reduction in splanchnic oxygenation after feeding.

68 9:30 AM

Nutritional Practices in Extremely Low Birth Weight Infants (ELBW, <1000g): 2002 vs. 2006

Rita M. Ryan, Jennifer A. Clark, Nancy Garrison, Alyssa Hermann, Anne Marie Reynolds. Pediatrics/Neonatology, Univ Buffalo - Women & Children's Hosp Buffalo, Buffalo, NY.

BACKGROUND: Severe under nutrition and postnatal growth failure are common in ELBW (<1000g). NICHD data indicate that at 36 weeks 89% have growth failure, and at 18-22 months corrected GA 40% are still <10th percentile.
OBJECTIVE: Compare nutrition-related data for ELBW infants born in 2002 vs. 2006. We hypothesized that ELBW infants born in 2006 received quality nutrition earlier.
DESIGN/METHODS: This was a retrospective review of 100 ELBW patients, 50 each selected randomly from 2002 and 2006. Continuous data were analyzed by t-test, categorical data analyzed using chi-square or Fisher exact test.
RESULTS: Mean weight percentile at birth was 35th in 2002 and 31st in 2006, with 14% and 30% of babies born at <10th percentile respectively (SGA). Parenteral nutrition improved with significantly earlier initiation of TPN, time to 3gm/kg/d protein and lipid in the 2006 cohort.

	2002	2006
Babies < 1000g	n=50	n=50
BW (g)	773	754
GA (wks)	26.1	26.5
survival	84%	96%
wt %ile at birth	35th	31st
<10th %ile at birth	14%	30%
TPN started	1.2	0.2*
reached 3 gm/kg/d TPN protein	5.5	2.5*
reached 3 gm/kg/d TPN lipid	7.8	4.2*
started enteral	6.2	7.3
reached 100 ml/kg/d enteral feedings	27	29
reached 120 kcal/kg/d enteral	40	41
wt at 14d (g)	844	899**
wt at 28d (g)	1037	1135**
wt at 36wks (g)	1956	1846
wt %ile at discharge	12th	14th
<10th %ile at discharge	50%	52%

data presented as means; *P<0.01 vs. 2002; **P<0.05; numbers are in days unless otherwise noted

There were no significant changes in time to attain enteral feeding goals. Human milk was the first feed for 50% of babies in 2002 and 44% in 2006. Time in days to reach 70kcal/kg/d (total TPN+enteral) was 8.3 in 2002 vs. 7.8 in 2006; 100kcal/kg/d: 16.3 vs. 17.3 days. In 2002, it took 27d to reach 100 ml/kg/d enteral feeds vs. 29d in 2006; 31 vs. 32d for 120 ml/kg/d. For 150 ml/kg/d enteral feeds, it took 46d in 2002 vs. 39d in 2006 (P=0.1). Although weights were significantly higher at 14d and 28d in 2006, they were not different at 42d, 56d or 36wks GA.
CONCLUSIONS: Approximately half of our ELBW babies leave our NICU at <10th percentile for their in utero target weights. Although we achieved earlier parenteral nutrition and higher weights at days 14 and 28 in 2006, the growth percentile for weight at discharge was 14th. Additional strategies to improve advancement of enteral nutrition are needed.

69 9:45 AM Fellow in Training

Growth Velocity in the Extremely Low Gestational Age Newborn

Yolanda F. Brown, Camilia R. Martin, Elizabeth N. Allred, Richard A. Ehrenkranz, Michael O'Shea, Mandy B. Belfort, Marie C. McCormick, Alan Leviton, ELGAN Study Investigators. Division of Newborn Medicine, Children's Hospital, Boston, MA; Department of Neonatology, Beth Israel Deaconess Medical Center, Boston, MA; Neuroepidemiology Unit, Children's Hospital, Boston, MA; Pediatrics, Wake Forest University School of Medicine; Pediatrics, Yale University School of Medicine.

BACKGROUND: Extremely low gestational age newborns (ELGANs, <28 weeks gestation) are at considerable risk for nutritional deficiencies and extrauterine growth restriction (EUGR). Previous studies of growth velocity (GV) have shown that the youngest infants have the slowest GV and are more likely to demonstrate EUGR.
OBJECTIVE: To describe GV and nutritional intake in the ELGAN by gestational age (GA).
DESIGN/METHODS: We studied 1196 infants from the ELGAN study, a multi-center, prospective, observational study of 1506 infants born before 28 weeks GA. Detailed nutritional and growth data were available each day for the first week of life, weekly to 28 days of life, and at the time of discharge. We defined GV as the difference between the weights at two specified times divided by the starting weight divided by the interval length in days. We calculated the GV at weekly intervals for the first 28 days and for the interval from day 28 to discharge.
RESULTS: During week 1, all GA groups lost weight (negative GV) (Table 1). During week 2, however, they all began to gain weight (positive GV). During weeks 2 and 3, and from day 28 to discharge, GV of infants born at 23 weeks GA are greater than GVs of infants born at later GAs. This difference is evident despite similar median daily total fluid volumes and caloric intakes across all GA groups at 28 days (Table 2).

Table 1. Median growth velocity by GA

	Median Growth Velocity(gm/kg/day)					
GA (weeks)	Week 1	Week 2	Week 3	Week 4	Day 28 - discharge	N
23	-15	17	20	15	28	57
24	-10	15	17	15	26	193
25	-9	16	14	17	24	251
26	-8	15	14	17	23	305
27	-10	16	15	19	22	390

Table 2. Total volume and caloric intake at day 28

GA (weeks)	Total volume	Total Calories	% calories from enteral intake
23	128	92	36
24	131	98	52
25	131	98	56
26	133	101	66
27	137	105	77

volume in mL/kg/d; calories in kcal/kg/d

CONCLUSIONS: In contrast to previous studies, we found that ELGANs of lower GA have greater GV than infants of higher GA despite similar caloric intakes. This finding may reflect the implementation of more aggressive parenteral nutritional strategies which may offset growth deficits due to delayed enteral feedings.

71 10:15 AM House Officer

Changing Epidemiology of Cholecystitis and Cholelithiasis in the Pediatric Population

Fadel Balawi, Robert Lee, Warren Rosenfeld. Pediatrics, Winthrop-University Hospital, Mineola, NY.

BACKGROUND: Cholelithiasis and cholecystitis are being recognized with increasing frequency in infancy, childhood and adolescence. Past studies implicated hemolytic diseases, use of total parenteral nutrition, distal ileal resection, adolescent pregnancy and birth control pills. Recently, obesity has been associated with gallbladder disease. No distinct age predilection nor predominance of males (M) or females (F) have been reported.
OBJECTIVE: We hypothesized that the epidemiology of gallbladder disease is changing. This review investigated sex, age of onset, associated conditions and family history.
DESIGN/METHODS: We conducted a retrospective chart review study of 85 consecutive inpatient cases with diagnosis of cholelithiasis and/or cholecystitis admitted over a 7 year period. Diagnoses were confirmed with ultrasonography with or without computed tomography.
RESULTS: There were 19 males (M) and 66 females (F). Males had a mean age of 12.7 ± 5.3 yrs, weight of 55.6 ± 39.3 kg, and BMI of 22 ± 8.7 kg/m2. Females had a mean age of 14.5 ± 3.7 yrs, weight of 70 ± 28.3 kg, and BMI of 27.3 ± 7.8 kg/m2. 75 patients (15 M, 60 F) were 11-21 yrs. Only 10 patients (5 M, 5 F) were < 11 years old. The majority were overweight (55%). 38 patients (13 M, 25 F) had BMI < 25; 17 patients (1 M, 16 F) had BMI 25-30 (overweight); 30 patients (5 M, 21 F) had BMI > 30 (obese). Presenting signs and symptoms included bilary colic (74) while 11 were asymptomatic at the time of diagnosis and cholelithiasis was an incidental finding on radiograph. 32 patients (8 M, 22 F) presented with pain < 2 weeks duration; 31 (6 M, 25 F) had symptoms > 2 weeks duration; 1 female had chronic symptoms for 3 years. Twenty-two (5 M, 17 F) had a family history for biliary disease. Associated diseases: hemolytic disease (5), TPN during the neonatal period (3), delivery within 3 months of diagnosis (4), oral contraceptives (4), biliary dyskinesia (2) and Down syndrome (4).The majority of patients had normal white cell count, 76% had normal AST levels, 53% had elevated ALT levels. Direct bilirubin was elevated in 40% of patients.
CONCLUSIONS: As in previous studies we evaluated inpatients with cholelithiasis/cholecystitis to determine its presentation in the pediatric population. Patients accounted for 1/200 admissions, were more frequently female (F/M=3/1), and in older children than previously described. Obesity/overweight occurred in 55% of cases and 85% had acute onset of biliary symptoms. Hemolytic disease was rare.

Infectious Disease Platform Session

Saturday, March 29, 2008 8:15 AM-10:30 AM

72 8:15 AM Fellow in Training

Rhinovirus Epidemiology, Disease Spectrum, and Association with Serious Bacterial Infections in Febrile Young Infants

Mark X. Cicero, Lei Chen, Carla Weibel, Caleb Korngold, Jeffrey Kahn. Pediatrics, Yale University School of Medicine, New Haven, CT.

BACKGROUND: Rhinovirus (RV) is a common cause of cough, wheeze, and fever. Recent work suggests RV is associated with more serious disease than the common cold. The disease spectrum and epidemiology of RV in febrile young infants are unknown, as is the association between rhinovirus infection and serious bacterial infection (SBI). New technology makes rapid RV detection more feasible.
OBJECTIVE: 1) Determine the frequency and severity of illness associated with RV in febrile infants < 61 days old.
2) Determine the incidence of SBI in febrile infants < 61 days old with and without RV infections.
DESIGN/METHODS: A cross-sectional study of all febrile infants < 61 days old was conducted in an urban academic pediatric emergency department. Demographic, symptomologic, and outcome data were recorded. Enrolled infants had evaluation of blood, urine, and cerebrospinal fluid (CSF), and nasal mucus sampled via swab. Reverse transcription was performed on RNA extracted from the nasal samples. Polymerase chain reaction was performed using RV primers. DNA sequencing was done for RV positive samples; sequences were compared to the known RV genome. Enrollment is ongoing.
RESULTS: Ninety-eight infants have been enrolled, of whom 14 (14.2%) had RV detected. The median ages of infants with and without RV detected were 34 and 39 days, respectively. For the 14 infants with RV, 8 (57%) were admitted to the hospital, one of whom had co-infection with respiratory syncytial virus. One infant (7%) had a urinary tract infection (UTI), the only SBI in the RV group. Among the 84 infants without RV, the admission rate was 74%, and there were six (7%) with SBIs: four UTIs, one episode of bacteremia, and one case of Listeria meningitis. Of the infants with RV, 4/14 (28.6%) had CSF pleocytosis and in the non-RV group, 10 (11.9%) had CSF pleocytosis (p= 0.112, Fisher exact test).
CONCLUSIONS: Rhinovirus is associated with febrile illnesses and hospitalization in infants < 61 days old. The data suggest that inflammation in the central nervous system (CNS) may occur in some infants < 61 days old who are infected with RV. To date, febrile infants in our cohort with RV were as likely to have SBI than those without RV. Rapid testing for RV may guide management of febrile young infants with meningitis. There is a trend toward CSF pleocytosis in the RV positive group, and further studies are required to determine if RV infection extends to the CNS.

73 8:30 AM

Individual Differences in the Concentration of Intracellular Metabolites of Anti-HIV Nucleoside Analogs

Elijah Paintsil, Rong Hu, Yung-Chi Cheng. Pediatrics and Pharmacology, Yale University School of Medicine, New Haven, CT.

BACKGROUND: Conventional antiretroviral therapy involves the administration of standard fixed doses. This approach does not take into consideration interpersonal variability in pharmacokinetic processes that may results in substantial differences in target site concentration among patients. We observed differences in the accumulation of metabolites of 4'-Ed4T, a recently discovered HIV-1 reverse transcriptase inhibitor (RTI), in different T-cell lines.

OBJECTIVE: We tested the hypothesis that the intracellular accumulation of triphosphate metabolites of nucleoside analogs will be different among different individuals.

DESIGN/METHODS: PBMCs were used *in vitro* since they are the target cells for HIV-1 infection. PBMCs were isolated from nineteen (9 females and 10 males) healthy HIV-seronegative individuals. 1 to 2 X 10^7 of PHA stimulated PBMCs were incubated with [3H]-4'-Ed4T, [3H]-AZT, or [3H]-3TC (1 μM [500 mCi/mmol]) for 24 hours. After acid extraction, the intracellular metabolites were analyzed by HPLC. The identity of the peaks of the radiolabeled-nucleotides of 4'-Ed4T, AZT and 3TC was determined by comparison with authentic elution-time standards of unlabeled nucleotides of the respective analog.

RESULTS: There were differences in the formation of total, and triphosphate metabolites among the donors tested. For each donor, the amount of NRTI-monophosphate formed correlated well with the amount of the triphosphate. The amount of 3TC (cytidine analog) metabolites formed were generally greater than that of the thymidine analogs (4'-Ed4T and AZT). AZT and 4'-Ed4T triphosphate concentrations demonstrated positive correlation (R^2 = 0.06) among the females, however, this was not statistically significant. Furthermore, there was a negative correlation between 3TC and AZT or 4'-Ed4T in the females. In the males, there was poor correlation between either AZT and 4'-Ed4T or a thymidine analog (AZT or 4'-Ed4T) and cytidine analog (3TC).

CONCLUSIONS: The individual differences in the intracellular accumulation of nucleoside analog metabolites may partly account for the interpersonal variation in response to anti-HIV activity of nucleoside analogs, evolution of drug-resistance, and the development of drug toxicity. The use of concentration-controlled dosing regimens may be necessary especially in heavily HAART-experienced individuals.

74 8:45 AM Fellow in Training

Variability in the Presence of CSF Pleocytosis Among Young Infants with Enterovirus Infections of the Central Nervous System

Jeffrey A. Seiden, Joseph J. Zorc, Richard L. Hodinka, Samir S. Shah. The Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Enteroviruses (EV) are the most common cause of aseptic meningitis in young infants. In older children, the absence of cerebrospinal fluid (CSF) pleocytosis has a high negative predictive value for EV meningitis. However, many young infants with EV meningitis do not have CSF pleocytosis.

OBJECTIVE: To identify factors associated with CSF pleocytosis among infants ≤90 days of age with EV meningitis.

DESIGN/METHODS: This was a retrospective cohort study performed at an urban academic children's hospital. Patients ≤90 days of age with a positive CSF EV polymerase chain reaction test obtained during the 2000-2006 EV seasons were included. Patients with serious bacterial illness (SBI) or herpes simplex virus infection were excluded. CSF pleocytosis was defined as CSF white blood cell (WBC) count >22/mm^3 for patients <1 month of age and >15/mm^3 for patients ≥1 month of age. Multivariable logistic regression was used to identify factors independently associated with CSF pleocytosis.

RESULTS: A total of 159 patients had a positive CSF EV PCR test during the study period; five (3.1%) were excluded for concurrent SBI: urinary tract infection (n=2), bacteremia (n=2), and bacterial meningitis (n=1). Median age of eligible patients was 36 days; 60% were female. Median CSF WBC count was 110/mm^3 (interquartile range, 11-311/mm^3). CSF pleocytosis was present in 109 (71%) patients. The proportion of infants with CSF pleocytosis accompanying EV meningitis increased with age; CSF pleocytosis was present in 59%, 74%, and 90% of infants aged 0-28, 29-56, and 57-90 days, respectively (p=0.007). Age and peripheral WBC count were independently associated with CSF pleocytosis (Table).

Results of logistic regression for CSF pleocytosis

Variable	Adjusted OR	95% CI	p-value
Age[a]	1.26	1.09 to 1.47	0.002
Peripheral WBC count[a]	3.03	1.52 to 6.05	0.002
CSF RBC count[a]	1.01	0.99 to 1.02	0.29
Fever	0.27	0.06 to 1.34	0.11

[a]Reflects the increase in odds of pleocytosis for each one week increase in age, each 5000 cell increase in peripheral WBC count, and each 1000 cell increase in CSF RBC count, respectively.

CONCLUSIONS: Among infants with EV meningitis, CSF pleocytosis is related to older age and higher peripheral white blood cell counts, perhaps reflecting the inability of younger infants to mount a robust inflammatory response to EV infection.

75 9:00 AM Fellow in Training

Sequential Evidence-Based Central Line Care Interventions Can Decrease Line Associated Sepsis

Sulaiman Sannoh, Barbara Clones, Jose Munoz, Boriana Parvez. RNICU, MFCH, WMC, Valhalla, NY.

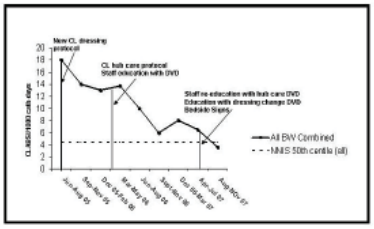
BACKGROUND: Central Lines (CL) are essential in critically ill neonates for providing TPN, medications and blood products but have increased risk of complications with high attributable mortality and cost. CL-associated bloodstream infections (CLABSI) are considered a marker for quality of healthcare. The annual CLABSI rate is higher in NICU (8.4/1000 vs 5.3/1000 catheter-days in all ICU). We hypothesized that he implementation of sequential evidence-based interventions for CL care will decrease CLABSI.

OBJECTIVE: To implement sequential evidence-based CL care interventions and observe CLABSI rates.

DESIGN/METHODS: This is a prospective interventional study from 06/05-11/07. Data of all neonates with CL are entered in the NICU CL database. In 6/05 NICU baseline CLABSI was 18/1000 catheter-days. We introduced series of sequential interventions for CL care: new CL dressing change protocol in 6/05, new CL hub care protocol using chlorhexidine and staff education using DVD in 2/06, Staff education on dressing change with DVD, DVD re-education on CL hub care protocol and bedside signs in 8/07. We are reporting the incidence of CLABSI before and after these sequential interventions and comparing it with 50% NNIS. X^2 was used to compare ratios and t-test for means, p<0.05 was significant.

RESULTS: 23% of all NICU patients had CL (497/2148 admissions). All CL sepsis rates decreased after sequential interventions by 55% (*p<0.05)* when device utilization remained the same. The percent of infected catheters decreased from 17% to 9% *(p<0.05)*. The cumulative infection rates decreased after every sequential interventions to as low as 3.6/1000 catheter-days, below NNIS 50th percentile (Fig 1). Sepsis caused by gram negative bacteria was also decreased.

Fig 1. Decreased CLABSI After Sequential Interventions



CONCLUSIONS: In this prospective study we were able to show significant decrease in CLABSI for all catheter types and BW categories.

76 9:15 AM

Prevalence and Characterization of HIV-Associated Nephropathy and Other Renal Disorders in a Cohort of Perinatally HIV-1 Infected Children

Murli U. Purswani, Charles Mitchell, James Oleske, Kathleen Kaiser, Miriam C. Chernoff, Hans Spiegel, Warren A. Andiman, George Seage. Bronx-Lebanon Hospital Center, Bronx, NY; University of Miami Medical School, Miami, FL; University of Medicine and Dentistry of New Jersey, Newark, NJ; Frontier Science Research Foundation, Buffalo, NY; Harvard School of Public Health, Boston, MA; Yale University School of Medicine, New Haven, CT; Children's National Medical Center, Washington, DC.

BACKGROUND: There is limited information describing the spectrum of non-urinary tract infection renal disease associated with perinatal HIV-1 infection (P-HIV). HIV-associated nephropathy (HIVAN) has been described in children, with a reported prevalence of 7-15%.

OBJECTIVE: 1. To describe types and prevalence of renal disease in a cohort of P-HIV children. 2. To determine risk factors associated with HIVAN.

DESIGN/METHODS: Pediatric AIDS Clinical Trials Group study 219/219C was a large, prospective cohort study of P-HIV children (opened 9/93, closed 5/07) collecting information using standardized criteria and structured forms every 3-6 months. In 9/06, additional clinical data was abstracted on children followed at least 30 months and identified with renal laboratory abnormalities or clinical diagnoses through 12/04. HIVAN was defined as persistent proteinuria with echogenic kidneys ± histologic evidence on biopsy (Bx). Comparisons were made using Fisher's exact, Pearson's χ^2 and Kruskal-Wallis tests.

RESULTS: Of 2,102 children entered, 72 carried a renal diagnosis yielding a prevalence of 3.4%. HIVAN was associated with non-Hispanic African American (AA) race (p=0.042), nadir CD4% <15% to event (p=0.001), higher baseline Log HIV RNA (p=0.012) and higher AUC Log HIV RNA to event (p<0.0001). There was a trend toward higher mean age (8.1 vs 6.3 yrs, p=0.065). Non-HIVAN renal diagnoses comprised the largest group (48/72, 67%). Indinavir (IND) toxicity occurred in 22 of 255 (8.6%) children receiving this drug. Bx-diagnosed immune-mediated etiology (HIV-Im) was noted in 8 children.

Diagnosis	No	Prevalence (%)
HIVAN	24	1.14
With Bx	14	
Focal Segmental Glomerulosclerosis	5	
Mesangial Glomerulonephritis (GN)	2	
Membranous GN	1	
Results N/A	6	
HIV-Im	8	0.38
Lupus GN	4	
IgA GN	2	
HCV GN	1	
Interstitial Nephritis (IN)	1	
IND Toxicity	22	1.05
Nephrolithiasis	15	
IN	3	
Nephropathy	4	
Other	18	0.86
Renal Tubular Acidosis	6	
Nephrolithiasis (non-IND)	4	
Acute Renal Failure	3	
Non-Hodgkin's Lymphoma	2	
Other	3	

CONCLUSIONS: A wide range of renal disorders was identified. HIVAN was most common, with lower prevalence for overt disease than previously reported. Risk factors included advanced HIV infection and AA race. Renal dysfunction in P-HIV should prompt consideration of other etiologies including drug-related nephrotoxicity and HIV-Im.

77 9:30 AM Fellow in Training

Human Papillomavirus Antibodies from Natural Infection Are Protective Against Subsequent HPV Species-Related Infections

Zainab A. Malik, Susan M. Hailpern, Robert D. Burk. Pediatric Infectious Diseases, Children's Hospital at Montefiore, Bronx, NY; Pediatrics, Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: HPV 16 is a member of the alpha papillomavirus species group 9 (α9) that is strongly associated with cervical cancer. Whether antibodies induced by natural infection with the α9 group are protective against subsequent infection is not known.

OBJECTIVE: This study examined whether immunoglobulin G (IgG) antibodies (Ab) to the α9 group (HPV16, 31, 33, 35 and 52) are protective against subsequent infection with phylogenetically-related types of HPV.

DESIGN/METHODS: In a longitudinal study of college women investigating the natural history of cervicovaginal HPV infection, exfoliated cervicovaginal cells were collected for HPV DNA detection and typing by MY09/11 polymerase chain reaction (PCR) and Southern blot at baseline and every 6 months.

Blood was collected for serology at baseline and yearly. HPV 16, 31, 33, 35 and 52 virus-like particles (VLPs) were used as antigens in a polymer enzyme-linked immunosorbent assay (ELISA) to measure IgG Ab to type-specific HPV capsid proteins. Relative risks (RR) and corresponding 95% confidence intervals (CI) were calculated directly.

RESULTS: Data from 533 women was available for analysis. 310 women (58%) had no detectable antibodies at baseline. The prevalence of VLP IgG to one, two, three and four or more types of HPV from the α9 group was 19% (n=99), 10% (n=54), 9% (n=46) and 3% (n=17), respectively. A reduced risk of incident infection with the α9 group was associated with the presence of two (RR: 0.94; 95%CI: 0.50, 1.76), three (RR: 0.85; CI: 0.42, 1.73) or $\geq$ four (RR: 0.69; CI: 0.19, 2.55) types of Ab to the α9 group (P-trend 0.04). Protection from incident infection with any type of HPV was associated with the presence of $\geq$4 types of Ab to the α9 group (RR: 0.52; CI: 0.22, 1.24).

CONCLUSIONS: VLP IgG antibodies to the α9 group protect against subsequent infection with related types of HPV. Serum antibodies induced by HPV vaccination may confer broad cross-protection against HPV strains not included in the vaccine.

78 9:45 AM

Phagocytosis and Oxidative Burst of Neonatal Neutrophils Confronted with *Candida albicans* and *Candida parapsilosis*

Kisha G. Destin, Matthew A. Maccani, Sonia S. Laforce-Nesbitt, Joseph M. Bliss.
Pediatrics, Women & Infants Hospital of Rhode Island, Providence, RI; Graduate Program in Pathobiology, Brown University, Providence, RI.

BACKGROUND: *Candida* species are the third leading cause of late-onset sepsis among premature neonates, with *C. albicans* and *C. parapsilosis* most commonly involved. The high prevalence of *C. parapsilosis* is a unique feature of this population. The neutrophil represents a key element in the control of systemic *Candida* infections, yet the specific neutrophil mechanisms that make the premature neonate particularly susceptible to *Candida* infections are not well understood.

OBJECTIVE: To compare two neutrophil functions, phagocytosis and oxidative burst, of term and preterm neonatal neutrophils exposed to *C. albicans* and *C. parapsilosis* to that of adult neutrophils.

DESIGN/METHODS: Neonatal neutrophils were isolated from cord blood immediately following placenta delivery and from peripheral blood of healthy adult volunteers. Phagocytosis activity of the neutrophils against unopsonized yeast forms of each species was quantified by light microscopy. Oxidative burst activity against *C. albicans* yeast and hyphae and *C. parapsilosis* yeast was measured by fluorescence intensity of the marker for intracellular reactive oxygen species, CM-H_2DCFDA.

RESULTS: Phagocytosis of *C. albicans* yeast was low in both adult and neonatal neutrophils (10-15%), but was more efficient with *C. parapsilosis* as target (80-85%). Neutrophils from both term and preterm infants (25-30 weeks) were capable of phagocytosis equivalent to adults, with the exception of one infant at 22 weeks. This infant had 65% of adult phagocytosis activity against *C. parapsilosis*. Oxidative burst activity of neutrophils from term neonates exposed to *C. albicans* hyphae was equivalent to that induced by PMA and was similar to adult neutrophils. Neutrophils from preterm neonates (25-30 weeks) also had burst activity similar to adults. Minimal burst was induced in either adult or neonatal neutrophils by exposure to *C. parapsilosis* yeast, and was attenuated in infant and adult neutrophils by exposure to *C. albicans* yeast.

CONCLUSIONS: Although the response to *C. albicans* and *C. parapsilosis* varied based on species and growth morphology, neutrophils from neonates and adults behaved similarly at most gestational ages. These findings suggest that a deficiency in phagocytosis or the ability to generate an oxidative burst are not responsible for the increased susceptibility of preterm neonates to infections with *Candida*, although infants as young as 22 weeks may be an exception.

79 10:00 AM Fellow in Training

Pro- and Anti-Inflammatory Cytokine Release by Circulating Monocytes in the Newborn: Control by Endogenous Interleukin-10 and Effects of Exogenous Interleukin-10 Versus Dexamethasone

Lina Elbash, Lucy Pereira-Argenziano, Veronika Miskolci, Ivana Vancurova, Dennis Davidson. Division of Neonatal-Perinatal Medicine, Schneider Children's Hospital, New Hyde Park, NY; Department of Biological Sciences, St. John's University, NY, NY.

BACKGROUND: Circulating monocytes (MONOs), in the fetus and newborn, migrate to tissues and play an important role in the fetal inflammatory response syndrome, bronchopulmonary dysplasia, and white matter injury. Little is known regarding the temporal release, balance, and control of pro- and anti-inflammatory (PI, AI) cytokines by human fetal MONOs.

OBJECTIVE: To determine: 1) the temporal release of PI and AI cytokines from MONOs stimulated by endotoxin (LPS); 2) if endogenous interleukin-10 (IL-10) has an autoregulatory AI role on PI cytokine release; and 3) to compare equimolar levels of exogenous IL-10 versus dexamethasone (DEX), in therapeutic ranges of the latter, on PI and AI cytokine release.

DESIGN/METHODS: MONOs (92% pure) were isolated from cord blood of term infants (N=5) after elective cesarean section. MONOs were stimulated in vitro with LPS (10 ng/ml) up to 18 hrs. Cytokine release was measured in media at 4 and 18 hrs by ELISA. LPS-stimulated MONOs, 10^6 cells/ml were pretreated (1 hr) with either control vehicle, IL-10 monoclonal antibody (mab), IgG control, or equimolar levels of exogenous IL-10 or DEX.

RESULTS: LPS produced significant changes in PI cytokines (IL-8, IL-1ß, and tumor necrosis factor-TNF) at 4 and 18 hrs, ranging from 45 to 304 fold increases. LPS produced significant increases in AI cytokines, IL-10 and IL-1 receptor antagonist (IL-1ra) by 7 and 6 fold at 4 hrs, then 128 and 22 fold at 18 hrs, respectively. The AI cytokine, IL-4 was not detected. IL-10 levels reached 896pg/ml/10^6 MONOs ($4.8x10^{-11}$M) by 18 hrs. IL-10 mab significantly increased release of IL-8, IL-1ß, and TNF at 18 hrs of LPS stimulation by 3 fold. DEX (10^{-8}M) had no effect on cytokine release. Exogenous IL-10 (10^{-8}M) significantly inhibited IL-8, IL-1ß, and TNF release at 4 and 18 hrs, ranging from 89-97%.

CONCLUSIONS: For LPS-stimulated MONOs of the newborn, large increases in PI cytokines are released early compared to the AI cytokines. Endogenous IL-10 inhibited maximal release of PI cytokines at 18 hrs. Surprisingly, under our study conditions, DEX had no effect on PI or AI release. However exogenous IL-10, at equimolar therapeutic levels of DEX, produced marked inhibition of the early and late release of PI cytokines. AI therapy with exogenous IL-10 may be potentially useful in serious disorders of the newborn.

80 10:15 AM Fellow in Training

Use of Umbilical Cord Blood Cultures for the Diagnosis of Early-Onset Sepsis

Secelela Malecela, Judith Palafoutas, Michelle Peterson, Zacharia Cherian, Jayashree Ramasethu. Neonatology, Georgetown University Hospital, Washington, DC; Neonatology, Washington Hospital Center, Washington, DC.

BACKGROUND: Each year 400,000 peripheral blood cultures (PBCx) are drawn from newborns for evaluation of early onset sepsis (EOS), with 0-2% positive yield and contamination rates of 0-6%. Even though EOS is acquired intrapartum, umbilical cord blood cultures (UBCx) are rarely done due to limited data and contamination rates of 2.5-12%. UBCx are less invasive and easy to perform.

OBJECTIVE: To describe the utility of UBCx for diagnosis of EOS.

DESIGN/METHODS: UBCx are routinely performed at an urban center in infants at risk for EOS using strict protocols to minimize contamination. Risks factors for EOS are chorioamnionitis, fever >38°C, rupture of membranes > 18 hours (PROM), positive or unknown group B hemolytic streptococcus (GBS) screen, and prematurity (<37 wks GA). Clinical and laboratory data on all infants with UBCx in a 6 month period were reviewed. Definitions: Confirmed sepsis- positive UBCx, treated with antibiotics (ABtx) for 7-14d. Presumed sepsis- negative UBCx, ABtx 7-14d based on clinical, laboratory or radiological data. R/O sepsis-asymptomatic, negative UBCx, observed only or ABtx for 48-72 hrs.

RESULTS: 569 infants had UBCx; 176 (31%) were preterm. 241 (42%) were born by C-section. Risk factors: Chorioamnionitis or fever 129 (23%), PROM 80 (14%), GBS+ with inadequate or no prophylaxis (IAP) 83 (14.6%) and preterm labor (PTL) 112 (63.6%). 9 UBCx were positive, 5 of these were contaminants (contamination rate 0.9%).

EOS Classification and UBCX Results

	< 36 weeks GA n(%)	≥ 37 weeks GA n(%)	Total n(%)
Confirmed Sepsis	2(1)	2(0.5)	4(0.7)
Presumed Sepsis	56(32)	50(12.5)	106(18.6)
R/O Sepsis UBCx-	117(66.4)	337(86)	454(79.8)
R/O Sepsis Contaminants	1(0.6)	4(1)	5(0.9)
Total	176(31)	393(69)	569

UBCx Results and Clinical Correlations

Isolate	GA	Risk Factors	IAP	Symptoms	Treatment
GBS	24	PTL,PROM,GBS?	Yes	Resp. distress	2d- died
GBS	40	GBS+	Yes	Resp. distress	10d
GBS	40	PROM	No	None	10d
Strep.Viridans	33	PTL,Chorioamnionitis,GBS?	Yes	Resp. distress	10d
Bacillus Spp.	36	PTL,GBS?	No	None	None
S.Aureus	37	GBS+	Yes	None	None (PBCx negative)
Strep.Viridans	40	GBS+	Yes	None	None
CONS	39	GBS?	No	None	None
CONS	40	GBS?	No	None	None

CONCLUSIONS: In this large series, the positive yield of UBCx was comparable to PBCx reported in the literature with lower contamination rates. With strict collection protocols, UBCx could be an alternative to PBCx at birth.

Neonatology I - Neonatal Pulmonology Platform Session

Saturday, March 29, 2008 8:15 AM-10:30 AM

81 8:15 AM

Carcinoembryonic Cell Adhesion Molecule 6: A New Human Surfactant Associated Protein

Philip L. Ballard, Cheryl J. Chapin, Linda W. Gonzales, Nicole Bailey, Jeffrey D. Merrill, Marye Godinez, Roberta A. Ballard. Pediatrics, University of California San Francisco, San Francisco, CA; Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; Pediatrics, Case Western Reserve University, Cleveland, OH; Neonatology, Childrens Hospital of Oakland, Oakland, CA.

BACKGROUND: Carcinoembryonic Cell Adhesion Molecule 6 (CEACAM6) is a glycophosphatidylinositol anchor glycoprotein that is upregulated during hormone-induced lung type II cell differentiation. In gastrointestinal epithelial cells, plasma membrane CEACAM6 functions in immune defense, cell adhesion and apoptosis.

OBJECTIVE: To determine the intracellular location of CEACAM6 in type II cells and its expression profile in infants.

DESIGN/METHODS: Epithelial cells were isolated from human fetal lung and treated with dexamethasone and cAMP to induce type II cell differentiation; CEACAM6 expression was assessed by confocal immunofluorescence. Large aggregate surfactant and supernatant fractions were isolated from tracheal aspirates of intubated premature infants (mean gestational age 25.5 wk, n=30) and term infants without lung disease (n=10) during the second postnatal week. CEACAM6 was measured by Western and immunodot analysis. Surface activity of commercial surfactant in the presence of inhibitory proteins with or without CEACAM6 (by siRNA knockdown or addition of rCEACAM6) was determined by pulsating bubble surfactometry.

RESULTS: By immunofluorescence, CEACAM6 localized to both plasma membrane and lamellar bodies of cultured fetal type II cells. In tracheal aspirates, CEACAM6 was present in both surfactant (65%) and supernatant (35%) fractions. In the supernatant, CEACAM6 was 0.48±0.05% (mean/se) of total protein for premature infants with lung disease vs 0.23±0.04% (p=0.02) for term infants without lung disease and was primarily the 60 kDa form. In surfactant of premies, CEACAM6 was 3.3±0.4% of total protein and 2.2±0.4% of phospholipid, similar to the value for SP-B (1.1%), and was primarily the 90 kDa form that presumably includes the GPI anchor. CEACAM6 concentration was inversely related to recovery of surfactant. In the presence of inhibitory proteins from conditioned epithelial cell culture medium, low minimum surface tension was obtained with but not without CEACAM6.

CONCLUSIONS: CEACAM6 is a newly identified surfactant-associated protein that is expressed during type II cell differentiation in vitro and is present in airways of infants. Production of CEACAM6 appears to be upregulated following premature birth and/or lung disease. CEACAM6 has a potential function in promoting surfactant stability as shown by its ability to reduce surface tension in the presence of inhibitory proteins.

82 8:30 AM Fellow in Training

Simulated Medical Transport Is Associated with Decreased mRNA Expression of Surfactant Proteins A, B & C and Higher Active Phospholipid Content in Neonatal Sprague-Dawley Rats

Ashraf Gad, J. Craig Cohen, Avinash Chander, Shetal Shah. Neonatology, Stony Brook University Medical Center, Stony Brook, NY.

BACKGROUND: Forces transmitted to the neonate as a consequence of accelerations during transport have been epidemiologically associated with adverse neonatal outcomes including broncho-pulmonary dysplasia. These accelerations measured per unit time (impulse) have been shown to adversely impact respiratory function in a dose-dependent manner. The mechanism for these changes in lung compliance after transport has not been well described.

OBJECTIVE: To examine if transport was associated with decreased levels of surfactant proteins and altered total phospholipid content.

DESIGN/METHODS: Seven Sprague-Dawley rat pups underwent a simulated medical transport on postnatal day of life 10 for one hour on a modified vortex transport simulator oscillating at a frequency of 2.8Hz & an average impulse of 27.4 m/sec^2-min – a level associated with ambulance transport based on real-world studies. Eight control animals were placed in the transported for one hour but not moved. Post intervention, rat lungs were harvested & processed for mRNA extraction & bronchoalveolar lavage (BAL). Total phospholipid content was examined in both BAL fluid supernatant & Pellet fraction. RT-PCR was performed on lung tissue of another cohort of animals to examine mRNA levels of surfactant proteins. Data was analyzed using unpaired *t* test.

RESULTS: Messenger RNA expression for all surfactant proteins in transported rat lungs were 48.6 ± 13%, 42.9 ± 10 % and 43.8 ± 12.8% of control levels for surfactant proteins A, B and C respectively ($p < 0.05$). Active phospholipid content in the pellet fraction of BAL fluid increased from 33.63 ± 5.13 mcg/g lung in control to 57.45 ± 6.97 mcg/g/lung in transported animals ($p<0.05$). Total phospholipid content, a measure of the phospholipid pool including inactive surfactant, was not significantly altered between the two groups (227.07 ± 20.07 mcg/g lung vs. 230.16 ± 31.93 mcg/g lung respectively).

CONCLUSIONS: In this model, transported neonatal rats experienced significant decreases in mRNA expression of three major surfactant proteins, potentially explaining the phenomenon of decreased lung compliance observed. Increases in the amount of active phospholipid, unaccompanied by a decrease in the inactive pool, suggest transport is associated with altered phospholipid homeostasis. Further studies are needed to more fully understand the mechanism of transport-mediated lung injury.

83 8:45 AM

ErbB4 Regulation of Type II Cell Maturation in Murine Lung

Lucia D. Pham, Sujatha M. Ramadurai, Washa Liu, Christiane E.L. Dammann, Heber C. Nielsen. Pediatrics, Tufts-New England Medical Center, Boston, MA.

BACKGROUND: The development of cell-cell communication is crucial for lung maturation. ErbB4, a member of the ErbB receptor family and its ligand Neuregulin (NRG) play an important role in this process. We have shown that ErbB4 is the preferred dimer partner for the other ErbB receptors in late gestation fetal rat lung. ErbB4 knockout animals are embryonic lethal due to heart and neural defects. In cardiac rescued ErbB4$^{-/-heart}$ fetuses, ErbB4 deletion produced altered alveolar structure, decreased DSPC synthesis and altered surfactant composition. However the fibroblast-initiated effect on type II cell maturation in the ErbB4$^{-/-heart}$ animals is unknown.

OBJECTIVE: We hypothesize that ErbB4 is involved in the fibroblast-initiated communication leading to fetal type II cell maturation.

DESIGN/METHODS: We prepared fibroblast conditioned medium (FCM) from d17 fibroblasts cultured from ErbB4$^{-/-heart}$ animals. We tested the ability of FCM from ErbB4$^{-/-heart}$ to stimulate surfactant DSPC synthesis in type II cells cultured from Swiss Webster day 17 (d17) fetal mouse lungs. Additional type II cells were treated with fetal lung FCM from 1) d18 Swiss Webster fibroblasts (known to stimulate DSPC synthesis); 2) d17$^{+/+}$ (WT fetal littermates of the ErbB4$^{-/-heart}$ fetuses); 3) culture media; or 4) NRG (10 ng/ml). After 24 hrs, type II cells were harvested for assay of cell proliferation (^{3}H-thymidine incorporation into DNA), surfactant synthesis (^{3}H-choline incorporation into DSPC) or SP-B and SP-C protein expression by Western blotting.

RESULTS: Thymidine Incorporation: There was no effect on thymidine incorporation by NRG, d17 ErbB4$^{-/-heart}$ FCM or d17$^{+/+}$ FCM as compared to control. D18 FCM produced a 40% decrease in thymidine incorporation. DSPC synthesis: As expected d18 FCM and NRG treatment produced a 250% increase in DSPC synthesis compared to control ($p<0.05$). d17$^{+/+}$ FCM had minimal stimulation of DSPC synthesis above control (130%). FCM from ErbB4$^{-/-heart}$ fibroblasts produced a 50% decrease in DSPC synthesis.

CONCLUSIONS: FCM from d17 ErbB4$^{-/-heart}$ fibroblasts decreased DSPC synthesis without altering proliferation. We conclude that ErbB4 signaling in fetal lung fibroblasts is an important component of fibroblast-type II cell communication leading to lung maturation. (Supported by NIH 37930, Peabody Foundation, Gerber Foundation).

84 9:00 AM Fellow in Training

Nitrolinoleate Acts as a Signaling Molecule in Pulmonary Cells Via Modification of Membrane Proteins

Jayshree Savla, ChangJiang Guo, Bruce Freeman, Andrew Gow. Neonatology, Robert Wood Johnson Medical School-UMDNJ, New Brunswick, NJ; Pharmacology and Toxicology, Rutgers University - UMDNJ, Piscataway, NJ; Pharmacology, University of Pittsburgh, Pittsburgh, PA.

BACKGROUND: Nitrated lipids, such as nitrolinoleate (LNO_2), are formed from the nitration of unsaturated fatty acids by nitric oxide and its derivatives. LNO_2 has been found in relatively abundant concentrations in the human vasculature. Within acute lung injury, such as ARDS, production of nitrated lipids is increased. However, the effects of these compounds in the lung are unknown.

OBJECTIVE: The goal of this study was to investigate the effects of LNO_2 on the pulmonary epithelial cells and macrophage function.

DESIGN/METHODS: Cytosolic calcium mobilization in human airway epithelial cells (A549) was measured by fura-2 AM labeling. The ability of LNO_2 to modify membrane proteins within A549 and THP-1 (human derived macrophage cells) cells was assessed utilizing a biotinylated form of the molecule. The atypical PKCζ and its downstream target ERK were determined by western blot.

RESULTS: LNO_2 but not linoleic acid (LA) caused inhibition of calcium influx in response to bradykinin in A549 cells. This effect was reversed by non selective PKC inhibitors such as chelerythrine chloride and calphostin C; but not by the classic PKC inhibitor G06976. Western blot analysis showed that atypical PKCζ was activated by LNO_2 stimulation. A PKCζ pseudosubstrate inhibitor reversed LNO_2-mediated regulation of calcium influx. LNO_2 was shown to activate PKCζ directly in vitro by direct binding. Treatment of THP-1 cells with biotinylated LNO_2 resulted in a labeling of membrane proteins, which was inhibited by incubation with unlabeled LNO_2 but not LA. A model in which LNO_2 acts a signaling molecule within pulmonary epithelial cells and macrophages by covalently binding to cell membrane proteins, including PKCζ, to further activate downstream targets, such as ERK, is proposed.

CONCLUSIONS: In conclusion, LNO_2 may act as a signaling molecule in the pathogenesis of pulmonary inflammatory disease by a novel mechanism that has not been previously described.

85 9:15 AM Fellow in Training

The Role of Reactive Oxygen Species (ROS) in A549 Respiratory Epithelial Cell Infection by Adenovirus Type 21 (ADV-21) and Parainfluenza Virus Type 3 (PIV-3)

Khalid S. Ahmad, Ansamma Joseph, Melodi B. Pirzada, Byung-Min Choi, Jeffrey A. Kazzaz, Leonard R. Krilov. Cardiopulmonary Research Institute, Departments of Pediatrics and Medicine, Winthrop University Hospital, Mineola, NY.

BACKGROUND: ADV-21 infection has been implicated in severe pediatric lower respiratory disease and death. Neonates have been particularly susceptible to severe pulmonary disease, extrapulmonary dissemination, and significant mortality. Gray et al demonstrated an increasing trend for ADV-21 detection amongst both civilian and military populations (CID 2007;45:1120-31). PIV-3 is the second most common cause of bronchiolitis in children. It is also associated with pneumonia. Although primary adenoviral infection pathology involves epithelial cell necrosis, the role of oxidant stress in viral infection is largely undefined.

OBJECTIVE: To compare the effects of ADV-21 and PIV-3 on their ability to induce oxidative stress in A549, a human alveolar type II cell line.

DESIGN/METHODS: A549 cells were infected for 4 hours with a range of multiplicity of infection (MOI) of ADV-21 (0.05 – 0.15) and of PIV-3 (8 – 80). At 2 days post infection, ROS production was assayed with superoxide-sensitive chemiluminescent dye MCLA and cell counts were determined by coulter counter. Values were compared to uninfected controls.

RESULTS: In the ADV-21 infected cells ROS production was significantly elevated (P values < 0.05) at each MOI of ADV-21 analyzed (0.05-0.15). A dose-dependent relationship was not noted. Mean cell viability was also markedly reduced at each MOI. The cell count for controls ranged from 4.2-5.4 x 10^5 cell/mm^3 and ↓'d to 2.4-4 x 10^4 cells/mm^3 in the ADV exposed cells ($P < 0.0003$).

In PIV-3 infected cells, ROS production was not significantly elevated compared to control at each MOI of PIV-3 tested. The reduction in cell viability was more modest compared to ADV-21 (controls 4.5-5.2 x 10^5; PIV-3 exposed 2.8-4.1 x 10^5 cell/mm^3).

CONCLUSIONS: ADV-21 resulted in markedly elevated oxidative stress and cell death compared to PIV-3 in human respiratory epithelial cells. These results may help explain the acute nature and severity of clinical disease induced by ADV-21. Since oxidative stress correlated with cell death, antioxidant therapy may help reduce the severity of disease induced by these viruses. Further studies correlating these findings with clinical disease are warranted.

86 9:30 AM

Angiopoietin 2 Release by Tracheal Aspirate Cells from Ventilated Premature Infants Is Not Regulated by Nuclear Factor-KappaB

Zubair H. Aghai, Judy G. Saslow, Tarek Nakhla, Gary Stahl, Riva Eydelman, Louise Strande, Vineet Bhandari. Pediatrics/Surgery, Cooper University Hospital-Robert Wood Johnson Medical School, Camden, NJ; Division of Perinatal Medicine, Yale University School of Medicine, New Haven, CT.

BACKGROUND: Angiopoietin 2 (Ang2) plays an important role in inflammation. Recently, we have shown that Ang2 is increased in tracheal aspirates (TA) of ventilated premature infants (VPI) who had an adverse outcome (bronchopulmonary dysplasia and/or death). Nuclear factor- kappaB (NF-κB) is a key regulator of inflammatory mediators. The role of NF-κB on Ang2 release in premature infants is not known.

OBJECTIVE: To study the effect of NF-κB activation on Ang2 release by TA cells obtained from VPI.

DESIGN/METHODS: TA cells obtained from 10 VPI {birth weight (mean±SD) 707±133 g, gestational age, 25.4±1.8 w} were incubated in 4 groups (C=control, TNF=TNF-α 2ng/ml, AZM (Azithromycin) 4=TNF-α 2ng/ml + AZM 4ug/ml and AZM8= TNF-α 2ng/ml + AZM 8ug/ml). AZM was used to suppress NF-κB activation. After 18 hours of incubation, activation of NF-κB in nuclear protein was measured by electrophoretic mobility shift assay (EMSA) and Ang2 levels in cell culture media by ELISA.

RESULTS: The predominant cells in TA samples were polymorphonuclear leukocytes (48%) and alveolar macrophages (43%). Baseline Ang2 levels (mean±SE) in the TA cell culture medium was 428±82 pg/ml, approximately three times higher than TA (supernatant) Ang2 concentrations of 162±13 pg/ml. Stimulation of TA cells by TNF-α increased the activation of NF-κB (Table, $p<0.001$) without a significant increase in Ang2 levels. Addition of 8 ug/ml of AZM suppressed the TNF-α stimulated activation of NF-κB ($p<0.001$) without significant decrease in Ang2 levels.

Table 1

	Control	TNF	AZM 4	AZM 8
NF-κB	1.0±0.0	3.1±0.2*	2.8±0.2	1.4±0.0 **
Ang2 (pg/ml)	428 ± 82	425 ± 82	361± 85	424 ± 80

Values are mean ± SE *p<0.001 compared with control group, **p<0.001 compared with TNF

CONCLUSIONS: Ang2 is secreted by TA cells (mostly inflammatory) obtained from VPI. Ang2 release by TA cells was not increased by TNF-α stimulation. In our *in vitro* study, Ang2 release by TA cells from VPI appears not to be regulated by NF-κB activation.

87 9:45 AM Fellow in Training

Nasal Continuous Positive Airway Pressure (NCPAP) vs Bi-Level NCPAP (SiPAP) in Preterm Infants: A Comparison of Work of Breathing (WOB) and Respiratory Function

Vita M. Boyar, Sherry E. Courtney, Jennifer Beck, Christer Sinderby, Robert H. Habib.
Neonatal-Perinatal Medicine, Schneider Children's Hospital, New Hyde Park, NY; Pediatrics, Stony Brook University Medical Center, Stony Brook, NY; Pediatrics, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; Pediatrics, Mercy Children's Hospital at St.Vincent's Mercy Medical Center/University of Toledo - College of Medicine, Toledo, OH; Critical Care, Keenan Research Center at the Li Ka Shing Knowledge Institute of St. Michael's Hospital, Toronto, ON, Canada.

BACKGROUND: Bi-level NCPAP (SiPAP) is now an option for non-invasive respiratory support in infants. Little data are available comparing SiPAP with NCPAP.

OBJECTIVE: To compare work of breathing (WOB) and other respiratory parameters during NCPAP and SiPAP, using matched mean airway pressures (MAP) in premature infants.

DESIGN/METHODS: 10 preterm infants on NCPAP or SiPAP for mild respiratory distress were studied. Study weight was 961±189g, gestational age 29.4±1.9 wks, study age 8±4 days, FiO_2 at study 0.26±0.06 (means+/- SD). Each infant was studied on both modes, applied in random order. There were 5 males and 5 females; 5 infants randomized first to NCPAP. SiPAP was provided at a sigh rate of 20/min, sigh time of 1.0sec. Matched MAPs between NCPAP and SiPAP were ensured via continuous intra-prong monitoring. Tidal Volumes(Vt) were obtained by calibrated respiratory inductance plethysmography. Intrapleural pressures were estimated by esophageal pressure monitoring. Breath-to-breath work of breathing was calculated from approximately 1 minute of pressure-volume data taken at the end of a 15 min period of CPAP or SiPAP support.

RESULTS: As seen in the Table, there were no differences in inspiratory or elastic WOB, or in resistive WOB (RWOB) between NCPAP and SiPAP. Similarly, no differences were found in respiratory rate (RR), Vt, phase angle, heart rate, or transcutaneous O_2 and CO_2 (TcO_2, $TcCO_2$).

NCPAP vs SiPAP (means±SD)

	NCPAP	SiPAP	P
MAP (cmH_2O)	5.4±0.6	5.6±0.5	0.13
Breaths analyzed, n	48±10	53±20	N/A
Inspiratory WOB/ml (cmH_20)	1.24±1.26	0.93±1.20	0.17
Elastic WOB/ml (cmH_2O)	0.97±0.95	0.71±0.88	0.14
Resistive WOB/ml (cmH_2O)	0.56±0.60	0.40±0.50	0.21
Phase angle (degrees)	28±28	21±22	0.50
Vt (ml)	3.1±1.9	3.3±3.46	0.8
RR (breaths/min)	57±12	53±17	0.33
Heart rate (beats/min)	133±64	131±70	0.84
TcO_2 (mmHg)	71±15	68±17	0.37
$TcCO_2$ (mmHg)	48±7	48±8	0.78

CONCLUSIONS: When compared to NCPAP, SiPAP appears to have no deleterious effects on WOB or other respiratory parameters over brief periods. Future studies must evaluate whether SiPAP will be beneficial in apnea reduction or provide other added benefit over NCPAP in preterm infants.

Supported in part by Viasys, Inc.

88 10:00 AM

High Flow Nasal Cannula in Preterm Infants: Effects of High Flow Rates on Work of Breathing

Kee H. Pyon, Zubair H. Aghai, Tarek A. Nakhla, Gary E. Stahl, Judy G. Saslow.
Pediatrics, Cooper University Hospital, Camden, NJ; Pediatrics, Our Lady of Lourdes Medical Center, Camden, NJ.

BACKGROUND: High flow nasal cannula (HFNC) has gained increased popularity as noninvasive respiratory support in the neonatal population. Our recent study on neonates has shown that at lower flow rates (3-5 L/min) of HFNC (Vapotherm 2000i©), there was no significant difference in the work of breathing (WOB) when compared to conventional nasal continuous positive airway pressure (NCPAP). However, higher flow rates of HFNC have been used on preterm infants without much available pulmonary mechanics data.

OBJECTIVE: Compare WOB and changes in end distending pressure (ΔP) in neonates on high flow rates using HFNC versus NCPAP.

DESIGN/METHODS: In this pilot study, 8 preterm neonates < 2000 grams were studied randomly on HFNC at 6, 7, 8 L/min (HFNC6, HFNC7, and HFNC8, respectively) and NCPAP at 6 cmH_2O (NCPAP6). The mean (± SD) birth weight was 873 ± 273 grams and gestational age 26.6 ± 2.1 weeks. At the time of study, weight was 1695 ± 458 grams, age 45.8 ± 19.3 days, and FiO_2 0.33 ± 0.10. Calibrated DC-coupled respiratory inductance plethysmography was used to measure tidal ventilation. An esophageal balloon estimated pleural pressure from which ΔP from baseline was calculated at each device setting. Using standard methods, inspiratory, elastic, resistive WOB (IWOB, EWOB, and RWOB, respectively) and lung compliance (C_L) were calculated.

RESULTS: The WOB parameters and ΔP at all HFNC flow rates were lower but not significantly different when compared to NCPAP6 (Table: mean ± SD). C_L was also similar for all the device settings.

	NCPAP6	HFNC6	HFNC7	HFNC8
IWOB (cmH_2O/ml)	3.99 ± 2.37	3.49 ± 1.07	3.07 ± 1.24	3.32 ± 1.30
EWOB (cmH_2O/ml)	3.12 ± 2.49	2.08 ± 0.44	1.90 ± 0.58	2.29 ± 0.82
RWOB (cmH_2O/ml)	3.46 ± 2.21	2.87 ± 1.15	2.34 ± 1.11	2.41 ± 1.04
C_L ($ml.kg^{-1}/cmH_2O$)	0.97 ± 0.49	1.26 ± 0.63	1.04 ± 0.24	1.13 ± 0.41
ΔP (cmH_2O)	1.71 ± 0.85	1.27 ± 0.92	1.63 ± 1.01	1.20 ± 0.50

Statistical Analysis: One Way RM ANOVA (NCPAP vs HFNC, no significance)

CONCLUSIONS: This pilot study shows that at flow rates > 5 L/min on HFNC, the WOB, ΔP, and C_L were not significantly different than NCPAP6. The low ΔP values reflect no significant lung overdistension with increasing HFNC flow rates. Additional infants will need to be enrolled and evaluated to determine conclusively whether higher flow rates on HFNC can be effectively and safely used in the preterm population.

89 10:15 AM Fellow in Training

Is There a Relationship Between the Initial (I) FiO_2 in the Delivery Room (DR) and Bronchopulmonary Dysplasia (BPD)?

Anita Stola, Jeffrey Perlman, Joseph Schulman. Department of Pediatrics; Division of Neonatology, New York Presbyterian Hospital Cornell MC, New York, NY.

BACKGROUND: BPD remains a common complication observed in up to 25% of VLBW infants (VLBWI).The pathogenesis is complex including O_2 toxicity, mechanical ventilation mediated via either volu/barotrauma or inflammation. A practice plan (PP) to ↓the I FiO_2 in the DR was introduced over the past year and has resulted in the use of a starting FiO2 of < 0.30 with up to 25% of VLBWI resuscitated with RA. We hypothesized that the use of lower I FiO_2 in the DR would be associated with reduction in BPD

OBJECTIVE: To determine whether ↓the I FiO_2 in the DR would modulate the development of BPD.

DESIGN/METHODS: VLBWI (n=53) ≤1500g who were part of the PP and admitted between 6/06-6/07 were evaluated. Data recorded included antenatal steroid (AS) use, BW, GA, DR respiratory support i.e.CPAP, intubation, I DR and admitting FiO_2, sex, I PaO2, pH and pCO2, surfactant use, duration of intubation and sepsis. BPD was defined as O_2 requirement at 36 weeks PCA. Data were analyzed using chi-square, t tests and logistic regression modeling.

RESULTS: 52/53 surviving VLBWI of BW 1051g,GA 28 wks were treated. The starting FiO_2 ↓ from 0.42±.06 to 0.28±.07 over 12 mo. 13/52(25%) were diagnosed with BPD. VLBWI with BPD vs No BPD were of ↓ GA i.e.26± 2vs 29± 2*, ↓ BW 825± 211vs1124±229*, received less AS 5/13 vs 2/39*, more likely male 9/13vs12/39*, intubated in DR i.e. 13/13 vs 14/39*, lesser initial PaO_2 58±16 vs 88 ±51* and pH 7.25±.07 vs 7.29±.07*, received more surfactant 12/13 vs 14/39*. Comparable I DR FiO_2 0.34±.10 vs0 .32±.10, admission FiO_2 0.54±.25 vs0.41±.28, pCO2 43±8 vs 49±6 were noted. By logistic regression analysis ventilation in DR, no AS use, male sex, BW was significantly related to BPD. The ROC using these four variables was O.85.

CONCLUSIONS: The data show that ↓the I FiO_2 in the DR is not associated with a reduction in BPD. Rather in this cohort BPD was predicted by male sex, lack of AS administration intubation in the DR and lesser BW with a predictive ROC value of 0.85. We speculate that a course of AS prior to birth in male VLBWI enhances lung development that translates into the ability to assist ventilation in a non-invasive manner. Importantly an initial step in reducing BPD in VLBWI is to ensure appropriate exposure to AS *p≤0.05.

Plenary II
Platform Session

Saturday, March 29, 2008 1:10 PM-4:00 PM

90 2:00 PM

Resuscitation of Neonatal Lambs with Pulmonary Hypertension with 21% and 100% Oxygen – Effect on Pulmonary Hemodynamics

Satyan Lakshminrusimha, Daniel D. Swartz, Sylvia F. Gugino, Karen Wynn, Robin H. Steinhorn, James A. Russell. Pediatrics, University at Buffalo, Buffalo, NY; Physiology and Biophysics, University at Buffalo, Buffalo, NY; Pediatrics, Northwestern University, Chicago, IL.

BACKGROUND: Ventilation with 21%O_2 is being adopted in more delivery rooms for initial resuscitation of term neonates. The effect of initial ventilation with 21%O_2 on pulmonary hemodynamics in neonates with *in-utero* pulmonary hypertension (PH) is not known. We recently reported that resuscitation with 21% or 100%O_2 for 30min results in a similar decrease in pulmonary vascular resistance (PVR) in normal lambs (Ped Res. Sep2007).

OBJECTIVE: To study the effect of resuscitation with 21% or 100%O_2 on PVR in lambs with PH.

DESIGN/METHODS: PH was induced in fetal lambs by antenatal ductal ligation at 126d of gestation (term ~ 145d). Lambs were delivered 9d later by C-section and ventilated with 21%O_2 (n=6) or 100%O_2 (n=8) for 30min. Control lambs without PH were ventilated similarly for comparison. Lambs were instrumented to measure PVR prior to delivery. After 30min, lambs with PH were ventilated with 50%O_2 and pulmonary vasodilator response to inhaled nitric oxide (NO) at 20 ppm was evaluated. Control lambs received an infusion of U46619 to increase their PVR and then exposed to inhaled NO.

RESULTS: PVR was significantly higher in lambs with PH compared to control (fig 1). PVR decreased significantly greater at 5min of age in PH lambs on 100%O_2 . However, there was no difference in PVR between 21% and 100%O_2 ventilated lambs beyond 10min of age. There was no difference in pulmonary arterial pressure and blood flow, systemic arterial pressure and left atrial pressure in PH lambs ventilated with 21% or 100%O_2. PVR prior to administration of inhaled NO was similar in all groups of lambs. Prior exposure to 100%O_2 impaired subsequent vasodilation to inhaled NO (fig 2) in both control and PH lambs.

CONCLUSIONS: 21%O_2 ventilation decreases PVR similar to 100%O_2 in neonatal lambs with PH by 10 min of age. We speculate that 100%O_2 ventilation results in an increase in reactive oxygen species and interferes with the vasodilator response to NO.

Figure 1. Change in pulmonary vascular resistance (PVR) in lambs with pulmonary hypertension (PH) and controls over 30 min of ventilation with 21% or 100% Oxygen

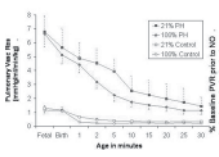
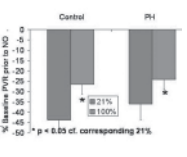


Figure 2. Relaxation response to 20 ppm of inhaled NO. PVR was increased in control lambs with an infusion of U 46619.



91 2:15 PM

Missense LEOPARD Syndrome Mutations in *PTPN11* Have Gain of Function Effects During Development

Kimihiko Oishi, Cindy J. Wang, Tabassum Rahman, Natalie Pica, Bruce D. Gelb.
Pediatrics, Center for Molecular Cardiology, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Missense mutations in the *PTPN11* gene, which encodes the protein tyrosine phosphatase SHP-2, cause LEOPARD syndrome (LS), an autosomal dominant disorder with pleomorphic developmental abnormalities including lentigines, cardiac defects, short stature, and deafness. LS resembles Noonan syndrome (NS), which can also be caused by missense *PTPN11* mutations. *In vitro*, LS SHP-2 proteins have reduced phosphatase activity (loss of function; LOF), while NS mutants result in gain of function (GOF), the latter attributable to perturbation of SHP-2 inactivation-activation mechanism. Our transgenic *Drosophila* model of NS, expressing the commonest mutation, N308D, in *corkscrew (csw)*, the fly homologue of *PTPN11*, has ectopic wing veins due to increased Egfr/Ras/MAP kinase (MAPK) signaling.

OBJECTIVE: To characterize the effects of LS mutant CSW during *Drosophila* development.

DESIGN/METHODS: We generated stable fly stocks of the genotypes *UAS-csw^{Mut}/CyO;tub-GAL4/TM2* for the following alleles: Y279C (LS), T468M (LS), Y279C/R465M (phosphatase-dead LS), and Y279C/Y542F (docking-deficient LS). Three independent lines were generated for each genotype. Wing phenotypes, assessed with light microscopy, were quantified and compared statistically using χ^2 testing. Immunoblotting and histochemistry was performed using anti-dpERK antibody.

RESULTS: Ubiquitous expression of the LS alleles Y279C and T468M resulted in ectopic wing veins as previously found for NS. MAPK activation was reduced in LS embryos compared to wild type CSW transgenic embryos but was more than in wild type embryos. Haploinsufficiency for Ras (*Ras85D*) and MAPK (*rolled*), achieved through intercrosses, suppressed the ectopic wing veins. Ectopic wing veins were not present in flies expressing the phosphatase-dead Y279C CSW but were present in flies expressing the docking-deficient Y279C CSW.

CONCLUSIONS: As in patients, the LS phenotype in flies closely resembled that observed in NS. The Y279C allele increased MAPK activation and required RAS-MAPK signaling for its phenotypic expression. These GOF effects could not be attributed to overexpression of minimally active CSW since similar expression of wild type CSW engendered no phenotype. Y297C's GOF effects required its minimal residual phosphatase activity. Thus, the LS alleles behave as developmental GOF alleles despite biochemical LOF, which we attribute to a dysregulated inactivation mechanism.

92 2:30 PM

Hospital Stays for Ambulatory Care Sensitive Conditions in Children with Sickle Cell Disease: 1997 to 2003

Suzette O. Oyeku, Ryan Conrad, Andrew D. Racine. AECOM, Children's Hospital at Montefiore, Bronx, NY; CUNY Graduate Center, NY, NY.

BACKGROUND: Ambulatory care sensitive conditions (ACSC) include diagnoses for which timely, quality ambulatory care might prevent hospitalization. Previous studies have shown that ACSC, particularly pneumonia account for a significant portion of discharges in sickle cell disease (SCD) patients. In the era of pneumococcal conjugate vaccine, it is not known whether the proportion of SCD discharges attributable to ACSC or whether lengths of stay (LOS) have changed over time among SCD patients.

OBJECTIVE: To assess trends and LOS in ACSC hospital discharges among children with SCD from 1997 to 2003.

DESIGN/METHODS: Hospital discharge data from 1997, 2000, and 2003 Kids' Inpatient Databases were used to assess trends in ACSC hospitalizations and LOS for patients' ages 3 months-20 yrs with a principal ICD-9 code for SCD. Multivariable logistic regressions were used to assess time trends in proportion of SCD discharges associated with ACSC controlling for covariate predictors. Log linear regressions were used to assess trends in LOS for ACSC among SCD patients controlling for patient level factors.

RESULTS: 58,007 discharges (1997 to 2003) among children with SCD were analyzed. The most frequent ACSC diagnoses during the entire period were pneumonia (13%), pharyngitis (3.9%), dehydration (3.8%), asthma (1.5%), seizures (1.4%) and otitis media (1.2%). The percent of discharges for non-pneumonia ACSC among SCD patients decreased from 14% in 1997 to 13.7% in 2003 (p=0.31). The unadjusted proportion of discharges for pneumonia declined from 13.7% in 1997 to 12.9% in 2003 (p<0.02). The proportion of discharges for ACSC increased by 10% from 1997 to 2003 when adjusted for age and other covariates (OR 1.10, p=0.005). No change in the adjusted proportion of discharges for pneumonia from 1997 to 2003 was observed (OR 1.04, p=0.196). Adjusted LOS among SCD patients declined by 0.3 days from 1997 to 2003 (p<0.001). Adjusting for this secular trend, LOS for SCD patients with non-pneumonia ACSC decreased by an additional 0.1 days (p=0.031) but LOS for pneumonia discharges did not decrease from 1997 to 2003 (p=0.731).

CONCLUSIONS: From 1997 to 2003, the percent of SCD discharges associated with ACSC increased while the percent of discharges for pneumonia remained unchanged. This may reflect treatment patterns for febrile illness in SCD. The relationship between these hospitalization trends and changes in ambulatory practice for the treatment of SCD warrants further study.

93 3:00 PM Fellow in Training

Oxidative Stress Disrupts Oligodendrocyte Maturation

Heather M. French, Polina Mamontov, Mary Reid, Judith Grinspan, Rebecca A. Simmons. Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Oligodendrocytes undergo a defined lineage progression from neural stem cell to mature oligodendrocyte. They display a maturation-dependent vulnerability to oxidative damage, inflammation and infection during the late oligodendrocyte progenitor stage. The mechanism by which oligodendrocyte injury occurs is unclear, but it is thought that altered regulation of key genes (Sox10, Shh, HDAC1-3) in the program of oligodendrocyte development disrupts normal maturation and subsequent myelinating abilities and may contribute to the pathogenesis of periventricular white matter injury (PWMI).

OBJECTIVE: Given the link between chorioamnionitis and PWMI, our objective is to determine if abnormal development of oligodendrocytes in the presence of oxidative agents is the result of altered epigenetic regulation of key genes regulating maturation.

DESIGN/METHODS: Mixed glial cultures were prepared from newborn rat brain (P1). After 7 days, oligodendrocyte precursors were isolated by immunopanning with monoclonal antibodies RAN2 and A2B5. Oligodendrocytes were treated with BSO (100mM) and t-BOOH (5mM) for 24-72 hours to induce oxidative stress. RNA was extracted from cultured oligodendrocytes (n=3) and expression of Sox10, Shh and HDAC 1-3 was measured by real-time PCR. Immunocytochemistry was performed on cultured oligodendrocytes to assess whether oxidative stress disrupted differentiation and altered histone acetylation patterns. TUNEL and caspase 3 staining was performed to determine whether cell death was responsible for decreased gene expression.

RESULTS: Oligodendrocyte precursor cells exposed to oxidants had significantly decreased expression of Sox10, Shh and HDAC3 (p<0.01), but there was no difference in expression of HDAC 1 and 2. Decreased gene expression was not due to cell death as demonstrated by TUNEL and caspase 3 staining (p<0.05). Oligodendrocyte differentiation was arrested in the oligodendrocyte precursor phase after exposure to oxidants (p<0.01). Oxidant exposure decreased global histone H3 and H4 acetylation (p<0.01).

CONCLUSIONS: The oxidative stress state in vitro leads to alteration of oligodendrocyte regulatory gene expression via epigenetic regulation, indicating that disrupted regulation of these genes may be causative in the pathogenesis of PWMI.

94 3:15 PM Fellow in Training

Enhanced Lung Maturation Using Intrauterine Gene Therapy

Gabriela I. Mihalache, Erin C. Killeen, Delon Callender, Janet E. Larson, J.C. Cohen, Manoj A. Biniwale. Pediatrics, Stony Brook University Medical Center, Stony Brook, NY.

BACKGROUND: In utero gene transfer is a successful method for transferring genes to the developing fetus. Our laboratory has previously shown that in utero adenoviral-mediated transfer of genes into the amniotic fluid results in sustained high-efficiency expression in rodent lung and intestine. The experience with in utero gene transfer in rodent models suggested that effective gene transfer was dependent upon the developmental stage of the target organ. For the lung the ideal time was immediately prior and during the early canalicular period. Swine model is ideal for preclinical experimentation as pigs share many physiological similarities to humans.

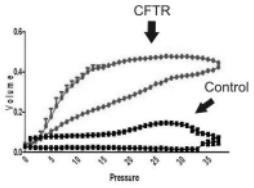
OBJECTIVE: To accelerate lung maturation to prevent lung disease related to prematurity using pig model.

DESIGN/METHODS: In utero gene therapy was performed in timed pregnant Yucatan pigs at canalicular stage (gestational age 9, 12 and 13 weeks). Cystic fibrosis transmembrane conductance regulator (CFTR) with luciferase and Enhanced Green Fluorescent Protein with beta-galactosidase (controls) were injected using adenovirus as a vector for gene transfer. At 48-96 hours after gene transfer, fetuses were delivered. Respiratory function tests were performed to assess the compliance of the premature lungs. Lung tissues were harvested for analysis of reporter gene expression using immunohistochemistry and gene assays. H and E staining was done to assess maturation of lung.

RESULTS: Respiratory function tests showed improved compliance of fetal lung tissue in CFTR treated animals as demonstrated by Pressure volume curves. The maturation of lung tissue was confirmed on H and E staining. Immunohistochemistry confirmed the presence of reporter genes differentiating CFTR treated animals from controls.

CONCLUSIONS: CFTR treated animals showed acceleration of lung maturation after in utero gene therapy performed at canalicular stage of lung development.

Figure 1: Results of respiratory function tests (Pressure volume loops) in CFTR treated premature pigs compared to controls



95 3:30 PM Fellow in Training

Oligodendrocyte Maturation in a Rabbit Model of Intraventricular Hemorrhage

Caroline O. Chua, Furong Hu, Hongmin Xu, Praveen Ballabh. Department of Pediatrics, Division of Newborn Medicine, RNICU, Maria Fareri Children's Hospital @ Westchester Medical Center, New York Medical College, Valhalla, NY; Department of Anatomy and Cell Biology, New York Medical College, Valhalla, NY.

BACKGROUND: Premature infants with germinal matrix hemorrhage-intraventricular hemorrhage (GMH-IVH) are predisposed to persistent motor deficits and developmental disabilities. These neurologic sequelae might be secondary to disturbances in myelination resulting from injury to maturing oligodendrocytes (OL).

OBJECTIVE: To evaluate OL lineage, including pre-OL (O4+) and immature OL (O1+), as well as myelination in premature rabbit pups with IVH compared to controls.

DESIGN/METHODS: Premature rabbit pups were delivered by C-section at 29 days (d) gestational age (term=32d), and alternately assigned to receive either intraperitoneal glycerol to induce GMH-IVH or no treatment (control) at 2 hours (h) postnatal age. The development of IVH and its severity were diagnosed by head ultrasound at 24h postnatal age. Corona radiata, corpus callosum, and internal capsule at the level of midseptal nucleus and ventro-lateral thalamus were evaluated for density of OL and myelination. Consecutive brain sections on d3 (corrected post-conceptional age, P1) and d5 (P3) were immunostained for O1 and O4. Sections on d14 (P11) and d21 (P18) were double-labeled with myelin basic protein (MBP) and panaxonal filament antibodies (n=3 pups at each time point). Myelination was measured by taking the ratio of myelinated (MBP) to unmyelinated fibers (panaxonal filament) using Metamorph software.

RESULTS: Pre-OL (O4+) counts were significantly lower in pups with IVH compared to controls in the three brain regions--corona radiata, corpus callosum and internal capsule-- on both d3 (p<0.05, p<0.001 and p<0.001, respectively) and d5 (p<0.001 each). Likewise, immature OL (O1+) were notably less in pups with IVH versus controls in the three brain regions both on d3 (p<0.01, p<0.01 and p<0.05) and d5 (p< 0.05, p<0.01 and p<0.01). Myelination was reduced in pups with IVH compared to controls on d14 in the corpus callosum and internal capsule (p<0.001 and p<0.01), but not in the corona radiata. On d21, myelination was decreased in all the three brain regions in pups with IVH versus controls (p<0.001 each).

CONCLUSIONS: There is histological evidence of reduced density of developing OL and decreased myelination in premature rabbit pups with IVH compared to controls. Thus, IVH might be attended by either cellular death of OL, its decreased proliferation and maturation, or both. We speculate that neuroprotection of OL might prevent white matter injuries and consequent cerebral palsy in infants with IVH.

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Transcription Factor Ap2δ Associates with Ash2l and ALR, a Histone Methyltransferase, To Activate *Hoxc8* Transcription During Development

Cheryl C. Tan, K.V. Sindhu, SiDe Li, Hitomi Nishio, Jason Z. Stoller, Kimihiko Oishi, Sahitya Puttreddy, Tamara J. Lee, Jonathan A. Epstein, Martin J. Walsh, Bruce D. Gelb. Pediatrics, Center for Molecular Cardiology, Mount Sinai School of Medicine, New York City, NY; Department of Cell and Developmental Biology, University of Pennsylvania School of Medicine, Philadelphia, PA; Cardiovascular Institute, University of Pennsylvania School of Medicine, Philadelphia, PA; Pediatrics, Children's Hospital of Pennsylvania, Philadelphia, PA.

BACKGROUND: The Ap2 family of transcription factors comprises five members with important roles during embryonic development. Aside from expression pattern differences, the specificity of their gene targets is unexplained, as all five share nearly identical DNA binding domains. *Tcfap2d*, which encodes Ap2δ, contains the most divergent transactivation domain, suggesting regulation through specific interactors.

OBJECTIVE: To identify and characterize a specific Ap2δ co-activator.

DESIGN/METHODS: A yeast two-hybrid screen was performed using Ap2δ's transactivation domain. Co-immunoprecipitation (co-IP) assays were performed using K562 cell lysates and anti-V5, -Ash2l and -Alr antibodies. *In vitro* histone methyltransferase (HMT) assays were performed. To identify targets, RNAi experiments were performed in N2A cells with *Tcfap2d*- or *Ash2l*-specific RNAi. Chromatin IP assays were performed using sonicated chromatin and incubated with antibodies as above.

RESULTS: Ash2l was identified as a potential co-activator of Ap2δ with a yeast two-hybrid screen and the interaction domain mapped to a small region of Ash2l. V5-tagged Ap2δ was expressed in K562 cells and co-immunoprecipitated endogenous ASH2L and ALR, an HMT known to complex with ASH2L. Moreover, these Ap2δ immunocomplexes possessed histone H3 methylase activity. Other Ap2 proteins failed to co-immunoprecipitate with Ash2l. Expression of *Hoxc8*, a known Alr target gene, was reduced when *Tcfap2d* or *Ash2l* expression was knocked down with RNAi. ChIP analysis showed that Ap2δ, Ash2l and Alr were present at two regions of the *Hoxc8* gene containing evolutionarily conserved, putative Ap2 binding sites. ChIP from *Tcfap2d* RNAi-treated cells documented a significant reduction of recruitment of Ash2l and Alr to those *Hoxc8* sites.

CONCLUSIONS: We provide the first evidence of an association between a gene-specific transcription factor and Alr. Furthermore, our studies reveal a functional role for Ap2δ in recruiting HMTs to specific gene targets such as *Hoxc8* that had not been previously documented for the Ap2 family. Taken as a whole, these findings provide a mechanism through which transcription factors can alter epigenetic marks in the histone code in order to achieve specific effects on gene regulation.

Adolescent Medicine Platform Session

Saturday, March 29, 2008 4:15 PM-5:45 PM

97 4:15 PM

Are There Neurocognitive Correlates of Risk Behaviors in Preadolescents?

Daniel Romer, Laura M. Betancourt, Joan M. Giannetta, Nancy L. Brodsky, Martha Farah, David Shera, Hallam Hurt. Adolescent Risk Communication Institute, The Annenberg Public Policy Ctr., The Univ. of PA, Phila., PA; Neonatology, The Children's Hosp. of Phila., Phila., PA; Ctr. for Cognitive Neuroscience, The Univ. of PA, Phila., PA; Div. of Biostatistics & Epidemiology, The Children's Hosp. of Phila., Phila., PA.

BACKGROUND: Numerous factors have been associated with risk behaviors (RB); however, data are few regarding the relation between neurocognitive functions (NCFn), especially frontal executive functions, and the initiation of RB.

OBJECTIVE: To assess NCFn in preadolescents and explore association of NCFn with initiation of RB.

DESIGN/METHODS: In a prospective study of developmental trajectories of NCFn, self-control, and risk-taking, youth ages 10-12 yrs. of mixed socioeconomic status were enrolled from Phila. schools. Self-control (SC) was assessed with the Eysenck I_7 Junior Impulsivity Scale (Imp) and Reduced Brief Sensation Seeking (SS) Scale. Three frontal executive function systems were assessed using 8 tasks: Cognitive Control (Counting Stroop, Erikson Flanker), Working Memory (Spatial Working Memory, 2-Back, Corsi Block Tapping, Digit Span) and Reward Processing (Reversal Learning, Balloon Analogue Risk Task). Four risk behaviors, fighting, gambling, alcohol, and cigarette use, were assessed through a self-report questionnaire based on the CDC Youth Risk Behavior Survey. Structural equation modeling (SEM) was used to test the relationships between NCFn, SC, and RB.

RESULTS: 384 participants (48% male; race 58% white, 28% African American, 8% Asian, 7% other; mean age 11.4 ± 0.9 yrs.) were enrolled. Assessment of risk behaviors showed: 28.9% were involved in fighting, 27.2% had gambled for money, 17.4% had used alcohol, and 2.9% had smoked cigarettes. Using SEM, our final model provided a good fit to the data (X^2/df = 1.30; RMSEA = 0.028; CFI = 0.942). In the model, both Imp (0.97) and SS (0.42) indexed SC, and all 4 risk behaviors loaded on a single factor, RB. SC was strongly related to RB (-0.67). Of the 3 frontal executive systems, Working Memory, composed of 4 tasks, was weakly associated with SC (0.16). Neither the Cognitive Control nor Reward Processing system was associated with SC. Of the 4 individual NCFn tasks from those 2 systems, only Reversal Learning was associated with SC (0.12).

CONCLUSIONS: In this cohort of preadolescents, self-reported Imp and SS are strongly associated with RB. In contrast, frontal NCFn is only weakly associated with these behaviors. The results suggest that, in preadolescents, characteristics such as IMP and SS rather than NCFn predict RB.

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98 4:30 PM

Predictors of Unstable Housing Among Adolescents with HIV

Jeffrey M. Birnbaum, Elizabeth A. Eastwood. Pediatrics, Downstate Medical Center, Brooklyn, NY; Health & Nutrition Sciences, Brooklyn College, City University of New York, Brooklyn, NY.

BACKGROUND: Adolescents with HIV are disproportionately in unstable housing. Adolescents in unstable housing cannot consistently adhere to HIV care regimes due to competing survival needs and are at risk for poor outcomes. Better understanding of the problems of adolescents has been hampered by research focusing on adults alone, so adolescents have remained underserved.

OBJECTIVE: (1) To examine the risk factors for antecedent and current housing instability; (2) describe which adolescents have stable versus unstable housing and changes in housing status; and (3) explore which factors predict continued housing instability.

DESIGN/METHODS: This study examines the housing status at two points in time of a sample of 224 adolescents with HIV aged 13-24 seen at an adolescent clinic in Brooklyn, NY. Participants were enrolled into treatment between January,1991- June, 2004. All participants were interviewed face-to-face by clinic staff using a standard intake interview. Univariate statistics were generated comparing prior unstable housing with stable housing and current unstable housing to stable housing. Multiple logistic regression equations were performed predicting prior unstable housing and current unstable housing.

RESULTS: Nearly 2 in 5 participants (38.6%, n=86) had a history of unstable housing, which was reduced to 12.9% (n=29) at the time of program entry. Housing status transitions revealed that 60.1% (n=134) continued to have stable housing, 11.7% (n=26) continued to have unstable housing, 26.9% (n=60) transitioned from unstable to stable housing, and three moved form stable to unstable housing. Multivariate logistic regression models predicting current and prior unstable housing, revealed four variables related to both outcomes: physical abuse; sexual abuse; referral from social services entities; and family member with substance abuse. Comparisons of those who remained in unstable housing versus transitioned to stable housing revealed higher rates of sexual abuse, suicide ideation, arrest, financial self-support, lack of family financial support, and younger age of sexual debut.

CONCLUSIONS: Adolescents' social problems associated with unstable housing include household member abuse and neglect. Social service referrals indicated the presence of unstable housing and other social problems resulting in treatment for HIV being a secondary concern. When adolescents in abusive situations come to the attention of programs for youth, they have a positive impact on transitioning adolescents to safer households.

99 4:45 PM

Low Literacy in Adolescents and Health Outcomes

Alexis Lieberman, Jennifer Cromley, Lauren Charles, Oscar Rodriguez, Maria Lopez-Marti, Srikanth Das, Diego Moguillansky.

BACKGROUND: Low literacy has been linked to poor health outcomes and poor health communication in adults; little is known about this association in adolescents.

OBJECTIVE: to determine the frequency of low literacy in an inner-city adolescent clinic, and its association with health communication, health outcomes, risk taking behaviors and nonadherence.

DESIGN/METHODS: We conducted a cross sectional survey of consecutively seen adolescents attending an inner-city clinic. Literacy level was assessed via a WRAT test; health communication by exit interview. Medical records were reviewed for health outcomes (uncontrolled asthma, obesity, caries); risk-taking behaviors (substance use, multiple sexual partners, STIs) and nonadherence (missed visits, non-response to abnormal test recall).

RESULTS: 81 teens participated: 93% female, 93% AA, mean age 17 (14–21), grades 7th- HS graduate. 33% scored >=2 grade levels below actual grade, 16% <=5th grade level. Age composition of the high- and the low-WRAT score groups was similar. Low literacy adolescents were significantly less likely to come to a visit with a question for the doctor, to ask any question of the doctor, to feel that all of their questions were answered, and to wish to change the way their doctor talked to them. There were no correlations between literacy level and health outcomes, risk-taking behaviors, and adherence.

CONCLUSIONS: Low literacy was common among adolescents at an inner-city clinic and was associated with poor health communication during the clinical encounter. Health communication strategies should include identification of low literacy and improved provider communication skills.

100 5:00 PM

Teen High-Risk Behaviors Improved by Patient-Centered Counseling Intervention

Kedron Horvath, Alexis S. Lieberman, Rebecca Merkh, Paul G. Whittaker. Department of Pediatrics, Thomas Jefferson University, Philadelphia, PA; Department of Pediatrics, Albert Einstein Medical Center, Philadelphia, PA; Family Planning Council, Philadelphia, PA.

BACKGROUND: Teens who present to an adolescent medicine clinic for "walk-in" visits often have a history of engaging in multiple high-risk behaviors, therefore offering an opportunity to assess risk and provide both immediate and on-going intervention.

OBJECTIVE: To assess the efficacy of a risk assessment and patient-centered counseling intervention for teens presenting on a walk-in basis.

DESIGN/METHODS: All walk-in patients seen 7/05-9/06 in an urban teen clinic completed a brief, written screen regarding contraception, substance use, violence, and depression. Patients who screened positive received immediate guidance and an invitation to on-going, on-site, patient-centered counseling, which included help setting personal behavior change goals. Progress in meeting goals was assessed using the Stages of Change model.

RESULTS: 1092 teens screened, 57% female. 74% had one or more risk factors, and were provided immediate guidance. 22% of those with risk factors agreed to on-going counseling; 32% of those who agreed to counseling actually participated in it. Males had a higher rate of risk factors, but female gender, partner abuse and depression were associated with accepting the intervention; younger age was associated with participating. The most common patient-chosen goals were increasing contraception and condom use, and improving communication with a partner or parent. At baseline, most teens were in pre-contemplation/contemplation stage; action/maintenance was achieved for >70% of goals, after an average of 4 counseling sessions.

CONCLUSIONS: An intervention of screening for risk behaviors, immediate guidance and on-site counseling was effective in assessing risk and providing intervention. Though a minority participated in counseling, those who did were likely to achieve personal goals.

101 5:15 PM House Officer

Internet Usage To Obtain Health Information Among Adolescents in an Urban Healthcare Network

Adeleye Afolayan, Cesar Mella, Zarlasht Manzoor, Cynthia Lewis, Ayoade Adeniyi, Ronald Bainbridge, Richard Neugebauer. Department of Pediatrics, Bronx Lebanon Hospital Center, New York, NY.

BACKGROUND: Limited data exists on the usage of the Internet to obtain health information by adolescents in an urban setting.

OBJECTIVE: The purpose of this study is to: 1) determine the frequency of Internet usage to obtain health information among adolescents in an urban health care network; 2) characterize how health information obtained is utilized; 3) identify which health topics are most commonly searched for.

DESIGN/METHODS: After obtaining informed consent, adolescents were recruited from an urban health care network in the South Bronx. Sites included 2 ambulatory health care centers and a hospital emergency department. Participants were 13–19 years old and English speaking. All participants completed an IRB approved, 19 item self-administered questionnaire. Questions assessed access to the Internet; Internet usage for health information; review of this information with the primary care provider; decision making based on information retrieved and view of its helpfulness. In addition, the questionnaire included demographic and general health items.

RESULTS: Among 100 respondents, mean age was 16 years, with 30% between 13-14 years and 40% over 16 years. Two thirds were girls; 80% Hispanic and the others were African-American. 80% were in grades 9 through 12. 92% reported that their household income was less than 40,000/year. All reported Internet use, of which 75% have used it for health information. 41% of which used the Internet "always, often or sometimes" to obtain health information. Over 20% averaged 10 or more hours a week of Internet usage, 30% less than 1 hour/week. Females use the Internet significantly more than males (65.8% vs. 34.2% p<. 001). 67% judged that Internet information improved their understanding of health problems; 58% thought that it improved their health. The six most commonly searched conditions in descending order were: STDs (44.8%); Exercise (44.2%); Acne (35.5%); Alcohol (35.1%); Pregnancy (33.8%) and Diet (33.8%).

CONCLUSIONS: Most of the teenagers surveyed in an inner city urban setting used the Internet to access health information and believe that it helps to improve their understanding of health problems. STDs and exercise were the most commonly searched topics. Findings suggest health care providers who care for adolescents in urban settings should discuss and provide anticipatory guidance on health information from the Internet.

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Outpatient (O) Directly Observed Therapy (DOT) for Children/Youth with Perinatally-Acquired HIV Infection (CYPAHIV) with Antiretroviral (ARV) Treatment Failure (TF) Due to Chronic Non-Adherence (CNA)

Eberechi I. Nwaobasi, Barry Dashefsky. Pediatrics, UMDNJ-NJMS, Newark, NJ.

BACKGROUND: CNA to prescribed ARV (due to many factors) accounts for most ARV TF in CYPAHIV. ODOT administered by professionals is standard management for tuberculosis. Coincidental DOT of ARV during hospitalization has been associated with short term reversal of TF due to CNA in CYPAHIV. Impact of systematic long term ODOT in this group has not been previously reported.

OBJECTIVE: To describe the impact of ODOT on the viral load (VL) & CD4 of a cohort of CYPAHIV with ARV TF due to CNA.

DESIGN/METHODS: Medical records of 13 CYPAHIV with ARV TF followed at FXB HIV Clinic (Newark, NJ) from 10/1/01-9/30/06 for whom ODOT was begun at the discretion of managing physicians because of CNA, were retrospectively reviewed to evaluate possible impact of this intervention on HIV control. TF was defined as failure to achieve a ≥ 3-fold decrement (D) in VL or an undetectable (U) VL and/or to maintain a stable CD4# & % within 4 months of start of an ARV regimen and standard attempts to ameliorate NA. Changes in VL & CD4 after start of DOT were primary outcome variables of interest. A successful intervention (SI) was defined as achievement and maintenance of a ≥ 3-fold D in VL or an U VL and/or a stable or increasing CD4 count within 4 months of starting ODOT.

RESULTS: Characteristics of 13 subjects (S) for whom DOT was initiated:13 African-Americans, 6 males, 5 DYFS involvement; DOT funded by DYFS (4), Medicaid (2), private insurance (2); mean age:12y (range:2-15y). Pre-DOT: mean/median VL:113,444/54,675; mean/median CD4# & %:302&11/164&3 . Post-DOT initiation (x6-9 m): mean/median VL:56,858 /3818; mean/median CD4# & %:403&17/272&14. For 6 of 13 S, ODOT was stopped within 12d-21m due to NA (3), change of residence (1), loss of funding (2); all 4 S for whom ODOT was stopped within 4m, remained TF (including 1 death); 1 S improved on ODOT but moved. 1 S improved on ODOT but had TF when ODOT was stopped. For 7 of 13 S, ODOT has continued for 9 -32m. Based on data 9m after start of ODOT, 6 of 7 S achieved SI: 4 achieved & maintained an U VL (within 1-4m) and 2 a ≥ 3-fold D in VL; all achieved a stable (4) or increased (3) CD4. The 1 non-SI had genotypic evidence of ARV resistance.

CONCLUSIONS: When implemented and maintained for >9m for patients with TF of ARV due to CNA , ODOT is associated with a high probability of significant virologic & immunologic improvement in response to ARV.

Developmental Biology Platform Session

Saturday, March 29, 2008 4:15 PM-5:45 PM

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The Cardiac L-Type Calcium Channel Is Required for Normal Cardiogenesis and Embryonic Survival

George A. Porter. Pediatrics, Yale University School of Medicine, New Haven, CT.

BACKGROUND: Cardiac function depends upon calcium transients which are initiated by the sarcolemmal L-type calcium channel (LTCC). These cyclic changes in calcium levels also appear to regulate gene expression in the developing and mature heart. We have previously shown that blockade of LTCCs in cultured embryos causes abnormalities in cardiac morphogenesis, particularly in the right ventricle (RV) and outflow tract (OFT), structures derived from the anterior heart field (AHF).

OBJECTIVE: To determine whether LTCCs are required for normal cardiac morphogenesis and embryonic survival.

DESIGN/METHODS: Global and conditional deletion of the major cardiac LTCC isoform, CaV1.2, was obtained using floxed-CaV1.2 mice mated to β actin-Cre or Mef2c-AHF-Cre mice. Mice were harvested at various stages of gestation and after birth and analyzed for genotype, survival, phenotype (gross morphology, histology, immunostaining), and apoptosis (TUNEL). Some litters were evaluated for cardiac function using *in vivo* mouse embryonic echocardiography.

RESULTS: Global deletion and conditional deletion of CaV1.2 from the AHF caused embryonic demise at around embryonic day (E) 14 and 15, respectively. In contrast, we observed normal survival and morphology in all heterozygotes and in CaV1.2-deleted embryos until about two days before death. Approximately one day before death, embryonic development slowed and the cardiac ventricles became globular. Although the RV and OFT had grossly normal structure, the ventricular myocardium became increasingly non-compacted starting approximately two days before death. TUNEL staining showed that apoptosis was increased in the OFT cushion and decreased in the trabecular myocardium. Finally, echocardiography demonstrated that cardiac function became increasingly disrupted and embryos developed pericardial effusions prior to death.

CONCLUSIONS: Deletion of CaV1.2 has no adverse effects during the early embryonic period but eventually leads to ventricular non-compaction, abnormal cardiac function with congestive heart failure, and late embryonic demise. These abnormalities may be due to altered apoptosis or differentiation of cardiac myocytes from their precursors.

104 4:30 PM Fellow in Training

Neonatal Ex4 Administration Normalizes Epigenetic Modifications at the Proximal Promoter of Pdx-1

Sara E. Pinney, HongShun Niu, Fenglen Li, Rebecca A. Simmons. Division of Endocrinology/Diabetes, The Children's Hospital of Philadelphia, Philadelphia, PA; Division of Neonatology, The Children's Hospital of Philadelphia, Philadelphia, PA; University of Pennsylvania, School of Medicine, Philadelphia, PA.

BACKGROUND: Intrauterine growth retardation (IUGR) has been linked to the development of type 2 diabetes in adults. The abnormal metabolic intrauterine environment affects the development of the fetus by permanently modifying gene expression and function of susceptible cells, like the Beta cell. Pdx-1, a pancreatic homeobox transcription factor, is critical to beta-cell function and development and its expression is permanently reduced in IUGR rats. USF-1, a ubiquitously expressed transcription factor known to mediate recruitment of chromatin remodeling enzymes, binds to the proximal Pdx-1 promoter and is obligate for Pdx-1 transcription. Previous studies have demonstrated that the reduction in Pdx-1 transcription in IUGR beta-cells is due to silencing epigenetic modifications at the proximal Pdx-1 promoter. Glucose dependent insulinotropic hormone (GLP-1) and its long acting agonist, Exendin-4 (Ex-4) prevent diabetes in the IUGR rat by normalizing Pdx-1 expression. The mechanism responsible for Ex-4 effects on Pdx-1 transcription has not been elucidated. The permanent increase in Pdx-1 transcription in the IUGR rat model after a 6-day course of Ex-4 treatment suggests an epigenetic mechanism may be responsible.

OBJECTIVE: Ex-4 normalizes Pdx-1 expression by reversing the aberrant chromatin modifications at the proximal Pdx-1 promoter known to be present in the IUGR state.

DESIGN/METHODS: IUGR and control newborn pups were treated with a 6-day course of Ex-4 or vehicle and neonatal islets were harvested for analyses. Histone modifications were analyzed by chromatin immunoprecipitation assays with antibodies to acetylated histone H3, acetylated histone H4 and USF-1

RESULTS: Ex-4 treatment of the IUGR pups significantly increased the acetylation of histone H3 and histone H4 at the PDX-1 proximal promoter compared to the IUGR vehicle group ($p<0.05$). In IUGR pups treated with vehicle, USF-1 binding was not detectable whereas IUGR animals treated with Ex-4 had measurable binding of USF at the site of the PDX-1 promoter.

CONCLUSIONS: Ex-4 treatment increases histone H3 and histone H4 acetylation at the proximal Pdx-1 promoter thereby increasing Pdx-1 expression and preventing the development of diabetes in the IUGR rat.

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A Novel Cre Reporter Mouse Reveals New Derivatives of Pax3-Expressing Precursors

Jason Z. Stoller, Karl R. Degenhardt, Li Huang, Min Min Lu, Jonathan A. Epstein. Cell and Developmental Biology, Penn Cardiovascular Institute, University of Pennsylvania, Philadelphia, PA; Pediatrics/Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Pediatrics/Cardiology, Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Pax3 is a transcription factor that is mutated in Waardenburg syndrome and has been implicated in rhabdomyosarcoma tumors. Pax3 precursors differentiate into many neural crest and somite derived tissues. Controversial Pax3 derivatives have been described in fate mapping studies using currently available reporter mice.

OBJECTIVE: To unequivocally identify novel and previously contentious Pax3 derivatives using a newly created Cre reporter mouse.

DESIGN/METHODS: A nuclear localized GFP-*LacZ* fusion gene (GNZ) was knocked-in to the ROSA26 locus in mouse embryonic stem cells to create GNZ reporter mice. GNZ mice were crossed with Pax3-Cre knock-in mice. Pax3 derivatives in the resulting embryos were visualized with X-gal staining, GFP fluorescence, immunohistochemistry and confocal microscopy.

RESULTS: The GNZ reporter mouse enabled the identification of Pax3 derivatives at a single cell resolution. Previously described Pax3 derivatives were identified by punctate nuclear staining in the dorsal neural tube, somites, kidney, bowel, outflow tract endocardial cushions and aortic smooth muscle. Controversial derivatives in the epicardium, myocardium and conduction system were notably absent. A previously unknown population of Pax3 derived venous endothelial cells were discovered in the cardinal vein derived left superior vena cava.

CONCLUSIONS: We show that the use of this newly developed GNZ reporter line allows for enhanced resolution, detection and co-localization. The reporter has certain advantages related to the nuclear expression and the combined expression of both β-galactosidase and GFP activities. We report a previously unrecognized subset of venous endothelial cells derived from Pax3 expressing precursors.

106 5:00 PM Fellow in Training

Identification of Progenitor Cell Characteristics in Naive Human Fetal Lung Epithelium

Kristen Glass, Linda Varghese, Linda Gonzales, Michael Beers, Cherie Foster. Pediatrics/Neonatology, Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, Philadelphia, PA; Pulmonary and Critical Care Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA.

BACKGROUND: Lung progenitor cells are characterized by proliferative capacity and expression of markers of multiple cell types. Bronchoalveolar stem cells (BASC) have been characterized by co-expression of the Type 2 (T2) cell marker, SP-C, and the Clara cell marker, CC10 (Kim et al, Cell, 2005) in both adult murine normal lung and lung cancer. Whether these characteristic markers identify BASC in human fetal lung (HFL) is unknown.

OBJECTIVE: To characterize potential progenitor cells in naive human fetal lung epithelium.

DESIGN/METHODS: We isolated naive fetal lung epithelial cells and cultured them for up to 7d in Waymouth's media (Way) ± Keratinocyte Growth Factor (KGF), 1% Fetal Bovine Serum (FBS) or both. Proliferation was assessed by immunostaining for Ki67 and counting the number of proliferating cells/total cells in 9 randomly selected high powered fields (hpf) at 60X (n=3 experiments). T2 (SP-B, PGC, SP-C), T1 (PAI-1) and Clara cell (CC10) marker expression was examined using real time RT-PCR. Results from three experiments were analyzed using ANOVA. SP-C and CC10 co-expression was assessed by immunostaining and confocal microscopy.

RESULTS: Together, KGF+FBS elicited marked proliferation in naive fetal lung epithelial cells at 4d (16.5±3.4% proliferating cells, mean±SE, $p<0.01$) and 7d (11.3±1.7%, $p<0.05$) vs. the background rate of 2.3±0.4% proliferating cells in Way alone. RT-PCR for lung epithelial cell markers identified detectable expression of all T1, T2, and Clara cell markers surveyed. SP-C mRNA was present at 0.09±0.03 ng/μl and CC10 at 152±66ng/μl. These findings were corroborated by the detection of CC10/SP-C dual positive cells using confocal microscopy.

CONCLUSIONS: Progenitor cells exist in naive human fetal lung epithelium. These cells are capable of proliferation, express markers of several alveolar epithelial cell types and co-express SP-C and CC10, a previously identified hallmark of BASC. HFL, therefore, is a potentially important source of BASC for the study of lung stem cell biology.

107 5:15 PM

Hypoxia Inducible Factor-1α Activity Is Increased in Neonatal Neutrophils

Anna Vetrano, Faith Archer, William Hoffman, Barry Weinberger. Pediatrics-Neonatology, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

BACKGROUND: Hypoxia inducible factor-1 (HIF-1) suppresses neutrophil apoptosis and regulates transcription of hypoxia-responsive genes, such as vascular endothelial growth factor (VEGF). Under normoxic conditions, the HIF-1α subunit is degraded by prolyl hydroxylases. On exposure to hypoxia, these enzymes are inactivated and HIF-1α translocates to the nucleus, where it binds to target genes. Neonates are exposed to relative hypoxia during gestation, labor and delivery. We have previously shown that neutrophils from neonates exhibit decreased apoptosis and clearance from inflammatory sites compared to adult cells, possibly increasing susceptibility to inflammatory diseases.

OBJECTIVE: We hypothesize that HIF-1α activity is increased in neonatal neutrophils, compared to adult cells, and that this contributes to impaired apoptosis and increased expression of HIF-1 target genes in these cells.

DESIGN/METHODS: Neutrophils were isolated by gradient centrifugation from umbilical cord and adult blood. Cells were cultured under hypoxic (95% N_2, 5% CO_2) or normoxic conditions, in the presence or absence of the prolyl hydroxylase inhibitor dimethyloxallyl glycine (DMOG; 500 μM). Apoptosis was quantified by Annexin-PI binding and flow cytometry. Expression of HIF-1α and VEGF was measured by real-time PCR. HIF-1α protein was quantified by indirect immunofluorescence.

RESULTS: We found that apoptosis was impaired in neonatal, relative to adult neutrophils, and that this difference was enhanced by hypoxia. HIF-1α gene expression was similar in adult and neonatal neutrophils. In contrast, HIF-1α protein was markedly increased in neonatal cells, under both normoxic and hypoxic conditions. Consistent with increased HIF-1α activity, expression of the HIF-1α target gene VEGF was significantly increased in neonatal neutrophils, compared to adults. VEGF was decreased in both adult and neonatal neutrophils after exposure to hypoxia. This effect was also observed under normoxic conditions in the presence of DMOG, indicating HIF-1α-dependence.

CONCLUSIONS: Neonatal neutrophils are more sensitive to hypoxia-induced suppression of apoptosis than adult cells, and this is associated with increased HIF-1α protein expression and transcriptional activity. Increased HIF-1α activity in neonatal neutrophils may be due, in part, to resistance of the protein to hydroxylase-mediated degradation. This may increase the risk of chronic inflammation in newborns under pathologic conditions.

108 5:30 PM

Static Stretch of Differentiated Human Fetal Type II Cells Promotes Transition to a Type I Phenotype

Cherie Foster, Linda Varghese, Linda Gonzales, Susan Margulies. Pediatrics, Division of Neonatology, The Children's Hospital of Philadelphia, Philadelphia, PA; School of Engineering and Applied Science, University of Pennsylvania, Philadelphia, PA.

BACKGROUND: Static stretch by fetal lung fluid is required for alveolar development. Animal models suggest that large static stretch, as with in utero tracheal obstruction or extreme ventilator PEEP, promotes upregulation of T1 and downregulation of T2 markers. Cellular pathways regulating this transition are not fully defined. One candidate family of messengers is the Rho GTPases, tightly coupled to the cytoskeleton and previously implicated in fetal lung branching morphogenesis (Moore, Dev Dyn, 2005).

OBJECTIVE: To characterize effects of static stretch on phenotype modulation and activation of Rho A in human fetal lung (HFL) T2 cells.

DESIGN/METHODS: HFL T2 cells were cultured on silastic using established models of T2 cells (Gonzales, Ped Path Mol Med, 2001) and equibiaxial stretch (Tschumperlin, AJP Lung, 1999) for 72h. Cells were subjected to a 10% (42% total lung capacity [TLC]) or 37% ↑ in surface area (SA, 100% TLC) for 24hr. T2 (SP-B and Pepsinogen C [PCG, Foster, AJRCMB, 2004]) and T1 cell (Claudin 7, PAI-1, and Caveolin-1) markers were analyzed by Western blotting (WB) and real time RT-PCR. Rho A activation was assessed by stress fiber quantitation and ELISA assay. Stress fiber changes were assessed with fluorescent phalloidin staining and Image Pro-Plus 6.0 software. 3-6 experiments were analyzed by student's t-test.

RESULTS: No changes were seen in T2 proteins by WB. T2 mRNAs decreased at both levels of stretch: [10%: SP-B (61 ±8%) and PGC (58±9%) of unstretched control, 37%: SP-B (50±5%) and PGC (52±8%) of unstretched control, all $p\leq0.05$]. T1 protein analysis revealed induction of Caveolin-1 at 10%↑SA(1.7±0.32-fold, $p=0.08$ vs. 24h no stretch) and both Caveolin-1 (1.8 ±0.29-fold, $p<0.05$) and PAI-1(1.4 ±0.19-fold, $p=0.08$) at 37%↑SA. T1 mRNAs (Claudin 7, PAI-1 and Caveolin-1)were induced with 10%↑S.A.(all $p<0.05$), with induction of Claudin 7 (1.7-fold) and PAI-1(3.4±0.42-fold, respectively ($p<0.05$ vs unstretched control) at 37%↑SA. ELISA revealed activation of Rho within 5 min for both stretch levels. Stress fibers increased with static stretch. At 37%↑SA, there was a 27% increase in stress fiber fluorescence intensity/ cell ($p<0.05$ vs. unstretched control).

CONCLUSIONS: Static stretch of differentiated T2 cells promotes transition to a T1 phenotype. Rho GTPase activation in this model identifies an attractive candidate second messenger system by which stretch-induced cytoskeletal stimulation could elicit phenotype changes.

General Pediatrics II Platform Session

Saturday, March 29, 2008 4:15 PM-5:45 PM

109 4:15 PM Fellow in Training

The Efficacy of EMLA Versus Synera for Venipuncture in Children

Ting A. Lee, C. Anthoney E. Lim, Kathy Freeman, Catherine C. Skae. General Pediatrics, Children's Hospital at Montefiore, Bronx, NY; Department of Epidemiology and Population Health, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY.

BACKGROUND: The Synera patch uses a controlled heating system to transcutaneously deliver a lidocaine/tetracaine mixture for analgesic effect. No published studies compare the efficacy of the Synera patch with other topical anesthetics.

OBJECTIVE: To compare the efficacy of the Synera patch with Eutectic Mixture of 5% Lidocaine-Prilocaine (EMLA) as a topical anesthetic for venipuncture in pediatric patients.

DESIGN/METHODS: We conducted a prospective, double-blind, randomized trial with patients 4-12 years old requiring venipunctures in outpatient subspecialty clinics of a large, academic, tertiary care Children's Hospital. After meeting inclusionary criteria, subjects were randomized to receive Synera for 20 minutes or EMLA for 60 minutes, after which the site was assessed for pruritus, erythema, edema, or pallor. Venipunctures were performed by one of two experienced phlebotomists. A blinded observer recorded pain scores using the 1-5 numerical rating scale (NRS) during tourniquet placement, needle insertion, and 5 minutes post-procedure. Child and parent assessed pain with the Wong-Baker FACES Scale and the NRS, respectively. The primary outcome was the proportion of subjects reporting "no pain" (pain=0). Secondary outcomes were parent and observer measures of the child's pain and the presence of skin reactions to the medications.

RESULTS: Fifty-six subjects have been enrolled with mean age 8.1yrs, 41% male, 58% with <10 venipunctures, and 9% with prior topical anesthetic use. There were no significant differences between groups in subject characteristics or procedural characteristics except Synera was placed for a significantly shorter period of time compared to EMLA. There was no significant difference between treatment groups in patients reporting "no pain" (27/28 Synera, 25/28 EMLA, $p=0.661$). There were significantly more patients with pallor at the site in the EMLA group (10 vs 2, $p=0.020$). There was no significant difference between groups in pain rating by subjects ($p=0.340$), parents ($p=0.196$), and observers (tourniquet $p=0.503$, needle stick $p=0.815$, post-procedure $p=0.159$). Pain scores were significantly correlated (child-parent $R=0.877$, $p<0.0001$; child-observer $R=0.399$, $p=0.0023$; parent-observer $R=0.551$, $p<0.0001$).

CONCLUSIONS: This ongoing equivalency study strongly suggests that Synera is as effective as EMLA for pain associated with venipuncture. Future studies will focus on the efficacy of Synera and other topical anesthetics for other common pediatric procedures.

110 4:30 PM

Nutritional Status of Children After a Food Supplementation Program Integrated with Routine Health Care in Migrant Communities of the Dominican Republic

Kavita Parikh, Gabriela Marein-Efron, Shirley Huang, Samir S. Shah, Geraldine O'Hare, Rodney Finalle. Division of General Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; School of Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA; Division of Gastroenterology, Hepatology and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; Departments of Pediatrics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, PA; Cobbs Creek Primary Care Center, Children's Hospital of Philadelphia, Philadelphia, PA; Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA.

BACKGROUND: Malnutrition in children lowers resistance to infection and increases mortality from common illnesses such as diarrhea and respiratory infections.

OBJECTIVE: To compare baseline and 1-year post-intervention acute and chronic malnutrition rates in children of migrant workers in the Dominican Republic after initiation of a food supplementation program given in conjunction with routine health care visits.

DESIGN/METHODS: This cross-sectional study was conducted in 5 rural communities or bateyes in the Dominican Republic. Children 0 to 18 years of age were eligible if they received routine care from local mobile clinics. Height and weight measurements from 2005 were baseline data and measurements from 2006 were data after initiation of a food supplementation program. Acute malnutrition was defined using 2006 WHO Child Growth Standards for <5 yr olds and the Waterlow criteria with 2000 US CDC growth charts for ≥5 yr olds. Chronic malnutrition was defined using the Kanawati and McLaaren criteria with 2000 US CDC growth charts. Chi-square or Fisher exact tests were used to compare rates of malnutrition.

RESULTS: Among 175 children in 2005, 52% were female, mean age was 5.3 years, and 59% were <5 years. Among 148 children in 2006, 48% were female, mean age was 5.6 years, and 57% were <5 years.

Compared to baseline, fewer overall children suffered from acute malnutrition after the food supplementation intervention [34 of 114 children (23%) vs. 70 of 175 (40%), p=0.001]. The reduction in malnutrition was noted in males (p=0.044) and females (p=0.010), in 4 of the 5 bateyes, and depended on patient age. Over the year, the nutritional status improved for children <5 years of age (p=0.002) and 6 to 11 years of age (p=0.033) but not children ≥12 years of age (p=0.8). Rates of chronic malnutrition decreased from 33% to 18% after food supplementation (p=0.003). This effect was seen in all 5 bateyes though the magnitude of effect varied substantially by bateye and was present in males (p=0.007) but not females (p=0.1). Chronic malnutrition rates were not different when stratified by age.
CONCLUSIONS: The concept of food supplementation in the context of routine health care visits decreased the prevalence of childhood acute and chronic malnutrition, and warrants further exploration as a way to reduce childhood malnutrition in resource scarce areas.

111 4:45 PM House Officer

Maternal Ethnicity, Education and Observation of Infant Sleeping Position in the Hospital Nursery as Correlates of Back-to-Sleep Practices

Irfan Ali, Gracia Marte, Gawin Tsai, Ram Kairam, Richard Neugebauer, Gerrad Augustine, Anantha Harijith, Ronald Bainbridge, Ayoade Adeniyi. Department of Pediatrics, Bronx Lebanon Hospital Center, Bronx, NY; Departments of Pediatrics, Columbia Universty Medical Center, Bronx, NY.

BACKGROUND: Sudden infant death syndrome (SIDS) is the leading cause of mortality in babies between one month and one year of age. Despite a substantial decline in the incidence of SIDS following "Back to Sleep" campaign, SIDS still results in about 2,500 deaths each year, a disproportionate number from low-income, ethnic minority neighborhoods.
OBJECTIVE: To examine whether maternal ethnicity, educational level, and observed sleeping position in the hospital nursery are associated with infants' sleeping positions at home.
DESIGN/METHODS: Socio-demographic data, information on infant's sleeping position observed in the hospital nursery and home sleeping position (current or planned), were obtained via interview from parents (n=541). Differences in proportions were tested using chi-square; maximum likelihood logistic regression was used for multivariate analyses. Statistical significance was set at p<0.05.
RESULTS: Among respondents 61% were Hispanic, 24% African American and 13% African. Overall, 37% of respondents always placed their infants to sleep on their back. Always placing the child to sleep on their back was most common among Africans (59%), than among African Americans (40%) or Hispanics (33%) (p<0.002). Higher education was associated with greater likelihood of correct practices, e.g., among women with 1-11 years of education, 32% place their infants to sleep on their back as compared with 42% among college graduates, p<0.08. However, specific knowledge of SIDS, as distinct from higher education generally, was not associated with correct sleeping position. In controlled analyses, their higher level of education explained the higher proportion of Africans employing correct Back-to-Sleep practices. Observation of hospital nursery practice was unassociated with practices later adopted in the home.
CONCLUSIONS: Among the ethnic groups, Africans were more likely to employ correct back-to-sleep practices. The data also suggest that women with more years of education employed correct practices more often than less educated women, albeit independently of any specific knowledge about SIDS. Back-to-Sleep practices at home were not correlated with those employed in the hospital nursery. The Back-to-Sleep campaign should increase efforts to reach the Hispanic and the less well-educated members of the US population.

112 5:00 PM

Under-Representation of Minority Children in Pediatric Statin Trials

Brook Belay, Andrew Racine, Peter F. Belamarich. Pediatrics, Temple University, Philadelphia, PA; Pediatrics, Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: Among those studies that report race, there is a marked under-representation of minority children in clinical trials of HMG CoA reductase inhibitors (statins) in heterozygous familial hypercholesterolemia (heFH).
OBJECTIVE: The purpose of this analysis was three fold: (1) to obtain and report the racial composition of pediatric statin trials; (2) to explore the hypothesis that known founder effects among populations of Caucasian children may have facilitated or favored their inclusion in statin trials; and, (3) to determine whether there was any evidence that the selective lipid screening guidelines based on family history may inadvertently identify less minority children who would otherwise qualify for this type of study.
DESIGN/METHODS: We conducted a MEDLINE search using relevant terms to identify all pediatric heFH statin trials. We contacted the corresponding authors to obtain race/ethnicity and the presence of founder effects. Studies meeting entry criteria were retrieved and data retrieved for each of the objectives.
RESULTS: Ninety-four percent (94%) of the 885 children with heFH enrolled in statin trials from around the world for whom we were able to obtain race were Caucasian. This was true even in study sites where there was a large population of minority children and where founder-effects have not been described. Strong but indirect evidence from both the adult literature and the pediatric literature suggest that the Family history based screening engenders a health care disparities for minority/ disadvantaged children.
CONCLUSIONS: Intensive efforts will be required to arrive at a fair representation of minority children in studies of pediatric FH. Moving forward, it will also be important to ensure that screening guidelines do not inadvertently engender health care disparities in minority children.

Study	Country	No. Patients	Black	Asian	Hispanic	Other	White
Steiner 1992	Austria*	15					15
Knipscheer 1990	Netherlands*	72	5	1	0	0	66
Couture 1998	Canada**	83					83
Stein 1999	Finland*, USA*	132					>96%/125
Athyros 2002	Greece*	16					16
Dreissner 2003	Austria**	20					20
McCrindle 2003	Canada*, Norway, South Africa, USA	187	3	3	0	9	172
Weissen 2004	Netherlands**	214	1	6	0	0	207
Hedman 2005	Finland*	30					30
van der Graaf 2005	Netherlands, South Africa*	84					84
Classo 2005	USA*	54				11	43

*Personal communication with corresponding author.
†Founder effect presence unknown.
‡Founder effect likely.
§Founder effect confirmed.

113 5:15 PM House Officer

Acute HIV Syndrome in a General Pediatric Practice: Missed Opportunities

Andres F. Camacho-Gonzalez, Natasa Milosavljevic, Barbara Kelly. Pediatrics, Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: Despite prevention efforts, improvement in sexual behavior among adolescents, and superior retroviral therapy, HIV rates have increased among youth yet most adolescents are unaware of their HIV status. Higher level of suspicion and identification of Acute HIV Syndrome may help reduce the spread in this high-risk population.
OBJECTIVE: To determine provider level of suspicion and identification of Acute HIV Syndrome among teens presenting with an acute illness to an inner city clinic in Philadelphia.
DESIGN/METHODS: We conducted a retrospective survey of 54 adolescents aged 15-23 seen at an inner city clinic from 7/07-10/07 and diagnosed with ICD-9 codes of pharyngitis, viral syndrome, mononucleosis, or lymphadenopathy. Charts were reviewed for demographic, risk factors for HIV, clinical and laboratory data.
RESULTS: Patients' mean age was 17; 72% female, 94% Afican American and 4% Hispanic. As per patient report all patients were heterosexual, 78% were sexually active with 61% with more than one partner; 52% used intermittent or no barrier contraception, 32% had a history of sexually transmitted infection (STI), 10% had a history of sexual assault and 24% had used illicit drugs (no IV drug use). Most (74%) had clinical symptoms compatible with Acute HIV Syndrome (2+ symptoms). Of these, 78% were sexually active and 35% had history of STI. Based on symptoms and sexual history 57% (31/54) were at risk for Acute HIV Syndrome. Most common diagnoses were pharyngitis (50%), viral URI (30%) mononucleosis (12%). Non-HIV diagnostic studies were sent on 84 % of patients diagnosed with pharyngitis (13% positive), 40% with URI (0% positive), 100% with mononucleosis (17% positive). Only 6.4% (2/31) of at risk patients were offered an HIV antibody test and none were offered RNA testing.
CONCLUSIONS: Missed opportunities for identification of Acute HIV Syndrome are common. Further studies need to explore provider knowledge and behavior, availability of HIV testing, and other barriers to implementing strategies to enhance acute HIV recognition in inner city clinics serving high-risk youth.

114 5:30 PM House Officer

Improving Tuberculosis Case-Finding in an Inner City Pediatric Clinic

Gina Montealegre, Guadaloupe Lopez-Marti, Krissa George, Erika Mendoza, Ryan Kotton, Barbara Black, Alan Schindler, Barbara Kelly. Department of Pediatrics, Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: The incidence of tuberculosis (TB) in Philadelphia is fifth highest in the US. The diagnosis of latent TB infection (LTBI) or TB disease in a child is a "sentinel healthcare event" representing recent TB transmission in the community. While screening is an important TB control measure, due to the low prevalence of TB among low-risk children the CDC recommends screening in high-risk children only.
OBJECTIVE: To evaluate the effect of a targeted TB screening program on identification of children with LTBI and TB disease in a pediatric practice serving a high-risk community.
DESIGN/METHODS: Prior to 4/07, screening PPDs were placed routinely on all children at age 9-12 months, when required for school physical exams, and on incidentally identified high-risk children. In 4/07, we redesigned our TB screening program to include: a brief screening questionnaire to identify high-risk patients at every well child visit; PPD placement only for children identified as high-risk and at least 12 months old; staff education; educational handouts and reminder wristbands; telephone recall for no shows. After 5/07, we discontinued wristbands and telephone recalls. We report on numbers of PPDs performed, show rates for PPD reading and number of cases of LTBI or TB disease identified.
RESULTS: From 8/1/06-12/31/06, 336 PPDs were placed (average 67/month): 137 (41%) patients were low risk; 76 (23%) high-risk; 121 (36%) unknown risk. Of these, 103 (31%) had their PPD read and 2 patients were identified with LTBI. From 4/23/07-5/21/07, 66 high-risk patients had PPDs placed; 45 (68%) returned for PPD reading and 2 patients were identified with LTBI. From 10/29/07-11/29/07, 76 high-risk patients had PPDs placed; 33 (43%) had their PPD read (2 by a school nurse) and 3 patients were identified with LTBI. No cases of TB disease were identified during the study periods.
CONCLUSIONS: While targeted PPD testing did not lead to a reduction in the number of children tested, it did result in increased efficiency in identifying LTBI (2/336 PPDs placed before targeting, 5/142 after targeting). Initial improvement in PPD reading rates declined when reminder wristbands and recalls were discontinued. Continued efforts for improving PPD reading rates are needed.

Metabolism/Obesity Platform Session

Saturday, March 29, 2008 4:15 PM-5:45 PM

115 4:15 PM Fellow in Training

Correlation of Weight Gain in First Ten Days of Life and Childhood Obesity

Riti S. Dayal, Fernanda E. Kupferman, Fernando Llopiz, Salimah Walani, Kanchana Roychowdhury. Pediatrics, Flushing Hospital Medical Center, Flushing, NY.

BACKGROUND: Previous studies have shown that rapid weight gain in infancy is associated with the development of childhood obesity. Furthermore, possibly critical periods may exist for the development of obesity, like early infancy and 5-7 years. These critical periods should serve to focus preventive efforts.
OBJECTIVE: To evaluate whether changes in weight in first ten days of life are associated with overweight status at 5 yrs of age.
DESIGN/METHODS: This is a descriptive, cross-sectional study. Medical records of 5 yr-old children were reviewed. Weight at birth, at 10 days of life, and Body Mass Index (BMI) at age 5 were recorded. Neonates were divided into those who gained weight during the first week of life, and those who did not. Five year-olds were classified by BMI into three groups: normal (BMI <=85th perc.), at risk (85th-95th perc.), and overweight (> 95th perc.). Weight change was compared with BMI percentile at 5 yrs of age. Parental weight and height, child's nutrition during first week of life, physical activity, hours of TV viewing, and socioeconomic status were obtained by telephone interview. Parental BMI was calculated.
RESULTS: Fifty subjects participated in the study; 52% were males. Fifty-four percent gained weight in first week of life. At 5 yrs of age 48% had normal BMI, 10 % were at risk, 42% were overweight. Thirty-four percent were breast-fed, and 66% were formula-fed. There was no significant association between weight change

from birth to ten days of life and BMI status at 5 yrs (Chi-square=0.34; p=0.58), between BMI of father and weight status at 5 yrs (T-statistic= -0.824; p= 0.268); or between mode of feeding and BMI status at 5 yrs (Chi-square=0.009; p=0.924). A significant association was found between gender and BMI status at 5 yrs (Chi-square =3.88; p=0.049), between BMI of mother and BMI status at 5 yrs (T-statistic= -2.4; p=0.018), and between mode of feeding and weight change in first 10 days of life (Chi-square =13; p=0.00).
CONCLUSIONS: We found no association between weight gain in first 10 days of life and overweight status at age 5. Formula-fed babies are prone to increased weight gain by ten days of life. Maternal BMI had an association with being overweight at 5 yrs. Formula vs breast feeding had no association with BMI status at 5 yrs of age. Females were found less likely to be overweight at 5 yrs.

116 4:30 PM House Officer

The Effect of an Intervention Program on Overweight Second and Third Grade Students in an Inner City Elementary School: A Pilot Study

Sister Melinda Lando, K. Nicole Jalandoni, Haydee Larralde, Nicholas Obiri, Ronald Bainbridge, Ayoade O. Adeniyi, Richard Neugebauer. Pediatrics, Bronx Lebanon Hospital Center, Bronx, NY.

BACKGROUND: Obesity is a growing epidemic in school-aged children. Effective intervention programs are lacking. In NY city, Hispanic children have the highest obesity rate among ethnic groups.
OBJECTIVE: The objective of this pilot study was to examine the efficacy of a nutrition and exercise program for overweight second and third grade students in a public elementary school in South Bronx: >50% of school attendees are Hispanic.
DESIGN/METHODS: After obtaining informed consent from caregiver and assent from the child, 28 2nd or 3rd grade students with BMI ≥85th percentile were randomized to intervention or control group. The control condition comprised nutrition classes; intervention offered the same nutrition classes plus 40 minutes physical activity, 3 times a week for 3 consecutive months. BMI was calculated at baseline, at the end of 3 months and 10 months post-baseline. Participants were administered a knowledge test on nutrition and exercise and the Piers-Harris Children's Self Concept scale at baseline and post-intervention.
The primary outcomes were mean within-subject change in BMI from baseline to the 3 and 10 month assessments. Secondary outcomes were mean within subject change in self-concept and knowledge regarding nutrition and exercise. Intention to treat analysis was performed using multiple regression. Statistical significance was $p<0.05$.
RESULTS: At 3 months, mean BMI in intervention group (N=14) decreased from 20.9 to 20.3 (-0.6); mean BMI increased in control group (N=14) from 20.5 to 22.2 (+1.7), $p<0.05$. At 10 months, the difference in change score was not significant. Mean change score in physical appearance was larger in intervention compared to control group (p=0.02). Mean change scores in knowledge test were not significantly different.
CONCLUSIONS: This short-term physical activity program was superior to the control condition in limiting BMI increase at 3 months but not at 10 months post-baseline. In the US, where 20% of children report a decrease in physical activity, this study emphasizes the need for changing that pattern in this population. Increasing physical activity in the school setting seems ideal. A full scale, longer term study is recommended to replicate these early findings and to develop techniques for sustaining at longer term follow-up the early benefits of this intervention.

117 4:45 PM

Effect of Caloric Information on Menu Selection by Caregivers in an Inner City, Minority Population

Wipanee Phupakdi, Jeremy Aiss, Stanley Cho. Pediatrics, St. Barnabas Hospital, Bronx, NY; Weill Cornell Medical College, New York, NY.

BACKGROUND: Caloric information on menus has emerged as a major legislative priority in an effort to curb rising obesity rates. Adult caregivers have the greatest impact on children's dietary routines. There is no data on the impact of caloric information on menu selection.
OBJECTIVE: To assess the impact of caloric information on menu selection and nutritional behaviors in an inner city community.
DESIGN/METHODS: A convenience sample of adult caregivers at 3 afterschool programs, 2 Head Start programs, and a public elementary school was surveyed. Participants were asked to select a lunch from a menu without calories, then select from a menu with calories posted. Analysis focused on univariate and bivariate associations between education level and responses to menu selections pre- and post- caloric information.

	Price
Grilled Chicken Sandwich	$3.99
Crispy Chicken Sandwich	$3.99
Fish Filet Sandwich	$3.29
Hamburger	$0.99
Cheeseburger	$1.39
Double Cheeseburger	$4.29
Fries – Small	$1.00
Fries – Large	$1.79
Nothing	---------

	Price	Calories
Grilled Chicken Sandwich	$3.99	400
Crispy Chicken Sandwich	$3.99	500
Fish Filet Sandwich	$3.29	380
Hamburger	$0.99	250
Cheeseburger	$1.39	300
Double Cheeseburger	$4.29	540
Fries – Small	$1.00	250
Fries – Large	$1.79	570
Nothing	---------	-----

RESULTS: 183 adult caregivers were surveyed (49% Hispanic, 37% African-American; 45% high school education). When given calorie information, 46% changed a hypothetical lunch order to reduce their calorie intake, 46% did not change their order, and 8% changed their order to increase their calorie intake. There was no effect of years of education on outcome. 47% of respondents reported eating fast food at least once a week.
CONCLUSIONS: Caloric information on menus would decrease calories in nearly half of this high risk community. With almost half of families eating fast food at least once a week, this could lead to a significant impact with reduction in caloric intake. More public health interventions aimed at nutrition education could reduce obesity and its complications in this community.

118 5:00 PM Medical Student

Acceptance of Referrals to an Obesity Management Program at an Inner-City Health Center

Maya Ilowite, Iman Sharif. Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Lack of acceptance of the diagnosis of childhood obesity is frequently cited as a barrier to the usefulness of obesity management programs in inner-city settings. We sought to determine the extent to which such beliefs may impact the acceptability of an onsite obesity management program at an inner-city community health center.
OBJECTIVE: To determine the proportion of families who accepted referral to an on-site obesity management program for their child.
DESIGN/METHODS: Over a 6 month period from February-July 2007, we flagged charts of all overweight (BMI>85th cile) children with a short survey prompting the provider to invite them to participate in an onsite obesity management program offered during evenings and Saturdays. Those who declined the referral were asked for a reason. Anonymous completed surveys were returned to a bin and collected by the investigators.
Descriptive statistics were performed, and bivariate analyses were used to determine whether BMI, age, or gender were associated with acceptance. Enrollment data from the program were used to determine a referral completion rate for the same period.
RESULTS: Over the 6 month period, 339 surveys were collected. Mean age of children in families surveyed was 12 years (range 6-18); 42% were male. Mean BMI was 27.4 (range 17.7, 62); 71% were obese. Overall, 223(66%) accepted the referral to the obesity program. Those who accepted the referral were more likely to be obese (76% vs. 62%, p=0.008). There were no differences in the rate of acceptance by age or gender.
For those who did not accept the referral, the following reasons were cited:
"too busy/inconvenient class times"(42%), "don't feel weight is a problem"(27%), "don't think it will help"(23%). Six percent of families cited medical or social concerns impeding participation, and 2% were dissatisfied with the quality of the program.
Prospectively collected enrollment data from the obesity program indicated that 80 children were enrolled during the 6 month period. This figure represents 36% of those who purportedly accepted the referral, resulting in an overall acceptance rate of 24%.
CONCLUSIONS: About 1 in 4 families at this inner-city health center accepted a referral to an on-site obesity management program, implying that the program fills a much needed service. On the other hand, "the glass is only 1/4 full." Reasons for lack of acceptance were consistent with a precontemplative stage of behavior change. Outreach efforts to increase referral acceptance are needed.

119 5:15 PM

The Relationship Between the Density of Food Sources in the Built Environment and Obesity Among Inner City School Children

James J. Burns, Jane Garb, Coleen Walsh, Thomas Yarsley. Pediatrics, Baystate Children's Hospital, Springfield, MA.

BACKGROUND: There has been an alarming increase in the rate of childhood obesity over the past 15 years. An increase in the availability of unhealthy food alternatives in the built environment is hypothesized to be a potential contributory factor.
OBJECTIVE: To determine if the density of regional food sources is related to obesity rates among inner city school aged children.
DESIGN/METHODS: Body Mass Index (BMI) percentiles were generated for 10,513 students grades K-12 in an inner city school district (2005-2006). Each student's home address and regional food source locations were entered into a Geographic Information System (GIS). Rates of obesity (BMI ≥ 95%ile) and density of food sources by block group were then mapped. Additionally, distance to nearest food source was calculated for all students. Spatial regression (controlling for age, gender, racial, socioeconomic and educational status) was performed using S+ and ArcView (GIS software) with food source as the predictor variable for obesity. Independent T-test compared mean distance to nearest food source (obese vs. non-obese).
RESULTS: The prevalence of obesity in this inner city school age population was 23.8%. There was a positive relationship between the density of total food sources and obesity rates by block group ($p = 0.001$). This was also true for the fast food sub-category ($p = 0.007$). This analysis controlled for age, gender, racial group, socioeconomic status and educational level. Additionally, obese students lived 57 feet closer to total food sources than those who were not obese (obese: 1105 feet vs. non-obese 1162 feet; $p = 0.005$).
CONCLUSIONS: This study demonstrates a statistically significant relationship between the density of total food sources (including fast food) and obesity. Further analysis is needed to evaluate how the built environment affects food choices in inner city children and their families. It is likely that the density of regional food sources has some influence.

120 5:30 PM Fellow in Training

Effects of a Lifestyle Plus Exercise Intervention on Metabolic Parameters in 7th Grade School Children: A Randomized Controlled Trial

Radhika Purushothaman, Amrit Bhangoo, Sunil Sinha, Viral Gala, Margarita Smotkin-Tangorra, Irina Kazachkova, Jessica Hileman, Neesha Ramchandani, Joyce Munga, Debbie Perez, Kate Pavlovich, Michael Rosenbaum, Svetlana Ten, Deborah DeSantis, Lisa Altshuler, Steven Shelov. Pediatrics, Infants and Childrens Hospital at Maimonides, Brooklyn, NY; Kids Weight Down Program, Infants and Childrens Hospital at Maimonides, Brooklyn, NY; Pediatrics, New York Presbyterian Medical Center, New York, NY.

BACKGROUND: Interventions targeting obesity in childhood are important in improving their metabolic profile and reducing risk of complications.

OBJECTIVE: To examine the effects of a school-baseddiet and exrcise intervention program on obesity & metabolic risk factors in 7th grade children

DESIGN/METHODS: 128 healthy students were divided into 3 groups based on intervention. Group 1 were controls (N= 46; Age = 12.1 +/- 0.5 yrs; Boys = 23); Group 2 (L group) received only life style intervention (N=24; Age = 12.2 +/- 0.5 yrs; Boys = 11 yrs) and Group 3 (LE group) children received life style and exercise intervention (N = 58; Age = 12.1 +/- 0.6 yrs; Boys = 22). The L group was a special needs class & not randomly selected: so excluded from the study. The LE group was further divided based on their BMI % as <85th % (Lean group; N= 28), 85th -95th %(overweight; N=7) or >95th % (Obese group; N=22). Due to the small number of overweight children, they were not used for comparison. The intervention was a 3-month, supervised exercise, nutrition & community intervention program for a period of 12 weeks. Detailed behavioral questionnaires & parameters reflecting obesity & metabolic syndrome were measured at baseline & post-intervention.

RESULTS: All parameters in both groups were similar at baseline. After intervention both groups showed a significant decrease in WC, systolic & diastolic blood pressure.

AIR & body fat decreased significantly in the LE group when compared to controls. Similarly, adiponectin & IGFBP1 decreased & GDI increased, but not in the C group.

Among the LE subgroups, the lean subgroup showed a decrease in body fat & blood pressure & increased IGFBP1, AIR and GDI, while obese group showed only a decrease in blood pressure.

In lean subgroup, there was a positive correlation between change in WC & adiponectin (R=0.48, p=0.019) and similar correlation with IGFBP1 (R=0.47; p=0.017), but not in the obese subgroup.

CONCLUSIONS: Obese children, especially with signs of metabolic syndrome, require more intensive intervention compared to lean children to achieve the same changes. Improvement in biochemical parameters can occur even before changes in BMI.

Neonatology II - Epidemiology and F/U Platform Session

Saturday, March 29, 2008 4:15 PM-5:45 PM

121 4:15 PM House Officer

Do Predischarge Bilirubin (BR) Measurements Predict Risk for Significant Hyperbilirubinemia Following Discharge?

Fadel Balawi, Amy Urban, Lynda Adrouche-Amrani, Warren Rosenfeld. Pediatrics, Winthrop-University Hospital, Mineola, NY; Pediatrics, Children's Hospital of Pittsburgh, Pittsburgh, PA; Pediatrics, Mt. Sinai Hospital, New York, NY.

BACKGROUND: The AAP Guideline for Hyperbilirubinemia (Pediatrics 2004;114:297) suggests "the best documented method for assessing the risk of subsequent hyperbilirubinemia is to measure the total serum bilirubin or transcutaneous bilirubin and plot the results on a (Bhutani) nomogram." Those in favor of universal screening have advocated this approach to identify neonates in the high risk zones of the nomogram and therefore prevent kernicterus. However, BR prior to discharge is only one risk factor and patients who develop significant hyperbilirubinemia, which may lead to kernicterus, may not be identified by this method.

OBJECTIVE: Will neonates in the low risk (LR) (<40th%tile) and low intermediate risk (LIR) (40th-75th%tile) zones on the (Bhutani) nomogram and who are presumed to be at no or low risk for subsequent hyperbilirubinemia develop significant jaundice?

DESIGN/METHODS: Charts of 84 consecutive patients with predischarge BRs who were readmitted for hyperbilirubinemia were reviewed for predischarge and readmission levels of BR and the presence of risk factors.

RESULTS: Neonates in LR group accounted for 14% (12/84) and LIR group 27% (27/84) of readmissions. Two or more risk factors were present in 80% of these patients and 3 or more in 44% of patients. Breast feeding, male gender, gestational age between 35-38 weeks and maternal age > 25 were the most common risk factors found. 5/12 LR patients rose to > 95th%tile and the remainder to just below 95th%tile. 19/27 LIR patients rose to >95th%tile and 8/9 remaining rose to just below 95th%tile.

CONCLUSIONS: 47% of patients readmittted for hyperbilirubinemia were from groups considered to be at no or little risk for significant jaundice post discharge according to the Bhutani nomogram. Predischarge BR may not always predict the risk of post discharge hyperbilirubinemia, especially when other risk factors are present. To successfully prevent kernicterus perhaps all babies need to be screened (examined) for hyperbilirubinemia 24-48 hours post discharge or new risk adjusted guidelines developed.

122 4:30 PM

Early Medical and Behavioral Characteristics of NICU Infants Later Diagnosed or Suspected with Autism Spectrum Disorder (ASD)

Bernard Z. Karmel, Judith M. Gardner, Lauren D. Swensen, Ira L. Cohen, Eric London, Elizabeth M. Lennon, Michael J. Flory, Santosh M. Parab, Anthony Barone. Infant Development, NYS Institute for Basic Research, Staten Island, NY; Psychology, NYS Institute for Basic Research, Staten Island, NY; Pediatrics, Richmond University Medical Center, Staten Island, NY.

BACKGROUND: Infants with obstetric/neonatal complications may be at a higher risk for ASD. Our longitudinal studies evaluate development of regulatory mechanisms from birth in NICU infants. Retrospective evaluation of records from 1995-present indicated ~1.5% of our population were suspect or diagnosed with ASD, with higher % after 2000 (1% vs 2%, X^2=3.9, p<.05).

OBJECTIVE: To identify demographic, medical, and behavioral variables for early diagnosis of ASD.

DESIGN/METHODS: NICU infants later suspected/diagnosed with ASD (n=37) were compared to non-ASD (n=2474) children on variables including gender, maternal education, gestational age (GA), birthweight (BW), CNS injury, neonatal neurobehavior, infant regulation and attention, and cognitive and motor behavior from birth to 3½ yrs.

RESULTS: ASD children were predominantly male (84% vs 54%), with higher-educated mothers (14.8 vs 13.9 yrs, F=4.01, p<.05). For ASD, mean GA=33.0 wks and mean BW=1897g; for non-ASD, mean GA=34.7 wks and mean BW=2290g. Differences remained controlling for gender and maternal education (GA: F=4.31, p<.04; BW: F=5.32, p<.03). ANCOVAs showed no differences between ASD and non-ASD on intrauterine growth, 1- or 5-min Apgar Scores, or severity of CNS involvement, controlled for GA or BW (p's>.05). Infants later suspected/diagnosed with ASD showed a pattern of behavioral deficits starting in the newborn period, with a higher incidence of visual asymmetry at 1 mo (corrected) (7.0% vs 1.5%; OR=4.7, p<.001) and poorer arousal modulation of visual attention at 4 mo (corrected) (F=7.39, p<.01), indicating potential deficits in development of visual and regulatory systems. Controlling for maternal education and CNS injury, assessments indicated lower scores on Bayley-II motor and mental scales starting at 7 and 10 mo respectively, and on Griffiths Mental Development Scales between 2 and 3½ yrs (p's<.01).

CONCLUSIONS: As early as newborns, infants suspected/diagnosed with ASD may form a distinct sub-population within NICU-assigned babies, with atypical visual and arousal regulation deficits when compared to other high-risk infants. Furthermore, disintegration on standardized testing may be expected as early as 7 mo, which typically only occurs in infants with the most severe CNS pathology. Such differences may be indicative of precursors to ASD at older ages.

123 4:45 PM Fellow in Training

Executive Function in Former Preterm Children at Preschool Age

Elise M. Lavery, Soraya Abbasi, Nancy L. Brodsky, Laura M. Betancourt, Hallam Hurt. Neonatology, Children's Hospital of Philadelphia, Phila, PA; Neonatology, Pennsylvania Hospital, Phila, PA.

BACKGROUND: Former preterm children are at risk for learning disabilities and poor achievement at school age. Investigating executive functions, such as those used in attentional control and organized exploration at preschool age, may help identify those children at greatest risk.

OBJECTIVE: To assess executive function in former preterm children at preschool age. To measure the effect of gender, race, perinatal morbidities and socioeconomic status on executive function.

DESIGN/METHODS: Inclusion criteria: ≤32 wks or ≤ 1500 grams, free of severe disabilities (MDI/PDI < 55, blind or deaf) and enrolled in developmental follow-up. Executive function was measured using the Goodman Lockbox (GLB), a free-play task that has 5 subscales investigating problem-solving abilities: Mental Organization, Aimless Actions, Nonadaptive Moves, Adaptive Moves and Number Unlocked. Cohort scores were compared, in 6-month epochs (30, 36 and 42 months), to similar epochs of the standardized data for the GLB. Neurodevelopmental outcome at 12 and 24 months was measured by the MDI and PDI scores of the Bayley Scales of Infant Development (BSID II). Data on socioeconomic status and perinatal morbidities were collected.

RESULTS: So far, in this cross-sectional evaluation, 35 preterm children (GA 29±2.5 weeks and BW 1270±470 gms) have been tested at mean age 38±5 months. Population demographics: 51% male; 49% African-American, 46% Caucasian and 5% other. MDI scores were 105 ±9 and 105±15 at 12 and 24 months, respectively; PDI scores were 96±18 and 101±20. Compared to the GLB norms, the preterm group performed less well in: Mental Organization at 36 and 42 months (all p<0.05); Aimless Actions at 30, 36 and 42 months (all p<0.001); Nonadaptive Moves at 30, 36 and 42 months (all p<0.0001) and Number Unlocked at 30, 36 and 42 months (all p<0.05). Overall, boys performed more poorly in Aimless Actions than girls (p<0.05). GLB scores did not correlate with either socioeconomic status, race or perinatal morbidities (p≥0.05).

CONCLUSIONS: In a relatively healthy cohort of preterm children with BSID II scores in the normal range, we found at preschool age: 1) executive function, measured by problem solving abilities, lower than GLB norms, 2) gender differences in measures of impulsive and unfocused behavior. These results argue for more comprehensive and extended follow up of "normal" former preterm children, as early poor performance in executive function may portend poor achievement in school.

124 5:00 PM

Shifts in the Relative Influence of Biological and Environmental Risk Factors on Developmental Outcome of High-Risk Infants

Judith M. Gardner, Bernard Z. Karmel, Elizabeth M. Lennon, Phyllis M. Kittler, Michael J. Flory. Infant Development, NYS Institute for Basic Research, Staten Island, NY.

BACKGROUND: High-risk infants are at risk for poor developmental outcome. It is important to understand shifts in the relative contributions of major risk factors affecting outcomes.

OBJECTIVE: To predict outcome based on major biological and environmental factors over first 5 yrs. To construct developmental models of how these factors interact over age.

DESIGN/METHODS: Longitudinal studies of >2600 infants born between 1994 and 2006 (54% boys, GA: 23-42 wks, BW: 400-5200g) were conducted using Bayley Scales of Infant Development (BSID-II) to 2 yrs, Griffiths Mental Development Scales (GMDS) from 2 to 3½ yrs, and Differential Abilities Scales (DAS) from 4 to 5 yrs. Relative effects of biological risk (CNS injury, BW, GA, relative intrauterine growth [RIUG: standardized BW for GA]), environmental risk (maternal education; MEd), and gender were studied.

RESULTS: Associations among different Scales were consistent. BSID Mental Development Index (MDI) at 2 yrs predicted GMDS (R^2=0.55) and all subscales (R^2=0.17-0.54) at 3 yrs, as well as DAS verbal and nonverbal scores at 4 and 5 yrs (R^2=0.34-0.43). Likewise, 2 yr BSID Psychomotor Developmental Index (PDI) predicted GMDS (R^2=0.12-0.25) and DAS (R^2=0.07-0.17). All p's<.001. At 1 yr, PDI was best predicted by biological risks. Biological effects on MDI declined steadily from 4 mo to 2 yrs as environmental influences increased: degree of CNS injury accounted for >80% of explained variance at 1 mo and 20% at 2 yrs. A comparable but later shift in predicting nonverbal outcomes occurred at the end of yr 3. After yr 4, MEd accounted for 90% of explained variance of verbal and 60% of nonverbal performance, except for those with more severe CNS involvement. Structural models revealed effects of male gender and RIUG on cognitive skills by yr 2, with later effects mediated by 2nd-yr performance. Gender and RIUG effects on motor skills appear toward end of yr 3. CNS injury had strong direct effects on cognitive and motor skills through yr 3, but also through its effect on early neurobehavioral status. MEd had strong direct effects on cognitive skills after yr 1 lasting well into yr 5, even controlling for intermediate effects. Its effects on motor skills began in yr 3.

CONCLUSIONS: Meaningful developmental trajectories were constructed, demonstrating changing influence of predictor variables and accurate predictions of behavior through the first 5 yrs.

125 5:15 PM Fellow in Training

Neurodevelopmental (ND) Outcomes of Moderately Low Birth Weight (MLBW) Infants

Melissa A. Woythaler, Marie C. McCormick, Vincent C. Smith. Division of Newborn Medicine, Harvard Medical School, Boston, MA; Division of Newborn Medicine, Beth Israel Deaconess Medical Center, Boston, MA; Division of Newborn Medicine, Harvard School of Public Health, Boston, MA.

BACKGROUND: Very low birth weight (VLBW) infants (<1500g) have poorer ND outcomes with lower ND scoring and more behavioral problems than normal birth weight (NBW) infants (>2500g). It has also been shown that ND outcomes of MLBW (1500-2499g) infants are worse compared to NBW infants, however there is limited data regarding their predictors of outcomes.

OBJECTIVE: We wanted to assess ND outcomes of MLBW infants and what modifiable predictors of outcome they have. We hypothesize that MLBW infants will have worse ND outcomes than NBW infants and that they will have some modifiable predictors of outcome.

DESIGN/METHODS: We studied 6183 infants (including 953 MLBW and 729 VLBW) from the National Maternal and Infant Health Survey (NMIHS) and its longitudinal follow-up. Over-sampling Black and low birth weight infants, the NMIHS provided early childhood morbidity and health data. We analyzed ND outcomes with non-parametric tests (Wilcoxon rank sum for continuous variables and Kruskal-Wallis for categorical variables). The outcome was the Denver Developmental Screening based Neurodevelopmental Score (DDSNS). The DDSNS ranged from 0-16 with higher scores being better. The DDSNS predictors were infant birth weight, gender, health insurance status, race, maternal depression, age, marital status, education, household income, and WIC status.

RESULTS: Mean DDSNS scores were higher as birth weight strata increased (VLBW 10.2; MLBW 11.7; and NBW 12.3 p<0.0001). In NBW infants, gender, maternal depression, age, education, and marital status were statistically significant predictors of DDSNS (p<0.05). For MLBW and VLBW infants, gender was the only statistically significant preductor of DDSNS (Females 12.3 Males 11.6 p<0.0003) and (Females 10.8 Males 9.5 p<0.0001) respectively.

CONCLUSIONS: MLBW infants have ND outcomes intermediate to NBW and VLBW infants. For MLBW infants, gender was the only significant predictor of ND outcome with no modifiable risk factors identified. We conclude that being MLBW is such a strong risk factor for a worse ND outcome that other predictors become insignificant. More research needs to be done to identify modifiable predictors of outcome.

126 5:30 PM Fellow in Training

Do Premature Females Really Do Better Than Their Male Counterparts?

Jody L. Kohut, Linda H. Green, Sharon Kirkby, David Webb, Kevin Dysart. Neonatology, Thomas Jefferson University and duPont Hospital for Children, Philadelphia, PA; ParadigmHealth, Upper Saddle River, NJ; Drexel University, Philadelphia, PA.

BACKGROUND: Premature male infants have been reported to have lower survival rates, increased chronic lung disease (CLD) and increased rate of intraventricular hemorrhage (IVH) when compared to female infants. It is not well understood whether male gender plays a role in other processes of care in the NICU.

OBJECTIVE: To compare survival rates and outcomes in process of care in female vs male infants born ≤32 weeks gestational age (GA).

DESIGN/METHODS: Data was obtained from the ParadigmHealth database for all infants born ≤32 weeks GA from 1/03-6/07. Females were compared to males for demographics, complications, and care processes while in the NICU. Univariate and multivariate analysis was conducted using chi square analysis, analysis of variance or logistic regression.

RESULTS: 12816 infants were included; 6086 females and 6721 males. Mean GA did not differ, (29.5 weeks female vs. 29.6 weeks male). Male were born larger than females (1437g vs 1350g, p<0.01) as females were more likely to be born SGA (11.1% vs. 7.7%, p<0.01). Males received more surfactant, developed more CLD, received more steroids and had more oxygen requirement at discharge. Females were more likely to develop a patent ductus arteriosus (PDA). After controlling for birth weight, GA, and SGA status females were still more likely to survive (95.4% vs. 93.6% OR 1.63, p<0.01). Male gender did not play a role in other processes of care except for weaning to a crib.

Outcomes in Processes of Care

	Male	Female	P value
Apnea %	66.1	66.7	0.3
CLD %	21.9	18.4	<.01
IVH (3-4) %	2.8	2.6	0.7
ROP (3-4) %	2.4	2.0	0.2
Infection %	18.7	18.9	0.4
Pneumothorax %	2.1	1.6	0.3
PVL %	0.8	1.0	0.5
Surfactant %	37.6	34.7	<0.01
Phototherapy %	64.9	65.0	0.20
Steroids %	7.5	6.2	0.01
NEC %	3.5	2.9	0.2
PDA %	20.5	22.7	<.01
Days NPO	8.3	7.9	0.1
Days To Start Feeds	7.0	6.5	0.2
Days to Full PO Feeds	40.8	40.7	0.7
Days To Crib	32.9	33.8	0.04
Ventilator Days	13.9	13.8	0.8
CPAP Days	10.1	10.2	0.5
Days To RA	23.7	22.6	0.06
Home On Oxygen	11.2	9.3	<0.01
LOS (days)	50.3	49.5	0.3

CONCLUSIONS: In comparing infants born ≤32 weeks GA males have a decreased rate of survival and an increased rate of respiratory morbidity in spite of higher birth weight distributions. Gender did not play a role in other processes of care including days to room air and LOS.

Pulmonary and Asthma Platform Session

Saturday, March 29, 2008 4:15 PM-5:45 PM

127 4:15 PM Ph.D. Student

Perfluorochemical (PFC) Liquids Decrease Diaphragm Stress in Hyperoxic Lung Injury

Daniel J. Malone, Jichuan Wu, Mary F. Barbe, Thomas H. Shaffer, Marla R. Wolfson. Physiology & Peds, Temple Univ Sch Med, Phila, PA; Anatomy and Cell Biology; Physical Therapy, Temple Univ Sch Med, Phila, PA; Nemours Res Lung Ct, Al duPont Hosp Child, Wilm, DE.

BACKGROUND: Hyperoxia (HO) alters pulmonary mechanics and gas exchange increasing demand of respiratory muscle. Excessive respiratory pump loading leads to ventilatory failure. PFC liquids support lung mechanics and gas exchange in acute lung injury.

OBJECTIVE: To test the hypothesis that diaphragm stress is reduced by PFC liquid attenuation of chronic HO-induced lung injury.

DESIGN/METHODS: Spontaneously breathing C57/BL6 mice (6-8 weeks, N=78) were randomized to sham or intratracheal PFC (PP2/PP9, 25%/75%, 10 ml/kg), and exposed to normoxia (N) (F_IO_2=0.21) or HO (F_IO_2>0.95) for 3 days. Lung compliance, room air O_2 response, inflammatory cytokines in muscle, and histomorphometry of lung (alveolar wall thickness, expansion index) and diaphragm (fiber diameter, muscle damage score) were assessed.

RESULTS: PFC attenuated the HO-induced decrease in lung compliance, gas exchange and altered lung architecture (Table 1). Preserved lung function was associated with reduced diaphragm inflammation, fiber size and percentage of abnormal muscle fibers (Table 2) compared to sham.

Table 1

Group	Compliance	SpO_2	Alveolar Wall Thickness	Expansion Index
(X ± SE)	(ml/cmH_2O/kg)	(%)	(μm)	
Sham/N	0.82±0.04†	94.5±1.4†	5.2±0.1†	1.29±0.11†
Sham/HO	0.51±0.05	76.0±5.9	8.6±0.2	0.69±0.05
PFC/N	0.81±0.05†	93.8±0.8†	4.9±0.2†	1.27±0.07†
PFC/HO	0.85±0.08†	91.9±0.6†	6.0± 0.2†	1.06±0.07†

† p< 0.05 versus Sham/ HO

Table 2

Group	Muscle Fiber Diameter	Muscle Damage Score	IL-6	MCP-1	IFN-γ
(X ± SE)	(μm)	(%)	(pg/mg protein)	(pg/mg protein)	(pg/mg protein)
Sham/N	13.8±0.1†	5.6±2.1†	3.7±0.5†	16.5±2.2†	4.0±1.5†
Sham/HO	15.2±0.1	24.3±2.3	22.1±4.5	137.5±18.9	54.1±12.1
PFC/N	13.5±0.1†	5.6±1.1†	3.5±0.5†	20.2±5.2†	8.3±3.7†
PFC/HO	13.8±0.2†	7.8±1.2†	7.6±1.94†	46.1±10.4†	6.8±2.2†

† p< 0.05 versus Sham/ HO

CONCLUSIONS: Preconditioning the lung with PFC liquid preserves lung compliance, gas exchange and lung architecture in chronic HO exposure. Thus, unloading the diaphragm reduces muscle stress, inflammation, and damage while preserving muscle fiber size. The direct effect of PFC liquid on the lung and indirect effect on respiratory muscle may play a role in further mitigating the progression of respiratory failure. (Temple Univ Fellowship).

128 4:30 PM Fellow in Training

Transport-Induced Biophysical Impulse Results in Long-Term Alterations of Respiratory Function in Neonatal Sprague-Dawley Rats

Joseph J. Hudak, Andrew Dylag, Shetal Shah. Pediatrics, Stony Brook University Hospital, Stony Brook, NY.

BACKGROUND: Forces experienced by neonates due to accelerations during transport are associated with adverse outcomes. These accelerations per unit time were shown previously to cause immediate alterations in respiratory function in rats in a dose-dependent. However, the long-term effects on respiratory function of transport-induced impulse is not well characterized.

OBJECTIVE: To determine if exposure to a standardized cumulative impulse during transport resulted in long-term alterations in respiratory function in a neonatal rat model.

DESIGN/METHODS: 3 groups of Sprague-Dawley rat pups underwent simulated transport on postnatal day 5 or 6. Each group was exposed to an average impulse of 27.4 m/sec^2-min, (determined from previous experiments to closely simulate ambulance transport) for 0, 30 or 60 minutes. During the trials, acceleration measurements in the X, Y, and Z planes were sampled with a computerized accelerometer. Animals were then allowed to grow under normal conditions.

At weaning the rats were paralyzed and ventilated on a SCIREQ small mammal ventilator. Using a forced-oscillation technique, measurements of elastance, tissue damping, airway resistance, ratio of damping to elastance (eta, hysteresivity) , and intertance were obtained at positive end expiratory pressures (PEEP) of 0, 3 and 6 cm of H_2O. Running averages for each respiratory parameter were compared among groups using 2x2 factorial ANOVA.

RESULTS: Overall, increased transport time resulted in a decrease in compliance at all levels of PEEP (p<0.0001). Statistically significant decreases in conducting airway resistance were seen after 60 minute transport for all levels of PEEP (p<0.03). Increased transport time resulted in a significant step-wise increase in tissue damping and elastance at all levels of PEEP (p<0.0001). Pressure-Volume Loops were statistically different at all levels of PEEP (p<0.0001). Inflammatory changes were seen on H & E staining.

CONCLUSIONS: Neonatal rats undergoing simulated transport experienced long-term alteration of respiratory function. Duration of transport correlated to larger alterations in a dose dependant manner. Transport-induced lung disease is related to cumulative impulse and is not eliminated with growth. The decreases in static compliance and increases in tissue damping are consistent with an inflammatory response. Further studies are needed to fully understand the response of the preterm neonate to transport-mediated stress.

129 4:45 PM

Discordance Between Reported Compliance and Knowledge Regarding Appropriate Home Management of Childhood Asthma in an Underserved Population

Cathleen Ballance, GianeCarla Montero, Anna Petrova. Pediatrics, Jersey Shore University Medical Center, Neptune, NJ; Pediatrics, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

BACKGROUND: Parental knowledge regarding home asthma management is critical for the proper control of childhood asthma. Identification of lacunae in asthma management knowledge and skills of the caregiver will help in the development and implementation of appropriate teaching strategies for healthcare providers.

OBJECTIVE: This study was designed to assess parental knowledge, attitudes and beliefs regarding home asthma management in association with severity of asthma presentation in an underserved population of children.

DESIGN/METHODS: A survey questionnaire that was designed to assess parental knowledge, attitude and beliefs regarding asthma home management was mailed to all listed pediatric asthma patients (2-18 years) seen at the Family Health Center from 2004-2006. Follow up phone calls were made to non-respondents. The medical record of the enrolled asthma patients was reviewed to collect demographic, clinical, and outcome data including asthma-related hospitalization and ED visits for the last 12 months.

RESULTS: Among the 159 listed asthma patients, 108 were unable to be reached because of change of residence, asthma was misclassified in 2 subjects and 49 completed questionnaires. We identified 32 (65.3%) children with mild (Group 1) and 17 (34.7%) with moderate/severe asthma (Group 2). A majority of parents from both groups preferred to bring their child to the clinic/ED without trying home treatment if the child began to have symptoms of an asthma attack. Moreover, 53% of parents in Group 2 reported using a controller medication as their first choice for treatment of an asthma attack. Approximately half of parents in both groups identified Albuterol as the medication they were giving their child to prevent asthma attacks and 30% of parents in Group 2 didn't know which medication their child was using to prevent attacks, despite reported compliance with prescribed home asthma management regimens. Hospitalizations/ED visits were identified in 37.5% vs. 76.5% of respective groups ($p<0.02$).

CONCLUSIONS: There is clear evidence of poor parental knowledge regarding appropriate home asthma management despite the reported compliance and understanding of the treatment regimens prescribed by primary care physicians. We speculate that these deficits in parental knowledge contribute to high rates of hosptialization/ED visits, especially for children with moderate/severe asthma.

130 5:00 PM Undergraduate Student

Improved Documentation of ED Asthma Severity

Michael A. Colon, John M. Corsi, James F. Wiley II, Sharon R. Smith. Pediatrics, Connecticut Children's Medical Center, Hartford, CT; University of Connecticut, Storrs, CT.

BACKGROUND: It is important to document the severity of an asthma exacerbation in the Emergency Department (ED). Assessment allows the provider to determine degree of severity, treatment, and response to treatment. Although assessment is frequently done in the ED, documentation in the medical record is often scant.

OBJECTIVE: To evaluate the effectiveness of an intervention in the electronic medical record (EMR) on the documentation of asthma severity. Also, to assess the frequency of major and minor deviations from the asthma treatment algorithm after intervention.

DESIGN/METHODS: This was a chart audit study assessing an EMR intervention designed to improve documentation of asthma severity in the ED. The intervention was three fold: 1) addition of a specific "tab" (documentation section) for the hospital's validated asthma severity score (Modified Pulmonary Index Score, MPIS), 2) addition of the evidence-based treatment algorithm into the EMR, and 3) addition of "remember algorithm" to title of asthma medication grouping. Major and minor deviations in following the treatment algorithm were predetermined. All children with asthma were included during 4-week periods before and after intervention. Categorical data was evaluated using chi-squared tests, and continuous data using t tests.

RESULTS: There were 355 children enrolled, 193 before and 162 after the intervention. The children were 37% female, 21% white, 44% Latino, 25% black and 10% other, and the mean age was 6.8 $\pm$ 4.3 years. The gender, ethnicity, and age were similar in both groups. There was a significant improvement in MPIS documentation among physicians from 24% (46/193) to 67% (109/162, $p<0.0001$). Documentation was also improved among all providers (MD, RN, and RT) from 65% (125/193) to 85% (137/165, $p< 0.0001$) after the intervention. The frequency of major and minor deviations was similar in both groups. Other than no MPIS documentation, the most common major deviation was an error in steroid dosing with 10% before and 5.5% after intervention ($p=0.14$). The most common minor deviation was not following weight-based recommendations for albuterol dosing with 33% before and 35% after intervention ($p=0.65$).

CONCLUSIONS: This simple intervention significantly improved the documentation of asthma severity for children in the pediatric ED. Similar interventions for other critical documentation may be effective. Adding the algorithm to EMR did not change adherence to recommendations.

131 5:15 PM Fellow in Training

Association of Obesity and Asthma in Inner City Minority Children

Nita Vangeepuram, John Doucette, Julie A. Britton, Maida Galvez, Barbara Brenner, Susan L. Teitelbaum, Mary S. Wolff. Community and Preventive Medicine and Pediatrics, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Asthma and obesity are more common in low-income minority communities such as East Harlem, New York City (NYC). Evidence for an association between increased body fat and asthma exists, and postulated mechanisms include inflammatory mediators, hormones, mechanics and genetics. Studies to date have only used body mass index (BMI) as a measure of obesity. BMI may not be ideal since actual body fat level varies by age, sex, maturity level, and ethnicity. Superior obesity measures include: (1) percent body fat and (2) waist circumference and waist-to-height ratio (indicators of fat distribution). In addition, few studies have looked at physical activity's association with asthma or its effect on the adiposity-asthma relationship.

OBJECTIVE: To study the association between asthma diagnosis and (1) BMI percentile, (2) percent body fat, (3) fat distribution and (4) physical activity.

DESIGN/METHODS: Cross-sectional data from Growing Up Healthy, a community based study of 6-8 year old NYC children, were used. Body measurements were performed using a standardized protocol. Asthma was defined as parental report of doctor-diagnosed asthma. Adiposity-asthma associations were estimated by multivariate logistic regression. Questionnaire-based physical activity information and pedometer measurements among asthmatics and non-asthmatics were compared using T-tests.

RESULTS: At baseline 39% of girls (155/398) and 53% of boys (56/105) had a BMI greater than the 85th percentile based on CDC normative values. Twenty-six percent of children had doctor-diagnosed asthma. In multivariate adjusted models, there were associations between each body fat measure and asthma diagnosis. The odds ratio (95% CI) for asthma for the highest quintile of body fat measure compared to the lowest was 3.70(1.79-7.66) for BMI percentile, 2.18(1.09-4.37) for percent body fat, 2.21(1.09-4.49) for waist circumference and 3.21(1.52-6.77) for waist-to-height ratio. There was no gender effect. Asthmatic children also had statistically significantly more sedentary activity and fewer metabolic hours per week from recreational activity.

CONCLUSIONS: This study found an association between each different adiposity measure and physical activity with doctor-diagnosed asthma. Prospective observations will allow study of asthma severity in relation to body fat measures and activity levels. Enhanced understanding could improve outcomes for both health conditions.

132 5:30 PM

Chitinase Activity in Bronchoalveolar Lavage Fluid from Children with Asthma and Other Allergic Lung Diseases

Alfin G. Vicencio, Zhongfang Du, Wang Yong Zeng, Mark Suhrland, Stacy Kipperman, David L. Goldman. Pediatrics, Children's Hospital at Montefiore and Albert Einstein College of Medicine, Bronx, NY; Pathology, Montefiore Medical Center, Bronx, NY.

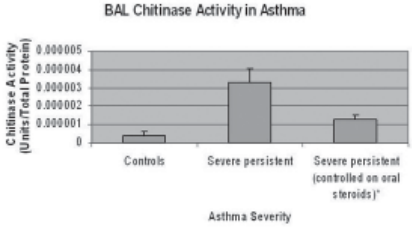
BACKGROUND: Acidic mammalian chitinase (AMCase) has been described as a critical downstream mediator of IL-13 induced asthma in a mouse model, and elevated serum levels of similar enzymes correlate with asthma severity and airway remodeling in adults. Furthermore, we have recently described that chronic pulmonary infection with a common chitin-containing organism (*C. neoformans*) results in airway hyper-reactivity, airway remodeling and increased activity/expression of AMCase in a rat model. Currently, it is unknown whether similar findings are present in children with allergic lung diseases.

OBJECTIVE: We sought to determine whether chitinase levels are increased in bronchoalveolar lavage (BAL) fluid from children with allergic lung diseases including asthma.

DESIGN/METHODS: BALfluid was saved from children undergoing flexible bronchoscopy with lavage as part of their routine evaluation. Chitinase activity was determined using an established fluorogenic assay and corrected for total protein concentration. The study was approved by the Committee on Clinical Investigations, Albert Einstein College of Medicine.

RESULTS: Chitinase activity was measured from the BAL fluid of 12 patients (chitinase activity listed in parentheses). 4 controls had large airway lesions ($3.87x10^{-7}$ +/- $2.59x10^{-7}$), 2 had severe-persistent asthma but were non-symptomatic with daily systemic steroids ($1.27x10^{-6}$ +/- $2.25x10^{-7}$), and 5 had severe-persistent asthma under poor control ($3.34x10^{-6}$ +/- $9.82x10^{-7}$). Interestingly, one patient with severe allergic alveolitis diagnosed by open lung biopsy demonstrated chitinase levels that were almost a log above all other groups ($2.07x10^{-5}$).

CONCLUSIONS: 1) Chitinase activity is detectable in BAL fluid from children with pulmonary disease. 2) Chitinase activity may be higher in patients with allergic lung conditions including severe asthma. 3) Steroid therapy may reduce the activity of AMCase and chitinase-like enzymes in the lung.



Poster Session II
Poster Session

Saturday, March 29, 2008 6:00 PM-7:30 PM

133 Medical Student

Comparative Readability of Spanish and English Patient Education Materials

Maya Ilowite, Iman Sharif. Social Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Physicians practicing in mainly Spanish-speaking populations often use the Spanish translation of patient education materials(PEM) to improve communication. While studies have shown that English language PEM are often at an inappropriately high reading level for patients, no studies have evaluated the reading levels of Spanish PEM. Our anecdotal experience from discussion with Spanish-speaking colleagues is that Spanish PEMs are written at even higher reading levels than the English materials.

OBJECTIVE: To compare the readability of PEMs written in Spanish vs. English.

DESIGN/METHODS: PEMs were selected from MD Consult and The Injury Prevention Program (TIPP). Through consultation with practitioners at an inner-city academic health center, we selected MD Consult sheets commonly used to explain pediatric skin conditions.We evaluated TIPP sheets for all age groups.

We used the Fry Readability Formula and Flesch Reading Ease to evaluate readability of English forms. Spanish handouts were evaluated using the Spanish-adapted Fry Readability Formula and the Fernandez-Huerta Formula (a Spanish adaptation of the Flesh Reading Ease). The Fry measures the grade level of the material. Reading Ease measurements are given as a number from 0-100, with a higher number denoting a greater ease of reading.

We used a paired t-test to compare mean readability of Spanish vs. English versions of PEMs overall, and for each source (MD Consult and TIPP).

RESULTS: We reviewed 28 PEMs, comprising the English and Spanish versions of 7 MD Consult handouts and 7 TIPP sheets.

Overall, Fry grade level was higher for Spanish vs. English versions [6.5(CI: 5.7,7.2) vs. 4.8(CI: 4.0,5.7), $p=0.0001$]. Fry was higher for Spanish versions of both MD Consult [6.4 (4.8, 8.0) vs. 4.3 (2.9, 5.7); $p=0.0007$] and TIPP [6.6(5.8, 7.3) vs. 5.4(4.2, 6.6); $p=0.03$] sheets.

Overall, Reading Ease was not significantly different for Spanish vs. English [78.5(75.2, 81.7) vs. 81.8(78.4, 85.2); p=0.08] PEMs. However, for MD Consult sheets, Spanish sheets were significantly more difficult [74.8 (69.4, 80.3) vs. 82.8(76.8, 88.9); p=0.004]. Reading Ease of the TIPP sheets were similar, Spanish vs. English [82.1(80.8, 83.5) vs. 80.7 (75.7, 85.7); p=0.40].
CONCLUSIONS: In this exploratory study, we found that Spanish versions of commonly used PEMs were consistently written at a more difficult reading level. Quality improvement efforts in the health literacy arena should target Spanish translations as another area to improve readability of PEMs.

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Communication and the Pediatric Residency Match

Catherine C. Skae, Marina Reznik, Philip O. Ozuah. Department of Pediatrics, Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: The National Resident Match Program (NRMP) has established guidelines regarding residency program and applicant communication during the Residency Match process. NRMP guidelines specifically state that participants "must not make statements implying commitment". We wondered how often medical students adhered to this regulation.
OBJECTIVE: To determine the frequency of applicant statements of commitment in violation of NRMP guidelines.
DESIGN/METHODS: We conducted a prospective study of thank you notes received over five recruitment seasons from 2002-2007 at a pediatric residency in a large academic Children's Hospital. We collected all notes sent by applicants to the Program Director (PD), faculty interviewer, and department Chair. We dichotomized the notes into those that had statements of commitment and those that did not. Of those that had statements of commitment, we categorized them as containing either "moderate" or "strong" statements of commitment. For example, a moderate commitment was, "I ranked your program highly". A strong commitment was, "I ranked your program at the top of my list" or "I ranked your program #1". Chi square was used to compare dichotomous variables.
RESULTS: A total of 1113 thank you notes were analyzed, of which 715 (64%) were sent to the PD, 375 (34%) were sent to the interviewer, and 23 (2%) were sent to the Chair. Overall, 262 (24%) notes contained statements of commitment, of which 51% were "strong" statements of commitment and 49% were "moderate" statements. The Chair and PD were significantly more likely to receive notes with statements of commitment: 30% of notes sent to Chair vs. 30% for PD vs. 10% for interviewer (p=.000). Similarly, the Chair and PD were also significantly more likely to receive notes with "strong" commitments: 57% of notes sent to Chair vs. 55% for PD vs. 32% for interviewer (p=.017). Applicants in the top 3rd of our rank lists were just as likely to make statements of commitment as those in the bottom 3rd.
CONCLUSIONS: Despite NRMP guidelines, there is a substantial amount of communication containing statements implying commitment by residency applicants, particularly communications to the Chair and PD. Medical students applying for residency do not appear to be deterred by the NRMP restrictions.

135 House Officer

The Effectiveness of Web-Based Learning During Pediatric Residency Training

Honey E. Sward, Carol P. Carraccio, Alison Falck. Pediatrics, University of Maryland Medical Center, Baltimore, MD.

BACKGROUND: Web-based learning tools are being utilized in many educational settings. Self-directed, web-based learning modules represent a novel approach to didactic teaching during pediatric residency training. In addition to addressing time constraints, self-directed learning is an important skill for residents to acquire for life-long learning. Studies have shown that web-based learning is an efficient teaching method in undergraduate medical education. However, there is scant literature addressing the efficacy of self-directed, web-based learning for pediatric residents.
OBJECTIVE: To determine whether a web-based, self-directed learning module on retinopathy of prematurity (ROP) is an effective educational tool for pediatric residents at The University of Maryland Medical Center (UMMC).
DESIGN/METHODS: Pediatric residents at UMMC completed a web-based learning module on ROP as a requirement for their NICU rotation. The module consisted of a pre-test, a PowerPoint presentation, a post-test, and a satisfaction survey. The same 10 questions based on AAP PREP content specifications were found on the pre-test and post-test, and were presented in random order. Residents completed a satisfaction survey after finishing the module, and participated in a discussion of the module. Mean pre-test and post-test scores were compared using a paired student t-test, and subjective data was obtained from the satisfaction surveys.
RESULTS: 17 residents completed the module between 7/07 and 12/07. There was an improvement between mean pre-test scores of 3.5 +/- 1.2 and mean post-test scores of 7.0 +/- 1.8 (p= <0.001). There was no statistically significant difference in mean pre-test and post-test scores when stratified by level of training. The majority of residents who completed the survey reported that this exercise was more beneficial than reading an article on ROP. All residents reported that their knowledge about ROP was enhanced by performing the module, and that they would find self-directed learning exercises like this one beneficial in other rotations.
CONCLUSIONS: A web-based module on ROP is an effective learning tool for pediatric residents. Web-based education will promote self-directed learning skills and provide an alternative to traditional teaching methods in the context of busy residency training programs. Future directions should include the assessment of long-term knowledge retention, and the incorporation of similar self-directed learning modules into other pediatric rotations.

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Documenting Resident Education in Systems-Based Practice

Sandra F. Braganza, Iman Sharif. Social Pediatrics, Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: Systems-based practice is an important teaching mandate of ACGME. Especially in underserved areas, social work (SW) referrals to link patients to community-based resources are one important aspect of this competency.
OBJECTIVE: To describe the number, types, and outcomes of referrals to social services by pediatric residents practicing in an underserved area.
DESIGN/METHODS: Setting: Inner-city academic health center where 80% of children are Medicaid recipients. 12 pediatric residents (4 PL1, 4 PL2, 4PL3) practice at the health center per academic year. In Oct 2005, as part of an inititative to teach systems-based practice, we instituted weekly SW rounds. Residents scheduled for continuity clinic met with SW and pediatric faculty to discuss social service referrals. A copy of every referral was kept in a log book, which was updated by the team.
We reviewed the log book and collected data for each referral made over 2 years. For each referral, an investigator recorded age of patient referred, level of training of the resident and coded the text of the "reason for referral" into referral themes(mental health, supplies, etc.) and comorbidity themes. Text in the "follow-up" section was coded into 3 possible outcomes: complete, incomplete, don't know. We used bivariate analyses to test whether types of referrals changed from year 1 to year 2, by level of training, or by age of patient.
RESULTS: Overall, 94 referrals were made by 14 residents over a 2-year period. (46-Year 1, 48-Year 2). 43% were made by PL2s; 41% by PL3s. Mean age of children referred was 7.4 years. Major referral themes included mental health (56%), need for medical supplies (15%), and need for home nursing services (10%). Major comorbidities included mental health (41%), chronic illness (31%), school failure (8%), and domestic violence (7%). Overall, 49% of referrals had completed outcomes. Of mental health referrals, 51% had completed outcomes. Referrals for mental health concerns involved older children (mean age 10.0(8.7, 11.4) vs. 4.9(3.4, 6.4). Referral patterns did not vary over time, or by resident level of training. Each resident recorded an average of 6.3 referrals over 2 years (range from 2 to 14).
CONCLUSIONS: The institution of SW rounds and a log book provided a feasible way to fulfill ACGME requirements to document teaching of systems-based practice. The data obtained can inform curriculum planning for teaching around this competency. Education on mental health would be an important part of the curriculum in this underserved setting.

137 House Officer

Resident as Teacher: Evaluation of a Teaching Curriculum for Pediatric Housestaff

Czer Anthoney E. Lim, Cristina E. Farrell, Catherine C. Skae. Department of Pediatrics, Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: Resident teaching workshops are an integral part of the housestaff curriculum. We propose a mechanism to measure their impact on educational interactions between members of the housestaff.
OBJECTIVE: To evaluate the efficacy of a curriculum for housestaff to increase the frequency of and confidence in teaching.
DESIGN/METHODS: Subjects completed pre-intervention surveys about their comfort with (1-5 Likert Scale) and number of teaching events per week, during daytime and night/weekend (N/W) hours; number of N/W shifts worked was collected to control for confounding effects of teaching opportunities. Over 4 weeks, subjects attended 4 interactive, power-point-based teaching workshops after which memory cues were placed in resident work areas and presentations placed online. Subjects then completed post-intervention surveys. Primary outcomes were confidence in and frequency of teaching. Frequency of being taught was a secondary measure. Paired t-tests were used to compare the mean changes from pre to post intervention.
RESULTS: In this paired groups, pre/post intervention study, 26 subjects with 23% PGY1, 34% PGY2, and 34% PGY3 enrolled. Significant increases occurred in comfort with teaching procedural skills (0.57, p=0.0016) and giving didactic sessions (0.54, p=0.0092). Without a significant difference in number of N/W shifts pre and post intervention (0.35, p=0.647), significant increases occurred in the number of teaching events during daytime precepting (0.96, p=0.0365), and bedside teaching (1.34, p=0.0157); significant increases occurred in N/W precepting (1.85, p=0.0003), bedside teaching (2.27, p=0.0004), procedures (1.31, p=0.0096), and providing feedback (1.46, p=0.0047). There was no significant change in daytime teaching received but the increased N/W frequency of being taught approached significance (1.0, p=0.0617).
CONCLUSIONS: This teaching curriculum resulted in increased confidence in teaching procedural skills and giving didactic sessions, and an overall increased frequency of precepting and bedside teaching. There were more dramatic increases in frequency of N/W teaching compared to daytime teaching and a trend suggesting that housestaff were taught more frequently on nights and weekends. These results suggest an educational benefit of N/W call and is a unique finding in the literature. Medical student evaluations are being used to objectively evaluate teaching skills and 3 and 6 month surveys will assess the longevity of these effects.

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An Intervention To Improve Neonatal Endotracheal Intubation Skills of Pediatric Residents

Colleen A. Hughes, Rose M. Viscardi, Alison J. Falck. Department of Pediatrics, University of Maryland Medical Center, Baltimore, MD.

BACKGROUND: Following delivery, 5-10% of infants require some degree of resuscitation and 1% need significant intervention to survive. Since pediatricians are often responsible for resuscitating newborns, endotracheal intubation (EI) is an important skill to acquire. Development of proficiency should be emphasized during residency training. Over the last decade, opportunity to perform EI during residency training has decreased. Recent published studies and data from our institution have shown that pediatric residents do not achieve competency in performing EI. A curriculum that maximizes EI opportunities while providing an optimal learning environment is necessary. The effect of this type of intervention to improve EI skills of pediatric residents has not been described.
OBJECTIVE: Implementation of a curriculum designed to improve exposure to neonatal EI with a formalized process of mentoring and feedback will improve EI success rates of pediatric residents at the University of Maryland Medical Center (UMMC).
DESIGN/METHODS: Pediatric residents at UMMC participated in an EI curriculum during their NICU rotation which included an educational module, EI schedule, and formalized mentoring with feedback. Residents were assigned a schedule during which they performed all EI procedures in the delivery room (DR) and NICU. EI procedures were supervised by experienced practitioners. EI procedure was defined as the effort of a practitioner to perform EI, regardless of number of attempts or whether success was achieved. Residents were given maximum of three EI attempts depending on the stability of the patient. Following the procedure, residents received structured feedback using an EI checklist. EI success rates of pediatric residents were compared to baseline data and statistical significance was determined by Chi-square analysis.
RESULTS: During the study period from 08/07-11/07, 52 EI procedures were observed. EI procedures performed by residents increased from 20% to 50% following the intervention. EI success rate for pediatric residents increased from 39% to 77% (p<0.05). This effect was seen in both the NICU and DR setting (p<0.05).
CONCLUSIONS: A structured curriculum that provides didactic review, increases opportunity to perform EI, and emphasizes mentoring can improve EI success rates of pediatric residents. Given current limitations on exposure, a novel approach is necessary to ensure competency in performing EI is achieved prior to completion of residency training.

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Education and Monitoring of Residents' Proficiency in Neonatal Resuscitation

Matthew A. Rainaldi, Yang S. Kim, Karen D. Hendricks-Munoz. Pediatrics, Neonatology, NYU Medical Center, New York, NY.

BACKGROUND: Since the emergence of Neonatal Intensive Care Units (NICUs), the American Academy of Pediatrics has emphasized the role of community hospitals to "recognize and provide initial management of infants requiring transfer to a NICU." One of the most important aspects of this management is proficiency in endotracheal intubation. It is an integral part of training and in a significant number of community hospitals a general pediatrician bares that responsibility.

OBJECTIVE: To: 1) determine the expectations of residents in acquiring proficiency in neonatal resuscitation. 2) assess self-perception of neonatal intubation skills by residents 3) measure residents' skill in intubating neonatal mannequins and 4) reevaluate intubation skills following the introduction of a structured educational curriculum.

DESIGN/METHODS: At total of 68/114 NYU Pediatric Residents were surveyed on neonatal resuscitation from 2005 to 2006. In 2006, a neonatal resuscitation curriculum consisting of monthly sessions (didactic and hands-on, 1½hour total) was implemented. Intubation proficiency was assessed before and after curriculum initiation. Longitudinal analysis of survey responses was performed to evaluate changes in expectations and/or skill over the two year period.

RESULTS: Most residents (94%) regardless of year of training, felt strongly that they should be proficient in neonatal resuscitation, yet fewer believed that this goal was attainable given the current curriculum and rotations in the NICU (70%). A majority of residents (63%) believed that intubation was a skill that a resident should be proficient in by second year (R2), but R2's reported only a 55% proficiency rate, and R3's only 68%. Perceived skill increased with higher training level during each academic year. After implementation of the resuscitation curriculum, R2's improved their intubation proficiency from 44 to 66%. Successful intubations (defined as first try and less than 30 seconds) were achieved by R1's (62.5%) and R2's & R3's (95%) immediately after NRP training. However, proficiency decreased to 36% for R2's & R3's when assessed during random periods not associated with NRP training.

CONCLUSIONS: Pediatric residents expect to reach proficiency in neonatal resuscitation, but find it challenging to do so. Education that includes an immediate practice period increases short-term confidence and success, however repeated education and practice experience is needed to maintain proficiency.

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Neonatal Resuscitation Simulation Measurement Tool Development

Jesse Bender, Karen Kennally, Sheree Lindgard, Jean Salera, Richard Tucker.
Pediatrics, Women & Infants' Hospital, Providence, RI.

BACKGROUND: Simulation based medical education is used increasingly to train pediatric residents to handle high risk, low frequency events. Assessment scales to evaluate their performance and team behaviors during simulated scenarios are used in Neonatal Resuscitation Program (NRP) training.

OBJECTIVE: Develop, refine and evaluate scenario-specific assessment tools with which to assess residents' performances.

DESIGN/METHODS: Four blinded NRP-certified instructors independently assessed the performance of pediatric and family medicine residents using a predetermined measurement tool. Indeterminate elements were identified, and modifications were made to create a revised assessment tool. The revised tool was used two months later to assess performance using the same videos. The initial tool was derived from the Megacode Assessment Form of the NRP textbook and published teamwork behavior checklists. Descriptive verbiage was assigned to a 5-point ordinal scale for each of 33 performance elements and 18 behavioral elements. Thirteen elements with the highest inter-rater variability were modified, and twelve other elements were clarified to improve discrimination between the 5 point scale.

RESULTS: Revisions did not change summary performance means for each resident, but did reduce the inter-rater variance between raters (table 1). Individual elements showed marked variation by pairwise comparisons kappa values. Kappa values across all test items, using Fleiss-Cohen weighting, showed markedly more concurrence with the revised tool than the initial tool (table 2).

Table 1: Summary of Performance Means

Resident	Version	Mean of all raters	Standard deviation
1	Initial	2.6	0.37
	Revised	2.4	0.29
2	Initial	2.4	0.71
	Revised	2.4	0.38

Table 2: Weighted Kappa Values for Three Raters vs Gold Standard Rater

Rater	Version	Kappa	Standard error	95% CI
A	Initial	0.5643	0.0371	0.4915 – 0.6371
	Revised	0.7687	0.0257	0.7183 – 0.8192
B	Initial	0.0897	0.0878	-0.0824 – 0.2618
	Revised	0.8292	0.0306	0.7691 – 0.8892
C	Initial	0.3742	0.0251	0.3250 – 0.4234
	Revised	0.6228	0.0274	0.5691 – 0.6765

CONCLUSIONS: While specifying more detail on a simulation performance assessment tool makes it less generalizable, it can markedly improve inter-rater agreement. This revised tool shows substantial inter-rater agreement.

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Antenatal Corticosteroids Are Associated with Decreased Odds of Death in Neonates Born at 23 Weeks

Edward J. Hayes, David A. Paul, Gary E. Stahl, Jolene Seibel-Seamon, Kevin Dysart, Benjamin E. Leiby, Amy B. Mackley, Vincenzo Berghella. Maternal Fetal Medicine/Obstetrics and Gynecology, Thomas Jefferson University, Philadelphia, PA; Neonatology/Pediatrics, Christiana Care Health Systems, Newark, DE; Neonatology/Pediatrics, Cooper University Hospital, Camden, NJ; Neonatology/Pediatrics, Thomas Jefferson University, Philadelphia, PA; Biostatistics/Pharmacology & Experimental Therapeutics, Thomas Jefferson University, Philadelphia, PA.

BACKGROUND: NICHD recommends antenatal corticosteroids for all pregnant women 24-34 weeks at risk for preterm delivery.

OBJECTIVE: Since a significant number of 23 week neonates are now undergoing resuscitation, our objective was to determine if exposure to antenatal corticosteroids decreased the odds of death in neonates born at 23 weeks gestation.

DESIGN/METHODS: Retrospective cohort study was performed of 23 0/7 to 23 6/7 week gestation neonates delivering between 1998-2007 at 3 tertiary centers. Neonates were excluded if they were stillbirths, terminations, or parents had elected non-resuscitation. Univariable logistic regression analysis was used to assess the association of clinical and demographic factors with the likelihood of death. A multivariable logistic regression model was used to assess the effect of steroids on the odds of death after adjustment for potential confounding variables.

RESULTS: The study sample included 181 infants. There were no significant associations between institutions (p=0.98), route of delivery (p=0.93), gender (p=0.89), race (p=0.90), maternal diagnosis at delivery (p=0.65), maternal drug use (p=1.0) , IVF (p=0.57) and survival. Multiple gestations were associated with increased odds of death, OR=3.66 (1.05,12,73). Multivariate logistic model revealed that infants exposed to antenatal corticosteroids had a decreased odds of death, OR=0.31 (0.12,0.83). In subsequent analysis, odds of death was related to completeness of course based on 2 doses of betamethasone or 4 doses of dexamethasone.

Antenatal Corticosteroids and Odds of Death: Multivariable logistic regression

Steroid Course	# of Patients	% that Died	Odds Ratio
Complete	45	80.0	0.15 (0.05,0.47)
Partial	36	88.9	0.64 (0.17,2.42)
None	100	93.0	1.0

CONCLUSIONS: Infants born between 23 0/7 and 23 6/7 weeks gestation, whose mothers received a complete course of antenatal corticosteroids, had an associated 85% reduction in the odds of death (p=0.001) compared to no steroids. This finding suggests the need for a large, multicenter prospective trial to confirm this observation, assess long-term morbidity and evaluate the cost-effectiveness of this intervention.

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Antenatal Smoking Does Not Affect the Severity of Apnea in Premature Infants

Zlatka Jeliazkova, Nosrat Razi, Judy G. Saslow, Barbara Amendolia, Gary Stahl, Kee Pyon, Nicole Kemble, Zubair H. Aghai. Pediatrics/Neonatology, Cooper University Hospital-Robert Wood Johnson Medical School, Camden, NJ.

BACKGROUND: Antenatal exposure to cigarette smoke is associated with increased risk of sudden infant death syndrome. Maternal smoking increases the rate of central apnea in full term infants. The effect of prenatal exposure of smoke on the severity of apnea in preterm infants is unknown.

OBJECTIVE: To study the effect of maternal smoking on apnea of prematurity.

DESIGN/METHODS: Preterm infants with a gestational age (GA) of 34 weeks or less born between January 1997 and September 2007 were included in this study. A four channel pneumogram was performed at the time of discharge. Relevant clinical data were collected from the infants' medical records. Premature infants who were exposed to cigarette smoke during pregnancy (study group) were compared with the infants who were not exposed to smoke (control group).

RESULTS: 1800 infants (GA ≤ 34 w) were born and admitted during the study period; 1656 infants survived and were discharged from the hospital. 263 infants (BW 1682±566 g, GA 31.0±2.8 w) were exposed to smoke and 1393 infants (BW 1638±575 g, GA 31.1±2.7 w) were not exposed to smoke. There was no significant difference in the baseline demographics and clinical characteristics (BW, GA, race, sex, prenatal steroid use, ventilator days and BPD) between the two groups. When comparing the smoking vs. control group, there was no difference in the incidence of apnea, number of infants treated with xanthines, the duration of xanthine therapy and the number of infants with abnormal pneumograms. There was also no significant difference in the number of infants discharged home on monitors, oxygen and xanthines.

Incidence and severity of apnea in preterm infants exposed to smoke vs. control

	Exposed to Smoke (n=263)	Control (n=1393)	p
Apnea (%)	154 (58.5)	773 (55.5)	0.4
Treated with Xanthine (%)	136 (51.7)	798 (57.3)	0.2
Duration of Xanthine (days)	18.5±27.7	19.9±27.8	0.5
Abnormal Pneumogram (%)	84 (31.9)	429 (30.8)	0.8
% Period Breathing	4.3±6.8	4.7±7.3	0.5
Apnea Density	1.9±2.8	1.8±2.1	0.6
Discharge on monitor	125 (47.5)	679 (48.7)	0.8
Discharge on O2 (%)	29 (11.0)	135 (9.7)	0.6
Discharge on Xanthine (%)	63 (24.0)	312 (22.4)	0.6

CONCLUSIONS: Prenatal exposure to cigarette smoking was not associated with increased incidence or severity of apnea in premature infants.

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Analysis of Cesarean Section Trends in Very Low Birth Weight Infants (VLBW) over Time and Impact on Birth Outcome (1994-2006)

Hashini R. Seneviratne, Charlan Kroelinger, David A. Paul. Delaware Department of Health and Social Services, Delaware Division of Public Health, Dover, DE; Pediatrics and Neonatology, Christiana Care Hospital, Newark, DE; School of Urban Affairs and Public Policy, University of Delaware, Newark, DE.

BACKGROUND: Cesarean section (CS) deliveries are becoming increasingly common for various reasons; including maternal or obstetrician preference, past delivery and medical history. The relationship between cesarean delivery and outcome in VLBW remains uncertain.

OBJECTIVE: To analyze the trend in CS deliveries over time, and determine whether there is an association between CS and poor outcomes in VLBW infants.

DESIGN/METHODS: This study is a cohort analysis of babies with birth weight <1500g, between 1994 and 2006, n= 2040. All infants were cared for at Christiana Hospital, the only level 3 NICU for VLBW infants in the State of Delaware. All infants had a cranial sonogram performed on the 4th day of life. Severe IVH was considered grade 3-4. For the purposes of this study, poor outcomes are defined as death, severe intraventricular hemorrhaging (IVH), or a combination of death and/or IVH. Data was analyzed based on 3-year cohorts. Logistic regression analysis was used to investigate CS trends over time, and the association between CS and poor outcomes.

RESULTS: Mean birthweight, gestational age, or inborn status did not change over the study period. When analyzing cohorts of VLBW patients it was found that cesarean delivery increased 22% from 1994 to 2006. When controlling for variables such as gestational age, maternal age, multiple gestation, preeclampsia, diabetes, PPROM, and infant position; the odds of cesarean delivery remained elevated in Cohort 4 compared to Cohort 1 (table). After controlling for the factors above, CS was not associated with death, severe IVH, or IVH and/or death (OR 1.2, 95% CI 0.9-1.6).

	Cohort 1 (1994-1997) n=419	Cohort 2 (1997-2000) n=526	Cohort 3 (2000-2003) n=530	Cohort 4 (2003-2006) n=565
Death and/or Severe IVH (%)	16%	21%	25%	22%
C/S Deliveries	58%	59%	62%	71%
Univariable Odds of C/S	reference	1.1 (CI = 0.8-1.4)	1.1 (CI = 0.96-1.3)	1.2 (CI = 1.1-1.3)
Multivariable Odds of C/S	reference	1.1 (CI = 0.8-1.4)	1.0 (CI = 0.9-1.2)	1.2 (CI = 1.1-1.3)

CONCLUSIONS: In our population of VLBW infants, the rate of CS delivery increased over time. This increased rate was not associated with any change in the odds of death and/or severe IVH. Our data suggest that further investigation is needed concerning the benefits and risks of increasing rates of cesarean delivery in VLBW infants.

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Duration of Caffeine Citrate Therapy Is Associated with Increasing Postnatal Growth Restriction in Very Preterm and Low Birth Weight Infants

Jennifer L. Lefner, Richard Tucker, Leslie McKinley, William Oh. Pediatrics, Women and Infants Hospital, Brown Medical School, Providence, RI.

BACKGROUND: • Premature infants are often treated with caffeine citrate for apnea of prematurity. Caffeine has been shown to cause increased oxygen consumption, increased energy expenditure, and decreased weight gain among infants treated for apnea of prematurity.

OBJECTIVE: • To assess the effects of caffeine on growth outcomes of very preterm and very low birth weight infants being treated with caffeine for idiopathic apnea of prematurity. Our hypothesis is that there is an inverse correlation between duration of caffeine citrate therapy and growth in very preterm and very low birth weight infants who are on such therapy for apnea of prematurity.

DESIGN/METHODS: We retrospectively reviewed the growth data of 136 infants less than 1500 grams birthweight, less than 32 weeks gestation, on caffeine for apnea of prematurity using chart review and information extracted from our Department of Pharmacy database, and our generic database over a 20 month period from April 2004 through December 2005. The data analysis included the pearson correlation of anthropometric growth outcomes (weight, length, and head circumference) at 36 weeks post conceptual age, growth velocity (gm/kg/day), caloric intake (kcal/kg/day), and duration of caffeine dosing (days). Infants were identified to be extra uterine growth restricted if they were <10% for weight at 36 weeks, and a T-test was performed to evaluate the differences between those who were EUGR and those non-EUGR infants. Multiple linear regression analysis was done looking at anthropometric outcomes at 36 wks post conceptual age.

RESULTS: There were 62 infants for whom data was available at 36 weeks corrected gestational age who were included in our analysis. There was no significant correlation of weight at 36 weeks or growth velocity and duration of caffeine dosing. There were no significant differences found between the extra-uterine growth restricted infants and those not growth restricted at 36 weeks. Multiple linear regression analysis revealed a relationship approaching significance between duration of caffiene dosing and growth velocity with a p value = 0.051.

CONCLUSIONS: • Duration of dosing with caffeine citrate does not have a significant effect on weight, length, or head circumference at 36 weeks post conceptual age. Duration of dosing with caffeine citrate is inversely related to growth velocity (gm/kg/day) in a manner which approaches significance.

145 Fellow in Training

Patent Ductus Arteriosus Ligation in the Neonatal Intensive Care Unit Versus the Operating Room: Short Term Morbidities

Sara D. Sibley, Martha C. Caprio, Pradeep V. Mally, Karen D. Hendricks-Munoz. Pediatrics, Division of Neonatology, New York University School of Medicine, New York, NY.

BACKGROUND: Surgical ligation of patent ductus arteriosus (PDA) is one of the most common types of surgery in preterm babies. It is performed in the NICU on Very Low Birth Weight (VLBW) infants (<1500gms) in many institutions as a standard of care. In 2006, NYU began performing surgical ligations on VLBW infants in the NICU, instead of the operating room (OR). There are no recent studies comparing the neonatal outcomes following PDA ligation in the NICU vs the OR.

OBJECTIVE: To compare outcomes of infants who underwent surgical ligation in the NICU to those who were transported to the OR.

DESIGN/METHODS: We conducted a retrospective chart review of VLBW infants who underwent surgical ligation of PDA at New York University Medical Center between 1/2004 and 5/2007. This group was divided into 2 cohorts: 1) OR and 2) NICU. Primary outcomes were length of time on oxygen and mechanical ventilation. Secondary outcomes were length of stay, surgical complications, IVH, sepsis, post-operative assessment of fluid, electrolytes, and vital signs. Data was compared using students t-test, and P-values of <0.05 were considered significant.

RESULTS: A total of 50 infants met th study criteria, 26 VLBW infants underwent PDA ligation in the NICU, and 24 infants were transported to the OR for the procedure. Background demographics were evenly matched between the groups, including birth weight, gestational age, antenatal steroids and Apgar scores. The primary outcome measures, which were days on oxygen (70.5±23 days for OR group vs 92.9±53 days for NICU group) and mechanical ventilation (35.5±18 days vs 50.9±50 days), were not significant. Weight at surgery was heavier in the OR group (1240±433gm vs 968±262gm, p=0.009), and their age in days at the time of surgery was older (35.2±16 days vs 21.4±10 days, p=0.0006). Postoperatively the OR group had lower temperatures (35.9±0.96 C° vs 36.7±0.51 C°, p=0.0006).

CONCLUSIONS: In this group of VLBW infants, temperature instability was an important post-operative factor in those infants who underwent PDA ligation in the OR. Since hypothermia may directly contribute to poor neurodevelopmental outcome in neonates the short and long term neurodevelopmental outcomes of these infants will be stratified for hypothermia. Finally,differences in clinical practice may have played a role in the OR ligated infants being larger and older than the NICU ligated infants at the time of surgery.

146 House Officer

Decrease in Number of PRBC Transfusions but Not Exposure in Very Low Birth Weight Infants Between 1994 and 2006

Celina C. Sindall, Robert G. Locke, Amy Mackley, David A. Paul. Pediatrics, Thomas Jefferson University/A.I. duPont Hospital for Children, Wilmington, DE; Neonatology, Christiana Hospital, Newark, DE.

BACKGROUND: Very low birth weight (VLBW) infants frequently require transfusions of packed red blood cells (PRBC). Transfusion practices have changed over time.

OBJECTIVE: To investigate trends in PRBC transfusions over the past 12 years.

DESIGN/METHODS: Retrospective cohort study from a single level 3 NICU between 1994 and 2006. The study sample included infants with birthweight less than 1500 grams. PRBC transfusions were ordered based upon clinical criteria. Data was analyzed using four 3-year cohorts. Illness severity on the day of birth was quantified by the Score for Neonatal Acute Physiology (SNAP.) Data analysis included ANOVA, Kruskal–Wallis test, and multivariable analysis using stepwise linear regression. Data are presented as mean ± sd.

RESULTS: The study sample included 2045 infants. Although there was no change in the proportion of babies transfused, mean number of transfusions/infant decreased over the 12 year study period (table.) Transfusions/infant decreased in both infants less than and greater than 1kg. During the study period there were no changes in birthweight, gestational age, or days of mechanical ventilation. Illness severity increased over time. After controlling for potential confounding variables including gestational age, mechanical ventilation, and illness severity, the birth cohort remained independently associated with PRBC transfusions. (Overall model: r^2=0.64, p<0.01).

	Cohort 1 (1994-1997 n=423	Cohort 2 (1997-2000) n=527	Cohort 3 (2000-2003) n=530	Cohort 4 (2003-2006) n=565	p
PRBC/infant	3.7 ± 4.9	3.0 ± 4.2	2.4 ± 3.6	2.1 ± 3.1	<0.001
Any PRBC (%)	54%	52%	49%	47%	0.15
Birthweight(g)	1051 ± 290	1040 ± 278	1040 ± 285	1012 ± 289	0.16
SNAP	10.8 ± 5.8	12.3 ± 6.9	14.2 ± 8.9	14.2 ± 9.0	<0.001
Mechanical Ventilation (days)	14.0 ± 19.8	14.4 ± 19.9	12.3 ± 21.4	11.9 ± 19.9	0.12
PRBC/infant BW<1000gms	7.5 ± 5.2	5.3 ± 4.6	4.4 ± 4.5	3.7 ± 3.7	<0.001

CONCLUSIONS: In our population of VLBW infants, the number of PRBC transfusions/infant has decreased over time, although the proportion of infants transfused has not. We speculate that changing transfusion threshold, blood banking and phelobotomy practices are responsible for the decrease. From our data, we can not determine the clinical impact of the decrease in transfusions.

147 Fellow in Training

Packed Red Blood Cell Transfusions Are Strongly Associated with Necrotizing Enterocolitis in the Very Low Birthweight Infant

Kelly J. Zook, Alexandra Remakus, Amy Mackley, Deborah Tuttle, Robert Locke, David A. Paul. Neontaology and Pediatrics, Christiana Care Health System, Newark, DE; Pediatrics, Thomas Jefferson Univ, Phila, PA.

BACKGROUND: Very low birthweight infants (VLBW) frequently require packed red blood cell transfusions (PRBC) throughout the NICU course. Previous studies have reported conflicting results regarding NEC in association with PRBC transfusions.

OBJECTIVE: The purpose of this study was to investigate the association between NEC and PRBC transfusions.

DESIGN/METHODS: Retrospective cohort study that included 2311 VLBW (<1500gm) cared for at Christiana Care Health System, a single level 3 NICU in Delaware between July 1993 and July 2007. NEC was defined as Bell's stage 2 or greater. Illness severity on the day of birth was quantified by SNAP. All PRBC transfusions were ordered by the medical team based on clinical indications. Statistical analysis included ANOVA, Chi-Square, Mann-Whitney U Test and multivariable analysis using logistic regression.

RESULTS: A total of 122 infants (5.2%) developed NEC. Those infants who developed NEC were of lower birthweight and gestational age, had longer length of time on the ventilator, were more likely to be exposed to postnatal steroids, and more likely to have PDA than those infants who did not develop NEC. There were no differences in antenatal steroids, SGA, SNAP, and Apgar scores between the infants with and without NEC. Infants who developed NEC were more likely to be transfused PRBC's (91% vs 48%, p<.01) and received an increased number of PRBC (5.6 ± 5.0 vs 2.7 ± 4.1, p<.01) compared to those infants without NEC. Separate logistic regression models were created. Model 1 used all variables associated with NEC on univariable analysis, and Model 2 eliminated postnatal variables such as PDA and ventilator days which may be part of the causal pathway for NEC.

Table 1 Odds of NEC with PRBC

	Univariable Analysis	Multivariable Analysis- Model 1: All variables	Multivariable Analysis- Model 2:antenatal variables only
Odds of NEC with any PRBC transfusion	8.9 (3.4-24.8)	9.6 (4.8-19.2)	9.6 (5.1- 18.2)
Odds of NEC per PRBC transfusion	1.1 (1.07-1.14)	1.09 (1.04-1.14)	1.07 (1.02-1.13)

Data are odds (95% CI)

CONCLUSIONS: In our population of VLBW infants, PRBC transfusions were strongly associated with NEC. From our data we can not determine whether PRBC are causal for NEC or a marker for other risk factors. Our data are important for hypothesis generation and suggest the urgent need to investigate the causality of PRBC with NEC.

148 Fellow in Training

Amplitude Integrated EEG (aEEG) Monitoring During Selective Hypothermia Has Potential Important Clinical and Prognostic Implications

Vivien L. Yap, Jeffrey M. Perlman, Murray Engel. Pediatrics, New York Presbyterian Hospital- Weill Cornell Medical Center, New York, NY; Neurology, New York Presbyterian Hospital-Weill Cornell Medical Center, New York, NY.

BACKGROUND: Selective hypothermia has been shown to improve survival and neurodevelopmental outcome in term newborns at risk for hypoxic ischemic encephalopathy (HIE). We implemented a practice plan in which a single-channel aEEG (Olympic Medical) and raw EEG (rEEG) was done from admission and throughout the 72h of head cooling. We hypothesize that continuous aEEG and rEEG monitoring will detect subclinical seizures (Sz) and that Δs in aEEG patterns during cooling may relate to abnormal (abnl) outcome.

OBJECTIVE: To determine the occurrence of subclinical Sz during cooling and the impact of cooling on aEEG characteristics in relation to short-term outcome.

DESIGN/METHODS: aEEG was done for ≥20min prior to initiating hypothermia and throughout cooling. Conventional EEG (cEEG) was done at intervals during and continuously after cooling. Enrollment criteria were consistent with head cooling protocol. aEEG characteristics [upper margin (UM), lower margin (LM), bandwidth (BW=UM-LM), Sz consistent on both aEEG and rEEG, sleep-wake cycling (SWC)] were recorded at admission, 0-12, 12-24, 24-48, 48-72, & >72h. Short-term outcome was defined as abnl MRI consistent with HIE.

RESULTS: 10 term infants were monitored with aEEG & rEEG for mean duration of 90h. At admission, the tracings for 5/10 infants were severely abnl (UM<10μV), 2 were moderately abnl (UM>10μV, LM<5μV), 1 had Sz, and 2 had motion artifact. All infants (n=4) with abnl MRIs had severe tracing or Sz at admission. Clinical Sz (n=7) or EEG Sz (n=9) were treated with phenobarbital (n=10), fosphenytoin (n=7), midazolam(n=9). Cooling and AED ↓ BW from 7.4μV at admission to 4.6μV at 12-24h. All infants with normal MRI (n=6) had ↑ BW by 24-48h, vs 1/4 with abnl MRI. SWC was present by 24-48h in 3/6 with normal MRI vs 0/4 with abnl MRI. All infants with normal MRI had Sz in first 24h, with resolution by 48-72h; 3/4 with abnl MRI had early Sz with persistence >72h in 2. The rEEG tracings correlated well with the conventional EEG.
CONCLUSIONS: aEEG and rEEG monitoring during cooling provides additional information related to Sz detection and pattern Δs that are related to abnl MRI findings. EEG Sz occur often without a clinical correlate. Recovery of normal aEEG BW & SWC and cessation of Sz indicate favorable short term outcome. Artifacts may contribute to an elevated tracing, which may be confused with Sz or limit induction of therapy-clinical evaluation is critical in this regard.

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Medical Student

Indicators of Compliance for Neonatal Follow-Up

Vedika Nehra, Paul Visintainer, Jordan S. Kase. School of Medicine, New York Medical College, Valhalla, NY; School of Public Health, New York Medical College, Valhalla, NY; Pediatrics, The Regional Neonatal Center Maria Fareri Children's Hospital Westchester Medical Center-New York Medical College, Valhalla, NY.

BACKGROUND: Outpatient screening of neonates at risk for developmental delay due to prematurity or other conditions in the perinatal period is imperative in identifying children with delays remidable by therapeutic services. Although it is known that early identification and treatment is beneficial in optimizing developmental outcome, close follow-up (f/u) is often overlooked.
OBJECTIVE: The objective of this study is to identify factors associated with compliance of outpatient f/u appointments in order to ensure future optimal care and attention to these children.
DESIGN/METHODS: This retrospective observational cohort study looked at all patients who were born between 07/01/2006 and 06/30/2007 admitted to the Regional NICU (RNICU) at the Maria Fareri Children's Hospital at Westchester Medical Center. Children referred for developmental f/u after discharge (d/c) were included in analyses. D/C summaries were reviewed to attain information regarding 3 antenatal factors, 2 transfer status variables, 18 neonatal morbidities, and 5 variables addressing coordination of d/c. Recording of data and analyses were performed utilizing the statistical software SPSS 11.5. Children were divided into two categories: compliant (C) or non-compliant (NC) with f/u appointments. Comparison of categorical variables between compliance groups was done with chi square analysis. T-test compared the means of continuous variables. Mann Whitney U Rank sum test compared ordinal variables. Significance defined as p<0.05.
RESULTS: A total of 329 patients were admitted to the RNICU, and referred to f/u upon d/c. Overall rate of compliance was 60%. Antenatal variables: maternal drug use and maternal age were significantly associated with compliance: drug use: C:11.7%; no drug use: C:62.2%; p<0.001; age: C:30years;NC:28years;p=0.02 . Transfer status: only patients transferred out correlate significantly: transfer out: C:10.3%; no transfer: C:62.2%; p<0.001. Neonatal co-morbidities: only mode of delivery was associated with compliance: C-section: C:64%;vaginal:52% p=0.038. D/C coordination: only patient contact by phone within a week of d/c improved compliance: no contact: C:34%; left message: C:55%; contacted: C:67%; p<0.001.
CONCLUSIONS: Maternal drug use and transfer of patient to a hospital closer to the family both decreased patient compliance. Contacting patients after d/c significantly improved compliance. Close attention to these indicators of compliance may help to optimize appropriate f/u and developmental outcomes of future patients.

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Benign Extra-Axial Fluid Collections in Ex-Preterm Children

Noah Cook, Nancy Brodsky, Jo Ann D'Agostino, Frances Orlando, Judith Bernbaum, Hallam Hurt, Robert Zimmerman. Neonatology, The Children's Hospital of Philadelphia, Phila., PA.

BACKGROUND: "Benign extra-axial fluid collection" (BEAF) has been associated with premature birth. Although generally regarded as innocuous, BEAF has also been linked to neurodevelopmental impairment. Inconsistencies in reported outcomes may be due to varying diagnostic criteria and to confounding factors such as hydrocephalus and cerebral atrophy. The identification of truly 'benign' fluid collections could prove highly valuable in the care of ex-preterm children.
OBJECTIVE: Characterize BEAF according to specific radiologic features, and determine whether BEAF is associated with a reassuring developmental outcome in ex-preterm children.
DESIGN/METHODS: A retrospective study of children born between 2001-2006 at ≤32 weeks gestation, who underwent cranial MRI or CT imaging and neurodevelopmental testing after term-corrected age. Images were characterized by an experienced neuroradiologist using 9 features and 20 measurements. *BEAF* was defined as isolated extra-axial fluid collection (EAF) or mild EAF with proportional ventriculomegaly, without features of overt hydrocephalus or cerebral atrophy. ROC analysis was used to identify measurements that distinguish BEAF from other abnormal forms of EAF (*Abnl EAF*). χ^2 analysis was used to compare imaging findings with clinical outcomes. The primary outcome was severe cognitive or motor impairment based on the Bayley Scales of Infant Development (BSID) II/III.
RESULTS: 72 subjects (mean 27.4±2.6 wks gestation, 1038±454 g birthweight) met inclusion criteria; 28 (39%) had EAF, including 13 BEAF and 15 Abnl EAF. Mean adjusted ages at the time of imaging and BSID testing were 10.9±8.6 and 21.3±8.9 months, respectively. Mean BSID scores for BEAF subjects were within the normal range, with only one BEAF subject having severe impairment vs. 8 Abnl EAF subjects (7.7% vs. 53.3%, p=0.016). Corpus callosum thickness and 3rd ventricle width were strong indicators of atrophy (AUC 0.74 ±0.07) and hydrocephalus (AUC 0.83±0.05), respectively. A composite of these and 3 other measurements (internal capsule, corona radiata and ambient cistern), when abnormal, was associated with Abnl EAF (p=0.002) and developmental impairment (p=0.036).
CONCLUSIONS: BEAF, as defined here, is associated with a reassuring developmental outcome in ex-preterm children. Specific intracranial measurements are useful in objectively distinguishing those with 'benign' EAF from those at risk for severe developmental impairment.

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Dermoid Cysts Following Fetal Myelomeningocele Closure: Clinical Implication and Follow-Up

Enrico Danzer, N. Scott Adzick, Natalie E. Rintoul, Deborah M. Zarnow, Erin M. Simon Schwartz, Jeanne Melchionni, Leslie N. Sutton, Alan W. Flake, Mark P. Johnson. The Center for Fetal Diagnosis and Treatment, The Children's Hospital of Philadelphia, Philadelphia, PA.

OBJECTIVE: To evaluate incidence and clinical implication of dermoid cysts (DC) after fetal myelomeningocele (fMMC) closure.
DESIGN/METHODS: Retrospective databases and parental questionnaire information (IRB#2006-2-4587) were used to determine the incidence, clinical presentation, and outcomes of children that developed DC following fMMC surgery.
RESULTS: Prior to the NIHCD-MOMS trial, 54 children underwent fMMC closure at our institution. Sixteen (29.7%) presented with symptomatic spinal cord tethering and required surgery at a median age of 24 months (range, 4-93). Of those, 11 (69%; 20% of total) developed tethering secondary to DC. In 10/11 DC was seen on preoperative MR imaging. In one, the cyst was found during surgical exploration. All but one (L3 lesion level) dermoids developed in children with L4 or L5 defects. Within a mean follow-up of 42±14.9 months, 4 children had recurrence of symptomatic DC and required reoperation. After surgery for DC, 5/11 (45.5%, 3 after primary DC removal) lost normal bladder function, now requiring clean intermittent catheterization. Four children with DIC experienced long-term loss of lower extremity function by one, three, one, and two neuromotor levels, respectively. However, these changes did not alter their overall ambulatory status (5 walking independently, 3 require bracing, 3 with walker). Four (7.4%) additional children with evidence of DC on surveillance MR imaging are currently asymptomatic. All four are continent and ambulatory (3 independent, 1 with walker) at a mean age at follow-up of 71.5±21.2 months (range, 48-94). Patients' demographics and frequency of Alloderm use at initial fMMC surgery in children with DC did not differ from entire group.
CONCLUSIONS: It is currently unknown, whether fMMC closure increases the incidence of DC, or perhaps the better than expected function and close follow-up allowed earlier recognition. The ongoing NIHCD-MOMS trial will be able to determine whether children that underwent fetal intervention are at increased risk of DC development compared to children that underwent postnatal MMC closure. Deterioration of bladder function is the most common long-term complication of DC after fMMC surgery. Patients undergoing prenatal counseling should be informed about the risk of DC formation following fetal surgery.

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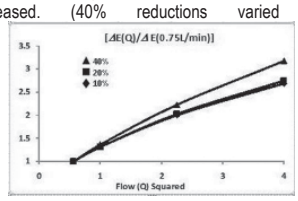
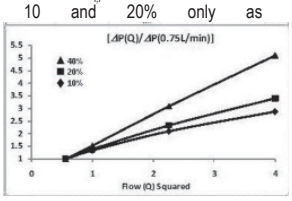
Pressure-Flow Relationship: Relevance to Bidirectional Glenn Shunt To Reduce Flow Across Pulmonary Outflow Obstruction

Joshua Wiesman, Nancy Ross-Ascuitto, Robert Ascuitto. Innovations, LLC, Hopkinton, MA; Pediatric Cardiology, LSU Health Sciences Center, New Orleans, LA.

BACKGROUND: A bidirectional Glenn shunt (BGS) was used in a two-ventricle repair of 10 patients (3-17 yrs old) having congenital heart disease with severe pulmonary outflow obstruction, thereby avoiding a pulmonary conduit. Doppler studies showed preop transpulmonary peak pressure drops of 70-100 (mean 84) mmHg; postop <10-16 (mean <12) mmHg.
OBJECTIVE: To obtain insight into using a BGS to volume unload an obstructed pulmonary ventricle, we employed a computer-based model of fluid flow, taken to simulate blood traversing passages with circumferential obstructions (10, 20 and 40% reductions in cross sectional area).
DESIGN/METHODS: Pressure distributions and velocity fields, determined from solutions (finite element analysis) to the Navier-Stokes equations, were used to assess the pressure-flow relationship (*i* to *f*). Pressure drop $\Delta P_{i,f}$ and flow-energy loss $\Delta E_{i,f}$ were described by: $\Delta P_{i,f}(Q) = (\langle P \rangle_i - \langle P \rangle_f)$; $\Delta P_{i,f}(Q) = (\langle K \rangle_f - \langle K \rangle_i) + \Delta E_{i,f}(Q)$, where $\langle P \rangle$ and $\langle K \rangle$ represent flow-averaged pressure and kinetic energy, respectively, Q flow rate. Model parameters: obstruction length 0.02m; pathway diameter 0.012m, fluid density 1050 Kg/m^3, viscosity 3.5x10^{-3} N-s/m^2, and flows 0.75, 1.0, 1.5 and 2.0 L/min.
RESULTS: Figs show increases in $\Delta P_{i,f}$ and $\Delta E_{i,f}$ as flow rate is increased. (40% reductions varied as Q^2; 10 and 20% only as Q).





CONCLUSIONS: Pressure drop and flow energy loss markedly increase as flow rate across obstruction increases. This finding supports the use of a BGS to reduce flow across residual outflow obstruction by volume unloading the pulmonary ventricle.

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Resident

A Prospective Cohort Study of Arrhythmias in the Neonatal Intensive Care Unit

Nadia Badrawi, Ranya Hegazi, Edisa Tokovic, Wael Lotfy, Fadya Mahmoud, Hany Aly. Neonatology, Cairo Children's Hospital, Cairo, Egypt; Cardiology, Cairo Children's Hospital, Cairo, Egypt; Pediatrics, Children's National Medical Center & George Washington University, Washington, DC.

BACKGROUND: Arrhythmias among newborns are not uncommon, but the exact incidence and types of arrhythmia in the neonatal intensive care unit (NICU) is not known. It is also not fully clear whether different medical conditions, interventions and medications administered to these ill infants could predispose to arrhythmias.
OBJECTIVE: To identify the incidence, common types, associated risk factors and presentations for arrhythmia in the NICU.
DESIGN/METHODS: We prospectively conducted 12-lead EKG studies on a random sample of 457 neonates who were >3 days old and >28 weeks gestation. All Infants were evaluated for the presence of arrhythmias. A 24-hour Holter monitoring was offered randomly to every 4th baby with normal EKG and to all of those who demonstrated arrhythmias on their EKG creating 3 groups: normal, benign and non-benign arrhythmia. Two-dimensional echocardiography (ECHO) was performed in all neonates clinically assessed with murmurs or electrophysiologically diagnosed with arrhythmia. Screening results were correlated with

maternal, obstetrical and neonatal data. Unpaired student t- test, Mann-Whitney test, Chi square test, Fisher's exact and analysis of variance testing were used for analysis. Correlation and regression analyses were also performed whenever appropriate.
RESULTS: Of the 457 patient EKGs studied, 39 (8.5%) had benign arrhythmia, and 7 (1.5%) had non-benign arrhythmia. Male gender, maternal age and maternal smoking were identified as risk factors for arrhythmia. Infants with benign arrhythmia had lower glucose levels (89± 38 mg/dl vs. 103 ± 29.2 mg/dl in the normal group, p=0.03).
A total of 139 infants had Holter monitoring, with 48 infants showing arrhythmia. None of the infants with arrhythmias were <32 wks, 12 (25%) were 32-37 wks, and 36 (75%) were >37 wks. Arrhythmia significantly correlated with severe hypoxic ischemic encephalopathy (p=0.03), high umbilical artery lines (p<0.01), and β-2 receptors agonist drugs used for nebulization (p=.023). Umbilical venous lines and dopamine infusion were not associated with arrhythmia.
CONCLUSIONS: Arrhythmias have higher prevalence among NICU population compared to previously reported figures in neonates. They are more common in male infants with older gestational age. Maternal smoking, high umbilical artery lines, lower glucose levels, and the use of the nebulized β-2 adrenergic treatment were associated with benign arrhythmia.

154 Fellow in Training

Clinical Significance of Neutropenia (N) in HIV Infected Children (HIVIC)

Tong Wei Ch'ng, Barry Dashefsky, Arry Dieudonne, James Oleske, J. Flyer, S. Keller. Pediatric Infecious Diseases, New Jersey Medical School (UMDNJ), Newark, NJ.

BACKGROUND: N, an absolute neutrophil count (ANC) < 1000/mm^3, is common in patients with HIV infection. Unlike in patients with malignancy, where N is associated with a 10-60 % risk of serious infection (SI), N is not consistently associated with SI in studies of HIV-infected adults. Rate of N and associated risk for SI in HIVIC is unknown.
OBJECTIVE: In a sample of HIVIC, to determine (1) rate of N; (2) risk factors (RF) for N; (3) any association between N and SI.
DESIGN/METHODS: In a retrospective observational cohort study, medical records from 2002-06 of 198 HIVIC aged 1- 27 yrs enrolled at FXB Pediatric HIV Clinic were reviewed. Specified demographic, clinical and laboratory data were recorded re each observational encounter (OE) at clinic visits or during hospitalizations. Each OE associated with N was counted as 1 episode of N (EN). SIs included are meningitis, blood stream, soft tissue and serious opportunistic infections. Rates of N and SI were calculated. Data were analyzed for associations between the two and for other potential RFs for each [eg, demographics, medications, CD 4 %, HIV viral load (VL)] by univariate and multiple logistic regression tests.
RESULTS: 3762 OEs (3650 outpatient; 112 inpatient) were recorded for 198 subjects (S). Mean OE/ S=19, range=1-54. 51% were male, 73% Black, 16% Hispanic, 7% White and 4% other. 285 (7.6%) of OEs were ENs. 74 S (37.4%) had ≥ 1 EN; 50% had ≤ 2 ENs, 30% had 3-6 and 20% had 7-17. Median ANC =2400 for non-ENs and 825 for ENs. ANC=500-999 in 93% of ENs (and 750-999 in 65%). Median CD4 % and $\log_{10}$ VL during ENs and non-ENs were 31% vs. 28%, and 3.1 vs. 2.9 respectively. 3 SIs occurred during 285 ENs (1.05%) and 70 SIs during 3477 non-ENs (2.01%) [OR=0.6; p=0.35]. Of examined potential RFs, only AZT (OR=2.1, p<0.01) and SMX/TMP (OR=2.6, p<0.01) were significantly associated with EN and only female gender (OR=3.7; p=0.02) and CD4 by every 10% decrease (OR=2.3; p<0.01) were significantly associated with SI.
CONCLUSIONS: 37.4% of a large sample of HIVIC observed for 5 years during HAART era experienced ≥ 1 EN; N was noted during 7.6% of 3762 OEs. Use of AZT and SMX/TMP were RFs for N. N was typically associated with ANC>500, self-limited and rarely associated with SI. Only 73 SIs noted during <2% of OEs; female and low CD4% were RFs for SI, but N was not. N appears to be less hazardous in HIVIC than in children with malignancy, perhaps reflecting the impact of HAART on reducing rates of SI.

155 Fellow in Training

Natural History of Progression of Metabolic Risk Factors in Uncomplicated Obesity in Urban, Inner City Children with Diet and Exercise Recommendations Alone

Minu M. George, Radhika Purushothaman, Shahid Malik, Arlene B. Mercado, Salvador Castells, Svetlana Ten. Department of Pediatrics, Maimonides Infants and Children's Hospital of Brooklyn, Brooklyn, NY; Department of Pediatrics, Children's Hospital at SUNY Downstate Medical Center, Brooklyn, NY.

BACKGROUND: Childhood obesity is a worldwide problem that has reached epidemic proportions. With obesity, the first line treatment is modification of dietary and exercise habits.
OBJECTIVE: To evaluate the natural progression of obesity with Dietary/Exercise therapy alone on BMI, lipid profile, BP, and insulin sensitivity in children from an urban, inner city population without biochemical complications at baseline.
DESIGN/METHODS: This is a retrospective study of 32 obese children 11.1 ± 3.4 yrs (22 boys, 11.7 ± 3.4 yrs, BMI 32.3± 5.4 kg/m^2 & 10 girls, 9.8 ± 3.2 yrs, BMI 27.3 ± 7.3 kg/m^2), who underwent dietary/lifestyle therapy alone. None of them received any pharmacological intervention. Children with elevated lipid profile, liver function, glucose, HbA1c were excluded from analysis. Weight, height, BMI, blood pressure (BP), HbA1c, lipid profile, liver function, fasting insulin and glucose were measured at first visit and at subsequent follow up visits. Their natural progression was evaluated 18 months later. Dietary/Exercise therapy was discussed with the family at several follow up visits. The data was analyzed by paired t-test. Children were analyzed as a whole group and divided into boys and girls to evaluate the differences.
RESULTS: BMI, systolic blood pressure (SBP), fasting insulin increased significantly in the boys group and in the total group ($p < 0.05$), but not in the girls group. HDL significantly decreased in boys and in the total group ($p < 0.05$), but not in girls. There were no changes in diastolic BP, cholesterol, triglycerides, LDL, glucose, HbA1c, ALT, and AST levels.
CONCLUSIONS: Dietary/Exercise therapy alone did not improve HDL, insulin, BMI, and SBP. Natural history, even of uncomplicated obesity, revealed a negative progression of cardiovascular risk factors such as HDL, insulin, BMI and SBP. More intensive intervention is indicated in early childhood to prevent the formation of metabolic syndrome in early adolescence. The girls group did not reveal statistically significant changes, only the same tendency as a whole group. This can be explained by the younger age of the studied girls and the protective effect of estrogens.

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The Relationship Between Healthy Land Use in the Built Environment and Body Mass Index (BMI) Percentiles Among Inner City School Children

James J. Burns, Jane Garb, Coleen Walsh, Thomas Yarsley. Pediatrics, Baystate Children's Hospital, Tufts University School of Medicine, Springfield, MA.

BACKGROUND: One explanatory hypothesis for the recent increase in childhood obesity is inadequate levels of physical activity. Healthy land use may be associated with less childhood obesity by providing more opportunity for such activity.
OBJECTIVE: To determine if living in a healthy land use region is related to lower BMI percentiles among inner city school aged children.
DESIGN/METHODS: Body Mass Index (BMI) percentiles were generated for 10,513 students grades K-12 in an inner city school district (2005-2006) using standardized age and gender norms. Each student's home address was entered into a Geographic Information System (GIS) and mapped. Healthy land use, defined as forest, open, recreational and medium or low density housing areas were derived from state GIS land-use maps. A comparison of mean BMI percentiles for students living in vs. not living in healthy land use regions was calculated using independent T-test.
RESULTS: Statistically significant lower mean percentiles in BMI were found between those who lived in healthy vs. unhealthy land use regions (mean BMI percentile in healthy land use 67.91 vs. mean BMI percentile not living in healthy land use 70.99; $p < 0.001$).
CONCLUSIONS: This study demonstrates lower BMI percentiles for children living in healthy land use regions. Further studies should be conducted to determine if this is due to increased physical activity.

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Childhood Obesity and Neighborhood Food Store Availability in an Inner City Community: The Growing up Healthy in East Harlem Study

Maida P. Galvez, Kimberly Morland, Laura Liao, Cherita Raines, Jessica Kobil, Nita Vangeepuram, James Godbold, Barbara Brenner, Mary S. Wolff. Community and Preventive Medicine, Mount Sinai School of Medicine, New York, NY; Pediatrics, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Prior studies have shown an association between fast food store availability and body size. Less is known about the relationship between the full spectrum of food store availability in the inner-city and body size.
OBJECTIVE: We hypothesized that in the inner-city, minority community of East Harlem, New York, an increased number of fast food stores and bodegas (convenience stores) in close proximity to a child's home is associated with increased risk for childhood obesity as measured by body mass index (BMI).
DESIGN/METHODS: Baseline data from a 3 year longitudinal study of 6-8 year old East Harlem boys and girls (n=323) were utilized. Anthropometry (height and weight) were conducted with a standardized protocol. Food store data on supermarkets, grocery stores, convenience stores, specialty stores, restaurants and fast food stores were collected via a walking survey of East Harlem. Stores located within the same Census block as the child's home address were identified using ArcGIS software version 8.3, which allowed for geocoding of both home and store address. We computed age- and sex-specific BMI-percentiles using CDC national norms. Using prevalence ratios, we estimated risk of a child's BMI-percentile being in the top third of the sample based on number and types of food stores on their Census blocks.
RESULTS: More than 75% of the 323 children lived in Census blocks with no grocery stores, specialty stores, or restaurants. Bodegas were present in 45% of their Census blocks, and fast food stores were present in 60%. Mean BMI-percentiles for each tertile were 32.7, 76.4, and 97.2, respectively. No associations were seen with BMI-percentile and number of grocery stores, specialty stores, restaurants or fast food restaurants on a child's Census block. Children (n=176) living on a block with one or more bodegas (range 1-6) were more likely to have a BMI-percentile in the top tertile (prevalence ratio1.20, 95% CI 1.00-1.45), compared with children having no bodegas (n=147).
CONCLUSIONS: The presence of bodegas within the same Census block as a child's residence was associated with a higher BMI-percentile. Individual demographic and behavioral factors will be assessed as possible confounders. This has potential implications for both child and neighborhood level interventions with respect to childhood obesity.

158 Fellow in Training

Clinical Manifestations of Obesity in a Sample of Urban Minority Children

Nita Vangeepuram, Allison Gault, Ellen Schranz, Danielle Laraque. Pediatrics, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Obesity disproportionately affects minority children, yet diagnosis rates of obesity comorbidities in traditionally underserved areas are unclear. Similarly, nutrition and physical activity knowledge, attitudes and behaviors must be better understood in urban obese children.
OBJECTIVE: To describe: (1) baseline medical and psychosocial characteristics and (2) knowledge, attitudes and behaviors of children enrolled in a new obesity program in a pediatric primary care practice in East Harlem, New York City.
DESIGN/METHODS: Children underwent a comprehensive baseline evaluation, which included medical history, physical exam, body measurements, labs, and psychosocial screening. Validated questionnaires were used to measure nutrition and physical activity knowledge, attitudes and behaviors (KAB).
RESULTS: Twenty-one obese children ages 8-14 years enrolled in the program. The sample was 57% male; 1/3 were black and 2/3 were non-black Latino. On history, 29% had at least two symptoms suggestive of obstructive sleep apnea. Child self report revealed that 71% worry about their weight. In addition, 62% are sad "sometimes or often" and 43% are down on themselves "sometimes or often" specifically about their weight.
Waist circumference was greater than the 90th percentile in 81% of program children and percent body fat was greater than the 85th percentile in 71% of program children based on published reference percentiles. The major positive physical findings were acanthosis (67%) and striae (29%). A total of 29% had high total cholesterol, 48% had a HOMA-IR score indicative of impaired glucose tolerance, and 10% had evidence of fatty liver. Dietary recall revealed that 57% of children had not eaten any vegetables and 38% had not eaten any fruit in the prior 24 hours. In addition, 71% had ≤ 2 days of vigorous activity/week and 91% had ≤ 2

days of gym/week. Half of the sample watched > 5 hours of TV per day. The KAB questionnaire revealed good knowledge of high fat foods and nutrition and physical activity self-efficacy but less healthy selection of foods.
CONCLUSIONS: In this sample of obese urban minority children, almost half had impaired glucose tolerance and almost a third had symptoms of obstructive sleep apnea. Most children reported sadness and worries about their weight. Children's nutrition and physical activity knowledge and self-efficacy were good, but actual habits were less healthy, highlighting an important disconnect between knowledge and behavior.

159 Fellow in Training

Parent and Pediatrician Input in the Development of an Obesity Program

Nita Vangeepuram, Allison Gault, Ellen Schranz, Danielle Laraque. Pediatrics, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: In the past, development of pediatric clinic-based obesity programs has not typically included all involved stakeholders. This project, based in an academic practice in East Harlem, NYC, describes the development of a novel obesity program by explicitly involving parent and pediatrician input from the project's inception.
OBJECTIVE: To describe parent and pediatrician input in the development of a novel obesity program.
DESIGN/METHODS: Semi-structured parent focus groups addressed cultural issues, barriers to healthy living, and program content. Primary care pediatrician surveys were administered to understand obesity treatment practices and barriers.
RESULTS: Parent Focus Groups: Three focus groups were held with a total of 13 parents. Barriers to healthy eating included cost of healthy food, differing family food habits, and children buying food on their own. Cultural issues included traditional diets rich in fried foods and rice and misperceptions of healthy weight. Barriers to exercise included unsafe outdoor play areas and limited indoor space. Parents liked games, recipes, tracking diet and exercise behaviors, and interactive problem solving. They wanted to be present at sessions to reinforce what was taught. Weekly updates were requested and a time commitment of one weekly 2 hour session was felt to be reasonable. Primary Care Pediatrician Survey: All 51 resident and attending pediatricians approached completed the survey. Only half reported discussion of the food pyramid or family meals. More than 75% of physicians reported screening for hypertension and lipid abnormalities most of the time. Fewer reported that they usually screen for orthopedic issues (8%), insulin resistance (59%), fatty liver (50%), and obstructive sleep apnea (18%). Most physicians do not routinely ask about self-esteem, eating disorders, depression, teasing and family dynamics. Physician-identified treatment barriers included time constraints, lack of referral resources, and inconsistent parent involvement.
CONCLUSIONS: Parents and pediatricians offered unique and differing insights into program planning. Parent suggestions were incorporated into program content (i.e. use of games and discussion of community specific barriers) and structure (i.e. session length and parent presence). The physician survey informed the medical assessment and program content. Future study will determine whether parent and provider input in program planning leads to increased program success.

160 Fellow in Training

Congenital Lead Poisoning Discovered by Routine Screening of a "High Risk" Pregnant Woman

Nachammai R. Chinnakaruppan, Allison K. Wawer, Eugene Shapiro, Eduardo Bautista, Steven Marcus. Pediatrics, UMDNJ Robert Wood Johnson Medical School, New Brunswick, NJ; Pediatrics, Jersey Shore Medical Center, Neptune, NJ; NJ Poison Information & Education System, UMDNJ-New Jersey Medical School, Newark, NJ.

BACKGROUND: Approximately 0.5% of women of childbearing age have blood lead levels > 10 mcg/dL. Lead freely crosses the placenta and can affect the fetus detrimentally. There are only a few cases of prenatal and congenital lead poisoning reported in the literature and management is controversial. We present a case of prenatally diagnosed lead poisoning and our management strategies are delineated.
OBJECTIVE: Report the case of an infant with congenital lead poisoning.
DESIGN/METHODS: Case report.
RESULTS: A screen for lead levels in a Mexican mother just before delivery revealed a blood lead level (BLL) of 58 mcg/dL and hemoglobin of 9.5g/dL. She received no treatment for the lead. She delivered a full term 3 kg normal female.The neonate's BLL on day of life (DOL) 2 was 73 mcg/dL and hemoglobin was 17g/dL. Peripheral smear showed no basophilic stippling and there were no long bone metaphyseal changes on X-ray. In an attempt to rapidly lower her BLL, we performed a double volume exchange transfusion on DOL 4. Her BLL post-exchange was 11.4 mcg/dL. To further lower her body burden of lead, we treated her with chelation therapy: a total of 6 doses of intramuscular dimercaprol (BAL), and a continuous infusion of calcium disodium ethylenediaminetetraacetate (CaNa2EDTA) was begun with the second dose of BAL and continued for 2 days. Oral succimer was then given by gavage for 19 days. BLL monitored daily showed a transient elevation to 23 mcg/dL on DOL 9 before leveling off to 15 mcg/dL prior to discharge on DOL 25. She remained active and fed well. Environmental investigation revealed multiple sources of lead in the mother's home which were removed. The infant was discharged on iron supplements and follow-up by local department of health and high risk infant development program.
CONCLUSIONS: This is a case of congenital lead poisoning treated by exchange transfusion and chelation therapy. This case documents the need for prenatal screening of at least at risk populations such as women who consume ethnic candies, folk remedies and who exhibit pica behavior.Prenatal identification of these high risk women allows for education, behavioral changes and removal of potential sources of lead, providing a safer home for the newborn and siblings. If prenatal screening becomes more common, obstetricians and pediatricians in cooperative efforts must develop protocols to delineate appropriate therapeutic intervention for mother and baby.

161 House Officer

Do Orphanage Children Exhibit Better Growth Than Those in Communities in Honduras?

Gilma Marimon, Erin Dahlinghaus, Christine Narad, Annie Kautza, Patrick Mason. Department of Pediatrics, Inova Fairfax Hospital for Children, Faifax, VA; Nuestros Pequeños Hermanos, Tegucigalpa, Honduras.

BACKGROUND: Growth stunting due to poor environmental conditions is known to be a problem in the developing world. There also appears to be a clear correlation between children living in an orphanage and poor growth. Anecdotal evidence from an orphanage in Honduras however had suggested an improved growth rate for the children as compared to their peers in the community. We found that inadequate nutrition, access to healthcare, and sanitary conditions were common concerns in these poor rural communities. We hypothesized that children living at the orphanage would exhibit better growth as measured by BMI than their peers living in rural villages, secondary to these factors.
OBJECTIVE: To conduct a pilot study comparing the nutritional status and growth of children living in either a rural community setting or an orphanage as measured by BMI.
DESIGN/METHODS: A survey consisting of 10 items was obtained from the parents of all children seen during a medical brigade in June 2007 at two different small, rural towns within Honduras ("community") and a privately funded orphanage ("orphanage"). The survey addressed issues related to the diet and nutritional status of the children within each setting. In addition, empirical data was collected including age, weight, height, and head circumference. Height and weight data were used to calculate BMI.
RESULTS: Mean BMI in the community was found to be 15.58 (± 2.7 standard deviation (SD)) compared to a mean BMI of 17.40 (± 1.87 SD) ($p<0.001$) within the orphanage. Ages in the children within the community ranged from 0.58 to 13 years of age with a mean of 6.69 (± 3.66 SD) while those in the orphanage ranged from 2.87 to 12 years with a mean of 8.86 (± 2.39 SD). Most of the children within the community received 3 meals per day and appeared to have less protein and fewer calories per meal than children in the orphanage.
CONCLUSIONS: Children in the orphanage had better growth than children living in a family setting in rural Honduras. This was likely secondary to improved nutrition, access to healthcare, and sanitary conditions at the orphanage. This pilot study lays the groundwork for future studies to further delineate the specific causes of why children living in rural Honduras exhibit stunted growth as compared to the orphanage population. The results of subsequent studies will aid in planning future brigades so that we may work with the local leaders to help them address these critical needs.

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Infant Growth and Child Cognition at 3 Years of Age

Mandy B. Belfort, Sheryl L. Rifas-Shiman, Janet W. Rich-Edwards, Emily Oken, Ken P. Kleinman, Matthew W. Gillman. Newborn Medicine, Children's Hospital; Obesity Prevention Program, Dept of Ambulatory Care and Prevention, Harvard Medical School/ Harvard Pilgrim Health Care; Division of Women's Health, Brigham and Women's Hospital; Depts of Epidemiology and Nutrition, Harvard School of Public Health, Boston, MA.

BACKGROUND: Infancy is a critical period for brain development. Few studies have examined the extent to which infant weight gain is associated with later neurodevelopmental outcomes in healthy populations.
OBJECTIVE: To examine associations of infant weight gain from birth to 6 months with child cognitive and visual-motor skills at age 3 years.
DESIGN/METHODS: We studied 872 participants in Project Viva, an ongoing prospective, longitudinal, pre-birth cohort. We excluded children born at <37 completed weeks gestation. We abstracted birth weight from the medical record and weighed infants at age 6 months. We derived weight-for-age z-scores (weight z-score) using the 2000 CDC growth charts. Our primary predictor was infant weight gain, defined as the weight z-score at 6 months adjusted for the weight z-score at birth. At age 3 years, we measured child cognition with the Peabody Picture Vocabulary Test III (PPVT-III) and visual-motor skills with the Wide Range Assessment of Visual Motor Abilities (WRAVMA).
RESULTS: Mean (SD) PPVT-III score was 104.2 (14.4) and mean (SD) total WRAVMA standard score was 102.8 (11.2). Mean (SD) birth weight z-score was 0.21 (0.94) and mean 6 month weight z-score was 0.39 (0.96). In multiple linear regression adjusted for child age, sex, gestational age, breastfeeding duration, and race/ethnicity; maternal age, parity, smoking status, and PPVT-III score; and parental education and income level, we found no association of infant weight gain with child PPVT-III or total WRAVMA standard scores [-0.4 PPVT-III points (95% CI -1.3, 0.6) and -0.4 total WRAVMA points (95% CI -1.2, 0.5) for each z-score increment in infant weight gain], or with the WRAVMA subscale scores. The lowest and highest deciles of weight gain were associated with mean PPVT-III scores of 104.6 and 101.1 points, respectively.
CONCLUSIONS: Slower infant weight gain was not associated with poorer neurodevelopmental outcomes in healthy, full term 3-year-old children. Even infants with the slowest rates of weight gain did not have lower cognitive test scores at age 3 years than infants with the fastest weight gain. These results should aid in determining optimal growth patterns in infants to balance risks and benefits of health outcomes through the life course.

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Adverse Asthma Outcomes in Pediatrics

Alan S. Weller, Kitaw Demissie. General Pediatrics, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ; Epidemiology, UMDNJ-School of Public Health, Piscataway, NJ.

BACKGROUND: Despite improvements in management of pediatric asthma, adverse outcomes continue to occur among children hospitalized for asthma. Although predictors of pediatric adverse asthma outcomes have been studied, analysis of a national representative sample is required.
OBJECTIVE: To determine the predictors of adverse outcomes for pediatric asthma hospitalizations using a national representative sample.
DESIGN/METHODS: The National Hospital Discharge Survey for 2001-2005 was used to examine predictors of adverse asthma outcomes among children 2-17 years. International Classification of Diseases 9th Revision, Clinical Modification (ICD-9) codes of 493.0 to 493.9 were used to identify primary hospitalization for asthma. Adverse outcome (intubation/death) is the dependent variable. Clinical predictors considered in our analyses comprised pneumonia, acute upper respiratory tract infection, sinusitis, bronchitis, and influenza. Non-clinical predictors were race, age, gender, region and insurance. Adverse outcome and comorbidities were also operationalized using appropriate ICD-9 codes. A logistic regression model was constructed to estimate the association between predictors and adverse outcomes.
RESULTS: A weighted sample of 641,354 children aged 2-17 years were studied. The prevalence of adverse asthma outcome was 0.45%. Adolescence as compared to children 2-4 years (OR=3.37; 95% CI: 3.10-3.66), black race as compared to white (OR=1.31; 95% CI 1.19-1.43) and male gender (OR=1.47; 95% CI:1.36-1.59) were found to be independent predictors of an adverse outcome. As compared to private medical insurance, children insured by Medicaid (OR=2.29; 95% CI: 2.07-2.54), HMO/PPO (OR=1.29; 95% CI: 1.14-1.45) and uninsured children (OR=1.42; 95% CI: 1.20-1.67) were more likely to exhibit an adverse outcome. Also, children who reside in the West (OR=5.07; 95% CI: 4.56-5.64) or the Northeast (OR=1.89; 95% CI: 1.68-2.13) as compared to the South of the US and those with concomitant influenza infection (OR=4.79; 95% CI: 3.59-6.39) were at increased risk of developing an adverse outcome.
CONCLUSIONS: Adolescence, male gender, black race, and Medicaid and lack of insurance are risk factors for adverse asthma outcome. Pediatricians should consider testing hospitalized asthmatic patients for influenza since those with concomitant influenza infection are at a higher risk of developing an adverse outcome. Further studies are required to characterize the role of these predictors in order to formulate appropriate interventions in these high risk groups.

164 House Officer

Breastfeeding Initiation and Weaning in a South Bronx Hospital: Influence of Knowledge, Attitude and Practices

Irfan Ali, Anthony Ani, Harleen Bhandhal, Priya Bhate, Ronald Bainbridge, Ayoade Adeniyi, Richard Neugebauer. Department of Pediatrics, Bronx-Lebanon Hospital Center, Bronx, NY.

BACKGROUND: Breastfeeding is practiced throughout the world. This is influenced by tradition, religious and cultural beliefs. It provides comprehensive nutrition and protection against many illnesses to the infants and also many benefits for mothers. Breast milk transfers to the infant maternal antibodies against a host of infections. Despite the awareness of such benefits, many women from lower income groups do not breastfeed.

OBJECTIVE: To examine the association between maternal age, educational level, receiving individual prenatal counseling or attendance in parenting classes and the likelihood of maternal breastfeeding after discharge from the hospital.

DESIGN/METHODS: After obtaining informed consent, mothers were recruited from our emergency room, outpatient clinic and maternity ward. All participants completed an IRB approved questionnaire. The questions were read to the mothers by the investigators. Infants' and maternal socio-demographic characteristics and sources of information regarding breastfeeding were obtained. Information on maternal breastfeeding practices was also obtained.

RESULTS: A total of 95 mothers were interviewed. 49% were born in United States. 96% have a least one child and 30% have more than two children. 92% were using formula but 44% among those were exclusively giving formula. Among mothers 20-29 years old (49%), 45% were bottle feeding exclusively while 51% gave both breast milk and formula; 24% of mothers were more than 30 years old, out of which 26% gave only formula but 65% gave both breast milk and formula. 70% of mothers attended school up to 11th grade. There was no association between educational level and breastfeeding. 34% attended breastfeeding classes and 40% have met breastfeeding counselors. We found no association between mothers' attendance in parenting classes or receiving individual counseling and subsequent breastfeeding practices. 85% believe that breast milk is better than formula but 74% stated that they continued formula feeding because it was started in the hospital.

CONCLUSIONS: Maternal age, education, prenatal classes and counseling have no correlation with initiation and continuation of breast feeding after hospital discharge. However, among those who were commenced on formula in the hospital, none were breastfeeding exclusively subsequently. This practice is clearly inconsistent with our mission as pediatricians.

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Referral Patterns for Victims of Intimate Partner Violence Identified in a Pediatric Hospital

Maria McColgan, Patricia Barry, Mario Cruz. St. Christopher's Hospital for Children, Philadelphia, PA; Lutheran Settlement House, Philadelphia, PA; Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: Due to the profound effects of Intimate Partner Violence (IPV) on children, the AAP recommends that pediatricians routinely screen for IPV and that residency programs include IPV education. While various efforts have addressed the issue of IPV screening in pediatrics, all of them have focused on the outpatient setting and none utilized an onsite IPV counselor.

OBJECTIVE: We describe our experiences after 2½ years of establishing the Children and Mom's Project (CAMP), a comprehensive, longitudinal IPV training and intervention program located at St. Christopher's Hospital for Children.

DESIGN/METHODS: Our intervention involved: establishment of an IPV counselor, hospital protocols to manage positive IPV screens, an IPV screening prompt on patient encounter forms in the outpatient clinic, IPV training of all hospital employees with emphasis on nursing staff, pediatric residents, social workers, and attending physicians, identification of resident and hospital "champions" to encourage IPV screening, and posting of IPV signage. Positive screens were identified by hospital staff and referred to the onsite IPV counselor. Demographic information on the IPV victims and data on the referral source were collected.

RESULTS: During the first 18 months of the program, 163 positive IPV screens were referred to the onsite IPV counselor. Of the referrals, 68% were obtained via routine screening and 32% via risk-factor based screening. Thirty percent of referrals came from an outpatient general pediatrics clinic, 22% from subspecialty clinics, 39% from inpatient services, 6% from the emergency department. Only 30% of all positive screens were called in by the social work department, while 65% were called in by physicians or nurses and 5% were self referred. Ninety-nine percent were female. Forty-eight percent were Latina, 38% African American, 11% Caucasian. Thirty-one percent percent had 1 child, 31% had 2, 34% had 3 or more children. Services provided included supportive counseling, legal help, shelter/housing resources, mental health referrals, and safety planning.

CONCLUSIONS: The presence of an onsite IPV counselor, establishment of IPV protocols, and widespread IPV training for hospital staff resulted in significant case finding. Most of the positive screens were identified through routine screening. A substantial percentage of referrals came from the inpatient setting. Future IPV interventions should focus on the inpatient setting as well as the outpatient setting.nt.

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Pubertal Assessment Methodology and Baseline Characteristics in a National Cohort of 6-8 Year Old Girls: The Breast Cancer and the Environment Research Center Cohort

Frank M. Biro, Maida P. Galvez, Louise C. Greenspan, Nita Vangeepuram, Larry Kushi, Susan Pinney, Mary S. Wolff. Division of Adolescent Medicine, Cincinnati Children's Hospital, Cincinnati, OH; Department of Community and Preventive Medicine, Mount Sinai School of Medicine, New York, NY; Division of Research, Kaiser Permanente, Oakland, CA; Department of Environmental Health, University of Cincinnati College of Medicine and Academic Health Center, Cincinnati, OH.

BACKGROUND: Identifying environmental factors that influence timing of puberty in girls will enhance our understanding of early childhood determinants for diseases incurred later in life including breast cancer. A major challenge to assessing the role of the environment on pubertal onset is standardization of pubertal assessment amongst a number of providers and clinical sites.

OBJECTIVE: A consortium of Breast Cancer and the Environment Research Centers (BCERC) was developed through a partnership between NIEHS and NCI in 2003. We describe (1) the methods and training of providers for determining pubertal stages and (2) the characteristics and maturation status of the baseline cohort of girls 6-8 years old and a subset of girls ages 7 years old.

DESIGN/METHODS: Three sites located in East Harlem, New York, Cincinnati, Ohio and San Francisco, California are jointly conducting a prospective study of pubertal development in 1200 girls ages 6-8 years old. Breast development is assessed by clinicians or trained research staff at each site. In order to optimize validity and comparability of pubertal staging, a standardized pubertal assessment protocol including a training curriculum and pubertal staging form was developed. The kappa statistic was utilized to evaluate the agreement between the master trainers and providers conducting examinations.

RESULTS: The baseline cohort included 1222 girls ages 6-8 years. The results of the dual examinations for agreement were combined across all three centers. For 110 paired pubertal ratings, the kappa statistic was 0.75 indicating "substantial" agreement. At age 7, the proportion of girls who had attained breast stage 2 or greater was 122/919, or 13.2%. The proportion of girls who have attained breast stage≥2 by age 7 is significantly greater than that reported by Herman-Giddens(1997); for White girls, 9.4% v 5.0%, p<.0001 (95% CI 3.0%-5.5%); for Black, non-Hispanic girls, 19.7% v 15.4%, p<.0001 (95% CI 4.1%-4.7%).

CONCLUSIONS: In this longitudinal, multi-site consortium, we standardized pubertal staging by provider and across sites in order to minimize error in our main outcome: timing of breast development. There were significant differences in pubertal status by race/ethnicity across sites and a trend in earlier breast development as compared to previous studies.

167 Medical Student

Administration of Tetanus, Diptheria, & Acellular Pertussis (Tdap) Vaccine to Parents of High-Risk Infants in the Neonatal Intensive Care Unit (NICU)

Andrew Dylag, Shetal Shah. Department of Pediatrics, Division of Neonatology, Stony Brook University Medical Center, Stony Brook, NY.

BACKGROUND: Infants with chronic respiratory illness that contract pertussis infection, particularly those discharged from the NICU, demonstrate significant morbidity & mortality. Tdap vaccination is recommended for adults in contact with infants < 12 months of age. Significant barriers to adult vaccination exist including cost, convenience, & access. To eliminate these barriers, we implemented NICU-based administration of Tdap to parents of admitted infants.

OBJECTIVE: To determine the feasibility of Tdap vaccine administration to parents in a tertiary-care, Level III NICU & measure its effect on vaccination rates among parents of this high risk population.

DESIGN/METHODS: For a four-month period from July to October 2007, all parents of admitted patients were informed of the risks & benefits of Tdap by placing an information letter at their infant's bedside. All staff were educated about the dangers of pertussis infection & instructed to reinforce the need to obtain vaccination. Parents were screened, medically consented, & immunized at their infant's bedside. Immunization was available for 20 hrs per day at no cost. Student's T-tests were used for data analysis.

RESULTS: Over the study period, 352 children (598 eligible parents) were admitted to the NICU with gestational ages ranging from 23 to 42 weeks & 489 parents (81.8%) were offered vaccine. Parents were not considered eligible in cases of palliative infant care, paternal absence, or Child Protective Services involvement. Overall vaccination rate was 72.3% (425 parents), reflecting 86.7% of the screened population. The 55 parents (9.2%) who refused the vaccine predominately cited pertussis as an insignificant health threat or disbelief in vaccination. There were no differences in vaccination rate based on parental age. No allergic reactions to vaccination were observed. The 54 infants whose parents were not offered vaccine had a significantly shorter length of stay (2.7 ± 2.0 vs. 22.1 ± 26.7 days, p<0.0001), higher birth weight (3116 ± 731 vs. 2439 ± 992 grams, p<0.0001), & higher gestational age (37 4/7 weeks ± 26 days vs. 34 5/7 ± 30, p<0.0001) than parents that were offered vaccine.

CONCLUSIONS: Administration of Tdap in the NICU is an effective means of increasing vaccination rates in parents of this population. Logistical barriers persist when implementing this program for infants with short (< 3 days) length of stay.

General Pediatrics III Platform Session

Sunday, March 30, 2008 9:45 AM-12:00 PM

168 9:45 AM Fellow in Training

PIC'M Study: Parental Influence in Clinical Management

Sean M. Bailey, George E. Fryer, Karen Hendricks-Munoz, Pradeep Mally. Pediatrics, New York University School of Medicine, New York, NY.

BACKGROUND: Many NICUs have changed from traditional care models to Family-Centered Care that involves interdisciplinary work rounds.Providers and families work as a team,sharing in management decisions.This model aims to promote communication and empower families in order to achieve the best outcome for infants.While Family-Centered approaches have been shown to lead to better outcomes and family satisfaction,we know of no studies examining the impact that this model of care has on actual physician management decisions.

OBJECTIVE: To determine:a) NICU care decisions discussed by neonatologists with families and b)the effect of parental opinion on management issues in the NICU.

DESIGN/METHODS: We conducted an anonymous web-based survey of 2,187 physicians self identified as members of the American Academy of Pediatrics section on perinatal pediatrics.Practicing US neonatologists with active e-mail accounts were eligible and allowed to answer once.

RESULTS: 1000 of 2,187 surveys were returned,for a response rate of 46%;978 were eligible.

Table 1.Interventions Most Discussed & Impact of Parental Opinion.

	% of Neonatologists discussing Intervention	% of Time Parents Influence Clinician's Decision Making Process if Conversation Takes Place
Steroids for CLD	(864/932) 92.7%	(664/864) 76.8%
Blood Transfusion	(902/932) 96.8%	(644/902) 71.4%
PDA Ligation	(851/932) 91.3%	(353/851) 41.5%
PICC Line Placement	(796/932) 85.4%	(314/796) 39.5%

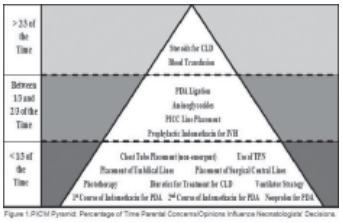


Figure 1.PICM Pyramid. Percentage of Time Parental Concerns/Opinions Influence Neonatologists' Decisions.

CONCLUSIONS: Parental opinion has a greater impact on clinical decision making in regards to some interventions more than others.Steroids for CLD and blood transfusion are discussed most frequently and are also the interventions in which parents have the most influence.Therapies such as TPN,umbilical lines,and phototherapy are often not discussed,and even when broached,parents do not greatly influence management. As we embrace Family-Centered Care and work with an increasingly sophisticated population,physicians may need to reevaluate how they allow parents to be included in the clinical management process.

169 10:00 AM

Availability and Accuracy of Spanish Language Medication Labels

Iman Sharif, Julia Tse. Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Studies have reported on the availability of medication labels in various languages, however none have reported on the accuracy of translations used.

OBJECTIVE: 1)To determine the availability of Spanish-language medication labels in the Bronx, NY, a borough with a very high Spanish-speaking population. 2) To test the accuracy of computer-translated Spanish medication labels.

DESIGN/METHODS: Using the NYS Education Department's listing of licensed pharmacies in conjunction with the Yellow Pages Online, we conducted a telephone survey of all pharmacies in the Bronx during September 2007. Respondents were asked whether the pharmacy could provide Spanish-language medication labels, the methods they used, and the frequency with which they did so. We then visited representative pharmacies and asked for Spanish-language medication labels for a series of prescriptions for iron drops, a topical cream, and a liquid antibiotic.

RESULTS: Of 316 pharmacies, 288(91%) participated. Respondents were pharmacists(86%), technicians (10%), managers(3%), or other staff(1%). Overall, 209(73%) stated that the pharmacy could provide Spanish-language medication labels. Of these, 179(86%) used a computer program, 24(11%) used lay staff , and 6(3%) used an interpreter, language line, pharmacist, or technician to translate into Spansh. Of those using computers, 170(95%) stated that someone always checked the translation for accuracy. Checkers were lay staff (57%), technicians(34%), pharmacists(8%), or medical interpreter(1%). Overall, only 5 of 14 pharmacists who checked the computer translations were fluent in Spanish. A wide variety of computer translation programs were reported, but 4 major companies accounted for about 75% of all programs used. Of those who said they could translate, 72% said they printed prescriptions in Spanish daily. Yet, 96% said they saw Spanish-speaking customers on a daily basis.

We analyzed 82 Spanish medication labels from 22 pharmacies using 14 different computer programs. Except for 2 individual labels, no two translations for one prescription agreed. 35(43%) of "spanish" prescription labels included English words and phrases, such as "Take", "give", "topically", "with juice", and "to affected area".

CONCLUSIONS: Pharmacies in the Bronx are frequently providing medication labels in Spanish, however the quality of these translations is questionable. More is needed to evaluate and improve the usefulness of computer translations of prescription instructions.

170 10:15 AM House Officer

Mental Health Care Needs of Latino Families in the South Bronx: Perspectives of Parents and Pediatricians

Anagha Loharikar, Iman Sharif, Sandra Braganza. Department of Family and Social Medicine, Montefiore Medical Center, Bronx, NY.

BACKGROUND: Latino communities in the United States suffer disparities in access to adequate mental health (MH) care, which has been attributed to systemic barriers and incoordination between health care providers and community based organizations. While some studies have reported on perspectives of the Latino community on MH, no studies have reported perspectives of pediatricians working in such communities. We present data collected as part of an AAP CATCH grant to develop a MH home for Latino families in the South Bronx, where 63% of the population is Latino.

OBJECTIVE: To understand and compare the perceptions of Latino parents and practicing pediatricians regarding 1) the causes of MH problems, 2) barriers to MH services , and 3) MH needs.

DESIGN/METHODS: We conducted a qualitative study. Parents of children with a history of MH services referral, use or need were recruited at a federally-qualified community health center to participate in a focus group. We conducted two 90-minute groups with parents. Next, we conducted one 90-minute focus group with pediatricians at the same health center. Focus groups were audio-taped and transcribed. Two investigators independently coded each transcript for thematic content. Differences in coding were resolved via consensus.

RESULTS: Causes: Parents and pediatricians both identified familial disruption as well as poverty/violence as etiologies of MH problems in Latino children. Parents also emphasized a causal relationship between the actions of "God" and "the devil" on MH. Barriers: Both parents and pediatricians acknowledged stigma associated with MH disorders. Parents described distrust of authority and public institutions and incompetence among MH providers, including lack of "caring." Pediatricians attributed lack of access to systemic barriers, such as lack of insurance. Needs: Both groups described a need for preventive services in the community. Parents described consequences of MH problems on self, family, and community. Parents emphasized a need to be heard and for community awareness about MH. Themes distinctive to the pediatricians included the high prevalence and range of MH problems of their patients and discomfort with personal experiences in managing MH.

CONCLUSIONS: Parents and pediatricians gave differing perceptions of the MH needs of the Latino population in this inner-city setting. Further exploration can inform the intervention-design of the CATCH initiative to improve access to MH care.

171 10:30 AM Resident

Integration of a Mandatory, Web-Based Neonatology Curriculum into Pediatric Residency Training

Priya Garg, Jamelah Tucker, Carol Carraccio, Alison Falck. Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

BACKGROUND: Duty hour requirements and demanding schedules create unique challenges for didactic teaching in pediatric critical care settings. Self-directed learning utilizing a web-based curriculum is ideal for this environment. Currently, little is known about the potential impact of web-based learning on pediatric resident education. A pilot study during 2005-2006 at the University of Maryland Medical Center (UMMC) demonstrated that self directed learning in the neonatal intensive care unit (NICU) was effective and well-received. However, motivation and participation were variable.

OBJECTIVE: To assess residents' participation, knowledge gain, and satisfaction with a required web-based NICU curriculum.

DESIGN/METHODS: Pediatric residents at UMMC completed four online NICU modules as a requirement of the rotation. Modules were developed from NICU curriculum topics as outlined in AAP PREP content specifications. Modules consisted of a pre-test, PowerPoint lecture, post-test, and satisfaction survey. Residents self-navigated the modules, and participated in case-based review during the NICU rotation. Pre- and post-tests consisted of the same ten questions. Quantitative data were analyzed using paired student t-tests. Qualitative data from the satisfaction surveys were summarized.

RESULTS: During the study period, 7/07 to 11/07, 24 of 26 residents rotating in the NICU completed at least one module. By the end of the NICU rotation, 76% of the required modules were completed. Fifty percent of residents completed all required modules. For the 78 data pairs (maximum score of 10), mean pre-test score was 5.4 (±2.10) and mean post-test score was 7.8 (±1.59). The mean change between pre- and post-test scores was +2.4 ($p<0.001$). 46% of satisfaction surveys were completed. Greater than 85% of residents found the modules effective teaching tools. Greater than 85% stated that the curriculum enhanced their learning experience and 93% stated that self-directed learning would be helpful on other rotations.

CONCLUSIONS: A web-based curriculum is an effective tool for pediatric resident education. In addition to addressing time constraints, self-directed learning is emphasized as an important skill for life-long learning. Future directions should focus on addressing etiologies of resident non-compliance, assessment of long-term knowledge gain, expansion of the web-based Neonatology curriculum, and incorporation of self-directed learning into other clinical settings.

172 10:45 AM

Experience with a Pediatric and Surgical Co-Management Model in Pediatric Residency Training

Anna M. Carr, Allan M. Arbeter, Matilde Irigoyen, Robert S. Wimmer. Department of Pediatrics, Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: Little is known of the experiences and perceptions of pediatric hospitalist faculty and residents participating in co-management models with surgical services.

OBJECTIVE: To describe pediatric hospitalists faculty and residents' experience with a surgical co-management model in a teaching service at a children's hospital.

DESIGN/METHODS: In 2003 Albert Einstein Medical Center established an inpatient teaching service at St Christopher's Hospital for Children in Philadelphia, PA, staffed by pediatric hospitalists and pediatric residents. On July 2005, we initiated a surgical co-management model. Residents perceptions of the strengths and weaknesses of the model were obtained through end-of-rotation evaluations and feedback at monthly meetings. Hospitalist faculty provided feedback quarterly.

RESULTS: Co-managed patients accounted for a third of admissions with 65% in orthopedics, 15% ENT, 10% neurosurgery, 5% plastics, 5% ophthalmology. Most (90%) co-managed patients had 1+ concurrent medical condition; 30% had multiple medical conditions (CP, genetic syndromes, obesity). The primary roles of the pediatric residents were in the areas of pain management, procedural sedation, peri-operative respiratory management, fluid and nutritional management, assessment of rehabilitation needs, discharge planning, psychosocial concerns, and patient safety. Overall faculty and residents felt the model had improved patient care and teaching. Strengths perceived included more exposure to complex patients, increased teaching opportunities with pediatric medical and surgical subspecialists, and increased pain management and procedural sedations skills. Perceived weaknesses were timely communication, lack of clarity of roles between pediatric and surgical residents, distrust of surgical (primarily adult-trained) resident skill in pediatric medication orders, and excess of menial tasks.

CONCLUSIONS: Exposure to a model of pediatric hospitalist and surgical co-management was overall a positive experience for residents, enhancing their educational opportunities with complex patients and surgical conditions. Challenges with regards to role and communication need to be addressed.

173 11:00 AM House Officer

Growth Assessment of Children Living in a Honduran Orphanage

Jillian Kunar, Christine Narad, Annie Kautza, Patrick Mason. Department of Pediatrics, Inova Fairfax Hospital for Children, Fairfax, VA; Nuestros Pequeños Hermanos, Tegucigalpa, Honduras.

BACKGROUND: Poverty, war and the HIV/AIDS crisis are forcing millions of abandoned children into worldwide orphanages. Studies have demonstrated that orphanages often lack adequate food, clothing and consistent care resulting in developmental delays and growth stunting. This study examines the growth outcome of children living within a "model" Honduras orphanage compared to those in orphanages around the world.

OBJECTIVE: We sought to determine the growth rate of children living in a Honduras orphanage and compared this rate to historical growth rates of children in Eastern European (EE) orphanages and children seen when adopted.

DESIGN/METHODS: Data was collected at the privately funded Nuestros Pequenous Hermanos orphanage in Honduras. Growth records were reviewed for each prepubertal child and compared to historical data for growth rates of children in EE orphanages and growth rates of children at their adoption. Age height (HT) and weight (WT) were obtained for each child at the time of arrival into the orphanage as well as current measurements. Growth z-scores were determined using EpiInfo (CDC).

RESULTS: Initial and current HT and WT data were collected on 96 children (56 males). Mean age on arrival to the orphanage was 4.96 yrs (range 2 mo to 10.8 yrs) and the children spent a mean of 4.14 years (range 1 mo-8.9 yrs) in the orphanage. Mean HT, WTand BMI z-scores from arrival and currently are listed in the table. HT growth velocity since arrival was noted to be 6.38 cm/yr $\pm$ 1.82 for girls and 5.34 $\pm$ for boys. We had previously shown that the children living in several orphanages in Romania had

HT z-scores of -4.13 for boys and -4.73 for girls. Additionally, our survey of children adopted from EE demonstrated a decrease in height z-scores from -0.14 on arrival at the orphanage to -2.03 4 years later.

	Boys		Girls	
	Arrival	Current	Arrival	Current
Height	-1.38 ± 1.7	-1.62 ± 1.0	-1.54±1.3	-1.37 ± 0.9
Weight	-0.53 ± 2.6	-0.69 ± 1.0	-0.8 ± 1.1	-0.73 ± 0.9
BMI	0.37 ± 1.2	0.44 ± 0.7	0.4 ± 1.0	0.11 ± 1.29

CONCLUSIONS: Unlike children living in EE orphanages, children living in the Honduras orphanage demonstrated a growth velocity similar to children living in the US. The absence of the expected growth stunting appears to be unique for an orphanage. It is hoped that by understanding the mechanisms that improve their growth, orphanages around the world may be restructured to better care for these vulnerable children.

174 11:15 AM

Communication of Care: Results of the District of Columbia American Academy of Pediatrics, Fetus and Newborn Committee Hepatitis B (HepB) Survey

Mary Revenis, Inez Reeves. Neonatology, Children's National Medical Center, Washington, DC; Neonatology, Shady Grove Adventist Hospital, Rockville, MD.

BACKGROUND: Prevention by pediatricians of perinatally acquired HepB and it's serious, sometimes fatal complications requires identification of infants at risk. In Washington DC in 2005, 33 births had HepB exposure (only 25 had prophylaxis at birth with HepB vaccine and HBIG, only19 fully immunized by 8 mo, and only 4 had post-vaccine serology (one HepBsAg +)).

OBJECTIVE: Communication of HepB risk factors and infant prophylaxis between birth hospitals and follow-up pediatric providers in Washington, DC was evaluated.

DESIGN/METHODS: Newborn discharge summary forms from Washington DC birth hospitals were reviewed for hard-coding of maternal HepB status (surface antigen, antibody or core antibody), and newborn HepB prophylaxis and date (vaccination and immune globulin (IG)). A survey for pediatric providers in Washington DC was developed to determine mode of receipt of newborn discharge summaries, and frequency of communication by the first office visit of: (maternal HepB surface antigen, antibody and core antibody; (2) newborn HepB vaccination and HepBIG administration; and (3) actual status of mothers initially classified as unknown.

RESULTS: Birth hospital discharge summary forms: 6 of 7 have newborn HepB vaccine hard-coded on the form (4 included date), and 0 of 7 have maternal HepB surface antibody or core antibody status.

Survey of follow-up physicians: 83 surveys were returned. Newborn discharge summaries are brought by mother (31% always, 64% sometimes, 5% never); by telephone (39% sometimes, 61% never); by mail (4% always, 34% sometimes, 63% never); and FAX (27% sometimes, 73% never). Receipt of information by the first office visit is 8% always, 72% sometimes, and 21% never for maternal HepB surface antigen; 5% always, 55% sometimes, and 40% never for maternal HepB surface antibody; 3% always, 57% sometimes and 41% never for maternal HepB core antibody; 14% always, 83% sometimes and 3% never for neonatal HepB vaccine; and 8% always, 83% sometimes and 9% never for HepBIG. By the one month visit 37% always, 42% sometimes and 21% never knew true maternal status if previously classified as unknown.

CONCLUSIONS: There are significant gaps in communication of newborn HepB risk factors and birth hospital care to the follow-up pediatric provider. This poses a barrier to identification and appropriate management of infants at risk for serious or fatal complications of HepB exposure.

175 11:30 AM

A Comprehensive Intimate Partner Violence Intervention Results in Sustained Improvement in Screening Rates by Pediatric Residents

Maria McColgan, Patricia Barry, Angelo P. Giardino, Mario Cruz, Sandra Dempsey, Martha Davis, Jessica McKee, Ana Lisa Yoder, Coleen Fitzpatrick, Dalvi Monique. Pediatrics, St. Christopher's Hospital for Children, Philadelphia, PA; Lutheran Settlement House, Philadelphia, PA; Texas Children's Health Plan, Houston, TX; Albert Einstein Medical Center, Philadelphia, PA; Institute for Safe Families, Philadelphia, PA; Philadelphia Health Federation, Philadelphia, PA.

BACKGROUND: The AAP recommends that pediatricians routinely screen for IPV and that residency programs should include IPV education. Unfortunately, only 8-21% of pediatricians routinely screen for IPV, and 31% of pediatricians never screen for IPV. Barriers to IPV screening include lack of experience, insufficient training, time, no office protocol, no referral source, and a fear of opening up "Pandora's box."

OBJECTIVE: We hypothesized that by instituting a comprehensive IPV intervention program within a pediatric residency program, we could demonstrate a sustained improvement in documentation of IPV screening among pediatric residents.

DESIGN/METHODS: Our intervention included IPV training for all pediatric residents at St. Christopher's Hospital for Children, establishment of an onsite IPV counselor and office protocol to handle positive IPV screenings, identification of resident "champions" to encourage IPV screening, and addition of IPV signage in the outpatient waiting areas. IPV screening rates were determined by retrospective chart review performed 12 months prior to the intervention, 3-months into the intervention, and 8-months into the intervention.

RESULTS: Chart review at baseline revealed documentation of IPV screening in 0.9% (4 of 439), 36% (217 of 599), and 33% (133 of 402) of patient charts at baseline, 3-months, and 8 months into the intervention. The mean number of times female caregivers were screened for IPV increased significantly from 0.01 at baseline to 0.41 at 3-months, and 0.42 at 8-months into the intervention. Documentation of a positive IPV screen occurred in 0.5% of charts at baseline, 1.5% of charts at 3-months, and 0.5% at 8 months into the intervention. Residents documented reasons why they did not screen for IPV in zero charts at baseline, 4 charts at 3 months, and 12 charts at 8 months into the intervention.

CONCLUSIONS: A comprehensive IPV intervention can significantly improve documentation of IPV screening among pediatric residents. Because issues of confidentiality and safety with IPV can limit documentation, this data may under-represent the true IPV screening rate of our residents.

176 11:45 AM House Officer

Infant Safe Sleeping in Homeless Family Shelters

Sonia Chaudhry, Nancy Miller. Pediatrics, Baystate Medical Center, Springfield, MA.

BACKGROUND: The October 2005 AAP Policy Statement outlines recommendations for infant safe sleeping environments designed to decrease sudden unexpected infant death syndrome. State medical examiners increasingly report infant deaths due to unsafe sleeping environments. Community members including homeless shelter staff and resident families may be unaware of the AAP recommendations. Homeless shelter resident families may have unmet needs for infant safe sleeping environments.

OBJECTIVE: Our purpose was to conduct a needs assessment for infant safe sleeping environments in homeless family shelters, to assess shelter staff knowledge, and to provide education about the AAP recommendations.

DESIGN/METHODS: An interactive presentation about the AAP recommendations for safe sleeping environments was conducted with the staff of 8 family shelters in Hampden County, Massachusetts. Fifty-nine staff members completed pre and post presentation quizzes designed to assess knowledge of the AAP recommendations. Parent brochures were created and distributed to shelters to be used by staff when teaching resident families about infant safe sleeping.

RESULTS: All staff members completed a 13 question pre- and posttest. The mean pretest score was 70% correct, with the mean posttest score (92%) significantly higher ($p<.001$). On pretest, 88% answered the question about co-sleeping correctly, while only 27 % answered the question about pacifier use correctly. Twenty-five percent of the shelters routinely had appropriate infant cribs available. Only 1 of 8 shelters allowed families to take the cribs upon finding permanent housing. Most shelters (80%) had no funding for cribs, sleepers, or pacifiers, all items included in the AAP recommendations. The majority of the shelters provided parenting classes, although none received staff education nor provided resident education about infant safe sleeping environments. Based on staff comments, the educational intervention was pertinent and beneficial to help families keep infants safe. The shelter staff intends to use the brochures for parent education for all resident families with infants.

CONCLUSIONS: The homeless family shelters of Hampden County do not receive staff education, do not provide parent education, or have the funding to provide safe infant sleep environments for resident families. Educational intervention for homeless shelter staff increased their knowledge about the AAP recommendations.

Genetic Basis of Disease Platform Session

Sunday, March 30, 2008 9:45 AM-12:00 PM

177 9:45 AM Fellow in Training

Single Nucleotide Polymorphisms (SNPs) of Interleukin-8 (IL8) and IL8 Receptors and BPD in ELBW Infants

J. Fisher, M. Brown, E. Kaoi, M. Singh, C. Pham, N. Ali, H. Maramreddy, S. Strassberg, L.A. Parton. Pediatrics, Div of Newborn Med, Maria Fareri Children's Hospital, Valhalla, NY; Pediatrics, New York Medical College, Valhalla, NY.

BACKGROUND: The genetic foundations for BPD have recently been demonstrated in twinning studies. Airway secretions from perterm infants destined to progress to BPD yield increased expression of the potent neutrophil chemotactic factor IL8 within the first 24 hours of life. This occurs even in the absence of clinical or histiologic chorioamnionitis or PPROM. This altered expression pattern found with BPD may be a consequence of genetic variations in IL8 and IL-8R genes.

OBJECTIVE: We tested the hypothesis that SNPs of IL8 and IL8R contribute to the development of BPD in ELBW infants.

DESIGN/METHODS: This is an ongoing prospective cohort study currently involving 95 ELBW infants from 2002 to present, weighing <1kg, without congenital or chromosomal anomalies. BPD is defined as oxygen requirement at 28 days of life; those with mild BPD do not require oxygen at 36 weeks PMA; those with moderate BPD require FiO_2 of <0.3 at 26 weeks PMA; those with severe BPD require pressure and/or a FiO_2 >0.3 at 36 weeks PMA. Buccal mucosa swabs were collected from each infant after informed parental consent was obtained. DNA was isolated from these samples. Probes specific for IL8 (-251, 396, 781, 1633, 2767 and 3331), IL8RA (M31R, R335C, +860) and IL8RB (+785 and +1235) were used during Real-time PCR for allelic discrimination. Statistical analysis utilized chi square and ANOVA, with $P<0.05$ indicating statistical significance.

RESULTS: As expected, lower gestational age ($P<0.001$) and lower birth weight ($P<0.001$) place ELBW infants at higher risk for more severe BPD. No differences in racial distribution were found between the groups. Infants with more severe BPD were more likely to have received surfactant. Genotypes for IL8 -251 and 396 were significantly associated with the severity of BPD ($P=0.04$, 0.01). The distribution of alleles at IL8 -251, 396 and 2767 were significantly associated with BPD severity ($P=0.03$, 0.02 and 0.03). There was an association between BPD severity and the incidence of PDA requiring treatment, sepsis, as well as the presence of ROP. SNPs of -251 were associated with the incidence of chorioamnionitis and PVL ($P=0.02$, 0.01); SNPs of 396 were associated with the incidence of IVH > 2 ($P=0.03$).

CONCLUSIONS: Genetic variations in the IL8 pathway are associated with BPD severity in ELBW infants.

178 10:00 AM Fellow in Training

Single Nucleotide Polymorphisms of Fas, Fas Ligand, and the Caspases and Bronchopulmonary Dysplasia in ELBW Infants

Hima Maramreddy, A. Yao, C. Pham, N. Ali, J. Fisher, S. Strassberg, L.A. Parton. Division of Newborn Medicine, Maria Fareri Children's Hospital at Westchester Medical Center, Valhalla, NY; New York Medical College, Valhalla, NY.

BACKGROUND: Apoptosis mediated by the Fas pathway, in which Fas and Fas ligand (FasL) are upstream mediators and caspases 8 and 3 are downstream mediators, is involved in normal lung development as well as the lung pathology involved in respiratory distress syndrome, the requisite antecedent to bronchopulmonary dysplaisa, BPD. The pathology of BPD results from interactions of lung immaturity and environmental stressors with genetic foundations. The hallmark hypoalveolarization of BPD may result from a dysregulation of apoptosis resulting from SNPs of genes in the Fas pathway.

OBJECTIVE: We tested the hypothesis that SNPs of Fas, FasL, caspases 8 and 3 contribute to the development of BPD in ELBW infants.

DESIGN/METHODS: This is an ongoing cohort study that has enrolled 114 infants from 2002 to present, weighing <1 kg at birth, without congenital or chromosomal anomalies. BPD is defined as need for O_2 at 28d. BPD severity is defined by oxygen need at 36 weeks postmenstrual age, PMA. Infants with mild BPD have no oxygen requirement at 36 weeks PMA. Infants with moderate BPD require FiO2 < 0.3 at 36 weeks PMA and infants with severe BPD require pressure and/or $FiO_2 \geq 0.3$ at 36 weeks PMA. DNA was isolated from buccal mucosal swabs via DNA adsorption to a silica gel based membrane. Allelic discrimination was then performed using specific probes for Fas (-1377,-691,-670), FasL (-844,1174,2777), caspase 8 (IVS 12-19),

and caspase 3 (-280,+567) with Real-time PCR. Chi square analyses and ANOVA were performed with $P<0.05$ denoting statistical significance.
RESULTS: Genotype distribution for the Fas -1377 SNP was significantly associated with BPD severity. Lower gestational age and birthweight, administration of antenatal steroids, and administration of postnatal surfactant and steroids were associated with BPD severity. The Fas -691 SNP was associated with AGA status and the Fas -670 SNP was associated with preeclampsia. There was an association between a clinically significant PDA and culture-positive sepsis and BPD severity. There was an association between FasL SNPs and PVL; and between genotypes of Fas -691 and FasL 1174 and severe ROP. There was an association between SNPs of caspase3 -280 and a clinically significant PDA.
CONCLUSIONS: The Fas -1377 polymorphism is associated with BPD severity. In addition, several co-morbidities of prematurity were correlated with Fas, FasL and caspase 3 SNPs.

179 10:15 AM

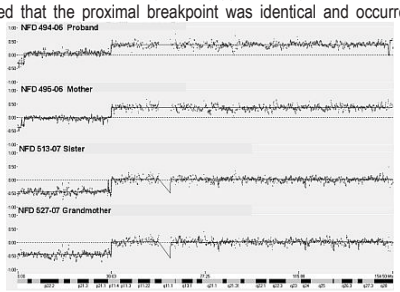
Role of Epigenetic Modifications in the Maturational Regulation of Lung HO-1

Sacha Kassovska-Bratinova, Phyllis A. Dennery. Children's Hospital of Philadelphia, Philadelphia, PA; Pediatrics, University of Pennsylvania, Philadelphia, PA.
BACKGROUND: Expression of lung heme oxygenase-1 (HO-1), the rate-limiting enzyme of heme degradation, is highest at birth and are lowest in adulthood. In hyperoxia, newborns have reduced inducibility of HO-1 mRNA, compared to adults (Dennery, et al Pediatr Res. 2002), which may be due in part to decreased transcription factor activation (Yang et al AJP Lung, 1999) and/or increased levels and binding of Bach1, a repressor of HO-1 transcription (Bratinova, unpublished). Because epigenetic regulation is important in controlling gene expression during development and in oxidative stress, we wondered whether this could also explain maturational differences in the regulation of lung HO-1.
OBJECTIVE: To evaluate maturational differences in epigenetic modifications of the mouse HO-1 gene at baseline and in hyperoxia
DESIGN/METHODS: Lung genomic DNA was isolated from newborn (< 12 hours) and adult FVB mice, exposed to air and hyperoxia (>95% O2) for 72 hours. Non-methylated cytosines in the genomic DNA were converted to thymidines, using 2.5 M sodium bisulfite. The mutagenized promoter region of HO-1 was amplified, cloned into a pCR2.1 TOPO vector (Promega) and sequenced. Ten separate clones per animal were sequenced from each experimental condition. Genomic DNA-histone protein crosslinking was achieved with 1% formaldehyde/2.5 mM EGS in PBS with protease inhibitors. Nuclei were isolated from lungs and chromatin was sheared and incubated with antibodies against dimethylated histone 3 at lysine 4 (H3K4me2) and acetylated H3 (Upstate) or rabbit IgG. Occupancy of the HO-1 promoter was assessed relative to the input on ethidium bromide stained 2% agarose gels.
RESULTS: Sequence comparison analysis showed that the CpGs of the mouse HO-1 promoter were hypomethylated in both the newborn and the adult mice and that there was no difference in HO-1 promoter methylation in response to hyperoxia. However, increased methylation was present in a region 150 bp from the start of intron 1 and this was decreased in hyperoxia, but only in the adults. Histone acetylation and methylation were increased at baseline in neonates.
CONCLUSIONS: Absence of HO-1 methylation in neonatal lungs at baseline suggests that methylation of HO-1 can contribute to the relatively enhanced basal expression in the neonates. The decreased methylation of intron 1 in adults exposed to hyperoxia is consistent with enhanced inducibility. Histone modifications were also consistent with enhanced neonatal HO-1 expression at baseline.

180 10:30 AM Fellow in Training

Familial Turner Syndrome Due to a Heritable Xp Deletion

Sreenivas Dutt Gunturu, Radhika Purushothaman, Henry Anhalt, Svetlana Ten, Harry Ostrer. Pediatrics, Infants and Childrens Hospital at Maimonides, Brooklyn, NY; Pediatrics, St. Barnabas Medical Center, Livingston, NJ; Department of Genetics, New York University, New York, NY.
BACKGROUND: Reports of familial Turner syndrome are rare, but these represent a unique opportunity to distinguish the effects of chromosome deletion. All previous reports have been in families with members affected in 2 generations. Here, we report the first family with 4 members affected in 3 generations.
OBJECTIVE: Analysis of location of deletion on Xp via array cGH and correlation with clinical characters.
DESIGN/METHODS: A grandmother, mother and 2 affected daughters were evaluated clinically. Echocardiography, kidney sonogram, auditory, neurological examination including fundi were normal in both sisters.
On evaluation the younger sister had high arched palate, cubitus valgus and one nevus. Pelvic sonogram revealed normal uterus and ovaries. She has euthyroid autoimmune thyroidits and short stature. The older sister had malformed teeth, genu valgus, borderline low hairline, rhizomelia and single nevus in the sacral region. She was euthyroid with short stature. She achieved final adult height on growth hormone and Lupron therapy of 156 cm, target height of159 cm. After discontinuation of Lupron she spontaneously developed periods at 15 6/12 yrs. The brother had multiple nevi, pectus excavatum. He was growing below 5th percentile for the age. IGF-1 was low (108 ng/mL), IGFBP-3 (2.1 mg/L) and euthyroid.
Conventional cytogenetic analysis using G-banding and array comparative genomic hybridization (aCGH) were preformed using the Affymetrix 500K array
RESULTS: The phenotypic presentation of TS was variable among the 4 affected members. By conventional cytogenetic analysis, all were found to have 46(XX, del(X)(p11.4-p23). This was confirmed by aCGH, which, in addition, demonstrated that the proximal breakpoint was identical and occurred at 38 Mb (figure 1).



CONCLUSIONS: This is the first case report of 3 generations with Turner's syndrome with a stable transmissible deletion denoting that they have normal puberty fertility. This gives us an opportunity to examine genes involved in reproduction on the X chromosome.

181 10:45 AM Fellow in Training

SHOX Gene Analysis in Families of Children with Short Stature

Genna W. Klein, Yeray Novoa, Sofia Shapiro, Elizabeth Wallach, Robert Rapaport. Pediatrics, Mount Sinai School of Medicine, New York, NY.
BACKGROUND: Haploinsufficiency of the *short stature homeobox-containing gene (SHOX)* is implicated in the short stature (SS) of Turner syndrome and Leri-Weill Dyschondrosteosis. *SHOX* variants (S+) are reported in 2-20% of patients (Pt) with growth failure of unknown etiology ("idiopathic SS"). Few families (Fm) with S+ have been studied.
OBJECTIVE: To analyze S+ in Fm of children with SS.
DESIGN/METHODS: Retrospective review of Pt with *SHOX* tested at Esoterix Laboratories (Calabasas Hills, CA) as part of clinical care from 7/30/01 to 7/12/07. Excluded: Fm with chromosomal or skeletal abnormalities. Fm was defined as *SHOX* tested in ≥2 members. S+ was a result other than "no mutation detected" (S-). Pt characteristics, mid-parental height (Ht) (MPH), laboratory, and *SHOX* were analyzed. If clinically indicated during follow up, growth hormone stimulation with 2 agents (GHstim) was done. Student t-tests and chi square were used for comparisons.
RESULTS: Of 47 Fm (74 Pt, 44 parents) tested, 36 (63/118 individuals) had S+; 14 Fm had 1 member S+ (Group 1); 22 Fm had ≥2 members S+ (Group 2), and 11 Fm had no S+ (Group 3). There were no significant differences between groups for Ht, MPH, gender, GH deficiency, nor when all S+ were compared to all S- Pt. 3 Fm had complete gene deletion, 5 Fm had c.63C>T, 19 Fm had c.277+17G>T, and 12 Fm had 8 previously unreported variants. 4 Fm had >1 type of S+. The 23 Pt who only had c.277+17G>T were not different from the S- Pt (Group 3). In this group 6/13 mothers (Mo) tested and 5/6 fathers (Fa) tested were similarly S+.

Group	1	2	3
#Fm (#Pt)	14 (20)	22 (32)	11 (22)
S+ Mo/Mo Tested*	2/11 (18)	7/16 (44)	0
S+ Fa/Fa Tested*	2/4 (50)	11/13 (85)	0
S+Sibs/Sibs Tested*	0/6 (0)	9/10 (90)	0/11 (0)
S+ Pt/Pts in Fm*	13/20 (65)	30/32 (94)	0/22 (0)
Male, %	54	53	55
GHstim done*	7/13 (54)	20/30 (73)	11/22 (50)
GH Peak <10, %	57	27	36
Ht SDS§	-1.87 (0.67)	-1.76 (0.70)	-1.71 (0.74)
MPH SDS§	-0.80 (0.55)	-0.76 (0.74)	-0.71 (0.61)

Data expressed as ratio (%)* or mean (SD)§

CONCLUSIONS: S+ were common. They were noted in ≥2 members in 22 families. S+ was not associated with significant difference in Ht, MPH, gender or GH deficiency. Further basic and clinical studies of S+ Pt will elucidate genotype/phenotype correlations in families.
We acknowledge the help of Dr. Frank Fujimura and funding by Eli Lilly & Co.

182 11:00 AM

Hemoglobin Fast Variant/Possible Bart's in Newborns: Correlation with DNA alpha-Thalassemia Testing

Fariha Kamran, Dominick Sabatino, Sujatha Kosuri, Stephen P. Katz, Harvey Aiges. Pediatrics, Nassau University Medical Center, East Meadow, NY.
BACKGROUND: Newborn hemoglobinopathy screening programs, in addition to picking up sickle hemoglobin detects other abnormal hemoglobins, such as hemoglobin Bart's, a "fast moving variant" associated with alpha-thalassemia, very common among people's who can trace their ancestry to the so-called "malarial belt", that is 20° N and 40° S of the equator.
OBJECTIVE: To determine if the application of alpha-thalassemia DNA testing can identify the "hemoglobin fast variant" as Bart's.
DESIGN/METHODS: Twelve infants referred by the New York State hemoglobinopathy program because of the presence of a "hemoglobin fast variant, possible Bart's" were studied over a one year period. Complete histories, physical exams were done along with alpha-thalassemia DNA testing were done. Three weeks later referrals were made for genetic counseling after the parents were informed of the results. At one year of age an interval history, physical,and complete blood count was done.
RESULTS: Age ranged from 1-7months. Ten infants were homozygous for the alpha-thalessemia 3.7 deletion, or $\alpha^{\cdot\cdot}\alpha/\alpha^{\cdot\cdot}\alpha$, also known as the alpha-thalassemia-1. Two were heterozygous for the alpha-thalassemia deletion on one chromosome, $\alpha^{\cdot\cdot}\alpha/\alpha\alpha$, also known as alpha-thalessemia-2. In all twelve infants there was a 100% correlation with the DNA-alpha thalassemia screening and confirmation of hemoglobin Bart's. The ethnicity of our patients consisted of eight african americans, two were hispanic, one was asian, and one was middle eastern. All had microcytic red cell indices, ranging from 63-72 fL, at one year of age.
CONCLUSIONS: 1. Alpha-thalassemia DNA testing is a reliable method for the confirmation of the presence of hemoglobin Bart's in newborns found to have a "fast moving variant" on screening. 2. Alpha-thalassemia DNA testing provides a quick, early diagnosis of alpha thalassemia. 3. Early, accurate diagnosis can prevent unnecessary further testing in the child because of microcytic red cell indices. 4. Genetic counseling can be offered as soon as the diagnosis of alpha thalassemia is made.

183 11:15 AM Fellow in Training

Effect of GH and IGF-1 Therapy in 3 Patients with Growth Hormone Insensitivity (GHI) Due to Mutation of the GH Receptor Gene

Nauman Basit, Sunil K. Sinha, Amrit Bhangoo, Svetlana Ten. Pediatric Endocrinology, Infants and Children's Hospital of Brooklyn at Maimonides and SUNY Downstate Medical Center, Brooklyn, NY.
BACKGROUND: Response to the recombinant GH and IGF-1 therapy in GHI is widely variable. We report the effect of GH and recombinant IGF-1 therapy in 3 non-classical cases of GHI.
DESIGN/METHODS: Subject A: Presented at age 8 yrs with height (Ht) -3.8 SD from a consanguineous Pakistani family with mild mid-facial hypoplasia. He passed GHRH stimulation test with peak of 28.4 mg/L, his IGF generation test revealed an increase from -2 SDS to -1.3 SDS. His GH receptor was found to have an intronic pseudoexon mutation consistent with GHI phenotype. GH was started at age of 8.1 yrs with 0.3 mg/kg/wk dose and gradually increased to 0.7 mg/kg/wk. On GH therapy over 4 yrs his Ht improved from -3.8 SDS to only -2.71 SDS. At 12.5 yrs IGF-1 was started at 0.12 mg/kg/dose BID, with improvement of growth velocity (GV) to 10 cm/yr, but 6 months after treatment GV decreased significantly to 1.2 cm/yr. His predicted Ht is 155 cm (-2.9 SDS). His Target Height is 163 cm (-1.93 SDS).
Subject B: Brother of Subject A presented with Ht -5.56 SD at age 3.3 yrs. He has significant mid-facial hypoplasia, frontal bossing. Same mutation was identified. He passed GHRH stimulation test with peak > 200 mg/L, his IGF generation tests revealed increase in IGF-1 from -4.0 SDS to only -3.9 SDS. GH therapy

started at 3.3 yrs with 0.3 mg/kg/wk dose and gradually dose was increased to 0.5 mg/kg/wk. On GH over 4 yrs his Ht improved from -3.8 SDS to -4.62 SDS. At 7.8 yrs IGF-1 was started at 0.12 mg/kg/dose BID, with no improvement of GV. His Ht at 9.8 yrs is -4.96 SDS, with predicted Ht at -5.37 SDS.

Subject C: An offspring of a consanguineous Pakistani parents presented at 8 yrs with Ht -3.29SDS. Target Ht -0.33 SDS. He was found to have a mutation in the GHR gene, exon 10. GH was started at age of 8.5 yrs with 0.3 mg/kg/wk; gradually increased to 0.5 mg/kg/wk. His Ht improved from -3.29 SDS to -2.9 SDS. Last 3 months he was treated with IGF-1 0.12 mg/kg/dose BID with GV 7.2 cm/yr. Ht now is -2.03 SDS, with predicted Ht at -1.05 SDS.

CONCLUSIONS: All three patients were started on a dose of 0.3 mg/kg/wk; after primary evaluation and gradually increased to maximum recommended dose. The above data reveals that, response to GH can be beneficial and response to IGF-1 therapy can be suboptimal. However, combined GH and IGF1 therapy maybe more beneficial in improving final adult height in cases of non-classical GHI.

184 11:30 AM Fellow in Training

Anti-Mullerian Hormone as a Marker of Ovarian Reserve in Young Girls with Turner's Syndrome

Radhika Purushothaman, Oksana Lazareva, Munazza Basit, Svetlana Ten. Pediatric Endocrinology, Infants and Childrens Hospital at Maimonides, Brooklyn, NY.

BACKGROUND: Spontaneous fertility is rare among Turner's syndrome patients. Karyotype 45 XO, mosaicism with XY and Xq deletions has been associated with hypoplastic ovaries and uterus whereas women with mosaicism, terminal p deletions or ring X chromosome have been shown to be fertile. Anti-Mullerian hormone (AMH) has been found to positively correlate with antral follicle count and has been used for that purpose in in-vitro fertilization.

OBJECTIVE: We sought to explore the relation between anti-mullerian hormone and other markers of ovarian function like ovarian structure via pelvic sonogram, FSH and LH and to further see whether there was a correlation between these levels and karyotype

DESIGN/METHODS: This is a retrospective chart review of all patients with Turner's syndrome in our clinic. Karyotype, AMH, inhibins A & B, pelvic sonogram findings were correlated.

RESULTS: We examined a total of 10 patients in our clinic with a mean age range of 13.4 +/- 4.6 years. The mean age at diagnosis was 7.9+/- 4.5 years. Two groups were identified: group 1 with a karyotype favorable to fertility and group 2 with a poor probability of fertility. In group 1: 3 had mosaicism, 1 had terminal Xp deletion & 1 had ring chromosome. In group 2: 3 patients had 45XO, 1 had 45XO/46XY and 1 had Xq deletion. Regardless of karyotype, all had undetectable anti-mullerian hormone, inhibins A and B. In group 1, pelvic sonogram findings revealed fairly developed uterus and ovaries and their FSH and LH remain prepubertal in 3 girls who are in their teens. In group 2, all showed hypoplastic ovaries and uterus and their gonadotropins were high

CONCLUSIONS: Pelvic sonogram findings and gonadotropins are good markers of ovarian function and correlated well with karyotype. To our disappointment, anti-mullerian hormone and inhibins A and B did not seem to be reliable predictors of ovarian function

185 11:45 AM Fellow in Training

Interfamily Phenotypic Difference in Familial Isolated Growth Hormone Deficiency Due to a Novel Homozygous Mutation of Growth Hormone Releasing Hormone Receptor (*GHRHR*) Gene

Sunil K. Sinha, Kyriaki S. Alatzoglou, Amrit Bhangoo, Svetlana Ten, Mehul T. Dattani. Pediatric Endocrinology, Maimonides Infants and Children's Hospital of Brooklyn and SUNY Downstate Medical Center, Brooklyn, NY, Brooklyn, NY; Developmental Endocrinology Research Group, UCL Institute of Child Health, London, United Kingdom.

BACKGROUND: Mutation of the gene encoding the GHRH receptor (*GHRHR*) is associated with familial isolated growth hormone deficiency (IGHD) type IB. We are report here two siblings with a novel homozygous mutation in *GHRHR* presenting with marked phenotypic variability.

Patient: The index case presented at 6 years of age with short stature (91.5 cm; SDS -5.44; mid-parental height 166.4 cm; +0.47SDS), whilst her younger sister presented at 2.6 years with the same problem (81.1 cm; SDS -2.8). The siblings were born at term with a birth weight of 3kg after uneventful pregnancies to consanguineous Pakistani parents. Physical examination revealed mild mid-facial hypoplasia with frontal bossing in the younger sibling, with no dysmorphic features noted in the older sibling in spite of more pronounced growth retardation. Laboratory evaluation in the older sister revealed low IGF-1 (-3.6 SD) and IGFBP3 (-3.05 SD) concentrations whilst those in the younger sister were slightly higher (IGF-1 -1.9 SD, IGFBP-3 --1.9 SD). Concentrations of all other pituitary hormones were within normal ranges. MRI revealed a hypoplastic anterior pituitary gland in the older sister but the size was within the normal range in the younger sister. Both siblings were initiated on GH replacement therapy and responded well with an excellent growth velocity on 0.3 mg/kg/week GH.

RESULTS: Mutation analysis of *GHRHR* identified a novel homozygous missense mutation in both siblings, whilst parents were heterozygous. This was a single base change (c.818G>C) in exon nine that results in the substitution of Tryptophan with Serine (W273S) at the extracellular domain of the receptor. The area is highly conserved and the change has not been reported in the SNP database, nor was it found in patients and controls screened as part of our study.

	Normal	Index	Sibling
Height		-5.44 SDS	-2.8 SDS
IGFBP- 3	2.8-6.9 mg/L	0.6 (-3.05SD)	2.7 (1.9 SD)
IGF-1	91-443 ng/ml	9 (-3.6 SD)	57 (-1.9 SD)
GHBP	267-1638 pmol/L	ND	899
ASL	0.9-9.3 mg/L	ND	6.7 (0.45 SD)
Free T4	0.8-2.2 ng/dl	1.2	0.95
TSH	0.27-4.2 uU/ml	2.12	2.4
Cortisol	4-22 ug/dl	9.4	ND

ND- Not done

CONCLUSIONS: GHRHR mutations should be screened for in patients with IGHD type 1B, and mutations may be associated with marked phenotypic variability both between pedigrees and within the same pedigree.

Neonatology III - Clinical Studies Platform Session

Sunday, March 30, 2008 9:45 AM-12:00 PM

186 9:45 AM House Officer

Utility of Measuring Direct Bilirubin at 12-24 Hours of Age in Neonates Admitted to the Neonatal Intensive Care Unit

Sukesh Sukumaran, Ronald Sutsko, Barbara Amendolia, Judy G. Saslow, Tarek Nakhla, Nicole Kemble, Nosrat Razi, Gary Stahl, Kee Pyon, Zubair H. Aghai. Pediatrics/Neonatology, Cooper University Hospital-Robert Wood Johnson Medical School, Camden, NJ.

BACKGROUND: The American Academy of Pediatrics recommends the measurement of direct bilirubin (DB) in near term and full term infants receiving phototherapy for jaundice, jaundice presenting at or beyond 3 weeks of age, and sick infants. A common practice at our institution is to measure the total bilirubin (TB) and DB levels at 12-24 hours of age for all infants admitted to the Neonatal Intensive Care Unit (NICU).

OBJECTIVE: To assess the utility of measuring DB at 12-24 hours of life in infants admitted to the NICU and to establish the reference range of DB concentration at various gestational age and birth weight.

DESIGN/METHODS: Infants born in the period (January, 2000- December, 2006) and admitted to the NICU were included in this study. Relevant demographic, laboratory and clinical data were collected. Abnormal DB was defined as: 1) DB level $\geq$ 1mg/dl with a corresponding TB of $\leq$5 mg/dl or 2) DB of >20% of the corresponding TB that is > 5 mg/dl.

RESULTS: A total of 2,760 infants were admitted to the NICU during the study period. The median gestational age was 35 weeks (w) (range, 22-42 w) and the median birth weight was 2400 g (range 365-5418 g). Total and direct bilirubin levels were measured in 2,044 (74 %) infants at 12-24 hours of life. Only 2 (0.098%) infants had abnormal DB. Extensive work-up in both infants was normal and the cholestasis eventually resolved. None of the 159 infants who developed cholestasis after the first week of life had an abnormal DB level on day 1. None of the infants with early sepsis (n=32) or low apgar score (<5) at 5 minutes (n=124) had abnormal DB on day 1.

CONCLUSIONS: The routine measurement of DB at 12-24 hours of age for infants admitted to the NICU has a very low yield and may not be cost-effective. Further research is needed to identify the risk factors in infants in whom the routine measurement of DB at 12-24 hours will be clinically warranted.

187 10:00 AM

Effect of a High Fidelity Simulation Curriculum on Pediatric Resident Competency in Neonatal Airway Management Skills

J. Arnold, M. Fiedor Hamilton, J. Kloesz, R. Clark, S. Kanter, B. Lowmaster, S. Wisneiski, D. Hofkosh, P. Kochanek. Ped, SBUMC, Stony Brook, NY; CCM, UPMC, PGH, PA; Ped, UPMC, PGH, PA; Education, UPMC, PGH, PA.

BACKGROUND: Pediatricians are responsible for delivery room resuscitation. Neonatal airway management skills are required competencies for pediatric trainees. Work hour restrictions have limited residents' opportunity to practice these skills. Falck (2003) and Leone (2005) report poor neonatal intubation success rates: 33-50%, 40-55%, and 40-62% for 1st, 2nd, and 3rd year residents respectively. Pediatric residents are not mastering this core clinical competency.

OBJECTIVE: Improve pediatric residents' ability to manage the airway of a critically ill neonate including 1) proper set up of resuscitation equipment, 2) bag-mask ventilation, and 3) endotracheal intubation using the infant simulator, *Simbaby* (Laerdal).

DESIGN/METHODS: 50 pediatric residents at Children's Hospital of Pittsburgh were randomized to participate in the curriculum (24 study and 26 controls [standard educational approach]). The intervention included a web-based module reviewing management of the newborn in respiratory distress and a simulation curriculum consisting of delivery room scenarios where residents practiced delivery room set up, bag-mask ventilation, and endotracheal intubation. The primary outcome was intubation success rates in the clinical arena as documented by respiratory therapists (blinded). Secondary outcomes included learner satisfaction, performance evaluation in the simlab, and neonatal intubation complication rates.

RESULTS: 163 intubations were performed by pediatric residents in the NICU during the study (82 intubations from the study group and 81 from controls). The success rate was higher in the study (65%) vs control (48%) groups for all residents ($p<0.05$, Chi-Square, Table). In the study group, trends toward higher success rates were seen across the spectrum of training level.

Intubation Success

	Intervention	Control
PGY I	58%	47%
PGY II	66%	45%
PGY III	83%	56%
All	65%	48% ($P<0.05$)

CONCLUSIONS: A simulation curriculum improved pediatric resident competency in neonatal intubation skills. This finding is strengthened by the observed intubation success rates in controls, which were similar to those previously reported across training levels. To our knowledge, this is the first study to evaluate directly the effect of high fidelity simulation on competency in the patient care environment.

Supported by NIH # T32 HD40686, Safar Center, and WISER Center, UPMC.

188 10:15 AM Fellow in Training

Impact of Instrumental Dead Space on Pressure Support Volume Guarantee (PS-VG) Mode of Ventilation in Extremely Low Birth Weight (ELBW) Infants

Rebecca J. Eick, Sepideh Montazami, Kabir M. Abubakar, Martin Keszler. Neonatology, Georgetown University Hospital, Washington, DC.

BACKGROUND: Volume targeted ventilation (VTV) is increasingly used in neonates with the potential for reducing volutrauma and hypocapnia. However, normative data for appropriate tidal volume (VT) settings are lacking, especially in ELBW infants in whom the added dead space (DS) of the flow sensor may be a concern. We previously reported retrospective data from 38 infants ≤800g and showed that an initial VT of 5 to 6 mL/kg achieved normocapnia when using VTV despite the use of a set VT only slightly larger than the estimated DS of ~3mL.

OBJECTIVE: To prospectively validate the concept that effective alveolar ventilation (AV) occurs at VT close to the dead space volume in ELBW infants and that the use of a flow sensor does not require excessively large VT.

DESIGN/METHODS: Infants with birth weights <1200g who required ventilation with the Babylog 8000 plus in the PS-VG mode in the first 3 days of life and had no leak around their endotracheal tube (ETT) were enrolled in this prospective study. Ventilation parameters [respiratory rate (RR), expiratory VT (Exp VT), set VT and minute ventilation (MV)] were downloaded continuously from the ventilator. Arterial and capillary blood gas values were recorded for the first 3 days of life. Mean VT, RR and MV for the 20 minutes prior to each blood gas were associated with pCO_2 as a sample set. Theoretical AV was calculated using the formula [measured VT minus estimated DS volume (2.7mL instrumental DS + 0.5mL/kg anatomic DS)] x RR. Simple descriptive statistics were used.

RESULTS: Data were available for 14 infants with gestational ages of 24 to 29 weeks and birth weights of 610-1180g (mean 853±184g). A total of 167 paired blood gas and ventilation data sets were available for analysis.

Exp VT(mL/kg)	Set VT(mL/kg)	Est. DS (mL)	PCO_2 (mmHg)	RR (br/min)	MV (mL/kg/min)	Alv Vent
4.65 ± 0.05	4.76 ± 0.05	3.14 ± 0.01	43.8 ± 0.6	64 ± 1.0	270 ± 1.0	59 ± 5

Data are Mean ± SEM; Alv Vent = theoretical alveolar ventilation (mL/kg/min)

CONCLUSIONS: An initial VT of 4.5 to 5 mL/kg in the first 3 days of life provides effective AV and normocapnia in ELBW infants using the PS-VG mode even with the instrumental DS associated with the required flow sensor. The calculated AV underestimates effective AV. We postulate that fresh gas penetrates through the dead space gas because of the high flow velocity generated in the narrow ETT.

189 10:30 AM

Predictors of Morbidity and Mortality in Infants with Congenital Diaphragmatic Hernia: A National Database Review

Hany Aly, Maria D. Bianco-Batlles, Anthony Sandler, Mohamed H. Mohamed. Neonatology, The George Washington University & Children's National Medical Center, Washington, DC; Surgery, The George Washington University & Children's National Medical Center, Washington, DC.

BACKGROUND: Improved outcomes are reported in patients with congenital diaphragmatic hernia (CDH). This observation could be related to the use of a more conservative and expectant management protocol during the first few days of life. Since regionalization of care has been proposed for difficult neonatal cases and since neonatal transport is not a risk-free procedure, understanding the outcomes of infants with CDH is an important model for understanding the effect of regionalization and transport.

OBJECTIVE: Utilizing a national database, we aimed to: 1) determine outcome of infants with CDH, 2) compare outcomes of infants who needed to be transported for their surgical repair to those who did not, and 3) validate the impact of delayed surgery on outcome.

DESIGN/METHODS: We analyzed the National Inpatient Sample and the "Kids" database for the years 1998- 2004. Infants included in this study are those: diagnosed with CDH according to the International Classification of Disease-9, age at admission <8 days, operated for CDH repair and/ or died before surgery. Variables of gender, race, geographic region, co-existing diagnoses, use of extracorporeal membrane oxygenation (ECMO), complications and length of stay (LOS) were obtained. Infants were stratified based on whether they were transported from another facility or were born at the same place of surgery. They were also further stratified into 3 groups according to their age at operation (<3 days, 3-7, and >7 days). Groups were compared using Pearson's ^{2}, t-test, Kruskal-Wallis test and logistic regression test.

RESULTS: A total of 2613 infants were included; of them 42% female, 55% Caucasian, and 30.8% mortality. There were 1138 infants transported and 1475 remained at their birth hospital. Only 1080 (73.2%) of the inborns were operated, compared to 941 (82.7%) of the transported infants (P <0.001, OR=1.7). Among the 2021 infants who were operated, 89.4% survived, and 17.8% required ECMO. Inborn infants had less ECMO (11.9% vs. 24.5%, P<0.001, OR=2.4), less mortality following surgery (8.1% vs. 13.3%, P<0.001, OR 1.75), and less LOS (21.6 vs. 32.8 days, P<0.0001). Mortality in relation to the 3 categories for operation age was 7.3% vs. 7.8% vs. 21.2%. Mortality with ECMO was 41% (OR=18 when compared to no-ECMO patients).

CONCLUSIONS: Need for transport is associated with poorer outcome. There was no advantage with delaying surgical repair.

190 10:45 AM

An Evaluation of an ROP Screening Program

Rachel Porat, Dafna Ofer, Dana Toib, Ahashta Johnson, David L. Schutzman. Pediatrics, Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: Recently, 20 million dollars were awarded to a baby blinded by retinal detachment from ROP following delayed eye exam (Philadelphia Inquirer), and we are aware of 2 additional cases elsewhere of detachment following missed appointments. Not much data are available regarding the adequacy of various practices and programs in ensuring appropriate eye care to infants at risk for ROP.

OBJECTIVE: To ensure the timeliness of eye examination in premature babies at risk for ROP, both before and after discharge.

DESIGN/METHODS: A retrospective survey was conducted on all infants born from January 2005 through December 2006 with gestational age ≤ 32-weeks and with birth weight ≤ 1500g. Records reviewed included initial hospital charts, f/u High-Risk Clinic charts, Pediatric Clinic charts, Ophthalmology records and parental phone interviews. Detailed clinical data were collected including eye exam results and treatments. Adequacy of ROP screening and f/u was assessed as per AAP guidelines and recorded as: on time, late-if >2 weeks past recommendation, never performed or not indicated.

RESULTS: A total of 166 infants needed eye exams during the 2 year period; of these 19 were transferred, 20 died and 7 had no records available, leaving a total of 120 patients. Their mean BW 1.19± 0.98Kg and GA 28.6 ± 2.84 wks. 57% required mechanical ventilation and 83% received supplemental O_2 74 required initial eye exam while inpatients. First eye exam was on time in 94% of the inpatients, late in 3% and not done in 3%. F/U exams in-house were on time in 87% and late in 13%. Of these 74, 64 required outpatient F/U eye exam after NICU discharge. Ophthalmology appointments were made for 59 (though documented in only 40 charts), 38 were seen and 14 were no-show (7 unknown).

Of the 46 with first eye exam indicated after discharge: 36 had appointments (though only 7 noted in the hospital records), 6 were seen and 30 were no show. No show rate was significantly higher among babies requiring initial eye exam after discharge. (OR 10.1).

CONCLUSIONS: Ophthalmology follow up after NICU discharge of preterm infants at risk for ROP is poor, particularly among infants whose initial exam occurs after D/C.

Strategies to improve follow up should include parental education, increased documentation and development of tracking systems to ensure compliance with AAP recommendations.

191 11:00 AM Fellow in Training

Amplitude Integrated Electroencephalography (aEEG) in Premature Infants (PREMS): Frequent Artifacts (ARTs) Limit a Role in Assessing Cerebral Function?

Debbie Suk, Alfred N. Krauss, Murray Engel, Jeffrey M. Perlman. Pediatrics, New York Presbyterian Hospital-Weill Cornell Medical Center, New York, NY; Child Neurology, New York Presbyterian Hospital-Weill Cornell Medical Center, New York, NY.

BACKGROUND: The aEEG, an integrated electrocortical activity monitor, is very sensitive in identifying high risk term infants as candidates for hypothermia treatment and for seizure (Sz) detection. In PREMS, the aEEG has been used for brain maturation assessment. We hypothesized that the aEEG would be suppressed during apnea and bradycardia (A&B) followed by an increase in amplitude in PREMS related to changes in CBF. 10 PREMS (mean BW 1085g, GA 31wks) were studied to determine the impact of A&B on the aEEG.

OBJECTIVE: Cerebral function monitors (CFM) now include a single channel raw EEG (rEEG). ART, however, was present in many rEEG tracings which limited interpretation of the derivative aEEG. The objective is to highlight this problem.

DESIGN/METHODS: aEEG was recorded with the Olympic CFM 6000 using bitemporal frontal electrodes, ≥ 1h duration on DOL 0-2, 3-6, 7-10, 11-14, 20-22, 28-30. ARTs were determined if the rEEG waves had a sharp appearance with a large amplitude changes. In contrast, normal brain waves (NBW) had smooth waves of small amplitude changes. To quantify the problem of ART, tracings of rEEG were selected every 2 min and categorized as NBW, ART, or indeterminate (IND) if the finding was at least 10s in duration. Three blinded readers reviewed the rEEGs of 5 random infants to determine interobserver agreement of ART.

RESULTS: 48 recordings, mean duration 83 min and impedance 6.1 kΩ, yielded 1683 points: 529 NBW (31%), 1013 ART (61%), 142 IND (8%). There was overall good interobserver agreement. Notably, ARTs were more common when there was a spike or upward shift in the aEEG, patterns that could otherwise be interpreted as Sz. When the aEEG was suppressed, it was most often classified as NBW.

CONCLUSIONS: ARTs are frequent in aEEG recordings of PREMS, thereby potentially limiting its role in assessing brain maturation or in Sz detection. ART may reflect muscle or eye movements, and do not appear to be electrical interference as they are usually absent with aEEG suppression. This observation is consistent with a recent case report (Pediatrics, Dec 06) describing ARTs present in the rEEG of a term baby with a resultant increased aEEG that became suppressed after elimination of ART with paralysis. These observations suggest caution when interpreting spikes or increases in the aEEG and perhaps incorrectly attributing them to Sz; clinical exam and the rEEG are critical correlates.

192 11:15 AM Fellow in Training

Ascorbic Acid Combined with Ibuprofen in Hypoxic Ischemic Encephalopathy: A Randomized Controlled Trial

Hany Aly, Mohamed El-Dib, Laila Abd-Rabboh, Fathy Nawwar, Hassan Hassan, Mohamed Aaref, Ahmad Elsayed. Department of Neonatology, The George Washington University and Children's National Medical Center, Washington, DC; Department of Pediatrics, Alazhar University, Cairo, Egypt.

BACKGROUND: Free oxygen radicals and pro-inflammatory cytokines are important causes for brain injury in neonates with hypoxic ischemic encephalopathy (HIE). In animals, ascorbic acid (Vitamin C) is protective against free radicals-induced neurotoxicity while Ibuprofen has been shown to be neuroprotective through modulation of leukocyte activity, reducing cytokine production, inhibition of free radicals and signaling transduction. The efficacy of these 2 drugs in protecting the human brain in HIE has not been studied.

OBJECTIVE: To test the hypothesis that a combination of anti-oxidants (Vitamin C) and anti-inflammatory (Ibuprofen) agents can ameliorate brain injury in HIE when given to infants immediately after birth.

DESIGN/METHODS: Sixty asphyxiated infants admitted at Bab El-Shariya University Hospital, Cairo, Egypt, were randomly assigned to one of two groups. Group A (n = 30); infants received intravenous Vitamin C (100 mg/kg/day for 3 days) and oral Ibuprofen (10 mg/kg on day 1, followed by 5 mg/kg on days 2 & 3), and Group B (n = 30), infants received similar volumes of placebo. Treatment drugs were administered within 2 hours after birth. A panel of cytokines were measured at enrollment. Neurological evaluations of all infants were done on admission, on discharge and at 6 months of age. Grades of HIE were assigned on admission using Sarnat and Sarnat grading and 6 months developmental screening was done using Denver Developmental Screening Test II (DDST II).

RESULTS: There was no difference between Group A and B in gestational age (38.4 ±1.3 vs. 38 ±1.1 wks), HIE grading (Severe HIE: n=11 vs. n=11, Moderate HIE: n=11 vs. n=9), serum IL-1β (11.1±3.1 vs. 10±3.4) and IL-6 levels (116.1±80.1 vs. 113.1±72.4). No difference between Group A and B was noted in mortality rate (37% vs. 33%), rate of abnormal neurological exam at discharge (47% vs. 55%) and rate of delayed scores on DDST II at 6 months (32% vs. 40%). Serum IL-1β and IL-6 levels correlated with the severity of HIE (P<0.01). Elevated Serum IL-6, but not IL-1β, correlated with poor neurodevelopmental outcome at 6 months (P<0.001).

CONCLUSIONS: Early administration of vitamin C and Ibuprofen did not reduce mortality or improve neurodevelopmental outcomes measured at 6 months of age. Mediators other than free radicals and inflammatory cytokines may have stronger role in brain damage in infants with HIE.

193 11:30 AM House Officer

Vinyl Bag vs. Thermal Mattress To Prevent Hypothermia in Extremely Low Birth Weight (ELBW) Infants

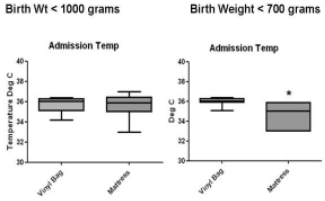
Bobby Mathew, Satyan Lakshminrusimha, Vivien Carrion. Neonatology/Pediatrics, The Women and Children's Hospital of Buffalo, Buffalo, NY.

BACKGROUND: Neonatal hypothermia in the delivery room (DR) has been associated with increased morbidity and mortality in ELBW infants. Present NRP recommendations include use of polyethylene bag in ELBW infants to maintain body temperature. Thermal mattesses can also be used to prevent hypothermia.

OBJECTIVE: To study and compare two methods of preventing hypothermia after birth in ELBW preterm infants.

DESIGN/METHODS: This randomized control trial enrolled infants <28wk gestation who were randomized to either vinyl bags (Vi-Drape®, $11.80/bag), or thermal mattress (Transwarmer®, $20/mattress). Both groups underwent drying of the head and placement of a stocking cap. Resuscitation and stabilization were carried out according to NRP guidelines. Infants were transferred to the NICU in prewarmed transport isolettes. Axillary temperature on admission to the NICU was recorded.

RESULTS: 27 infants were enrolled in the study and admitted to the NICU between 7/2005 and 7/2007 and randomized to vinyl bags (n=14) or thermal mattresses (n=13). Baseline characteristics such as gestational age (25.6±0.4 & 25.9±0.3 wk), birth weight (691±25 & 705±35g) and cord pH were similar for both groups. There was no difference in the admission temperature between the two groups. However in infants with birth weight < 700g (n=8 vinyl bag and n=6 warmer group), vinyl bags were more effective than mattresses in preventing hypothermia (vinyl bags 36±0.1°C vs. thermal mattress 34.7±0.6°C, p=0.015).



* P < 0.02 compared to Vinyl bag group by unpaired 't' test

	Transfer time (DR to NICU in min)	Admission temp °C	Hypothermia <35°C	Worst pH in first 6h	Worst Base deficit in first 6h mEq/L	Hypotension
Vinyl Bag	22.5 ± 2	35.75 ± 0.2	2	7.28 ± .02	-6 ± 0.8	7
Thermal Mattress	22.6 ± 3	35.52 ± 0.4	3	7.29 ± .02	-6 ± 1.2	8

CONCLUSIONS: The use of thermal mattress does not confer any improvement in admission temperature compared to the vinyl bags in <28wk gestation infants. It appears that in ELBW infants <700g, vinyl bags may be preferred over thermal mattresses to prevent hypothermia in the DR.

194 11:45 AM

Use of Chemical Warming Packs During Delivery Room Resuscitation and Admission Temperatures in Very Low Birth Weight Neonates

Joaquim M. Pinheiro, Susan Boynton, Susan A. Furdon, Robin Dugan, Sharon Jensen, Christine Reu-Donlon, Mary A. Miller, Andrea Degnan. Pediatrics; Quality Management; Obstetrics & Gynecology, Albany Medical Center, Albany, NY.

BACKGROUND: Hypothermia is an independent contributor to neonatal mortality. Yet, recently available data indicate that while receiving standard delivery room care, the majority of very low birthweight (VLBW) newborns undergo cold stress, and a substantial proportion become severely hypothermic. This has prompted clinicians to use multiple adjuncts aimed at maintaining normothermia in VLBW neonates, though the efficacy and safety of these methods remains to be established.

OBJECTIVE: 1) to characterize the effectiveness of thermoregulation procedures in maintaining normothermia during delivery room resuscitation; 2) to assess the impact of an unanticipated change in equipment at our institution on the admission temperatures of VLBW newborns.

DESIGN/METHODS: Retrospective analysis of Quality Assurance data submitted to the Vermont-Oxford Network (VON), for 21 consecutive months starting January 2006; IRB-approved. We compared the rate of hypothermia (admission temperature < 36.5°C) in our NICU during 2006 to the aggregate rates reported by VON. We then compared the rates of hypothermia and mean admission temperatures in our NICU during Period 1 (when chemical warming packs were used routinely, in addition to plastic wrapping and warm blankets) and Period 2 (after packs were discontinued due to an incident of focal skin injury possibly related to a chemical leak).

RESULTS: In 2006, 42% of VLBW babies in our NICU had admission temperature < 36.5°C, compared with the VON rate of 61% (IQR 48%, 76%). No change in practice other than discontinuation of the warming packs was instituted during Period 2. During Period 1, 38% of 190 VLBW neonates were hypothermic, compared with 64% of 86 during Period 2 (p<0.001). Mean admission temperatures during the 2 periods were 36.5°C and 36.2°C, respectively (p=0.002). A control chart showed the shift in temperatures occurring as Period 2 began. The incidence of temperatures >38°C was 2% during both periods.

CONCLUSIONS: The results associated with this isolated change in practice at our institution suggest that chemical warming packs were a useful adjunct in achieving above-average rates of normothermia during delivery room resuscitation of VLBW newborns. Their potential adverse effects should be weighed against the increased risk of mortality associated with hypothermia in this population.

Neurobiology Platform Session

Sunday, March 30, 2008 9:45 AM-12:00 PM

195 9:45 AM Fellow in Training

Cardiac Troponin I (cTnI) Levels in Asphyxiated Infants Undergoing Selective Head Cooling Correlate with Mortality and Neurodevelopmental Outcome

Constance G. Andrejko, Vidula Damle, Susan C. Adeniyi-Jones. Pediatrics, Thomas Jefferson Univ./duPont Hospital for Children, Philadelphia, PA.

BACKGROUND: Infants with perinatal asphyxia are at risk for multi-organ dysfunction, neurologic sequelae, and death. cTnI is a cardiomyocyte-specific protein and marker for myocardial injury. In adults with ischemic and hemorrhagicstroke, elevated cTnI levels are associated poor neuroligical outcome. Neonates with perinatal asphyxia and RDS have higher serum cTnI than normal infants. Little is known about cTnI levels in infants with hypoxic ischemic encephalopathy (HIE) undergoing head cooling (HC).

OBJECTIVE: To determine if elevated cTnI levels are associated with an increased risk of morbidity and mortality in infants with HIE undergoing HC.

DESIGN/METHODS: A retrospective chart review of 91 asphyxiated infants ≥ 36 weeks gestation and ≥ 1.8 kg undergoing HC at Thomas Jefferson University Hospital, Philadelphia, PA was performed. All infants who had at least one Troponin level measured (n = 86) and met criteria for head cooling (pH < 7.0 or base deficit of > -16 on any blood gas within one hour of life, or a 10 minute Apgar score of ≤ 5 or ongoing need for mechanical ventilation, and signs of encephalopathy and a moderate to severely abnormal amplitude-integrated EEG tracing) were included in the analysis. Patients were categorized as normal / mild disability (Group I) or non-survivors/moderate to severe disability (Group II). The relationship between cTnI levels and outcome was determined using the Mann-Whitney U test.

RESULTS: Eighty-six infants with undergoing HC for HIE had one or more cTnI levels measured. The mean gestational age (GA) was 39.0 weeks, mean birthweight was 3252 grams, and the median 5 minute APGAR score was 3. cTnI levels ranged from 0.00 to 13.9 ng/ml and were undetectable in 4 infants. cTnI levels were higher in infants who died (n=11, median 1.12, interquartile range 0.43-1.38) compared to those who survived (n=75, median 0.27, interquartile range 0.12-0.47, p=0.003). cTnI levels were found to be higher in Group II infants (n=26, median 0.64, interquartile range 0.35-1.32) than Group I infants (n=32, median 0.16, interquartile range 0.07-0.30, p<0.001). A cTnI level of ≥ 0.3 a sensitivity of 81%, specificity of 73%, PPV of 70% and a NPV of 84% for severe neurologic disability or death.

CONCLUSIONS: cTnI, a marker of myocardial injury, may be a valuable predictor of outcome among infants undergoing HC for HIE.

196 10:00 AM Fellow in Training

Altered Fractional Anisotropy Caused by Neonatal Hypoxia Ischemia Is a Result of Increased Radial Diffusivity in Injured White Matter

Brian S. Stone, Jiangyang Zhang, Susumu Mori, Frances J. Northington. Pediatrics, Division of Neonatology, Johns Hopkins Hospital, Baltimore, MD; Radiology, Johns Hopkins School of Medicine, Baltimore, MD.

BACKGROUND: Diffusion tensor imaging (DTI) provides indices that are used to examine the integrity of white matter (WM) microstructure. These include fractional anisotropy-FA, axial and radial diffusivity-Da and Dr). Adult animal studies suggest that decreases in Da are associated with axonal damage, while increases in Dr are associated with myelin damage.

OBJECTIVE: We used ex-vivo DTI MR imaging and histopathology to determine how neonatal HI affects the microstructure of the developing WM following injury.

DESIGN/METHODS: We used the Rice-Vannucci model, (unilateral carotid ligation + 45 min of hypoxia, FiO2=0.08) to cause brain injury in p7 C57B6 mice and performed ex-vivo DTI and histopathology at p8, p11, p15, p21, and p28 (n≥4/time point). Regions of interest were placed on coronal sections of fiber tracked fimbria fornix (FF) and measures of FA, Dr, and Da were calculated using in-house DTI Studio Software. Post imaging, brain tissue was sectioned and stained for neurofilament-M (NF-M) expression.

RESULTS: In the contralateral FF, FA increases from p8 to p28 (p< 0.001), Dr decreases (p=0.002) with no significant change in Da. Axonal injury to the ipsilateral FF is evident at p11 in histological sections stained with NF-M. By p15, FA of the ipsilateral FF is less than FA in the contralateral FF (0.55±0.13 vs 0.70±0.07, p=0.04). This difference persists at p21 and p28. There is no difference in the Da between the ipsilateral and contralateral FF. However, there is an increase in Dr in the ipsilateral FF compared to the contralateral FF. At p15 Dr is 0.006±0.002 vs. 0.004±0.001 (ipsilateral vs. contralateral, p=0.07), at p21 Dr is 0.005±0.001 vs. 0.003±0.0009 (p=0.05) and at p28 Dr is 0.007±0.002 vs. 0.002±0.0003 (p=0.07).

CONCLUSIONS: This study illustrates that neonatal HI blocks the normal developmental increase in FA in the ipsilateral white matter during the 3 weeks following HI, simultaneously with loss of a major neurofilament protein from axons in the ipsilateral white matter. Despite histopathologic evidence for axonal injury, HI in the immature brain does not alter Da; rather it causes an increase in Dr in the ipsilateral FF. These results are consistent with those found in a fetal model of hypoxic brain injury, but in contrast to results in adult models of HI. It is unclear what the neuropathologic substrate of alterations in FA and Dr are in the developing brain following neonatal HI.

197 10:15 AM Fellow in Training

A Randomized Controlled Trial To Determine the Lowest Effective Dose for Adequate Mydriasis in Premature Infants

Monisha Bahri, Gonzalo C. Vicente, Judith J. Palafoutas, Nitin R. Mehta. Neonatology, Georgetown University Hospital, Washington, DC; Pediatric Ophthalmology, Georgetown University Hospital, Washington, DC.

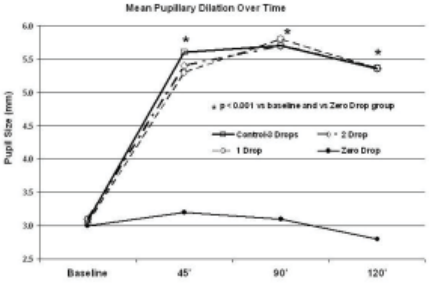
BACKGROUND: Adverse effects of the anticholinergic and adrenergic agents used to dilate pupils of infants screened for retinopathy of prematurity (ROP) have been reported. To reduce the potential for adverse effects we sought to determine the minimal effective dose needed to achieve clinically adequate mydriasis.

OBJECTIVE: To compare the mydriatic efficacy of different number of eyedrops.

DESIGN/METHODS: Preterm infants scheduled for ROP screening were enrolled and randomized at each exam to one of three groups. Pupils were dilated using a combination eyedrop of Phenylephrine 1% and

Cyclopentolate 0.2% commercially available as Cyclomydril [R]. In all groups, the right (control) eye received 3 eyedrops per our current NICU protocol, while the left (test) eye received either: 0, 1 or 2 drops. Pupil size in mm was measured by a single examiner at: 0 (baseline), 45, 90 and 120 min after instillation. Comparison of the means was calculated using ANOVA.

RESULTS: 29 study exams were performed in 11 enrolled infants; 55% caucasian, 37% male, median GA 27.9 weeks. There was no significant difference in mean pupil size between 1, 2 and 3-drop groups at baseline and up to 120 min. All but 6 eyes (3-control, 3-test) achieved ≥ 5mm pupil by 45 mins. Two eyes (same infant, 2-drop and control) stayed < 5mm to 120 mins. This infant had brown irises and stage 2, zone 2 ROP. The Zero-drop group maintained baseline size indicating lack of a crossover effect and was the only group requiring additional drops to complete the ROP examinations.



CONCLUSIONS: Effective mydriasis was achieved with 1 or 2 drops between 45 and 90 minutes and was sustained to 120 minutes. This effect was independent of the contralateral control eyedrops. Therefore, retinal exams could be completed by 90 minutes in most infants using less than 3 drops. A larger study is needed to determine any effect of iris color and ROP severity on these findings.

198 10:30 AM Fellow in Training

A Comprehensive Analysis of Protein Secretion by Neonatal Murine Astrocytes After Inflammatory Stimulation

Sarah D. Keene, Todd Greco, Harry Ischiropoulos. Department of Pediatrics and Pharmacology, Children's Hospital of Philadelphia and the University of Pennsylvania, Philadelphia, PA.

BACKGROUND: The causal relationship between prenatal infection, inflammation, and brain injury is one of active investigation. Astrocytes provide neuronal scaffolding, trophic support, and modulate central nervous system (CNS) responses to systemic inflammation. It is believed that the majority of astrocyte functions are carried out by the actions of secreted proteins.

OBJECTIVE: The goal is to develop a comprehensive inventory of proteins secreted by neonatal astrocytes in culture, and to allow comparison of secreted proteins after acute or prolonged inflammatory stimulation.

DESIGN/METHODS: Primary astrocyte cultures were isolated from neonatal mice and either treated with cytokines or left untreated. A proteomic approach composed of in-gel digestion and liquid chromatography interfaced directly with a linear ion trap mass spectrometry was used. A multi-step computational analysis was employed to identify the proteins in astrocyte-conditioned media. For semi-quantitative comparisons we employed MS spectral counting.

RESULTS: The study generated a comprehensive list of 169 secreted proteins across all conditions, more than quadrupling the number reported presently. The secretome contained components of the extracellular matrix, regulators of cellular development and growth, signaling molecules and enzymes involved in the processing of glycoproteins and glycosaminoglycans. Deficiencies in these classes of proteins are associated with various lysosomal storage diseases. Lower relative amounts of these were noted in the media of cytokine treated cells. Twelve proteins were detected exclusively in the inflammatory response secretome, including four members of the chemokine ligand families that modulate inflammation and migration of oligodendrocyte precursors and neural stem cells.

CONCLUSIONS: The advanced proteomic approach combined with a computational workflow analysis resulted in the identification of a significant number of proteins not previously ascribed to astrocytes. This comprehensive compilation of extracellular/secreted proteins is a rich, valuable resource that can be mined for factors that regulate neuron/glia networks and the release of neurotoxic factors. Control of inflammation may indeed be a key treatment strategy, which potentially can include the replacement or augmentation of secreted proteins inhibited during inflammation.

199 10:45 AM

Regional Tissue Oxygenation in Association with Alterations in the Physiologic Parameters in Preterm Infants

Anna Petrova, John Chuo, Uday Nadgir, Mayoor Bhatt, Rajeev Mehta. Pediatrics, Robert Wood Johnson Medical School-UMDNJ, New Brunswick, NJ.

BACKGROUND: The association between pathophysiological changes in arterial oxygen delivery and hemodynamics, and alterations in regional tissue oxygenation in extremely premature neonates is not very well understood. Non-invasive monitoring of oxygen delivery and utilization allows the investigation of tissue oxygenation and perfusion during alterations of oxygen supply and pathophysiological changes in hemodynamics.

OBJECTIVE: To determine the extent to which cerebral and renal tissue oxygenation is dependent on alterations in peripheral oxygen supply and hemodynamics.

DESIGN/METHODS: Near infrared spectroscopy (NIRS) measurements (recorded every 5 seconds over 4 hours) of cerebral (rSO_2-C) and renal (rSO_2-R) tissue oxygenation were linked with the corresponding physiologic parameters of peripheral oxygen saturation (SaO_2), systolic (SBP), diastolic (DBP), mean (MBP) blood pressure and heart rate (HR) in seven extremely preterm infants on nasal CPAP for apnea of prematurity. The cerebral and renal fraction oxygen extraction (FOE-C) and (FOE-R) was calculated using the SaO_2 and rSO_2-C and rSO_2-R data. The cerebral and renal oxygenation and extraction was evaluated in association with alteration in peripheral oxygen saturation and hemodynamic parameters.

RESULTS: No episodes of hypotension or apnea were recorded during the continuous monitoring. The episodes of bradycardia corresponded with SaO_2 <80% in 13% of the measurements (N=2130). Multiple regression analysis did not reveal any significant impact of the short (duration of 5-seconds) of bradycardia on the cerebral and renal tissue oxygenation and oxygen extraction. However, the rSO_2-C and rSO_2-R were significantly dependent on the normal variation in SBP and MBP. Although regional tissue oxygenation was less likely to be associated with alterations in SaO_2, oxygen extraction by the cerebral and renal tissue decreased significantly when the SaO_2 was <70%.

CONCLUSIONS: The maintenance of adequate cerebral and renal oxygenation during the transient but severe arterial desaturations in stable normotensive preterm infants receiving CPAP is at the expense of reduced tissue oxygen extraction. Although the clinical impact of such an association was not evaluated in the present study, the decreased cerebral oxygen extraction could be prognostically unfavorable for the development of hypoxia-related cerebral insults.

200 11:00 AM Fellow in Training

Blood Glucose Levels and ROP in ELBW Infants

Raul Chavez-Valdez, Christoph U. Lehmann, Elizabeth A. Cristofalo, Jane E. McGowan. Pediatrics, The Johns Hopkins Univ School of Medicine, Baltimore, MD; Neonatology, St. Christopher's Hospital for Children/DUCOM, Philadelphia, PA.

BACKGROUND: Hyperglycemia (blood glucose >150 mg/dl) occurs in up to 45% of extremely low birth weight (ELBW) infants. Some studies suggest that hyperglycemia increases risk for severe retinopathy of prematurity (ROP).

OBJECTIVE: The objective of the present study was to investigate the relationship between blood glucose levels and development of ROP in a cohort of ELBW infants.

DESIGN/METHODS: Data were collected retrospectively from a cohort of infants with BW <1000g born between March 1, 2004 and February 28, 2007 and admitted to the NICU at Johns Hopkins Hospital within the first 24h after birth. Data extracted from the electronic medical record or by chart review included demographics, Apgar scores, use of O2, steroid Rx, inotrope Rx, infections, and insulin Rx, in addition to all recorded laboratory and bedside blood glucose measurements during the first 10 d after birth. Univariate logistic regression was performed to identify potential ROP risk factors. Significant variables were then used in a multivariate logistic regression. Analysis of effect of glucose levels was performed using episodes of high (>200 or >150 mg/dL) and low (<50 and <40 mg/dL) glucose, and, separately, using a cumulative, time-weighted glucose level (TWGL) derived from a plot of glucose values v time for each 24h period.

RESULTS: Data from 123 infants were included in the analysis (55% male; 59% African American; mean GA 26.6 wk; mean BW 782g and median APGAR 1/5 min 4/7). In the initial univariate regression, TWGL, low blood glucose level, steroid exposure, inotrope Rx and history of gram(+) sepsis had significant effects on incidence of severe, but not mild, ROP. In the multivariate logistic regression including these 4 variables, 3 reached significance [OR (CI)]: TWGL > 50th percentile for the cohort [4.8 (1.2-19.0)], gram (+) sepsis [5.1 (1.6-16.10] and any episode of blood glucose <50 mg/dL [0.17 (0.06-0.51)].

CONCLUSIONS: We conclude that single or multiple episodes of hyperglycemia during the first 10d after birth are not associated with increased risk for severe ROP in ELBW infants. However, overall glycemic status during the first 10 d, as represented by TWGL, was a more significant predictor, of severe, but not mild, ROP. In contrast, infants with low glucose levels (as suggested by values <50 mg/dl) in the first 10d may be less likely to develop severe ROP. Degree of illness, as indicated by sepsis and/or inotrope use, may also contribute to ROP risk in this population.

201 11:15 AM

Childhood Syncope

Cristina S. Wheeler Castillo, Francis J. DiMario. Health Fellows Program, Trinity College, Hartford, CT; Pediatrics and Neurology, CT Children's Medical Center, Hartford, CT.

BACKGROUND: Syncope is a sudden, self-limited loss of consciousness and postural tone produced by cerebral hypoperfusion/hypoxia. Approximately 30-50% of children experience at least one episode of syncope by adolescence. The pathophysiology of syncope can be stratified into several groups: autonomic neurally mediated reflex syncope, cardiogenic (1^0, 2^0), cerebrovascular insufficiency, orthostatic, pseudosyncope, and suffocation. Convulsive syncope is common in children and may be misdiagnosed as epilepsy.

OBJECTIVE: The primary aim of the study was to systematically categorize the etiology of syncope in pediatric outpatients referred for neurological evaluation and to determine the frequency of concurrent epilepsy. A secondary aim was to determine what clinical/laboratory information is most useful in distinguishing syncopal etiologies.

DESIGN/METHODS: In this IRB approved retrospective study we applied uniform diagnostic criteria to ascertain the frequencies of specific etiologies of syncope found in children referred for neurological evaluation. Subjects were identified by chart review of ICD-9 codes 780.2 and 786.9 over the period 2003-2006. One hundred twenty-nine items of data concerning; demographics, family history, triggers, symptoms, event descriptions, examination and ancillary testing results for each subject were coded and analyzed using descriptive statistics and frequencies.

RESULTS: There were 141 subjects, [90 girls (63.8%)] with a mean age of 10.9(s.d. ± 4.96) years. Prior to referral, 36/141 subjects (25%) were evaluated in the ER for syncope. There were 92 patients referred for syncope, 18 for epilepsy, 29 for syncopal convulsions, and 2 for both syncope and epilepsy. Of the syncope referrals, 83/92 were found to have syncope, and 9/92 were found to have syncopal convulsions. Of those referred for epilepsy, 5/18 were found to have syncope alone, 11/18 were found to have syncopal convulsions, 1/18 was found to have epilepsy and syncopal convulsions, and 1/18 was found to have epilepsy, syncope, and syncopal convulsions. An EEG was obtained in 64.7%, MRI/CT in 34%, and EKG in 25.5%, all were normal or non-diagnostic. In subjects who underwent; head-upright tilt table test (HUTT), Holter monitoring and ancillary blood testing only 4/192 tests (2.1%) were diagnostic. A mechanism of primary Neurocardiogenic syncope was identified in 78% (112/141) subjects.

CONCLUSIONS: Although 38% of subjects had syncopal convulsions only 1.4% (2/141) had concurrent epilepsy. A detailed medical history was the most useful diagnostic tool.

202 11:30 AM

Peak-To-Peak Amplitude in Neonatal Brain Monitoring of Premature Infants

Deirdre O'Reilly, Michael Navakatikyan, Marcia Filip, Deirdre Greene, Linda J. Van Marter. Newborn Medicine, Children's Hospital Boston, Boston, MA; Pediatrics, Harvard University School of Medicine, Boston, MA; BrainZ Instruments, Ltd., Auckland, New Zealand; Newborn Medicine, Brigham and Women's Hospital, Boston, MA.

BACKGROUND: Advances in newborn intensive care have not led to prevention of brain injury among preterm infants. Ultrasound, the primary diagnostic tool currently used to assess brain injury, is of limited utility in early detection of white matter disease. A relatively new modality, reduced-montage electroencephalography (EEG), such as 2-channel EEG monitors, have been used to detect seizures and predict neurodevelopmental outcome among term infants following hypoxic-ischemic injury. Brain monitoring among preterm infants using these devices has been less widely investigated. In this study, we investigate whether a new representation of brain monitoring – called rEEG, measuring peak-to-peak amplitude (Navakatikyan, Proceedings of 8th World Congress on Perinatal Medicine, 9/2007), reduces artifact and yields information useful in assessing

brain activity in preterm infants.
OBJECTIVE: To investigate a method for analyzing data that focuses on amplitude of raw EEG tracing.
DESIGN/METHODS: 17 premature infants enrolled as part of a large prospective trial of brain monitoring and MRI outcomes at term equivalent gestational age underwent recordings at weekly intervals through 36 weeks postmenstrual age. (BrainZ BRM II) 121 recordings between 4-6 hours in length on 17 infants from 23 to 36 weeks' gestation were analyzed using rEEG, which produces a measurement of peak-to-peak amplitude sampled from 2 second intervals of the raw EEG trace. This was accomplished by assessing median, upper and lower amplitude margins, bandwidth, and by constructing amplitude bands: A (0-10 μV), B (10-25 μV), C (25-50 μV), D (50-100 μV) and E (>100 μV). Parameters were analyzed against gestational age by calculated linear coefficient of correlation.
RESULTS: Peak-to-peak amplitude in this cohort of preterm infants was characterized by the presence of very low and very high amplitudes, represented by the A and E amplitude bands. These bands gradually decreased with increasing gestational age and a middle amplitude band (C) became more prominent. The bandwidth of semi-log transformed margins (upper margin - lower margin) correlated strongly with gestational age (r = 0.902).
CONCLUSIONS: Peak-to-peak amplitude as assessed on rEEG correlated strongly with increasing gestational age. This method might prove useful in establishing normative data that can serve as a basis for evaluating maturation of brain activity among preterm infants.

203 11:45 AM Ph.D. Student

Effect of Relative Intrauterine Growth Restriction (RIUG) and Relative Discordancy (RDIS) on Auditory Brainstem Evoked Responses (ABRs) in Newborn Twins

Ha T.T Phan, Bernard Z. Karmel, Judith M. Gardner, Phyllis Kittler, Inna Miroshnichenko, Anthony Barone, Anantham Harin, Santosh Parab. Infant Dev, NYS Institute for Basic Research, Staten Island, NY; Pediatrics, Richmond University Medical Ctr, Staten Island, NY; Ctr for Dev Neuroscience, College of Staten Island, Staten Island, NY; PhD in Biology, CUNY Graduate Ctr, New York, NY.

BACKGROUND: Chronic stress in utero has been linked to myelin growth associated with neural maturation. ABRs represent neural transmission speeds at successive loci along the auditory brainstem pathway. Thus they provide a means by which to address early effects on CNS maturation.
OBJECTIVE: To examine the effect of RIUG and RDIS on early neural development of the auditory brainstem in newborn twins.
DESIGN/METHODS: ABRs were studied in 175 newborn NICU twin sets (N=350) from 09/00-10/06. RIUG=z-score normalized birth weight for gestational age based on Fenton (2003) growth curve. RDIS=percent difference in birth weight relative to larger twin. Infants' post-conceptional age (PCA) at test was 32-43 wks (M=1.4 wks post birth). Measures: Component latencies (CLs) of Waves III and V were determined for the first ABR study. Analysis: Data were analyzed using General Linear Models (GLM). Since PCA and structural CNS injury affect ABR CLs, they were included as covariates.
RESULTS: RIUG produced shorter Wave III ($F_{(1,341)}$=11.4, p<.001) and Wave V ($F_{(1,340)}$ =10.1, p<.002) CLs, controlled for PCA and structural CNS injury as covariates. RDIS likewise produced shorter CLs when similarly analyzed (Wave III: $F_{1,342)}$=5.73, p<.02; Wave V: $F_{(1,341)}$=16.7, p<.001). No significant interactions of RIUG with RDIS for either Wave III or V CLs were found. Dropping the interaction term, analyses with only the two main effects but still controlling the covariates indicated Wave III CL was affected by RIUG ($F_{(1,340)}$=6.76, p <.01, controlled for RDIS), while Wave V CL was affected by RDIS ($F_{(1,339)}$=9.1, p <.01, controlled for RIUG).
CONCLUSIONS: RIUG and RDIS affect ABR transmission speeds as indicated by shorter Wave III and Wave V CLs during the neonatal period. These effects are in contrast to prolonged CLs associated with immaturity and perinatal CNS injury. Moreover, the differential effects of RIUG and RDIS on Waves III and V might indicate underlying differences in susceptibility at specific loci of CNS for these two intrauterine chronic stress factors.

Pulmonary Development and Injury Platform Session

Sunday, March 30, 2008 9:45 AM-12:00 PM

204 9:45 AM

Role of the NF-κB Subunit p50 in Postnatal Lung Development

Guang Yang, Maurice Hinson, Jessica Bordner, Tiangang Zhuang, Clyde Wright, Phyllis A. Dennery.

BACKGROUND: Nuclear factor kappa B (NF-κB) regulates genes involving inflammation, apoptosis, proliferation and oxidative stress. One of the NF-κB subunit proteins, p50, lacks the trans-activation domain typical of the other subunits and has been categorized as a repressor of transcription. We previously observed that neonatal p50 null mutants (KO) mice were more susceptible to hyperoxia-induced lung injury.
OBJECTIVE: To establish the role of p50 during lung maturation.
DESIGN/METHODS: Heterozygote p50 mice were bred to generate litter mates of wild type (WT) and KO. The lungs were obtained at gestational age of 15 (E15), 17 (E17), 19 (E19) and also on postnatal days of 1 (p1), 7 (p7) and 2 month (adult). Lung protein levels of p50, p65 and I-κB were determined by Western analysis and nuclear protein binding to NF-κB was determined by EMSA. Lung morphological changes were evaluated by hematoxylin and eosin staining and radial alveolar counts (RAC). A vascular marker platetelet cell adhesion molecule (PCAM) was evaluated on tissue slides. Additionally lung total RNA was evaluated for surfactant protein B (SPB) and C (SPC) as well as VEGFR2 and Tie1 using RT-PCR. Lastly lung samples from P1 pups were subjected to microarray analysis using an Affymetrix gene chip (GeneChip® Mouse Genome 430A 2.0)containing 14000 mouse genes.
RESULTS: Evaluation of NF-κB binding through development revealed increased binding activity at E15 and p7 despite unchanged lung p50 protein levels. Disruption of p50 did not result in obvious lung morphological changes at E15-19, however enlarged alveoli and decreased RAC were evident at postnatal day 7. Although mRNA levels of SPB and SPC were not different between groups, VEGFR2 and Tie1 mRNA levels were significantly decreased in the p50 KO at p1 and p7. This was further supported by decreased PCAM staining on p7. P50 KO pup lung showed a significant decrease in 312 genes as compared to the WT. Of note there was a 1.6 fold decrease in VCAM1, 3.2 fold in NR1D1, 2.9 fold in TIPIN and 3.0 fold in DHCR24 among others. There was no difference in levels of protein carbonyls or inflammatory markers between WT and KO.
CONCLUSIONS: We conclude that p50 regulates vascularization and DNA replication in the developing lung and that this impacts susceptibility to hyperoxia.

205 10:00 AM Fellow in Training

Inhibition of NF-κB Activation by Preventing IκB-β Degradation Improves Neonatal Survival in Hyperoxia and Preserves Lung Architecture

Clyde J. Wright, Guang Yang, Phyllis A. Dennery. Pediatrics, Children's Hosp of Philadelphia, Phila, PA; Pediatrics, Univ of Penn SOM, Phila, PA.

BACKGROUND: The transcription factor NF-κB regulates the cellular response to inflammatory and oxidant stress. Multiple studies have shown exaggerated NF-κB activation in preterm and neonatal models when compared to adults. The pathway leading to hyperoxia-induced NF-κB activation remains to be elucidated, and it is unknown whether altering the exaggerated NF-κB activation in the neonate would protect against oxygen toxicity.
OBJECTIVE: Using wild type(ICR) and IκBβ knock-in mice(AKBI), in which the IκBα gene is replaced by IκBβ cDNA, we sought to characterize differences in the timing, degree and mechanism NF-κB activation following exposure to hyperoxia, and the effect on lung architecture and survival.
DESIGN/METHODS: ICR and AKBI mice were exposed to hyperoxia(>95% O2) or room air beginning on the day of birth. Control and treated mice were sacrificed at 8/24/72 hrs(n=3/time pt). Cytosolic and nuclear extracts were prepared from homogenized lung specimens. Cytosolic levels of the inhibitory proteins IκBα and IκBβ were determined by Western blot. Nuclear extracts were evaluated for NF-κB consensus sequence binding by electrophoretic mobility shift assay(EMSA). Radial alveolar counts were performed on samples obtained at 72 hrs(n=3/time pt). Survival curves for ICR(n=36) and AKBI(n=30) mice were generated through 14 days of hyperoxia.
RESULTS: ICR mice showed no change in IκBα protein levels with hyperoxia. As expected, AKBI mice lacked IκBα. Baseline levels of IκBβ were not different between groups. In the ICR mice, IκBβ protein decreased after 8 hrs of hyperoxia, and recovered by 24 hrs. In contrast, AKBI mice showed significantly increased IκBβ after 8 hrs of hyperoxia compared to ICR(p<.05). ICR mice showed increased NF-κB consensus sequence binding after 8 and 24 hrs of hyperoxia by EMSA compared to AKBI. Following 72 hrs of hyperoxia, ICR mice showed a significant decrease in RAC(p<.01), while AKBI had preserved lung architecture compared to controls. ICR mice had 80% mortality after 14 days of hyperoxia, while AKBI displayed 60% survival(p<.005).
CONCLUSIONS: We report for the first time that hyperoxia-induced IκBβ degradation results in NF-κB activation. Specific inhibition of this NF-κB activation pathway resulted in preserved lung architecture and marked improvements in neonatal survival following hyperoxic exposure. Manipulation of this pathway could have therapeutic applications for neonates exposed to hyperoxia.

206 10:15 AM

ErbB Signaling in Hypoxia- and Hyperoxia-Induced Lung Epithelial Cell Injury

Washa Liu, Hshi-chi Koo, Jonathan M. Davis, Heber C. Nielsen, Christiane E.L. Dammann. Newborn Medicine, Floating Hospital for Children, Boston, MA; Pediatrics, Hannover Medical School, Hannover, Germany.

BACKGROUND: Hypoxia causes cell injury or cell death secondary to ATP depletion following the switch to anerobic metabolism. Oxygen therapy is widely used to treat disease processes that cause hypoxia. However, prolonged exposure to hyperoxia leads to the generation of excessive reactive oxygen species that cause acute lung injury and contribute to the development of bronchopulmonary dysplasia. ErbB receptors (ErbB1, ErbB2, ErbB3, and ErbB4) have key roles in fetal lung development and repair to maintain the homeostatic integrity of lung structure and function. Little is known about ErbB receptor regulation in hypoxia- and hyperoxia-induced lung injury and repair.
OBJECTIVE: We hypothesize that exposure to hypoxia influences the development of hyperoxia-induced lung injury. ErbB signaling is important in regulating repair from hypoxia and hyperoxia-induced lung injury.
DESIGN/METHODS: Mouse lung epithelial (MLE)12 cells were treated with 10%O_2 for 1 hour, followed by 21% or 95%O_2 treatment for 48 hours. Control cells were either exposed to 21%O_2 or 95%O_2 only. ^{3}H thymidine or ^{3}H choline were added in the last 24 hours to measure cell proliferation and choline incorporation, respectively. Cell viability was assessed by MTS assay. Effects on ErbB receptor expression were studied by Western blot.
RESULTS: Exposure to 95%O_2 significantly reduced MLE12 cell viability (by 50%), proliferation (by 37%), and choline incorporation (by 33%) compared to room air controls. This was accompanied by an overall ErbB receptor down-regulation (by 25-77%), most prominently of ErbB4. An initial exposure (pre-conditioning) to 10% O_2 followed by 95%O_2 significantly improved cell viability (by 25%) and ErbB4 protein expression (by 25%) compared to hyperoxia alone, but cell proliferation was inhibited even further. Hypoxia pre-treatment did not affect choline incorporation compared to cells exposed to 95%O_2 alone. After 48 hours of recovery in room air, cells pre-treated wtih 10%O_2 showed a recovery of cell proliferation and ErbB4 receptor expression.
CONCLUSIONS: Hyperoxia causes lung epithelial cell damage, impaired surfactant phospholipid synthesis, and downregulation of ErbB receptor expression. Pre-conditioning with short term hypoxia improved cell viability and increased ErbB4 expression, suggesting that hypoxia may stimulate signaling pathways involved in ErbB4 upregulation that protect against hyperoxic cell injury. (NIH HL 04437, HL37930, DFG 378/3-1).

207 10:30 AM

Bach-1 Modulates Heme Oxygenase-1 (HO-1) Transcription in the Newborn in Hyperoxia

Sacha Kassovska-Bratinova, Guang Yang, Kazuhiko Igarashi, Phyllis A. Dennery. Pediatrics, CHOP, Phila, PA; Pediatrics, Univ of Penn SOM, Phila, PA; Biochemistry, Tohoku Univ SOM, Sendai, Japan.

BACKGROUND: Heme oxygenase-1 (HO-1), the rate-limiting enzyme of heme degradation and a phase II antioxidant defense, is induced in the lungs of animals exposed to hyperoxia. However, in a rat model, newborns show reduced inducibility of HO-1 mRNA after hyperoxic exposure, compared to adults. While mild overexpression of this enzyme is protective against hyperoxic lung injury, high levels are detrimental.
OBJECTIVE: In order to understand more about the differential response of newborn and adult animals to oxygen, we studied the effect of hyperoxia on the expression of HO-1 in a mouse model.
DESIGN/METHODS: Wild type FVB mice and transgenic FVB mice (HO-1-luc), expressing the luciferase reporter under the control of 15 kb from the mouse HO-1 promoter region and upstream regulatory sequences (gift from Dr. C.Contag) were used. Adult (2 month old) and newborn(<12 h) mice were exposed to >95% oxygen over a period of 72 hrs. HO-1 promoter activity was assessed by in vivo imaging. Lung total mRNA

and whole lung lysates and nuclear extracts were prepared. HO-1 mRNA levels were determined by RT- PCR (ABI). Protein levels were detected by Western blot analysis using antibodies against HO-1 and Bach-1, the repressor of HO-1 transcription. Bach-1 binding to HO-1distal enhancers at basal levels was evaluated relative to input, using chromatin immunoprecipitation (Upstate). Bach-1 binding to the antioxidant response element (ARE; 5'TTTTATGCTGTGTCATGGTT3' was detected by supershift gel retardation assay.
RESULTS: HO-1- luc mice had no increased light emission in hyperoxia, compared to the adult mice, which showed a significant (2 fold) increase at each time point tested. Newborns had a smaller (3.5 fold) increase, compared to the adults (7.9 fold) in hyperoxia. Bach-1 protein levels were significantly higher in the neonatal lung at baseline. In hyperoxia there was enhanced nuclear protein-DNA binding to the ARE, and this binding increased in a time-dependent manner. Supershift gel retardation demonstrated that Bach-1 contributed to this complex. In the newborn lung at baseline chromatin immunoprecipitation revealed increased Bach-1 binding to the HO-1 distal enhancers and in hyperoxia enhanced binding was observed.
CONCLUSIONS: The negative modulation of HO-1 gene transcription in the newborn in hyperoxia may be related to enhanced Bach-1 binding to the ARE. This may serve to more tightly regulate HO-1 expression in the newborn in response to oxidative stress.

208 10:45 AM

Heparin-Binding VEGF Isoforms Attenuate Hyperoxic Lung Injury in Explanted Mouse Embryonic Lung

Americo E. Esquibies, Alia Bazzy-Asaad, Lloyd G. Cantley. Pediatrics, Section of Respiratory Medicine, Yale University, New Haven, CT; Medicine. Section of Nephrology, Yale University, New Haven, CT.

BACKGROUND: Oxygen tension has been shown to modulate physiologic and structural properties of lung morphogenesis, a process that is tightly regulated by numerous factors and cytokines. Among the latter is vascular endothelial growth factor (VEGF) which is present in rodent airway epithelium as early as embryonic day 11.5 (E11.5) and plays an important role in vascular development and epithelial cell morphogenesis.
OBJECTIVE: Because hyperoxia a) reduces VEGF expression in airway epithelial cells, and b) can impair airway development (levels of 50% in the explanted lung can cause a moderate decrease in lung growth), we asked whether heparin-binding VEGF isoforms might alter the effect of hyperoxia (50%O2) on the growth of lung explants.
DESIGN/METHODS: Explants were harvested from E11 mouse embryos and infected with adenovirus (150 viral particles/cell) encoding either VEGF165, VEGF188, or DsRed (control), and cultured at 37ºC in a sealed chamber with 3%O2 (to mimic in vivo lung oxygenation) for 2 days to allow for protein expression. Subsequently, explants were cultured in oxygen levels of 3%O2 or 50%O2 for another 2 days. Total number of lung bud branches and total branch length were quantitated.
RESULTS: Number of branches and total branch length were significantly reduced after 2 days in 50%O2 as compared to 3%O2 (17.4±2.8 vs 27.8±2.4 and 2.6±0.5 mm vs 4.5±0.3 mm p<0.05). Explants that were infected with adenovirus-encoding VEGF 165 or VEGF 188 and grown for 2 days in 50%O2 resulted in partial reversal of the decrease in bud branching and total branch length (3%O2: 27.8±2.4 and 4.5±0.3 mm; 50%O2: 17.4±2.8 and 2.6±0.5 mm; 50%O2+VEGF 165: 24±3.7 and 3.5±0.5 mm p< 0.05 vs 50%O2 alone for total number of branches; 50%O2+VEGF 188: 22.3±2.9 and 3.1±0.4 mm p< 0.05 vs 50%O2 alone).
CONCLUSIONS: We conclude that moderate hyperoxia impairs lung bud branching morphogenesis and growth, effects that are partially reversed by expression of heparin-binding VEGF isoforms and suggest that manipulation of this pathway might provide a therapeutic approach for the prevention of hyperoxic airway toxicity.

209 11:00 AM

Lung Contusion Alters Pulmonary Vasoreactivity in Rats

Satyan Lakshminrusimha, Bruce A. Davidson, Rita M. Ryan, Jadwiga D. Helinski, Krishnan Raghavendran. Pediatrics, SUNY, Buffalo, NY; Anesthesia, SUNY, Buffalo, NY; Surgery, SUNY, Buffalo, NY.

BACKGROUND: Lung contusion is a common complication of blunt chest trauma. We recently described a rat model for isolated bilateral lung contusion from blunt chest trauma (Anesth Analg 2005;101:1482) and showed an inconsistent correlation between the extent of inflammation and hypoxemia. We set out to investigate the alteration in pulmonary arterial (PA) reactivity in lung contusion.
OBJECTIVE: To study the reactivity of third generation PA following lung contusion in rats.
DESIGN/METHODS: Lung contusion was induced in anesthetized spontaneously breathing adult male rats by dropping a hollow aluminum cylindrical weight (300 g) onto the chest with a protective shield placed over the precordium. Rats were allowed to recover and sacrificed at 4h and 24h (n=6-9) and compared to uninjured controls. Third generation PA rings were dissected and placed in a bath with modified Krebs solution, connected to a transducer and bubbled with 21% O_2+ 6% CO_2. Some rings were pretreated with a non-specific NO synthase (NOS) inhibitor, L-nitro arginine (LNA 10^{-3} M). Rings were constricted with norepinephrine (NE) and relaxed with either a NOS agonist (A 23187) or NO donor (SNAP) at 10^{-6} M.
RESULTS: Rats were hypoxic at 4h post-contusion compared to controls, but recovered 24h after contusion (table). Pretreatment with LNA increased baseline tension significantly more in control PA compared to 4h or 24h post-contusion PA indicating higher basal NOS activity in controls. Constriction response to NE in the presence of LNA was significantly higher 4h after contusion compared to controls. Relaxation to A23187 and SNAP were significantly impaired 24h after contusion compared to controls.

Oxygenation and Pulmonary Vasoreactivity Following Lung Contusion

Group	A-a gradient (mmHg)	Constriction to LNA (10^{-3} M) force	Constriction to LNA+NE$^{-7.5}$M g/g force	Relaxation to A23187 (10^{-6}M) %	Relaxation to SNAP (10^{-6}M) %
Control	196 ± 29	130 ± 14	392 ± 77	73 ± 5%	88 ± 7%
4 hr post contusion	337 ± 49*	112 ± 22	671 ± 114*	52 ± 7%	73 ± 8%
24 hr post contusion	217 ± 22	66 ± 16*	452 ± 27	33 ± 7%*	45 ± 12%*

* p < 0.05 compared to control

CONCLUSIONS: Hypoxemia and increased PA contractility are observed 4h after lung contusion in rats with recovery by 24h. Production of, and response to NO are significantly diminished in PA following lung contusion. Inhaled NO may be a potential therapeutic modality to alleviate hypoxemia in patients following lung contusion.

210 11:15 AM Medical Student

Surfactant Administration Does Not Normalize Respiratory Function Changes Associated with Transient *In Utero* Knockout (TIUKO) of the CFTR Gene in Sprague-Dawley Rats

Andrew Dylag, Joseph Hudak, Shetal Shah, J. Craig Cohen. Department of Pediatrics, Division of Neonatology, Stony Brook University Medical Center, Stony Brook, NY.

BACKGROUND: TIUKO of the cystic fibrosis transmembrane conductance regulator (CFTR) gene was previously shown to result in short-term histologic & physiologic changes in the lungs of Sprague-Dawley rats. Previous studies of this rat model demonstrated altered surfactant homeostasis with increased phosphatidyl choline and decreased mRNA of surfactant proteins A & B. Respiratory function testing is a previously validated means to assess physiologic performance of this disease model.
OBJECTIVE: To determine the effect of exogenous, intra-tracheal surfactant administration on respiratory function in CFTR TIUKO Sprague-Dawley rats.
DESIGN/METHODS: Four groups of time-pregnant Sprague-Dawley rat pups underwent TIUKO of CFTR by anti-sense CFTR (ASCFTR) using an adenovirus vector at 16 days gestation or control procedure with EGFP. At weaning on day of life 21 or 22, the rats were paralyzed & mechanically ventilated on a SCIREQ small mammal ventilator. A dose of 4cc/kg of either bovine-derived surfactant or phosphate-buffered saline (PBS) control was administered and the animals were allowed to equilibrate on the ventilator for 5 minutes after treatment. Measurements of elastance, tissue damping, airway resistance, & hysteresivity (eta) were subsequently obtained at PEEP of 3 & 6 cm of H_2O using a forced-oscillation technique. Running averages for each respiratory parameter were compared among groups using 2x2 factorial ANOVA.
RESULTS: Compared with ASCFTR control, ASCFTR animals who received surfactant demonstrated no statistically significant changes in mean airway resistance, tissue damping, compliance, elastance, or hysterivity at any PEEP value. Compared with control animals who received surfactant, ASCFTR animals who received surfactant demonstrated increased compliance at a PEEP of 3 & 6 cm H_2O ($p<0.01$, $p<0.001$, respectively). Pressure-Volume loops of the ASCFTR surfactant animals showed improvement in hyperinflation and air trapping compared to ASCFTR controls but failure to normalize to EGFP control values.
CONCLUSIONS: Transient *in utero* knockout of CFTR causes alteration in the organogenesis of lungs & surfactant dysfunction resulting in physiologic alterations of respiratory function. These changes are not fully attenuated by administration of exogenous surfactant. This data strengthens the paradigm that the CFTR gene plays a developmental role in the lung.

211 11:30 AM Fellow in Training

Transient In-Utero Exposure to Nicotine Directly Stimulates Expression of Proteins Necessary for Mechanico-Sensory Dependent Lung Development

Shruti Gupta, Shanthy Sridhar, Craig J. Cohen, Janet E. Larson. Pediatrics, University Hospital at Stony Brook, Stony Brook, NY.

BACKGROUND: Smoking during pregnancy continues to be largely prevalent in general population. Most studies suggest that nicotine derived from smoking is responsible for deficiencies in the fetus including low birth weight, premature delivery, significant neonatal morbidity and mortality. Collins et al showed that in rats, smoke exposure caused a reduction in lung volume, number of saccules and septal crests. These studies, however, focused on continuous exposure of nicotine on fetal lung development. Sekhon et al showed the presence of nicotinic receptors in the developing lung and that nicotine interacts directly with these receptors. Thus, the transient role of these nicotine receptors in normal lung development has not been addressed. Although it is known that off springs of mothers who smoked throughout pregnancy have altered pulmonary function tests compared to age matched controls, the molecular mechanisms behind these changes are unknown. In this study nicotine's direct effect on smooth muscle contraction necessary for mechanicosensory-dependent fetal lung development is examined after transient nicotine stimulation.
OBJECTIVE: To determine the relationship between nicotine, smooth muscle contraction , and fetal lung development.
DESIGN/METHODS: Timed pregnant Sprague-Dawley rats at 16 days gestation were treated in-utero with five different concentrations of nicotine or DMEM (control).
Fetal lungs were harvested at six hours and twenty four hours post-injection. Immunohistochemistry localization in the fetal lung, western blots and 2D gel electrophoresis were performed on protein extracts from treated lungs.
Also treated rats were allowed to deliver and pulmonary function tests were performed on rat pups from day 10-16 of life.
RESULTS: When 100 micromoles of nicotine is injected at 16days gestation, an increase in unphosphorylated regulatory myosin light chain (LC-20) is seen compared to control in both lungs harvested at 6 hours and 24 hours post-injection. This was confirmed both by Western blot analysis and Immunohistochemistry. Pulmonary function tests on rat pups showed a statistically significant decrease in airway resistance and increase in static compliance pointing towards structural maturation of the lung.
CONCLUSIONS: Transient nicotine exposure during intrauterine life stimulates stretch induced lung organogenesis by altering phosphorylation of muscle contraction proteins.

212 11:45 AM

Airway Injury Resulting from Repeated Endotracheal Intubation: Possible Prevention Strategies

Adebayo A. Oshodi, Kevin Dysart, Alison Cook, Elena Rodriguez, Yan Zhu, Thomas H. Shaffer, Thomas L. Miller. Pediatrics, Thomas Jefferson University Hospital, Philadelphia, PA; Nemours Research Lung Center, Alfred I duPont Hospital for Children, Wilmington, DE; Physiology and Pediatrics, Temple University School of Medicine, Philadelphia.

BACKGROUND: Intubated neonates on ventilatory support are at risk for airway injuries. Such injuries involve inflammatory mediators that are implicated in worsening of lung disease in this population. Reintubation and prolonged intubation are known risk factors for such injuries, and it is likely that the act of intubation and reintubation alone may contribute to airway and lung injury.
OBJECTIVE: To show the effect of repeated intubation on airway injury and to examine the effect of inhaled or intravenous (IV) anti-inflammatory steroids on reintubation injury.
DESIGN/METHODS: Neonatal piglets (2-5 d old; 2.5 ± 0.4 kg), were intubated and randomized to 4 groups (n=8 each) to be followed over 4 hr. Groups were SHAM (not reintubated), injured (INJ) i.e., reintubated every

0.5hr with no pretreatment, and injured but pretreated with 1mg nebulized budesonide (Pulmicort; PULM) or 0.3mg/kg IV dexamethasone (DEX). Each pig was sedated for the duration of study, and had a 2.5Fr catheter placed in the femoral artery for blood sampling and blood pressure measurement every 0.5 hour. After 4 hrs, each pig was sacrificed and tissue harvested for histology and IL-6 assays.
RESULTS: Airway tissue IL-6 content was greater in the INJ group compared to SHAM ($p < 0.01$). In the laryngeal tissue, DEX reduced IL-6 to control levels but PULM did not ($p < 0.05$). The reintubation injury resulted in plasma IL-6 levels that, compared to SHAM, were greater in the INJ and PULM groups ($p < 0.05$). Quantitative histology showed that airway mucosa was thinner in INJ and DEX compared to SHAM ($p<0.05$).
CONCLUSIONS: Intubation alone results in significant tracheal trauma and systemic inflammation. IV but not inhaled steroids attenuated the inflammatory response; however, histology responded to inhaled steroids not IV. These data suggest that intubation alone may contribute to problems of ventilator induced lung injury.
Funded by Nemours and NIH COBRE P20-RR20173-01.

Endocrinology/Metabolism Platform Session

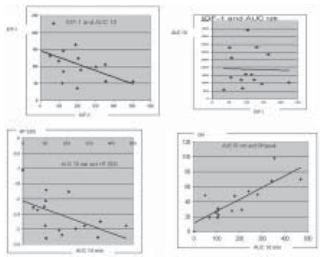
Sunday, March 30, 2008 9:45 AM-12:00 PM

213 9:45 AM House Officer

A Short Version GHRH Stimulation Test as a Novel and Effective Tool in Children with Idiopathic Short Stature

Amrit Bhangoo, Nauman Basit, Vijay Chickajaju, Svetlana Ten. Division of Pediatric Endocrinology, Infants' and Children's Hospital of Brooklyn at Maimonides, Pediatric Endocrinology Division of SUNY Downstate, Brooklyn, NY.

BACKGROUND: Growth Hormone (GH) stimulation test is gold standard yet cumbersome & not always reliable for evaluating children with short stature.
OBJECTIVE: We studied if a short version GHRH (Growth Hormone Releasing Hormone) stimulation test could be a potential alternative of evaluation in these children.
DESIGN/METHODS: A total of 19 children with Idiopathic Short Stature (Age 8.6 ± 3.2 yrs; 5 girls; HT -2.5 ± 0.6 SDS) underwent GHRH stimulation test (Dose 1 mcg/kg IV) after an over night fast. Serum GH samples were obtained at 0 (baseline) and then at 3, 5, 10, 30, 60, 90 and 120 mins after administration of GHRH. Area under curve (AUC) for the GH levels was also calculated for time intervals specified above. Subjects' height, IGF-1, target & predicted height data was collected.
RESULTS: A strong correlation was found between AUC at 10 min (AUC 10 GH) values and GH peaks ($r=0.83$, $p<0.001$), with HT SDS ($r=0.52$, $p=0.038$), AUC 10 GH correlated with baseline IGF-1. Correlation between AUC 120 GH and GH peak was lower (0.62, $p= 0.01$) while AUC 120 GH did not correlate with HT SDS and IGF-1 levels.
CONCLUSIONS: The modified 10 min GHRH stimulation test approach is novel, convenient, safe and more precise. We suggest that a shorter version GHRH stimulation test is a better diagnostic aid than the conventional 120 min version.



214 10:00 AM

Markers of Insulin Reserve in Pediatric Type 2 Diabetes (T2DM)

Lorraine E. Levitt Katz, Marcia Hernandez, Heather M. McKnight, Paul R. Gallagher, Kathryn M. Murphy. Pediatrics and Biostatistics, Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Despite the rapid rise in childhood T2DM, the natural history of insulin reserve is not known. In order to develop treatments aimed at delaying β-cell failure, it is imperative to define the pattern and predictors of changes in insulin secretion.
OBJECTIVE: To determine the timeline of β-cell failure in pediatric T2DM by defining changes in hemoglobin A1c and dose of exogenous insulin as well as fasting markers of insulin reserve: Insulin-like Growth Factor Binding Protein-1 (IGFBP-1) and C-peptide.
DESIGN/METHODS: T2DM subjects were recruited in 3 groups:
1. Non-acidotic (NA) and antibody negative (Ab-) at presentation (*n=46)*
2. DKA and Ab- at presentation *(n=13)*
3. NA and Ab+ at presentation *(n=7)*

At diagnosis, fasting levels of C-peptide and IGFBP-1, A1c level and dose of insulin were obtained. Subjects were treated with Metformin and/or insulin. Follow-up fasting assessments were performed every 3-6 months for 4 years. The effect of group on repeated outcomes was analyzed using a mixed longitudinal effects approach (SAS Proc).
RESULTS: 66 subjects (30M, 36F), (age 14±2.7y) participated. Baseline A1C and IGFBP-1 levels were similar between groups. Insulin doses at baseline differed, with the DKA group requiring the most. Baseline insulin dose correlated with IGFBP-1 ($p=0.029$) and C-peptide ($p=0.004$). A1C and insulin dose changed significantly over time in a complex curvilinear manner, and demonstrated differences among the 3 groups. The nature and rate of change of IGFBP-1 across time was different in the 3 groups, $p=0.016$. While baseline fasting C-peptide differed between groups ($p=0.014$), over time, C-peptide did not change significantly nor exhibit group effects.

		Baseline	0-0.5 years	1.5-2 years	3-4 years
Group 1	Insulin (u/kg/day)	0.58±0.58	0.44±0.38	0.39±0.4	0.56±0.7
NA/Ab-	IGFBP-1(ng/ml)	7.2±11.9	7.3±14.2	8.6±10.3	4.1±3.1
Group 2	Insulin (u/kg/day)	1.06±0.49	0.59±0.36	0.55±0.46	0.8±0.38
DKA/Ab-	IGFBP-1(ng/ml)	21±42	4.1±3.7	9.8±9.4	97±52
Group 3	Insulin (u/kg/day)	0.31±0.24	0.48±0.26	0.48±.09	0.72±0.21
NA/Ab+	IGFBP-1(ng/ml)	5.6	10.9±5.4	33±33	86±106

CONCLUSIONS: Over a 4 year period, children with T2DM require high doses of insulin, differing from adults. Group characteristics, such as positive antibodies or DKA at diagnosis, affect how insulin reserve changes across time.

215 10:15 AM Fellow in Training

HbA1c as a Screening Tool for Pediatric Type 2 Diabetes

Alisa B. Schiffman, Kristen T. Sonnek-Schmelz, Sarah J. Ratcliffe, Lorraine Levitt-Katz, Steven M. Willi. Department of Endocrinology/Diabetes, The Children's Hospital of Philadelphia, Philadelphia, PA; Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, PA.

BACKGROUND: The American Diabetes Association recommends screening children at risk for type 2 diabetes (T2DM) with fasting plasma glucose (FPG) or oral glucose tolerance test (OGTT). These tests present logistical challenges when compared with random HbA1c.
OBJECTIVE: To evaluate the ability of HbA1c to identify children with T2DM.
DESIGN/METHODS: Ninety-three consecutive children (40M/53F; mean age 12.7±3.9 years) undergoing OGTT to evaluate the risk for T2DM at the CHOP Diabetes Center for Children were reviewed for FPG, fasting insulin, 2 hr PG and HbA1c. Fasting insulin and glucose were used to calculate indices of insulin sensitivity via HOMA and QUICKI. Beta cell function was assessed using HOMA. Data were analyzed and exhibited a normal distribution after log transformation. ROC analysis was performed to identify optimal cut point for HbA1c.
RESULTS: HbA1c was 5.4±0.1% for subjects with normal glucose tolerance (NGT; n=62), 6.1±0.2% for those with impaired glucose tolerance (IGT; n=22) and 6.8±0.3% for T2DM (n=9). This was statistically significant ($p<0.001$). Trends in beta cell function via HOMA were likewise significant (488±63, 356±98 and 202±66 for NGT, IGT and T2DM respectively; $p=0.003$). Insulin sensitivity did not differ across these groups when calculated using HOMA or QUICKI. Analysis of fasting and 2 hour insulin values showed no significance. ROC analysis of HbA1c revealed that a cut point of 6.0% was 100% sensitive and 80% specific in identifying children with T2DM (AUC=0.94).
CONCLUSIONS: Along the continuum from NGT to IGT to T2DM, HbA1c increases, beta cell function decreases and insulin sensitivity remains constant. In this limited study, T2DM was effectively excluded by a HbA1c below 6.0%.

216 10:30 AM House Officer

Hypoglycemia in Critically Ill Children

E. Vincent Faustino, Clifford Bogue. Department of Pediatrics, Yale University School of Medicine, New Haven, CT.

BACKGROUND: Tight glucose control (TGC) at 80-110 mg/dl with insulin improves outcome in critically ill adults. In children, blood glucose in the same range is associated with lower mortality rates. Insulin use, however, is limited by hypoglycemia which can lead to increased mortality and morbidity. Maximizing the benefits of TGC entails a better understanding of hypoglycemia in critically ill children prior to its systematic use.
OBJECTIVE: (1) to determine the prevalence of hypoglycemia in a population of critically ill children; (2) to assess the prognostic significance of low blood glucose in this population; and, (3) to identify risk factors associated with hypoglycemia.
DESIGN/METHODS: A retrospective cohort with nested case-control study design was employed with data extracted from point-of-care blood glucose measurements, hospital administrative databases and computerized information systems. 1088 non-diabetic PICU admissions prior to TGC in the unit (January 2000 to December 2004) were included. Prevalence of hypoglycemia, relative risks of mortality (RRM) and lengths of stay were based on blood glucose thresholds of <40, <50 and <60 mg/dl. Risk factors were identified using 73 patients with glucose <50 mg/dl matched with non-hypoglycemic patients in the cohort with glucose of 80-110 mg/dl. Matching was based on the number of PICU days until the first hypoglycemic event.
RESULTS: Hypoglycemia occurred in 3.1% (<40 mg/dl) to 9.8% (<60 mg/dl) of the cohort. Patients with blood glucose below the cut-off values had significantly higher RRM. At glucose <40 mg/dl, RRM was 5.93 (95% confidence interval (CI), 3.65-9.62). Comparison of patients with glucose <40 mg/dl with the patients with all glucose values between 80-110 mg/dl resulted in a greater RRM at 19.69 (4.68-82.89). Lower blood glucose at all threshold values correlated with longer stays in the PICU and in the hospital. Univariate and multivariate analyses identified insulin use (odds ratio: 3.74, 95% CI: 1.16-12.08), liver dysfunction (2.94, 1.32-6.55), sepsis (2.68, 1.13-6.38) and age <1 year (2.26, 1.11-4.57) as risk factors for hypoglycemia. Gender, severity of illness, admission type, endocrine disorders or inborn errors of metabolism, malignancy, renal dysfunction, inotrope use, nutritional status and mechanical ventilation were not associated with low glucose.
CONCLUSIONS: The present study is the first report on the prevalence, prognostic significance and risk factors for hypoglycemia at glucose values <40, <50 and <60 mg/dl prior to TGC in critically ill children.

217 10:45 AM Fellow in Training

Hypoglycemia Associated Autonomic Failure: Are Free Fatty Acids (FFA) Responsible?

A.S. Nayak, B.B. Nankova, E.F. LaGamma. Newborn Med, Maria Fareri Child's Hosp, Valhalla, NY.

BACKGROUND: During hypoglycemia, epinephrine is released from the adrenal medulla after cholinergic stimulation of nicotinic & muscarinic receptors followed by induction of epinephrine synthesis to replenish stores.Repeated episodes attenuate Epi responses (Inouye, 2005) due to inhibition of release or decreased synthesis. Infants of diabetic mothers fail to release epinephrine in response to either stress of birth or hypoglycemia. Counterregulatory mechanisms also increase plasma free fatty acids(FFA). Our previous work showed that tyrosine hydroxylase, rate limiting enzyme in Epi synthesis, is subject to dose-dependent regulation by FFA: enhanced by low physiological concentrations and suppressed by high levels in a PC12 cell model (pheochromocytoma; Nankova, 2003); c/w inability to synthesize epinephrine. Since sympathetic nerve impulses continue, we hypothesize that inability to release Epi in vivo is due to failed synthesis.
OBJECTIVE: To determine whether: i) muscarinic, nicotinic or both receptors are involved & ii) blockade of cholinergic receptors alters effects of butyrate (FFA) on TH mRNA levels.
DESIGN/METHODS: PC12 cells differentiated with low 1 mM/high 6 mM concentrations of butyrate were treated with nicotine/carbachol (muscarinic agonist). Rats were injected with butyrate. Total RNA was analyzed by northern blot & genome-wide microarray analysis.

RESULTS: Addition of nicotine to low butyrate-differentiated PC12 cells resulted in increased TH mRNA. Combined nicotine + high butyrate treatment caused marked suppression.Unlike nicotine, carbachol had no significant effect on TH mRNA levels either in the presence/absence of butyrate. Butyrate affected TH mRNA independent of cholinergic receptor blockade. Rats injected with low butyrate had an increase in TH mRNA levels in adrenal medulla vs vehicle c/w data from PC12 cell model. Microarray analysis showed significant overlap of gene expression between *in vivo & in vitro* experiments.
CONCLUSIONS: TH gene expression is suppressed as a result of *combined* cholinergic-nicotinic (but not with muscarinic) + high FFA stimulation. Butyrate acts on TH independent of cholinergic receptor blockade & affects expression of similar genes in animals/PC12 validating the *in vitro* model. Speculation: Failed epinephrine release appears to be due to decreased TH synthesis, not release. Modification of FFA blood levels or partial nicotinic receptor blockade either by diet/pharmacologically may preserve the epinephrine responses during hypoglycemia.

218 11:00 AM Fellow in Training

Does One Enteral Feeding Correct Asymptomatic Hypoglycemia in the Newborn?

Yesenia Morales, Debra Potak, Richard J. Schanler. Neonatal-Perinatal Medicine, Schneider Children's Hospital, New Hyde Park, NY; Neonatal-Perinatal Medicine, Schneider Children's Hospital at North Shore, Manhasset, NY; Pediatrics, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Although feeding is the treatment for asymptomatic neonatal hypoglycemia, some clinicians give intravenous therapy if the glucose value is very low and enteral feeding only if the value is minimally low. The amount of such feeding rarely is specified. In addition, common nursery interventions, such as glucose screening, may affect breastfeeding initiation and duration adversely.
OBJECTIVE: To evaluate the effect of one enteral feeding on the correction of asymptomatic hypoglycemia in newborn infants and to determine whether the intervention of glucose screening affects the initiation of breastfeeding.
DESIGN/METHODS: The records of all infants in the newborn nursery who had bedside glucose screening during a 2 month period were reviewed. The protocol specifies glucose screening for infants who are small and large for gestational age, of diabetic mothers, late preterm, and with thermoregulation issues. The Accu-Chek Inform (Roche, Mannheim, Germany) was used for screening. Infants with low screening glucose values (<45 mg/dL) were compared with infants having normal values. The following data were collected: reason for glucose screen, birth weight, gestational age, mode of delivery, age and value of glucose screen, intervention (method of feeding) for low glucose screen, outcome, number and type of feedings. Maternal data included age, parity, medical history, duration of hospital stay, breastfeeding for the last 5 feedings before discharge.
RESULTS: Most infants (81%) were screened per protocol. Of 121 consecutive infants screened, 38 (31%) had a glucose screen value <45 mg/dL. There was no relationship between glucose value and birth weight, gestational age, maternal age, or infant diagnoses. One feeding normalized the glucose screen in all but 3 infants (7.8%) and subsequent screens identified only 1 additional infant (screen value of 42 mg/dL). The quantity of enteral feeding varied from 10 to 50 mL, mean 21 ± 9 mL. Infants with initial glucose screens <31 mg/dL received the same quantity of milk (20 ± 4 mL) as those with screens 31 to 44 mg/dL (21 ± 10 mL). Exclusive breastfeeding rates did not correlate with the number of glucose screens and were not significantly different in infants with low (13%) vs normal (24%) glucose screens.
CONCLUSIONS: A single enteral feeding normalized a low glucose screen in most infants. The response to an enteral feeding was the same despite the glucose level. This intervention did not affect exclusive breastfeeding rates at discharge.

219 11:15 AM Ph.D. Student

Disruption of Late Rat Intestinal Organogenesis Leads to Adult Onset Obesity and Insulin Resistance

Malgosia Skowron, Janet E. Larson, Haihong Zong, Jeffery E. Pessin, J. Craig Cohen. Neonatology/Pediatrics/Pharmacology, Stony Brook Univ. School of Medicine, Stony Brook, NY.

BACKGROUND: Organogenesis requires the sequential development of specialized cells and structures for full function. Delaying or disrupting this developmental cascade can lead to an organ that retains some fetal characteristics leading to adult onset diseases. The lung and intestines are two organs whose normal differentiation were shown by this laboratory to be dependent upon cystic fibrosis transmembrane conductance regulator (CFTR) dependent regulation of mechanicosensory differentiation. Using in utero gene therapy with either sense or antisense adenovirus constructs we have shown that both lung and intestinal development is dependent upon the levels of CFTR expression.
OBJECTIVE: CFTR deficiency is known to result in intestinal obstruction and altered function. Transient effects of reduced CFTR late in development have not been examine for changes in metabolic function that are independent of the role of CFTR post-natally. This study evaluated the role of epigenetic disruption of CFTR in the intestines and the adult onset metabolic effects.
DESIGN/METHODS: To analyze the precise temporal aspect of cftr requirement, we transiently suppressed CFTR expression in the intestine of rat fetuses using adenoviral-based in utero gene therapy. Individual rat fetuses were treated at E16 -E17 with sufficient antisense CFTR containing adenovirus to achieve inhibition of CFTR. Animals were allowed to deliver. Oral and systemic glucose tolerance tests were performed as well as insulin resistance assessed.
RESULTS: Depending on the timing of this treatment, reduction of CFTR function resulted in phenotypes ranging from meconium ileus and subsequent death to metabolic imbalance and weight gain. We are focusing on fetuses treated during day 16 of embryonic development. After birth, the animals display elevated fasting blood glucose levels, impaired glucose metabolism, significant insulin insensitivity, and excess body fat. This disease state had many of the hallmarks of Metabolic Syndrome.
CONCLUSIONS: These data demonstrate that transient disruption of CFTR function in utero permanently changes the developmental fate of progenitor cells of the intestine. Experiments are underway to further characterize the metabolic defect, as well as the underlying functional deficiency of intestinal cells.

220 11:30 AM

Effects of Maternal Depression or SSRI Use on Placental NET and SERT Gene Expression

Kathryn L. Ponder, Bethany McGonnigal, Jennifer Bauer, Alyse Laliberte, Amy Salisbury, James Padbury. Pediatrics, Alpert Medical School at Brown University, Providence, RI.

BACKGROUND: Selective serotonin reuptake inhibitor (SSRI) use is widespread among women of childbearing years to treat the symptoms of depression. An informal survey in Women and Infants' Hospital of Rhode Island revealed that up to 30% of pregnant women used SSRIs. Placental gene expression is crucial to the regulation of the neuroendocrine environment *in utero*. The placenta expresses the neurotransmitter transporters for norepinephrine (NET) and serotonin (SERT) in greater abundance than the central nervous system of the developing fetus. Placental expression of NET and SERT blocks passage of maternal norepinephrine or serotonin. In previous studies, we and others have determined that placental NET is downregulated by adverse intrauterine conditions, such as cocaine use, pre-eclampsia, or intrauterine growth restriction (IUGR). Maternal depression and drug use have been shown to affect fetal neurobehavior and biophysical responses.
OBJECTIVE: There are no studies to date on the effects of maternal depression and/or SSRI use on placental SERT and NET. Therefore we sought to examine the effects of maternal depression and SSRI use on these placental genes.
DESIGN/METHODS: We used quantitative, real-time PCR to examine SERT and NET in RNA extracted from term placenta. Thus far we have enrolled 8 control patients, 3 SSRI patients, and 1 depressed, non-medicated patient. To control for confounding effects of other drug use, we also included placental samples from 4 fetuses exposed to nicotine.
RESULTS: According to our preliminary data, NET and SERT expression in the depressed patient was increased relative to controls. SSRI use was associated with a return of NET and SERT expression towards control levels. SSRI use alone was associated with no change in SERT expression and an increase in NET expression compared to controls. Nicotine use was not associated with altered gene expression.
CONCLUSIONS: Dysregulation of placental gene expression may be associated with altered fetal neuroendocrine status. This may result in changes in fetal and later neonatal neurobehavioral development. To confirm these preliminary observations, we are continuing to enroll patients. In future studies we plan to correlate placental expression with neonatal neurobehavioral tests.

221 11:45 AM

Vitamin D Responsiveness Is Impaired in Neonatal Neutrophils

Daniel Hirsch, Faith Archer, Barry Weinberger, Anna Vetrano. Pediatrics-Neonatology, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

BACKGROUND: Neutrophils are key effectors of the inflammatory response. Previous studies have shown that neutrophil removal by apoptosis is impaired in neonates, possibly increasing susceptibility to inflammatory diseases. Although vitamin D is commonly associated with calcium metabolism and bone homeostasis, recent studies have shown that vitamin D is important in the down-regulation of inflammation. The active metabolite of vitamin D, 1,25-dihydroxyvitamin D3 (1,25-vit D3), is generated by the action of both renal and extra-renal forms of 1∝hydroxylase (CYP27B1), and is inactivated by the enzyme CYP24A1. 1,25-vit D3 induces gene expression by binding to the vitamin D receptor (VDR).
OBJECTIVE: We hypothesize that neonatal neutrophils have impaired responsiveness to 1,25-vit D3 and that this may be due to decreased expression of VDR and CYP27B1, and/or to increased expression of CYP24A1.
DESIGN/METHODS: Neutrophils from term umbilical cord and adult blood were isolated by gradient centrifugation and cultured in the presence or absence of 1,25-vit D3. In some experiments, lipopolysaccharide (LPS) was added to induce inflammation. Expression of VDR, CYP27B1 and CYP24A1 was measured by real-time PCR.
RESULTS: Compared to adult neutrophils, basal expression of VDR, CYP27B1 and CYP24A1 was significantly lower in neonatal cells. LPS or 1,25-vit D3 significantly up-regulated VDR and CYP27B1 expression in adult but not neonatal neutrophils. In contrast, while CYP24A1 expression was suppressed by LPS in both adult and neonatal neutrophils, its expression was increased by 1,25-vit D3 only in neonatal cells.
CONCLUSIONS: Expression of CYP27B1 and VDR, key proteins up-regulating the generation of and responsiveness to 1,25-vit D3, respectively, is decreased in neonatal neutrophils, compared to adult cells. However, the counter-regulatory enzyme CYP24A1, which degrades vitamin D, is induced by 1,25-vit D3 only in neonatal cells. These findings suggest that responsiveness to vitamin D is impaired in neonatal neutrophils. This may play a role in the prolonged activity and delayed apoptosis of neonatal neutrophils, contributing to inflammatory disorders.

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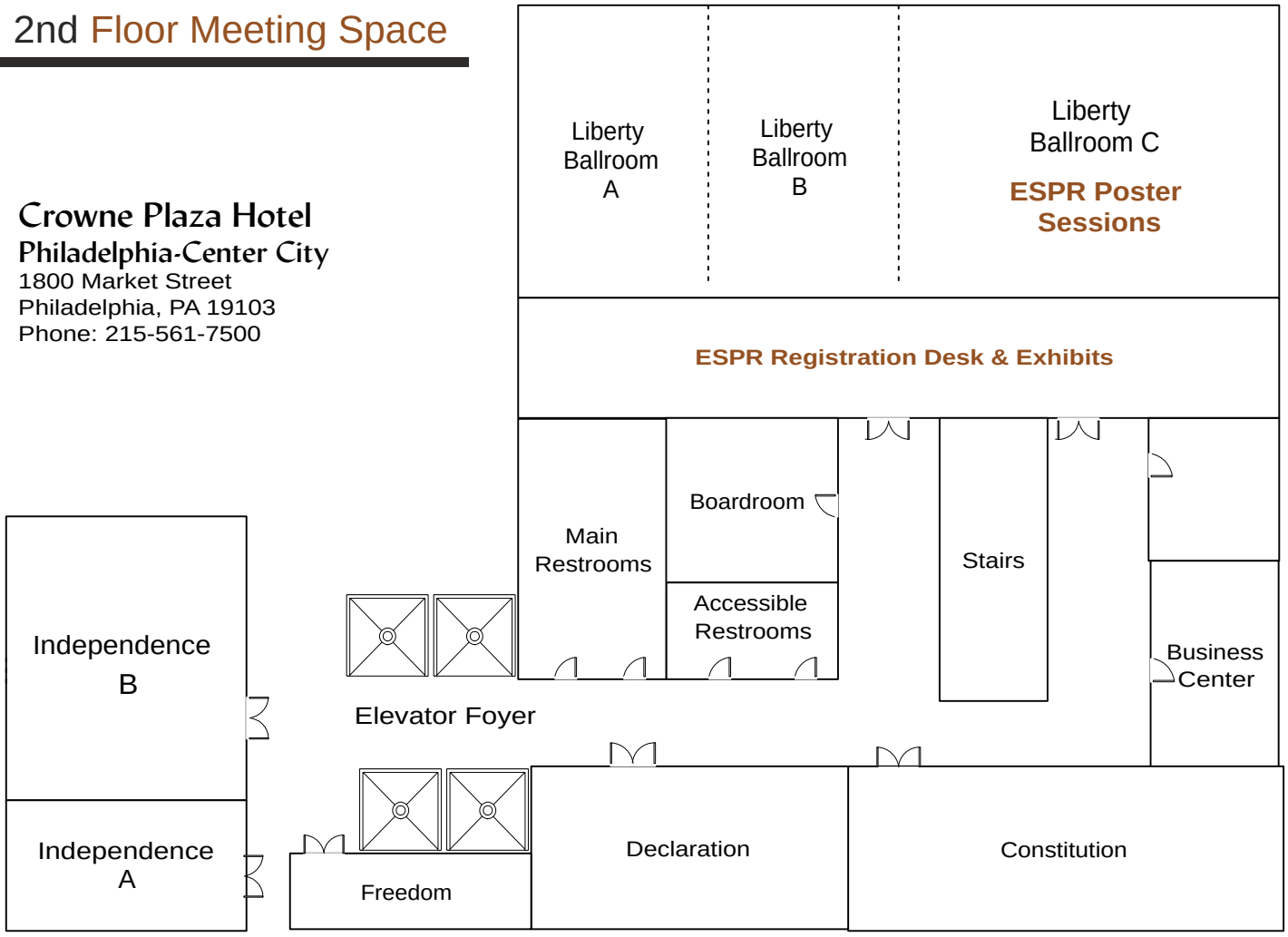

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