2004
Eastern Society for Pediatric Research
16th Annual Meeting

Program Guide

March 26–28, 2004
Hyatt Regency
Old Greenwich, CT

In cooperation with the New York Academy of Medicine

New for 2004

We are pleased to announce that we have engaged the services of the New York Academy of Medicine (NYAM) to run our 2004 meeting. They will also sponsor the CME program. While our recent meetings have been terrific, the administrative burden has exceeded what could reasonably be expected of our volunteers. We expect the engagement of the professional meeting planners at the NYAM will further enhance our meeting. This will include improved informatics enabling presenters to load their PowerPoint presentations at a central station in advance, avoiding some of the glitches we encountered last year.

ESPR Officers and Council 2003–2004

President
Luc P. Brion, M.D.
Albert Einstein College of Medicine and
Children's Hospital at Montefiore,
Bronx, New York

Secretary-Treasurer
Rashmin C. Savani, M.B.Ch.B.
The University of Pennsylvania School of Medicine,
Philadelphia, Pennsylvania

Chairperson, Planning Committee
Bruce D. Gelb, M.D.
Mount Sinai School of Medicine
New York, New York

Council Members
Anthony Alario, MD
Clifford Bogue, MD
Bruce D. Gelb, MD
Ian Holzman, MD
Philip Larussa, MD
Lawrence M. Nogee, MD

Planning Committee
Bruce D. Gelb, MD *(Chair)*
Clifford W. Bogue, MD
Luc P. Brion, MD
Heber Nielsen, MD
Lawrence M. Nogee, MD
Daniel Notterman, MD

Immediate Past President
Mitchell J. Kresch, MD

Past Presidents
Laurence Finberg, MD
Joseph B. Warshaw, MD
Marc Yudkoff, MD
Alan R. Fleischman, MD
Ira H. Gewolb, MD

Sponsorship Honor Roll

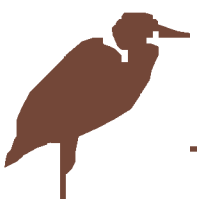
The ESPR expresses its appreciation to all of our sponsors of the 2004 ESPR Annual Meeting

Established Sponsors
Curative Pharmacy Services
Mead-Johnson Nutritionals
MedImmune, Inc.
Philips Medical Systems
Ross Products Division of Abbott Laboratories, Inc.

Additional Sponsors
Dey L. P.
INO Therapeutics, Inc.
Mercury Medical
Viasys Healthcare

Academic Sponsors
Alan R. Cohen, MD
The Children's Hospital of Philiadelphia
Philadelphia, Pennsylvania
Gabriel Haddad, MD
Children's Hospital at Montefiore, Bronx, New York
Margaret K. Hostetter, MD
Yale University, New Haven, Connecticut
Thomas R. Welch, MD
SUNY Upstate Medical University, Syracuse, New York

Contents



Welcome to the 16th Annual Meeting!

Dear Colleagues:

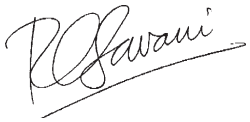
Welcome to the 16th Annual Meeting of the Eastern Society for Pediatric Research (ESPR)! We are sure that this will be an exciting meeting with excellent State-of-the-Art Plenary Talks, a Lunch with the Professors Educational Program, featured speakers at subspecialty sessions and a large number of high-quality abstracts.

The organization of this meeting would not have been possible without the help of the American Pediatric Society and the Society for Pediatric Research, especially Deborah Atwood, Information Services Director of the APS/SPR, and Debbie Anagnostelis, APS/SPR Executive Director, as well as Marathon Multimedia. We would like to acknowledge the ESPR Planning Committee and the other members of the ESPR Council for their help. We appreciate the meeting planning and provision of CME accreditation by the New York Academy of Medicine Office of Continuing Medical Education, especially Donald Morcone. We would like to thank our corporate and academic sponsors who were instrumental in making this meeting possible.

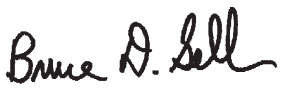
We are confident that this meeting continues to satisfy the mission of the ESPR in providing a forum for young investigators to present their research in a structured, yet informal and relaxed atmosphere, and by offering timely educational programs that address important current clinical and basic science questions in Pediatrics.

Thank you for attending! We look forward to sharing this time with you.

Luc P. Brion, MD
President



Rashmin C. Savani, MB, ChB
Secretary-Treasurer



Bruce D. Gelb, MD
Chair, Planning Committee

Faculty

Michael F. Artman, MD
New York University
School of Medicine
New York, New York

Diane Bianchi, MD
Tufts-New England Medical Center and
Tufts University School of Medicine
Boston, Massachusetts

Luc P. Brion, MD
Albert Einstein College of Medicine and
Children's Hospital at Montefiore
Bronx, New York

William Carroll, MD
New York University
School of Medicine
New York, New York

Marie M. Egan, MD
Yale University School of Medicine
New Haven, Connecticut

Bruce D. Gelb, MD
Mount Sinai School of Medicine
New York, New York

Danielle Laraque, MD
Mount Sinai School of Medicine
New York, New York

Stephen Ludwig, MD
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Laura R. Ment, MD
Yale University School of Medicine
New Haven, Connecticut

Ed Morrisey, PhD
University of Pennsylvania
School of Medicine
Philadelphia, Pennsylvania

Heber Nielsen, MD
Tufts-New England Medical Center and
Tufts University School of Medicine
Boston, Massachusetts

Lawrence M. Nogee, MD
Johns Hopkins University
Baltimore, Maryland

Philip O. Ozuah, MD
Albert Einstein College of Medicine
Bronx, New York

Alice S. Prince, MD
Columbia University College of
Physicians and Surgeons
New York, New York

Michael Rosenbaum, MD
Columbia University College of
Physicians and Surgeons
New York, New York

Karen Santucci, MD
Yale University and New Haven
Children's Hospital
New Haven, Connecticut

Rashmin Savani, MBChB
University of Pennsylvania
School of Medicine
Philadelphia, Pennsylvania

Tor Savidge, PhD
Massachusetts General Hospital
and Harvard Medical School
Boston, Massachusetts

Howard Spivak, MD
Tufts University School of Medicine
and New England Medical Center
Boston, Massachusetts

Alda Tufro, MD, PhD
Albert Einstein College of Medicine and
Children's Hospital at Montefiore
Bronx, New York

Registration and CME Desk Hours

Registration will be held in the Lobby of the Hyatt Regency. Registration hours are as follows:

Friday, March 26	<< >> – 7:00pm
Saturday, March 27	7:30am – 7:00pm
Sunday, March 28	7:30am – << >>

<<THE TIMES ABOVE NEED TO BE SUPPLIED BY ESPR >>

Abstract Publication

All abstracts being presented at the 2004 Eastern Society for Pediatric Research Annual Meeting are printed in this Program Guide, beginning on page 12.

All abstracts *submitted* to the 2004 ESPR Annual Meeting, whether presented or not, are being published in the April 2004 Supplement to *Pediatric Research*. Abstracts submitted to the PAS as well as to the ESPR are included in the *Pediatric Research* publication and are noted by a superscripted "ESPR" after the publication number (i.e., 236^{ESPR}). ESPR abstract publication numbers in *Pediatric Research* will NOT be the same number that is indicated in this publication. Abstracts submitted only to the ESPR appear under the Eastern Society for Pediatric Research heading in the *Pediatric Research* publication.

Audio/Visual Information IMPORTANT!

All presentations must be made using PowerPoint. Computers and LCD projectors will be provided. Slide projectors will not be provided. Speakers will need to bring their presentations on a CD-ROM, ZIP drive, or flash memory. Presentations will be loaded onto a central computer during the session prior to the presentation (i.e., Friday evening for Saturday morning presentations, Saturday morning for Saturday afternoon presentations, and Saturday afternoon for Sunday morning presentations).

Speaker Check In REQUIRED!

Speakers must have their presentations loaded onto a central computer during the session prior to the session in which the presentation is to be made. Please take your materials to the Speaker Ready Room/Area in <<LOCATION>>.

<<ADDITIONAL INFO NEEDS TO BE SUPPLIED BY ESPR >>

Business Center

The Business Center at the Hyatt Regency is located on the Ground Floor, near the Grand Staircase and Gift Shop.

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 The New York Academy of Medicine and the Eastern Society for Pediatric Research. The New York Academy of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The New York Academy of Medicine designates this educational activity for a maximum of 11.0 Category 1 credits toward the Physician's Recognition Award of the AMA. Each physician should claim only those credits that he/she actually spent in the activity.

Disclosure

The New York Academy of Medicine relies upon invited faculty participants to provide educational information that is objective and as free from bias as possible. In this spirit, and in accordance with the guidelines of the session sponsor, faculty participants are required to indicate any commercial relationship that might be perceived as a real or apparent conflict of interest.

CME Procedure

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

- **Upon arrival**, pick up your verification form at the Continuing Education Desk. (Lobby–Hyatt Regency)
- **On your departure date**, turn in your completed verification form. <<Where to Turn in Fom?>>

A record of credit will be emailed to each registrant after the activity concludes.

THINGS TO DO WHILE IN GREENWICH

Bush-Holley Historic Site
Home of Connecticut's first art colony, the Historical Society's facilities include the circa 1730 National Historic Landmark Bush-Holley House; the circa 1805 visitor center, housed in a former village post office; the Hugh and Claire Vanderbilt Education Center, set in a mid-19th century barn and artists' studio. The grounds and gardens have been restored to their appearance during the Cos Cob Impressionist art colony that thrived between 1890 and 1920.

Future Meetings

March 18 – 20, 2005 ~ Old Greenwich, CT (tentative)

Friday, March 26

5:30pm–7:30pm

Poster Session I
Conde's Room

8:30am–11:00am

Cardiology I	Developmental Biology	General Pediatrics I	Infectious Diseases	Neonatology I	Nephrology
	FEATURED TALK: Signaling Mechanisms That Regulate Lung Development	FEATURED TALK: Psychosocial Issues in Primary Care	FEATURED TALK: Bacterial Activation of Airway Inflammation	FEATURED TALK: Inborn Errors of Surfactant Metabolism	FEATURED TALK: Kidney Vascularization: The Role of VEGF and Semaphorins
Putnam	Winthrop A-B	Mead A	Riverside	Mead B	Mead C

11:00am–12:00pm

Plenary Session I

Announcement of the Mentor of the Year Award
Plenary Lecture: CPR—Past, Present and Future ~ Stephen Ludwig

Regency DEFG

12:00pm–1:00pm

Lunch with the Professors Educational Program
ESPR Business Meeting
Regency DEFG

1:30pm–3:30pm

Plenary Session II

Plenary Lecture: Fetomaternal Trafficking of Cells and Nucleic Acids: Biology and Diagnostic Applications ~ Diane Bianchi
Young Investigator Award Finalists Presentations
Regency DEFG

3:45pm–6:00pm

Adolescent Medicine	Gastroenterology	General Pediatrics II	Hematology/ Oncology	Pulmonology	Rheumatology/ Genetics
			FEATURED TALK: Omics and Outcome in Childhood Cancer	FEATURED TALK: The Effects of SERCA Inhibitors	
Riverside	Mead B	Mead A	Winthrop A-B	Mead C	Putnam

6:00pm–7:30pm

Poster Session II
Conde's Room

Sunday, March 28

8:30am–9:30am

Plenary Session III

Announcement of the Young Investigator Award
Plenary Lecture: Murder Is No Accident ~ Howard Spivak
Regency DEFG

9:45am–12:15pm

Cardiology II	Emergency Medicine	Endocrinology	General Pediatrics III	Neonatology II	Neurology
		FEATURED TALK: The Prevalence of Pre-diabetic Phenotypes in Early Adolescence: The El Camino Diabetes Prevention Study		FEATURED TALK: ErbB Receptors in Development of the Lung	FEATURED TALK: MRI Studies of Developing Brain
Mead C	Riverside	Winthrop A-B	Mead A	Mead B	Putnam

Friday, March 26

5:30pm–7:30pm Conde's Room

Poster Session I

1 A Randomized, Cross-Over Efficacy Trial of the Injex Jet Injector in Comparison to Needle Syringe in the Management of Pediatric Patients with Type 1 Diabetes Mellitus
Ashutosh Gupta, Neven Pesa, Henry Anhalt. — *Abstract 1*

2 Withdrawn

3 Effect of Introduction of Synchronized Nasal Intermittent Positive Pressure Ventilation (SNIPPV) on Growth and Short-Term Outcome of Babies in the Newborn Special Care Unit
Ameya Kulkarni, Richard A. Ehrenkranz, Vineet Bhandari. — *Abstract 3*

4 Cord Unbound Fatty Acid Concentrations as a Biomarker for Fetal Distress
Jose Yuvienco, Emily Dizon, Alan Kleinfeld, Thomas Hegyi. — *Abstract 4*

5 Basal Ganglia Hyperechogenicity in Preterm Infants
Lamia Soghier, Karim Aref, Mordicai Koenigsberg, Melanie Kogan, Jacqueline Bello, Jacques Romano, Tom Hoffman, Luc P. Brion. — *Abstract 5*

6 Stress Hyperglycemia in Pediatric ICU Patients Who Die
Kristen Ognibene, Peter M. Trinkaus, Charles L. Schleien.—*Abstract 6*

7 Pulse Oximetry Screen for Serious Neonatal Illness in the First Day of Life
Muraleedharan Sivarajan, Nick Wild, Muhuntha Gnanalingham, Bimal Mehta, Chris Bedford. — *Abstract 7*

8 MOVED TO SUNDAY POSTER SESSION

9 Parents' Views on Pediatric Advice and Counsel: A Cross-Cultural Perspective
Thyde M. Dumont-Mathieu, Bruce A. Bernstein, Paul H. Dworkin, Lee M. Pachter. — *Abstract 9*

10 Effect of Fetal Echocardiography and Pulse Oximetry Screening on Age at Diagnosis of Congenital Heart Disease
Ejiro Diejomaoh, Charlotte M. Druschel, Tonia Carter, Angela Romano, Yehuda Shapir, Mysore Gandhi, Fredrick Z. Bierman, Robert Koppel. — *Abstract 10*

11 Spanish Health Literacy of Inner-City Latino Parents
Melissa Leyva, Iman Sharif, Philip O. Ozuah. — *Abstract 11*

12 Variation in Nutritional Suppport Impacts Growth Outcomes of 30–35-Week Gestation Infants in 10 California and Massachusetts NICUs
Mary T. Blackwell, Marie C. McCormick, John Zupancic, Gabriel Escobar, Douglas K. Richardson. — *Abstract 12*

13 Rubbing Ointments and Asthma Morbidity in Adolescents
Marina Reznik, Iman Sharif, Philip O. Ozuah. — *Abstract 13*

14 Longitudinal Studies of Inter-Alpha Inhibitor Proteins (Iaip) Levels in Septic Newborn Infants
Kultar Singh, Edward Siryaporn, Kreso Bendelja, Yow-Pin Lim, James F. Padbury. — *Abstract 14*

15 Diversity of the SH and G Glycoprotein Genes in Isolates of the Human Metapneumovirus
Frank P. Esper, Carla Weibel, Jeffrey S. Kahn. — *Abstract 15*

16 Predictors of Early Readmission for Asthma in an Inner-City Population
Marina Reznik, Philip O. Ozuah. — *Abstract 16*

17 Cytokine Expression in Neonatal Cord Blood in Response to Lactobacillus plantarum (Lp299v) and Staphylococcus epidermidis (S.epi)
A. M. Francesca Tatad, John Peoples, Sandy Cheung, Mirjana Nesin, Susana Cunningham-Rundles. — *Abstract 17*

18 Assessment of the Effectiveness of Mock Codes in Improving Residents' Competency
Sujata Chakravarti, Chrysanthe Gaitatzes, Laura Dattner, Philip O. Ozuah. — *Abstract 18*

19 Ghrelin, Leptin and Growth Hormone During Growth Hormone Stimulation Testing in Children
Deborah A. Bowlby, Robert Moghaddas, Sudha Reddy, Elizabeth Wallach, Fenella Greig, Alisa Sokoloff, Michael Wajnrajch, Robert Rapaport. — *Abstract 19*

20 Does Mode of Transport or Location of Birth Affect the Occurrence of Severe IVH in ELBW Infants?
Santosh M. Parab, Ravi Mishra, Muhammad T. Zia, Kathy Rogan, Edmund F. LaGamma. — *Abstract 20*

21 Can Tidal Volume and Flow-Loop Mechanics Identify the Ability To Survive Off-ECMO in Restrictive Lung Disease?
Abdul Haleem, Ravi Mishra, Muhammad T. Zia, Edmund F. LaGamma. — *Abstract 21*

22 Nitric Oxide: Friend or Foe to Pulmonary Epithelium?
Dhruti Pandya, Ioana Godi, Sonya Strassberg, Lance A. Parton. — *Abstract 22*

23 Disparate Exposures to Allergens and Allergists for Inner-City Children with Asthma
Karen L. Warman, Ellen J. Silver. — *Abstract 23*

24 Ontogeny of Bilirubin Binding Capacity in Low Birthweight Neonates
Jesse Bender, William J. Cashore, William Oh. — *Abstract 24*

25 Nosocomial Transmission of the Human Metapneumovirus
Frank Esper, Richard A. Martinello, Derek Boucher, Carla Weibel, Jeffrey S. Kahn. — *Abstract 25*

26 Does Steroid Resistance Predict Cyclosporine Resistance in Primary Focal Segmental Glomerulosclerosis?
Ibrahim F. Shatat, Noosha Baqi. SUNY-Downstate Medical Center, Brooklyn, NY — *Abstract 26*

27 Evaluation of Pediatric Residents' Competency in Recognition of an Innocent Murmur
Sujata Chakravarti, Philip O. Ozuah. — *Abstract 27*

28 Residency Applicant Love Letters...What Do They Really Mean?
Catherine C. Skae, Marina Reznik, Philip O. Ozuah. — *Abstract 28*

29 Parental Attitudes to Inhaled Corticosteroid Use for Asthma
Anne Gordon, Valerie Lewis, Katherine O'Connor, Kristen Wade, Marina Reznik, Philip O. Ozuah. — *Abstract 29*

30 17-Alpha-Hydroxyprogesterone as Placental Immunoregulator: From Cell to Potential Clinical Benefit
Lea Bonifacio, Jill Schak, Eric Forman, Suli Han, Sherif Mishriky, Barry Weinberger, Nazeeh Hanna. — *Abstract 30*

Saturday, March 27

8:30am–10:00am Putnam

Cardiology I

Moderator: Bruce Gelb, Mount Sinai School of Medicine, New York, NY

8:30 Beta-Adrenergic Receptor Subtype Densities in Preterm Newborn, Term Newborn, and Adult Baboon Myocardium
David P. Treece. — *Abstract 31*

8:45 Selective Upregulation of Activator Protein-1 (AP-1) in Heart Failure Due to Chronic Volume Overload in Rats
Grace A. Freire, Catherina B. Ocampo, Yianna Kazakos, Madhu Gupta. — *Abstract 32*

9:00 Bedside Measurement of B-Type Natriuretic Peptide as a Marker for Patent Ductus Arteriosus in Preterm Infants
Patrick A. Flynn, Ralph L. da Graca, Mirjana Nesin, Rubin S. Cooper, Peter A. M. Auld, Charles S. Kleinman. — *Abstract 33*

9:15 The Use of the V to HRA Interval To Predict Sidedness of an Accessory Pathway in Children with SVT
Christa L. Miliaresis, Christopher Snyder. — *Abstract 34*

9:30 Short-Term Surgical Outcomes in Adults with Congenital Cardiac Anomalies
Bevin Weeks, Gary S. Kopf, Christopher S. Snyder. — *Abstract 36*

9:45 Predictors of High-Cost Admissions for Congenital Heart Surgery
Jean A. Connor, Kimberlee Gauvreau, Kathy J. Jenkins.—*Abstract 35*

8:30am–10:45am Winthrop A–B

Developmental Biology

Moderator: Ed Morrisey, University of Pennsylvania School of Medicine, Philadelphia, PA

8:30 Production, Activation and Signaling of TGF-b During Lung Type II Cell Maturation
Theresa M. McDevitt, Linda W. Gonzales, Rashmin C. Savani, Philip L. Ballard. — *Abstract 37*

8:45 Role of Thyroid Transcription Factor (TTF-1) in SP-B Expression During Differentiation of Human Fetal Lung Type II Cells
Venkat Kolla, Linda W. Gonzales, Ping Wang, Sree Angampalli, Philip L. Ballard. — *Abstract 38*

9:00 Hop, a New Target Gene for Thyroid Transcription Factor (TTF-1) in Fetal Lung Epithelial Cells
Linda W. Gonzales, Venkatadri Kolla, Kelly C. Wade, Ping Wang, Sreedevi Angampalli, Jonathan A. Epstein, Philip L. Ballard. — *Abstract 39*

9:15 Break

9:30 ErbB Receptor Heterodimerization in Fetal Rat Lung Epithelial Type II Cells and Fibroblasts
Washa Liu, Sandy Murray, Heber C. Nielsen, Christiane E. L. Dammann. — *Abstract 40*

9:45 Presence of Gamma-Interferon-Inducible Lysosomal Thiol Reductase (GILT) in Human Alveolar Type II Cells
Sabrina McGary, Emily Fischer, Amana Akhtar, Peggy Zhang, Susan Guttentag. — *Abstract 41*

10:00 Structure: Function Correlations During Hormonal Regulation of Alveolarization
Samuel J. Garber, Joseph P. Foley, Rashmin C. Savani. — *Abstract 42*

10:15 FEATURED TALK:
Signaling Mechanisms That Regulate Lung Development
Ed Morrisey
University of Pennsylvania School of Medicine
Philadelphia, PA

8:30am–11:00am Mead A

General Pediatrics I

Moderator: Danielle Laraque, Mount Sinai School of Medicine, New York, NY

8:30 Evaluating Attitudes About Research: An Analysis of Parent–Child Dyads
Robert M. Nelson, William W. Reynolds. — *Abstract 43*

8:45 Behavior of Kindergarten Children in Stepfamilies: Is Having Two Parents at Home Better Than One?
Prashil H. Govind, Ruth E. K. Stein. — *Abstract 44*

9:00 Behavior in Kindergarten Children: Is Having an Additional Adult Relative Protective in Single Parent Families?
Prashil H. Govind, Ruth E. K. Stein. — *Abstract 45*

9:15 The Relationship of Maternal Methadone Use to Early Developmental Outcomes
Jo-Ann B. Bier, Doranne Grenon, Theresa Johnson, Ellen Mullane. — *Abstract 46*

9:30 Break

9:45 What Do Adults Know About the Harmful Effects of Smoking on Child Health?
Meg Parker, Iman Sharif. — *Abstract 47*

10:00 Racial/Ethnic Disparities in Child Health: Another Failed Explanation!
Michele J. Siegel, Laurie J. Bauman, Ruth E. K. Stein. — *Abstract 48*

10:15 Children's Short Tenures in Medicaid Managed Care
Gerry Fairbrother, Heidi L. Park, Arfana Haidery, Bradford H. Gray. — *Abstract 49*

10:30 FEATURED TALK:
Psychosocial Issues in Primary Care
Danielle Laraque
Mount Sinai School of Medicine, New York, NY

8:30am–11:00am Riverside

Infectious Diseases

Moderator: Alice S. Prince, Columbia University College of Physicians and Surgeons, New York, NY

8:30 Impact of Cervical Secretions on HSV Infection
Minnie John, Marla Keller, Kathleen Hogarty, Natalia Cheshenko, Sarah Ferris, Sylvan Wallenstein, Mary Klotman, Betsy C. Herold. — *Abstract 50*

8:45 Demographic, Clinical, and Resource Utilization Characteristics of a Multisite Sample of HIV+ Children
Richard Rutstein, Kelly Gebo, George Siberry, Patricia Flynn, Victoria Sharp, Steven Spector. — *Abstract 51*

9:00 Incidence, Types and Risk Factors for Malignancy in Perinatally HIV Infected Children
Helen Kest, Susan Brogly, Barry Dashefsky, George Mcsherry, James Oleske, George Seage. — *Abstract 52*

9:15 Incidence and Outcome of CMV Infection in Pediatric Liver Transplantation Recipients Managed with Preemptive Ganciclovir Therapy
Cindy Goldberg, Andrew Campbell, Umberto Conte, Maria Tan, Sukru Emre, Betsy Herold. — *Abstract 53*

9:30 **Seroepidemiology of Human Metapneumovirus in Children**
Jessica W. Leung, Carla A. Weibel, Jeffrey S. Kahn. — *Abstract 54*

9:45 **Break**

10:00 **Effects of Respiratory Syncytial Virus (RSV) and Hyperoxia on Apoptosis in Cord and Adult Peripheral Mononuclear Cells (PBMCs)**
Leonard R. Krilov, Thomas W. McCloskey, S. Hella Harkness, Paul J. Lee, Jonathan M. Davis. — *Abstract 55*

10:15 **Beneficial Effects of Inter-Alpha Inhibitor Proteins (Iaip) in an In Vivo Animal Model of Neonatal Sepsis**
Kultar Singh, Kreso Bendelja, Yow-Pin Lim, James F. Padbury. — *Abstract 56*

10:30 **FEATURED TALK:**
Bacterial Activation of Airway Inflammation
Alice S. Prince
Columbia University College of Physicians and Surgeons
New York, NY

8:30am–11:00am Mead B

Neonatology I

Moderator: Lawrence M. Nogee, Johns Hopkins University, Baltimore, MD

8:30 **Neonatal Interleukin-1 Receptor Antagonist (IL-1ra) and Interleukin-4 (IL-4) Gene Polymorphisms and Spontaneous Preterm Birth**
Marcelo Y. Nabong, Santosh Vardhana, Mehmet Genc, Mirjana Nesin, Steven S. Witkin. — *Abstract 57*

8:45 **Influence of Census and Patient-to-Nurse Ratios on the Decision To Discharge Moderately Premature Infants**
Jochen Profit, Marie C. McCormick, John A. Zupancic, Kim Coleman-Phox, Rebecca H. Roberts, Gabriel J. Escobar, Douglas K. Richardson. — *Abstract 58*

9:00 **Growth Variation at Discharge and 3 Months Post-Discharge in Moderately Premature Infants**
Mary T. Blackwell, Marie C. McCormick, John Zupancic, Gabriel Escobar, Douglas K. Richardson. — *Abstract 59*

9:15 **Break**

9:30 **Treatment of Severe Retinopathy of Prematurity: A New Approach**
Talkad S. Raghuveer, Peng Chen, Pantea Mahtosh, Merrill Stass-Isern, Trudi Grin, Keith Warren. — *Abstract 60*

9:45 **Ouabain Prevents Excitotoxicity-Mediated Apoptosis in the Newborn Striatum**
W. Christopher Golden, Lee J. Martin. — *Abstract 61*

10:00 **Effect of Antenatal Steroids on Tight Junction Protein Expression in the Cerebral Cortex of Ovine Fetuses With In Utero Brain Ischemia**
Shadi N. Malaeb, Stephanie A. Newton, Grazyna B. Sadowska, Edward G. Stopa, Halit Pinar, Barbara S. Stonestreet. — *Abstract 62*

10:15 **Genetic and Pharmacologic Modulation of Nitric Oxide-Hemoglobin Reactivity**
Eric J. Frehm, J. Eric Russell, Andrew J. Gow. — *Abstract 63*

10:30 **FEATURED TALK:**
Inborn Errors of Surfactant Metabolism
Lawrence M. Nogee
Johns Hopkins University, Baltimore, MD

8:30am–10:45am Mead C

Nephrology

Moderator: Alda Tufro, Albert Einstein College of Medicine and Children's Hospital at Montefiore, Bronx, NY

8:30 **Erythropoietin and Its Receptor During Kidney Development in Mice**
Mihail M. Subtirelu, Alda Tufro. — *Abstract 64*

8:45 **Increased Glomerular Expression of Notch1, Jagged1 and Transforming Growth Factor b (TGF- b) Isoforms in Mice Lacking CD2-Associated Protein (CD2AP), Model of Focal Segmental Glomerulosclerosis (FSGS)**
Robert P. Woroniecki, Mario Schiffer, Frederick J. Kaskel, Andrey S. Shaw, Erwin P. Bottinger. — *Abstract 65*

9:00 **Alterations in F1F0 Atpase Levels in Renal Ischaemia**
Shirley A. Wang, Michael Riordan, Gunilla Thulin, Michael Kashgarian, Kevin L. Behar, Norman J. Siegel. — *Abstract 66*

9:15 **The Risk of Cardiovascular Disease in Adults Who Have Had Childhood Nephrotic Syndrome**
Brent Lee Lechner, Detlef Bockenhauer, Sandra Iragorri, Thomas L. Kennedy, Norman J. Siegel. — *Abstract 67*

9:30 **Break**

9:45 **Ambulatory Blood Pressure (ABP) Abnormalities Correlate with the Presence of Microalbuminuria (MA) in Minority Adolescents with Type 2 Diabetes Mellitus (T2DM)**
Leigh M. Ettinger, Mehul B. Patel, Katherine Freeman, Joan R. Di Martino-Nardi, Joseph T. Flynn. — *Abstract 68*

10:00 **Beneficial Effect of Combination Therapy with Angiotensin Converting Enzyme Inhibitors (ACEI) and Angiotensin Receptor Blockers (ARB) on Proteinuria in Pediatric Patients**
Tania Mucci, Rachel Frank, Suzanne Vento, Bernard Gauthier, Marcela Vergara, Howard Trachtman. — *Abstract 69*

10:15 **FEATURED TALK:**
Kidney Vascularization: The Role of VEGF and Semaphorins
Alda Tufro
Albert Einstein College of Medicine
Children's Hospital at Montefiore, Bronx, NY

11:00am–12:00pm Regency DEFG

Plenary Session I

11:00 **Welcome and Announcement of the Mentor of the Year Award**

Sponsored by an educational grant from Ross Products Division of Abbott Laboratories, Inc.

11:10 **PLENARY LECTURE:**
CPR—Past, Present and Future
Stephen Ludwig
Associate Physician-in-Chief for Medical Education, Jensen Professor of Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA

12:00pm–1:00pm Regency DEFG

Lunch with the Professors Educational Program & ESPR Business Meeting

Sponsored by an educational grant from Mead Johnson Nutritionals

1:30pm–3:30pm Regency DEFG

Plenary Session II

Moderators: Luc Brion, Albert Einstein College of Medicine and Children's Hospital at Montefiore, Bronx, NY; and Bruce Gelb, Mount Sinai School of Medicine, New York, NY

1:30 PLENARY LECTURE:
Fetomaternal Trafficking of Cells and Nucleic Acids: Biology and Diagnostic Applications

Diane Bianchi
Chief, Division of Genetics, Tufts-New England Medical Center, Natalie V. Zucker Professor of Pediatrics, Obstetrics and Gynecology, Tufts University School of Medicine, Boston, MA

Sponsored by an educational grant from Dey, L.P.

Young Investigator Award Finalists

2:30 The Impact of Maternal Immune Status on the Development of Allergic Disease
A. Matson, L. Zhu, E. Breen, R. Clark, C. Schramm, B. Lingenheld, L. Puddington. — *Abstract 70*

2:45 Identification of a Novel POSH Homologue, POSH2 and Its Role in Neuronal Apoptosis. Possible Implications for Developmental Brain Injury
Michael Wilhelm, Nickolay V. Kukekov, Zhiheng Xu, Susan Vannucci, Lloyd A. Greene. — *Abstract 71*

3:00 Colony-Stimulating Factor 1 (CSF-1) Role in a Model of Proteinuria-Induced Tubulointerstitial Disease (TID)
Corina Nailescu, Frederick J. Kaskel, E. Richard Stanley. — *Abstract 72*

3:15 A Novel Promoter Element in the Tyrosine Hydroxylase Gene Mediating the Response to the Dietary Short Chain Fatty Acid Butyrate
Pranav Patel, Bistra Nankova, Edmund F. LaGamma. — *Abstract 73*

Sponsored by an educational grant from MedImmune, Inc.

3:45pm–5:00pm Riverside

Adolescent Medicine

Moderator: <<To be announced>>

3:45 Emergency Contraception: Are Pediatric Residents Counseling and Prescribing to Teens?
Sylvia W. Lim, Lori Legano, Kelechi N. Iheagwara, Susan M. Coupey. — *Abstract 74*

4:00 Opportunistic Screening for *Chlamydia trachomatis* (CT) Infection in Adolescent Males in a Non Inner City School-Based Health Clinic
Dalan S. Read, Amy L. Suss, April Lee, Edward McCabe, Tamara Reznik, Margaret R. Hammerschlag. — *Abstract 75*

4:15 The Association of Dietary Glycemic Index and Load with Pediatric Overweight and the Metabolic Syndrome: A National Perspective
Carolyn J. Tabak, Peggy Auinger, Stephen Cook, Michael Weitzman. — *Abstract 76*

4:30 A Rose by Any Other Name: "Underdiagnosis" of Overweight in U.S. Adolescents Using Pediatric Standards
Carolyn J. Tabak, Peggy Auinger, Susanne Tanski, Michael Weitzman. — *Abstract 77*

4:45 Effect of Complementary Therapies on Lung Function in Adolescents with Acute Asthma Exacerbation
Marina Reznik, Iman Sharif, Philip O. Ozuah. — *Abstract 78*

3:45pm–5:00pm Mead B

Gastroenterology

Moderator: Tor Savidge, Massachusetts General Hospital and Harvard Medical School, Boston, MA

3:45 Effect of Antenatal Placental Insufficiency on Postnatal Preterm Infant Gastrointestinal Function
Elena Wachtel, Karen Hendrics-Munoz, Ilan Timor. — *Abstract 79*

4:00 Serum Phosphate Levels During the First Four Weeks of Age in Premature Infants
Nirupama Laroia, Nahed El Hassan, Rita M. Ryan. — *Abstract 80*

4:15 The Effects of Curcumin on the Expression of DF508-CFTR in Gastrointestinal Epithelia of a Cystic Fibrosis Mouse Model
Scott A. Weiner, Marilyn A. Pearson, Emanuela Bruscia, Diane Krause, John P. Geibel, Michael J. Caplan, Marie E. Egan. — *Abstract 82*

4:30 FEATURED TALK:
<<Title to come>>
Tor Savidge
Massachusetts General Hospital and Harvard Medical School Boston, MA

3:45pm–5:30pm Mead A

General Pediatrics II

Moderator: Philip O. Ozuah, Albert Einstein College of Medicine Bronx, NY

3:45 Complementary Therapies vs. Albuterol: Does Severity of an Acute Asthma Attack in Adolescents Predict the Choice of Therapy?
Marina Reznik, Iman Sharif, Philip O. Ozuah. — *Abstract 83*

4:00 Quality of Care and Racial Disparities in Hospitalized Asthmatic Patients
Susan A. Fisher-Owens, Wendy M. Turenne, William Pastor, Kathleen Chavanu, Anthony D. Slonim. — *Abstract 84*

4:15 Inpatient Pain Management Practices at a Children's Hospital
Catherine C. Skae, Sharon Calaman, Philip O. Ozuah. — *Abstract 85*

4:30 Negative Life Events and Reduced Quality of Life in Children with HIV Infection: A Longitudinal Analysis
Lois C. Howland, Sybil L. Crawford, Deborah S. Storm, Yunsheng Ma, James M. Oleske. — *Abstract 86*

4:45 A Comparison of the Pain Associated with Simultaneous (SIM) vs. Sequential (SEQ) Immunization Injections Given at the 9- and 12-Month Well Child Visits
Frederick J. Bogin, Bruce A. Bernstein, Jessica S. Payton, Neil L. Schechter, Benjamin Ristau. — *Abstract 87*

5:00 The Vaccines for Children Program: Taking a Shot at Disparities in Immunization Status
Andrew D. Racine, Theodore J. Joyce. — *Abstract 88*

5:15 Does a Schedule of Pentavalent DTaP-IPV-Hepatitis B (Pediarix), Conjugate Pneumococcal (PCN7), and Conjugate H. influenza (Hib) Vaccines Cause Excess Emergency Visits and Hospitalizations in Young Infants?
Lindsay A. Thompson, Matilde Irigoyen, L. Adriana Matiz, Philip S. LaRussa, Shaofu Chen, Frank Chimkin. — *Abstract 89*

3:45pm–5:45pm Winthrop A-B

Hematology/Oncology

Moderator: William Carroll, New York University School of Medicine New York, NY

3:45 Antiendothelial and Antiangiogenic Properties of QW1624F2-2, a Low-Calcemic Hybrid Analog of 1,25-Dihydroxyvitamin D_3
Claire Rodriguez, Paul Furigay, Gary Posner, Michael Fannon, Narasimha Swamy. — *Abstract 90*

4:00 Somatic *PTPN11* Mutations Are Prevalent in Common B-Cell Precursor Acute Lymphoblastic Leukemia
Marco Tartaglia, Simone Martinelli, Giovanni Cazzaniga, Viviana Cordeddu, Monica Spinelli, Claudio Carta, Giuseppe Masera, Giuseppe Basso, Mariella Sorcini, Andrea Biondi, Bruce D. Gelb.— *Abstract 91*

4:15 Binding of Zinc Proptophyrin to Serum Proteins and Effect on Apoptosis
Adia G. George, Guang Yang, Phyllis A. Dennery. — *Abstract 92*

4:30 N-MethylNitrosourea Induced Lymphomas in Circadian Clock Function Deficient Mice
Gautam Malkani, Mark Meyer, H. Michael Ushay, Zhong Sheng Sun, Bruce M. Greenwald. — *Abstract 93*

4:45 Iron Chelators Deferoxamine (DFO) and Diethylene-triaminepentaacetic Acid (DTPA) Inhibit Endothelial Cell Proliferation and Angiogenesis
Paul Furigay, Claire Rodriguez, Laurent Brard, Narasimha Swamy. — *Abstract 94*

5:00 In Vivo Evaluation of Zinc Protoporphyrin on Tumor Supression
Ameen Salahudeen, Guang Yang, Phyllis A. Dennery. — *Abstract 95*

5:15 FEATURED TALK:
Omics and Outcome in Childhood Cancer
William Carroll
New York University School of Medicine, New York, NY

3:45pm–6:00pm Mead C

Pulmonology

Moderator: Marie M. Egan, Yale University School of Medicine New Haven, CT

3:45 Vascular Endothelial Growth Factor (VEGF) Enhances Maturity in the Developing Mouse Lung
Vineet Bhandari, Chun G. Lee, Chuyan Tang, Seamus A. Rooney, Robert J. Homer, Jack A. Elias. — *Abstract 96*

4:00 Overexpression of Bioactive TGF-b1 in Neonatal Mouse Lung: A New Model for BPD?
Alfin G. Vicencio, Chun Geun Lee, Oliver Eickelberg, Ying Chuu, Gabriel G. Haddad, Jack A. Elias. — *Abstract 97*

4:15 Heliox Attenuates Lung Inflammation and Structural Alterations in Acute Lung Injury
Ursula S. Nawab, Suzanne M. Touch, Tami Irwin-Sherman, Thomas J. Blackson, Jay S. Greenspan, Guangfa Zhu, Thomas H. Shaffer, Marla R. Wolfson. — *Abstract 98*

4:30 A Serpin Protects Against Death from Pseudomonas Pneumonia
Lawrence M. Rhein, Dave Askew, Greg P. Priebe, Gary A. Silverman. — *Abstract 99*

4:45 Evidence That Human Metapneumovirus Does Not Contribute to the Severity of Respiratory Syncytial Virus Disease
Isaac Lazar, Carla Weibel, David Ferguson, Marie Landry, Jeffrey S. Kahn. — *Abstract 100*

5:00 Pro-Inflammatory Mediators Amplify the Apoptotic Response of Human Lung Cells During Hypoxia
Sonya S. Strassberg, Ioana Godi, Asgar Dudhbhai, Dhruti Pandya, Lance A. Parton. — *Abstract 101*

5:15 Cytokine Stimulation of Lung Epithelial Cells Induces iNOS and Results in Cell Death
Michael A. Posencheg, Linda W. Gonzales, Andrew J. Gow. — *Abstract 102*

5:30 FEATURED TALK:
The Effects of SERCA Inhibitors
Marie M. Egan
Yale University School of Medicine, New Haven, CT

3:45pm–5:45pm Putnam

Rheumatology/Genetics

Moderator: Rashmin Savani, University of Pennsylvania School of Medicine, Philadelphia, PA

3:45 Juvenile Dermatomyositis: IVIG as Part of Standard Treatment Regimen
C. April Bingham, Deborah M. Levy, Lisa F. Imundo.—*Abstract 103*

4:00 Three Year Follow-Up of Mycophenolate Mofetil Therapy in Childhood SLE Indicates Effectiveness as a Maintenance Agent
Leigh Serra, Yuki Kimura, Marilyn Punaro, Lisa Imundo.—*Abstract 104*

4:15 Quality of Life in Pediatric Lupus
L. N. Moorthy, E. Leibowitz, L. Robbins, M. Harrison, M. Peterson, N. Cox, K. Onel, T. J. Lehman. — *Abstract 105*

4:30 Short Stature in Patients with Chronic Granulomatous Disease Is Associated with X-Linked Genotype, Granulomatous Gastrointestinal Disease and Phagocyte Metabolic Activity
David M. Lang, Steven M. Holland, Beatriz E. Marciano, Douglas B. Kuhns, Deborah P. Merke. — *Abstract 106*

4:45 Expression Studies and Homology Modeling of GPIb beta
Jingrong Tang, Po-Ching Liu, Peter J. Steinbach, Naomi L. C. Luban, Stephen G. Kaler. — *Abstract 107*

5:00 DBP-maf, a Potent Activator of Osteoclasts, Is Deficient in Juvenile Osteopetrosis
Prema R. Madyastha, Lyndon L. Key, Narasimha Swamy. — *Abstract 108*

5:15 Noonan Syndrome-Causative Gain-of-Function Mutations in *PTPN11* Result in Wing Abnormalities and Embryonic Lethality in *Drosophila*
Kimihiko Oishi, Marco Tartaglia, Mark E. Lieb, Leslie Pick, Bruce D. Gelb. — *Abstract 109*

5:30 Functional Absence of *TBCE* Causes Loss of Parathyroid Glands in the Syndrome of Hypoparathyroidism, Mental and Growth Retardation, and Facial Dysmorphism
Melissa C. Huang, Mark Rubinstein, Bart Loeys, Ruti Parvari, George A. Diaz. — *Abstract 110*

THINGS TO DO WHILE IN GREENWICH

Putnam Cottage
Revolutionary War leaders gathered at the former Knapps Tavern, which is preserved today as a local history museum.

6:00pm–7:30pm Conde's Room

Poster Session II

31 Relation of Intrapartum Magnesium Sulfate to Memory in Adolescents Born at Low Birth Weight
Jordan S. Kase, Judith F. Feldman, John M. Lorenz, Nigel Paneth, L. H. Lumey, Agnes H. Whitaker. — *Abstract 111*

32 Prediction of Neonatal Hyperbilirubinemia with a Transcutaneous Bilirubin Nomogram
Nidal Humoee, Anna Petrova, Rajeev Mehta, Thomas Hegyi. — *Abstract 112*

33 Effects of Discordance in Birth Weight on Postnatal Growth in Very Low Birth Weight Twin Infants
Gunjeet M. Sahni, Micheal A. Guiliano, Dominique Jean-Baptiste, Vinayak Govande, Myungduk R. Kim. — *Abstract 113*

34 Rapid Toxicity to *Candida albicans* Mediated by Human Peripheral Blood Mononuclear Cells
Joseph M. Bliss, Sonia Laforce-Nesbitt. — *Abstract 114*

35 New Model for Insulin Initiation in Type I Diabetes
John Ching, Neven Pesa, Golali Nejati, Ashutosh Gupta, Nicole Matthews, Henry Anhalt, Svetlana Ten. — *Abstract 115*

36 Preterm Neonatal Thrombocytopenia Causes and Outcome
Shakuntala Nanjundaswamy, Anna Petrova, Rajeev Mehta. — *Abstract 116*

37 Hypothyroidism Due to Autoimmune Thyroiditis in Very Young Children
Ashutosh Gupta, Harvey Mermelstein, Svetlana B. Ten, Henry Anhalt. — *Abstract 117*

38 Routine Parenteral Intake of Vitamin E in Very Low Birth Weight Infants in the U.S.: Too Much or Too Little?
Luc P. Brion, Edward F. Bell, Talkad S. Raghuveer. — *Abstract 118*

39 The Competency of Pediatric Residents in the Evaluation and Treatment of Childhood Obesity
Anthony F. Porto, Peter Belamarich, Andrew D. Racine. — *Abstract 119*

40 Trimming of Percutaneous Central Venous Catheters Prior to Insertion and Risk of Catheter Related Sepsis in the NICU
Archana P. Bilagi, Jotishna Sharma, Jeanne Rorke, Martin Keszler. — *Abstract 120*

41 Infants with Persistent Pulmonary Hypertension of the Newborn (PPHN) Are at Increased Risk for Subsequent Systemic Hypertension
Anne Marie Reynolds, Mahesh Bommaraju, Kirsten Blessing-Hanagan, Rita Ryan. — *Abstract 121*

42 Effect of Parental Health Literacy on Child Asthma Morbidity
Lisa Wilks-Gallo, Iman Sharif, Philip O. Ozuah. — *Abstract 122*

43 Does Posting Asthma Guidelines in Physician Examination Rooms Improve Anti-Inflammatory Therapy Use?
Sandra F. Braganza, Iman Sharif, Philip O. Ozuah. — *Abstract 123*

44 Risk Factors for Retinopathy of Prematurity (ROP) in Very Low Birth Weight (VLBW) Neonates
Shital Doshi, Khaja Raziuddin, Vesna G. Sutija. — *Abstract 124*

45 Hematologic Characteristics of Infants with Trisomy 21: A Case for Platelet Underproduction
Timothy A. Kline, Amy Mackley, David A. Paul. — *Abstract 125*

46 Urinary Peroxide and Nitrite/Nitrate Levels in Newborn Infants
Christiana R. Farkouh, Scott A. Lorch, Jeffrey Merrill, Philip L. Ballard, Harry Ischiropoulos, Roberta A. Ballard. —*Abstract 126*

47 Growth of Retinal Blood Vessels Is Altered in "Sick" vs. "Well" Premature Infants
Naveed Hussain, Ricardo Jean-Baptiste, Marta Barker, Christopher Kelley. — *Abstract 127*

48 The Comparision of Effect of Incomplete and Complete Course of Antenatal Steroids on Morbidity and Mortality in Premature Infants
Harpreet Kaur, Chhavi Agarwal, Lourdes Cohen, Susana Rapaport. — *Abstract 128*

49 Breastfeeding in 30–35-wk Infants from Birth to 3 Months After NICU Discharge
Mary T. Blackwell, Marie C. McCormick, John Zupancic, Gabriel Escobar, Douglas K. Richardson. — *Abstract 129*

50 Alveolar Type 1 Cell Marker Expression in an In Vitro Model of Human Alveolar Type 1 Cell Transdifferentiation
Cherie D. Foster, Linda Varghese, Susan H. Guttentag. — *Abstract 130*

51 Comparison of Two Methods of Screening for Iron-Deficiency Anemia in Inner City Children
Reva Snow, Philip O. Ozuah. — *Abstract 131*

52 Use of a Neonatologist's Time After Regular Working Hours at Two NYS Level One Community Hospitals
Catherine Ekwa-Ekoko, Praveen Ballabh, Lakshmi Modipalli, Edmund F. LaGamma. — *Abstract 132*

53 Can We Improve Neonatal Outcomes of Extremely Low Birth Weight Infants Born at Community Hospitals?
Nadine M. El-Khoury, Muhammad Zia, Sergio G. Golombek. — *Abstract 133*

54 Barriers to Implementation of ADHD Guidelines in Inner City Primary Care Settings
Candace J. Erickson, Paola Carugno, David A. Perlstein, David H. Rubin. — *Abstract 134*

55 Perinatal Outcomes of Singletons Versus Twin Premature Newborns <1000g at Birth
Muhammad T. Zia, Ravi Mishra, Edmund F. LaGamma. — *Abstract 135*

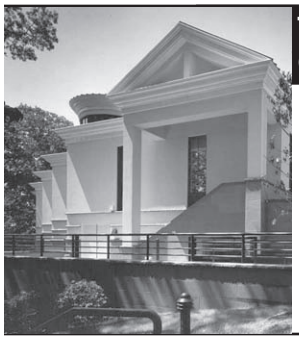
56 Longitudinal Changes of B-Type Natriuretic Peptide (BNP) in Preterm Neonates
Ralph L. da Graca, Denise C. Hassinger, Patrick A. Flynn, Mirjana Nesin, Peter A. M. Auld. — *Abstract 136*

57 Interleukin (IL)-6 to Vascular Endothelial Growth Factor (VEGF) Ratio Predicts the Development of Brochopulmonary Dysplasia (BPD)/Death in Premature Infants
Jonathan H. Nedrelow, Vineet Bhandari. — *Abstract 137*

58 Asialotransferrin as a Biochemical Marker for Subarachnoid-Pleural Fistula Diagnosis
Isaac Lazar, Carlos Knopf, Michael Halberthal, Gad Bar-Joseph. — *Abstract 138*

59 Pediatrician Knowledge of School Asthma Policies
Marian Larkin, Iman Sharif, Philip O. Ozuah. — *Abstract 139*

60 Mother and Infant Outcomes with Prenatally Detected Choroid Plexus Cysts
Elizabeth A. Cristofalo, Janet DiPietro, Kathleen Costigan, Jude Crino, Marilee C. Allen. — *Abstract 8*



THINGS TO DO WHILE IN GREENWICH

Bruce Museum
Situated in a beautiful park setting at the foot of Greenwich Avenue, the Bruce presents 14 changing exhibitions annually. Its permanent exhibitions feature a minerals gallery, a marine tank, and displays that explain the environmental and historical development of the area.

Sunday, March 28

8:30am–9:30am Regency DEFG

Plenary Session III

8:30 Announcement of the Young Investigator Award

Sponsored by an educational grant from Medimmune, Inc.

8:40 PLENARY LECTURE: Murder Is No Accident

Howard Spivak
Professor of Pediatrics and Community Health, Tufts University School of Medicine; Adjunct Professor, Eliot-Pearson Department of Child Development; Chief of the Division of General Pediatrics and Adolescent Medicine at New England Medical Center, Boston, MA

Sponsored by an educational grant from INO Therapeutics, Inc.

9:45am–12:00pm Mead C

Cardiology II

Moderator: Michael F. Artman, New York University School of Medicine, New York, NY

9:45 Strategy for Molecular Genetic Stratification of Familial Hypertrophic Cardiomyopathy
Sheila J. Carroll, Emerson Whittington, Daphne T. Hsu, Wendy K. Chung. — *Abstract 141*

10:00 Doc-2, a Tumor Suppresor Protein Represses MAP Kinase Activation and Collagen Gene Expression in Cardiac Fibroblasts; Implications in Heart Failure
Mohamad K. Al-Ahdab, Deepa Chandrashekar, Rene A. Arcilla, Mahesh P. Gupta, Madhu Gupta. — *Abstract 142*

10:15 Non-Invasive Localization of Mouse Embryos by Ultrasound Biomicroscopy (UBM)-Doppler Allows Genotype-Phenotype Correlation
Rui Ping Ji, Colin K. L. Phoon. — *Abstract 143*

10:30 Break

10:45 Tfap2b Plays a Critical Role in the Development and Remodeling of the Mouse Ductus Arteriosus
Feng Zhao, Thomas Lufkin, Reinhard Buettner, Bruce D. Gelb. — *Abstract 144*

11:00 Neural Crest Cell Migration and Patterning in a Mouse Model of Persistent Truncus Arteriosus
Kathryn Maschhoff, Theresa Lubas, Paris Ward, Paul Anziano. — *Abstract 145*

11:15 Calcium Regulation During Early Cardiac Development
George A. Porter, Jr., Ryan F. Makuck. — *Abstract 146*

11:30 FEATURED TALK: Maturational Changes in the Regulation of Cardiac Contractile Function
Michael F. Artman
New York University School of Medicine, New York, NY

9:45am–11:30pm Riverside

Emergency Medicine

Riverside

Karen Santucci, Yale University and New Haven Children's Hospital, New Haven, CT

9:45 Serious Bacterial Infections (SBI) in Older Febrile Infants (FI): Incidence and Predictors
Allen L. Hsiao, Lei Chen, M. Douglas Baker. — *Abstract 147*

10:00 Predictors of Pneumonia in Young Febrile Infants
S. Platt, D. Levine, N. Fefferman, P. Dayan, C. Macias, J. Zorc, W. Krief, J. Schor, D. Bank, K. Shaw, N. Kuppermann. — *Abstract 148*

10:15 Break

10:30 Urine Leukocyte Esterase as a Predictor of Urinary Tract Infections in Febrile Infants in the Emergency Department
Lei Chen. — *Abstract 149*

10:45 Utility of Bedside Bladder Ultrasound Prior to Urethral Catheterization in Infants
Lei Chen, Allen L. Hsiao, Christopher L. Moore, Karen A. Santucci. — *Abstract 150*

11:00 Initial Fluid Resuscitation for Patients with Diabetic Ketoacidosis: How Dry Are They?
Michele J. Fagan, Jeffrey R. Avner, Hnin Khine. — *Abstract 151*

11:15 Patterns of Injury Associated with Routine Childhood Falls
Melanie L. Pitone, Magdy W. Attia. — *Abstract 152*

9:45am–12:15pm Winthrop A-B

Endocrinology

Moderator: Michael Rosenbaum, Columbia University College of Physicians and Surgeons, New York, NY

9:45 Vitamin D Deficiency in Obese Children
Ashutosh Gupta, Svetlana B. Ten, Golali Nejati, Neven Pesa, Amrit P. S. Bhangoo, Irina Kazachkova, Nicole A. V. Matthews, Henry Anhalt. — *Abstract 153*

10:00 Elevated Liver Transaminases Are a Frequent Complication of Obesity in Children Referred to the Kids Weight Down Program
Nicole A. V. Matthews, Irina Kazachkova, Shivinder Narwal, Graciela Wetzler, Golali Nejatii, Henry Anhalt, Svetlana Ten. — *Abstract 154*

10:15 Is Microalbuminuria (MA) in Childhood Obesity Related to Glucose Toxicity?
Tania S. Burgert, Catherine Yeckel, William Tamborlane, Sonia Caprio. — *Abstract 155*

10:30 The Impact of Redefining Impaired Fasting Glucose in Children at Risk for Impaired Glucose Tolerance and Type 2 Diabetes Mellitus
Stasia Hadjiyannakis, Sarah E. Lawrence, Leanne M. Ward, Margaret L. Lawson. — *Abstract 156*

10:45 Break

11:00 Insulin and TSH Levels Can Predict Short-Term Response to Behavioral Intervention in Obese Children
Amrit Bhangoo, Golali Nejati, Lisa Altshuler, Susan Beren, Chaya Silverstein, Deborah DeSantis, Yanick Joseph, Henry Anhalt, Svetlana Ten. — *Abstract 157*

11:15 Childhood Obesity: Diabetes Risk in an Urban Hispanic Caribbean Population
Abeer Hassoun, Daisy Chin, Sadana Balachandar, Alexandra M. Manibo, Nicole Sherry, Phillip M. Pierorazio, Lenore S. Levine, Sharon E. Oberfield, Ilene Fennoy. — *Abstract 158*

11:30 Oral Glucose Tolerance Test (OGTT) Findings in Minority Youth [African American (AA) and Caribbean Hispanic (CH)] at Risk for Type 2 Diabetes Mellitus (T2DM)
Mireya H. Garcia, Hadassa Nussbaum, Patricia Vuguin, Roy Grant, Joan Di Martino-Nardi. — *Abstract 159*

11:45 FEATURED TALK:
The Prevalence of Pre-diabetic Phenotypes in Early Adolescence: The El Camino Diabetes Prevention Study
Michael Rosenbaum
Columbia University College of Physicians and Surgeons
New York, NY

9:45am–11:30am Mead A

General Pediatrics III

Moderator: <<To be determined>>

9:45 Structured vs. Unstructured Data Entry: Measuring Attitudes and Comparing Documentation Completeness in Primary Care Pediatrics
Robert W. Grundmeier, Anthony A. Luberti, Susan E. Coffin, Curtis P. Langlotz, Kevin B. Johnson. — *Abstract 160*

10:00 Helping Teachers Breathe Easier: Improving Asthma Knowledge and Competencies Among Elementary School Teachers
Reva Snow, Sarah Kimball, Philip O. Ozuah. — *Abstract 161*

10:15 Break

10:30 The Vaccines for Children Program: A Difference-in-Difference Analysis of Changes in Immunization Status Disparities
Andrew D. Racine, Theodore J. Joyce. — *Abstract 162*

10:45 Improving Residents' Competency in Pain Management
Sharon Calaman, Catherine C. Skae, Philip O. Ozuah. — *Abstract 163*

11:00 Utility of 360-Degree Assessment of Competencies of Pediatric Residents
Sandra F. Braganza, Iman Sharif, Philip O. Ozuah. — *Abstract 164*

11:15 Impact of Interventions Aimed at Compliance with New ACGME Resident Work Hour Regulations
Daniel Finkelstein, Philip O. Ozuah. — *Abstract 165*

9:45am–12:30pm Mead B

Neonatology II

Moderator: Heber Nielsen,Tufts-New England Medical Center and Tufts University School of Medicine, Boston, MA

9:45 Bronchopulmonary Dysplasia (BPD): Impaired Expression of Interleukin-1 Receptor Antagonist (IL1Ra)?
Deepika K. Kakkera, Mustafa M. Siddiq, Lance A. Parton.— *Abstract 166*

10:00 Relationship Between Markers of Nitric Oxide Metabolism and Pulmonary Function in Infants at Risk of BPD
Andrew J. Gow, Philip L. Ballard, Michael Norberg, William E. Troug, Roberta A. Ballard. — *Abstract 167*

10:15 Natriuretic Peptide Clearance Receptor Is Downregulated in the Pulmonary Epithelium After Birth in Preterm and Full Term Lambs
Bobby Mathew, Christopher A. D'Angelis, Daniel D. Swartz, Vasanth H. Kumar, Peter A. Nickerson, Huamei Wang, Karen A. Wynn, Bruce A. Holm, Rita M. Ryan. — *Abstract 168*

10:30 Inhaled Carbon Monoxide Preserves Alveolarization and Improves Pulmonary Mechanics in Neonatal Murine Hyperoxia-Induced Lung Injury
Veniamin Ratner, Serguei V. Kishkurno, Maxim Fedarau, Richard A. Polin, David J. Pinsky, Vadim S. Ten. — *Abstract 169*

10:45 Break

11:00 Effects of Surfactant (SF)-Augmented CPAP Therapy on Lung Structure and Inflammation
U. S. Nawab, T. Irwin-Sherman, S. M. Touch, T. J. Blackson, G. Zhu, T. H. Shaffer, M. R. Wolfson.— *Abstract 170*

11:15 Gene Expression Profiling of Human Lung Type II Cell Differentiation
Kelly C. Wade, Linda W. Gonzales, John Gonzales, Susan H. Guttentag, Philip L. Ballard. — *Abstract 171*

11:30 SP-A Deficient Mice Exhibit a Biphasic Response to Bleomycin-Induced Lung Injury
Jennifer H. Kaplan, John A. Casey, Yaniv Tomer, Francis R. Poulain, Samuel Hawgood, Michael F. Beers. — *Abstract 172*

11:45 Current AAP Vitamin D Supplementation Guidelines May Be Inappropriate for Some Breastfeeding Term Hispanic Neonates
Daniel S. Hirsch, Christine Dillon, John M. Lorenz, Michael F. Holick. — *Abstract 81*

12:00 FEATURED TALK:
ErbB Receptors in Development of the Lung
Heber Nielsen
Tufts-New England Medical Center and Tufts University School of Medicine, Boston, MA

9:45am–12:00pm Putnam

Neurology

Moderator: Laura R. Ment, Yale University School of Medicine New Haven, CT

9:45 C1q Gene-Deleted Neonatal (but Not Adult) Mice Are Protected Against Hypoxic-Ischemic Brain Injury
Vadim S. Ten, Sergei A. Sosunov, Sergei V. Kishkurno, Raymond I. Stark, Marina Botto, E. Sander S. Connoly, Jr., David J. Pinsky. — *Abstract 173*

10:00 Multiple Periods of Hypoxic Preconditioning Prevents Hypoxic-Ischemic Energy Depletion and Expands Protection in Immature Rat Brain
Susan J. Vannucci, Robert M. Brucklacher, Robert C. Vannucci. — *Abstract 174*

10:15 Renal Effects of Topiramate in Children with Seizures
Sarah M. Barnett, Anthony H. Jackson, Jane L. Garb, Herbert E. Gilmore, Beth A. Rosen, Dina H. Kornblau, Gregory L. Braden.—*Abstract 175*

10:30 Delayed Rolling Over Skill Associated with Deformational Plagiocephaly
Dakshayani R. Guttal, Rami R. Grossman, Susana Rapaport. — *Abstract 176*

10:45 Break

11:00 Dietary Factors Influence Catecholamine Synthesis Via Second Messenger Pathways Converging on the CAMP-Response Element Binding Protein (CREB)
Parul V. Shah, Bistra B. Nankova, Edmund F. LaGamma. — *Abstract 177*

11:15 Maturational Switch in Gene Expression of Blood Brain Barrier (BBB) Nutrient Transporters
Katherine V. Biagas, Ichha Sethi, Susan J. Vannucci. — *Abstract 178*

11:30 FEATURED TALK:
MRI Studies of Developing Brain
Laura R. Ment
Yale University School of Medicine, New Haven, CT

Poster Session I

Friday, March 26 5:30pm–7:30pm Conde's Room

1

Fellow

A Randomized, Cross-Over Efficacy Trial of the Injex Jet Injector in Comparison to Needle Syringe in the Management of Pediatric Patients With Type 1 Diabetes Mellitus

Ashutosh Gupta, Neven Pesa, Henry Anhalt. Pediatrics, Maimonides Medical Center, Brooklyn, NY.

BACKGROUND: A jet injector can administer medications subcutaneously without a needle. This may reduce pain, eliminate needle stick injuries and need for needle disposal. A needle-less jet injector (injex) has been shown to produce blood levels of insulin equivalent to that produced by a standard needle syringe.

OBJECTIVE: To assess the efficacy of injex in maintaining glycemic control in comparison to a needle syringe in children with type 1 diabetes mellitus (T1DM) and to determine the patient preference for insulin delivery system.

DESIGN/METHODS: 14 patients (7 male, 7 female) with T1DM for >1 yr, taking ≥2 insulin injections/day with HbA1c <10% were enrolled. Those with bleeding diathesis, diabetic complications, obesity and pregnancy were excluded. 6 (5 male, 1 female; age 13.2±3.1 yr) completed the study. 2 were randomized to group 1 (injex first) and 4 to group 2 (syringe first) (visit 1).Except for the possible gender bias, the weight (kg) (50.5±13.3 vs 52.3±21.6, p>0.05) and HbA1c (%) (9.5±0.6 vs 8.2±1.3, p>0.05) matched between the two groups. 3 mo. later the delivery devices were switched (visit 2). At the end of the study (visit 3), 3 mo. later, all patients completed a preference questionnaire. Insulin dose was changed as needed. Weight, HbA1c and daily insulin dose (units) were measured at visits 1, 2 and 3. Mann-Whitney test was used to perform pair wise comparison of HbA1c and weight. Wilcoxon signed-rank test between pairs was used to compare patient injector preference.

RESULTS: HbA1c and weight did not change between groups 1& 2 (HbA1c 9.5±0.6 vs 8.2±1.3, 9.6±0.7 vs 7.7±2.4 and 9.1±0.6 vs 7.6±2.0 and weight 50.5±13.3 vs 52.3±21.6, 50.5±12.7 vs 52.8±9.0 and 51.5±2.1 vs 54.3±19.7 at visits 1, 2 and 3 respectively; all p>0.05). As a whole the HbA1c and weight remained stable (HbA1c 8.6±1.2, 8.3±2.1and 8.1±1.8 and weight 51.7±16.9, 52.0±16.1 and 53.3±15.4 at visits 1, 2 and 3 respectively; all p>0.05). The total daliy insulin dose did not differ with either device (40.4±12.8 vs 43.0±15.4; p>0.05). There was no statistically significant preference for either device although there was a trend towards preference for the syringe.

CONCLUSIONS: Glycemic control is similar in children with T1DM with the use of injex or needle. Our results are based on a small group and need to be validated in a larger group.

Funded by Equidyne Systems, Inc., San Diego, California.

2 Withdrawn

3

Student

Effect of Introduction of Synchronized Nasal Intermittent Positive Pressure Ventilation (SNIPPV) on Growth and Short-Term Outcome of Babies in the Newborn Special Care Unit

Ameya Kulkarni, Richard A. Ehrenkranz, Vineet Bhandari. Pediatrics; Division of Perinatal Medicine, Yale University School of Medicine, New Haven, CT.

BACKGROUND: SNIPPV has been shown to be superior to nasal continuous positive airway pressure (NCPAP) as a mode of extubation (Pediatrics 2001;108:13-17). Concerns have been raised that SNIPPV, while being associated with decreased BPD, may compromise growth because of increased work of breathing.

OBJECTIVE: To study the effect of introduction of this novel modality at an institution with no prior experience with it.

DESIGN/METHODS: Babies extubated to SNIPPV for at least 24 hours were identified (8/01-2/02). Controls (never received SNIPPV) were matched by gestational age (GA) and birth weight (BW) (5/00-2/02). Data including demographics, neonatal outcomes, caloric intake, weights on days (d) 1-14, then weekly until d84, were collected . Standard diagnostic criteria were used for PDA, air leaks, IVH, PVL, NEC, ROP, GER and BPD. Statistical analyses included chi-square, student's t test and repeated measures ANOVA; p value <0.05 was considered significant.

RESULTS: Neonatal demographics and outcomes are shown in the table. In addition, there were no differences between the 2 groups in maternal demographics, use of antenatal steroids, exposure to antenatal antibiotics, Apgars, incidence of PDA, air leaks, IVH, PVL, NEC, ROP, and GER.

	Control (n=25)	SNIPPV (n=25)	p value
GA (weeks)	26 ± 0.4	26.5 ± 0.5	0.5
BW (grams)	843 ± 53	906 ± 69	0.5
Surfactant doses	2.6 ± 0.3	1.9 ± 0.3	0.2
ET PPV (hrs)	718 ± 114	515 ± 97	0.2
SNIPPV (hrs)	0 ± 0	266 ± 47	<0.001
NCPAP (hrs)	546 ± 75	284 ± 53	<0.01
O2 days	85.3 ± 7.7	64.6 ± 6.4	0.04
BPD (#, %)	17 (68)	9 (36)	0.02
Hospital days	98.8 ± 7.3	86.8 ± 9.7	0.3

Data expressed as mean ± sem, except BPD

Overall, there were no differences in the caloric intake (total, carbohydrate, protein or fat) or weight gain between the 2 groups. However, from d21-28, babies in the SNIPPV group (mean age of receiving SNIPPV) had better weight gain than controls (on ETT) (16.1±1.7 vs. 7.4 ± 2.3 g/kg/d; p=0.003). No differences in weight gain were noted from d35-42 (both on NCPAP) or d49-56 (SNIPPV group off respiratory support; controls on NCPAP).

CONCLUSIONS: Introduction of SNIPPV at Yale resulted in babies having signifcantly less supplemental oxygen and BPD, without compromising on their weight gain. We would recommend SNIPPV as a preferred mode of extubation.

4

Fellow

Cord Unbound Fatty Acid Concentrations as a Biomarker for Fetal Distress

Jose Yuvienco, Emily Dizon, Alan Kleinfeld, Thomas Hegyi. Pediatrics, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ; Torrey Pines Institute for Molecular Studies, San Diego, CA.

BACKGROUND: Most serum FFA are transported bound to albumin, and only a small fraction of the total FFA is unbound. Serum unbound FFA (FFAu) levels are regulated by the ratio of the total serum FFA to the serum albumin concentration and are profoundly sensitive to alterations in homeostasis. FFAu constitute the biologically active compartment of the total serum FFA, which are known to be inhibitory for a variety of cellular and immune processes. Increased levels of FFAu have been found in adults undergoing coronary angioplasty as a result of acute hypoxia-ischemia.

OBJECTIVE: We hypothesized that fetal hypoxia at the time of delivery, manifested by an Apgar Score of less than 5 at 1 minute, will be associated with elevated FFAu levels in the cord blood.

DESIGN/METHODS: On hundred ninety-nine infants between 25-41 weeks gestational age were enrolled in the study. Infants with an Apgar score of less than 5 at 1 minute served as the study group. Blood samples were collected from the umbilical cord and the serum was frozen at -70 F. At the time of enrollment, maternal clinical (Group B Streptococcal status and pregnancy induced hypertension) and neonatal data (gestational age, birth weight, mode of delivery, gender, Apgar score, rupture of membranes, cord pH, meconium stained amniotic fluid, nuchal cord and intrauterine growth retardation) were recorded.Serum [FFA_u] determinations were done with the fluorescent probe ADIFAB. Upon binding FFA_u the ADIFAB fluorescence shifts from 432 nm to 505 nm and therefore the concentration of FFA_u can be determined from the ratio of 505 to 432 nm fluorescence as: [FFA_u] =0.44 Q(R-Ro)/(Rmax-R).

RESULTS: The low Apgar score group (n=31, BW 3132+/-761 g, GA 37.9+/-3.1 wks) and normal Apgar score group (n=168, BW 3074+/-850g, GA 37.5+/-3.5 wks) were significantly different with respect to Apgar score at one minute (3.0+/-1.0 vs. 8.4+/-1.1) Apgar score at five minutes (6.9+/-2.1 vs. 8.8+/-0.5), cord pH (7.15+/-0.13 vs.7.28+/-0.07), and in the frequency of meconium passage (41.9% vs. 14.9%). Cord FFAu levels were 8.02+/-4.27 vs. 4.01+/-2.21 nM (p<0.01) respectively. Cord FFAu correlated significantly with Apgar score at 1 minute (r=-.45) and cord pH (r=-.26), but not with BW or GA.

CONCLUSIONS: In infants with low one minute Apgar scores, cord free fatty acid levels were significantly greater than in controls, suggesting that FFAu levels may be a biomarker for fetal hypoxia.

5

Fellow

Basal Ganglia Hyperechogenicity in Preterm Infants

Lamia Soghier, Karim Aref, Mordicai Koenigsberg, Melanie Kogan, Jacqueline Bello, Jacques Romano, Tom Hoffman, Luc P. Brion. Pediatrics, Albert Einstein Coll Med, Children's Hosp at Montefiore (AECOM/CHAM), Bronx, NY; Radiology, AECOM/CHAM, Bronx, NY.

BACKGROUND: In neonates, transient basal ganglia hyperechogenicity (BGH) may result from edema/ischemia, whereas persistent BGH may result from ischemic infarction, hemorrhage, or perivascular lesions.

OBJECTIVE: To determine the incidence of BGH in preterm infants <34 weeks (wk) gestational age (GA), to compare perinatal characteristics of neonates with BGH with those of matched controls and to determine the incidence of various presumed pathologic entities causing BGH.

DESIGN/METHODS: This case-control retrospective study included infants with a GA <34 wk admitted 7/00-3/02. In cases, BGH was diagnosed and confirmed by US, and a CT/MRI, obtained when stable, was read by a neuroradiologist, and later re-read blindly by two neuroradiologists (JB and JR). Controls were selected as the 3 infants of the same GA group (23-25, 26-28, 29-31, 32-33$^{6/7}$ wk) admitted closest to one with BGH. Severity of germinal matrix-intraventricular hemorrhage (GMH/IVH) was classified as none, mild-moderate (grades I-II), and severe (grades III-IV). The incidence of potential risk factors was compared in cases and controls by logistic regression analysis.

RESULTS: Average GA was 27.3 ± 3.0 wk (mean ± SD) and 27.7 ± 2.9 wk in patients and controls, respectively, and birth weight was 1072 ± 398 and 1080 ± 428 grams. Among 289 infants <34 wk, 25 (8.6%) were diagnosed with BGH at a median age of 6 (1-82) days. All patients had associated GMH/IVH by US and 3 developed a porencephalic cyst involving BG. Logistic regression showed that BGH was significantly associated with chorioamnionitis, high-frequency oscillation (HFO), and severity of GMH/IVH. Initial CT/MRI reading lead to a diagnosis of BG hemorrhage in 16 and was normal in 9/25, whereas blinded reading showed severe IVH with porencephalic cyst in 1 patient, ischemic infarction in 1 patient, and was normal in 18/20. Among patients with normal CT/MRI, 1 was diagnosed with vasculitis (congenital cytomegalovirus infection) and 1 with edema/ischemia based on US findings.

CONCLUSIONS: In this retrospective study, BGH occurred in 8.6% infants < 34 wk GA, and was associated with chorioamnionitis, HFO, and severity of GMH/IVH. In most infants BGH was observed without anomaly on CT/MRI. In some infants BGH resulted from ischemic infarction, edema/ischemia, vasculits, or severe IVH with porencephalic cyst. The long-term prognosis of VLBW infants with BGH needs to be determined.

6

House Officer

Stress Hyperglycemia in Pediatric ICU Patients Who Die

Kristen Ognibene, Peter M. Trinkaus, Charles L. Schleien. Department of Pediatrics, Columbia University College of Physicians and Surgeons, New York, NY; Department of Pediatrics, Division of Critical Care, Columbia University College of Physicians and Surgeons, New York, NY.

BACKGROUND: Stress hyperglycemia (SHG) contributes to sepsis and death in adult ICU patients. Improved outcome can be noted by 5 days of tight glucose control. SHG occurs in PICU patients but its frequency, precipitants and role in outcome are unknown. SHG may be a causative factor or may be only an epiphenomenon of severe illness and the use of known precipitants (P), e.g.:corticosteroids (CS), epinephrine or norepinephrine (Epi), or high glucose load (HGL).

OBJECTIVE: We suspect that SHG is common in severely ill PICU patients and sought to characterize its frequency, patterns of presentation and role of known precipitants in children dying in the PICU as these children represent a highly stressed group.

DESIGN/METHODS: We conducted a retrospective chart review of all patients dying over a 6 month period in the PICU at the Children's Hospital of NY. Frequency, patterns of SHG, and P were identified. Definitions: SHG - glucose > 120, diabetic range hyperglycemia (DHG) – glucose ≥ 200, high glucose loads = ≥8 mg/kg/min glucose delivery. SHG pattern definitions: pre-terminal only (PT) – SHG only in last 4 days of life; recurrent sustained (RS) – persistent SHG for ≥ 5 consecutive days, recurrent intermittent (RI) – SHG for ³ 5 non-consecutive days of PICU stay; cardiac arrest related (CA); cardiopulmonary bypass related (CPB). Total non-PT = RS + RI. Patients with CA or CPB may be in more than one group.

RESULTS: There were 31 deaths. No patient had pre-existing diabetes. SHG occurred in 28/31 (90%) and DHG in 23/31 (74%). Insulin was used in 3. SHG patterns frequencies were: PT - 14, RS - 9, CA – 5, CPB – 4, IR – 3. Of the 28 pts with SHG, 26 (93%) had at least one P: Epi - 22, CS - 12, HGL - 12. In the PT group: DHG - 12/14, Epi - 9, CS - 4, LOS>7 days - 4. In the non-PT group: DHG - 11/14, LOS > 7 days - 9. In the RS group: Epi - 9/9, CS - 6, Sepsis - 6.

CONCLUSIONS: SHG and DHG are common in PICU patients who die. P usage was present in most of these. Patterns of SHG can be identified. SHG limited to PT, CA or CPB most likely represents an epiphenomenon of stress and may not contribute to poor outcome. SHG was non-PT (RS+RI) in 45% of patients: 6 of these had sepsis and SHG may be a causative factor contributing to poor outcome, sepsis, multi-organ failure and death as seen in adults. Further investigation is warranted including comparisons with survivng patients, trials of tight glucose control and investigation of mechanisms of casuative effects.

7

Fellow

Pulse Oximetry Screen for Serious Neonatal Illness in the First Day of Life

Muraleedharan Sivarajan, Nick Wild, Muhuntha Gnanalingham, Bimal Mehta, Chris Bedford. Pediatrics, Warrington Hospital NHS Trust, Lovely Lane, Warrington, Cheshire, United Kingdom; Pediatrics, Lincoln Medical Center, Bronx, NY. (Sponsored by Steven William Piecuch)

BACKGROUND: Early detection of serious neonatal illness can be difficult. Presentation can be subtle and insidious in a seemingly well neonate. Delay in diagnosis can increase morbidity and mortality.

OBJECTIVE: Pulse oximetry is a safe, non-invasive and inexpensive method of assessing oxygen saturation. We evaluated the efficacy of pulse oximetry during the first day of life as a screening tool for the detection of serious neonatal illness.

DESIGN/METHODS: Prospective cohort study conducted from September 1999 to August 2000 in a regional hospital setting. Midwives were trained in the use of pulse oximeters. Oxygen saturation in room air was measured in the foot between 30 minutes and 6 hours of age on all live-born infants who were admitted to the well baby nursery. Pulse oximetry values <90% were rechecked. Infants who had 2 pulse oximetry readings <90% were evaluated by a pediatric resident. Admissions to the general pediatric unit and tertiary cardiac referral center were reviewed to identify infants with significant neonatal illness who may have been missed by screening.

RESULTS: 1421 of the 3218 infants (44.2%) who met the inclusion criteria completed the study. Mean birth weight was 3416 grams and mean gestational age was 39.4 weeks. Mean saturation was 96.6%. Initial saturation was <92% in 81 (6%), <91% in 46 (3%) and <90% in 31 (2%) of cases. 18 of the 31 infants (58%) with saturation <90% were clinically normal on further evaluation. Of the other 13, 1 (8%) had congenital heat disease (disconnected right pulmonary artery), 8 (62%) had TTN or mild RDS, 2 (15%) had asymptomatic GBS infection and 2 (15%) were hypoglycemic. Two infants with normal saturations were subsequently found to have congenital heart disease. One, a patient with Tetralogy of Fallot, had a saturation of 97% at age 1 hour. The other, a patient with pulmonic stenosis with atrial septal defect, had a saturation of 97% at age 2 hours.

CONCLUSIONS: 31 of 1421 asymptomatic infants (2%) screened in the first day of life had oxygen saturation <90%. Of these, 13 (42%) were found to have significant illness. Specificity was 98.8% and sensitivity was 86.7%. Pulse oximetry is a potentially effective screening tool in the first day of life. Pulse oximetry may not be an effective method for identifying cyanotic heart disease in the first day of life, when the ductus arteriosus may be open.

8

Mother and Infant Outcomes With Prenatally Detected Choroid Plexus Cysts

Elizabeth A. Cristofalo, Janet DiPietro, Kathleen Costigan, Jude Crino, Marilee C. Allen. Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD; Population and Family Health Sciences, Johns Hopkins University School of Public Health, Baltimore, MD; Obstetrics and Gynecology, Johns Hopkins University School of Medicine, Baltimore, MD.

BACKGROUND: Prenatal ultrasound is a positive, reassuring experience when no abnormalities are detected. Improved technology has facilitated frequent detection of structural variants of unclear functional significance. Such diagnoses can raise parental anxiety because there is no information available to counsel them about outcomes. Choroid plexus cysts (CPC) are detected in 1-2% of fetuses. CPCs are noted with greater frequency in fetuses with Trisomy 18 or 21. However, the significance of a CPC in the absence of other abnormalities has not been systematically studied.

OBJECTIVE: To determine the clinical significance of prenatally detected, isolated CPC. We hypothesize that there will be no difference in birth outcomes or fetal/neonatal neurodevelopment (ND).

DESIGN/METHODS: A prospective longitudinal study of 32 mother/infant pairs with isolated, prenatally detected CPC compared with 64 race and SES-matched controls. Fetal ND was evaluated monthly by monitoring patterns of fetal heart rate (FHR), motor activity and behavior. Three weeks after delivery, we performed a comprehensive ND exam, including assessment of posture, tone, reflexes, reactions, sensory responses, visual tracking and attention (Allen & Capute, Pediatrics 83: 490, 1989).

RESULTS: CPC mothers had lower pre-pregnancy weights than control mothers (60.0 kg vs. 64.3 kg), and a greater proportion had BMI<19.8 kg/m^2 (30.4% vs. 13.3%). CPC fetuses had higher FHR, but no differences in FHR variability, FHR/movement coupling or activity. CPC infants had shorter gestational ages (GA) at birth (38.3 vs. 39.2 weeks, p=0.009). Three week old CPC infants had higher Abnormality Scores (AS, 3.5 vs 2.6, p=0.028) and borderline lower Maturity Scores (MS, 138.3 vs. 142.8, p=0.065) on ND exam. Because of lower GA, exams were performed earlier in CPC infants (postmenstrual ages, PMA 41.4 vs. 42.6 weeks, p=0.001). When corrected for PMA at the time of exam, the differences in MS and AS were no longer significant.

CONCLUSIONS: Infants with isolated, prenatally detected CPCs delivered one week earlier than controls. The lower maternal weight and BMI raises the question whether CPCs are more easily detected in thin women. We are further analyzing fetal data to determine the significance of higher FHRs. The significance of earlier delivery and differences in exam at 3 weeks with respect to ND outcome will be determined by a ND evaluation at 18 months.

9

Fellow

Parents' Views on Pediatric Advice and Counsel: A Cross-Cultural Perspective

Thyde M. Dumont-Mathieu, Bruce A. Bernstein, Paul H. Dworkin, Lee M. Pachter. Pediatrics, University of Connecticut School of Medicine, Farmington, CT.

BACKGROUND: Child health providers (CHPs) are encouraged to provide parenting advice and counsel during health supervision visits (HSV). Limited research data, primarily from surveys of non-minority parents, suggest that parents are receptive to receiving such anticipatory guidance. Sparse data are available on the views of minority parents from different ethno-cultural groups (ECGs). The extent to which findings from White parents are applicable to other groups is unclear.

OBJECTIVE: To explore the views of minority parents from 4 ethno-cultural groups (ECGs) regarding parenting and their expectations for receiving parenting advice during the HSV.

DESIGN/METHODS: Focus Groups (FGs) were conducted with mothers from 4 ECGs - African-American (AA), Jamaican (J), Haitian (H), Puerto Rican (PR) - of various SES in the greater Hartford, CT area. Trained moderators of the same ECG elicited perspectives on parenting; expectations for the HSV; and parenting advice from their CHP. Transcripts of the FGs (translated into English when appropriate) were analyzed by a team of 3 pediatricians and 1 anthropologist using a combination of Expert Thematic Analysis and Grounded Theory.

RESULTS: 91 mothers participated in 20 FGs (5 AA, 5 H, 4 J, and 6 PR). Analyses of the transcripts indicate that minority parents would not routinely seek advice from CHPs about many aspects of parenting. In contrast, CHPs are considered experts in matters of physical health. In this study, ECG membership was associated with subtle, but not major differences in attitudes towards receiving parenting advice from CHPs. The parents in this study identified several determinants of the role of the CHP as a primary source of parenting advice: the CHP's interpersonal skills; the rapport of the CHP with the parent and child; the presence of shared cultural values; and systemic issues (i.e., CHP's office operations).

CONCLUSIONS: This study of parents from 4 minority ECGs challenges the conventional wisdom, based on data from the majority population, that parents desire parenting advice from their CHPs. When providing anticipatory guidance on parenting in the multi-cultural context, CHPs should first assess the parent's attitudes and beliefs towards receiving this advice.

10

Fellow

Effect of Fetal Echocardiography and Pulse Oximetry Screening on Age at Diagnosis of Congenital Heart Disease

Ejiro Diejomaoh, Charlotte M. Druschel, Tonia Carter, Angela Romano, Yehuda Shapir, Mysore Gandhi, Fredrick Z. Bierman, Robert Koppel. Pediatrics, Schneider Children's Hospital, New Hyde Park, NY; Congenital Malformation Registry, New York State Department of Health, Troy, NY. (Sponsored by Dennis Davidson)

BACKGROUND: The incidence of severe congenital cardiovascular malformation (CCVM), i.e., requiring treatment in the neonatal period, is 1.4-3/1000. Not all cases are detected prior to nursery discharge. Pulse oximetry screening at 24 hours of age to detect severe CCVM in asymptomatic newborns was introduced in our well-baby nursery (WBN) in 1998. Despite an annual delivery rate of about 6000, to date only one infant with a severe CCVM has been detected through the use of oximetric screening.

OBJECTIVE: To determine the impact of fetal echocardiography (FE) on the prevalence of severe CCVM in the WBN and on the performance of the oximetric screening test..

DESIGN/METHODS: The databases of the divisions of Pediatric Cardiology and Neonatal-Perinatal Medicine were reviewed in order to evaluate changes in FE rates and the WBN prevalence of severe CCVM during 2 time periods. Period 1:1993-1998 before screening, and period 2: 1998-2003, following the introduction of oximetric screening. The New York State Congenital Malformation Registry was searched for cases of severe CCVM requiring readmission that had not been detected prior to discharge.

RESULTS: The rate of FE/live birth increased from 1.7% in '93 to 9.5 % in '03. The proportion of severe CCVM cases detected by FE increased from 33% in '93 to 83% in '03. The prevalence of severe CCVM in the WBN fell from 1/1043 to 1/5204 during this time interval. In period 1, the mean age at the time of detection of severe CCVM was 27.7 hours (range 0-94) with 50% of cases undetected at 24 hours. In period 2, mean detection time was 10.4 hours (range 0-24). Five patients in period 1 and 2 in period 2 required readmission for undetected severe CCVM.

CONCLUSIONS: Screening test performance depends on the prevalence of the screened disorder. Increasing rates of FE have resulted in decreased WBN prevalence of severe CCVM. The earlier detection of severe CCVM in period 2 may be attributable to increased knowledge and skill of nursery staff in recognizing early subtle signs. Minimally symptomatic infants that were previously observed until signs became obvious are now checked for desaturation prior to the 24 hour screening timepoint. Oximetric screening appears to have indirectly reduced the time to detection of severe CCVM and is likely to have a higher yield in regions with less access to FE.

11

House Officer

Spanish Health Literacy of Inner-City Latino Parents

Melissa Leyva, Iman Sharif, Philip O. Ozuah. Pediatrics, Children's Hospital at Montefore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Few studies have measured the Spanish health literacy skills of Latinos; none have measured the relationship of Spanish health literacy to comprehension of routinely dispensed medication instructions.

OBJECTIVE: 1) To determine how well Latino parents comprehend medication instructions 2) To determine whether health literacy in Spanish is related to parental comprehension of routinely dispensed medication instructions.

DESIGN/METHODS: Cross-sectional survey of Spanish speaking parents of children attending two urban pediatric clinics. A bilingual investigator presented subjects with a bottle of liquid ferrous sulfate. The prescription label on the bottle was written in English, the medication instruction sheet was in Spanish. This simulated the experience of Latino patients receiving care in this community. Subjects were asked to read the instructions, and then demonstrate the amount of medication and number of times/day to give it. Subjects also answered questions regarding preparation, administration, side effects, and precautions as described in the instructions. The Short Test of Functional Health Literacy in Adults - Spanish (STOFHLA-S)(range 0-36, adequate literacy >22) was then administered.

We computed Odds Ratios and 95% Confidence Intervals (CI) for correct demonstration of medication use by demographics and by adequate vs. inadequate health literacy. A summary score was computed for responses to the medication comprehension questions (range 0-7). Linear regression tested STOFHLA-S, age, languages spoken, and education as predictors of comprehension.

RESULTS: 100 subjects participated. 92% were female, 97% immigrants (Dominican, Mexican, Puerto Rican), mean # years in US= 12. 86% spoke only Spanish, 59% had not completed HS.

Overall, 22% of subjects demonstrated correct medication use. Bilingual subjects were more likely than monolinugal Spanish speakers to demonstrate correct use (OR=4.7, CI 1.4, 15.5).

66% of subjects had adequate health literacy by the STOFHLA-S. Subjects with adequate literacy were more likely to demonstrate correct medication use (30% vs. 6%, OR 6.96, CI 1.5, 32). Linear regression controlling for demographics found STOFHLA-S to independently predict the medication comprehension score (B=.658, p=.000).

CONCLUSIONS: Few Latino parents in this study understood the medication instructions. Scores on a standardized test of Spanish health literacy correlated with comprehension, but only 30% of subjects with "adequate" literacy demonstrated correct medication use.

12

Variation in Nutritional Suppport Impacts Growth Outcomes of 30-35 Week Gestation Infants in 10 California and Massachusetts NICUs

Mary T. Blackwell, Marie C. McCormick, John Zupancic, Gabriel Escobar, Douglas K. Richardson, Department of Maternal and Child Health, Harvard School of Public Health, Boston, MA; Department of Neonatology, Beth Israel Deaconess Medical Center, Boston, MA; Harvard Newborn Medicine Program, Children's Hospital and Harvard Medical School, Boston, MA; Division of Research, Perinatal Research Unit, Kaiser Permanente Medical Care Program, Oakland, CA.

BACKGROUND: Little study has been focused on NICU care of moderately premature infants in the last 2 decades. Despite low morbidity and mortality, these infants comprise ~50% of NICU patients.

OBJECTIVE: To measure variation in NICU nutrition support and its impact on growth outcomes in moderately premature infants.

DESIGN/METHODS: We studied a prospectively identified cohort of 850 infants,30-35 wks GA, born 9/01 thru1/03 in 10 NICUs, 5 each in California (CA) and Massachusetts (MA), 60-100/NICU . Demographic, hospital course and nutritional care data were obtained by medical record review. Post-discharge data was collected by standardized phone interview. Multivariate models and comparisons between NICUs were controlled for BW, GA, weight for GA and illness acuity (SNAP2 score).

RESULTS: Enteral feedings were provided to 27, 91 and 98% of study infants on days 0,3 and 7 with mean energy intake of 16+/-15, 48+/-32 and 93+/-33 kcal/kg/d. Infants *not* fed were younger, smaller and sicker than those who *were* fed but there remained substantial variation between NICUs in feeding volume (cc/kg), caloric density of feedings (kcal/oz) and total enteral energy intake (kcal/kg) through 28 days,p<0.01. *Peak* enteral energy intake of 120+/-26 kcal/kg was recorded at *28* days. Parenteral nutrition was provided to 39% of all subjects. NICUs with *lowest enteral energy intake* through 2 wks,(191+/-73 and 201+/-66 kcal/kg compared to population mean of 239+/-73 kcal/kg),had *highest rates of parenteral nutrition* use (43 and 82%). Gavage (pg) feedings were provided to 84% of subjects with pg feedings *ending* at mean GA of 35.27+/-1.18 wks (inter-NICU range >7 days,p<0.01). Caloric density of feedings at discharge averaged 22 kcal/oz with range of NICU means from 20.6 to 23.5 kcal/oz.,p<0.001. Increased weight gain from birth to discharge was associated with increased calorie intake in the first two weeks(+5.8g/k/d / 100kcal/kg), use of parenteral nutrition (+2.4g/k/d) and prolonged gavage feeding (0.27 g/k/d / wkGA) while breast milk feedings at discharge were associated with a growth deficit of 1.1 g/k/d, adjR2=0.21, p<0.001.

CONCLUSIONS: Inter-NICU variation in nutritional support significantly impacts inpatient weight growth velocity in this population of moderately premature infants from 10 CA and MA NICUs.

supported by AHRQ R01 HS10131

13

Fellow

Rubbing Ointments and Asthma Morbidity in Adolescents

Marina Reznik, Iman Sharif, Philip O. Ozuah, Pediatrics, The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Rubbing ointments, such as Vicks VapoRub, are the Complementary or Alternative Medicine (CAM) most commonly used by adolescents with asthma. The association between the use of rubbing ointments and asthma morbidity has not been evaluated.

OBJECTIVE: To test the hypothesis that use of rubbing ointments is associated with reduced asthma morbidity.

DESIGN/METHODS: We conducted a prospective cohort study of adolescents with asthma at an inner-city high-school. For a total of six months, we contacted the subjects monthly via telephone to determine whether thay had asthma attacks in the previous month. If the answer was "yes", then subjects were asked about the first treatment they used for their last asthma attack. Responses were coded dichotomously for the use of rubbing ointments and use of albuterol. Subjects were also asked about Emergency Department (ED) visits, hospitalizations, and courses of systemic steroids (proxies for asthma morbidity). National Heart, Lung, and Blood Institute guidelines were used to assign asthma severity classification for each subject based on symptom frequency at baseline. Odds ratios (OR) and 95% Confidence Intervals (CI) were computed for the likelihood of ED use, hospitalizations, and corticosteroid use for attacks where subjects used rubbing ointments vs. albuterol as the first treatment. Logistic regression analysis controlled for asthma severity.

RESULTS: 165 subjects participated. 940 follow-up phone calls were completed over the six months period. Subjects reported on a total of 229 asthma attacks for which they used either rubbing ointments (n=34) or albuterol (n=195) as the first treatment. After controlling for baseline asthma severity, use of rubbing ointments as the first treatment for an acute asthma attack was associated with decreased likelihood of ED visit (OR= .84, 95% CI .79; .89) and systemic corticosteroid use (OR .83, 95% CI .78; .88). No significant association was found between the use of rubbing ointments and hospitalizations.

CONCLUSIONS: After controlling for asthma severity, use of rubbing ointments by adolescents as the first treatment for an acute asthma attack was associated with lower asthma morbidity. More studies are needed to determine if rubbing ointments have an efficacious role in management of adolescents with asthma.

14

Fellow

Longitudinal Studies of Inter-Alpha Inhibitor Proteins (IaIp) Levels in Septic Newborn Infants

Kultar Singh, Edward Siryaporn, Kreso Bendelja, Yow-Pin Lim, James F. Padbury, Department of Pediatrics, Women & Infants Hospital, Brown Medical School, Providence, RI; Division of Medical Oncology, Rhode Island Hospital, Brown Medical School, Providence, RI; Prothera Biologics, East Providence, RI.

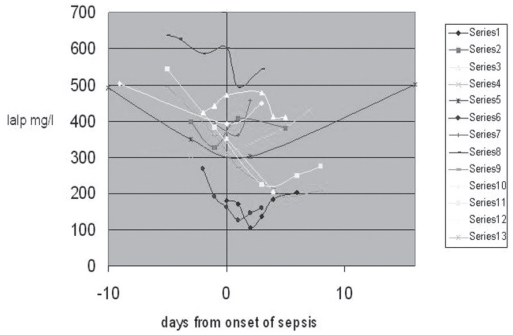
BACKGROUND: IaIp are group of serine proteases inhibitors. They are important modulators of endogenous proteases including trypsin, human leukocyte elastase, plasmin and cathepsin G. Release of endogenous proteases play an important role in inflammation, sepsis, wound healing and metastasis. Our previous study (Lim YP *et al. J Pediatr 2003;143:11-5*) demonstrated levels of IaIp(400-800 mg/l) in newborn infants comparable to those in healthy adult controls.There were similar levels in infants 24 weeks gestation up to full term. Documented sepsis was associated with a significant reduction in IaIp (613 ± 286 in control and 169 ± 126 mg/l is septic newborn infants, p<0.0001). The duration of this reduction in IaIp levels and the effects of different causes of sepsis on IaIp levels were not known.

OBJECTIVE: To measure the level of Inter-alpha Inhibitor protein (IaIp) longitudinally during the progression of sepsis in newborn infants and to examine the effects of different causes of sepsis to altertion in IaIp.

DESIGN/METHODS: We prospectively collected residual blood samples of 13 septic newborn infants before, during and after the onset of sepsis. Sepsis was defined as positive blood culture. IaIp levels were measured by a competitive ELISA.

RESULTS: In most of the newborn infants, IaIp levels decreased significantly at the time of onset of sepsis and subsequently returned to 'normal levels' following the treatment of sepsis.

CONCLUSIONS: A significant decrease of plasma IaIp levels occurs in the neonatal sepsis. There is a subsequent rise in its levels with the treatment of sepsis. This may be due to its consumption and reduced production at the time of infection. Plasma IaIp level might be clinically useful as a diagnostic marker during the therapy of neonatal sepsis.



One of the co-authors, Yow-Pin Lim, has an equity in Prothera Biologics.

15

Fellow

Diversity of the SH and G Glycoprotein Genes in Isolates of the Human Metapneumovirus

Frank P. Esper, Carla Weibel, Jeffrey S. Kahn, Pediatrics, Yale University School of Medicine, New Haven, CT; Epidemiology and Public Health, Yale University School of Medicine, New Haven, CT.

BACKGROUND: Respiratory tract infections are a major cause of morbidity and mortality worldwide. The human metapneumovirus (hMPV) is a newly discovered pathogen that has been reported worldwide and has been associated with both upper and lower respiratory tract disease. We have previously reported the clinical manifestations and epidemiology of hMPV in Connecticut. Our group and others have reported that at least 2 major genotypes of hMPV circulate during seasonal outbreaks. The genetic diversity within each genotype is poorly defined.

OBJECTIVE: To determine the genetic diversity of hMPV between and within genotypes.

DESIGN/METHODS: Respiratory specimens were collected from the Clinical Virology Laboratory at Yale-New Haven Hospital. Samples were screened for the presence of hMPV by RT-PCR using F gene primers. A complementary DNA library, using random hexamer primers, was made for each hMPV isolate identified. Amplicons spanning the SH and G genes of each isolate were sequenced. Genetic heterogeneity of the SH and G gene were established by sequence comparison.

RESULTS: Over 60 hMPV isolates were identified. Phylogenetic analysis revealed 2 major genotypes designated A and B. Two clusters were observed in the B genotype (B1 and B2). For the HMPV G gene, the majority of the nucleotide and amino acid diversity was observed in the extracellular domain of the G protein. Within the B1 and B2 clusters, amino acid identity of the hMPV G gene extracellular domain varied from 78.6% to 95.7%. The amino acid identity between B1 and B2 clusters ranged from 51.3% to 62.4%. The amino acid identity between the A and B genotypes was 22.2% to 26.5%. Less diversity in the amino acid sequence of the SH gene was observed. The amino acid identity between B1 and B2 clusters ranged from 80.5% to 86.4%. The amino acid identity between the A and B genotypes was 57.4% to 59.2%.

CONCLUSIONS: Significant genetic diversity was observed within the G genes of hMPV and to a lesser extent the SH gene. Based on G gene sequences, three distinct groups of hMPV appear to be circulating in Connecticut. Further studies are required to establish if antigenic diversity of the SH and G proteins take part in the natural history of hMPV respiratory disease.

16

Fellow

Predictors of Early Readmission for Asthma in an Inner-City Population

Marina Reznik, Philip O. Ozuah, Pediatrics, The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Asthma is one of the most frequent causes of preventable hospital readmissions among children. Factors associated with hospital readmission within 30 days of discharge for children with asthma have not been evaluated.

OBJECTIVE: To identify predictors of early readmission in children with asthma.

DESIGN/METHODS: A case-control study of a cohort of children hospitalized for asthma at a Children's Hospital between 1/1/02 and 11/6/03. Computerized health records identified children with a primary discharge diagnosis of asthma (ICD-9 493.0). Cases were defined as children with asthma readmitted with the same diagnosis within 30 days of the index admission. For each case, we identified a control which was a child hospitalized for asthma but not readmitted within 30 days. Cases and controls were matched for age, gender, ethnicity, season and year of index admission. Data were extracted from the medical records. Bivariate analyses (paired t-test, McNemar test) were performed. Logistic regression analysis determined the contribution of independent variables.

RESULTS: 100 subjects were identified (50 cases, 50 matched controls). Mean age was 6.9 yrs (SD 5.9) for cases and 6.8 yrs (SD 5.8) for controls. For both groups, 70% were male, 62% Hispanic, and 32% African American. Cases had a longer mean length of stay during the index admission than controls (3.0 days vs. 2.4 days, p=.05). Cases had a greater mean number of lifetime asthma admissions (12.2 vs 3.4, p=.005), were more likely to have been seen by a pulmonologist prior to the index admission (32% vs 10%, p=.019) and to receive a pulmonary consultation during the index admission (34% vs 8%, p=.007). Receipt of a pulmonary consultation during the index admission was found to be an independent predictor of readmission. Exposure to environmental triggers was not associated with readmission. No significant difference was found between the two groups on mean oxygen saturation at index admission or discharge, need for oxygen supplementation during the index admission, and presence of wheezing at discharge.

CONCLUSIONS: Results of this study suggest that early readmission occurs among a subset of children with greater disease severity. Receipt of pulmonary consultation, prolonged length of stay, history of multiple admissions may identify children who are more likely to be readmitted and thus, guide asthma management to enhance discharge planning, outpatient care and ultimately prevent early readmissions.

17

Fellow

Cytokine Expression in Neonatal Cord Blood in Response to Lactobacillus plantarum (Lp299v) and Staphylococcus epidermidis (S.epi)

A. M. Francesca Tatad, John Peoples, Sandy Cheung, Mirjana Nesin, Susana Cunningham-Rundles, Pediatrics, Weill Medical College of Cornell University, New York, NY.

BACKGROUND: Neonates encounter potential pathogens and normal commensal organisms which may support development of normal immune response. Antigens activate innate inflammatory responses mediated by interleukine-6 (IL-6) and IL-8. Effective immune response in adults is characterized by a predominantly T helper type 1 (Th-1). Th-1 response is positively regulated by IL-12 and negatively by IL-10.

OBJECTIVE: To examine cytokine expression in response to activation with an agent common to neonatal sepsis, S.epi, and a commensal bacteria whose early colonization is thought to provide protection against allergies to the growing child, LP299v, in order to understand signaling responses to these bacteria and their

impact on neonatal host defense.
DESIGN/METHODS: Cord blood (from seven term and three premature infants) was incubated for 4 or 18 hours without activators and with S.epi and LP299v. Cells were stained with monoclonal antibodies specific for mononuclear cells and then permeabilized and monoclonal antibodies specific for IL-8, IL-6, IL-10 and IL-12 were added. Samples were analyzed with flow cytometery for percentage of specific cells producing specific cytokines and geometric mean fluorescence of cytokine expression.
RESULTS: Intracellular cytokine production of unstimulated monocytes was significantly greater for IL-8 (p=0.02) and IL-6 (p=0.003) compared to T lymphocyte response, which was generally low at both 4 and 18hrs. In response to LP299v T lymphocyte IL-8 production was significantly higher (p=0.04) at 18hrs compared to unstimulated cells. LP299v induced strong IL-6 response in monocytes at 4 (p=0.01) and 18hrs(p=0.01). S.epi induced significant amounts of IL-10 (p=0.02) and IL-12 (p=0.04) in monocyte and a trend towards significance was seen for IL-6 responses at 4 and 18 hours. No T cell cytokine production was seen. Cord blood from premature neonates incubated for 18hrs showed a cytokine response robustly skewed towards mononuclear cells, with strong IL-6 and IL-8 production in response to both antigens.
CONCLUSIONS: These preliminary findings suggest that response to bacteria elicits specific cytokine patterns in both term and premature infants that may modulate development of the adaptive immune response. More samples are being collected to confirm these findings and elucidate if premature birth is correlated with a hyperactive immune response.

18

House Officer

Assessment of the Effectiveness of Mock Codes in Improving Residents Competency

Sujata Chakravarti, Chrysanthe Gaitatzes, Laura Dattner, Philip O. Ozuah. The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Many teaching institutions utilize mock codes to provide residents with the knowledge necessary to resuscitate and stabilize acutely ill children. However, it is not known if this method is effective in improving residents' competency in particular aspects of resuscitation, such as managing arrhythmias.
OBJECTIVE: To assess the relationship between pediatric resident attendance at mock codes and their ability to identify cardiac arrhythmias.
DESIGN/METHODS: We conducted a cross-sectional study using a convenience sample of PGY-1 and PGY-2 level residents in an ACGME accredited pediatric residency training program at a large, tertiary care children's hospital. Competency in the diagnosis of arrhythmias was assessed using an anonymous questionnaire, which displayed rhythm strips illustrating five common pediatric arrhythmias. Residents were asked to identify each rhythm. Participants provided self-reports of the number of times that they had attended mock code exercises within the current training year. Chi-square analyses tested differences in proportions of categorical variables.
RESULTS: Twenty-four residents participated. Subjects were divided into four groups based upon the number of mock codes that they had attended. Groups A, B, C, and D consisted of residents who had attended 0, 1, 2, or 3 or more mock code exercises, respectively. As shown in the Table, participation in mock codes was significantly correlated with competency in identifying 3 common arrhythmias. There was no significant difference in resident performance based upon level of training.
CONCLUSIONS: Participation in mock codes was associated with increased competency in the identification of normal sinus rhythm, supraventricular tachycardia, and ventricular fibrillation among residents. Also, with participation in mock codes, there was a trend towards increased ability to identify sinus bradycardia and ventricular tachycardia. These findings have implications for efforts aimed at improving residents' competency in pediatric resuscitation.
Percent of Residents Correctly Identifying Arrhythmia

Rhythm	Group A	Group B	Group C	Group D	P Value
Supraventricular Tachycardia	33%	63%	100%	100%	.008
Normal Sinus Rhythm	0%	50%	100%	100%	.001
Ventricular Fibrillation	67%	63%	100%	100%	.048
Sinus Bradycardia	0%	13%	33%	40%	.114
Ventricular Tachycardia	33%	75%	100%	80%	.105

19

Fellow

Ghrelin, Leptin and Growth Hormone During Growth Hormone Stimulation Testing in Children

Deborah A. Bowlby, Robert Moghaddas, Sudha Reddy, Elizabeth Wallach, Fenella Greig, Alisa Sokoloff, Michael Wajnrajch, Robert Rapaport. Division of Pediatric Endocrinology and Diabetes, Mount Sinai Medical Center, New York, NY; Weill Cornell Medical College, New York, NY; Pfizer Global Pharmaceuticals, New York, NY.
BACKGROUND: Ghrelin, a potent stimulator of growth hormone (GH), is an acylated peptide hormone of predominant gastric origin and is the endogenous ligand for the GH secretagogue receptor. Ghrelin levels are elevated in GH deficient (GHD) patients (adults), suggesting an inverse relationship between ghrelin and GH. Leptin is a peptide hormone secreted from adipose cells that acts directly on the hypothalamus to control food intake and body weight. Leptin levels are elevated in obesity and perhaps in GHD (adults). The complex interaction between GH, ghrelin and leptin has not been frequently investigated in children.
OBJECTIVE: To test the hypothesis that ghrelin and leptin levels are affected inversely by acute changes in GH.
DESIGN/METHODS: 14 patients, 12 male, (mean age, 12.1 ± 2.6 yr) (mean BMI SD, -0.26) had GH stimulation with arginine and L-dopa. Plasma levels of ghrelin and leptin were obtained by enzyme immunoassay (Pheonix Pharmaceuticals Inc., CA) after an overnight fast (T=0) and at time=30, 60, 120 and 180 minutes. GH levels were measured at the same time points by radioimmunoassay. Mann-Whitney rank analysis was used for calculating differences between groups.
RESULTS: Peak GH ranged from 2.9 to 48.0 ng/ml. No patients had other pitiatry hormone deficiencies. 6 patients (mean age 11.3 ± 2.6 yr; mean BMI SD -0.58) had peak GH response < 8 (mean 5.4 ± 2.0 ng/ml) (Group A). 8 patients (mean age 12.8 ± 2.6 yr; BMI SD -0.09) had peak GH ≥ 8 (mean 21.3 ± 14.4 ng/ml) (Group B). Mean ghrelin levels were significantly greater in Group A (1.50 + 0.72 ng/ml) than Group B (0.70 ± 0.35 ng/ml) (P=0.020). Leptin levels were not different between the groups (Group A: mean 6.3 ± 4.6 pg/ml; Group B mean 14.7 ± 23.7 pg/ml). There were no significant correlations between GH responses, ghrelin, leptin and BMI. Glucose levels remained constant thoughout the testing period. Head MRI was normal in all but 2 patients in whom GHD was suspected, they had small pituitary gland volumes.
CONCLUSIONS: Higher ghrelin levels were found in patients with lower GH responses during GH stimulation, without a significant change in leptin, suggesting a possible role for ghrelin, but not leptin, in the rapid GH response in children. Additional studies in a larger number of patients are needed to confirm these findings.

20

Fellow

Does Mode of Transport or Location of Birth Affect the Occurrence of Severe IVH in ELBW Infants?

Santosh M. Parab, Ravi Mishra, Muhammad T. Zia, Kathy Rogan, Edmund F. LaGamma. Pediatrics, Division of Newborn Medicine, Westchester Medical Center, New York Medical College, Valhalla, NY.
BACKGROUND: Antenatal maternal transport is generally preferred over postnatal transport of the neonate due to an anticipated better outcome. However, despite perinatal regionalization, a substantial number of extremely low birth weight (ELBW) infants are born in the community setting.
OBJECTIVE: To determine whether the incidence of intraventricular hemorrhage (IVH) differed at the time of first head ultrasound between inborn vs outborn infants with respect to mode of postnatal transport.
DESIGN/METHODS: Charts were reviewed from admissions between June 1998 and Dec 2002 with birth weight <1000g. Outborn infants transferred <48 hours after birth were compared to inborn infants for demographics, maternal illness, use of steroids, IVH detected by first head sonogram, metabolic derangements and mode of transport. IVH was classified according to Papille et al. A comparison of long-term neurological outcome is in progress.
RESULTS: A total of 259 infants <1000g at birth were evaluated during this review period. The higher incidence of severe IVH at the time of first head ultrasound scan (*p < 0.05) occurred in the transported vs inborn group as were fewer women treated with antepartum steroids. No significant differences were observed between helicopter vs ground transport except for a preponderance of male births.
CONCLUSIONS: Despite many obstetrical and delivery room resuscitation advances in the last 20 years, our data suggests that transport of the ELBW neonate in the *"maternal incubator"* is still the best alternative; however, the mode of transport (ground or air) did not affect outocme. It is also possible that ELBW's not transported to us were less sick. Further analyses of management approaches of care providers and how decisions about transport from our 15 hospital community network are made will help clarify the reason for this difference.

IVH in Inborn vs. Outborn ELBW Neonates

	n	Wt: Grams (mean ± SEM)	Male n (%)	C-Section n (%)	No antenatal steroids n (%)	IVH Grade1-2 n (%)	IVH Grade3-4 n (%)
Inborn	200	754 ± 10	98 (49%)	118 (59%)	33 (17%)	29 (15%)	8 (4%)
Outborn	59	772 ± 19	29 (49%)	29 (49%)	29 (49%)*	7 (12%)	9 (15%)*

IVH in Ambulance vs. Helicopter Transported ELBW Neonates

	n	Wt: Grams (mean ± SEM)	Age: Weeks (mean ± SEM)	Male n (%)	C-Section n (%)	IVH Grade 1-2 n (%)	IVH Grade3-4 n (%)
Ambulance	37	801 ± 21	25.6 ± 0.2	24 (65%)	18 (49%)	3 (8%)	5 (14%)
Helicopter	22	722 ± 33	25.7 ± 0.5	5 (23%)*	11 (50%)	4 (18%)	4 (18%)

21

Fellow

Can Tidal Volume and Flow-Loop Mechanics Identify the Ability To Survive Off-ECMO in Restrictive Lung Disease?

Abdul Haleem, Ravi Mishra, Muhammad T. Zia, Edmund F. LaGamma. Pediatrics, Division of Newborn Medicine, Westchester Medical Center - New York Medical College, Valhalla, NY.
BACKGROUND: Decisions to utlize advanced life support like ECMO involve assesment of the severity of pulmonary hypertension and the adequacy of pulmonary blood flow by ECHO & oxygenation index (OI). However, successful weaning from ECMO requires reversible parenchymal disease and a minimum lung alveolar capacity, independent of issues of lung perfusion. Either low functional residual capcity or low compliance reduce survival or "readiness to wean." While these tests require specialized equipment, bedside pulmonary mechanics allow for determination of tidal volume (TV) and dynamic compliance *continuously*. It would be important to know whether bedside parameters could be used to predict the minimal lung volume necessary to sustain life before applying or after initiating ECMO.
OBJECTIVE: To determine whether measurement of TV & dynamic compliance on-line using bedside pulmonary graphics from a conventional ventilator (VIP Bird Gold) could predict subsequent ability to wean from ECMO.
DESIGN/METHODS: Demographic data were collection from all neonates considered for or treated with ECMO at our center over the last 2 years (n= 11). OI > 30 or progression were the reasons to start ECMO. "*Bedside-TV*" was measured at the peak pressure where "*beaking*" began with a PEEP of 4 cm H_20.
RESULTS: 8 ECMO patients (2 PPHN, 2 CDH, 1 ACD, 2 MAS and 1 GBS Pneumonia) had their hospital course and pulmonary mechanics tracked. All were begun on ECMO < 72h postnatal age. Independent of ECMO, all patients with TV < 3 ml/kg died (n=3) while 2 additional deaths occurred (TV >3 ml/kg) due to a hemorrhage at a gortex graft (CDH; 9 d/o) and another due to E.coli meningitis (14 d/o).
CONCLUSIONS: These data suggest that bedside flow-loop mechanics are sufficiently robust to warrant further study using a larger sample size to validate the approach before prospectively applying the concept in order to limit care
Lung Function Indices Just Prior to ECMO

X±SEM	n	Birth Wt. (g)	pH	BE	OI	TV/Kg (ml/ccH2O/kg)	Compliance
Non-Surviors	3	3231±105	7.25±0.03	-3.3±1.8	25±6	1.8±1.0	0.14±0.11
(range)		(3080 to 3544)	(7.19 to 7.34)	(-7 to 0.8)	(19 to 31)	(0.4 to 3.8)	(0.03 to 0.25)
Survivors	5	3248±217	7.28±0.03	-2.2±2	37±5	5.3±0.8	0.27±0.05
(range)		(2230 to 3810)	(7 to 7.48)	(-12 to 2.7)	(21 to 50)	(3.4 to 7.9)	(0.19 to 0.46)
p		NS	NS	NS	NS	<0.04	NS

22

Fellow

Nitric Oxide: Friend or Foe to Pulmonary Epithelium?

Dhruti Pandya, Ioana Godi, Sonya Strassberg, Lance A. Parton. Pediatrics, New York Medical College/ Westchester Medical Center, Valhalla, NY. (Sponsored by Sergio Golombek)
BACKGROUND: Nitric oxide (NO) may have pleiotropic effects-either cytotoxic or cytoprotective-on the pulmonary milieu, depending on its concentration and interactions with other signaling messengers in this environment. The lungs of preterm infants are exposed to a relative hyperoxic environment that may be exposed to high levels of pro-inflammatory mediators, with little developmental capacity for protection. The effects of NO on pulmonary epithelium during this relative hyperoxia are poorly understood.
OBJECTIVE: To study the short-term (0-6 h) apoptotic effects of NO exposure on lung epithelial cells *in vitro* during hyperoxia.
DESIGN/METHODS: A549 cells (human adenocarcinoma cells) were treated with NO donor (DETANONOate) at concentrations from 0 mM to 1 mM, in a defined media. Apoptosis was quantitatively assessed at 0, 2, 4, and 6 h using TUNEL (Terminal deoxynucleotidyl transferase-mediated dUTP Nick End Labeling) assay; and qualitatively assessed by DNA laddering. Data for TUNEL is expressed as Mean ± SD. Significance between groups was determined by one-way ANOVA. A *P* value of 0.05 was considered statistically significant.
RESULTS: Apoptosis during Normoxia and Hyperoxia

	0 NO	0.1 NO	0.4 NO	1.0 NO
Room Air-2h	31.7 ± 14.5	39.8 ± 7.0	51.3 ± 13.6*	65.2 ± 16.1**
Hyperoxia-2h	37.3 ± 11.9	46.0 ± 8.4	56.0 ± 7.3	83.0 ± 3.2**
Room Air-4h	36.0 ± 11.5	51.0 ± 13.9	70.0 ± 1.0**	84.0 ± 3.6**
Hyperoxia-4h	35.0 ± 11.3	54.0 ± 9.1	62.0 ± 4.2*	84.0 ± 2.0**

* P value <0.05, ** P value<0.001
Accelerated apoptosis was noted with increasing concentrations of NO in the presence of both normoxia and hyperoxia. Little differences in rates of apoptosis were seen in the presence of hyperoxia, when compared to normoxia. Nearly complete apoptosis (> 90%) was observed at 6h (data not shown). Qualitative

confirmation of apoptosis was performed by DNA laddering.
CONCLUSIONS: Exposure to increasing concentrations of DETANONOate accelerated apoptosis over a period of 6 hours in this *in vitro* pneumocyte model. We speculate that this *in vitro* model may provide insights into the effects that NO may have on lung epithelium, particularly for acute lung injury.
Funded by the Children's and Women's Physicians of Westchester

23

Disparate Exposures to Allergens and Allergists for Inner-City Children With Asthma

Karen L. Warman, Ellen J. Silver. Pediatrics, AECOM/Children's Hospital at Montefiore, Bronx, NY.
BACKGROUND: The NHLBI Asthma Guidelines specifically recommend skin testing or in vitro testing for patients with persistent asthma exposed to perennial indoor allergens. Recommendations also include that people with asthma avoid exposure to inhaled allergens to which they are sensitive and to smoke.
OBJECTIVE: To describe 1) the presence of home environmental exposures to allergens/irritants in inner-city children with asthma and 2) to investigate adherence to guideline recommendations for allergy testing for children with persistent asthma seen in an inner-city, general pediatric practice.
DESIGN/METHODS: 105 children with asthma ages 5-11 were recruited 7/01 - 11/03 from an inner-city practice by physician referral, self-referral and during hospitalization. Prior to a CDC- sponsored intervention, the 37- item Children's Asthma Risk Assessment Tool© was verbally administered to parental caretakers by a trained asthma counselor. Environmental allergen exposures, smoke exposure, and the availability of allergen skin testing results were assessed by parental report. In addition, the presence of persistent asthma was determined by either physician report or parental symptom inventory.
RESULTS: Caretakers reported the presence of the following home environmental exposures: roaches (58%), visible mold on the walls (35%), ceilings (23%), and windows (15%); rugs in the child's bedroom (25%) or family room (29%); gas stove used for heating the home (23%); mice (35%), rats (3%), dogs (14%), cats (13%), hamster, guinea pig or rabbit (10%); smokers (30%) and childcare smokes (34%). Of the 105 children enrolled, only 20% had had skin testing done. Of these children, reported skin sensitizations included: dust mite (81%), mold (71%), cat (62%), roach (52%), rat (43%) and dog (29%). Of the 105 children enrolled, 85 were categorized as having persistent asthma, 6 as intermittent and data were missing for 14. Of the 85 children identified as having persistent asthma, only 20% had had skin testing. Prevalence of skin testing did not differ between children with and without persistent asthma (20% vs 17%).
CONCLUSIONS: In this sample of inner-city children, exposure to perennial indoor allergens and smoke is common. Allergen skin testing is not being performed as frequently as recommended. Interventions which increase the use of allergy testing may help in the identification of specific allergen sensitivities and encourage evidence-based modifications of the home environment.

24

Fellow

Ontogeny of Bilirubin Binding Capacity in Low Birthweight Neonates

Jesse Bender, William J. Cashore, William Oh. Neonatology, Women & Infants' Hospital, Providence, RI.
BACKGROUND: Unbound, unconjugated bilirubin (UB) is most likely the toxic fraction responsible for neonatal encephalopathy due to hyperbilirubinemia. Changes in Auditory Brainstem Evoked Response have been noted in term and preterm infants with UB > 1.0 and 0.5 μg/dl, respectively. For a given total serum bilirubin (TB), UB may vary widely. Bilirubin binding values have been described for neonates over 28 weeks gestational age (GA), but not for the earlier GA neonates who now have a relatively higher survival rate than in previous decades.
OBJECTIVE: To demonstrate in-vitro serum bilirubin binding capacity and affinity in neonates 23-30 weeks GA.
DESIGN/METHODS: Fifty neonates 23-30 weeks GA (530-1300g) have been enrolled. On the 5th day of life (DOL 5), serum TB and UB were measured with an UB-A1 analyzer (Arrows Co, Tokyo, Japan) and serum albumin with bromocresol purple. A subset of patients had repeat measurements of TB and UB at 2 weeks. Curves for Scatchard analysis were titrated by addition of bilirubin to the sera.
RESULTS: 1) At DOL 5, serum TB was 8.7 ± 2.1 mg/dl, albumin was 2.6 ± 0.4 g/dl and UB was >0.5 μg/dl in half of the sera, of which four had UB >1.0 μg/dl.
2) Upon in vitro bilirubin titration, at B:A ratio> 0.68 every serum sample had an UB in excess of 1.0 μg/dl.
3) The affinity of the primary bilirubin binding site on albumin, K_1, averaged 12.4 ± 8.29 x10^7. The slope changed at a bilirubin:albumin (B:A) molar ratio of 0.68 ± 0.20, or TB 15.4 ± 4.9 mg/dl. Second site affinity (K_2 = 1.95 ± 1.29 x 10^7) was 6-fold lower than K_1. Still weaker binding (K_3 = 7.52 ± 5.51 x 10^6) was seen at TB over 26.8 ± 6.9 mg/dl.
4) Primary site bilirubin binding capacity (BBC), estimated by K_1 intercept, occurred at B:A molar ratio of 0.85 ± 0.22.
5) BBC increases with increasing GA (r=0.52, p<0.001).
6) Same-patient sera had 4-fold higher affinity at two weeks of age.
CONCLUSIONS: Bilirubin binding appears non-saturable in neonatal sera of very low birthweight infants at B:A ratio <2.0. Progressively weaker affinities may reflect binding at primary then secondary albumin binding sites. High affinity binding occurs below a B:A ratio of 0.68, above which UB increases rapidly to potentially toxic levels. Gestational age correlates directly with BBC but not with binding affinity. Bilirubin binding affinity appears to increase with postnatal age.

25

Fellow

Nosocomial Transmission of the Human Metapneumovirus

Frank Esper, Richard A. Martinello, Derek Boucher, Carla Weibel, Jeffrey S. Kahn. Pediatrics, Yale University School of Medicine, New Haven, CT; Internal Medicine, Yale University School of Medicine, New Haven, CT; Epidemiology and Public Health, Yale University School of Medicine, New Haven, CT.
BACKGROUND: Respiratory viruses cause nearly 35% of pediatric nosocomial infections and nosocomial outbreaks of influenza, respiratory syncytial virus (RSV), parainfluenza and adenovirus have been previously reported. Human metapneumovirus (hMPV) is a recently discovered paramyxovirus causing upper and lower respiratory tract infections.
OBJECTIVE: As part of an ongoing epidemiological investigation of human respiratory viruses, we sought to determine whether there was evidence of nosocomial hMPV transmission.
DESIGN/METHODS: Patients less than 5 years-old admitted to our hospital whose nasopharyngeal (NP) specimen tested negative for RSV, influenza A and B, parainfluenza 1, 2 and 3 and adenovirus by direct immunofluorescence assay were tested for hMPV by RT-PCR. NP specimens were obtained at the discretion of the patient's clinical team. Nosocomial hMPV was defined as a patient with positive hMPV RT-PCR hospitalized greater than 96 hours before the respiratory illness.
RESULTS: From November 1, 2001 to October 31, 2002 NP specimens were collected from 668 children and hMPV was identified in 34 hospitalized patients. Five (14.7%) met the nosocomial case definition and 29 patients were considered community acquired. Analysis of the 5 nosocomial cases revealed that hMPV was possibly acquired in an intensive care unit (ICU). All 5 nosocomial hMPV patients received ICU care while only 1 of the 29 community acquired hMPV patients was exposed to the ICU. The 5 nosocomial cases were hospitalized a mean 54 days (range 20 to 196 days) prior to illness. Two nosocomial cases occurred in infants hospitalized since birth. Three nosocomial cases were cared for in a hospital ward concurrent with another hMPV patient prior to the onset of their nosocomial illness. However, no nosocomial case shared a room with another hMPV patient. Phylogenetic analysis noted no strain difference between the nosocomial and community acquired cases they were potentially exposed to and multiple strains were identified during the study period.
CONCLUSIONS: Nosocomial transmission of hMPV occurs. Nosocomial transmission occurred despite lack of direct patient-to-patient contact suggesting that; 1) healthcare workers and visitors may play a significant role in the nosocomial transmission of HMPV and 2) transmission may occur via fomites similar to RSV. Rapid hMPV diagnostic methods and interventions are needed to prevent nosocomial transmission.

26

House Officer

Does Steroid Resistance Predict Cyclosporine Resistance in Primary Focal Segmental Glomerulosclerosis?

Ibrahim F. Shatat, Noosha Baqi. Department of Pediatrics, SUNY- Downstate Medical Center, Brooklyn, NY. (Sponsored by Stephen Wadowski)
BACKGROUND: For more than 15 years Cyclosporine (CsA) has been used in the treatment of resistant Nephrotic syndrome (NS) cases. Physicians continued to use CsA to treat steroid-resistant (SR) Focal segmental golmerulosclerosis (FSGS) despite data supporting poor response in those patients.
OBJECTIVE: We intended to statistically test our observations that most steroid-resistant FSGS patients do not respond to CsA, and to compair thier reponse to children with steroid-dependent (SD) FSGS NS. This would permit targeting resistant FSGS patients in whom CsA treatment-related risks are justifiable.
DESIGN/METHODS: We reviewed the clinical and labaratory features of more than Forty SD and SR FSGS patients who received CsA treatment at our pediatric nephrology clinics over the last 15 years. Sixteen patients met the criteria; data documentation, biopsy proven FSGS diagnosis, primary FSGS cases were only included, all patients recieved 4-6 weeks of 2 mg/kg/day prednisone, followed by CsA treatment aiming at trough levels in the order of 200ng/ml.
These features (including response to steroids) at presentation and pre CsA treatment were evaluated to determine if they predict CsA responsiveness at 8-12 weeks, 22-26 weeks.
Ttwelve patients were males (75%), mean age was 8.8 years (2-16), seven patients were African-Americans (43%), six patients were Hispanic (37%), three patients (18%) had a family history of NS, Seven patients (43%) had hypertension, and 13 patients (81%) had edema on presentation.
RESULTS: Of the 16 patients, nine patients (56%) were steroid resistant; of whom seven patients (78%) were CsA resistant and two patients (22%) were CsA responsive. Seven patients (44%) were steroid dependent; all of them (100%) were CsA responsive.
Three patients had family history of FSGS, they did not respond to steroids and did not respond to CsA subsequently.
CONCLUSIONS: Our data showed that steroid resistance predicted CsA resistance (Fisher's exact test P= 0.003) in our small (n=16) primary FSGS NS pediatric patients. Further large prospective studies to test these results,and to generate selection criteria for CsA treatment in SR FSGS NS are needed.
CsA Responsiveness in relation to Response to Steroids

	Steroid Responsive	Steroid Resistant
CsA Responsive	7	2
CsA Resistant	0	7

27

House Officer

Evaluation of Pediatric Residents' Competency in Recognition of an Innocent Murmur

Sujata Chakravarti, Philip O. Ozuah. The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Heart murmurs are common findings in children and are the most frequent reason for referral to a cardiologist. Studies have demonstrated sub-optimal cardiac auscultation skills in pediatrics residents. However, the ability of residents to differentiate between innocent and common pathologic murmurs has not been examined.
OBJECTIVE: To assess pediatric residents' competency in diagnosing murmurs innocent versus pathologic murmurs.
DESIGN/METHODS: We conducted a criterion-referenced study of residents in an ACGME accredited pediatric residency training program at a tertiary care children's hospital. All participants listened to four cardiac events taken from an instructional cardiac auscultation compact disc, which contained real murmurs recorded from patients. The 4 murmurs represented conditions commonly seen in the pediatric population: ventricular septal defect, patent ductus arteriosus, atrial septal defect, and an innocent systolic ejection murmur. These murmurs served as the criterion stnadard for this study. After listening to each murmur, residents were asked to identify whether the murmur was innocent or pathologic, and if pathologic, to state the specific diagnosis. Responses were scored and differences in proportions of dichotomous varialbes were testd by chi-square analyses.
RESULTS: Forty-seven residents participated. Overall, residents demonstrated high levels of competency in the identification of pathological murmurs, including VSD (87% correct), PDA (82% correct), and ASD (63% correct). In contrast only 48% of residents correctly identified an innocent systolic ejection murmur. Residents were less competent at correctly identifying the diagnosis of pathological murmurs: VSD (62% correct), PDA (47% correct), and ASD (53% correct). There was no significant difference in performance of the residents by level of postgraduate training.
CONCLUSIONS: In this study, residents showed high levels of competency in recognizing pathologic murmurs to be pathologic. However, their ability to correctly classify an innocent murmur was suboptimal. Given that innocent murmurs are the most common reason for referral to cardiology, these findings have implications for efforts aimed at improving resident physical diagnostic skills, as well as for efforts aimed at improving utilization of medical resources.

28

Residency Applicant Love Letters...What Do They Really Mean?

Catherine C. Skae, Marina Reznik, Philip O. Ozuah. Pediatrics, The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: The NRMP sets guidelines regarding residency program and applicant conduct and communication during the Residency Match process. At our program, one area of debate throughout the years has been how to interpret and whether to respond to "Thank You" notes written by applicants.
OBJECTIVE: To analyze Thank You notes received at one residency program.
DESIGN/METHODS: We conducted a descriptive study of Thank You notes were collected over the course of the 2002-3 recruitment season. These notes were sent to the Program Directors, Interviewers, Chairman, and/or Residency Program Coordinator. Descriptive statistics were performed.
RESULTS: A total of 262 thank you notes were analyzed. 119 were either electronic or computer generated, while 143 were hand written. There no differences in content between these two forms of letters. 65 (25%) mentioned the phrases regarding "ranking at the top of the list". 8% of all applicants said they would rank us highly but then chose to match to other programs. Overall, 6% of all applicants used the phrase and matched at our program. 61% of all letters came to the program director.
CONCLUSIONS: Applicant Thank You notes do not necessarily mean what they say. Program directors should not bank on matching applicants who express a "Love" for their programs.

29 House Officer

Parental Attitudes to Inhaled Corticosteroid Use for Asthma

Anne Gordon, Valerie Lewis, Katherine O'Connor, Kristen Wade, Marina Reznik, Philip O. Ozuah. The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Of all patients with persistent asthma, only 26% report current use of anti-inflammatory medicine. Parental concerns may be a barrier to use of inhaled corticosteroids (ICS). No prior U.S. studies have examined the knowledge and attitudes of inner city parents about ICS use for asthma.

OBJECTIVE: To examine parental knowledge and attitudes to ICS use for asthma among an inner city population

DESIGN/METHODS: We employed a cross-sectional study of a convenience sample of parents at an inner-city clinic in the Bronx, NY. First, we conducted an open-ended interview with 24 parents to elicit areas of concern about ICS. Then we developed a questionnaire using the information gathered from the interviews. Parents in the waiting room were approached and surveyed regarding their knowledge, attitudes and barriers to the use of ICS. Chi-square test was used to compare categorical variables. We compared responses among 3 groups: 1) all participants, 2) those experienced with asthma and 3) those experienced with ICS.

RESULTS: 151 subjects participated, of whom 86% were female, 50 % African American, 45% Hispanic, and the mean age was 35 yrs. Overall 63% of respondents believed that ICS were effective in controlling asthma and 56% believed that ICS lead to fewer emergency department visits. Subjects who had used ICS were more likely to believe that it was effective (88% vs. 63%, $p < .01$). However, 85% believed that ICS produced "bad side effects"; 83% said it made children "hyperactive", and 81% believe that ICS led to weight gain. Patients who had used ICS were more likely to report fears of adverse effects from ICS as compared to others (27% vs. 15%, $p < .05$).

CONCLUSIONS: The results of this study suggest that parents, despite understanding how to administer ICS and believing that ICS work to control asthma, are still worried about the side effects of ICS. Lack of knowledge does not appear to be a major barrier. The results of this study provide useful information for addressing barriers to ICS use in this population. Future efforts may be targeted at parental fears and misconceptions about ICS use.

30 Fellow

17-Alpha-Hydroxyprogesterone as Placental Immunoregulator: From Cell to Potential Clinical Benefit

Lea Bonifacio, Jill Schak, Eric Forman, Suli Han, Sherif Mishriky, Barry Weinberger, Nazeeh Hanna. Pediatrics, UMDNJ- Robert Wood Johnson Medical School, New Brunswick, NJ.

BACKGROUND: Preterm labor is the leading cause of neonatal morbidity and mortality. A recent study demonstrated the possible role of 17-alpha-hydroxyprogesterone in treatment of premature labor although the exact mechanism of action is not fully understood. The pro-inflammatory cytokine interleukin IL-1 has been shown to stimulate the production of prostaglandins (PG) in gestational tissues. Increased PG synthesis is considered a key step in the initiation of labor both at term and preterm.

OBJECTIVE: This study was designed to investigate the effect of 17-alpha-hydroxyprogesterone on the pro-inflammatory mediators in the placenta.

DESIGN/METHODS: Cultured placental explants and placental macrophages from term pregnancies after labor were treated with 17-alpha-hydroxyprogesterone with and without LPS for 48 hours. Production of proinflammatory mediators: IL-1 alpha, IL-1 beta, macrophage inflammatory protein-1 alpha (MIP1-alpha) and MIP1-beta were quantified in the supernatants by ELISA. We also investigated the effects of 17-alpha-hydroxyprogesterone on isolated placental macrophages (Hofbauer cells) since these cells are the main source of COX-2 production, the rate limiting enzyme for production of PGE2. Using flow cytometry, we investigated the possible effect of 17-alpha-hydroxyprogesterone on placental macrophage cell survival.

RESULTS: Using ELISA, 17-alpha-hydroxyprogesterone significantly down regulated the production of proinflammatory mediators: IL-1 alpha, IL-1 beta, MIP1-alpha and MIP1-beta in placental explants. However, in placental macrophages, only IL-1 alpha production was decreased in response to 17-alpha-hydroxyprogesterone treatment suggesting that the interactions between different cell types in the placenta play an important role in modulating the response to exogenous signals. Interestingly, treating placental macrophages with 17-alpha-hydroxyprogesterone increased cell survival by decreasing placental macrophage apoptosis as shown by flow cytometry.

CONCLUSIONS: 17-alpha-hydroxyprogesterone effectiveness in preventing preterm labor may be related to its ability to alter the inflammatory milieu in the placenta as well as its protective effect of placental macrophages from apoptotic cell death.

Cardiology I
Platform Session

Saturday, March 27 8:30am–10:00am Putnam

31 Presentation Time 8:30 AM

Beta-Adrenergic Receptor Subtype Densities in Preterm Newborn, Term Newborn, and Adult Baboon Myocardium

David P. Treece. Pediatrics, Norwalk Hospital, Norwalk, CT. (Sponsored by Mitchell J. Kresch)

BACKGROUND: To survive preterm birth, infants must quickly achieve and sustain near maximal cardiac output. The β-adrenergic-adenylate cyclase system plays a major role in directing this vital increase in performance.

OBJECTIVE: This work tests the hypothesis that there are developmental changes in myocardial β-adrenergic receptors.

DESIGN/METHODS: This study evaluates the ontogeny of myocardial β-adrenergic receptor number, subtype, and affinity in a surviving primate model of prematurity. Myocardial tissue from 76 baboons (*papio cynocephalus*) was included in the evaluation. 18 baboons were born at term gestation, the remaining 58 born prematurely at 78% of term. Preterm animals were treated with mechanical ventilation and typical neonatal support prior to tissue collection at various time points up to 16 days of age. Term newborn animals were studied up to 4 days of age with adult animals included as a term animal group. Ventricular tissue from each animal was homogenized and purified to obtain both surface and intracellular membrane fractions. Receptor number and affinity were determined utilizing the β-adrenergic antagonist (-)iodocyanopindolol I 125 (ICYP). Receptor subtype analysis utilized ICYP and the subtype selective antagonists ICI89406 (β-1) and ICI118551 (β-2).

RESULTS: Surface membrane receptor density was significantly less in preterm (**P**) vs. term (**T**) animal groups (**P-0d**: 67.3 ± 21.9; **P-2-4d**: 57.2 ± 29.0; **P-16d**: 70.5 ± 15.8// **T-0d**: 139.6 ± 56.2; **T-2-4d**: 283.9 ± 193.3; **T-Adult**: 147.9 ± 43.4 fmol/g heart; $p<0.000001$ **P vs. T**). Similar findings were noted in the intracellular membrane fractions. β-1 to β-2 ratios from data combining membrane fraction results showed a predominance of β-2 receptors at birth, greater in the preterm animals, with subsequent increase in β-1 receptor percent (**P-0d**: 19:81 ± 14.2; **P-2-4d**: 45:55 ± 7.9; **P-16d**: 42:58 ± 11.7// **T-0d**: 35:65 ± 10.1; **T-2-4d**: 70:30 ± 5.2; **T-Adult**: 61:39 ± 6.0). Receptor affinity for radioligand (Kd) was not significantly different among the preterm and term groups.

CONCLUSIONS: Total β-adrenergic receptors are substantially reduced in preterm vs. term/adult baboons hearts. At birth, β-2 receptors dominate in both preterm and term animals. With age β-1 receptor presence increases, markedly in term, modestly in preterm baboons. In preterm baboons, β-2 receptors continue to dominate the β-adrenergic profile for the first two weeks of life. Receptor affinity was not significantly different among the preterm and term groups.

32 Presentation Time 8:45 AM Fellow

Selective Upregulation of Activator Protein-1 (AP-1) in Heart Failure Due to Chronic Volume Overload in Rats

Grace A. Freire, Catherina B. Ocampo, Yianna Kazakos, Madhu Gupta. Pediatric Cardiology, The Heart Institute for Children, Hope Childrens Hospital, Oak Lawn, IL; Physiology and Biophysics, University of Illinois, Chicago, IL. (Sponsored by Rene A. Arcilla)

BACKGROUND: Heart failure (HF) is the clinical end-stage of acquired and congenital cardiac disease. It is associated with specific changes in gene expression depending on underlying etiology. Reprogramming of gene expression involves changes in the DNA binding activity of specific transcription factors (TFs). Individual analysis of TFs have shown changes in DNA binding activity of NFATc, MEF2-C, P53, RXR, Egr-1, STAT1,5, Smad2,4, GATA4, and simultaneous activation of AP-1 and NFKB, in ischemic cardiomyopathy, dilated cardiomyopathy and in heart failure. Their status in HF from volume overload (VO) has not been examined.

OBJECTIVE: To determine molecular basis of VO induced HF by examining simultaneous changes in DNA binding activity of 54 different TFs, utilizing transcription factor microarray.

DESIGN/METHODS: VO was induced in male Sprague Dawley rats (300 ± 20 gm) by aorto-caval shunt for 6 wks and 10 wks. Cardiac function was assessed by echocardiography (echo) and heart/body wt and liver/body wt ratios. At 10 wks, cardiac nuclear extract was prepared from sham and VO hearts, analyzed by Panomics TF microarray, where consensus binding sequences of 54 TFs are spotted in duplicates at different dilutions. After nuclear protein/DNA interaction, the bound DNA was isolated, purified, identified by Southern analysis and quantified by densitometry. Results were confirmed by mobility gel shift assay.

RESULTS: In VO, echo showed increased LVEDd at 6 wks (43%) and 10 wks (67%) ($p<.001$), LV mass increased 68% at 6 wks and 91% at 10 wks($p<.001$), Mass/volume ratio declined by 37% at 6 wks ($p<.001$) and by 43% at 10 wks ($p<.002$), indicating predominant LV dilatation, Fractional shortening remained in normal range but the heart/body wt ratio was increased by 87% ($p <.005$), and liver/body wt ratio by 64% ($p <.01$) at 10 wks of VO. Nuclear protein/DNA array analysis of 10 wk VO hearts demonstrated increased expression of AP-1 and Smad 4 and decreased expression of GRE, NFATc, P53, RXR, STAT1 and TR, but no changes in Egr-1, GATA4 and NFKB.

CONCLUSIONS: Unlike cardiomyopathies, VO induced HF is predominantly associated with increased activity of AP-1 TF which does not accompany simultaneous activation of NFKB, Egr-1 and GATA-4, indicating a differential response at the molecular level that may account for specific differences in gene expression. (Supported by a grant from Med-Fund of Christ Hospital).

33 Presentation Time 9:00 AM

Bedside Measurement of B-Type Natriuretic Peptide as a Marker for Patent Ductus Arteriosus in Preterm Infants

Patrick A. Flynn, Ralph L. da Graca, Mirjana Nesin, Rubin S. Cooper, Peter A. M. Auld, Charles S. Kleinman. Pediatric Cardiology, Weill Medical College of Cornell University, New York, NY; Perinatology, Weill Medical College of Cornell University, New York, NY; Pediatric Cardiology, Columbia University College of Physicians and Surgeons, New York, NY; Pediatric Cardiology, Columbia University College of Physicians and Surgeons, New York, NY.

BACKGROUND: Patent ductus arteriosus (PDA) is a significant co-morbidity in premature neonates. Echocardiography (ECHO) is employed to assess the presence and magnitude of PDA in these patients. ECHO is costly, may be invasive to ill newborns and has limited availability in many centers. B-Type Natriuretic Protein (BNP) is an established marker for congestive heart failure in adults. BNP can be rapidly measured by a commercially-available bedside monitor using 0.25 cc of whole blood.

OBJECTIVE: To determine usefulness of bedside BNP to predict magnitude of PDA in preterm neonates.

DESIGN/METHODS: A prospective, blinded, observational study was performed on all preterm infants admitted to the Neonatal Intensive Care Unit (NICU) during a 5 month period. Infants with congenital heart disease besides PDA were excluded. ECHO and BNP were performed at 4-5 day intervals on each infant from enrollment until documented closure of PDA. Magnitude of PDA was assessed by grades of: diameter relative to the pulmonary artery branches (PDA/PAB), ratio of the diameter of the left atrium to aorta (LA:AO), ratio of the left ventricle to aorta (LVED:AO), diastolic reversal of flow in the descending aorta (DAO) and superior mesenteric artery (SMA) and overall magnitude (PDA). Measures of systolic (fractional shortening, FS), diastolic (transmitral flow, E:A) and combined (Tei Index) LV function were recorded. Variables were compared to BNP using Spearman Correlation Coefficients(r).

RESULTS: A total of 79 echocardiograms were performed in 18 preterm infants (gestational age 25-35 wks, birth weight 715 to 2200 g) from age 0 to 72 days. BNP correlated with PDA ($r=.6798, p<.0001$), PDA/PAB ($r=.5377, p<.0001$), LA:AO ($r=.3787, p=.0012$), DAO ($r=.5388, p<.0001$), and SMA ($r=.4870, p=.0003$). BNP >300 pg/ml (n=22) corresponded to a moderate or large PDA (PPV 95%, NPV 67%, Sensitivity 53%, Specificity 97%). The patient with BNP>300 and no PDA had decreased LV function.

CONCLUSIONS: Bedside quantification of BNP is a useful screening tool for hemodynamically significant PDA in preterm neonates. BNP > 300 pg/ml predicts presence of a moderate or large PDA. Routine NICU use of BNP identifies preterm infants who require cardiac evaluation. BNP may be used to follow ductal trend, resulting in fewer echocardiograms, thus lowering health care cost.

34 Presentation Time 9:15 AM Fellow

The Use of the V to HRA Interval To Predict Sidedness of an Accessory Pathway in Children With SVT

Christa L. Miliaresis, Christopher Snyder. Pediatric Cardiology, Yale New Haven Hospital, New Haven, CT. (Sponsored by Marie Egan)

BACKGROUND: SVT is a common occurrence in pediatric patients. Due to the safety and efficacy of radiofrequency ablation (RFA) and in an effort to avoid side-effects of medications, many patients elect RFA. During routine RFA, catheters (ventricle, V, coronary sinus, CS, high right atrium, HRA and his, H) are placed to determine the properties and sidedness of the accessory pathway, right versus left.

OBJECTIVE: The hypothesis is that the V to HRA interval is less for right-sided pathways than for left-sided pathways. If true, then electrophysiology studies could be performed without a CS catheter and save vascular access.

DESIGN/METHODS: The study was performed using data aquired from a single center tertiary care, university-affiliated children's hospital. We retrospectively collected data from all patients who underwent RFA for their SVT due to an accessory pathway between December 19, 2000 and November 5, 2003. Patients ranged in age from 4 to 21 years. Data collected includes demographic information, intracardiac timing intervals, type of SVT and sidedness of the accessory pathway.

RESULTS: We studied 27 patients who had an accessory pathway. Of these 27, 16 were found to have right-sided pathways and 11 were found to have left-sided pathways. Comparisons between right and left pathways revealed that all right-sided pathways (16/16) had a V to HRA interval less than 160 ms (range: 6-159 ms) with a sensitivity of 100% and a specificity of 89%. The average cycle length of their tachycardia

for right-sided pathways was 338 ms (range: 231-453). 82% of left-sided pathways (9/11) had a V to HRA greater than 160 ms (range 119-180 ms), with a sensitivity of 82% and a specificity of 100%. The average cycle length of left-sided pathways was 320 ms (236-410 ms).
CONCLUSIONS: The V to HRA interval is a useful predictor of sidedness of the accessory pathway in SVT in children. A V to HRA interval less than 160 ms is 100% sensitive and 89% specific for right sided pathways. EP studies where the V to HRA interval in SVT is less than 160 ms may not require a CS catheter.

35 Presentation Time 9:45 AM — Fellow

Predictors of High Cost Admissions for Congenital Heart Surgery

Jean A. Connor, Kimberlee Gauvreau, Kathy J. Jenkins. Pediatric Cardiology, Childrens Hospital Boston, Boston, MA.
BACKGROUND: Although survival after congenital heart surgery has improved, little is known regarding predictors of high cost admissions.
OBJECTIVE: To identify patient, institutional, and regional factors associated with high cost admissions for congenital heart surgery.
DESIGN/METHODS: We used hospital discharge data from the Healthcare Cost and Utilization Project (HCUP) Kid's Inpatient Database (KID) year 2000(data from 27 states). Cases of congenital heart surgery < 18 years of age were identified using ICD-9-CM codes. High cost admissions were defined as those in the highest decile for total hospital charges. Univariate and multivariate analyses with and without patients who died were used to determine demographic and hospital predictors for an increased frequency of high cost cases. Case mix severity was approximated using RACHS-1 risk groups. Regional and state differences were also examined.
RESULTS: Among 10,569 cases of congenital heart surgery identified, median hospital charges were $53,828. Statewide differences in the number of high cost admissions were present; CA, CO, FL, HI, PA and TX had more high cost cases and ME and SC had fewer. Subsequent analyses were performed adjusting for baseline state effects. Multivariate analyses with and without patients who died using generalized estimating equations revealed RACHS-1 risk category (OR 1.69-14.7), age (OR 3.9), prematurity (OR 4.7), the presence of other major non-cardiac structural anomalies (OR 2.5), Medicaid insurance (OR 1.47) and admission during a weekend (OR 1.64) to be independent predictors of a higher frequency of high cost cases ($p<0.05$). Although some institutional differences were noted in univariate analyses, bedsize, teaching and children's hospital status, hospital ownership, and hospital volume of cardiac cases were not independently associated with greater numbers of high cost admissions.
CONCLUSIONS: States varied in the frequency of high cost admissions for congenital heart surgery. Patients with greater disease complexity, younger age, prematurity, other anomalies, Medicaid and admitted during a weekend were more likely to result in high cost. Institutions of various types did not differ in frequency of high cost admissions, regardless of children's hospital or teaching status.

36 Presentation Time 9:30 AM — Fellow

Short-Term Surgical Outcomes in Adults With Congenital Cardiac Anomalies

Bevin Weeks, Gary S. Kopf, Christopher S. Snyder. Department of Pediatrics, Yale University School of Medicine, New Haven, CT; Department of Surgery, Yale University School of Medicine, New Haven, CT. (Sponsored by Clifford W. Bogue)
BACKGROUND: Adults with congenital cardiac anomalies (CCA) needing surgical intervention represent a challenging and growing segment of the population. As these patients live longer and require additional operative procedures, physicians and surgeons increasingly are required to address the issue of surgical mortality in a unique and aging population.
OBJECTIVE: The purpose of the present study is to review short-term (≤30 days) outcomes in adult patients undergoing surgical intervention for CCA at our institution.
DESIGN/METHODS: Patients 18 years of age and older who underwent surgical repair of CCA at Yale-New Haven Hospital from 9/98 through 8/03 were identified using the congenital cardiac surgery database. Cardiopulmonary bypass pump sheets and cardiothoracic surgery clinic follow-up appointments were reviewed. Data recorded included patients' age, anatomy, operation, cardiopulmonary bypass and aortic cross-clamp times, survival at 30 days post-op, and cause of death.
RESULTS: Ninety-one patients had 97 surgeries. The most common procedures included atrial septal defect closure (35), aortic (14) and pulmonary (19) valve/conduit replacement, ventricular septal defect repair (9), pacemaker generator/lead insertions (17), and replacement of Fontan circuit (6). Thirty day follow-up information was available for 85 patients. One death was reported as a complication of post-operative bleeding following aortic replacement and a second death occurred due to hypotensive shock following Fontan replacement. Surgical mortality, 2.4% in adult patients, is comparable to overall mortality, 2.5%, in patients undergoing surgery (p=ns).
CONCLUSIONS: The increasing prevalence of adults with CCA presents a challenge to the physician and surgeon. Our experience has led us to anticipate positive short-term outcomes for those individuals presenting for surgery. As the incidence of adults undergoing initial or subsequent repair or palliation of CCA continues to increase we expect a mortality rate similar to overall mortality rate for all patients undergoing cardiac surgery.

Developmental Biology Platform Session

Saturday, March 27 8:30am–10:45am Winthrop A-B

37 Presentation Time 8:30 AM

Production, Activation and Signaling of TGF-b During Lung Type II Cell Maturation

Theresa M. McDevitt, Linda W. Gonzales, Rashmin C. Savani, Philip L. Ballard. Neonatology, University of Pennsylvania, Children's Hospital of Philadelphia, Philadelphia, PA.
BACKGROUND: TGF-β is a multifunctional growth factor that is secreted as an inactive latent complex and requires activation to elicit its biological effects. TGF-β has been implicated in fetal lung development and disease. In fetal lung explants, TGF-β inhibits hormone-induced expression of surfactant proteins, phospholipid synthesis and lamellar body formation. However, the role of endogenous TGF-β activity in epithelial cell differentiation is unclear.
OBJECTIVE: We hypothesized that endogenous TGF-β is an autocrine negative modulator of type II cell differentiation and that blockade of endogenous TGF-β signaling would promote epithelial cell maturation.
DESIGN/METHODS: Epithelial cells isolated from human fetal lung were cultured for 2-4 days in serum-free medium without hormones (control) or containing dexamethasone (dex 10nM), cAMP (0.1mM) or dex + cAMP (DCI). TGF-β content was determined using the mink lung epithelial cell (MLEC) bioassay. The role of the β6 integrin subunit in TGF-β activation was determined by co-culturing lung epithelial cells with MLEC in the absence or presence of a specific β6-blocking antibody. For TGF-β blocking studies, epithelial cells were cultured for 2-3 days in the absence or presence of specific blocking antibodies to TGF-β (anti-PAN-TGF-β and anti-TGF-β receptor II) with isotype specific IgG as controls. SP-B mRNA was quantitated by dot blot analysis.
RESULTS: Cells produced TGF-β, which was predominately secreted in the latent form (75 %). Epithelial cells cultured with a combination of hormones (DCI) or dex alone demonstrated a 75% decrease in total TGF-β content compared to control cells (no hormones) while cAMP alone caused a 15% decrease (n=2). TGF-β activation was significantly inhibited in cells that were co-cultured with the anti-β6 antibody as demonstrated by a 50% reduction in luciferase activity (fold-increase control 11.5 ± 1.5 vs anti-β6 5.7 ± .25, $p< 0.005$, n=3). TGF-β blockade in cells cultured for 2-3 days with anti-TGF-β blocking antibodies in the absence of hormones had increased SP-B mRNA content (2.8-fold, $p<0.05$ vs control, n= 3).
CONCLUSIONS: Expression of TGF-β by human fetal lung epithelial cells is largely in the latent form, is inhibited by glucocorticoids, and is activated in part via the β6 integrin. We speculate that decreased TGF-β production and signaling contributes to epithelial cell maturation by alleviating TGF-β repression of key target genes such as SP-B.

38 Presentation Time 8:45 AM

Role of Thyroid Transcription Factor (TTF-1) in SP-B Expression During Differentiation of Human Fetal Lung Type II Cells

Venkat Kolla, Linda W. Gonzales, Ping Wang, Sree Angampalli, Philip L. Ballard. Neonatology, The Children's Hospital of Philadelphia, Philadelphia, PA; School of Medicine, The University of Pennsylvania, Philadelphia, PA.
BACKGROUND: Thyroid transcription factor-1 (TTF-1, product of the Nkx2.1 gene) is essential for both early lung morphogenesis and *in vitro* surfactant protein (SP) expression by type II epithelial cells. We previously described induction of TTF-1 by hormone treatment of fetal lung epithelial cells, preceeding the increase in surfactant protein expression.
OBJECTIVE: To further characterize the role of TTF-1 in expression of SP-B in differentiating human fetal lung type II cells.
DESIGN/METHODS: Epithelial cells from 14-20 wk gestation human fetal lung were isolated and cultured for up to 7 days in serum-free Waymouth's media alone or with DCI (dexamethasone,10 nM, + 0.1 mM 8-Br-cAMP and isobutylmethylxanthine) to induce type II cell differentiation. Some cells were transduced with adenovirus (1-20 pfu/cell) expressing either the long (CMV-5E) or short (CMV-12A2) isoform of TTF-1 or were transfected with anti-TTF-1 small inhibitory (si)RNA oligos (5 μg/35 mm dish, $1x10^6$ cells). Gene expression was analyzed by semiquantitative RT-PCR, immunohistochemistry and Western blot analysis.
RESULTS: To examine the effect of increased TTF-1 in the absence of hormone treatment, we transduced cells with adenovirus expressing TTF-1. Both isoforms of TTF-1 resulted in nuclear localization of TTF-1 immunoreactivity and increased nuclear protein content (5 to 20-fold) by immunoblot analysis. Expression of recombinant TTF-1 in control, dexamethasone-treated and cAMP-treated cells did not significantly increase either SP-B mRNA or protein content vs control. To inhibit TTF-1 expression, we used antisense RNA interference (siRNA) strategy, transfecting each of 4 different oligos into cells prior to addition of DCI. At 72 h, expression of TTF-1 mRNA was inhibited >75% by this strategy, and TTF-1 protein was inhibited 70% . Similarly, SP-B mRNA was inhibited 75% and SP-B protein (8 kDa) was inhibited ~90%. Expression of GAPDH and β-actin were unaffected.
CONCLUSIONS: We conclude that TTF-1 is required but not sufficient for induction of SP-B during differentiation of human type II cells. Other early responding factors are likely involved in transcriptional regulation of SP-B as well as other TTF-1 target genes.
Funded by NIH HL56401, P01 HL19737

39 Presentation Time 9:00 AM

Hop, a New Target Gene for Thyroid Transcription Factor (TTF-1) in Fetal Lung Epithelial Cells

Linda W. Gonzales, Venkatadri Kolla, Kelly C. Wade, Ping Wang, Sreedevi Angampalli, Jonathan A. Epstein, Philip L. Ballard. Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Medicine, University of Pennsylvania, Philadelphia, PA.
BACKGROUND: Homeodomain-only protein (Hop) is a non-DNA binding protein initially identified as an inhibitory regulator of cardiac-restricted genes (*Cell* 110:713, 2002). Hop is a down-stream target of Nkx2.5, which is related to Nkx2.1 (TTF-1) that is critical for surfactant protein expression in lung type II cells.
OBJECTIVE: To determine expression and regulation of Hop in fetal lung.
DESIGN/METHODS: Isolated epithelial cells were prepared from 14-18 wk gestation human fetal lung and cultured for up to 7 days in serum-free medium alone (control) or with dexamethasone (10 nM), CI [8-Br-cAMP (0.1 mM) + isobutylmethylxanthine (0.1 mM)], or all 3 agents (DCI) present for the final 72 h. This treatment causes precocious differentiation of type II cells. Some cells were transduced with adenovirus expressing TTF-1 (either the 12A2 or 5E isoforms with CMV promoter) at concentrations of 1-20 pfu/cell. Gene expression was studied in lung cells by DNA microarray analysis (Affymetrix), immunoblotting, immunohistochemistry, and in fetal mouse lung by in situ hybridization.
RESULTS: In initial microarray analyses of DCI-treated cells, Hop was identified as an early responding gene with mRNA content induced 17-fold at 72 h (mean, n=3). By Western analysis, Hop content of cell cytoplasm increased linearly between 2 h and 24-48 h of DCI exposure, with a 14±3-fold increase vs control (n=3) after 72 h. Immunostaining of DCI-treated fetal lung explants with anti-Hop antibody showed perinuclear localization, primarily in epithelial cells. Hop was also identified by in situ hybridization in airway epithelium of 16.5 d gestation mouse lung and signal intensity increased during fetal development. To examine the role of TTF-1 in Hop expression, cells were transduced with adenovirus expressing either the 12A2 or 5E isoforms of TTF-1 and then cultured 4 d in control medium (without hormones). Hop expression was induced by both forms of recombinant TTF-1 in a dose-dependent manner (maximal induction 13-fold vs control).
CONCLUSIONS: We conclude that Hop is upregulated during lung type II cell differentiation both *in vitro* and *in vivo*, likely secondary to increased TTF-1 enhancer activity. We speculate that Hop participates in differentiation of type II cells through inhibitory effects on yet unidentified transcriptional regulators.

40 Presentation Time 9:30 AM — Fellow

ErbB Receptor Heterodimerization in Fetal Rat Lung Epithelial Type II Cells and Fibroblasts

Washa Liu, Sandy Murray, Heber C. Nielsen, Christiane E. L. Dammann. Newborn Medicine, Floating Hospital at Tufts-NEMC, Boston, MA; Pediatrics, Hannover Medical School, Hannover, Germany.
BACKGROUND: The four ErbB receptors (ErbB1, ErbB2, ErbB3 and ErbB4) form homo- and heterodimers in response to ligands. ErbB heterodimerization expands signaling potential and diversity causing different biological responses. ErbB2 is the preferred heterodimer partner for the other ErbB receptors in tumor cell lines. Despite the importance of ErbB signaling in development (CNS, heart, lung) little is known about heterodimer formation in primary non-tumor cells. We are studying ErbB receptors in cell-cell communication during fetal lung development. We showed that the four ErbB receptors are expressed in alveolar epithelial type II cells and fibroblasts, affect proliferation and differentiation, and differ in phosphorylation and cellular response after treatment with different ligands, emphasizing the importance of understanding ErbB receptor heterodimerization in fetal lung development.
OBJECTIVE: We hypothesized that ErbB receptor ligands (EGF, TGFα, neuregulin (NRG)) elicit cell- and ligand-specific heterodimers in fetal lung type II cells and fibroblasts.
DESIGN/METHODS: Type II cells and fibroblasts were isolated from day 19 fetal rats, grown to confluence, serum starved, then stimulated 5 min with EGF (100ng/ml), TGFα (100ng/ml), or NRG (33nM). Cell lysates

were co-immunoprecipitated (Co-IP) to bring down receptor dimers and separated by SDS-PAGE. Blots were probed with anti-phosphotyrosine and ErbB receptor antibodies.
RESULTS: In fetal lung fibroblasts ErbB1 and ErbB2 Co-IP revealed dimers with ErbB4 in response to EGF and TGFα. For ErbB3 Co-IP, ErbB4 was the major dimer partner after NRG and TGFα stimulation. ErbB4 Co-IP did not show dimers. In contrast, in fetal type II cells ErbB1 Co-IP showed dimers with ErbB2 and ErbB4 and ErbB3 Co-IP showed dimers with ErbB4 after stimulation with EGF and TGFα. ErbB2 Co-IP showed ErbB4 dimers and ErbB4 Co-IP showed only ErbB1 dimers in response to all three ligands. Receptor tyrosine phosphorylation correlated with dimerization findings.
CONCLUSIONS: ErbB4 is a major heterodimer partner in fetal lung fibroblasts and type II cells. Type II cells also express ErbB2 heterodimers. Responses to EGF, TGFα, and NRG support the concept of signal diversification through ErbB heterodimers. We speculate that ErbB4 heterodimers are important in fetal lung cell-cell communication. Supported by NIH HL37930, HL04436, Peabody Foundation, and Charles Hood Foundation.

41 Presentation Time 9:45 AM

Presence of Gamma-Interferon-Inducible Lysosomal Thiol Reductase (GILT) in Human Alveolar Type II Cells

Sabrina McGary, Emily Fischer, Amana Akhtar, Peggy Zhang, Susan Guttentag, Dept of Pediatrics, Univ of Penn School of Medicine, Philadelphia, PA.
BACKGROUND: The thiol reductase GILT functions within the late endosomes and lysosomes of antigen presenting cells to catalyze the reduction of disulfide bonds in foreign peptides. Previous works demonstrated GILT expression in lung, yet its presence was attributed to macrophage expression (Science, 294:1361, 2001). Limited evidence suggests that type II pneumocytes (T2) may participate in antigen presentation and regulation of T-cell activation (J Investig Med 48:66, 2000).
OBJECTIVE: We therefore hypothesized GILT expression to be specific to human T2, localizing to late endosomes and lamellar bodies (LB).
DESIGN/METHODS: To examine GILT expression in human lung, we used adult lung tissue and bronchoalveolar lavage, second trimester fetal lung tissue, hormone-induced fetal lung explants and fetal lung epithelial cells differentiated in vitro using 10nM dexamethasone, 0.1mM 8-Br-cAMP, and 0.1 mM isobutylmethylxanthine (AJP Lung, 283:L940, 2002).
Funded by NIH HL59959
RESULTS: Immunoblotting demonstrated the presence of 30 kDa (mature) GILT in bronchoalveolar lavage and adult lung tissue. Mature GILT was detected in fetal lung tissue, increasing from 12-32 wk of human gestation and reaching maximal levels in adult lung. Immunostaining of adult lung confirmed GILT in alveolar macrophages. However, GILT was also seen in T2, with a similar alveolar distribution as SP-B. Immunofluorescence studies on isolated T2 demonstrated colocalization of GILT with LAMP-1, a LB and multivesicular body marker.
CONCLUSIONS: The developmental onset of GILT production suggests that this protease is a novel, non-surfactant related biomarker of T2 cells. Furthermore, GILT expression in T2 provides additional supporting evidence that T2 may assist in antigen presentation within the alveolar space of developing and mature lung.

42 Presentation Time 10:00 AM Fellow

Structure:Function Correlations During Hormonal Regulation of Alveolarization

Samuel J. Garber, Joseph P. Foley, Rashmin C. Savani, Division of Neonatology, Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA.
BACKGROUND: Bronchopulmonary dysplasia (BPD) is associated with an arrest of lung development. In animal models, multiple factors inhibit (e.g. glucocorticoids) or stimulate (e.g. retinoic acid, RA) alveolarization. While some effects of hormonal treatments on lung architecture are known, the functional consequences of these changes are unclear.
OBJECTIVE: To correlate hormonal alteration of alveolarization to changes in pulmonary function in rats.
DESIGN/METHODS: Neonatal rat pups were treated with dexamethasone (Dex, d1-14) and/or RA (d3-14) with appropriate controls. Lung structure was studied by histology and radial alveolar counts (RAC) at d15 and d30. Pulmonary function was evaluated by plethysmography (d13), exercise swim testing (d28) and arterial blood gases (d30).
RESULTS: Day 15 histology revealed a simplified distal lung architecture in Dex-treated rats and smaller, more numerous alveoli in RA-treated pups. A partial restitution of Dex-induced changes was seen in Dex+RA pups. RAC were significantly lower in Dex-treated pups at both d15 and d30 and higher in RA-treated rats at d15 but not d30. Dex+RA treated pups were not different from controls at both times. Respiratory rates (RR) and minute ventilation (MV) were significantly higher in Dex- vs. saline-treated animals. While RR were lower, MV remained elevated in Dex+RA pups.

	RR (bpm) d13	MV (ml) d13	RAC d15	RAC d30
Saline	180±5	23.5±4.4	8.7±0.2	8.8±0.3
Dex	211±11^	36.8±4.4"	6.6±0.2*	7.3±0.2*
RA	180±6	23.1±3.6	11.6±0.3*	8.9±0.7
Dex+RA	195±9	35.8±3.6"	8.9±0.4	8.5±0.1

^p<0.05 vs saline; "p=0.05 vs saline; *p<0.01 vs saline; n=9-16 for RR & MV; n=3-4 for RAC
At d30, Dex-treated rats had respiratory acidosis compared to control or saline-treated pups (pH 7.32±0.01 vs 7.38±0.01, p<0.01 and pCO2 57.0±2.4 vs 47.0±1.2 mmHg, p<0.01, n=5-6) and had a 30% increase in lung volume in pressure-volume studies as compared to saline and Dex+RA groups. In exercise swim testing, time to fatigue was not different between treatment groups.
CONCLUSIONS: Dex treatment of neonatal rats is associated with decreased alveolarization and increased dead space resulting in hypercarbia and acidosis that is not compensated for by increased respiratory rate and minute ventilation. These experimental changes in pulmonary function may be relevant to premature infants with prolonged glucocorticoid treatment or BPD who may fail to complete alveolar development.
Funded by NIH HL62868 and HL075930

General Pediatrics I
Platform Session

Saturday, March 27 8:30am–11:00am Mead A

43 Presentation Time 8:30 AM

Evaluating Attitudes About Research: An Analysis of Parent-Child Dyads

Robert M. Nelson, William W. Reynolds, Department of Anesthesia and Critical Care Medicine, Children's Hospital of Philadelphia, Philadelphia, PA. (Sponsored by Eric David Kodish)
BACKGROUND: Parent permission and child assent are often required for children to participate in research. Eliciting child assent ensures that the standard of voluntary participation is met. However, there are limited data on how children and parents view research and decide to participate.
OBJECTIVE: To explore the relationship between child assent and parent permission about child participation in hypothetical research scenarios of varying levels of risk.
DESIGN/METHODS: A semi-structured interview guide with 4 research scenarios and multiple prompts about decision making was developed. Separate interviews were conducted with 17 children (age 4-15, m=10.1) with either diabetes, asthma, seizures, or no condition, and 17 of their parents (11 mothers, 6 fathers). Interviews explored child-parent willingness to participate in hypothetical research studies of varying levels of risk (blood test, PK study, placebo-controlled drug trial, non-therapeutic bronchoscopy). Interviews were audio-taped, transcribed, and coded for specific themes using Nvivo qualitative analysis software.
RESULTS: 17 parent-child dyads (68 scenarios) were analyzed for themes related to decision making about research participation. Excluding non-responses (10/68), parents and children agreed with each other about participation in 39/58 (67%) scenarios (with 72% in favor). There was disagreement in 19/58 (33%) scenarios. Although 3 of 4 scenarios involved non-beneficial research, parents were often willing (56%) for the child to participate, even when the child was hesitant. For example, a mother said "I'd give a little coaxing…She doesn't like it, but she'll do it," reflecting the view of several parents who would persuade their children to participate. Some children believed they could not say no to their parents. For example, one 5 year old girl says she would have to do what her mom wanted because "she's a grown-up." Another 9 year old girl said, "I would try to [talk them out of it] but they would probably say I would have to. [Why?] Because they're parents."
CONCLUSIONS: Parents and children may not agree about the decision to participate when presented with hypothetical research scenarios. At times, the principle of voluntariness may be compromised through parental efforts to persuade, and children's unwillingness to dissent. To avoid potential coercion and undue influence, investigators should seek child assent independently of parental permission.
Supported in part by a Mentored RSDA from NINDS (K01 NS02151).

44 Presentation Time 8:45 AM Fellow

Behavior of Kindergarten Children in Stepfamilies: Is Having Two Parents at Home Better Than One?

Prashil H. Govind, Ruth E. K. Stein, Pediatrics, Albert Einstein College of Medicine, Children's Hospital at Montefiore, Bronx, NY.
BACKGROUND: Children living in single parent (SP) families are at increased risk for psychosocial and behavioral problems compared to children with both biological (BB) parents. It is not clear if children living in stepfamilies (SF) fare better than children living in single parent families.
OBJECTIVE: To test the hypothesis that children living in stepfamilies have similar behavioral profiles to children in single parent families.
DESIGN/METHODS: Early Childhood Longitudinal Study, Kindergarten class 1998-99 (ECLS-K) is a nationally representative cohort of 22,782 kindergarten children. From this cohort, a sample of married stepfamilies (n=1029), single parent families (n=4046), and married both biological families (n=11,841) was obtained. Child behavior was measured by the psychometrically sound Social Skills Rating Scale (SSRS) completed by the teacher. It includes negative behaviors such as externalizing and internalizing problems, and positive behaviors such as prosocial behaviors (*interpersonal skills and self-control*). Parent reported information regarding family demographics, race, and parental characteristics (education and parental emotional well being) were controlled in the analysis.
RESULTS: Children in SF had mean standard scores that were similar to children in SP families on both the internalizing and externalizing behavior subscales. Both groups had significantly higher (worse) scores than children in BB parent families on both behavior subscales. With regard to prosocial behaviors, BB had significantly more prosocial behaviors than all other groups. SF had significantly higher (better) mean scores than SP on the interpersonal skills subscale.
Family Structure and Mean Standard Behavior Scores

	BB n=11,841	SF n=1029	SP n=4046
Externalizing	1.57**	1.80	1.82
Internalizing	1.51**	1.65	1.65
Interpersonal	3.20**	3.04*	2.96
Self Control	3.27**	3.07	3.02

**p<0.05 significantly different (s.d.) from all other groups; *p<0.05 s.d. from SP
These results did not change when family demographics, income, and parental characteristics were controlled in multiple regression analyses.
CONCLUSIONS: Children in stepfamilies experience similar negative behaviors as children in single parent families. The fact that the biological parent has committed to a long-term relationship (as evidenced by marriage) with another partner seems to be protective for prosocial behaviors but not for internalizing and externalizing behaviors.

45 Presentation Time 9:00 AM Fellow

Behavior in Kindergarten Children: Is Having an Additional Adult Relative Protective in Single Parent Families?

Prashil H. Govind, Ruth E. K. Stein, Pediatrics, Albert Einstein College of Medicine, Children's Hospital at Montefiore, Bronx, NY.
BACKGROUND: Children living in single parent (SP) families are at increased risk for psychosocial and behavioral problems. Little is known about this risk across different SP family structures.
OBJECTIVE: To test the hypothesis children living in SP families that contain an additional adult related to the child have lower levels of problem behaviors than children living in other SP family structures.
DESIGN/METHODS: Early Childhood Longitudinal Study, Kindergarten class 1998-99 (ECLS-K) is a nationally representative cohort of 22,782 kindergarten children. From this cohort, a sample of mothers in SP families (n=3,321) and in both biological (BB) parent families (n=12,229) were compared. Mothers < 18-years old at the time of child's birth were excluded. The SP families were further subcategorized into single mother alone (SA), single mother living with relative (SR), and single mother living with non-relative (SnR). Child behavior was measured by the psychometrically sound Social Skills Rating Scale (SSRS), a teacher reported scale. It includes externalizing behaviors, internalizing problems and pro-social behaviors (interpersonal skills and self-control). Income, family demographics and parental characteristics (education and emotional well being) as reported by the mother were controlled in the final analysis.
RESULTS: Children in BB parent families had significantly fewer behavioral problems than all SP families. Within SP families, children in the SR group had fewer behavioral problems than SA group and SnR group. Based on ANOVA, the SR group had lower mean standard scores signifying fewer externalizing and internalizing problems (p<0.05) than SA and fewer internalizing problems (p<0.05) than SnR.
Family Type and Mean Standard Behavior Scores

	BB** n=12,229	SR n=913	SA n=2219	SnR n=135
Externalizing†	1.58	1.75	1.83	1.89
Internalizing††	1.52	1.60	1.67	1.74

For following relationships p<0.05:†BB<SR<SA; †† BB<SR<SA<SnR; **BB < (SR, SA, SnR)
Similar trend existed for prosocial behaviors but was not statistically significant. When family demographics, income and parental characteristics were controlled in multiple regression models, SR was significantly different from SA and SnR, and similar to BB.
CONCLUSIONS: These result suggests that an additional adult relative may moderate the risk for child behavioral problems in single parent families**.** However, a longitudinal study is needed to confirm such a relationship and to identify other explanatory variables.

46 Presentation Time 9:15 AM

The Relationship of Maternal Methadone Use to Early Developmental Outcomes

Jo-Ann B. Bier, Doranne Grenon, Theresa Johnson, Ellen Mullane. Medicine, Children's Hospital, Boston, MA; Pediatrics, St. Lukes Hospital, New Bedford, MA.

BACKGROUND: Infants born to mothers who have abused illicit drugs may be at risk for developmental delay. Many of these women receive methadone maintenance during pregnancy. Little information is available regarding the relationship of maternal methadone use to developmental outcomes in their infants.
OBJECTIVE: We sought to examine this relationship by comparing growth and developmental parameters in 46 consecutive infants of mothers on methadone maintenance to 184 consecutive premature but otherwise normal infants.
DESIGN/METHODS: All infants were evaluated prospectively in our neurodevelopmental clinic. Premature but otherwise normal infants were used as controls to minimize a bias toward negative developmental outcomes in term infants referred to our clinic. Growth and neurodevelopmental data were collected at three and seven months corrected age. Standardized testing included the Bayley Scales of Infant Development (MDI) and the Alberta Infant Motor Scale (AIMS).
RESULTS: Birthweight (2666±681g vs 1691±493g) and gestational age (37±4w vs 32±3w) were higher in the methadone group based on the study design. Maternal age was similar compared to control while socioeconomic status (SES) was lower in the methadone group (19.3±7.5 vs 29.6±10.1, $p<0.001$). By 3 and 7 months infant weight and length were similar. Head circumference, however, was smaller in the methadone group at both time points (7m: 42±1cm vs 44±2cm, $p<0.001$). At 3 months both the AIMS (32±21 vs 47±23, $p<0.01$) and MDI (93±12 vs 102±8, $p<0.01$) were lower in the methadone group. At 7 months the MDI remained lower in the methadone group (92±10 vs 100±7, $p<0.01$) while the AIMS scores had improved (43±26 vs 52±27, $p = 0.1$). In order to determine the importance of methadone use to the depression in developmental indices a multivariate analysis was performed analyzing the relationship between 3 month MDI to gestational age, birthweight, SES and methadone use. Although SES ($p=0.023$) and methadone use ($p=0.008$) were independent predictors of decreased MDI , methadone use was the strongest predictor of a reduced developmental index.
CONCLUSIONS: Maternal methadone use places infants at risk for impaired developmental outcomes. This impairment persists well into the first year of life. All children exposed to in utero methadone exposure should undergo routine developmental assessment and be referred to the appropriate early intervention program.

47 Presentation Time 9:45 AM Student

What Do Adults Know About the Harmful Effects of Smoking on Child Health?

Meg Parker, Iman Sharif. Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: The American Academy of Pediatrics (AAP) recommends that pediatricians educate parents about the harmful effects of smoking on children's health. However, children are often exposed to cigarette smoke at home by other adults, besides their parents. No reports have documented what adults know about the effects of smoking on children's health.
OBJECTIVE: 1) To determine what adults know about the harmful effects of smoking. 2)To determine whether knowledge about the effects of smoking on child health would motivate adults to quit smoking.
DESIGN/METHODS: Setting: inner-city community health center. We conducted a cross-sectional survey of adults with children living in their homes. First, we presented subjects with a list of 14 conditions, and asked them to indicate the ones they believed were worsened by cigarette smoking. Then, we asked current/past smokers whether they had ever cut down or quit smoking; using another list, we asked those who had cut down/quit to indicate all their reasons for doing so.
Bivariate analyses compared knowledge for each survey item for current smokers vs. non-smokers/quitters.
RESULTS: 684 subjects participated. 48% were Latino, 34% African-American; 74% had completed high school.
21% were current smokers, 19% had quit; 60% had never smoked.
Overall, knowledge of the effects of cigarette smoking was high regarding: lung cancer (93%), low birth weight (86%), asthma (79%), household fires (75%), and incidence of smoking in children (73%). Few subjects knew that cigarette smoking increased: sudden infant death syndrome (34%), colds (27%), ear infections (25%).
Compared to nonsmokers and quitters, current smokers reported more knowledge about smoking's effect on ear infections (37% vs. 25%, $p= 0.026$).
Of the 274 current/past smokers, 78% reported having ever cut down or quit smoking. The following reasons were cited most frequently: harmful to my health (57%), harmful to children(53%), harmful to babies during pregnancy (40%). Few subjects cited the following reasons: household fires (21%), air pollution (20%), laws restricting public smoking (8%).
CONCLUSIONS: In this study, the majority of smokers did not know about the effects of smoking on child health. Subjects who had cut down/quit smoking frequently cited concern about effects on child health. These findings have implications for public health education regarding the effects of cigarette smoking.

48 Presentation Time 10:00 AM

Racial/Ethnic Disparities in Child Health: Another Failed Explanation!

Michele J. Siegel, Laurie J. Bauman, Ruth E. K. Stein. Pediatrics, Albert Einstein College of Medicine/CHAM, Bronx, NY.

BACKGROUND: Black and Hispanic children are more likely to be rated by their parents to be in poorer health than White children but little is known about what influences parent ratings.
OBJECTIVE: To test the hypothesis that differences in parental rating of health status by race/ethnicity can be explained by other indicators of health (functional limitations, chronic conditions and hospitalizations).
DESIGN/METHODS: Data on a nationally representative sample of children age 0 to 12 from the 1999 Medical Expenditure Panel Survey were used for the analyses (N=5023). The sample included 2405 Non-Hispanic White, 754 Non-Hispanic Black and 1694 Hispanic children. Within each racial/ethnic category, the percentage of children identified as being in good, fair or poor health was calculated, and cross tabulated with combinations of 3 indicators of poor health. The indicators were functional limitations, chronic condition, and hospitalization.
RESULTS: Black and Hispanic children are more likely to be rated to be in poorer health than White Children (22.15%, 30.70% vs 16.09%, Chi-Sq p-value < .0001). Within each racial/ethnic group, children with more indicators were more likely to be rated in poorer health. However, the distribution of indicators did not account for the difference in ratings across groups (see table).
Percent Children Rated In Good, Fair, Poor Health By Number of Other Health Indicators

Number of Indicators of Poor Health	Whites (n=2405)	Blacks (n=754)	Hispanics (n=1694)	Chi-Sq p-value
0	14.06%	20.18%	29.09%	< .0001
1	22.29%	34.78%	36.89%	.026
2+	42.19%	54.17%	66.67%	.011

Replicating these analyses with children rated to be in fair or poor health versus excellent, very good or good health, did not significantly change the results.
CONCLUSIONS: Greater frequency of a health limitation, chronic condition or hospitalization does not account for the higher proportion of children rated to be in poorer health by Black and Hispanic parents. It is unclear whether these differences are due to other unmeasured aspects of health, poorer documentation of health limitations and chronic conditions among Black and Hispanic children, or differences in the conceptualization of the meaning of good, fair or poor health among respondents of different racial/ethnic backgrounds.

49 Presentation Time 10:15 AM

Children's Short Tenures in Medicaid Managed Care

Gerry Fairbrother, Heidi L. Park, Arfana Haidery, Bradford H. Gray. Health and Science Policy, New York Academy of Medicine, New York, NY.

BACKGROUND: Recent studies have shown that children's tenures in Medicaid managed care are dramatically shorter than tenures in Medicaid itself.
OBJECTIVE: To examine the reasons for short tenures and for the differences in tenures in Medicaid and Medicaid managed care, and to propose practices that may reduce the gap.
DESIGN/METHODS: This was a qualitative study, conducted in five states chosen to provide variation in tenure in Medicaid managed care, as well as to afford geographical variation and experience with managed The five states were: Arizona, Michigan, New York, Oregon, and Pennsylvania. In each state we conducted on-site, in-depth interviews with State Medicaid and managed care offices, including medical directors, eligibility and enrollment specialist, and enrollment brokers.
RESULTS: Two factors emerged as the major contributors to short tenures in Medicaid managed care: (1) the gap between the time Medicaid coverage begins and enrollment in a health plan and (2) the frequency and ease of Medicaid eligibility renewal. With respect to the gap, this occurs because Medicaid eligibility must be established before a child is enrolled in a health plan. Medicaid coverage begins *retroactively* at the date of the application (and sometimes earlier). Health plan enrollment can only begin *prospectively* after Medicaid eligibility has been determined, a process that can date up to 45 days. In our five study states the interval between the Medicaid coverage beginning and date of enrollment in a health plan typically was from two to four months. Because neither applicant nor provider can be sure of eligibility during this period, care may be delayed.
Frequent and burdensome Medicaid renewal processes exacerbated the problem, resulting in breaks in enrollment and the need to re-enroll.
CONCLUSIONS: Our current enrollment policies are creating a gap between Medicaid and health plan enrollment, which will inevitably result in short tenures in health plans. As long as health plan enrollment happens after Medicaid coverage retroactively begins, the only real remedies for achieving adequate tenures in health plans is to extend eligibility periods for Medicaid and/or make the Medicaid renewal process simpler. While these measures may be difficult for budget-strapped states to implement, it is important to realize the implications for quality of health care and accountability. The task of managing the care for Medicaid children is not possible without adequate tenures in health plans

Infectious Diseases Platform Session

Saturday, March 27 8:30am–11:00am Riverside

50 Presentation Time 8:30 AM Fellow

Impact of Cervical Secretions on HSV Infection

Minnie John, Marla Keller, Kathleen Hogarty, Natalia Cheshenko, Sarah Ferris, Sylvan Wallenstein, Mary Klotman, Betsy C. Herold. Department of Pediatrics, Mount Sinai School of Medicine, New York, NY; Department of Medicine, Mount Sinai School of Medicine, New York, NY; Department of Statistics, Mount Sinai Scool of Medicine, New York, NY. (Sponsored by Roberto Posada)

BACKGROUND: Cervical secretions have intrinsic anti-microbial activity, which may be important in protecting women against sexually transmitted infection (STI). Knowledge of these innate factors is critical for development of topical microbicides, drugs applied vaginally to prevent the transmission or acquisition of STI. The anti-HSV activity of cervicovaginal secretions is unknown.
OBJECTIVE: To evaluate the impact of cervicovaginal lavage fluid (CVL) on HSV infection and explore the mechanism(s) of anti-viral activity.
RESULTS: CVL was obtained from 20 women (ages 18-25 and 26-45) on two visits 14days apart. We found that CVL (pH~5.0) inhibits HSV infection in all subjects. There was a geometric mean reduction of >10-fold in HSV-2 recovered in cells cultured in the presence of CVL compared to cells cultured in the presence of control (saline, pH 5.0+0.2 mg/ml BSA) ($p<0.0001$). There was no significant difference in anti-HSV activity in samples obtained on Day 0 compared to Day 14 and between the two age groups. CVL inhibits laboratory and clinical isolates of HSV-2 using human immortalized cervical cells. HIV infection is also reduced in the presence of CVL. CVL appears to target the host cell and inhibit viral entry post-binding. This is supported by the following observations: (1) CVL does not reduce specific binding activity; (2) CVL prevents nuclear transport of the viral tegument protein VP16; (3) anti-HSV activity is retained if cervical cells are pre-treated with CVL, washed, and then inoculated with HSV-2; (4) the activity is reduced if virus is pre-treated with CVL and diluted prior to inoculating cells. Candidate components include lactoferrin, mucins, secretory leucocyte protease inhibitor (SLPI) and defensins. We quantified SLPI and α-defensins (HNP1-3) in the CVL samples by ELISA (Cell Sciences, R&D). Previously, we showed that NP1 inhibits HSV infection post-binding (Sinha *et al* AAC 2003). Also, recombinant SLPI inhibits HSV infection in vitro at concentrations that are not cytotoxic. The quantities of SLPI and HNP1-3 in CVL tended to correlate with anti-viral activity.
CONCLUSIONS: CVL has significant intrinsic anti-HSV activity, independent of pH. CVL targets the epithelial cell preventing nuclear transport of incoming capsids. Both SLPI and HNP1-3 may contribute to the anti-viral activity; other candidates include lactoferrin and mucins.

51 Presentation Time 8:45 AM

Demographic, Clinical, and Resource Utilization Characteristics of a Multisite Sample of HIV+ Children

Richard Rutstein, Kelly Gebo, George Siberry, Patricia Flynn, Victoria Sharp, Steven Spector. Children's Hospital of Philadelphia, Philadelphia, PA; Johns Hopkins University, Baltimore, MD; St. Jude's Children's Research Hospital, Memphis, TN; St. Luke's-Roosevelt Hospital System, New York, NY; University of California San Diego, San Diego, CA.

BACKGROUND: Little data have been reported on health care utilization patterns of HIV+ children,especially since the advent of new therapies.
OBJECTIVE: To identify demographic, clinical, and resource utilization patterns of 365 HIV perinatally infected children followed in the HIV Research Network (HIVRN).
DESIGN/METHODS: Clinical data were collected on patients attending 5 academic pediatric sites during CY 2001. Outpatient (OP) utilization=mean OP visits per patient/year. Inpatient (IP) rates are reported as number of hospitalizations/100 patient years (100 PY). Bivariate statistical comparisons of individual

variables with resource utilization were done using negative binomial regression.
RESULTS: Our sample has a slight predominance of females (56%); the majority were African-American (AA) (70%). The median age was 8 yrs (range 0-18). Mean CD4 count=911 cells/mm^3. 40% had HIV-1 RNA <400 copies/ml, 22% had <50 copies/ml. 22% were AIDS defined. 93% were on HAART with 88% on two classes and 41% on three classes of HAART. 37% were on PCP and 12% were on MAC prophylaxis. Mean annual OP visits were 8.1 per person per year for those >2 years and 9.6 for those <2 years. Overall mean IP utilization was 22.4/100 PY; 20.0/100 PY for those ages >2 years and 44.4 per 100 PY for those <2 years. Mean length of stay =3.9 days. In a similar cohort of adult patients followed in the HIVRN, mean IP utilization was 36.3 per 100 PY and OP utilization was 5.1 visits per patient per year in 2001. Children ≤2, AA, those not on HAART or with CD4 counts <50, CD4% <15%, AIDS, or VL>100,000 copies/ml had significantly higher IP utilization (p=.001). In addition, AA and Hispanics, those with CD4 <50, CD4% <15, or VL>100,000 copies/ml had higher OP utilization than Caucasians, those with higher CD4 counts, CD4%, or lower VL (p<.01). There was no difference in OP or IP based on insurance.
CONCLUSIONS: We report much lower OP and IP for HIV+ children compared to previously available data, reflecting benefits of newer therapies. HIV+ children have lower levels of IP utilization and higher levels of OP utilization compared to HIV+ adults. These rates also vary with age and race. While ART use is high, adequate viral suppression is achieved in <50% of patients.

52 Presentation Time 9:00 AM

Incidence, Types and Risk Factors for Malignancy in Perinatally HIV Infected Children

Helen Kest, Susan Brogly, Barry Dashefsky, George Mcsherry, James Oleske, George Seage. Pediatric Infectious Diseases, St. Joseph Hospital, Paterson, NJ; Center for Biostatistics in AIDS Research, Department of Biostatistics/Epidemiology, Harvard School of Public Health, Boston, MA; Pediatric Infectious Diseases and Immunology, University of Medicine and Dentistry, Newark, NJ.
BACKGROUND: Limited data address incidence, types and risk factors for malignancies among perinatally HIV-infected children(PHIV). Existing data are limited to case series and reports. This study uniquely focuses on long-term prospectively followed PHIV from multiple sites in US and Puerto Rico
OBJECTIVE: To determine incidence, types and risk factors for malignancies in a cohort of PHIV followed by the Pediatric AIDS Clinical Trial Group (PACTG) 219/219C from 5/93 to 12/02
DESIGN/METHODS: The PACTG data base was reviewed to identify all cases of malignancy. Demographic data, CD4 counts and %, antiretroviral therapy use and mortality were recorded for identified cases. Malignancy incidence rates (MIR) were calculated by gender, race, year, age and histology. Kaplan-Meier product limit method was used to determine cumulative incidence of death following a diagnosis of malignancy for incident cases
RESULTS: Among 2,719 PHIV enrolled in the cohort, 17 incident malignancies were diagnosed, for an incidence rate of 1.55/1000 person years (py) (95% CI: 0.90-2.47) including lymphomas (13), CNS neoplasms (2), leukemia (1), leiomyosarcoma (1). 15 subjects diagnosed before enrollment were excluded. MIR did not significantly differ by age, gender or race and ranged from 0/1,000py in 1993 and 2000, to 3.29/1,000 py in 1998. Compared with non-HIV-infected controls, MIR in the cohort was significantly elevated for all histological types. Among black children, incidence rate ratio(IRR) was highest for lymphomas, 90.98 (95% CI: 40.16, 206.12); in white children it was highest for leiomyosarcomas 87.86 (95% CI: 12.28, 628.47). Although 1/3 of malignancies occurred in patients with normal CD4%, severely suppressed CD4% was the single most important risk factor for malignancy-related mortality. There was no difference in MIR between pre HAART (highly active antiretroviral therapy) [1993-97] compared with HAART eras [1998-2002]; the IRR of MIR in the pre to the HAART era was 1.49 (0.57, 3.92)
CONCLUSIONS: Compared with non-HIV infected children, there is an increased MIR especially lymphomas and leiomyosarcomas in PHIV; cases were more likely to be associated with severe immune suppression. Malignancies occurred both in children with and without immune suppression, indicating that HIV-infection maybe the most important risk for immune suppression related malignancies

53 Presentation Time 9:15 AM Fellow

Incidence and Outcome of CMV Infection in Pediatric Liver Transplantation Recipients Managed With Preemptive Ganciclovir Therapy

Cindy Goldberg, Andrew Campbell, Umberto Conte, Maria Tan, Sukru Emre, Betsy Herold. Pediatrics, Mount Sinai Medical School, New York, NY.
BACKGROUND: CMV infection following transplantation accounts for significant morbidity despite rapid diagnostics and antivirals. Strategoes to prevent CMV are universal prophylaxis (100 days of anti-virals), pre-emptive therapy (short course therapy for detectable virmeia) and combinations. There is little information regarding the efficacy of these strategies in pediatrics.
OBJECTIVE: To determine the prevalence of CMV infection, disease ,and outcome in a cohort of pediatric liver transplantation recipients who were managed preemptively.
DESIGN/METHODS: A retrospective review identified 80 pts. who received a liver transplant between 1/ 1 01 and 11/1/03; a subset of 36 were managed preemptively This subgroup received 14 days of iv GCV perioperatively and were followed biweekly for CMV DNA using a quantitative competitive PCR assay (qcPCR) (Amplicor assay; ViroMed). Charts were reviewed for: CMV detecton by PCR and culture; CMV disease defined as presence of compatible signs or symptoms confirmed by viral isolation; episodes of rejction; immunosuppressive therapy; treatment with immunoglobulin and antiviral therapy.
RESULTS: The most common indications for transplant were biliary atresia (n =10), fulminant hepatitis (n =8), autoimmune hepatitis (n =3). Mean age at transplant was 6.6. Pre-transplant evaluation of recipients (R) included urine for CMV shell vial (all children < 1 year) and IgG (> 1 year). Of the 36 recipients, 5 were D-/R+; 8 D+/R+, 13 D+/R- and 10 D-/R-. All recieved 14 days of iv GCV and CMV hyperimmunoglobulin (150 mg/kg 72 h of transplant and at weeks 2, 4, 6, and 8 post-transplantation and 100 mg/kg at weeks 12 and 16). 11/36 (31 %) children have had CMV detected by qcPCR at least once (6 D+/R+, 5 D+/R-) and 3/11 had evidence of invasive disease (D+/R+). The 3 diseases were hepatitis confirmed by biopsy and culture; all recovered fully. No patient developed CMV disease without viremia. CMV viremia was preemptively treated with 14-21 days of iv GCV.
CONCLUSIONS: Preemptive monitoring is effective at preventing CMV disease in pediatric liver transplantat patients. This strategy may limit the number of children exposed to prolonged anti-viral therapy and its associated morbidity and may reduce the emergence of resistance. These data provide the framework for prospective controlled studies.

54 Presentation Time 9:30 AM Student

Seroepidemiology of Human Metapneumovirus in Children

Jessica W. Leung, Carla A. Weibel, Jeffrey S. Kahn. Epidemiology and Public Health, Yale University School of Medicine, New Haven, CT; Pediatrics, Yale University School of Medicine, New Haven, CT.
BACKGROUND: Human metapneumovirus (hMPV) is a newly discovered respiratory pathogen that is associated with both upper and lower respiratory tract disease in infants and children. Our studies and others suggest that hMPV infection is common in childhood though the incidence of hMPV in the general population is not known. To further investigate the epidemiology of hMPV, we developed an ELISA assay based on recombinant hMPV virion glycoproteins to determine the seroepidemiology of hMPV in the pediatric population.
OBJECTIVE: To define the seroepidemiology of hMPV in children in Connecticut.
DESIGN/METHODS: The fusion (F) glycoprotein gene from the two major genotypes of hMPV was amplified from respiratory specimens that tested positive for hMPV and cloned into a vesicular stomatitis virus expression vector. Lysates from cells infected with these recombinant viruses were used as antigen in an ELISA. Serum from children was screened for the presence of hMPV specific antibody using the recombinant antigen ELISA.
RESULTS: hMPV F was efficiently expressed by the recombinant viral vector. Metabolic labeling and western blot analysis confirmed expression of a 58kDa protein, corresponding to the molecular weight of hMPV F. This recombinant protein based ELISA was specific for hMPV. Antibodies that bind to the closely related paramyxovirus respiratory syncytial virus were not detected with this method. The percentage of individuals who were seropositive for hMPV F antibodies was 83.3% in children < 6 months old, declined to 46.2% in children 6-12 months old, and rose steadily in children 1-20 years old. The percentage of children 10-20 years of age who were seropositive for hMPV F antibodies was > 95%.
CONCLUSIONS: Our seroepidemiological data suggest that hMPV infection is common in childhood. The lower percentage of seropositive children in the 6-12 months old age group compared to the <6 month old age group likely reflects waning maternal antibody. The percentage of children who were seropositive for hMPV antibodies increased with age. These findings suggest that hMPV is widespread in our population. Further studies are required to determine whether hMPV infection confers protective immunity.

55 Presentation Time 10:00 AM

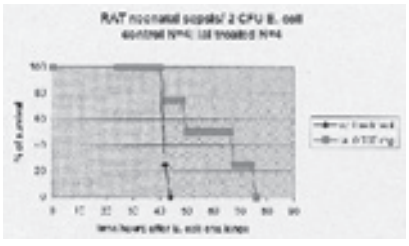
Effects of Respiratory Syncytial Virus (RSV) and Hyperoxia on Apoptosis in Cord and Adult Peripheral Mononuclear Cells (PBMCs)

Leonard R. Krilov, Thomas W. McCloskey, S. Hella Harkness, Paul J. Lee, Jonathan M. Davis. Pediatrics and the CardioPulmonary Research Institute, Winthrop University Hospital, SUNY Stony Brook School of Medicine, Mineola, NY; Immunology Center, NS-LIJ Research Institute, Manhasset, NY.
BACKGROUND: RSV causes marked inflammation with mononuclear cell infiltrates in the lower respiratory tract in infants. Hyperoxia is used in the treatment of RSV infections, but may further contribute to inflammatory changes in the small, peripheral airways.
OBJECTIVE: To assess the combined effects of RSV and hyperoxia on apoptosis in PBMCs in vitro.
DESIGN/METHODS: PBMCs from adult or cord blood (n=10 each) were separated over Ficoll and 2x10^6 cells were exposed to RSV (MOI=1) or media (mock). After 24 hrs of incubation, cells were maintained in room air (RA) or 95% FiO_2 up to 6 days. Aliquots of cells were sampled at 24-hr intervals, labeled with CD-14 APC and a TUNEL assay was performed utilizing an in vitro cell detection kit with FITC-labeled dUTP. The % of apoptotic cells were assessed by flow cytometry and are expressed as median % (25-75 IQR).
RESULTS: As previously reported (JID 2000;181:349), RSV significantly ↓'d apoptosis (vs. mock) at 24-72 h in RA. When exposed to hyperoxia, a significant ↓ in % apoptosis in RSV-exposed cells was seen at 24 h [cord lymphs: mock 23% (20-39) vs. RSV 15.5 (11-25); p<0.04; adult lymphs: mock 11% (6-15) vs. RSV 4% (2-8); p<0.02], but was lost by 48 h in cord lymphs [mock 26% (25-46) vs. RSV 23.5% (18-43)] and 72 h in adult lymphs [mock 14% (10-19) vs. RSV 18% (8-24)]. By 144 h, an ↑↑ in apoptosis was observed in O_2 vs. RA (RSV and mock): Cord lymphs: O_2 mock 82% (73-86), O_2 RSV 81% (78-81) vs. RA mock 38% (29-55), RA RSV 35% (18-41). Adult lymphs: O_2 mock 57% (34-64), O_2 RSV 43% (16-84) vs. RA mock 8% (0-10), RA RSV 7% (1-11). Similar changes were seen in the monocytes. At 144 h an ↑↑ in apoptosis was seen in the monocytes under O_2, but was greater with O_2 RSV than O_2 mock. Cord monos: O_2 mock 65% (37-79), O_2 RSV 81% (49-88), RA mock 26% (12-50), RA RSV 31% (13-65). Adult monos: O_2 mock 47% (21-66), O_2 RSV 80% (29-95), RA mock 7% (0-10), RA RSV 10% (5-27). At all time points, the % of apoptotic cells was significantly higher in cord vs. adult cells under the same conditions.
CONCLUSIONS: Hyperoxia and RSV both appear to have regulatory effects on apoptosis in PBMCs. The higher % apoptosis in cord vs. adult cells could contibute to the inflammation seen in infants with RSV disease. These effects may contribute to the pathophysiology of RSV infecton. Further studies of these interactions are warrranted.

56 Presentation Time 10:15 AM Fellow

Beneficial Effects of Inter-Alpha Inhibitor Proteins (IaIp) in an *In Vivo* Animal Model of Neonatal Sepsis

Kultar Singh, Kreso Bendelja, Yow-Pin Lim, James F. Padbury. Department of Pediatrics, Women & Infants Hospital, Brown Medical School, Providence, RI; Division of Medical Oncology, Rhode Island Hospital, Brown Medical School, Providence, RI.
BACKGROUND: IaIp are group of serine proteases inhibitors. They are important *in vivo* modulators of endogenous proteases including trypsin, human leukocyte elastase, plasmin and cathepsin G. Release of endogenous proteases plays an important role in inflammation, sepsis, wound healing and metastasis. A significant decrease of plasma IaIp levels occurs in adult and newborn sepsis. Our previous animal studies using the polymicrobial sepsis rat (adult) model of cecal ligation and puncture demonstrated the beneficial effects of intravenous IaIp adminitration in improving morbidity and mortality.
OBJECTIVE: The aim of this study is to evaluate the effects of parenterally administered IaIp in an *in vivo* animal model of neonatal sepsis.
DESIGN/METHODS: Sepsis was induced in 2-3 days old Fischer rats with a subcutaneous injection of E. Coli (BORT). A bacterial dose response curve of lethality was determined. 2 CFU/gram body weight was lethal at 40-50 hours after the infection. In the subsequent experiment, three day old animals (n=8) were injected with this dose of E. Coli and then randomized into two groups. The treatment group (n=4) received three intraperitoneal injections of 250 micrograms of purified human IaIp, at 6, 12 and 24 hours after the infection. The control group received equal amount of human albumin at the same time intervals.
RESULTS: All pups in the control group died within 40-44 hour after the infection. Animals in the treatment group survived up to 78 hours.
CONCLUSIONS: These results suggest that IaIp offers a beneficial effect in septic newborn rats and warrant further investigation. Questions being persued include: optimal dose vs. response to IaIp, optimal timing of IaIp administration, pharmacokinetics of IaIp, effectiveness of IaIp in other models of sepsis (E.g. Group B strep, LPS).
One of the co-authors, Yow-Pin Lim, has an equity in Prothera Biologics.



Neonatology I
Platform Session

Saturday, March 27 8:30am–11:00am Mead B

57 Presentation Time 8:30 AM Fellow

Neonatal Interleukin-1 Receptor Antagonist (IL-1ra) and Interleukin-4 (IL-4) Gene Polymorphisms and Spontaneous Preterm Birth

Marcelo Y. Nabong, Santosh Vardhana, Mehmet Genc, Mirjana Nesin, Steven S. Witkin. Department of Pediatrics and Obstetrics and Gynecology, Weill Medical College of Cornell University, New York, NY.

BACKGROUND: Spontaneous preterm birth is accompanied by marked increases in the levels of pro-inflammatory cytokines. Production of these cytokines is regulated by the levels of anti-inflammatory cytokines. Previous studies have demonstrated that IL1RN*2 is the IL-1ra allele with the lowest level of anti-inflammatory activity. Conversely, IL4*T is the IL-4 allele associated with the highest level of anti-inflammatory activity. This may affect the rate of spontaneous preterm birth.

OBJECTIVE: To determine the association between spontaneous preterm birth (SPTB) and polymorphisms at position -590 in the IL-4 promoter and the intron 2 of the IL-1 receptor antagonist (IL-1 ra) gene.

To determine whether polymorphisms in the neonatal or maternal genes coding for two anti-inflammatory cytokines - IL-1 ra and IL-4 influence the risk of spontaneous preterm birth (SPTB).

DESIGN/METHODS: DNA from buccal swabs were obtained from 57 mother-infant pairs who delivered <37 weeks and from 221 term birth pairs. Polymorphisms were analyzed by polymerase chain reaction (PCR) and restriction length polymorphism analysis.

RESULTS: IL-1ra allele 2 (IL1NR*2) was more frequent in the neonates who were born prematurely (26.4%) than in the term neonates (15.4%) (p=.01). IL-4 allele T (IL4*T) was less frequent in the premature neonates (23.1%) than in the term babies (33.8%) (p=.03). There was no relation between maternal IL1RN*2 or IL4*T and SPTB. Neonates who were positive for IL4*T had a lower mean birthweight (1886 g) than did neonates homozygotic for IL4*C (2345 g) (p=.04). There was no relationship between IL-1ra alleles and birthweight or between alleles of IL-4 or IL-1ra and respiratory distress syndrome.

CONCLUSIONS: These data suggest that neonatal possession of alleles associated with reduced anti-inflammatory activity in two polymorphic genes may increase susceptibility to SPTB.

58 Presentation Time 8:45 AM Fellow

Influence of Census and Patient-To-Nurse Ratios on the Decision To Discharge Moderately Premature Infants

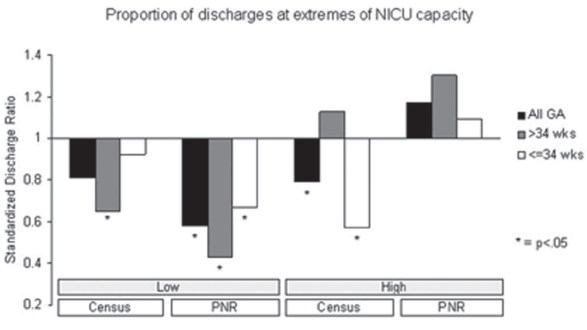
Jochen Profit, Marie C. McCormick, John A. Zupancic, Kim Coleman-Phox, Rebecca H. Roberts, Gabriel J. Escobar, Douglas K. Richardson. Newborn Medicine, Harvard Medical School, Boston, MA; Newborn Medicine, Beth Israel Deaconess Medical Center, Boston, MA; Division of Research, Perinatal Research Unit, Kaiser Permanente Medical Care Program, Oakland, CA.

BACKGROUND: Timely discharge of moderately premature infants has important economic implications. We hypothesized that the decision to discharge these infants is influenced by the organizational make-up of neonatal intensive care units (NICUs).

OBJECTIVE: This study evaluates the impact of daily census and dayshift patient-to-nurse ratios (PNR) on the decision to discharge moderately premature infants.

DESIGN/METHODS: In a prospective multi-center cohort study, we enrolled 850 infants born between 30 and $34^{6/7}$ weeks gestational age at ten level II and III NICUs. We obtained daily census and nurse staffing information from each hospital. Census and PNR were divided into deciles at the unit level, establishing busy (upper decile) and non-busy (lower decile) days. We used a test of binomial proportions to calculate whether 10% of discharges occurred within each of these deciles. The ratio of observed to expected discharges was calculated and expressed as a standardized discharge ratio (SDR).

RESULTS: We had complete census and PNR data on 800 and 774 patients, respectively. Figure 1 summarizes the results of our analyses. Considering all gestational ages, a smaller proportion of infants than expected were discharged when unit census was either high or low. On high census days, infants below 34 weeks fully accounted for this finding. In contrast, on low census days, fewer infants above 34 weeks were discharged. Discharges on days with high PNRs occurred at expected rates. However, when PNRs were low, fewer patients than expected were discharged. This observation remained significant among all gestational ages.



CONCLUSIONS: We demonstrated significantly lower than expected discharge rates at both extremes of NICU capacity. Organizational changes may attenuate these inefficiencies.

59 Presentation Time 9:00 AM

Growth Variation at Discharge and 3 Months Post-Discharge in Moderately Premature Infants

Mary T. Blackwell, Marie C. McCormick, John Zupancic, Gabriel Escobar, Douglas K. Richardson. Department of Maternal Child Halth, Harvard School of Public Health, Boston, MA; Department of Neonatology, Beth Israel Deaconess Medical Center, Boston, MA; Harvard Newborn Medicine Program, Children's Hospital and Harvard Medical School, Boston, MA; Division of Research, Perinatal Research Unit, Kaiser Permanente Medical Care Program, Oakland, CA.

BACKGROUND: Inter-NICU variation in growth outcomes has been well reported for VLBW infants but has been little studied in moderately premature infants comprising ~50% of NICU patients.

OBJECTIVE: To measure and compare growth outcomes of moderately premature infants in 10 NICUs at discharge *and* 3 months after discharge(D/C).

DESIGN/METHODS: Medical record review and post-D/C interview of a prospectively identified cohort of 850 infants,born between 9/01 and 1/03 at 30-35 wks GA in 10 NICUs, 5 each in California and Massachusetts, n=60-100/NICU . We measured weight and HC growth rates thru NICU D/C and weight gain 3 months (mos) after D/C. Comparisons between NICUs were controlled for BW, GA, weight percentile for BW, gender, and SNAP2 score.

RESULTS: Net weight(WT) gain from birth to D/C for 778 infants with LOS>6 days(d) was only **6.5+/-6.2 g/k/d** with individual study site means ranging from **4.5+/-5.9 to 8.6+/-4.7**, p<0.001. At 7 d subjects had lost 3.4+/-4.7% of BW with WT *gain* from 7d to D/C of 14.4+/-6.0 g/k/d. We found significant inter-NICU differences in WT change for each interval (p<0.001). Head circumference (HC) growth also varied between NICUs (0.35+/-0.79 to 0.71+/-0.48 cm/wk, p<0.05). HC growth was correlated with WT growth rate, p<0.001. Weight gain 3 mos after NICU D/C averaged 8.8+/-2.2 g/k/d, with smaller but still significant differences between NICUs, p<0.05. Three mos after D/C (49+/-5 wks corrected GA) 87% of infants were at or above their BW percentile (inter-NICU range 76-94%,p<0.05). Despite increased WT growth rate after D/C the 2 sites with slowest NICU growth remained 9th and 7th in rank 3 mos after D/C but NICU growth was *not* strongly predictive of post-D/C growth overall.

CONCLUSIONS: Growth outcomes varied significantly between study NICUs after controlling for differences in BW, GA and illness acuity. Less than 10% of subjects achieved intra-uterine weight goals while in NICU. Post-D/C weight gain approached normal rates and achieved some catch-up growth. Mean in-patient HC growth exceeded the *minimum* goal of 0.5cm/wk in only 40% of subjects and was highly correlated with weight gain. NICU care in these California and Massachusetts study sites does not support the achievement of standard intra-uterine growth goals. However there are other major predictors of post-D/C growth not identified in this study.

supported by AHRQ R01 HS10131

60 Presentation Time 9:30 AM

Treatment of Severe Retinopathy of Prematurity: A New Approach

Talkad S. Raghuveer, Peng Chen, Pantea Mahtosh, Merrill Stass-Isern, Trudi Grin, Keith Warren. Pediatrics, University of Kansas Medical Center, Kansas City, KS; Ophthalmology, University of Kansas Medical Center, Kansas City, KS; Pediatric Eye Care, P.A., Overland Park, KS. (Sponsored by Cheng Cho)

BACKGROUND: Severe Retinopathy of Prematurity (ROP) continues to occur due to increasing survival of extremely premature infants. The STOP-ROP trial failed to show benefits of supplemental oxygen to prevent progression of ROP. However, prevention of hypoxia and decreasing reactive oxygen species (ROS) downregulates vascular endothelial growth factor (VEGF), which in turn halts neovascular proliferation. Preterm infants are deficient in antioxidants and breast milk(BM) is rich source of antioxidants, though levels of docosahexaenoic acid (DHA) are low in BM of American women. We postulate that prevention of hypoxia combined with DHA-enriched breast milk may halt the progression of ROP.

OBJECTIVE: The aim of this study was to prevent the progression of ROP from reaching threshold and avoid laser.

DESIGN/METHODS: The study period was from January 2002 to November 2003. Infants who reached prethreshold ROP were offered the following: a) Maintaining oxygen saturation between 94%-98%, b) Supplementing mother and infant with DHA if the infant was BM fed, c) Switching to BM from a bank if infant was formula fed (IF) and supplementing with DHA. The primary outcome was development of threshold ROP and need for Laser therapy

RESULTS: Seven preterm infants (GA: 24-29 weeks, BW 604-1018g) have been treated with above protocol; 5 female and 2 male (Table 1). None progressed to threshold and none needed Laser therapy. Follow up (1-18 months) showed complete regression of ROP with no residual scarring in all 7 infants. In the same period 6 other infants (GA:24-27 weeks, BW:390-762g, 2 female and 4 male) reached prethreshold ROP with no intervention and all 6 progressed to threshold ROP and required laser surgery.

CONCLUSIONS: The combination of DHA-enriched breast milk and prevention of hypoxia seems to halt the progression of prethreshold ROP. This finding warrants further study in a randomized clinical trial.

Table 1 showing details of infants with ROP who were treated with new protocol

Gestation age (wks)	Birth Weight (grams)	Sex	Diet	ROP status	Result
29	1018	F	BM->BM+DHA	Stage 3	Resolved
26	604	F	IF->BM+DHA	Stage 3	Resolved
24	679	F	IF->BM+DHA	Stage 3	Resolved
25	755	M	IF->BM+DHA	stage 3	Resolved
25	736	M	IF->BM=BM+DHA	stage 3	Resolved
24	670	F	BM->BM+DHA	stage 3	Resolved
27	786	F	IF->BM+DHA	stage 3	Resolved

Diet: Baseline diet ->Interventional diet; ROP status: Stage 3 in Zone 2.

61 Presentation Time 9:45 AM

Ouabain Prevents Excitotoxicity-Mediated Apoptosis in the Newborn Striatum

W. Christopher Golden, Lee J. Martin. Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD; Pathology and Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD. (Sponsored by Edward E. Lawson)

BACKGROUND: Hypoxia-ischemia (HI) is a significant cause of neonatal encephalopathy and childhood neuromotor abnormalities. Excess activity of excitatory amino acids, a process known as excitotoxicity, significantly contributes to central nervous system damage in the newborn after HI. In brain regions vulnerable to HI (such as the striatum [basal ganglia]), excitotoxicity causes neuronal degeneration via apoptosis, a form of programmed cell death. In a rodent model of excitotoxicity, levels of sodium-potassium ATPase (Na, K ATPase), a vital cell membrane enzyme, remain normal prior to and during the morphological evolution of neuronal apoptosis. Furthermore, in non-neuronal tissues, low-doses of the Na, K ATPase inhibitor ouabain trigger intracellular signals that stimulate cell growth and activate cell-survival factors (such as NF-κB).

OBJECTIVE: To determine if sub-lethal doses of ouabain protect against neuronal apoptosis in a newborn model of excitotoxic brain injury.

DESIGN/METHODS: Newborn (7 day old) rat pups received unilateral intrastriatal co-injection of the gluatamte receptor agonist kainic acid (KA, 4 or 8 nanomoles [nmol]) and ouabain (Oua, 0.01 nmol) and were recovered at 24 hours post injection. Animals injected with KA alone (at both concentrations), Oua alone, or phosphate buffered saline (PBS) served as controls. Brains were subsequently fixed, harvested and sectioned. Mid-striatal sections (40mm) from each animal were stained with cresyl violet to detect apoptotic profiles and subjected to an *in situ* Na, K ATPase assay to detect enzyme activity.

RESULTS: Striatal neuron apoptosis after KA injection (4 or 8 nmol) is significantly increased (p<0.05) relative to sham and internal control at 24 hours post injection. In contrast, co-injection reduces apoptosis in animals receiving Oua/4 nmol KA (by 45-77%) or Oua/8 nmol KA (by 73-90%). The reduction in apoptosis, based on number of apoptotic profiles per high power field, was statistically significant at both KA doses (p<0.05 vs. KA alone). This dose of ouabain did not decrease Na, K ATPase activity.

CONCLUSIONS: Low doses of the cardiac glycoside ouabain block neuronal apoptosis after an excitotoxic insult without loss of Na,K ATPase activity. These findings suggest that the actions of ouabain (either dependent or independent of Na, K ATPase) are neuroprotective and that ouabain stimulates intracellular signals that promote neuronal survival.

62 Presentation Time 10:00 AM Fellow

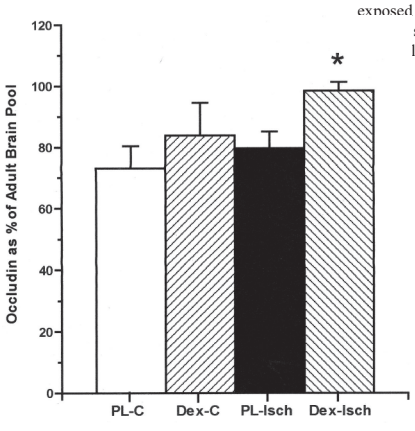
Effect of Antenatal Steroids on Tight Junction Protein Expression in the Cerebral Cortex of Ovine Fetuses With *In Utero* Brain Ischemia

Shadi N. Malaeb, Stephanie A. Newton, Grazyna B. Sadowska, Edward G. Stopa, Halit Pinar, Barbara S. Stonestreet. Pediatrics, Brown University and Women & Infants Hospital of Rhode Island, Providence, RI; Pathology, Brown University and Women & Infants Hospital, Providence, RI; Pathology and Cytopathology, Brown University and Rhode Island Hospital, Providence, RI.

BACKGROUND: Steroids may act on the intercellular tight junctions (TJ) of endothelial cells that form the blood-brain barrier (BBB). We have shown that antenatal steroids reduce BBB permeability, but do not attenuate pathological ischemic brain injury in the ovine fetus. Occludin is an important transmembrane TJ protein. The effects of antenatal steroids on TJ proteins have not been examined in the fetal brain.

OBJECTIVE: To test the hypothesis that antenatal steroids increase the expression of TJ proteins in ovine fetuses with and without exposure to *in utero* brain ischemia (Isch).

DESIGN/METHODS: Chronically instrumented ovine fetuses at 80% of gestation were studied 18 h after the last of four 4-6 mg dexamethasone (Dex) or placebo (PL) injections were given over 48 h to ewes. Groups (gps) were PL-Control (C, n=6), Dex-C (n=5), PL-Isch (n=6), and Dex-Isch (n=6). Ischemia consisted of 30 min of fetal bilateral carotid artery occlusion and 72 h of reperfusion. C gps were not exposed to Isch. Coronal brain sections were stained scored in Isch gps for cerebral cortex (CC) lesions by two pathologists. CC scores (0-5) were 0=0%, 1=1-10%, 2=11-50%, 3=51-90%, 4=91-99%, 5=100% of the area damaged. Frontal CC was snap frozen. Occludin protein expression was examined by Western blot, densitometry performed and results expressed as % of adult brain pool, which was an internal control.



RESULTS: Occludin protein expression was higher (Fig, M±SEM,*p=0.01) in the Dex-Isch than in PL-Isch gp. Ischemia scores did not differ between PL-Isch (2.6±0.7) and Dex-Isch (3.2±0.8) gps.

CONCLUSIONS: Maternal corticosteroid pretreatment increased TJ protein expression in the cerebral cortex of fetuses exposed to *in utero* brain ischemia. However, these changes were not associated with attenuation of pathological brain ischemia.

63 Presentation Time 10:15 AM Fellow

Genetic and Pharmacologic Modulation of Nitric Oxide-Hemoglobin Reactivity

Eric J. Frehm, J. Eric Russell, Andrew J. Gow. Department of Pediatrics, Division of Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Department of Hematology, University of Pennsylvania, Philadelphia, PA; Department of Pediatrics, Division of Neonatology, University of Pennsylvania, Philadelphia, PA.

BACKGROUND: NO's interactions with hemoglobin (Hb) are critical to its role in the circulation. Three fundamental NO-Hb reactions exist: conservation (FeIINO formation); consumption (FeIII and NO_3^- formation); and *S*-nitrosylation of Cys. Hb's capacity for cooperative ligand binding relies upon intramolecular heme communication. This is mediated by the bond between heme iron and the proximal His and requires Hb to be capable of conformational change. When NO is the only ligand, adult Hb (HbA) loses cooperativity despite undergoing conformational change; EPR studies indicate proximal His bond disruption.

OBJECTIVE: We propose that the lack of cooperative NO binding to HbA is due to cleavage of the proximal His bond. Therefore, we have assessed how alterations of the proximal His bond affect NO binding to Hb.

DESIGN/METHODS: NO binding characteristics were assessed in both HbA and the embryonic Hb Portland-2 (HbP2), obtained from transgenic mice, with tonometry to control gas tensions. The nature of bound NO was also assessed by EPR and Raman Resonance spectroscopy (RRS).

RESULTS: In the absence of O_2, HbA bound NO non-cooperatively. The addition of the allosteric regulator inositol hexaphosphate (IHP), which cleaves proximal His bonds, further diminished HbA's affinity for NO with no effect on cooperativity. HbA-NO binding became cooperative when O_2 was present; IHP eradicated this cooperativity. HbP2, in which embryonic ζ chains replace HbA's alpha chains, had a left-shifted O_2 equilibrium curve (P_{50}=1.9 mm Hg vs 3.2 for HbA), indicating increased O_2 affinity. Even in the absence of O_2, HbP2 demonstrated cooperative NO binding (Hill coeff=3.75). RRS confirmed the integrity of the proximal His bond, even when the fully nitrosylated molecule was subjected to negative allosteric regulators (i.e., low pH with chloride and phosphate ions). Under these conditions, RRS revealed proximal His bond breakage in $HbA(NO)_4$.

CONCLUSIONS: We have demonstrated the proximal His bond's centrality to Hb cooperativity and provided a mechanism for the maintenance of NO's bioactivity in the presence of Hb. We also show that the proximal His bond of the embryonic ζ chain, but not the adult alpha chain, resists breakage upon NO-heme binding. Further, we have shown that allosteric regulators alter NO handling by Hb, which may subserve vasodilation. We speculate that embryonic gene switching may allow for alternative NO handling by Hb during vascular development.

Nephrology Platform Session

Saturday, March 27 8:30am–10:45am Mead C

64 Presentation Time 8:30 AM Fellow

Erythropoietin and Its Receptor During Kidney Development in Mice

Mihail M. Subtirelu, Alda Tufro. Department of Pediatrics - Division of Pediatric Nephrology, The Children's Hospital at Montefiore - Albert Einstein College of Medicine of Yeshiva University, Bronx, NY.

BACKGROUND: Erythropoietin has been shown to be an angiogenic factor in addition to its well known role in hematopoiesis.

OBJECTIVE: The purpose of this study is to examine the role of erythropoietin during kidney vascular development. The mouse offers an ideal model for such a study because of the post natal component of kidney development.

DESIGN/METHODS: Whole kidney tissue was obtained from mice at pre and post natal ages ranging from embryonic day 12 (E12) to 28 days after birth (P28) and adults (A). The ontogeny of erythropoietin and its receptor expression were assessed by western blot (WB). Mouse glomerular endothelial cells were cultured, the expression of erythropoietin system was evaluated by WB, and using modified Boyden chambers their migratory response to recombinant erythropoietin, vascular endothelial growth factor (VEGF), or both was examined and compared to control conditions.

RESULTS: Erythropoietin is expressed in mouse kidney from E17 to adulthood and is not developmentally regulated. In contrast, erythropoietin receptor expression is very high at E12, decreases 10-fold during embryonic life, shifts from a ~100 kD isoform to the mature isoform (~66KD) and increases 3-fold from P7 to adulthood. Mouse glomerular endothelial cells in culture express erythropoietin ant its receptor. Migration assays showed that recombinant erythropoietin induces a glomerular endothelial cell migration similar to VEGF.

CONCLUSIONS: 1) a complete erythropoietin system is expressed during kidney organogenesis and vascularization; 2) the erythropoietin receptor is developmentally regulated whereas the ligand is not; 3) an isoform shift from a large to the mature erythropoietin receptor occurs during the first postnatal week; 4) erythropoietin is a chemoattractant for mouse glomerular endothelial cells in vitro. Taken together, these data suggest that the erythropoietin system may be involved in directional endothelial cell migration and kidney vascular development. Experiments to define the function of the large erythropoietin receptor isoform will be pursued.

65 Presentation Time 8:45 AM

Increased Glomerular Expression of Notch1, Jagged1 and Transforming Growth Factor b (TGF-b) Isoforms in Mice Lacking CD2-Associated Protein (CD2AP), Model of Focal Segmental Glomerulosclerosis (FSGS)

Robert P. Woroniecki, Mario Schiffer, Frederick J. Kaskel, Andrey S. Shaw, Erwin P. Bottinger. Pediatric Nephrology at the Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY; Department of Nephrology and Medicine, Albert Einstein College of Medicine, Bronx, NY; Pathology and Immunology, Washington University School of Medicine, St. Louis, MO; Albert Einstein Biotechnology Center, Bronx, NY.

BACKGROUND: CD2AP(-/-) knockout mice (KO) develop glomerular lesions resembling human FSGS between 3-4 weeks and die at 6 weeks of age from massive proteinuria and renal failure. The mechanisms involved in the glomerular injury in this model are unclear. Notch and TGF-β signaling pathways are important for the control of cellular differentiation and apoptosis, which has been shown to play a role in podocyte injury and progression of glomerulosclerosis.

OBJECTIVE: To examine involvement of TGF-β and Notch signaling pathways in the development of glomerular injury in CD2AP KO mice.

DESIGN/METHODS: Kidneys of 7 CD2AP (+/+) wildtype (WT), and 8 KO mice were harvested at 4 weeks of age in duplicate experiments (E1, E2). 30 glomeruli from one kidney of each mouse were laser captured and microdissected (LCM), and pulled for analysis. Total RNA was extracted from whole kidney, and glomerular RNA was isolated with DNAse treatment. Quantity and quality of RNA were verified by Bioanalyzer. Primers specific for amplification of TGF-β;1and 2, TGF-β receptor type; I, and II (TGF-β;RI, RII), Notch1, Jagged1, as well as housekeeping gene, ribosomal protein 13A (Rpl-13A) were used for quantitative real-time PCR gene expression analysis. Immunohistochemistry was performed on glomerular samples with specific anti-TGF-β;1antibodies.

RESULTS: Total RNA yield from 30 glomeruli was 10.78ng, SD (5.45) in WT, and 4.20ng, SD (2.04) in KO. Whole kidney mRNA expression of TGF-β; 2, RI, RII, Notch1 and Jagged1 was not different between WT and KO. However, TGF-β;1 mRNA was increased 1.44 and 1.66-fold (E1, E2) in whole kidney KO. KO glomeruli revealed increased TGF- β;1 by immunohistochemistry, and by mRNA expression; 2.00 and 2.15-fold (E1, E2). Glomerular mRNA expression was also increased 2.9 and 3.25-fold (E1, E2), for TGF-β;2, and 2.17 and 6.17-fold for TGF-β;RI, RII respectively . KO glomerular Notch1 mRNA expression was increased 4.53 and 9.27-fold, and Jagged1 was increased 14.76 and 9.95-fold (E1, E2).

CONCLUSIONS: By using LCM we demonstrated glomerular specific changes in Notch and TGF-β signaling pathways that were not evident in whole kidney mRNA. We report increased glomerular expression of TGF-β isoforms, Notch1 and Jagged1 not previously described in CD2AP KO, mice model of FSGS.

66 Presentation Time 9:00 AM Student

Alterations in F1F0 Atpase Levels in Renal Ischaemia

Shirley A. Wang, Michael Riordan, Gunilla Thulin, Michael Kashgarian, Kevin L. Behar, Norman J. Siegel. Magnetic Resonance Research, Yale University, New Haven, CT; Pediatrics, Yale University, New Haven, CT; Pathology, Yale University, New Haven, CT.

BACKGROUND: Renal ischaemia is associated with a rapid fall in cellular ATP levels in vivo. In response mitochondria change from being ATP producers to avid ATP consumers – using the reversible ATP synthase (also known as the F1F0 ATPase) in an attempt to maintain membrane potential.

OBJECTIVE: Changes in the expression and distribution of this proton pump were observed in an in vivo model of renal ischaemia.

DESIGN/METHODS: Male Sprague-Dawley rats (n=28) underwent 45 minutes bilateral renal artery occlusion. Kidneys were removed at reflow intervals of 15 minutes, 2, 6 and 24 hours. Non ischaemic control kidneys were obtained from sham operated rats. Aliquots of renal cortex underwent homogenization in protein and mitochondrial extraction buffers to allow comparison of expression between total and mitochondrial protein fractions. F1F0 ATPase expression was assessed by Western blotting using an antibody to the F1 subunit.

RESULTS: Consistent baseline expression of F1 ATPase was detected in sham operated rats and protein levels were comparable at each of the time points. Total cortical F1 ATPase levels increased by 46% of control values at 2 hours of reperfusion, remained elevated at 6 hours, but fell below 40% of control levels at 24 hours. Mitochondrial isolates demonstrated a fall in F1 ATPase to 25% of control levels by 2 hours of reflow; gradually returning to normal by 24 hours reflow.

CONCLUSIONS: Mitochondrial levels of renal cortical F1F0 ATPase decrease following ischaemic renal injury. Potential factors underlying reciprocal changes in total F1ATPase levels include decreased cytosolic degradation of mobilized protein or extra-mitochondrial synthesis. Recovery of mitochondrial F1 ATPase levels is associated with a marked fall in total cortical F1 ATPase; this could reflect mobilization, phosphorylation or degradation. Changes in mitochondrial F1F0 ATPase concentration may be important in determining the direction in which the F1F0 ATPase exerts its pivotal dual role in regulating cellular energetics in extremis.

67 Presentation Time 9:15 AM Fellow

The Risk of Cardiovascular Disease in Adults Who Have Had Childhood Nephrotic Syndrome

Brent Lee Lechner, Detlef Bockenhauer, Sandra Iragorri, Thomas L. Kennedy, Norman J. Siegel. Division of Pediatric Nephrology, Department of Pediatrics, Yale University School of Medicine, New Haven, CT.

BACKGROUND: The increased risk of cardiovascular disease (CVD) in patients with long-term hyperlipidemia is well documented. However, patients with hyperlipidemia as a transient consequence of intermittent relapses of nephrotic syndrome (NS) have not been studied. No long-term studies have provided data pertaining to the incidence of CVD in adults who had had relasping steroid sensitive childhood NS (R-SSNS).

OBJECTIVE: To determine if patients with R-SSNS are at increased risk for the non-renal long-term complication of CVD as adults.

DESIGN/METHODS: Forty patients who are currently between 25 and 53 years of age but had R-SSNS during childhood participated in a telephone interview specifically targeting CVD. Symptoms or events (angina, shortness of breath, arrhythmias, cardiomyopathy, cardiac arrest, myocardial infarction and pulmonary edema) that were sought, were the same as those obtained by the National Center for Health Statistics. During the course of childhood NS, these patients were exposed to factors which might have contributed to an increased risk of CVD: recurrent episodes of proteinuria and hyperlipidemia along with intermittent treatment with high dose steroids, which may be associated with transient elevations in blood pressure.
RESULTS: At the time of follow-up, 23-46 years after cessation of NS, none of these patients had end-stage renal disease or chronic kidney disease. Three patients had experienced a myocardial infarction (MI): a 32 year old male with a strong family history of cardiovascular disease; a 41 year old male with history of heavy smoking, hypertension, diabetes mellitus, and elevated cholesterol and a 31 year old male after a cocaine overdose. No mortality in the study population as a result of CVD was ascertained.
CONCLUSIONS: The occurrence of events and mortality from CVD is not different in this cohort of patients with R-SSNS compared to patients of a similar age in the general population. The occurrence of CVD mortality is lower than that of patients in the same age groups who are on dialysis. In the three cases who developed CVD and an MI, other well known risk factors for CVD were present. The data suggest that factors associated with relapsing NS, such as intermittent therapy with steroids or transient hyperlipidemia, are not independent risk factors and do not place patients with R-SSNS at increased risk for CVD or mortality compared to the general population.

68 Presentation Time 9:45 AM — Fellow

Ambulatory Blood Pressure (ABP) Abnormalities Correlate With the Presence of Microalbuminuria (MA) in Minority Adolescents With Type 2 Diabetes Mellitus (T2DM)

Leigh M. Ettinger, Mehul B. Patel, Katherine Freeman, Joan R. Di Martino-Nardi, Joseph T. Flynn, Pediatric Nephrology, Children's Hospital at Montefiore, Bronx, NY; Biostatistics, Montefiore Medical Center, Bronx, NY; Pediatric Endocrinology, Children's Hospital at Montefiore, Bronx, NY.
BACKGROUND: Adults with T2DM have been shown to have abnormalities of ABP that correlate with incipient diabetic nephropathy, as reflected by the presence of MA. Little is known about whether similar manifestations of end organ damage are present in the growing cohort of children with this disease.
DESIGN/METHODS: We enrolled 22 (12 female) minority (7 African-American, 13 Hispanic Carribean, 2 other)postpubertal adolescents (14.7±1.9 years of age, range 11.8 to 18.1) diagnosed with T2DM within the past three years. Their mean body mass index was 34.8±7.2 (range 22.0-51.7) kg/m^2 and their mean hemoglobin A1C was 7.6%±2.0 (range 5.5-13.6). ABP monitoring was performed and a 24 hour urine was collected. Blood was obtained for a fasting lipid profile, blood urea nitrogen, creatinine, hemoglobin A1C, homocysteine, and C reactive protein.
RESULTS: We found that 36.4% of subjects had MA (defined as ≥30mg of microalbumin/24 hour). 68.2% were classified as systolic nondippers (nocturnal decline in mean systolic BP<10%). There were significant associations between the presence of MA and the presence of a mean daytime systolic BP (SBP) >95th percentile (p=0.007, by Fisher's Exact test) and a mean nocturnal SBP >95th percentile (p=0.022). There was also a significant association between the presence of MA and the daytime SBP load (p=0.022) and nighttime diastolic BP load (p=0.031) being greater than 40%. The mean daytime SBP was significantly greater in subjects with MA compared to those without MA (127±9 mmHg vs 118±7 mmHg, p=0.014, by Mann-Whitney test). Those with MA had a mean daytime SBP load that was significantly higher than those without MA (49.1%±20 vs 17.9%±16.8, p=0.005). There were no significant differences between those with and without MA regarding their sex, race, age, family history of hypertension, duration of T2DM, diabetes medications, waist-hip-ratio, hemoglobinA1c, homocysteine, or C reactive protein.
CONCLUSIONS: This study is the first to examine the prevalence of ABP abnormalities and MA in adolescents with T2DM. As in adults, adolescents with T2DM exhibit abnormalities of ABP that are associated with evidence of incipient nephropathy. Long term follow-up studies are needed to further delineate the renal and cardiovascular sequelae of T2DM in this population.

69 Presentation Time 10:00 AM

Beneficial Effect of Combination Therapy With Angiotensin Converting Enzyme Inhibitors (ACEI) and Angiotensin Receptor Blockers (ARB) on Proteinuria in Pediatric Patients

Tania Mucci, Rachel Frank, Suzanne Vento, Bernard Gauthier, Marcela Vergara, Howard Trachtman, Pediatrics, Schneider Children's Hospital, New Hyde Park, NY.
BACKGROUND: Persistent proteinuria in patients with chronic renal disease is considered a poor prognostic sign. Administration of ACEI reduces proteinuria and protects renal function. ARB therapy, as a single agent, also lowers proteinuria. There are no data about the effects of combined ACEI-ARB treatment on renal function or urinary protein excretion in pediatric patients.
OBJECTIVE: To determine whether addition of ARB therapy to children and adolescents already receiving an ACEI safely and effectively reduces proteinuria.
DESIGN/METHODS: A chart review was performed on patients who had persistent proteinuria after treatment with steroids and/or other immunosuppressive agents and who were then given an ACEI and ARB. The following data were tabulated — age, gender, race, BP, serum K^+ concentration, estimated GFR, and early morning urine sample protein:creatinine ratio (Up/c) — at initiation of ACEI, prior to addition of ARB, and at the last assessment on combined ACEI-ARB therapy. Data are provided as mean±SD.
RESULTS: Thirteen patients (10 M: 3 F), age 13.4 ±5.9 yr, were included in this review. Children treated were 9 Whites, 2 Blacks, 1 Asian, and 1 Hispanic. The underlying disease was FSGS in 8 children, Alport syndrome 2, HSP 1, MCNS 1, and obstructive uropathy 1. Patients were initially treated with enalapril, 11±5 mg/day, for 30±5 months. Losartan was added, 24±10 mg/day, for 4±2 months. Up/c at the start of ACEI was 2.9±1.4 and declined to 2.1±1.1 prior to addition of ARB (P=0.13). At the last evaluation on combined ACEI-ARB therapy, Up/c fell 48% to 1.1±0.8 (P=0.0006 *vs* initial value and P=0.02 *vs* ACEI alone). Combination therapy was effective (>15% decline) in children with nephrotic-range (3/4) or sub-nephrotic-range proteinuria (7/8). Mean BP, serum K^+ level, and estimated GFR were not altered by the ACEI or combined ACEI-ARB therapy regimens.
CONCLUSIONS: The findings of this open-label,non-randomized trial suggest that combined ACEI-ARB therapy is well tolerated and decreases proteinuria in pediatric patients without adverse effects on BP, estimated GFR, or serum K^+ concentration. Further work is needed to determine whether combined ACEI-ARB treatment is effective in all forms of kidney disease, yields a sustained reduction in proteinuria, and results in long-term stabilization of kidney function.

Plenary Session II and Young Investigator Award Competition

Saturday, March 27 1:30pm–3:30pm Regency DEFG

70 Presentation Time 2:30 PM — Fellow

The Impact of Maternal Immune Status on the Development of Allergic Disease

A. Matson, L. Zhu, E. Breen, R. Clark, C. Schramm, B. Lingenheld, L. Puddington, Neonatology, University of Connecticut Health Center, Farmington, CT; Immunology, University of Connecticut Health Center, Farmington, CT; Pediatrics, University of Connecticut Health Center, Farmington, CT; Rheumatology, University of Connecticut Health Center, Farmington, CT.
BACKGROUND: Epidemiologic studies suggest that there exists a "sensitization window" in infancy, during which exposure to environmental antigens maximizes the risk for allergic symptoms upon re-exposure to the same antigen later in life. This may partially be explained by the production of Th2 cytokines by the uterus or amnion during gestation. High levels of maternal Th2 cytokines could divert the developing immune system away from Th1 polarization and toward the production Th2 cytokines and the development of allergy.
OBJECTIVE: The goal of this project was to determine the impact of maternal immune status on the development of allergic airway inflammation in a murine model of asthma.
DESIGN/METHODS: Female C57BL/6J mice were immunized with OVA/Alum or OVA/CFA in order to generate antigen-specific memory T cells capable of producing predominantly Th2-type cytokines (OVA/Alum priming) or Th1-type cytokines (OVA/CFA priming). Females sensitized under Th1 or Th2 conditions were subjected to challenge with aerosolized OVA (Aer) and 6 wk later were bred with nonsensitized C57BL/6J males and subjected to repeat OVA Aer while pregnant. Offspring from both groups and additional age and sex-matched controls (without exposure to OVA-sensitized mothers) were subjected to OVA-induced allergic airway disease starting at 1month of age, then analyzed for differences in airway inflammatory cells and for OVA-specific antibodies by ELISA.
RESULTS: Offspring born to Th1 polarized females exhibited significantly lower levels of OVA-specific IgE, IgG1 and IgA as compared to controls after antigenic challenge. These mice also exhibited significantly lower numbers of leukocytes and eosinophils in bronchoalveolar lavage fluid. In contrast, offspring born to Th2 polarized females showed higher levels of OVA-specific IgE, but lower levels of IgG1 and IgA as compared to controls. These mice had increased numbers of leukocytes and eosinophils in bronchoalveolar lavage fluid.
CONCLUSIONS: These results suggest that the status of the maternal immune system during pregnancy affects development of Th2-type allergic responses in offspring during postnatal life. Perinatal antigen exposure within an accentuated Th2 environment during pregnancy may increase the risk for allergic responses later in life, while exposure to antigen within an accentuated Th1 environment may be protective against future allergic expression.

71 Presentation Time 2:45 PM — Fellow

Identification of a Novel POSH Homologue, POSH2 and Its Role in Neuronal Apoptosis. Possible Implications for Developmental Brain Injury

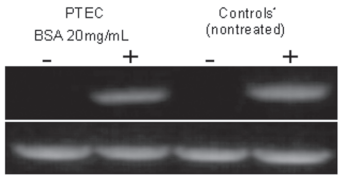
Michael Wilhelm, Nickolay V. Kukekov, Zhiheng Xu, Susan Vannucci, Lloyd A. Greene, Pediatric Critical Care Medicine, Columbia University Health Sciences, New York, NY; Pathology, Columbia University Health Sciences, New York, NY. (Sponsored by Charles Schleien)
BACKGROUND: Neuronal apoptosis plays important roles in normal development and following hypoxia-ischemia (HI). The c-Jun N-terminal kinase (JNK) cascade has been implicated in neuronal apoptosis and several scaffold proteins, including POSH (Plenty of SH3s), enhance JNK signaling.
OBJECTIVE: To identify and characterize a homologue of the scaffold protein POSH and determine whether the proapoptotic protein Nix (19 kDa-interacting protein) interacts with these scaffolds. We also investigated changes in JNK pathway activation and scaffold proteins following neonatal HI.
DESIGN/METHODS: POSH2 was cloned from total rat brain RNA, flag-tagged and inserted in the pCMS-EGFP vector. Mutations were made using site-directed mutagenesis. Mutliple tissue northerns were probed with specific POSH and POSH2 oligonucleotides to determine their tissue distribution. To inhibit the proteasome we used lactacystin. Immunpoprecipitation determined protein interactions. Nix was identified as a POSH-binding protein by yeast two-hybrid analysis. Apoptosis was identified by strip counting of GFP+ cells and Hoechst staining to determine nuclear morphology. Neonatal HI was performed in the P7 rat using the Rice-Vannucci model to examine changes in JNK activation and levels of POSH/POSH2, Nix and its homolgue BNip3.
RESULTS: POSH2 contains a Zn-ring domain, a rac-binding domain and three SH3 domains. The predicted protein shares 33% identity and 81% similarity with POSH. Targeting of POSH2 for proteasomal degradation is mediated by the ring domain and inhibited by lactacystin. POSH2 and POSH have differential tissue distribution, though POSH2 is present in cortical neurons and PC12 cells by PCR. POSH2 interacts with members of the JNK pathway and promotes apoptosis, which is blocked by a dominant negative c-Jun, in neuronal PC12 cells. Furthermore, POSH2 increases JNK phosphorylation. Nix/BNip3 also promote apoptosis of neuronal PC12 cells and increase JNK activation. Neonatal HI increased phosphorylated JNK in the ipsilateral hemisphere compared to total JNK and decreased levels of POSH proteins and Nix/BNip3.
CONCLUSIONS: POSH2 is a functional homologue of POSH. Nix/BNip3 activate the JNK pathway. We speculate that this activation occurs through interaction with POSH proteins. The JNK pathway is activated early following neonatal HI. POSH scaffold proteins may potentiate this activation.

72 Presentation Time 3:00 PM — Fellow

Colony-Stimulating Factor 1 (CSF-1) Role in a Model of Proteinuria-Induced Tubulointerstitial Disease (TID)

Corina Nailescu, Frederick J. Kaskel, E. Richard Stanley, Pediatric Nephrology, Children's Hospital at Montefiore, Bronx, NY; Developmental and Molecular Biology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY.
BACKGROUND: Proteinuria stimulates proximal tubular epithelial cells (PTEC) to produce cytokines that recruit monocytes, giving rise to macrophages (Mφ) that have a role in inducing TID. We have previously shown that exposure of PTEC to bovine serum albumin (BSA) induces a dose/time dependent increase in the protein expression of CSF-1, the primary regulator of the survival and proliferation of Mφ (unpublished).
OBJECTIVE: 1. Investigate the mechanism of BSA induced CSF-1 overexpression *in vitro.*
2. Determine if CSF-1 is required for proteinuria-induced TID *in vivo.*
DESIGN/METHODS: 1. PTEC were incubated with serum free medium or BSA. CSF-1 mRNA was measured by RT-PCR.
2. CSF-1-deficient *($Csf1^{op}/Csf1^{op}$)* and wild type *($Csf1^{op}/+$)* adult mice were injected for 10 days with 10 mg BSA/g body weight or saline. Mφ were immunostained using anti-F4/80 antibody and Mφ in S phase were identified using anti-PCNA antibody.
RESULTS: 1. There was no CSF-1 mRNA expression in nontreated PTEC, but BSA stimulated it.
2. All BSA treated mice developed proteinuria. CSF-1-deficient mice had an ~ 50% reduction of the interstitial Mφ infiltrate compared with wild type mice and less proliferating Mφ.

Protein Stimulated CSF-1 mRNA Expression



*Controls:
- negative: nontransfected 293T cells
- positive: 293T cells transfected with CSF-1

CONCLUSIONS: BSA activates CSF-1 mRNA and protein expression *in vitro. In vivo*, in the absence of CSF-1, proteinuria-induced interstitial Mφ infiltrate is significantly reduced. CSF-1 is an important mediator of TID in proteinuric diseases and could be a therapeutic target in chronic glomerulopathies.

Interstitial Mφ Infiltrate is Reduced in CSF-1-deficient Proteinuric Mice

	BSA Wild Type	BSA Op/Op	Saline Wild Type	Saline Op/Op
Urine BSA (μg/μmol creatinine)	1.8±0.4	2.1±0.5	0±0	0±0
Interstitial Mφ infiltrate (cells/HPF)	228±46•	124±28	34±5	12±3
Proliferating Mφ (cells/HPF)	32±4♦	12±2	12±4	4±1

Results are mean±1 SD. P< 0.05 compared with BSA-injected Op/Op mice•. P< 0.05 compared with BSA-injected Op/Op mice♦

73 Presentation Time 3:15 PM Fellow

A Novel Promoter Element in the Tyrosine Hydroxylase Gene Mediating the Response to the Dietary Short Chain Fatty Acid Butyrate

Pranav Patel, Bistra Nankova, Edmund F. LaGamma. Pediatrics, Division of Newborn Medicine, Westchester Medical Center - New York Medical College, Valhalla, NY.

BACKGROUND: Butyrate is widely recognized as progressively accumulated byproduct of postnatally-acquired enteric bacterial carbohydrate fermentation in the first week of life. Abundant evidence documents its role in genetic reprogramming of colonic epithelial cells, as a tumor suppressor agent, in apoptotic cell death and in gene regulation. The molecular mechanisms of butyrate action remain unknown, yet, in addition to chromatin remodeling, combinations of trancription factors are engaged by butyrate to regulate transcription of specific genes in a cell- and promoter-specific context. Our previous studies in a PC12 cell model system revealed that butyrate at physiological concentrations can regulate the transcription of tyrosine hydroxylase (TH; see Nankova, Peds Res 53:113,2003 & Mally, Peds Res In press)

OBJECTIVE: To identify the promoter element(s) mediating the transcriptional effects of butyrate on the TH gene.

DESIGN/METHODS: PC12 cells (rat pheochromocytoma) were either left untreated or treated with 1mM sodium butyrate. All cells were electroporated the next day with a TH-promoter driving expression of a CAT reporter gene. CAT activity was determined by a liquid scintillation method. DNA-protein interactions were examined by electrophoretic mobility shift assay (EMSA). Mutations were introduced by PCR-based site directed mutagenesis.

RESULTS: Two motifs exist in the rat TH promoter homologous to the butyrate response element (BRE) previously identified in the enkephalin gene (LaGamma Peds Res A2420, 2000). No such motifs were found in DBH or PNMT promoters, and both genes were not affected by butyrate. The regions in the TH promoter overlapping the BRE sites confer butyrate responsiveness to a CAT reporter gene in transient transfection studies. Using EMSA, we identified a characteristic pattern of sequence-specific DNA-protein interactions in butyrate-differentiated PC12 cells. Competition with TH-CRE oligonucleotides changed the mobility pattern, suggesting involvement of CREB/ATF factors. Single base mutation of the BRE sequence abolished the binding.

CONCLUSIONS: We identified two novel functional elements in the TH promoter mediating transcriptional responses to butyrate. Thus, dietary butyrate may have an extended role in the development of the nervous system function linking gut-derived exogenous regulatory signals to neuronal plasticity, cardiovascular functions, stress adaptation and behavior.

Adolescent Medicine Platform Session

Saturday, March 27 3:45pm–5:00pm Riverside

74 Presentation Time 3:45 PM

Emergency Contraception: Are Pediatric Residents Counseling and Prescribing to Teens?

Sylvia W. Lim, Lori Legano, Kelechi N. Iheagwara, Susan M. Coupey. Pediatrics, Albert Einstein College of Medicine/CHAM, Bronx, NY; Pediatrics, New York University Medical Center, NY, NY.

BACKGROUND: Emergency Contraception (EC) can be a good option for preventing teenage pregnancy and abortion. However, many teens are unaware of the availability of EC. Pediatric residents provide health care for many teens but we know very little about residents' attitudes, counseling and prescribing practices related to EC.

OBJECTIVE: To assess pediatric residents' attitudes and practices related to EC counseling and prescribing for teens.

DESIGN/METHODS: An anonymous self-administered survey was administered to pediatric residents (PGY 1-3) from two large inner-city academic medical centers. Both centers serve a predominantly low-income Hispanic and African-American population.

RESULTS: 72/120 residents participated in the survey; 36% PGY1, 39% PGY2, 25% PGY3. 81% female; 85% aged 25-30 years. Less than a third (30%) reported counseling teens about the availability of EC during routine non-acute care visits and 53% provided EC counseling during visits for contraception. Respondents counseled 39% of girls versus 9% of boys ($p<0.05$). 6% of pediatric residents reported that they prescribed EC often, 52% rarely and 42% never. When residents were asked whether prescribing EC would encourage teens to practice unsafe sex or would discourage compliance with other contraceptive methods, the majority answered "No" (73% and 70%, respectively). Just over half of the pediatric residents (54%) reported that they would prescribe EC for teens to have on hand prior to unprotected sex. However, the majority (72%) did not think that EC should be available over the counter, without prescription. Further analysis by year of residency training showed that more PGY 1 than 2 and 3 believed that EC should not be available over the counter (92% vs 60%, $p<0.05$). Also, more PGY 1 than 2 and 3 thought that giving EC would discourage compliance with other contraceptive methods (48% vs 21%, $p<0.05$) and they would consider not giving EC to adolescents to have prior to unprotected sex (65% vs 35%, $p<0.05$).

CONCLUSIONS: Pediatric residents are missing many opportunities to counsel and prescribe EC to teens. We found that less than one-third of pediatric residents routinely counseled teenaged patients about the availability of EC and the large majority rarely or never prescribed this contraceptive method. First year residents had more conservative attitudes towards EC than more senior residents, possibly reflecting less experience with this method.

75 Presentation Time 4:00 PM Fellow

Opportunistic Screening for *Chlamydia trachomatis*(CT) Infection in Adolescent Males in a Non Inner City School-Based Health Clinic

Dalan S. Read, Amy L. Suss, April Lee, Edward McCabe, Tamara Reznik, Margaret R. Hammerschlag. Pediatrics, State University of New York Downstate Medical Center, Brooklyn, NY; Pediatrics, Staten Island University Hospital, Staten Island, NY.

BACKGROUND: The prevalence of CT is highest among sexually active (SA) adolescent females 15-19 y.o., with prevalences in the USA and NYC ranging from 10-46%. Comparable data for adolescent males are limited, as males appear to access the health care system less frequently than their female counterparts. Use of nucleic acid amplification tests (NAATs) has allowed for non invasive testing for CT in nontraditional settings. This strategy has been recommended as a public health opportunity to reduce CT infection in at risk youth.

OBJECTIVE: The purpose of this study was to determine the prevalence of CT infection in SA males in a non inner city urban high school-based clinic by opportunistic screening with an NAAT.

DESIGN/METHODS: Non-invasive urine testing with a NAAT for CT was performed on SA males coming to the clinic for either a routine, problem oriented or sports physical, sexually transmitted infection (STI), or STI counseling with a social worker. Urine specimens with no unique identifiers were collected and transported to the laboratory for NAAT testing.

RESULTS: From 1/03 to 11/03, 131 males 14-19 y.o.(mean 16.7 yrs) were enrolled; only 1(0.76%) was positive for CT. Thirty boys (22.9%) came for a routine physical, 28 (21.4%) for a sports physical, 15 (11.5%) for a problem oriented visit, 3 (2.3%) for a STI, and 55 (42%) were seen by the social worker. Thirty-seven (28.2%) reported ≥ 1 sex partner during their lifetime, 54 (41.2%) reported first intercourse at the mean of 14.5 yrs, 107 (81.6%) reported regular condom use, and the majority (>90%) reported intercourse with same aged female partner(s).

CONCLUSIONS: Non-invasive testing with NAATs have facilitated STI screening, especially in adolescent populations. Urine screening was well accepted by the students. The prevalence of CT (0.76%) was considerably lower compared to females in the same geographic area (2.8%). These prevalences are lower than what has been previously reported in other non inner-city populations. This could be due, in part, to high condom use (81.6% vs. ~50% nationally) or first intercourse with sexually inexperienced same aged partners. These results also demonstrate that one cannot extrapolate from one adolescent population to another even in the same city; opportunistic screening of males for CT infection may not be a cost effective strategy in this population.

76 Presentation Time 4:15 PM Fellow

The Association of Dietary Glycemic Index and Load With Pediatric Overweight and the Metabolic Syndrome: A National Perspective

Carolyn J. Tabak, Peggy Auinger, Stephen Cook, Michael Weitzman. Strong Children's Research Center, University of Rochester, Rochester, NY; AAP Center for Child Health Research, University of Rochester, Rochester, NY.

BACKGROUND: Glycemic index (GI) is a food property, measured directly by the blood glucose response to the carbohydrates in a food compared to a standard. Glycemic load (GL) is the product of the GI and the amount of carbohydrate in the food. Low GI and GL diets have received much interest as a potential treatment for pediatric overweight. However, high GI and GL diets have not been shown to be associated with pediatric overweight or any of its complications. One such complication is Metabolic Syndrome, which is recognized as a risk factor for heart disease and diabetes in adults.

OBJECTIVE: To determine whether high GI or GL diets are associated with overweight and/or Metabolic Syndrome in adolescents.

DESIGN/METHODS: Data from 2277 adolescents ages 12-19 yrs in the Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994) were analyzed with SUDAAN. GI and GL were determined based on food frequency questionnaires (FFQ) using previously published methods. We defined subjects with a BMI≥95%ile for age and sex as overweight, and identified adolescents with Metabolic Syndrome as those having abnormalities in 3 or more of the following 5 domains: central adiposity, hypertension, fasting glucose, HDL, and triglycerides. Multivariate logistic regressions were performed to determine if GI and GL were independent predictors of overweight or Metabolic Syndrome. Subjects were excluded if they did not complete FFQ, had not fasted, were pregnant, or were taking glucose-regulating medicines.

RESULTS: 10.6% of adolescents were overweight, and 4.6% met criteria for Metabolic Syndrome. Subjects with higher GI diets were more likely to be overweight (OR=434, 95%CI 3.0-62860). GL was not a significant predictor of overweight. However, a higher GL diet appeared to be protective for Metabolic Syndrome (OR=0.35, 95%CI 0.16-0.78).

CONCLUSIONS: A high GI diet increases the likelihood of overweight in adolescents. The finding that a high GL diet did not predict overweight may be due to differences in caloric expenditure or the nature of the FFQ, which did not specify serving size. It has been observed that obese adults underreport food intake. If this phenomenon occurs in adolescents, this could explain why a high GL diet did not predict overweight or Metabolic Syndrome, and instead appeared to protect against Metabolic Syndrome. These results justify further research in this area.

77 Presentation Time 4:30 PM Fellow

A Rose by Any Other Name: "Underdiagnosis" of Overweight in U.S. Adolescents Using Pediatric Standards

Carolyn J. Tabak, Peggy Auinger, Susanne Tanski, Michael Weitzman. Strong Children's Research Center, University of Rochester, Rochester, NY; AAP Center for Child Health Research, University of Rochester, Rochester, NY.

BACKGROUND: The prevalence of pediatric overweight has risen dramatically in recent years and estimates indicate that 15.5% of ages 12-19 years are overweight. Overweight in children is defined as having a body mass index (BMI)≥95%ile by age and sex. In contrast, in adults it is defined as a BMI greater than 25 kg/m^2. Some teens with BMIs over 25, however, are not ≥95%ile for age and sex and thus do not meet the pediatric definition of overweight. Overweight is a risk factor for the Metabolic Syndrome, which has been implicated in the development of diabetes and heart disease. Therefore, accurate, early diagnosis and treatment are critically important.

OBJECTIVE: To determine the prevalence of teens with BMI≥25 who do not meet the pediatric definition of overweight, and to determine the prevalence of Metabolic Syndrome and its components within this "underdiagnosed" population.

DESIGN/METHODS: Data from 2392 teens ages 12-19 years from the Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994) were analyzed. BMI percentiles (from CDC growth charts, 2000) were divided into categories of <95%ile and ≥95%ile by age and sex and compared with the adult overweight criteria of BMI≥25. Measurements of waist circumference, fasting glucose levels, HDL, triglycerides, and blood pressure were used to determine the prevalence of Metabolic Syndrome, defined as abnormalities in 3 or more of these 5 domains.

RESULTS: In this sample, 10.8% of adolescents had BMI≥25, but did not meet the pediatric standard for

overweight. Of this population, 8.3% had hypertension, 28.2% had low HDL, 33.6% had hypertriglyceridemia, 2.3% had fasting glucose ≥110 mg/dL and 19% had a waist circumference>90%ile by age. Metabolic Syndrome was present in 6.9%. In contrast, in normal weight adolescents (BMI<85%ile and <25), only 0.05% (p=.03) had Metabolic Syndrome. Of these "underdiagnosed" adolescents, 23% had BMIs<85%ile, and were therefore classified as normal weight.
CONCLUSIONS: On a population basis, the sole use of pediatric BMI growth charts to determine overweight will "underdiagnose" 2.1 million teens in the US. Metabolic complications of overweight as defined by BMI≥25 are already evident in teens. While applying CDC growth charts for screening for overweight in teens is important, using a BMI value of 25 may be a quicker method to trigger providers to screen for components of metabolic syndrome in teens.

78 Presentation Time 4:45 PM — Fellow

Effect of Complementary Therapies on Lung Function in Adolescents With Acute Asthma Exacerbation

Marina Reznik, Iman Sharif, Philip O. Ozuah. Pediatrics, The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Complementary or Alternative Medicine (CAM) use is prevalent in adolescents with asthma. However, the effect of CAM use on objective measures of lung function in adolescents with acute asthma attack has not been studied.
OBJECTIVE: To determine the effect of commonly used CAM on an objective measure of lung function in adolescents with acute asthma..
DESIGN/METHODS: Prospective cohort study of inner-city high school students with asthma. Over a 6-month period, we asked subjects to record each asthma attack and all the therapies used. Using a Respironics Healthscan peak flow meter, for each attack, subjects recorded their peak flow (best of three) before, 10 and 20 minutes after using a treatment for an acute asthma attack. We also asked subjects to rate their self-perceived effectiveness of each treatment, using a 5-point Likert scale. The outcome measure was the therapeutic effect (L/min increase in peak flow), calculated as the difference between pre- and post-treatment measurements. For each therapy, we compared the mean change in peak flow. Linear regression controlled for the use of more than one therapy at a time, and for the severity of the acute attack (measured by the percent predicted pre-treatment peak flow). We used spearman correlation analysis to compare the objective increase in peak flow with the patient's perception of feeling better.
RESULTS: 161 individual peak flow measurements were obtained from 52 subjects. Mean change in peak flow was highest for syrups (104 L/min), followed by massage (66 L/min), albuterol (63 L/min), prayer (60 L/min), and rubs (58 L/min). Linear regression analysis revealed the following as independent predictors of a therapeutic effect: syrups (B= .28, p<.0001), albuterol (B= .20, p=.008) and water (B= -.16, p=.037). After controlling for severity of the acute attack, the following remained as independent predictors of a therapeutic effect: syrups (B= .30, p<.0001) and albuterol (B= .19, p= .009). Increase in peak flow measurements corresponded to a perception by a subject of feeling "better" (r = .244, p=.002).
CONCLUSIONS: These results suggest that CAM syrups may have a therapeutic effect on an objective measure of lung function. This therapeutic effect correlated with the subjective perception of feeling better. Further research is needed to determine the effectiveness of specific components found in CAM syrups used by adolescents with asthma.

Gastroenterology Platform Session

Saturday, March 27 3:45pm–5:00pm Mead B

79 Presentation Time 3:45 PM — Fellow

Effect of Antenatal Placental Insufficiency on Postnatal Preterm Infant Gastrointestinal Function

Elena Wachtel, Karen Hendrics-Munoz, Ilan Timor. Pediatrics, NYU Medical Center, New York, NY. (Sponsored by Robert Schacht)
BACKGROUND: Uteroplacental insufficiency leads to fetal growth retardation, which is a major cause of perinatal and postnatal morbidity. Current responses of the fetal intestine to intermittent or sustained vascular insufficiency, is not well understood.
OBJECTIVE: To determine if antenatal placental insufficiency in infants ≤ 34 weeks gestation leads to postnatal intestinal dysfunction. To determine if, the degree of, placental insufficiency is associated with varying intestinal functional outcome. To assess if intestinal dysfunction affects infant growth and the length of hospital stay.
DESIGN/METHODS: All infants≤ 34 weeks gestation were retrospectively identified from prospective NICU data. Infants were divided into two groups based on the results of Doppler studies. Patients with documented normal Doppler studies were Group I while infants with any degree of placental insufficiency (AEDF, REDFor elevated S/D ratio) were noted as Group II. Infants in Group II were further subdivided into Group II A, with elevated S/D ratio and Group II B, with AEDV or REDF. Medical outcome and demographic data was obtained from individual charts.
RESULTS: A total of 46 infants ≤ 34 weeks gestation were included in the study. 27 in Group I (Normal) and 19 in Group II. Group II A had 8 infants while Group II B had 11. The infants in Group II and II B experiencing a significant delay in meconium passage (>3 days) of 21% and 27% versus 3% for normal infants; the delay in tolerating enteral feeding within the first week of life was 64% and 82% for groups II and IIB versus 45% for normals; infants in Group I only 8% did not reach full feeding by 6th week of life, while 37% of infants in Group II and 55% in Group IIB have not reach full feeding by 6th week, the requirement for TPN > 3 weeks was 52% and 82% for groups II and IIB, versus 18% for normals. The lengths of stay for Group II and IIB, with mean values of 43 and 59 days were significantly longer than the 23 days for infants in group I.
CONCLUSIONS: There is a strong correlation between antenatal uteroplacental insufficiency and postnatal intestinal dysfunction, in premature infants. Neonates with AEDF or REDV are especially at risk for postnatal intestinal dysfunction, which may affect infant growth and length of hospital stay. This may occur as a result of antenatal redistribution of blood flow to vital organs, leading to altered postnatal gastrointestinal motility or maturation.

80 Presentation Time 4:00 PM

Serum Phosphate Levels During the First Four Weeks of Age in Premature Infants

Nirupama Laroia, Nahed El Hassan, Rita M. Ryan. Department of Pediatrics, University of Rochester and Golisano Children's Hospital at Strong, Rochester, NY; Department of Pediatrics, SUNY-Buffalo and Women and Children's Hospital of Buffalo, Buffalo, NY.
BACKGROUND: Phosphate is important for many metabolic functions. The only article reporting phosphate norms in premature infants was published in 1968.
OBJECTIVE: To describe phosphate levels for the first 4 weeks of life for infants with birthweights 500-1500 grams.
DESIGN/METHODS: This observational study included 52 consecutively born premature infants with birthweights 500-1500 grams: Group A, 500-1000 grams (n=24) and Group B, 1001-1500 grams (n=28). Phosphate levels were measured daily for the first 5 days and then weekly until 4 weeks of age. Phosphate levels were correlated with clinical data including demographic characteristics, need for respiratory support, and total phosphate supplementation by parenteral and enteral routes.
RESULTS: Mean birthweight and gestational age were 781 grams, 26.5 weeks in Group A and 1350 grams, 30.4 weeks in Group B. Two measures of acuity (need for ventilatory support and amount of oxygen supplementation) were measured and found to be statistically higher in Group A vs. B. The total amount of phosphate supplementation per kg was comparable on a daily basis in both groups. Phosphate levels are summarized below. With the exception of the first two days of life, phosphate levels were statistically lower in group A in comparison to B.
Serum Phosphate Levels

Age (days)	Phosphate levels (Group A) mg/dl	Phosphate levels (Group B) mg/dl
1	6.16 ± 1.33	5.73 ± 0.90
2	5.96± 1.55	6.14± 1.13
3	5.21±1.53	6.15± 1.22
4	4.84±1.60	5.86±1.07
5	4.41±1.69	5.66±1.39
12	5.13±1.23	6.79±1.16
19	5.97±1.17	7.35±0.91
26	5.98±1.12	6.79±0.71
33	5.73±1.21	6.58±0.60

CONCLUSIONS: The hospital course of Group A was more acute than Group B as reflected by a higher need of mechanical ventilation or amount of oxygen supplementation. This entails increased metabolic demands in Group A and possibly more need of high-energy bonds of Adenosine Triphosphate and thus may contribute to lower phosphate levels. An important question is whether phosphate levels can be used as a marker of level acuity and if aggressive phosphate replacement would be associated with an improvement of the status of the acutely ill neonate. A prospective study is required to study signs of hypophosphatemia and the effects of phosphate repletion in this age group.

81 Moved to Sunday – Presentation Time 11:45 AM - Neonatology II Platform Session

Current AAP Vitamin D Supplementation Guidelines May Be Inapproporiate for Some Breastfeeding Term Hispanic Neonates

Daniel S. Hirsch, Christine Dillon, John M. Lorenz, Michael F. Holick. Pediatrics, Columbia University, New York, NY; Cornell Medical College, New York, NY; Medicine, Boston Univerity, Boston, MA. (Sponsored by Richard A. Polin)
BACKGROUND: In April 2003, the AAP recommended that, "… all infants have a minimum intake of 200 IU of vitamin D (Vit D) per day beginning in the first 2 months of life." Vit D and its metabolites play an important role in pre- and postnatal growth and development. The fetus is entirely dependent upon the mother for its supply of Vit D. Recent national surveys have revealed that Vit D deficiency (Vit D def) is common in Hispanic women of childbearing age. Due to the paucity of dietary sources of Vit D and the minimal cutaneous Vit D synthesis ocurring in our region from November through February the incidence of Vit D def, determined by measuring serum 25-hydroxyvitamin D (25-OH D) levels, is greatest in the winter.
OBJECTIVE: The incidence of Vit D def in healthy term Hispanic newborns was compared at the end of winter and summer.
DESIGN/METHODS: During March and September 2003, cord blood was collected from term (37-42 weeks) appropriate- and large-for gestational age (AGA and LGA) white-Hispanic neonates born at Palisades Medical Center (located at a latitude of approximately 40°N). Measurement of 25-OH D was performed via chemiluminescence protein binding assay. Prospectively, Vit D def was defined as a 25-OH D of <11ng/ml. Neonatal and maternal data were obtained from the hospital record and birth certificate.
RESULTS: In both groups, most mothers took prenatal vitamins. In March-born neonates, there was a significantly lower median 25-OH D level and a greater incidence of Vit D def.
CONCLUSIONS: In March, Vit D def is common among normal white-Hispanic AGA and LGA term neonates in Northern New Jersey. Further study is warranted to determine the actual incidence and potential fetal effects of Vit D def in this population. Due to human milk's low Vit D content, current AAP Vit D supplementation guidelines may result in a prolongation of Vit D def in breastfeeding Hispanic term neonates born at a latitude of 40°N in March. In order to minimize the duration of Vit D def in this group, modification of AAP guidelines is warranted.
Patient Characteristics & Vit D Levels

	End of Winter (n=74)	End of Summer (n=61)
Maternal Age	26 (6)	28 (7)
Prenatal Vitamin Intake (%)	85ε	97
Birth Weight	3442 (415)	3433 (418)
Gest Age	39.7 (1.3)	40 (1.2)
% AGA	78	79
Median 25-OH D	6*	24
% 25-OH D <5ng/ml	42*	0
% Vit D Deficient	69*	3

(std dev), * p ‹0.001, ε p = .048

82 Presentation Time 4:15 PM — Fellow

The Effects of Curcumin on the Expression of DF508-CFTR in Gastrointestinal Epithelia of a Cystic Fibrosis Mouse Model

Scott A. Weiner, Marilyn A. Pearson, Emanuela Bruscia, Diane Krause, John P. Geibel, Michael J. Caplan, Marie E. Egan. Pediatrics, Yale University School of Medicine, New Haven, CT; Surgery, Yale University School of Medicine, New Haven, CT; Cellular and Molecular Physiology, Yale University School of Medicine, New Haven, CT; Laboratory Medicine and Pathology, Yale University School of Medicine, New Haven, CT; Cell Biology, Yale University School of Medicine, New Haven, CT.
BACKGROUND: The most common mutation of the CFTR gene, ΔF508, results in the synthesis of a CFTR protein that is unable to fold correctly and assume its appropriate tertiary conformation. Consequently, the protein is retained in the endoplasmic reticulum (ER) and targeted for degradation. We have previously shown that ER calcium pump (SERCA) inhibitors, such as thapsigargin and DBHQ, can increase the surface expression and functional activity of ΔF508 in CF affected cells. Furthermore, in a ΔF508 mouse model, we have also shown that treatment with aerosolized ER calcium pump inhibitors normalizes the nasal epithelial potential defect, suggesting that we have altered the localization of ΔF508 CFTR in this in vivo model.
OBJECTIVE: Curcumin, a natural polyphenolic phytochemical, inhibits SERCA. Our objective is to investigate the effects of curcumin on the expression of ΔF508-CFTR in gastrointestinal epithelia.
DESIGN/METHODS: We have treated the ΔF508 CF mouse model with curcumin (orally fed three times/day for three days) and assessed functional expression of CFTR using the rectal epithelial potential difference (RPD) assay. RPD was performed on wild-type, heterozygous, and CF (ΔF508) mice pre and post treatment to determine if there is an increase in CFTR activity.

RESULTS: Untreated CF mice (n=7), had a mean baseline RPD value (-0.2 ± 0.6mV). The RPD did not significantly chnage after the addition of forskolin, an adenylate cyclase activator (-0.2 ±1.2mV). All of these findings are consistent with the CF phenotype. After treatment with curcumin, the RPD significantly decreased in response to forskolin (-5.3 ± 2.0mV, p<0.01). These findings are consistent with a correction of the CF phenotype. Preliminary immunohistochemical studies support these electrophysiologic findings.
CONCLUSIONS: Our preliminary data suggests that curcumin alters the expression of ΔF508-CFTR in the gastrointestinal epithelia in the mouse model. Presently short circuit current (Isc) studies, further immunohistochemical assays, and calcium signaling studies are underway to further characterize this observation.
M.E. Egan and M.J.Caplan are consultants for SEER Pharmaceuticals which supports this work.

General Pediatrics II Platform Session

Saturday, March 27 3:45pm–5:30 PM Mead A

83 Presentation Time 3:45 PM Fellow

Complementary Therapies vs. Albuterol: Does Severity of an Acute Asthma Attack in Adolescents Predict the Choice of Therapy?

Marina Reznik, Iman Sharif, Philip O. Ozuah. Pediatrics, The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Prior reports suggest a high prevalence of Complementary or Alternative Medicine (CAM) use among adolescents with asthma. However, no prior studies have investigated the relationship between the severity of an asthma attack and the choice of CAM vs. albuterol use for an acute asthma exacerbation in adolescents with asthma. We hypothesized that adolescents with more severe asthma attacks will be more likely to use albuterol as first line therapy.
OBJECTIVE: To test the hypothesis that adolescents with a more severe acute asthma attack are more likely to use albuterol preferentially over CAM as a first line treatment.
DESIGN/METHODS: We conducted a prospective cohort study of adolescents with asthma at an inner-city high school in the Bronx, NY. At enrollment, we asked subjects to maintain a diary of their asthma attacks for a consecutive period of six months. For each attack, we asked subjects to record all therapies used to treat it. We gave each subject a Respironics Healthscan peak flow meter and trained all subjects on its proper use. For every asthma attack, subjects were asked to record their pre-treatment peak flow (best of three). This peak-flow measurement was used as a proxy for the severity of the acute attack. Height was also recorded. We determined the mean pre-treatment peak flow measurements (percent predicted based on height) for each therapeutic modality.
RESULTS: 161 pre-treatment peak flow measurements were obtained form 52 subjects. 69% were female, mean age was 15.1 years (SD 1.2). Mean pre-treatment peak flow measurements (percent predicted) were similar between subjects who used CAM and those who used albuterol as first line therapy (Table).
CONCLUSIONS: In this study, severity of an acute asthma attack did not predict a preferential choice of albuterol treatment over CAM.

Mean pre-treatment peak flow measurements and first-line treatment for asthma

First-Line Treatment (N)	Mean Pre-Treatment Peak Flow (% Predicted)
Water (8)	359 (88)
Foods (15)	352 (77)
Syrups (10)	347 (76)
Albuterol (106)	311 (72)
Rubs (40)	308 (71)
Prayer (21)	303 (71)
Massage (19)	296 (69)
Teas (22)	293 (61)
Steam (6)	254 (66)

84 Presentation Time 4:00 PM House Officer

Quality of Care and Racial Disparities in Hospitalized Asthmatic Patients

Susan A. Fisher-Owens, Wendy M. Turenne, William Pastor, Kathleen Chavanu, Anthony D. Slonim. Children's National Medical Center, Washington, DC. (Sponsored by Michael Bell)
BACKGROUND: Asthma is a leading cause of acute and chronic illness in children and adults, almost tripling the mean cost of the asthmatic patient's healthcare and affecting quality of life measures including school attendance. It also disparately affects children of color. The Institute of Medicine has highlighted racial/ethnic inequities in care as a quality issue. Studies have looked at disparities in the care of asthmatic children before admission and after discharge, but not while in-patient.
OBJECTIVE: To describe racial inequities in asthmatic children admitted to pediatric academic hospitals.
DESIGN/METHODS: The Pediatric Health Information System (PHIS) dataset was used for these analyses. These data, from fiscal year 2003, represent detailed hospital-based data from 32 independent, academic pediatric hospitals. Patient-level, institution-level, and utilization variables were examined to determine their association with racial disparities in the care of ICD-9 coded asthmatic patients. Bivariable testing using a p-value <.05 was performed.
RESULTS: Of 17,406 recorded admissions for asthmatic patients between the ages of 2-21 years, Blacks represented 51% of the population; Whites, 40% (p<.01). In both racial groups, the outcomes were similar, with 99% of each racial group discharged home (p=NS). The average age for Blacks was higher than that for Whites (7.7 ± .1 vs 6.2 ± .1 years, p<.01). Black patients were insured by Medicaid more often than Whites (44 vs 33%, p< .01). More Blacks were admitted through the Emergency Department than Whites (61 vs 50%, p<.01). The mean length of stay (LOS) was shorter for Blacks than for Whites (2.2 ± .04 vs 2.5 ± .10 days, p<.01); when comparing observed to expected LOS, the difference between Blacks and Whites was still statistically significant, but not clinically relevant (.86 vs .90, p<.01). Mean charges per person were lower for Blacks than Whites ($7494 ± 207 vs 9114 ± 315, p<.01), but this difference was minimized when analyzed per person per day ($3271 ± 30 vs 3508 ± 37, p<.01).
CONCLUSIONS: This study demonstrates some differences related to race; however, there are no substantial clinical differences in terms of care parameters. In summary, pediatric academic institutions do not show marked racial disparities in the care of hospitalized asthmatic children.

85 Presentation Time 4:15 PM

Inpatient Pain Management Practices at a Children's Hospital

Catherine C. Skae, Sharon Calaman, Philip O. Ozuah. The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Studies suggest that patients in US hospitals do not receive adequate pain management. The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) has made pain management a major area of attention.
OBJECTIVE: To determine the frequency of pain assessments and the appropriateness of pain interventions at a major children's hospital.
DESIGN/METHODS: We conducted an observational study at a major children's hospital. Data were collected over a seven-month period on patients admitted to the inpatient service with either a medical or surgical diagnosis consistent with pain. Data collected included: patient demographics, pain assessments, medications used, re-evaluations for elevated scores, and physician documentation in the medical record. Medication appropriateness was defined in accordance with WHO and AHCPR Guidelines. We tested differences in continuous and categorical variables using t-test and Chi-square respectively.
RESULTS: 5673 observations (on 407 patients) were analyzed, of which 54% were medical diagnoses and 45% were surgical. The mean overall age was 11.3 years (range= 0.1-21 years). The mean age for medical diagnoses was 9.9 years and 12.5 for surgical diagnoses. On a Scale of 0-10, 65% of pain scores were ≤ 3. 87.9% were ≤ 6. Overall, interventions were considered appropriate 68.5% of the time. However, interventions were significantly less likely to be appropriate when Pain Scores were higher: Pain Scores 1-3 (98% appropriate) vs. Pain Scores 4-6 (48% appropriate) vs. Pain Scores ≥7 (35% appropriate), p= .000. Of note, 20% of patients with Pain Scores ≥7 had no interventions.
CONCLUSIONS: Patients with higher pain scores were less likely to have appropriate interventions. Our results provide evidence in support of JCAHO attempts to address the issue of pain management.

86 Presentation Time 4:30 PM

Negative Life Events and Reduced Quality of Life in Children With HIV Infection: A Longitudinal Analysis

Lois C. Howland, Sybil L. Crawford, Deborah S. Storm, Yunsheng Ma, James M. Oleske. Graduate School of Nursing, University of Massachusetts Medical School, Worcester, MA; Department of Preventive and Behavioral Medicine, University of Massachusetts Medical School, Worcester, MA; School of Nursing, University of Medicine and Dentistry of New Jersey, Newark, NJ.
BACKGROUND: Once viewed as progressively fatal, HIV infection is currently considered a chronic illness with an uncertain prognosis; quality of life (QOL) is a salient outcome for pediatric primary care and research. Among children and adults with chronic illness, negative life events (NLE's) are related to lower levels of QOL. NLE's have been found to predict the risk of immune suppression in children with HIV infection. It is important to identify the effects of NLE's on QOL in children with HIV disease.
OBJECTIVE: Using longitudinal data from the Pediatric Late Outcomes Study (Pediatric AIDS Clinical Trials Group Protocol #219), we examined the effects of NLE's on **three domains of QOL** (*general health perceptions, psychological function*, and *symptom distress)* in **1560** children age **5-21** years who had documented HIV infection.
DESIGN/METHODS: In a prospective cohort design, subject data was collected between **April 1993** and **September 2000**. Children 6 months to 21 years who had previously been enrolled in a PACTG clinical trial were eligible for enrollment in PACTG219. QOL data was collected by parent/guardian self-report at each annual study visit. NLE's were reported by study nurses verifying information with parent/guardian. Using random effects longitudinal modeling, we estimated the average within-subject change in QOL associated with occurrence of NLE's. Ceiling effects were addressed by Tobit analysis.
RESULTS: Occurrence of **2 or more NLE's** was consistently related to **decrease in QOL in all 3 domains (p<0.0001)** with average decreases of 3.1 to 6.7 points (scale 0-100). Specific NLE's related to **family disruption** (family member leaving home, loss of housing, sick and/or hospitalized family member*)* were significantly related to **decreased** QOL for all 3 domains **(p-value range = <0.007 to <0.0001).** Further analyses will adjust for important sociodemographic and disease-related variables (to be presented).
CONCLUSIONS: Children with HIV infection with 2 or more reported negative life events have significant decreases in QOL scores in the domains of general health perceptions, psychological function, and symptom distress. It is important to consider strategies that may be effective in attenuating the impact of NLE's on QOL in this vulnerable population.
Research supported by the National Institutes for Nursing Research (RO1 NR07975)

87 Presentation Time 4:45 PM

A Comparison of the Pain Associated With Simultaneous (SIM) vs. Sequential (SEQ) Immunization Injections Given at the 9 and 12 Month Well Child Visits

Frederick J. Bogin, Bruce A. Bernstein, Jessica S. Payton, Neil L. Schechter, Benjamin Ristau. Pediatrics, University of Connecticut School of Medicine, Farmington, CT; Pediatrics, Saint Francis Hospital and Medical Center, Hartford, CT.
BACKGROUND: Many well child visits in the first year of life include multiple injections as a part of current immunization practice. It has been hypothesized that SIM administration of vaccines may be less painful/distressing than SEQ injections. One published study (Horn & McCarthy, 1999) explored this question with 4-5 year olds receiving 2 injections. No data are available for infants on the pain of SIM versus SEQ injection.
OBJECTIVE: 1. to assess whether pain/distress associated with administration of 2 vaccines is significantly different with SIM versus SEQ injection in a sample of 9 and 12 month olds, and. 2. to ascertain whether parents prefer either method.
DESIGN/METHODS: We conducted a prospective, randomized, non-blinded comparative study in our pediatric Primary Care Center. Infants whose parents gave informed consent received the standard (2) immunizations simultaneously (2 providers) or sequentially (1 provider, 20 sec between injections). Preparation of the vaccine, needles and syringes, injection site, temperature of the injectate, and sequence of the injections were standardized. Cardiac monitoring leads were placed prior to the injections. Video cameras (2) recorded the infant's face and the cardiac monitor from 20 seconds prior to 90 seconds post injection. Outcome measures included heart rate (HR), characteristics and duration of crying, and pain/distress assessed with a 4 point facial response scale. At the trial's conclusion demographic, pain rating and shot strategy preference data were collected.
RESULTS: 64 infants (31 SEQ, 33 SIM; 25 9-month-olds, 39 12-months-olds) were included in the study. No significant differences between HR and cry parameters were found between age or injection groups, with one exception: maximum HR (expressed as actual HR and % increase over baseline) was greater for the sequential group (p < .04). 80% of parents preferred simultaneous injection.
CONCLUSIONS: Our study does not clearly identify a difference between SEQ and SIM administration of 2 injections in minimizing pain/distress in infants. The finding of increased maximum HR in the SEQ group may suggest some subtle advantage for the SIM technique. However, all other outcome differences were minimal and a large sample size would be required for significance. Most parents expressed a preference for SIM injection.

88 Presentation Time 5:00 PM

The Vaccines for Children Program: Taking a Shot at Disparities in Immunization Status

Andrew D. Racine, Theodore J. Joyce. Pediatrics, Albert Einstein College of Medicine / Children's Hospital at Montefiore, Bronx, NY; National Bureau of Economic Research, New York, NY; Economics and Finance, Baruch College, City University of New York, New York, NY.

BACKGROUND: The Vaccines for Children Program (VFC) provides free vaccines to uninsured, Medicaid eligible, Alaskan Native, American Indian, and certain underinsured children under 18 years of age. Analyses using national data that test the effectiveness of VFC in improving income or race/ethnicity disparities in immunization status are lacking.

OBJECTIVE: To characterize the differential impact by income and race/ethnicity that VFC providers had on the likelihood of being up-to-date (UTD) for the 4:3:1:3:3 (DTaP, IPV, Measles containing vaccine, Hib, HepB) immunization series among a nationally representative sample of 19-35 month olds.

DESIGN/METHODS: We used 1997-2002 data from the National Immunization Survey (NIS), a nationally representative population based survey of over 30,000 households per year containing demographic and immunization-receipt information on 19-35 month-old children. NIS data indicate which providers participated in VFC enabling identification of any child who received some or all vaccines from a VFC provider (ANYVFC). NIS income categories were used to code children from poor (< 100 % of the Federal Poverty Level, FPL), near-poor (>= 100% FPL but < 250% of FPL) and non-poor (> 250% of FPL) families. Multivariate OLS regressions with state and year fixed effects characterized the percent of 19-35 month-olds in each state who were UTD for the 4:3:1:3:3 series as a function of ANYVFC and demographic covariates. Interaction terms captured the marginal ANYVFC effect on poor/near-poor children relative to non-poor and on black and Hispanic children relative to whites.

RESULTS: Poor/near-poor, black, and Hispanic children were less likely to be UTD for the 4:3:1:3:3 series than non-poor or white children by 8.9, 4.2 and 4.2 percentage points respectively. Although receipt of vaccines from a VFC provider did not make children more likely to be UTD in general, it disproportionately increased the likelihood of poor/near-poor children being UTD relative to non-poor children by an additional 3.2 percentage points($p<0.05$). Neither black nor Hispanic children showed evidence of a disproportionate benefit from the VFC program relative to whites.

CONCLUSIONS: From 1997-2002, receipt of vaccines from a VFC provider preferentially increased the likelihood that poor and near-poor 19-35 month old children were UTD for the 4:3:1:3:3 vaccine series relative to non-poor children. No increased benefit to minority children could be confirmed.

89 Presentation Time 5:15 PM

Does a Schedule of Pentavalent DTaP-IPV-Hepatitis B (Pediarix), Conjugate Pneumococcal (PCN7), and Conjugate H. influenza (Hib) Vaccines Cause Excess Emergency Visits and Hospitalizations in Young Infants?

Lindsay A. Thompson, Matilde Irigoyen, L. Adriana Matiz, Philip S. LaRussa, Shaofu Chen, Frank Chimkin. Division of General Pediatrics, Columbia University, NY, NY; Population and Family Health, Mailman School of Public Health, NY, NY; Pediatric Infectious Diseases, Columbia University, NY, NY.

BACKGROUND: In an effort to reduce the number of immunization injections an infant receives, the new schedule recommends Pediarix, PCN7 and Hib at 2, 4, and 6 months. Because this combination is known to increase the incidence of fever, it may also increase medical visits and hospitalizations for infants <3 months, when aggressive medical intervention is indicated.

OBJECTIVE: To examine whether infants who received Pediarix, PCN7, and Hib (new schedule) have excess emergency department (ED) visits, hospitalizations and procedures compared to the same age cohort during the prior year who received the previously recommended DTaP, Comvax (Hepatitis B and Hib), IPV and PCN7, (old schedule).

DESIGN/METHODS: Infants 6-10 weeks in the hospital immunization registry who received the new schedule between April 1 - September 30, 2003 (n=676; ED visits=44) were compared to those receiving the old schedule between April 1- September 30, 2002, (n=1047; ED visits=82). Outcome measures for those with ED visits were fever, hospitalization, antibiotic use, septic work ups and positive cultures or chest x-ray within one month of primary immunization.

RESULTS: Infants on the new schedule were significantly more likely to receive a partial work up (CBC and urine), get antibiotics, and be hospitalized than those on the old schedule. There were no differences in rates of ED visits, fever, full sepsis work ups (including lumbar puncture) or positive cultures. See Table, below.

CONCLUSIONS: The new schedule leads to increased hospitalizations, antibiotic use and partial work ups without evidence of increased infection. Infants on the new schedule did not receive the full work up (including lumbar puncture) as recommended for febrile infants <3 months. Further research is necessary to determine if the new schedule causes either unnecessary intervention or a change in management without supportive evidence.

Outcomes of infants on new schedule presenting to ED (old schedule= referent)

Outcome:	Odds Ratio	95% CI
Fever	1.54	(0.77, 3.06)
Partial Work up (CBC & Urine)	1.86	(1.04, 3.36) *
Full Work Up (with LP)	2.33	(0.66, 8.23)
Antibiotics	2.62	(1.23, 5.60)*
Hospitalization	2.66	(1.09, 6.51)*
Positive cultures or chest x-ray	1.86	(0.70, 4.97)

* p< 0.05 by Pearson's Chi square

Hematology/Oncology Platform Session

Saturday, March 27 3:45pm–5:45pm Winthrop A-B

90 Presentation Time 3:45 PM

Antiendothelial and Antiangiogenic Properties of QW1624F2-2, a Low-Calcemic Hybrid Analog of 1,25-Dihydroxyvitamin D_3

Claire Rodriguez, Paul Furigay, Gary Posner, Michael Fannon, Narasimha Swamy. Pediatrics, Women and Infants' Hospital of Rhode Island, Brown University, Providence, RI; Chemistry, School of Arts and Sciences, The Johns Hopkins University, Baltimore, MD; Division of Surgical Research, Children's Hospital, Boston, MA. (Sponsored by James F. Padbury)

BACKGROUND: The proliferation and migration of endothelial cells (EC) are essential steps for angiogenesis. Inhibition of angiogenesis shows promise in the treatment of hyperproliferative disorders such as tumor growth and metastasis. The antiproliferative activity of calcitriol is well established. However, the hypercalcemic side effects of calcitriol have lead to the synthesis of analogs with reduced calcemic activity. QW1624F2-2 (QW), a 1-beta-hydroxymethyl-3-epi-16-ene-24,24-difluorinated-26,27-bis-homo hybrid analog of calcitriol, is one such analog with low calcemic activity. (Carcinogenesis, 2000, 21, 1341-1345).

OBJECTIVE: To demonstrate that QW inhibits angiogenesis by reducing proliferation and inducing apoptosis in endothelial cells.

DESIGN/METHODS: Human umbilical vein endothelial cells (HUVEC) were cultured in complete endothelial growth medium-2 containing vascular endothelial growth factor (VEGF) and treated with 1 to 500 nM QW or calcitriol for 48 hours. Cell viability was assessed by MTS formazan reduction and proliferation by BrdU incorporation assays. Apoptosis was assessed by DNA fragmentation and caspase-3 activity. Cell cycle analysis was performed by flow cytometry (FACS). Signaling pathways were elucidated by western blot and semi-quantitative PCR. Vehicle treated cells were included as controls. The effect on angiogenesis was assessed by chick chorioallantoic membrane (CAM) assay.

RESULTS: QW inhibited the VEGF stimulated proliferation of EC. At 10 and 100 nM, QW inhibited 55% ($p<.05$) and 90% ($p<.01$) of proliferation, whereas calcitriol inhibited 5% ($p<.05$) and 25% ($p<.05$), respectively. The inhibition of EC proliferation by QW was associated with apoptosis. QW induced a significant G0/G1 arrest accompanied by increased apoptosis and a concomitant decrease in the percentage of cells in S phase. QW increased transcription of the CDK inhibitors p21 and p27, while decreasing the transcription of cyclin D1 which is essential for proliferation. QW also inhibited the phosphorylation of ERK1/2 and AKT, but increased the phosphorylation of JNK1/2, thus demonstrating the role of MAPK and PI3K pathways.

CONCLUSIONS: QW is a potent antiproliferative agent in endothelial cells and it inhibits angiogenesis. QW is potentially more useful as a therapeutic antiangiogenic calcitriol analog because of its low calcemic activity.

91 Presentation Time 4:00 PM

Somatic *PTPN11* Mutations Are Prevalent in Common B-Cell Precursor Acute Lymphoblastic Leukemia

Marco Tartaglia, Simone Martinelli, Giovanni Cazzaniga, Viviana Cordeddu, Monica Spinelli, Claudio Carta, Giuseppe Masera, Giuseppe Basso, Mariella Sorcini, Andrea Biondi, Bruce D. Gelb. Metabolismo e Biochimica Patologica, Istituto Superiore di Sanita, Rome, Italy; Centro Ricerca M. Tettamanti, Universita di Milano Bicocca, Monza, Italy; Pediatria, Universita di Padova, Padua, Italy; Pediatrics and Human Genetics, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Acute lymphoblastic leukemia (ALL) accounts for ≈75% of pediatric leukemias, with B-lineage ALL being most prevalent. The molecular events contributing to malignant transformation in ALL remain poorly understood. Recently, we demonstrated that somatic gain-of-function mutations in *PTPN11*, which encodes the protein tyrosine phosphatase SHP-2, represent the most frequent lesion in juvenile myelomonocytic leukemia (JMML).

OBJECTIVE: To determine the prevalence of *PTPN11* mutations in the subtypes of pediatric ALL.

DESIGN/METHODS: The ALL cohort (n=353) included 309 children with B-lineage ALL (Common immunophenotype, n= 183; Pre-B, n= 112; Pro-B, n=9;Pre-pre-B, n= 5) and 44 with T-lineage ALL. Genomic DNA was isolated from bone marrow mononuclear cells at diagnosis and during follow-up (33 days and/or 78 days). The *PTPN11* coding sequence (exons 1-15) was analyzed using DHPLC and direct sequencing. *MLL-AF4, BCR-ABL, TEL-AML1*, and *E2A-PBX1* fusion gene transcripts were assayed with RT-PCR. *NRAS* and *KRAS2* were assayed for exon 1 and 2 mutations. Mutation distributions were compared using X^2 analysis with a significance threshold of $p<0.05$.

RESULTS: *PTPN11* mutations were identified in 23/309 cases (7.4%) of B-cell precursor ALL at presentation but in no T-lineage sample. Mutations were not present during remission. All mutations were missense changes (exon 3, n=18, exon 13, n=5) and overlapped with the gain-of-function defects observed previously in JMML. *PTPN11* mutations were associated with the common immunophenotype (20/183, 11%; $p<0.005$). The *TEL-AML1* fusion gene, which had a prevalence of 24% in common B-cell ALL, and the other gene rearrangements never coincided with *PTPN11* mutations. No *NRAS* and one *KRAS2* mutation was observed among the 23 cases with *PTPN11* mutations, while *RAS* mutations were present in 23% of common B-cell ALL, a significant difference ($p<0.05$).

CONCLUSIONS: Gain-of-function *PTPN11* mutations are associated with common B-cell precursor ALL, defining a novel subgroup with low prevalence for the *TEL-AML1* rearrangement. Combining *RAS* and *PTPN11* mutation prevalence, dysregulation of RAS signaling is present in >1/3 of common B-cell precursor ALL. *PTPN11* mutations appear to play minimal role in T-lineage ALL oncogenesis.

92 Presentation Time 4:15 PM Student

Binding of Zinc Proptophyrin to Serum Proteins and Effect on Apoptosis

Adia G. George, Guang Yang, Phyllis A. Dennery. Pediatrics, School of Medicine, Stanford University, Stanford, CA; Pediatrics, Neonatology, Children Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Zinc protoporphyrin (ZnPP), a competetive inhibitor of heme oxygenase (HO), is a metabolite formed in heme biosynthesis. ZnPP demonstrates specificity to GC-rich regions of DNA and may form a complex with the HO protein.

OBJECTIVE: To understand: 1) whether there are differences in binding of ZnPP to other erythrocyte proteins including hemoglobin (Hb), 2) whether protein binding differs between neonates and adults and 3) the role of protein binding in cellular toxicity.

DESIGN/METHODS: Blood was collected from neonates (fetal cord blood) and adult healthy human volunteers. RBC and serum proteins were separated by centrifugation. Hemoglobin (Hb) was isolated by immunoprecipitation with a monoclonal pan anti-Hb antibody (Novus Biologicals, Littleton, CO). RBC, serum proteins, and Hb were incubated with ZnPP and subjected to 10% glycine non-denaturing gel electrophoresis. ZnPP binding was measured using the IVIS imaging system (Xenogen Alameda, CA). In other experiments, neonatal (<12h old, neo) C57BL/6 mice were injected intraperitoneally with 0-40 µmol/kg body weight of ZnPP. Genomic DNA was isolated from livers at 0, 24, 48, and 72 hrs, using a commercially available kit (Maxim Biotech, So. San Francisco, CA). DNA fragmentation was enhanced by ligation of dephosphorylated adaptors using PCR and visualized on an agarose/EtBr gel (Maxim Biotech, So. San Francisco, CA). Neo liver slices were evaluated under light microscopy with hematoxylin and eosin staining.

RESULTS: Multiple serum proteins demonstrated ZnPP binding in both neonates and adults but the predominant area of binding was different between the two groups. There was a dose dependent increase in the intensity of ZnPP binding in the neonates. No significant binding was observed on adult or fetal Hb. Along with the ZnPP-protein binding, in the neo liver, there was a dose dependent increase in DNA laddering after ZnPP injection. Light microscopy also showed increased hepatocellular vacuolization and necrosis in a dose and time dependent manner.

CONCLUSIONS: ZnPP binds differentially to neonatal and adult serum proteins but there is no predilection for binding to Hb. ZnPP binding occurs in a dose-dependent fashion to neo serum proteins. High doses of ZnPP may be responsible for hepatacellular injury.

We speculate that ZnPP may mediate its cytotoxic effects by binding to specific serum proteins.

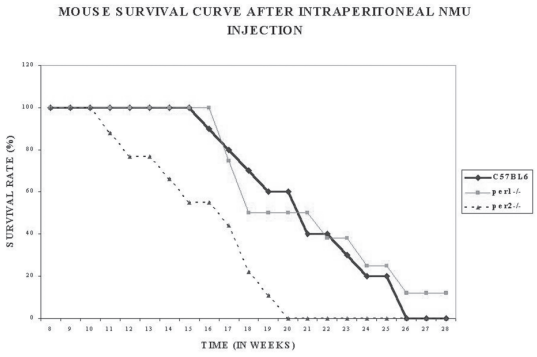
Funded by the NIH (1RO1 HL-070285, PAD)

93 Presentation Time 4:30 PM — Fellow

N-Methylnitrosourea Induced Lymphomas in Circadian Clock Function Deficient Mice

Gautam Malkani, Mark Meyer, H. Michael Ushay, Zhong Sheng Sun, Bruce M. Greenwald. Pediatric Critical Care Medicine, Weill Medical College of Cornell University, New York, NY. (Sponsored by Susan B. Bostwick)

BACKGROUND: Circadian rhythms are the daily oscillations of multiple biological processes driven by endogenous clocks. The master circadian clock in mammals resides in the suprachiasmatic nucleus (SCN) of the anterior hypothalamus. Molecular clockwork in the SCN is composed of interacting positive and negative feedback loops of clock genes. To date, ten core circadian genes have been identified (Period1 and Period2 being 2 of the 10). Similar clockwork has been found in all peripheral tissues studied.
It has been demonstrated that irregular circadian cycles, such as night-shift work in humans or constant exposure to light in rodents, increases mammary tumorigenesis.
OBJECTIVE: To demonstrate that circadian clock function deficient mice have increased susceptibility to tumor development induced by N-methylnitrosourea (NMU), a known carcinogenic DNA alkylating agent.
DESIGN/METHODS: 3 groups of mice were injected intraperitoneally with 50mg/kg NMU: C57BL6 (control), per2-/- (mice homozygous for the Per2 mutation), and per1-/-(mice homozygous for the Per1 mutation). Mice were observed for signs and symptoms of lymphoma development and sacrificed prior to death.
RESULTS: All mice showed evidence of massive thymic enlargement, lymphadenopathy, and hepatosplenomegaly. Histology confirmed the presence of diffuse lymphomatous changes. The per2-/- mice showed mortality 11 weeks after injection with 100% mortality by 20 weeks, whereas the control showed mortality 16 weeks after injection with 100% mortality by 26 weeks. The per1-/- mice had a survival similar to the control.



CONCLUSIONS: 1. Period2 gene deficient mice have increased susceptibility to tumor development after exposure to NMU. 2. Period1 gene deficient mice do not demonstrate any increased susceptibility. 3. The circadian clock system plays a role in cancer. 4. Disruption of circadian-controlled physiological systems can result in cancer.

94 Presentation Time 4:45 PM — Fellow

Iron Chelators Deferoxamine (DFO) and Diethylenetriaminepentaacetic Acid (DTPA) Inhibit Endothelial Cell Proliferation and Angiogenesis

Paul Furigay, Claire Rodriguez, Laurent Brard, Narasimha Swamy. Pediatrics, Women and Infants' Hospital of Rhode Island, Brown University, Providence, RI; Program in Women's Oncology, Women and Infants' Hospital of Rhode Island, Brown University, Providence, RI. (Sponsored by James F. Padbury)

BACKGROUND: Angiogenesis, a process by which new blood vessels are formed from preexisting vessels, depends upon the viability, proliferation and migration of endothelial cells. Compounds that inhibit growth factor stimulated proliferation of endothelial cells (EC) and angiogenesis, are potentially useful in the treatment of hyperproliferative disorders such as tumor growth and metastasis, psoriasis, and retinopathy of prematurity. Iron chelators are widely used in the treatment of iron-overload conditions and inhibit proliferation by depriving cells of iron and disrupting normal metabolism.
OBJECTIVE: To demonstrate that the iron chelators deferoxamine (DFO) and diethylenetriaminepentaacetic acid (DTPA) inhibit angiogenesis by reducing proliferation and inducing apoptosis in EC.
DESIGN/METHODS: Human umbilical vein endothelial cells (HUVEC-p) were cultured in complete endothelial growth medium-2 containing vascular endothelial growth factor (VEGF) and treated with 6.25 to 200 μM DFO or DTPA for 48 hours. Cell viability was measured by MTS formazan reduction and proliferation by BrdU incorporation assays. Apoptosis was assessed by DNA fragmentation and caspase-3 activity. Cell cycle analysis was performed by flow cytometry (FACS). Vehicle treated cells were included as controls. Inhibition of angiogenesis was demonstrated by chick chorioallantoic membrane (CAM) assay.
RESULTS: DFO and DTPA effectively inhibited the viability and proliferation of endothelial cells in a dose-dependent manner. Treatment with 25μM DFO and 100μM DTPA resulted in a 50% reduction in viability ($p<.01$ for each). Both compounds induced apoptosis in EC demonstrated by fragmentation of genomic DNA in treated cells at 48 hours. Pro-apoptotic caspase-3 activity was also increased in DFO and DTPA treated cells. Cell cycle analysis of EC treated with DTO and DTPA revealed an increased fraction of cells in the sub-G0/G1 and apoptotic phases. Treatment of CAMs with DFO or DTPA inhibited growth factor (bFGF) induced angiogenesis.
CONCLUSIONS: DFO and DTPA decreased EC proliferation and induced apoptosis which lead to the inhibition of angiogenesis. These results suggest that iron chelators may be developed as therapeutic agents for cancer and other angiogenesis-dependent disease states.

95 Presentation Time 5:00 PM — Student

***In Vivo* Evaluation of Zinc Protoporphyrin on Tumor Supression**

Ameen Salahudeen, Guang Yang, Phyllis A. Dennery. Pediatrics, School of Medicine, Stanford University, Stanford, CA; Pediatrics, Neonatology, Children Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Zinc Protoporphyrin (ZnPP), an endogenous metalloporphyrin that inhibits heme oxygenase activity, alters bone marrow cell proliferation. We have previously shown that ZnPP induces Early Growth Factor-1 gene expression, resulting in increased apoptosis in fibroblasts. This suggests that ZnPP could serve as a tumor suppressor.
OBJECTIVE: To evaluate the effects of ZnPP on the growth of lymphoma tumor cells (BCL_1) in mice.
DESIGN/METHODS: BCL_1 were transduced with a recombinant retroviral vector pGC-gfp/luc and passed through 4 generations of BALB/c mice in order to generate a stable GFP and luciferase expression line (BCL_1 gfp/luc). Female BALB/c mice (5 weeks old) were then transfected with 5×10^3 BCL_1 gfp/luc cells i.v. Five days post transfection the mice were injected with ZnPP (0, 40 or 80 μmol/kg body weight) i.p. The mice were imaged for tumor growth at 0, 24, 48 and 72 hours of ZnPP administration using the *in vivo* imaging system (IVIS) (Xenogen, Alameda, CA). After 72 hours, the spleens were removed for evaluation of DNA fragmentation by DNA laddering assay. Liver and spleen 6 μm slides were also evaluated for evidence of cellular injury and apoptosis using the TUNEL. assay.
RESULTS: By 72 hours, ZnPP treated mice showed a significant decrease in tumor cell growth as compared to the vehicle controls in a dose dependent manner (50% and 7% of vehicle control tumor size for 40 and 80 μmol/kg ZnPP respectively). ZnPP injection also resulted in increased BCl_1cell apoptosis.
CONCLUSIONS: These data demonstrate that ZnPP can result in suppression of tumor growth in an animal model. We speculate that ZnPP increases tumor cell apoptosis and suppresses tumor cell proliferation.
Funded by the NIH (1RO1 HL 070285; PAD)

Pulmonology Platform Session

Saturday, March 27 3:45pm–6:00pm Mead C

96 Presentation Time 3:45 PM

Vascular Endothelial Growth Factor (VEGF) Enhances Maturity in the Developing Mouse Lung

Vineet Bhandari, Chun G. Lee, Chuyan Tang, Seamus A. Rooney, Robert J. Homer, Jack A. Elias. Pediatrics, Yale University School of Medicine, New Haven, CT; Pulmonary and Critical Care Medicine, Yale University School of Medicine, New Haven, CT; Pathology, Yale University School of Medicine, New Haven, CT.

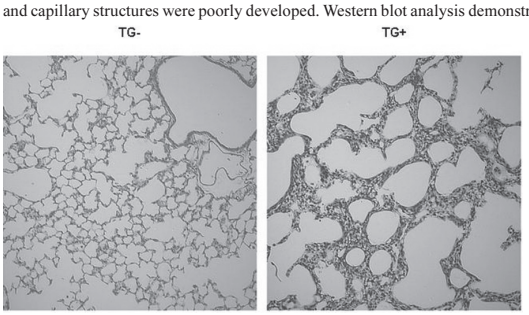
BACKGROUND: We have previously reported that activation of VEGF in adult CC10-rtTA-VEGF165 mice by Doxycycline (Dox)-water resulted in impressive increases in surfactant proteins (SP) B and C (but not A and D) and total phospholipid content in the broncho-alveolar lavage fluid, compared to controls. Furthermore, the vascular effects (pulmonary edema, hemorrhage, mucus metaplasia) of VEGF, but not the increase in SP, could be abrogated by nitric oxide (NO) inhibition.
OBJECTIVE: We wanted to evaluate the effect of VEGF165, when activated in utero, on alveolar maturation in the developing lung.
DESIGN/METHODS: Adult CC10-rtTA-VEGF165 were mated with wild type female mice. Since Dox crosses the placental barrier and is also excreted in breast milk, exposure of the VEGF transgenic (+) fetus allowed the VEGF to be "turned on" in utero as well as postnatally. Timed pregnant mice (vaginal plug noted on d0) were exposed to Dox water at embryonic (E)16, 18, 19, 20 and full term (21d) newborn (NB), up to postnatal (PN) d7.
RESULTS: Out of 43 mice pups born at term, obtained after in utero activation on E16, 41 were wild type (WT) and 2 were transgenic (TG); the latter 2 died on PN d1. Out of 32 pups similarly obtained after E18 activation, 7 were TG; 6 of the latter died on PN d1 while one survived up to PN d7 (day of sacrifice). All 7 mice pups after E19 activation were WT. Out of 7 obtained after E20 activation, 6 were WT and one TG mice; all were sacrificed on PN d7. Histology of the fresh deaths of the TG mice activated on E16 and E18 show pulmonary hemorrhage. The lungs of E20 and NB activation TG mice pups show evidence of lung maturation as evidenced by thinner alveolar walls, increased alveolar space, and decreased intervening mesenchyme. On lung morphometry, mean linear intercept was significantly increased in the E20 TG ($p=0.0002$) and NB TG ($p<0.05$) mice pups, compared to litter-mate controls. There was increased SP and NOS3 staining on immunohistochemistry in the TG mice pups lungs, compared to controls.
CONCLUSIONS: We conclude that VEGF165 enhances alveolar maturation in the developing lung. We speculate that for VEGF to be clinically useful for lung maturation, inhibition of its vascular effects via NO inhibition would be required.

97 Presentation Time 4:00 PM

Overexpression of Bioactive TGF-b1 in Neonatal Mouse Lung: A New Model for BPD?

Alfin G. Vicencio, Chun Geun Lee, Oliver Eickelberg, Ying Chuu, Gabriel G. Haddad, Jack A. Elias. Pediatrics, Children's Hospital at Montefiore/AECOM, Bronx, NY; Internal Medicine, Yale University School of Medicine, New Haven, CT; Internal Medicine, University of Giessen, Giessen, Germany.

BACKGROUND: Transforming growth factor-β (TGF-β) has been implicated in the development of bronchopulmonary dysplasia (BPD), yet its effects on early postnatal lung development have been difficult to investigate with traditional transgenic models. Thus, we have utilized a triple transgenic construct to conditionally overexpress bioactive TGF-β1 in the mouse lung specifically during the first two weeks of postnatal life.
OBJECTIVE: To describe the effects of TGF-β1 overexpression in neonatal mouse lung and compare the resulting phenotype with the pathological characteristics described in BPD.
DESIGN/METHODS: Mice bearing a triple transgenic construct coupled to a CC10 promoter were utilized for this study. This construct allows for lung-specific overexpression of TGF-β1 only when the animals are fed doxycycline. For the current investigation, neonatal mice were fed doxycycline starting at postnatal day (P) 7 and continuing until P14. Transgene-negative littermates, also maintained on doxycycline, served as the control group. Following the study period, animals were sacrificed, and lungs were pressure fixed and examined by histologic and immunohistochemical methods. Lung tissues from other study animals were processed for western blot analysis.
RESULTS: Neonatal overexpression of TGF-β1 resulted in histologic alterations similar to those seen in BPD (figure 1). Specifically, alveolar structures were abnormal, septae were thickened and hypercellular, and capillary structures were poorly developed. Western blot analysis demonstrated a decrease in platelet-endothelial cell adhesion molecule (PECAM), findings consistent with traditional models of BPD.



CONCLUSIONS: Overexpression of TGF-β1 in neonatal mouse lungs results in a phenotype consistent with BPD, suggesting that this cytokine plays an important role in development of disease.

98 Presentation Time 4:15 PM — Fellow

Heliox Attenuates Lung Inflammation and Structural Alterations in Acute Lung Injury

Ursula S. Nawab, Suzanne M. Touch, Tami Irwin-Sherman, Thomas J. Blackson, Jay S. Greenspan, Guangfa Zhu, Thomas H. Shaffer, Marla R. Wolfson. Neonatology, Thoms Jefferson Univ, Phila., PA; Nemours Lung Center, A.I duPont Hosp Child, Wilm., DE; Physiol. and Peds., Temple Univ Sch of Med, Phila, PA.

BACKGROUND: Low density gas mixtures have been shown to reduce work of breathing and facilitate the distribution of inspired gas. Lower pressure, volume, and supplemental oxygen requirements are associated with reduced lung injury.

OBJECTIVE: To test the hypothesis that Heliox breathing would attenuate alterations in lung structure and the inflammatory profile of the lung injured piglet.

DESIGN/METHODS: Spontaneously breathing neonatal piglets (2.52 ± 0.19 kg) were anesthetized, instrumented, supported with CPAP and injured with oleic acid (0.08 mL/kg). The animals were randomized to receive Nitrox (n=6) or Heliox (n=5) in which the F_IO_2 was regulated to maintain $SaO_2 = 95 \pm 5\%$ for 4 hrs. Arterial blood gases and pulmonary mechanics were measured serially. At termination, lungs were harvested, sectioned, and samples were prepared for analyses of MPO, IL – 8 and histomorphometery [EI = Expansion Index; EUA = Exchange Unit Area]. Relationships between physiologic indices over time, and cumulative lung structure and inflammatory indices were evaluated.

RESULTS: During Heliox breathing, compliance was significantly greater (1.03 ± 0.19 vs 0.62 ± .06 mL/cmH_2O/kg) while tidal volume (4.09 ± 0.26 vs 5.53 ± 0.47 mL/kg), frequency (103 ± 14 vs 131 ± 15 br/min), and F_IO_2 (0.39 ± 0.08 vs 0.57 ± 0.08), and $PaCO_2$ (33.7 ± 0.22 vs 44.8 ± 1.5 mm Hg) were significantly lower with Heliox as compared to Nitrox . MPO was significantly and positively correlated with F_IO_2 (r = 0.76), EUA (r = 0.63), and negatively correlated with # open EU/field (r = -0.73). mean ±SE; *p < 0.05 by t-test

	Minute Vent. [mL/min/kg]	a/A [%]	MPO [U/gm]	IL - 8 [pg/gm]	EI [%]	# EU [#]	EUA μm^3
Nitrox	693±45	52±10	2.16±0.36	6424±757	19±2.5	448±31	272±26
Heliox	426±76*	49±22	1.38±0.44*	4872±755*	26±3.8*	872±97*	189±40*

CONCLUSIONS: Compared to breathing Nitrox, Heliox improved the distribution of the inspired gas (> EI%) thereby recruiting more gas exchange units (> # EU). This resulted in improved gas exchange efficiency, reduced ventilatory and oxygen support, and attenuated lung inflammation. These data suggest that Heliox breathing may have combined therapeutic benefits of attenuating lung inflammation by reducing mechanical and oxidative stress in the clinical management of acute lung injury.

Hill-Rom, Pa. Dept. of Health ME-01-328

99 Presentation Time 4:30 PM — Fellow

A Serpin Protects Against Death From Pseudomonas Pneumonia

Lawrence M. Rhein, Dave Askew, Greg P. Priebe, Gary A. Silverman. Divison of Newborn Medicine, Children's Hospital, Boston, Boston, MA; Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Boston, MA.

BACKGROUND: Serine proteinase inhibitors (SERPINS) are members of a superfamily that share a conserved structure and unique inhibitory suicide-substrate mechanism. Serpinb3a is a mouse serpin that is orthologous to human SERPINB3 and SERPINB4, and has inhibitory activity against both papain-like cysteine proteases and chymotrypsin-like serine proteases. While the biochemical activity of Serpinb3a has been well-described, and it is highly expressed in the lung, its biological function is unknown.

OBJECTIVE: Protease-mediated injury is a major component of lung injury in bacterial pneumonias. The objective of this study is to determine whether an inhibitory serpin is protective against *Pseudomonas* (PSA) pneumonia.

DESIGN/METHODS: Serpinb3a-/- (KO) and wild-type (WT) mice (Balb/c background) were inoculated intranasally with 10^9 CFU/ml of PSA (PA01) and survival curves were determined.

Lung and spleen homogenates were prepared and serially diluted to determine bacterial outgrowth.

Lungs were harvested for histological analysis. Single-cell suspensions of splenocytes were stained with antibodies for CD4, CD8, and B220 and sorted by FACS analysis pre- and post-inoculation.

RESULTS: Serpinb3a KO mice showed increased mortality in comparison with WT mice. (Figure 1) Total bacterial counts in the lungs did not differ significantly between KO and WT mice. Histopathologically, the severity of bronchopneumonia was indistinguishable between groups. In contrast, KO mice had ~10-fold increase in bacterial counts in the spleen (39.4 CFU/gm vs 3.8 CFU/gm, p<0.046). T and B-cell subsets did not vary pre- or post-bacterial challenge in either group.

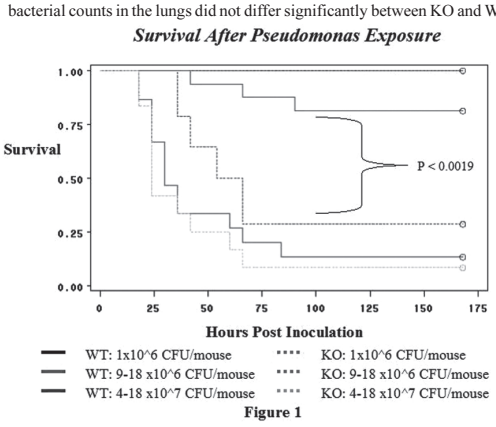


Figure 1

CONCLUSIONS: Serpinb3a plays an important role in protection against bacteremic invasion in PSA pneumonia. Further studies are underway to determine whether Serpinb3a contributes to clearance of PSA in the lungs or plays a role in inflammatory response regulation.

100 Presentation Time 4:45 PM — Fellow

Evidence That Human Metapneumovirus Does Not Contribute to the Severity of Respiratory Syncytial Virus Disease

Isaac Lazar, Carla Weibel, David Ferguson, Marie Landry, Jeffrey S. Kahn. Pediatrics, Yale University School of Medicine, New Haven, CT; Laboratory Medicine, Yale University School of Medicine, New Haven, CT; Epidemiology and Public Health, Yale University School of Medicine, New Haven, CT.

BACKGROUND: Respiratory syncytial virus (RSV) is a major pathogen of young children worldwide. The spectrum of disease caused by RSV ranges from mild upper respiratory tract disease to severe respiratory failure that requires intensive respiratory support. The pathogenesis of RSV disease is poorly understood. A previous study reported that 70% of children with severe RSV disease were co-infected with human metapneumovirus (hMPV), a newly discovered respiratory pathogen.

OBJECTIVE: To compare the frequency of hMPV infection in children with either mild or severe RSV disease.

DESIGN/METHODS: As part of an ongoing epidemiological study of viral respiratory infections in children, we collected all of the RSV direct fluorescent antibody (DFA) positive respiratory specimens from the Clinical Virology Laboratory at Yale-New Haven Hospital from November 1, 2001 to October 31, 2002. All RSV-positive children admitted to the PICU during this yearlong period were identified. Because the peak time of infection with RSV and with hMPV may differ, each RSV-positive child from the PICU was matched by date of diagnosis with a child with mild RSV disease (not requiring PICU admission). Respiratory specimens from all children were screened for hMPV by RT-PCR. Severity of illness was assessed with a clinical severity score (CSS).

RESULTS: Twenty-three RSV DFA-positive children admitted to the PICU and 23 RSV-DFA positive children non-PICU admitted children were identified and screened for hMPV. Statistically significant difference between the PICU group and the non-PICU group were observed in admission age (23.3 weeks vs. 55.6 weeks, p = 0.014), hospital admission rate (23/23 vs. 8/23, p = 0.004) and CSS (mean CSS 4.9 vs. 1.6, p < 0.001). Positive pressure ventilation (PPV) was required by 17/23 PICU patients (73.9%) and 10 of these 17 patients needed PPV for longer then 5 days. None of the patients with mild RSV disease required PPV (p < 0.001). None of the individuals screened in either group of RSV-DFA positive patients had evidence of hMPV infection (p=1.0) though our previous studies have established that hMPV was circulating in the community at the time of the study.

CONCLUSIONS: Although hMPV was circulating in our community, none of the 46 RSV-infected individuals had a positive test for hMPV. In our study population, hMPV did not contribute to the severity of RSV disease.

101 Presentation Time 5:00 PM — Fellow

Pro-Inflammatory Mediators Amplify the Apoptotic Response of Human Lung Cells During Hypoxia

Sonya S. Strassberg, Ioana Godi, Asgar Dudhbhai, Dhruti Pandya, Lance A. Parton. Neonatology, New York Medical College: Westchester Medical Center, Valhalla, NY. (Sponsored by Sergio Golombek)

BACKGROUND: Hypoxic exposure of premature infants may contribute to acute lung injury as well as to chronic lung injury, particularly in the presence of a net pro-inflammatory milieu. The premature respiratory tract is exposed to both of these potentially deadly elements. Apoptosis is a genetically encoded program of cell death that can be activated under physiological conditions such as hypoxia. Apoptosis in the presence of hypoxia may be involved in the mechanism of injury that leads to vascular changes, and therefore to degenerative diseases, such as chronic lung disease (CLD). Also, excessive pro-inflammatory stimulation or lack of anti-inflammatory suppression in developmentally immature infants may perpetuate the inflammatory response and contribute to the pathogenesis of CLD.

OBJECTIVE: Pro-inflammatory cytokines amplify and accelerate the cellular response to hypoxia via apoptosis. Anti-inflammatory cytokines protect the cells from apoptosis.

DESIGN/METHODS: Human lung cells (A549) are exposed to hypoxia (15%O_2) in the presence of pro-inflammatory (IL-6 or IL-8) or anti-inflammatory mediators (IL-10 or IL-1Ra). This is done in a 2% fetal bovine serum media. Apoptosis is quantified by the TUNEL (Terminal deoxynucleotidyl transferase (Tdt), mediated dUTP Nick End Labeling) method.

RESULTS: Data is expressed as mean ± SD. Short-term (4-6 h) hypoxia results in significant augmentation of apoptosis (*p<0.05, **p<0.01) compared to room air exposure. The presence of pro-inflammatory mediators IL-6 or IL-8 result in significant increase in apoptosis (•p<0.01) compared to the presence of anti-inflammatory mediators IL-1Ra or IL-10.

	IL-6	IL-8	IL-1Ra	IL-10
Room Air	48.7±13.2	48.7±13.2	36.0±5.3	26.0±4.6•
Hypoxia	75.0±5.6*	80.0±7.0*	47.0±4.0*•	51.0±7.0**•

CONCLUSIONS: Significant apoptosis is demonstrated following short-term hypoxic exposure of lung epithelial cells in culture. Pro-inflammatory cytokines enhance and anti-inflammatory mediators decrease apoptosis in air and also in the presence of hypoxia. These findings of an *in vitro* model of short-term hypoxic lung injury in the presence of various pro- and anti- inflammatory mediators may provide insights into the combinatorial mechanisms of apoptosis in acute and chronic lung injury and vascular remodeling, that may help to evaluate future clinical interventions.

Funded by the Children's and Women's Physicians of Westchester

102 Presentation Time 5:15 PM — Fellow

Cytokine Stimulation of Lung Epithelial Cells Induces iNOS and Results in Cell Death

Michael A. Posencheg, Linda W. Gonzales, Andrew J. Gow. Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Bronchopulmonary Dysplasia (BPD) and Necrotizing Enterocolitis (NEC) are responsible for significant morbidity and mortality in preterm infants. The pathogenesis of both of these diseases involves an inflammatory response that begins at the mucosal surface, making epithelial cells a prime target. The involvement of nitric oxide (NO) and its metabolites has been implicated in both BPD and NEC. Inducible nitric oxide synthase (iNOS), an enzyme responsible for NO production during inflammation, has been detected in the mucosa of neonates with BPD and NEC.

OBJECTIVE: We propose that epithelial cells respond to inflammatory stimuli with expression of iNOS and associated cell death, which may play a role in diseases of prematurity. The purpose of this study was to test this proposal in lung epithelial cells.

DESIGN/METHODS: We stimulated A549 cells, a transformed human lung epithelial cell line that expresses iNOS in response to cytokines, with a mixture of IL-1β, TNF-α, and Interferon-γ and measured iNOS expression by western blot and cell death by fluorescence photomicroscopy. In addition, we utilized a primary cell culture model of fetal human alveolar epithelial cells. Cells were cultured in the presence/absence of dexamethasone, cAMP, and IBMX (DCI), which facilitates differentiation of cells into mature type II cells.

RESULTS: Cell death increased in A549 cells stimulated with cytokines vs. controls at both 24 h (4.9% vs. 2.6%, p<0.05) and 48 h (6.9% vs. 3.8%, p<0.05), with associated iNOS expression. Cytokine stimulation of fetal cells also resulted in increased cell death (24 h: 60.4% vs. 12.5%, p<0.05; 48 h: 61.1% vs. 18.7%, p<0.05). Cytokine stimulation of DCI-treated cells also produced cell death at 24 h (18.8% vs. 8.2%, p<0.05), and was increased at 48 h (47.3% vs. 12.5%, p<0.05) vs. controls. In both fetal and DCI-treated cells, this increase in cell death was associated with an increase in iNOS expression and activity. Cell death was apoptotic as demonstrated by caspase-3 activation (inhibitable by L-NAME) and flow cytometry.

CONCLUSIONS: These data show that human lung epithelial cells respond to inflammatory stimuli by the production of iNOS and concomitant cellular injury and death via apoptosis. Fetal cells are more susceptible to this injury. We conclude that inflammatory stimulation of the immature epithelium may play a key role in the pathogenesis of prematurity-associated diseases.

Rheumatology/Genetics Platform Session

Saturday, March 27 3:45pm–5:45pm Putnam

103 Presentation Time 3:45 PM Fellow

Juvenile Dermatomyositis: IVIG as Part of Standard Treatment Regimen

C. April Bingham, Deborah M. Levy, Lisa F. Imundo. Pediatric Rheumatology, Children's Hospital of New York-Presbyterian, Columbia University College of Physicians and Surgeons, New York, NY. (Sponsored by Philip LaRussa)

BACKGROUND: Treatment of Juvenile Dermatomyositis (JDM) is variable and depends on disease severity. Although IVIG has traditionally been used for refractory disease, there is evidence to indicate it is useful as a first line, steroid-sparing agent.

OBJECTIVE: To examine the use of IVIG in JDM and its effect on disease outcome, steroid use, and medication side effects.

DESIGN/METHODS: The charts of all JDM patients treated at Children's Hospital of NY between 1990 and 2003 were reviewed.

RESULTS: Seventeen patients who received IVIG as a first-line agent for JDM were analyzed. Twelve of 17 (71%) received steroids at onset, 8/12 received IV pulse steroids. Three patients with mild disease received IVIG alone without steroids; 2/3 of those patients are in remission on no medications, and the other patient is asymptomatic on monthly IVIG. Two patients with moderate disease at onset were effectively treated with IVIG and weekly methotrexate (MTX) in a steroid-sparing manner. Presently, patients with moderate-severe disease receive monthly IVIG, MTX, and pulse IV followed by oral steroids. Five patients have received this combination from onset of disease. At presentation, 5/5 patients had weakness and rash, 4/5 had arthritis, and none had calcinosis. The initial mean steroid dose was 1.6 mg/kg/day (+/- 0.5). The mean steroid doses at 6 months, 1 year, and most recent follow up were 0.9 (+/-0.6), 0.2 (+/-0.3), and 0.6 (+/-0.7) mg/kg/day, respectively. Complications in the patients receiving IVIG as a first-line agent were calcinosis (4/17), ulcerative disease (3/17), lipodystrophy (1/17), and 1 death resulting from a ruptured cerebral AVM. Side effects from IVIG were headache in 8/17 (47%), vomiting in 2/17, and anaphylaxis in 1 patient. Complications related to steroid use included a hip fracture in one immobile patient, and growth restriction and insulin resistance in one child with lipodystrophy. There were no serious infections, and growth was adequate in 11/12 patients receiving steroids.

CONCLUSIONS: IVIG alone appears effective in controlling mild JDM, and in combination with MTX has recently been effective as steroid-sparing therapy in moderate disease. Side effects of IVIG were not serious, and in combination with other medications it has been effective as both initial and maintenance therapy. Further prospective controlled studies of IVIG as first-line therapy, with and without concurrent steroid therapy, are warranted.

104 Presentation Time 4:00 PM House Officer

Three Year Follow-Up of Mycophenolate Mofetil Therapy in Childhood SLE Indicates Effectiveness as a Maintenance Agent

Leigh Serra, Yuki Kimura, Marilyn Punaro, Lisa Imundo. Pediatric Rheumatology, Children's Hospital of NY, Columbia University, NY, NY; Pediatric Rheumatology, Hackensack University Medical Center, Hackensack, NJ; Pediatrics, Texas Scottish Rite Hospital, Dallas, TX. (Sponsored by Philip LaRussa)

OBJECTIVE: To determine the long-term tolerability and continued effectiveness of Mycophenolate Mofetil (MMF) in a cohort of pediatric SLE patients.

DESIGN/METHODS: A retrospective chart review of all SLE patients at our Pediatric Rheumatology Centers initiated MMF prior to May 2001.

RESULTS: Nineteen patients were identified. The average length of treatment was 31m (23-40). At the start of therapy, the average age was 15.3 yrs (5-20), disease duration 3.5yrs (0.4-11). The average dose of MMF given was 35mg/kg/d, actual dose:0.5-3 grams/d. Active disease manifestations included lupus nephritis (12), CNS symptoms (3), and vasculitis (3). Fourteen patients had received prolonged Cyclophosphamide(CYC) therapy, prior to MMF treatment. At 9.3m (2-20) we reported stabilization or improvement with MMF in 8/9 patients with improved SLEDAI scores(SLE activity index), urine protein excretion, C3, and serum creatinine and urinary sediment. The 10 patients continuing treatment for 31m (23-40) had improvement in SLEDAI score from 11.6 - 4.3 and were able to decrease steroids by 98% (1.6mg/kg/d to 0.04mg/kg/d). Patients with severe lupus nephritis had a sustained response to treatment and 8/12 had excellent control of renal disease. Adverse events in 12/19 patients including mild leukopenia (4), uncomplicated herpes zoster (5), abdominal pain (3), bacterial infections (3). On continued follow-up, 31m (23-40m) 4 patients flared and discontinued MMF. Three had a significant flare of lupus nephritis with biopsy proven activity, one had new onset of lupus pneumonitis and severe vasculitis. The average time to flare was 11.2m (5-17). One patient with lupus nephritis had failed to improve with MMF or CYC and withdrew from treatment. Two patients did not tolerate MMF, two additional patients were non-compliant and discontinued MMF without a flare of symptoms.

CONCLUSIONS: Initial experience with MMF in childhood SLE indicates it is well tolerated and appears to offer an effective, less toxic alternative to CYC treatment for selected patients. The majority of patients, includung those with lupus nephritis, continuing treatment over 3 years have a sustained response. Longer follow up has also revealed an increased incidence of flares(4/19),and noncompliance(2/19) while on therapy. Further study is needed to establish the role of MMF in the treatment of childhood lupus.

105 Presentation Time 4:15 PM

Quality of Life in Pediatric Lupus

L. N. Moorthy, E. Leibowitz, L. Robbins, M. Harrison, M. Peterson, N. Cox, K. Onel, T. J. Lehman. Pediatrics, Robert Wood Johnson Medical School-UMDNJ, New Brunswick, NJ; Rheumatology, Valley Hospital, Ridgewood, NJ; Psychology, Hospital for Special Surgery, New York, NY; Biostatistics, Hospital for Special Surgery, New York, NY; Pediatric Rheumatology, Hospital for Special Surgery, New York, NY; Rheumatology, Hospital for Special Surgery, New York, NY; Research, Hospital for Special Surgery, New York, NY. (Sponsored by Dayla Chefitz)

BACKGROUND: Pediatric systemic lupus erythematosus (SLE) is associated with significant morbidity and has biopsychosocial implications resulting from the disease and its treatment.

OBJECTIVE: Identify domains of quality of life (QOL) impacted by SLE in children.

DESIGN/METHODS: Children with SLE and their parents were asked a single open-ended question related to SLE. Qualitative analysis was performed by open coding using grounded theory. Concepts were extracted, grouped under categories, which were linked to identify overlying themes. Data triangulation was performed by corroboration. Demographic characteristics, disease activity (SLE disease activity index- SLEDAI), damage (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index- SDI), and duration were measured.

RESULTS: 38 children with SLE (30 girls, age 6-20 years SLEDAI 0-24, SDI 0-6, SLE duration 5-108 months) and 27 parents were approached. Their ethnicities were as follows: 10 (26%) Black non-Latino, 7 (18%) Asian or Pacific Islander, 14 (37%) Mexican/Latino, 6 (16%) White, Non-Latino and 1 (3%) other. Their educational statuses were as follows: 1 (2.8%) in kindergarten, 27 (75%) between fourth to twelfth grade in school and 8 (22%) in college. Thirty-five children (92%) had used (previous/current use) a disease modifying anti-rheumatic drug.

21 children and 16 parents responded to the open-ended questions. Themes derived from children's responses focused primarily on coping and with SLE and attempting to gain control of it, touched upon by the following overlapping categories: Limitations; Impact of/on social/family relationships; Effect on self; Fear of future/Long-term goals. Themes from the parents' responses were twofold-(A) Efforts to cope with their child having SLE, which included the following categories: Psychological; Accommodating disease; Shifting expectations; Social support; Worry/Fear of future; Medical care; (B) Appreciation/sadness in connection with their children's coping process.

CONCLUSIONS: Qualitative exploration of different facets of QOL in these children is critical for the understanding of specific factors that assist/ease the coping process and formulating interventions for improving children's/family's self-efficacy and disease management.

106 Presentation Time 4:30 PM

Short Stature in Patients With Chronic Granulomatous Disease Is Associated With X-Linked Genotype, Granulomatous Gastrointestinal Disease and Phagocyte Metabolic Activity

David M. Lang, Steven M. Holland, Beatriz E. Marciano, Douglas B. Kuhns, Deborah P. Merke. Warren Grant Magnuson Clinical Center, NIH, Bethesda, MD; National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD. (Sponsored by Jeffrey Baron)

BACKGROUND: Growth impairment and short stature are often observed in patients with chronic granulomatous disease (CGD). It is unknown if the growth status of patients with CGD is related to genotype or clinical characteristics of the disease. This report evaluates 25 years of growth data in relation to genotype, clinical characteristics, and an in vitro measure of phagocyte metabolic activity.

OBJECTIVE: To assess height and identify factors related to short stature in patients with chronic granulomatous disease.

DESIGN/METHODS: Medical record review was performed for all patients with CGD seen at the NIH between January 1978 and June 2003. Height data, genotype and history of granulomatous GI disease were obtained on 102 children (92 male, 10 female) and 76 adults (57 male, 19 female). Height-for-age standard deviation score (SDS) was calculated using 2000 CDC growth data. Phagocyte metabolic activity was measured in vitro as a dihydrorhodamine (DHR) stimulation index on 73 patients. Height SDS were evaluated by age, and most recent or adult height SDS were compared by gender, genotype, history of GI disease, and DHR stimulation index.

RESULTS: Significant short stature (height < -2 SDS) was present in 21% (general population = 2%, $p<0.001$), and had an odds ratio of 9.2 (95 % CI: 2.6-33.2) in patients with a history of granulomatous GI disease. The mean adult height was 169.1 cm (population mean = 176.9, $p<0.0001$) for males and 160.8 cm (pop. mean = 163.4, NS) for females. For males, the mean height at the most recent visit was -1.1 SDS for children (95 % CI: -1.3, -0.8) and adults (95 % CI: -1.5, -0.6). There was no significant change in height SDS by age. Final adult height was significantly decreased in patients with X-linked CGD but not autosomal recessive CGD. DHR stimulation index was significantly correlated with height SDS ($p<0.05$).

CONCLUSIONS: A significant proportion of patients with CGD have adult height below the population norm. Males with X-linked CGD and CGD patients with a history of granulomatous GI disease have an increased incidence of short stature, while patients with autosomal recessive CGD often have normal stature. The DHR index may be a predictor of growth impairment. Further research is needed to evaluate the relationship between disease characteristics, treatment, and growth in patients with CGD.

107 Presentation Time 4:45 PM

Expression Studies and Homology Modeling of GPIb beta

Jingrong Tang, Po-Ching Liu, Peter J. Steinbach, Naomi L. C. Luban, Stephen G. Kaler. Unit on Pediatric Genetics, NICHD, NIH, Bethesda, MD; Ctr for Molecular Modeling, Ctr for Information Technology, NIH, Bethesda, MD; Depts of Lab Medicine & Hematology-Oncology, Children's National Medical Center, Washington, DC.

BACKGROUND: Haploinsufficiency for genes on chromosome 22q11.2 is associated with velocardiofacial syndrome. Glycoprotein Ib beta (GPIb beta), a component of the von Willebrand factor (vWF) receptor, is among the genes in the 22q11.2 critical region. Deficiency of GPIb beta causes the bleeding disorder Bernard-Soulier syndrome in which the vWF receptor is inactive. The receptor normally requires assembly of several gene products (GPIb alpha, GPIb beta, GPIX). We report studies in a child with velocardiofacial syndrome due to 22q11 microdeletion, and congenital thrombocytopenia consistent with Bernard-Soulier syndrome.

OBJECTIVE: 1. To delineate the molecular basis of a severe bleeding disorder in a newborn infant. 2. To understand the effects of haploinsufficiency for the velocardiofacial syndrome critical region on chromosome 22q11. 3. To evaluate the structure and function of platelet glycoprotein Ib beta.

DESIGN/METHODS: The patient was studied under a protocol approved by the Institutional Review Board of the NICHD, NIH. We used flow cytometry, DNA sequencing, expression in CHOalphaIX cells, confocal microscopy, and protein homology modeling in these investigations.

RESULTS: We identified and characterized a novel mutation (Pro96Ser) in the carboxy-terminal flanking domain of a leucine-rich repeat in GPIb beta. We transfected the mutant allele in CHO cells that stably express two other components of the vWF receptor, GPIb alpha and GPIX. Flow cytometry and confocal imaging showed that P96S abrogates surface assembly of the vWF receptor. Based on homology to the human Nogo receptor, we built a model of GPIb beta that reveals the location of P96 within the protein structure, as well as seven other residues recently reported as missense mutations. The model predicts a hydrophobic patch, the burial of which may contribute to proper conformation of the vWF receptor complex.

CONCLUSIONS: We describe a syndrome of thrombocytopenia and dysmorphism in a newborn and trace the cause to mutations on chromosome 22. We present a model of the GPIb beta protein structure based on homology to the crystal structure of the human Nogo receptor. Further study of GPIb beta and its critical role in platelet adhesion is needed to enable novel therapeutic approaches for Bernard-Soulier syndrome patients, and as a potential target for anti-thrombotic drug development. Patients with VCF should be screened for platelet dysfunction.

108 Presentation Time 5:00 PM

DBP-maf, a Potent Activator of Osteoclasts, Is Deficient in Juvenile Osteopetrosis

Prema R. Madyastha, Lyndon L. Key, Narasimha Swamy. Pediatrics, Medical University of South Carolina, Charleston, SC; Pediatrics, Medical University of South Carolina, Charleston, SC; Pediatrics, Women and Infant's Hospital, Brown University, Providence, RI. (Sponsored by James F. Padbury)

BACKGROUND: Juvenile osteopetrosis is an inherited skeletal disorder characterized by abnormally dense bones which leads to impaired bone marrow development. It is caused by osteoclast dysfunction and is lethal in the first decade of life. The activation of osteoclasts is known to promote bone resorption, and alleviate the disease and its associated symptoms. Vitamin D-binding protein-macrophage activating factor (DBP-maf) is a newly discovered osteoclast activator, which has shown therapeutic potential in animal models.

OBJECTIVE: To demonstrate that DBP-maf activates osteoclasts and endogenous levels of DBP-maf are low in osteopetrotic patients.

DESIGN/METHODS: Osteoclasts from juvenile osteopetrotic patients and normal subjects (n=20) were generated *in vitro* using peripheral white blood cells (PWBC) on bone slices. The cytochemical identification of osteoclasts was carried out by staining for tartarate resistant alkaline phosphatase (TRAP). Osteoclast activity was measured by the ability to form resorption pits on bone substrate (pit resorption assay). DBP-maf in patient sera was quantified by lectin-ELISA. Lectin-ELISA was standardized to quantify DBP-maf in patient serum using DBP specific antibodies, N-acetylgalactosamine specific lectin from *Helix pomatia*, and standard DBP-maf.
RESULTS: When compared to osteoclasts from normal subjects, osteoclasts generated from juvenile osteopetrotic patients were approximately nine times smaller in mean diameter (183 m^2 *vs.* 16118 m^2) and stained four times lighter for TRAP (A_{405}= 0.460.19 *vs.* 1.830.21). Normal osteoclasts generated characteristic resorption pits while juvenile osteopetrotic osteoclasts failed to form resorption pits on bone slices. DBP-maf activated osteoclasts *in vitro* in a dose dependent manner. There was a 211% increase in the pit resorption by 0.5 ng DBP-maf treated osteoclasts when compared to untreated control (p = 0.05). DBP-maf content in the serum of normal subjects ranged between 5.5 to 8.0 ng/ml (p=.006) whereas osteopetrotic serum samples showed a 50-fold decrease in the content of DBP-maf (0.05-0.1 ng/ml, p=0.009).
CONCLUSIONS: Osteoclasts derived from osteopetrotic patients were morphologically abnormal and functionally defective as compared to normal osteoclasts. DBP-maf was found to be a potent activator of osteoclasts and DBP-maf serum levels in juvenile osteopetrotic patients were significantly lower than in normal subjects.

109 Presentation Time 5:15 PM — Fellow

Noonan Syndrome-Causative Gain-of-Function Mutations in *PTPN11* Result in Wing Abnormalities and Embryonic Lethality in *Drosophila*

Kimihiko Oishi, Marco Tartaglia, Mark E. Lieb, Leslie Pick, Bruce D. Gelb. Pediatrics and Human Genetics, Mount Sinai School of Medicine, New York, NY; Metabolismo e Biochimica Patologica, Istituto Superiore di Sanita, Rome, Italy; Medicine, Mount Sinai School of Medicine, New York, NY; Etomology, University of Maryland, College Park, MD.
BACKGROUND: Noonan syndrome (NS) is a developmental disorder with facial dysmorphia, short stature, as well as cardiac, skeletal and hematological defects. Missense mutations in *PTPN11*, encoding the protein tyrosine phosphatase SHP-2, cause 50% of NS cases. NS-related SHP-2 mutants have increased basal phosphatase activity and ligand-dependent increased RAS/MAP kinase signaling. SHP-2's homologue in fruitfly is corkscrew (csw). Existing *csw* mutant alleles are null or hypomorphic and affect several receptor tyrosine kinase pathways during development.
OBJECTIVE: To generate NS mutations in *csw* and characterize their effects during *Drosophila melanogaster* development.
DESIGN/METHODS: Two NS mutations, A72S and N308D, were introduced into *csw* using site-directed mutagenesis. Wild type (wt) and mutant cDNAs were cloned into a vector containing a Gal4-inducible *UAS* transcription regulatory element. Transgenesis was performed using P-element mediated transformation. Promoter-*Gal4* alleles (*engrailed, en; tubulin, tub*) were used to drive transgene expression. Immunoblotting and immunohistochemistry were performed with an anti-csw antibody.
RESULTS: Two or three independent lines were derived for each *csw* construct; stable stocks were generated with balancer chromosomes. Immunostaining of *en-Gal4;UAS-csw^{N308D}* embryos revealed the en striped pattern and immunoblotting of *tub-Gal4;UAS-csw^{N308D}* lysates showed increased csw compared to non-transgenic samples, documenting transgene expression. Intercrosses of *tub-Gal4*/balancer x *UAS-csw^{transgene}*/*UAS-csw^{transgene}* revealed Mendelian ratios for *csw^{wt}* lines, diminished survival of flies expressing *csw^{N308D}* and complete lethality with the *csw^{A72S}* alleles. Lethality occurred at the embryonic stage. Surviving *tub-Gal4;UAS-csw^{N308D}* flies had ectopic wing veins in peripheral areas of L2 and L5, similar to the phenotype observed with hypermorphic *Egfr* alleles.
CONCLUSIONS: Expression of two NS-related csw mutants altered fly development while overexpression of wt csw did not. Gain-of-function varied with the mutant allele (A72S being stronger than N308D). Since csw^{N308D} altered Egfr signaling, the pathway relevant for semilunar valvulogenesis in mammals, this fly model provides a tool for understanding NS disease pathogenesis. Epistatic studies with alleles for Ras-Map kinase pathway members are in progress.

110 Presentation Time 5:30 PM — Student

Functional Absence of *TBCE* Causes Loss of Parathyroid Glands in the Syndrome of Hypoparathyroidism, Mental and Growth Retardation, and Facial Dysmorphism

Melissa C. Huang, Mark Rubinstein, Bart Loeys, Ruti Parvari, George A. Diaz. Department of Human Genetics, Mount Sinai School of Medicine, New York, NY; Ben Gurion University of the Negev, Beer Sheva, Israel; Institute of Genetic Medicine, Johns Hopkins Hospital, Baltimore, MD. (Sponsored by Bruce Gelb)
BACKGROUND: The syndrome of hypoparathyroidism, mental retardation, facial dysmorphism and growth failure (HRD or Sanjad-Sakati syndrome (SSS), MIM 241410; AR-KCS, MIM 244460) is caused by mutations in *TBCE* (tubulin-binding cofactor E), a chaperone protein required for the proper folding of tubulin. Parathyroid glands are derived from endodermal endothelial cells and are responsible for the production of parathyroid hormone (PTH), the primary regulator of serum calcium. Parathyroid tissue is absent in patients with HRD, although the mechanism of loss is unclear. Homozygosity for a deletion in a microtubule (MT)-binding domain (del52-55) and compound heterozygous mutations predicted to effectively express only a truncated protein (C371X) have been reported. Del52-55 fibroblasts exhibited disruption of MT organization and the MT-dependent Golgi apparatus (GA) distribution. Despite the deletion in the α-tubulin binding domain, del52-55 overexpression sequestered α-tubulin from MTs and tubulin monomers, leading to loss of cellular tubulin and suggesting the involvement of this domain in a novel function for TBCE. In contrast, staining of GA in C371X fibroblasts displayed a more normal distribution, although MT density was decreased in C371X cells relative to wildtype and del52-55 cells. When overexpressed, the C371X mutant did not destroy MTs despite accumulating to high levels in transfected cells, implicating the C-terminal end of the protein in α-tubulin regulation. However, immunoblotting with antibody to TBCE revealed that protein levels were greatly decreased in the disease cells, suggesting that both mutant proteins were unstable. Despite differences in cell culture, the near complete absence of expressed protein implies a common pathogenic mechanism leading to the shared clinical manifestations. The parathyroid gland aplasia in HRD suggests that TBCE has a critical role in parathyroid cell precursor migration and/or differentiation and represents a novel mechanism of hypoparathyroidism. Minor features of the syndrome involving facial anomalies and T-cell lymphopenia raise the possibility that the developmental defect is not completely selective for parathyroid precursors, but may represent a more limited neurocristopathy than that leading to the DiGeorge syndrome.

Poster Session II

Saturday, March 27 6:00pm–7:30pm Conde's Room

111 — Fellow

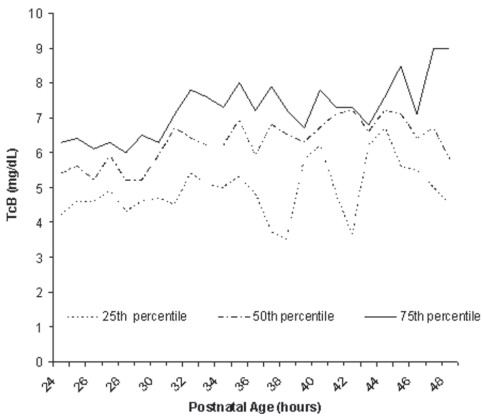
Relation of Intrapartum Magnesium Sulfate to Memory in Adolescents Born at Low Birth Weight

Jordan S. Kase, Judith F. Feldman, John M. Lorenz, Nigel Paneth, L. H. Lumey, Agnes H. Whitaker. Pediatrics, Columbia University College of Physicians and Surgeons, New York, NY; Psychiatry, New York Psychiatric Institute and Columbia University College of Physicians and Surgeons, New York, NY; Epidemiology and Pediatrics and Human Development, Michigan State University College of Human Medicine, East Lansing, MI; Epidemiology, Mailman School of Public Health at Columbia University, New York, NY. (Sponsored by Richard A. Polin)
BACKGROUND: Intrapartum magnesium (Mg) has been shown in some studies to be associated with a reduced risk of CP. No studies thus far have assessed the relation of intrapartum Mg with cognitive outcome in adolescents. We hypothesized that intrapartum Mg would protect against memory deficits in facial recognition and spatial location. Mg has been shown in animal studies to be protective against necrosis and apoptosis of neurons brought about by over activation of NMDA receptors. These receptors are particularly rich in the neonatal hippocampus. The hippocampus has been shown to be important for the types of memory mentioned above.
OBJECTIVE: Our objective is to investigate the relation between intrapartum Mg and memory in adolescents who were born at low birth weight (LBW).
DESIGN/METHODS: The source cohort was LBW (501-2000g) newborns admitted to any of 3 regional NICUs in central New Jersey from 1984-1987 and enrolled in the Neonatal Brain Hemorrhage Study (n= 1105). 864 survived to age 15; of these, 497 underwent IQ and memory testing at 15 yr. Multiple analysis of variance with covariates was done. Subtests of the Weschler Memory Scale which test memory for facial recognition and spatial location were dependent variables. Mg and maternal pregnancy induced hypertension (PIH) were independent variables. Covariates included variables reflecting risk for over activation of NMDA receptors (APGAR scores at 5 minutes; lowest base excess in the first 24 hours; lowest blood pressure in the first 24 hours; thyroid hormone status) and variables which correlated significantly with memory subtests such as gender, neonatal cranial ultrasound diagnosis, and maternal social risk factors.
RESULTS: Controlling only for IQ and the variables reflecting risk for over activation of NMDA receptors, both Mg and PIH had significant multivariate effects on memory. However, the effects were opposite of those predicted by our hypothesis. Intrapartum Mg and PIH were associated with somewhat lower memory scores. When all variables that correlated with the memory subtests were additionally included in the model, the multivariate significance for Mg, but not PIH disappeared.
CONCLUSIONS: This study does not support a beneficial effect of intrapartum magnesium upon memory for facial recognition and spatial location. PIH was associated with memory impairment.

112 — Fellow

Prediction of Neonatal Hyperbilirubinemia With a Transcutaneous Bilirubin Nomogram

Nidal Humoee, Anna Petrova, Rajeev Mehta, Thomas Hegyi. Department of Pediatrics, Robert Wood Johnson Medical School/Bristol-Myers Squibb Children's Hospital @ RWJUH, New Brunswick, NJ.
BACKGROUND: Transcutaneous bilirubin (TcB) values have a significant relationship with serum bilirubin but with wide variation in the reported correlation coefficients. An hour-specific TcB nomogram is essential if bilirubin values are to be utilized for clinical decision-making.
OBJECTIVE: To create an hour-specific neonatal bilirubin nomogram based on TcB measurements and to estimate, by using the pre-discharge TcB percentile distribution, the likelihood of developing post-discharge neonatal hyperbilirubinemia.
DESIGN/METHODS: We analyzed data on 703 TcB measurements in 367 healthy term and near-term neonates with birth weights from 2045 to 4705 grams (3339+/-428 grams), and postnatal age between 24-48 hours. TcB measurements were obtained from the infant's forehead using a Bilicheck®. A post-discharge phone survey was conducted on day 7 and 30 of life on 322 neonates (87.7%). Neonatal hyperbilirubinemia developed in 13.4% of the responders (n=43).
RESULTS: A graphic representation (nomogram) of the numerical relationship between the distribution of TcB values and post-neonatal age in hours is presented. TcB percentile greater than 75 was considered as being above normal. Sensitivity, specificity, positive predictive value, and negative predictive value were 62.8%, 69.5%, 24.1%, and 92.4%, respectively. Likelihood Ratio (LR) that has an advantage over sensitivity and specificity (because it is less likely to change with the prevalence of disease), was calculated as 2.1 with pre-test odds of 16% and post-test odds of 33%. Post-test probability for the development of neonatal hyper-bilirubinemia was 25% if the pre-discharge TcB was above the 75 percentile.



CONCLUSIONS: TcB values in conjunction with this TcB nomogram could be utilized for ruling out post-discharge neonatal hyperbili-rubinemia with a high probability. The likelihood that a pre-discharge TcB value could rule in post-discharge neonatal hyperbilirubinemia is low.

113 — House Officer

Effects of Discordance in Birth Weight on Postnatal Growth in Very Low Birth Weight Twin Infants

Gunjeet M. Sahni, Micheal A. Guiliano, Dominique Jean-Baptiste, Vinayak Govande, Myungduk R. Kim. Department of Pediatrics, Brookdale University Hospital and Medical Center, Brooklyn, NY; Department of Pediatrics, Lenox Hill Hospital, New York, NY. (Sponsored by Rakesh Sahni)
BACKGROUND: Discordance in birth weight is known to occur in 10% of twin pregnancies. Postnatal catch up growth has been reported in term appropriate and small for gestational age discordant twins ranging from early infancy to adolescence. Whether the disparity in birth weight affects postnatal growth in very low birth weight twin infants, is not known.
OBJECTIVE: To evaluate the influence of intrapair differences in birth weight on the pattern of postnatal growth of very low birth weight twin infants.

DESIGN/METHODS: Using the Vermont Oxford database, we reviewed data on all very low birth weight twin infants (birth weight <1500g) born at Brookdale University Hospital and Lenox Hill Hospital between Jan 1995 and Dec 2002. Of the 38 pairs born during the period 28 pairs were discharged home. Of these 28 pairs only 16 pairs were discordant at birth [i.e., (Birth weight difference / Birth weight of larger twin) X 100 > 8%]. Gender, gestation age, growth characteristics at birth and discharge, and the duration of hospitalization were recorded for each infant. Similar feeding strategies had been followed in all infants. Growth velocity, i.e. weight gain/day during the hospital stay was computed and compared between the smaller and the larger twin, using paired t-test.

RESULTS: The mean birth weight and gestational age of the 16 pairs of discordant twin infants who were discharged home were 1141 ± 223g and 29.0 ± 3.0wks respectively. The intrapair birth weight difference varied from 8.6-45.4% (70-681g) with a mean difference of 17.9% (236g). The comparative growth characteristics, gender distribution and duration of hospitalization of the smaller and the larger very low birth weight twin infants are shown in the table below.

	Smaller Twin	Larger Twin	p
Birth Weight (g)	1024 ± 211	1259 ± 261	<0.0001
Females (%)	68.7	56.2	NS
Discharge Weight (g)	2204 ± 239	2236 ± 163	NS
Duration of Hospitalization (d)	60.1 ± 22	56.0 ± 23	NS
Growth Velocity (g/d)	20.2 ± 3.4	18.2 ± 3.3	<0.01

mean ± SD

CONCLUSIONS: Despite comparable discharge weight and duration of hospitalization the smaller of the discordant very low birth weight twin infants show significantly higher postnatal growth velocity, suggesting catch up growth. We speculate that the intrauterine growth restriction in the smaller twin infant may program postnatal growth in order to catch up with the larger twin infant.

114

Rapid Toxicity to *Candida albicans* Mediated by Human Peripheral Blood Mononuclear Cells

Joseph M. Bliss, Sonia Laforce-Nesbitt, Pediatrics, Women and Infants' Hospital of Rhode Island, Providence, RI. (Sponsored by Lewis P. Rubin)

BACKGROUND: *Candida albicans* is a significant cause of serious infections among the immunocompromised, especially the premature infant. The cellular and innate immune systems have important roles in defense against these infections, and accumulating evidence also supports a role for antibody in host defense. The premature infant has impaired humoral immunity, as the majority of immune globulin is acquired transplacentally in the third trimester. Our general hypothesis is that the hypogammaglobulinemia of prematurity contributes to these patients' increased susceptibility to fungal infections.

OBJECTIVE: To investigate mechanisms of antibody-dependent cell-mediated cytotoxicity (ADCC) in host defense against infection with *Candida albicans*.

DESIGN/METHODS: *Candida albicans* was grown in the presence of serially diluted, heat-inactivated human serum. Bright fluorescence in immunofluorescence assays at the same dilutions used in these experiments confirmed that the human serum contained *C. albicans* specific IgG. Cells were washed and then incubated in the presence of freshly isolated peripheral blood mononuclear cells (PBMC). PBMC were lysed with water, and viability of *C. albicans* was determined by an assay of metabolic activity (XTT).

RESULTS: Heat-inactivated serum at concentrations as low as 1% (v/v) resulted in approximately 50% inhibition of *C. albicans* viability after 2 hours of incubation with PBMC at an effector:target (E:T) ratio of 8. Lower but measurable toxicity was achieved at lower E:T ratios and lower serum concentrations. However, the cytotoxic effect was seen neither in the absence of serum nor in the absence of PBMC and required both components. Media recovered and filtered following incubation was not capable of inducing toxicity in fresh *C. albicans* cultures, suggesting that the toxicity is not mediated by a soluble factor. Experiments to determine the specific host cell type(s) responsible for the effect and to confirm that antibody is the required serum component are currently underway.

CONCLUSIONS: The rapidity with which toxicity to *C. albicans* can be elicited in these studies provides evidence for an ADCC mechanism of host defense. Additional studies are aimed to determine the cellular and molecular interactions responsible for mediating this effect. These observations may provide additional insights into the mechanisms that increase the susceptibility of premature infants to these serious infections.

115

House Officer

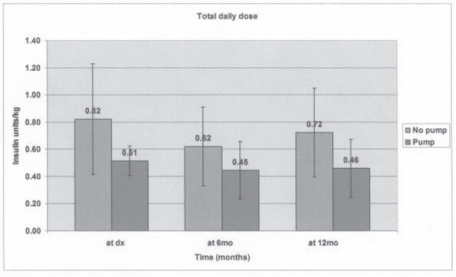
New Model for Insulin Initiation in Type I Diabetes

John Ching, Neven Pesa, Golali Nejati, Ashutosh Gupta, Nicole Matthews, Henry Anhalt, Svetlana Ten, Pediatric Endocrinology, Infants and Children's Hospital of Brooklyn, Brooklyn, NY.

BACKGROUND: Continuous subcutaneous insulin infusion (CSII) for pediatric patients is not novel. However, there is a lack of consensus on length of initial hospitalization, when to start pump therapy, and some skepticism on its utility especially at the onset of diabetes.

OBJECTIVE: The purpose of our study is to compare two algorithms of management of newly diagnosed diabetes patients in our clinic.

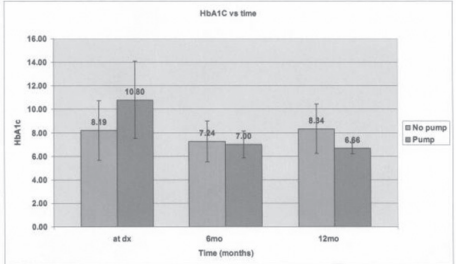
DESIGN/METHODS: We evaluated HbA1c level and total daily insulin dose (TDD) in 2 groups of patients (n=35, age 15 month to 16 years) with new onset diabetes type 1 (confirmed with GAD or islet cell antibodies) at diagnosis, 6 months, and 12th months after diagnosis.[figure 1]



RESULTS: HbA1c levels after 12 months of therapy in-Group 2 (6.66±0.46) were significantly lower than Group 1 (8.34±2.10) [p<0.05]. There were no differences in HbA1c levels after 6 months of therapy (Group 1 - 7.24±1.74 vs. Group 2 - 7.0±1.14).

TDD was significantly lower in Group 2 (0.45±0.21 at 6 months and 0.46±0.21 at 12 months of therapy) than Group 1 (0.62±0.29 and 0.72±0.33 respectively)[p<0.05].

There were no reported cases of DKA in Group 2 within the first year while Group 1 reported 2 cases (8.3%). [figure 2]



CONCLUSIONS: Intensive teaching, 24 hour support, and CSII within 2 weeks of diagnosis improved HbA1c levels and decreased TDD of insulin over traditional therapy. CSII was beneficial for newly diagnosed diabetes patients at the onset of disease.

Treatment algorithm Group 1 (number of patients = 24)	Treatment algorithm Group 2 (number of patients = 11)
All patients with new onset diabetes were discharged within 3-5 days.	All patients with new onset diabetes were discharged within 24 hours.
Patients and parents were taught within 3 to 5 days in-hospital how to manage diabetes by pediatric endocrinology team.	Patients and parents were taught within first 24 hours in-hospital how to manage diabetes by pediatric endocrinology team.
Patients were started on Humalog and NPH in the hospital after correction of diabetic ketoacidosis.	Patients were started on Humalog and Lantus after correction of diabetic ketoacidosis and regiment was continued for the first 1-2 weeks. CSII was started within first 14 days after diagnosis.
A pediatric endocrinologist was available 24 hours a day 7 days a week to support insulin dose adjustment and education over the phone for the patients and parents.	A pediatric endocrinologist was available 24 hours a day 7 days a week to support insulin dose adjustment and education over the phone for the patients and parents.

116

Fellow

Preterm Neonatal Thrombocytopenia Causes and Outcome

Shakuntala Nanjundaswamy, Anna Petrova, Rajeev Mehta, Department of Pediatrics, Robert Wood Johnson Medical School, New Brunswick, NJ.

BACKGROUND: Thrombocytopenia is the second commonest hematological abnormality in the neonatal period after anemia.

OBJECTIVE: To investigate the impact of placenta pathology and neonatal conditions on the development of thrombocytopenia, and to define the risk of thrombocytopenia on preterm neonatal morbidity and mortality.

DESIGN/METHODS: Cases and controls were defined from a discharge database of 1054 neonates with gestational age < 32 weeks . Medical records (maternal, neonatal, and placental pathology reports) of 82 thrombocytopenia cases (platelets levels less than 100 X (10)9/L) and 82 controls were analyzed.

RESULTS: The proportion of neonates with gestational age < 28 weeks was higher among the cases (68.3% vs17.1%, P<0.0001). More neonates with bacterial or candida septicemia were found in the cases versus controls (54.9% vs 30.5% and 17.1% vs 3.7%, respectively, P<0.01). No significant differences were seen between cases and controls in the percentage of placental infection related pathology and pathological findings reflecting abnormalities of placental-fetal blood flow (hematomas, infarction, and villous edema). Variables such as sepsis, maternal infection and other conditions (hypertension, diabetes), fetal distress (FD), placental pathological lesions, maternal and neonatal antibiotic use, heparin and indomethacin were included in the regression model to investigate the risk factors for the development of thrombocytopenia. Gestational age and FD were independently associated with thrombocytopenia (b=0.465 and b=0.205). Regarding the association between thrombocytopenia and outcome, platelet counts less than 100 X 10(9)/L, after controlling for gestational age, bacteriological proven sepsis, maternal and neonatal anrtibiotic administration, and placental pathological findings, were found to be an independent risk factor for neonatal mortality (b=0.515, P<0.001). The probability of developing intraventricular hemorrhage, necrotizing enterocolitis, and bronchopulmonary dysplasia among preterm neonates with thrombocytopenia was not any higher than in the infants without.

CONCLUSIONS: Our findings that show the impact of thrombocytopenia as an independent factor for preterm mortality may have practical implications for the development of new strategies and intervention programs to reduce the adverse outcomes in the at-risk neonates.

117

Fellow

Hypothyroidism Due to Autoimmune Thyroiditis in Very Young Children

Ashutosh Gupta, Harvey Mermelstein, Svetlana B. Ten, Henry Anhalt, Pediatrics, Maimonides Medical Center, Brooklyn, NY; Pediatrics, 1266 51st street, Brooklyn, NY.

BACKGROUND: Hypothyroidism (HT) in neonates or infants usually results from congenital aberrations. Discovery of HT before the age of 3 usually denotes failure of newborn screening (NBS) and is rarely caused by chronic autoimmune thyroiditis (AIT).

OBJECTIVE: We present 2 children, <3 yr. old, with HT due to AIT.

DESIGN/METHODS: Case 1: A 2 yr. 7 mo. old male, born at term (B.wt. 3.2 kg) to non-consanguineous parents presented with short stature. His NBS tests were normal. His length and weight had decelerated over time and milestones were delayed. He was constipated and lethargic. His height was 77 cm (-5.9 SDS) and weight 10.8 kg (-3.5 SDS). He had a small goiter, macroglossia and umbilical hernia. Hair was coarse and skin sallow, dry and cool. The total T4 was <1 µg/dl (N = 4.5-12) and TSH >150 mIU/ml (N = 0.4-6.9). the anti-thyroglobulin (anti-TG) (90 U/ml) and anti-TPO antibodies (ab.) (70 U/ml) were elevated (N<2.0). Case 2: A 2 yr. 4 mo. old female, first of twin, born at 26 wks. (B.wt. 891 gm) to non-consanguineous parents presented with failure to thrive. Her NBS tests were normal. She had Down syndrome (47, XX, +21). She had undergone surgery for Hirschprung's disease. Her milestones were delayed. She had typical features of Down syndrome, a protuberant tongue, but on goiter. She was hypotonic. Her free T4 was low (1.23 ng/dl; N = 0.75-2.0) and TSH elevated (15.97 mIU/ml; N = 0.23-5.24). The anti-TG (7.8 U/ml) and anti-TPO ab. (>70 U/ml) were elevated (N<2.0).

None had mucocutaneous candidiasis. Chemistry including LFT and s. calcium, CBC, islet cell ab. and adrenal ab. were normal. A neck sonogram showed normal thyroid in both. Few wks. after starting thyroxine the T4 and TSH levels normalized and both gained height rapidly.

CONCLUSIONS: HT due to AIT is rare in very young children; less than a dozen cases have been described. It should be distinguished from late-onset congenital HT. Although pathologically distinct, both have similar presentation and risk of neurological deficits, if left untreated. HT in young children may be a component of autoimmune polyendocrinopathy syndromes. It has also been described with IPEX syndrome (immune dysregulation, polyendocrinopathy, enteropathy, X-linked). The clinical and laboratory findings indicate that, at this point, our patient's HT is due to isolated AIT. Significantly improved growth after starting thyroxine delineates its important role in growth.

118

Routine Parenteral Intake of Vitamin E in Very Low Birth Weight Infants in the U.S.: Too Much or Too Little?

Luc P. Brion, Edward F. Bell, Talkad S. Raghuveer. Pediatrics, Albert Einstein Coll Med, Child. Hosp. Montefiore, Bronx, NY; Pediatrics, Univ. Iowa, Iowa City, IA; Pediatrics, Univ. Kansas Med. Ctr., Kansas City, KS.

BACKGROUND: An adequate intake of vitamin E is required by very low birth weight (VLBW) infants to prevent hemolytic anemia and other manifestations of deficiency. Infants who cannot be given adequate vitamin E enterally reguire parenteral multivitamins containing vitamin E. Recommended doses of parenteral multivitamins in VLBW infants vary considerably and may provide vitamin E intakes known to be associated with toxicity. The American Academy of Pediatrics (AAP) until recently has recommended 2.8 IU/day vitamin E for infants ≤ 2.5 kg. This intake would provide 7 IU/kg/day for a 0.4-kg infant. Intakes of parenteral vitamin E > 4 IU/kg/day often yield potentially toxic levels (>3.5 mg/dl) after 2-3 weeks of administration. Our Cochrane review has shown that vitamin E supplementation resulting in levels > 3.5 mg/dl, but not ≤ 3.5 mg/dl, significantly reduces the risk for severe retinopathy among VLBW infants examined but increases the risks of sepsis and of necrotizing enterocolitis (NEC) among infants treated for > 1 week.

OBJECTIVE: This study was designed to assess the frequency with which potentially inadequate or toxic doses of intravenous vitamin E are used by NICUs in the U.S.

DESIGN/METHODS: A questionnaire was sent 3 times by email to US neonatal division directors and twice by fax to the 100 neonatal perinatal training program centers listed in the 2003 directory (AAP, Section on Perinatal Pediatrics). We compared the responses to doses currently recommended (2.8 IU/kg/day, max 7 IU/day) by the American Society for Clinical Nutrition (ASCN) and the AAP.

RESULTS: We received a response from 69 centers (69%). Thirty centers followed the ASCN recommendation, 12 that from Astra Phamaceuticals, 4 the 1998 AAP recommendation, and 23 another protocol. Altogether, 37 centers used a dose per kg, 24 used a weight-based scale, 6 a fixed dose and 2 a TPN-rate-dependent dose. In 500-g infants, 9 centers (13%) used doses < 2.8 IU/kg/day, 31(45%) doses > 2.8 IU/kg/day, and 29 (42%) doses > 4 IU/kg/day. The dose of i.v. tocopherol acetate was 3.6 ± 1.4 IU/kg/day (mean± SD, range 0.7-9.1) at 500 g, 3.3 ± 1.0 (0.7-6.5) at 1 kg and 2.9 ± 0.8 (0.7-5.3) at 1.5 kg.

CONCLUSIONS: In the U.S., 42% of the NICUs provide VLBW infants with doses of vitamin E that may yield high serum levels of vitamin E with potential risk for sepsis and NEC, while 13% use doses that are too low and may yield deficiency in vitamin E.

119

House Officer

The Competency of Pediatric Residents in the Evaluation & Treatment of Childhood Obesity

Anthony F. Porto, Peter Belamarich, Andrew D. Racine. Pediatrics, Albert Einstein College of Medicine/CHAM, Bronx, NY.

BACKGROUND: Pediatricians identify multiple barriers to the care of obese patients including limited knowledge about the appropriate work-up and management. The evaluation and treatment of obesity as practiced by pediatric residents have never been studied.

OBJECTIVE: To determine the current evaluation and treatment practices of residents and to compare them with current obesity guidelines.

DESIGN/METHODS: A survey was created based on expert panel recommendations published in Pediatrics in 1997. The survey was given to all pediatric residents working at two main clinic sites at an urban academic medical center in an area of high obesity prevalence. Questions focused on: evaluation for complications of obesity; assessment of family, diet and exercise histories; recommendation of behavior changes; referral patterns. Likert scale responses were used to elicit self-reported behavior in evaluating obese patients. Information on site of practice, year of training (PL-1, 2 or 3), and career plans (primary care vs subspecialty) was also obtained. χ^2 analysis was used to evaluate categorical variables and logistic regression was used for multivariate analysis.

RESULTS: Fifty-six of 57 pediatric residents completed the survey. Fifty-seven percent of residents calculated a BMI. Of possible complications of obesity, 4% of residents thoroughly evaluated for orthopedic disorders; 27% for genetic; 29% for pseudotumor cerebri; 38% for endocrinologic; 41% for sleep; 59% for metabolic syndrome; and 66% for gastrointestinal. In terms of history, 11% of residents obtained a thorough family history while 55% and 88% obtained an exercise and diet history, respectively. Over 90% of residents recommended changes in eating and exercise patterns. Most residents referred patients to a nutritionist (96%) or pediatric subspecialist (81%) while less than half referred patients to an obesity specialist. Relative to PL-1 residents, PL-2 and 3s more frequently examined patients for endocrinologic disorders, asked about family history of diabetes, and referred patients to a nutritionist.

CONCLUSIONS: Most pediatric residents training in an urban setting demonstrate some awareness of the appropriate evaluation for childhood obesity. Although there is improvement over the course of their training, few achieve systematic competence in this area. Studies of potential interventions to improve the approach to the evaluation of childhood obesity in residency training are warranted.

120

Fellow

Trimming of Percutaneous Central Venous Catheters Prior to Insertion and Risk of Catheter Related Sepsis in the NICU

Archana P. Bilagi, Jotishna Sharma, Jeanne Rorke, Martin Keszler. Pediatrics/Neonatal-Perinatal Medicine, Georgetown University Hospital, Washington, DC.

BACKGROUND: Catheter-related sepsis (CRS) is a common complication of Percutaneous Central Venous Catheters (PCVCs) in the NICU, with reported incidence of 15-31%. Clinicians vary in their practice of trimming catheters to a premeasured length or leave them untrimmed prior to insertion. When untrimmed, the excess length is coiled at the site of insertion and secured; this excess length could be a potential source of infection.

OBJECTIVE: To determine if trimming PCVCs prior to insertion decreases the risk of CRS.

DESIGN/METHODS: Eligible infants requiring a PCVC as determined by the attending neonatologist, were prospectively randomized following informed consent, to either trimmed or untrimmed PCVC group. Data collected included demographics, diagnoses, complications, duration of dwell, episodes of CRS and reasons for removal of PCVC. Data were analyzed by t-test, Fisher's exact test and multiple logistic regression. Power analysis projected a sample size of 140 infants but the study was stopped after an interim analysis with 68 infants (34 in each group).

RESULTS: There were no significant differences in gestational age, birth wt., wt. and age at insertion of PCVC, number of attempts at insertion and dwell time in the two groups.

	Gestational age (weeks)	Birth weight (grams)	Weight at insertion (grams)	Age at insertion (days)	Dwell time (days)	Number of attempts
Trimmed	29.4 ± 5.6	1429 ± 1186	1522± 1216	9.8±17.4	13.5±9.7	1.7±1.0
Untrimmed	31.7± 6.0	1845 ± 1206	1955 ± 1238	9.0±10.8	14±9.7	1.6±0.8
P value	0.10	0.16	0.15	0.81	0.84	0.49

Data presented as mean±SD.

Incidence of CRS in the study population was 17.6% with 6/34 infants affected in each group. In infants <1000 g at insertion of PCVC, there was an small increase in CRS in the untrimmed group (trimmed: 3 / 18 (16.6%), untrimmed 4/13 (30.8%); Fisher's exact test: 2-tailed p = 0.413, OR = 0.45, 95% CI 0.0544 and 3.4346). However, by multiple logistic regression, this apparent difference was explained by birth weight, gestational age, dwell time and number of attempts at PCVC insertion; inclusion of trimming PCVCs did not improve the predictive value of the model (p = 0.98).

CONCLUSIONS: Trimming of PCVCs prior to insertion does not decrease the risk of CRS based on this interim analysis. Given the lack of any trend at all, enrolling further infants to meet the calculated sample size will not alter the conclusion.

121

Fellow

Infants With Persistent Pulmonary Hypertension of the Newborn (PPHN) Are at Increased Risk for Subsequent Systemic Hypertension

Anne Marie Reynolds, Mahesh Bommaraju, Kirsten Blessing-Hanagan, Rita Ryan. Pediatrics, Division of Neonatology, State University of New York at Buffalo and Women and Children's Hospital of Buffalo, Buffalo, NY.

BACKGROUND: Systemic hypertension (HTN) is reported as relatively rare in the Neonatal Intensive Care Unit (NICU) (overall incidence of 0.81%). HTN has been described in patients with Persistent Pulmonary Hypertension (PPHN) treated with Extracorporeal Membrane Oxygenation (ECMO). Clinically, we have suspected that non-ECMO PPHN infants also have HTN once the PPHN has resolved.

OBJECTIVE: To test the hypothesis that infants who have had PPHN are more likely to have HTN compared to matched controls.

DESIGN/METHODS: This is a retrospective case-control study, with potential PPHN cases screened by ICD-9 code. We then included infants with echocardiographic evidence of PPHN who did not receive ECMO. Controls were non-PPHN patients with the closest birth date matched for race, sex, gestational age +/- 1 week, and birth weight +/- 500grams. Data was collected daily from birth to day 14, then on days 16, 18, 20, 24 and 28 or until discharge, and included blood pressure measurements of highest, lowest and average systolic (SBP), diastolic (DBP) and mean; weight; fluids given; respiratory status including type of ventilator, settings and oxygen requirement; medications given including nitric oxide (NO), steroids, vasopressors and antihypertensives.

RESULTS: Our population includes 60 infants with an average birth weight of 3155 gms and gestational age of 37 weeks; 65% were male. PPHN infants had significantly higher FiO2 requirements, were more likely to receive NO, and were more likely to have systemic hypotension early in their course. In the overall population, 25% of infants had a SBP >100 at some time from day 4-28. During this time there was a significant difference in the average peak SBP between PPHN patients and controls (99.2 vs. 90.9, P = 0.03), and PPHN patients were more likely to have a SBP >95 than were controls (59% vs. 26%, P=0.02). These findings were corroborated by a trend toward a difference in peak DBP (64.2 vs. 59.3, P=0.07) and by a trend toward PPHN infants (21% vs. 4%, P=0.07) being treated with an anti-hypertensive medication.

CONCLUSIONS: Elevated blood pressure during hospitalization was relatively common in our population. Infants recovering from PPHN were more likely to have systemic hypertension than matched non-PPHN controls. Regulation of systemic blood pressure may be disrupted during the acute illness of PPHN, with an adjustment period required during recovery.

122

House Officer

Effect of Parental Health Literacy on Child Asthma Morbidity

Lisa Wilks-Gallo, Iman Sharif, Philip O. Ozuah. Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: No studies have looked at the impact of parental health literacy on child health outcomes.

OBJECTIVE: To test the hypotheses that lower parental health literacy is related to poor understanding of metered dose inhaler with spacer (MDI-S) use and increased child asthma morbidity.

DESIGN/METHODS: Setting: Inner-city pediatric outpatient clinics. We invited parents with and without asthmatic children to participte in a study about readability of asthma instructions. Subjects read instructions accompanying an MDI-S device, and then demonstrated its use. Subjects with an asthmatic child demonstrated MDI-S use both before and after reading the instructions. All subjects were administered the Short Test of Functional Health Literacy in Adults (STOFHLA; range 0-36, "adequate" literacy>23) . Demographics and data on child asthma morbidity were collected.

We used the manufacturer's instructions to code correct demonstration for each step of MDI-Spacer use. Students t-test compared mean STOFHLA for subjects who correctly vs. incorrectly demonstrated MDI-S use. For subjects who had a child with asthma, we compared # of ED visits and hospitalizations for those who demonstrated each step correctly vs. incorrectly at baseline demonstration. Linear regression tested STOFHLA, education and insurance status as predictors of the # of ED visits.

RESULTS: 117 subjects participated. Mean STOFHLA was higher for subjects who correctly : Removed the inhaler cap (33 vs 29, p=.08), Inserted inhaler into spacer (33 vs. 27, p=.05), Covered nose and mouth (33 vs 28, p=.06), Depressed the inhaler once at start of inhalation (33 vs. 30, p=.007), and Maintained seal for 6 breaths (34 vs 31, p=.006).

64 subjects had a child with asthma. At baseline demonstration, lower mean # of asthma hospitalizations was correlated with correctly : Removing cap (3 vs. 7, p=.13), Inserting inhaler (3 vs. 8, p=.11), and Depressing inhaler at start of inhalation (2.5 vs. 5, p=.21). Mean # ED visits was lower for subjects who,after reading the instructions, correctly: Removed cap (8 vs. 35, p=.002), Covered nose and mouth (9 vs. 32, p=.007). ED visits did not differ for the baseline demonstration.

After controlling for demographics, parental STOFHLA predicted # ED visits (*B*= -.873, p=.012). For every 1 point decrease in STOFHLA, ED visits increased by one.

CONCLUSIONS: Lower parental health literacy correlated with incorrect MDI-S use and increased child asthma morbidity, even within the range of "adequate" health literacy.

123

Does Posting Asthma Guidelines in Physician Examination Rooms Improve Anti-Inflammatory Therapy Use?

Sandra F. Braganza, Iman Sharif, Philip O. Ozuah. Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: We previously reported low levels of accurate classification and management of persistent asthma. In response, a 2-stage intervention was developed.

OBJECTIVE: To investigate the impact of a 2 stage intervention on increasing 1) physician documentation of asthma severity, 2) correct classification of asthma severity and 3) appropriate anti-inflammatory therapy use.

DESIGN/METHODS: We conducted a cross sectional study at an inner-city academic health center. After collecting baseline data, an educational intervention was made. One year later we posted asthma classification guidelines in all clinical examination rooms. Follow-up data were collected 10 months after the educational intervention and 6 months after posting the guidelines. All data were obtained by consecutive sampling over 14 day periods. Charts of patients with asthma were identified and documentation of asthma severity classification was recorded. Parents were then directly surveyed regarding the child's asthma symptoms and current asthma therapy.

We used the NAEPP (National Asthma Education and Prevention Program) guidelines to classify asthma severity. Chart classification of asthma severity was compared to the NAEPP-applied classification. Similarly, we used the NAEPP guidelines to code whether anti-inflammatory therapy use was appropriate for severity classification.

Bivariate analysis compared documentation of asthma severity, correct classification and appropriate

therapy use across the study period.
RESULTS: 428 subjects participated (176 at baseline; 109 post-educational intervention; 143 after the guidelines were posted). Severity classification was similar for all groups (persistent asthma: 56% vs.58% vs 61%, p=.57)
As shown in Table 1, documentation of asthma severity, correct classification and appropriate anti-inflammatory therapy use increased following the 2 interventions.
CONCLUSIONS: Our 2-stage interventions resulted in sustained improvements in the documentation, classification, and manamgement of persistent asthma. These findings have implications for the implementation of asthma quality improvement efforts.
Table 1

	Baseline, November 2001	After educational intervention, November 2002	After posting guidelines, November 2003	p value
Documentation of asthma severity	77%	86%	91%	0.002
Correct classification	39%	44%	53%	0.03
Appropriate anti-inflammatory therapy use	63%	82%	73%	0.002

124

House Officer

Risk Factors for Retinopathy of Prematurity (ROP) in Very Low Birth Weight (VLBW) Neonates

Shital Doshi, Khaja Raziuddin, Vesna G. Sutija. Pediatrics, New York Methodist Hospital, Brooklyn, NY.
(Sponsored by Leonard Glass)
BACKGROUND: While survival of VLBW neonates has improved , ROP remains a major clinical problem.
OBJECTIVE: The purpose of this study was to assess the relationship of several factors such as gestational age (GA), birth weight (BW), blood blucose concentration, supplemental oxygen and mean airway pressure(MAP) to the risk of developing ROP.
DESIGN/METHODS: A retrospective cross sectional study of 207 neonates with BW of <1250g born between January 1990-December 1999 at New York Methodist Hospital was performed. The daily glucose intake was adjusted to maintain glucose levels of <120mg/dL to a maximum of 23.9 g/kg/day. A minimum and maximum level for each day during 28 postnatal days was recorded and the mean maximum for each neonate computed. $PaCO_2$ was maintained in a range of 40-50 Torr. GA, BW and the need for supplemental oxygen and assisted ventilation were assessed. The results of cranial ultrasound and ophthalmologic exams were recorded.
RESULTS: Nineteen neonates (9.1%) developed ROP. They had lower GA and BW than neonates without ROP (GA: 26.1 vs 27.0 wks; p=0.0003; BW: 781.3 vs 944.3 g; p<0.0001). The proportion of neonates in whom hyperglycemia could not be controlled was higher in the ROP group (36.8% vs 0.5%; p<0.0001). Average maximum glucose levels during 28 postnatal days were higher in neonates with ROP (p<0.0001). Supplemental oxygen was discontinued later in the neonates with ROP (p=0.03) and they required it longer (9.0 vs 7.2 wks, p=0.04). The MAP did not differ in the two groups. Intravenricular hemorrhage (IVH) was present in 8 (42%) of ROP group compared to 16 (8.5%) in non ROP group. 75% of IVH in ROP group were Grade 1. Periventricular leukomalacia was present in 3 neonates without ROP.
CONCLUSIONS: In addition to lower GA and BW, prolonged oxygen supplementation and the presence of IVH, hyperglycemia appears to play a major role in the pathogenesis of ROP.

125

Fellow

Hematologic Characteristics of Infants With Trisomy 21: A Case for Platelet Underproduction

Timothy A. Kline, Amy Mackley, David A. Paul. Neonatology and Pediatrics, Christiana Care Health Services, Newark, DE; Pediatrics, Thomas Jefferson University, Philadelphia, PA.
BACKGROUND: It is well documented that infants with Trisomy 21 have multiple hematologic abnormalities. The reasons for this finding are unknown. For example, it is unknown whether the associated thrombocytopenia results from platelet destruction or underproduction.
OBJECTIVE: To characterize the hematologic characteristics of infants with Trisomy 21 and compare them with matched controls.
DESIGN/METHODS: A retrospective review of all infants with Trisomy 21 and admitted to the Christiana Care Hospital Special Care Nursery from 1997-2003. Infants were compared with a control group matched for gestational age. CBC results, including WBC, hemoglobin (Hb), hematocrit (Hct), platelet count, mean corpuscular volume (MCV) and mean platelet volume (MPV) on admission and again at hospital day 3-7, if obtained, were compared. Values were compared using analysis of variance and Chi Square tests. Data are presented as mean ± sd.
RESULTS: Infants with Trisomy 21 (n=30) were compared with controls (n=30) matched for gestational age. Platelet count on admission for Trisomy 21 patients were 155,000 ± 66,000/µl, while controls were 211,000 ± 54,000/µl.(p<.01). Platelet count on day 3-7 was 195,000 ± 140,000/µl for infants with Trsiomy 21 and 270,000 ± 58,000/µl for controls (p=.15). Admission Hct for trisomy 21 infants was 55 ± 6%, and for controls 50 ± 6% (p<.01). WBC count did not differ between the two groups on admission or day 3-7. Mean MCV for Trisomy 21 infants was 112 ±5.6 fl, and for controls 104.7 ±4.6 fl. (p<.01). Mean MPV for Trisomy 21 infants was 8.5 ± 1.1 fl, and for controls mean MPV was 10.8± .74 fl. (p<.01). 17% of infants with Trisomy 21 had thrombocytopenia (platelets <100,000/µl) at birth, compared with 0% of controls (p=.01).
CONCLUSIONS: Our data confirm the common findings of lower platelets and a higher hematocrits at birth in infants with Trisomy 21. Of note, infants with Trisomy 21 had lower mean platelet volumes compared to controls, suggesting decreased platelet production. Similiar to findings in infants born to mothers with pre-eclampsia, the high hematocrit, low platelet count, and low MPV may suggest placental insufficiency leading to red cell hyperplasia and decreased megakaryocyte production.

126

Fellow

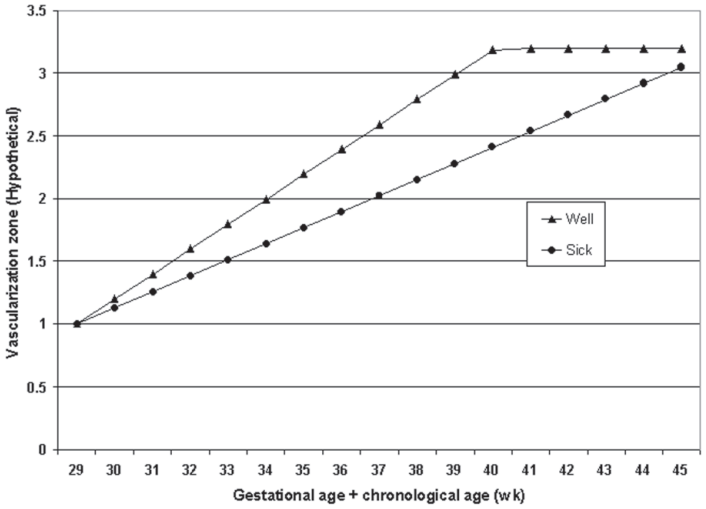
Urinary Peroxide and Nitrite/Nitrate Levels in Newborn Infants

Christiana R. Farkouh, Scott A. Lorch, Jeffrey Merrill, Philip L. Ballard, Harry Ischiropoulos, Roberta A. Ballard. Pediatrics, Childrens Hospital of Philadelphia, Philadelphia, PA.
BACKGROUND: Urinary peroxide (UP) has been associated with in vivo oxidative status. Urinary nitrite and nitrate (UN), byproducts of endogenous nitric oxide production, reflect in vivo nitric oxide (NO) production and metabolism. Limited data exists on UP and UN levels in newborn infants.
OBJECTIVE: Evaluate effects of gestational age and clinical status on the levels of UP and UN.
DESIGN/METHODS: A single urine specimen was obtained in the first 72 hours of life in healthy term infants not requiring respiratory support or supplemental oxygen (well term, Group 1, n=11); premature infants under 33 weeks gestation requiring either no respiratory support, nasal canula oxygen or Nasal CPAP with an FiO2<0.3 (well preterm, Group 2, n=10); and in preterm infants 24-32 weeks gestation admitted from 1998-2003 requiring mechanical ventilation from day one of life (sick preterm, Group 3, n=67). No infant received inhaled NO. All urine samples were stored at –70 until analysis. UP was quantified by a fluorometric method and UN was measured by reduction of nitrate and nitrite using acidified vanadium (III) and detection of released NO by chemiluminesence. Both UP and UN were standardized to urinary creatinine. Kruskal-Wallis tests were used to determine differences between groups. Log transformed regression models estimated the effects of gestational age on UP and UN levels.
RESULTS: UP concentrations were significantly lower in group 1 (median 3 umol/mmol Cr, range 0.6-21.8) when compared to group 2 (12.8, range 0-37, p=0.02) and group 3 (9.4, range 0.3-66.2, p=0.006). Group 2 had significantly higher UN levels (median 320 umol/mmol Cr, range 223-628, p< .01) when compared to group 1 (216, range 144-316, p=0.004) and group 3 (232, range 28-720, p=0.009). Both UP (r^2=0.37, p=0.004) and UN (r^2=0.37, p= 0.003) were inversely correlated with GA in well infants, but not in sick premature infants.
CONCLUSIONS: Among well newborn infants, urinary markers of oxidative status and NO metabolism may decrease with advancing gestational age. Biosynthesis or metabolism of NO to urinary nitrate and nitrite may be decreased in sick premature infants with respiratory disease, supporting the possible association of relative NO deficiency and newborn lung disease.
Funding support from GCRC grant (M01-RR00240).

127

Growth of Retinal Blood Vessels Is Altered in "Sick" vs. "Well" Premature Infants

Naveed Hussain, Ricardo Jean-Baptiste, Marta Barker, Christopher Kelley. Pediatrics, University of Connecticut Health Center, Farmington, CT; Biology, Universtiy of Hartford, Hartford, CT.
BACKGROUND: Retinal vascularization (RV) is incomplete in premature infants and continues after birth from the center (Zone 1) out to retinal periphery (Zone 3). Adverse events such as hyperoxia or sepsis predispose the infants to neovascularization, leading to retinopathy of prematurity (ROP). However, it is unknown how this may be associated with an alteration of RV.
OBJECTIVE: Determine whether the rate of growth of retinal blood vessels is altered in "sick" vs. "well" premature infants.
DESIGN/METHODS: A retrospective study of infants born at the Univ. of CT Health Center between 1998 and 2002 was done including all surviving infants with birth weight < 1600 g, GA ≤32 wk who had eye exams done starting at 6 weeks of age and continuing every 1-2 wk until discharge. Infants with at least 1 eye exam were included. All exams were done by a single pediatric ophthalmologist (CK). RV was assessed as per the ICROP definition of zones. Since, degree of illness correlates with growth in premature infants, they were classified as "well" if their rate of growth by weight gain was ≥10 gm/kg/day or "sick" if growth was <10 gm/kg/day. Data were analyzed for differences using univariate and regression analyses.
RESULTS: Rate of RV was slower in "sick" vs "well" premature infants (0.13 zone/wk vs 0.20 zone/wk; p<0.0001), based on a calculated projection of retinal vessel growth as shown below. Infants with ROP had slower rate of RV than those without ROP. RV was significantly slowed by lower GA at birth (p<0.0001), lower birth weight (p<0.0001), longer duration of oxygen requirement (p<0.001). RV was not affected by race, sex or the presence of IVH/PVL.
CONCLUSIONS: The overall poor growth and illness of the premature infant not only influences the development of ROP but also the rate of retinal vascularization. We speculate that, this may be correlated to recent reports of lower IGF-1 levels in "sick" premature infants.



128

The Comparision of Effect of Incomplete and Complete Course of Antenatal Steroids on Morbidity and Mortality in Premature Infants

Harpreet Kaur, Chhavi Agarwal, Lourdes Cohen, Susana Rapaport. Pediatrics, Flushing Hospital Medical Center, Flushing, NY.
BACKGROUND: The prevalence of preterm birth has increased (7-10% of the total pregnancies) over the last 2 decades due in part to advances in reproductive technology and obstetrical intervention. Immature infants have numerous complications associated with prematurity such as: IVH, NEC, ROP, CLD, sepsis and RDS. Several studies have been done to look at the neonatal outcomes with complete course of antenatal steroids but none of the studies have been done for incomplete course.
OBJECTIVE: To determine if an incomplete course of steroid shows the same clinical benefits when compared to complete course as measured by Pulmonary (RDS, CLD) and Non-Pulmonary outcomes (NEC, IVH, ROPand mortality).
DESIGN/METHODS: A Retrospective chart review of all mothers who presented in preterm labor and delivered at <34 weeks gestation at FHMC from January 1997 to May 2003.
Total of 159 charts were reviewed . 58 were excluded because of absence of prenatal steroid administration or presence of congenital malformations. A total of 101 subjects were included in the study and were divided into 2 groups- subjects that received incomplete course of steroids and subjects that received complete course of steroids .
The 2 groups were then compared looking into the morbidity and mortality.
RESULTS: An incomplete course of prenatal steroids does not have a significant difference in neonatal outcomes(RDS, NEC, ROP and IVH) as compared to a complete course though a complete course significantly decreases mortality rate in the gestational age group below 30 weeks as compared to an incomplete course.

	< 30 Weeks & complete course of Steroids<	< 30 Weeks & incomplete course of Steroids	> 30 Weeks & complete course of Steroids	>30 Weeks & incomplete course of Steroids
Mortality	9%	26%	0%	0%
RSD	81%	82%	43%	35%
CLD	42%	53%	0%	8%
IVH	16%	2%	0%	5%
ROP	60%	63%	11%	0%
NEC	13%	18%	35	4%

CONCLUSIONS: There is no significant difference on morbidity in group that received incomplete versus complete course of antenatal steroid although mortality was lower with complete course. Further studies will be helpful.

129

Breastfeeding in 30-35wk Infants From Birth to 3 Months After NICU Discharge

Mary T. Blackwell, Marie C. McCormick, John Zupancic, Gabriel Escobar, Douglas K. Richardson, Department of Maternal and Child Health, Harvard School of Public Health, Boston, MA; Department of Neonatology, Beth Israel Deaconess Medical Center, Boston, MA; Harvard Newborn Medicine Program, Children's Hospital and Harvard Medical School, Boston, MA; Division of Research, Perinatal Research Unit, Kaiser Permanente Medical Care Program, Oakland, CA.

BACKGROUND: Most literature on breastfeeding in NICU patients reports on specific interventions to support breastfeeding thru and after discharge. Less is known of the care, course and outcome of unselected NICU cohorts especially the large but less visible moderately premature population.

OBJECTIVE: To describe the course and outcome of 30-35wk GA breastfed infants from birth thru 3 months after NICU discharge(D/C).

DESIGN/METHODS: Demographic and NICU care and outcome data were obtained by medical record review for a prospectively identified cohort of 850 infants,30-35 wks GA, born 9/01 thru1/03 in 10 NICUs, 5 each in California and Massachusetts, 60-100/NICU. Post-D/C data was collected by standardized phone interview. Breastfed(bf) and formula fed infants were compared using Student's t-test. NICU comparisons were controlled for BW, GA, weight for GA and illness acuity (SNAP2 score); maternal age, parity, language and education level.

RESULTS: While in NICU, 76% of subjects were bf with 74% still *bf at D/C,* inter-NICU range=57-93%. By *3 months (mos) after D/C*, 231/676 (34%) of mothers interviewed were still breastfeeding (NICU range 12-56%). GA and illness acuity did not differ between formula and bf infants at D/C but those still bf at 3 mos had lower illness acuity at birth, p<0.01. Infants bf at D/C had slower *NICU weight gain* (-2.1 g/k/d,p<0.001) but those still bf 3 mos later did not. *Head circumference growth* was enhanced in infants bf in NICU, p=0.009. Energy intake was 7-15kcal/kg lower in bf infants on each day assessed,p<0.001, despite *feeding at breast less than 2x/day* on average. Parenteral nutrition conferred a growth advantage of >7 g/k/d, p<0.001, but was not used more often in bf infants or associated with continued breastfeeding. Breastfeeding was *not* associated with longer hospital stay in this population. *Post-discharge weight gain* was not affected by breastfeeding. Infants still bf 3 mos after D/C *fed at breast* 2.3-3.4x more often on days 0,3,7,14,21,28 and at 35 wks GA than those who did not continue to breast feed.

CONCLUSIONS: NICU weight gain was slower in breastfed infants but weight gain at 3 months did not differ from formula fed infants. Maintaining breastfeeding after NICU discharge remains problematic but increased opportunities in NICU to feed directly at breast appear to enhance breastfeeding persistence.

130

Alveolar Type 1 Cell Marker Expression in an In Vitro Model of Human Alveolar Type 1 Cell Transdifferentiation

Cherie D. Foster, Linda Varghese, Susan H. Guttentag, Dept. of Pediatrics, Division of Neonatology, Univ. of Penn. School of Med, Children's Hospital of Phila., Philadelphia, PA.

BACKGROUND: Alveolar type 1 (T1) cells cover 90% of the lung surface and are exquisitely sensitive to damage from toxins, inflammatory mediators and excessive stretch, as in ventilator induced lung injury. T1 are characterized by the expression of markers such as Aquaporin 5 (Aqp5) and Caveolin 1(Cav1), and recently, Plasminogen activator inhibitor 1 (PAI1). There is a paucity of information on the expression of these markers in human T1 cells due in part to a lack of in vitro cell culture models.

OBJECTIVE: To describe a novel model of human T1 transdifferentiation and characterize the expression of known T1 markers.

DESIGN/METHODS: Human alveolar type 2 cells (T2) were prepared from human fetal lung explants that had been induced for 3 days in 10 nM dexamethasone, 0.1 mM each of 8-Br-cAMP and IBMX (DCI). T2 were cultured for an additional 72 h in DCI to insure stable phenotype post-isolation. Transdifferentiation was then induced over a 4 day period by removing DCI from the culture media. We recently reported rapid down-regulation of RNA for the T2 markers SP-B and PGC (Foster, C et al, Am J Resp Cell Molec Biol, 2003) using this method. Cells were sampled before hormone withdrawal and on each of the subsequent 4 days in culture. RNA was prepared and analyzed by real time RT-PCR and proteins were analyzed by immunoblotting, and compared to cultured T2. Results are expressed as group mean for all time points±SE for 2 experiments and analyzed by paired t-test.

RESULTS: Aqp5 mRNA increased 4.03±0.32 –fold after withdrawal of hormones, although there was no discernable change in Aqp5 protein. Both RNA and protein increased after withdrawal of hormones for Cav1 (2.03±0.49 –fold) and PAI1 (3.50±0.87 –fold). Although all RNAs were induced within 24 h, there were no significant differences over time on subsequent days. These data are consistent with our report of increased P2X4, another T1 marker, expression in this model.

CONCLUSIONS: Our model of transdifferentiation of human T1 cells from T2 cells, via withdrawal of hormones known to be critical in maintaining human T2 phenotype in vitro, replicates results from similar animal models, making it possible to now study effects of interventions, such as stretch, on human T1 cells in culture. In addition to the reproducible down-regulation of T2 cell markers, markers of T1 cells are reliably induced during transdifferentiation in vitro.

Funded by NIH HL56401,HL59959,HD043245.

131

House Officer

Comparison of Two Methods of Screening for Iron-Deficiency Anemia in Inner City Children

Reva Snow, Philip O. Ozuah, The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Iron deficiency anemia (IDA) is a common cause of anemia in inner city children. Screening for IDA may be accomplished via a complete blood count (CBC) or HemoCue ™ hemoglobin (Hgb) determination. While the CBC provides additional information, there is a 98% concordance in hemoglobin measurements obtained by the two methods. No prior studies have compared the utility of both approaches to screening for IDA.

OBJECTIVE: To test the hypothesis that utilizing the CBC to screen for IDA would result in less follow-up testing and fewer unnecessary iron treatments.

DESIGN/METHODS: Retrospective chart review involving a consecutive sample of healthy children presenting to an inner city clinic at their 1-yr routine visit or their initial visit if after 1 year of age. At this clinic, such children are routinely screened for anemia with a CBC. We abstracted data on diagnosis, treatment and follow-up of anemia. Based on data obtained form the CBC screening, we modeled a hypothetical scenario for outcomes of screening with Hgb alone. We calculated the number of patients who: 1)would have been identified with IDA; 2) would have received appropriate versus inappropriate iron therapy; and 3) would have required further testing if anemia in these children were diagnosed instead with the HemoCue Hgb analysis. We assumed that all such children would have received a trial of iron therapy, as recommended by the Centers for Disease Control..

RESULTS: 198 subjects were studied, of whom 42% were African-American and 56% Latino and the mean age was 4.4 years. 28 (14%) cases of anemia were identified (mean Hgb=10.6). 24/28 (86%) cases of anemia were IDA and 23 were treated with iron. 7 subjects did not respond to iron therapy and 4 underwent further testing. One subject was diagnosed with beta-thalassemia minor. Based on our model, we calculated that had all patients had been tested with only a fingerstick Hgb, 25 would have been treated with iron, none would have underwent further testing, and only one patient would have been incorrectly treated with iron. The same number of patients in both groups would have required further evaluation predicated on poor response to iron treatment.

CONCLUSIONS: Contrary to our hypothesis, screening for IDA with the CBC resulted in more laboratory testing and did not reduce the number of patients who recieved an unnecessary course of iron. Our results suggest that screening with Hgb would be more efficient.

132

Use of a Neonatologists Time After Regular Working Hours at Two NYS Level One Community Hospitals

Catherine Ekwa-Ekoko, Praveen Ballabh, Lakshmi Modipalli, Edmund F. LaGamma, Pediatrics, Division of Newborn Medicine, Westchester Medical Center - NY Medical College, Valhalla, NY.

BACKGROUND: Two level I hospitals (2000 births/yr) affiliated with a Regional Perinatal Center (RPC) with 24 h out-of-house on-call neonatology coverage. Neonatologists called to attend all C/S & high-risk deliveries & to evaluate newborns (NB) with abnormal physical exams.

OBJECTIVE: To assess the use of neonatology time between 5:00 pm & 7:00 am at 2 NYS Level I community hospitals & its relation to NB outcomes.

DESIGN/METHODS: A call-log was completed from Aug '01 to May '03 tabulating: hospital, date, time & reason for call, time of birth, DR resuscitation, Apgar scores, gestational age, birth weight, NB diagnosis, interventions, time spent on the call, transfer to the RPC.

RESULTS: During the period of review there were 3303 births. Neonatology attended 616 births/NB (18.6% births). 35% calls occurred between 7:00 am & 5:00 pm, 65% between 5:00 pm & 7:00 am & 23% after midnight. 23% calls were made during the weekend. Reasons for calls included: C/S for failure to progress (FTP): 21%, C/S for non-reassuring fetal tracing:12%, preterm deliveries <36 weeks: 7%. Apgars <5 at one min. & <7 at 5 min. were noted in 4% & 2% consulted NB respectively. Most babies were term, with 11% <37 wks & 0.6% <30 wks. Diagnoses included: preterm (7%), rule out sepsis (7.5%), transient tachypnea of the NB (3.5%), depressed at birth (2%). The 13 term babies diagnosed depressed at birth (0.4% total births) were born vaginally & were attended by the neonatologist only after their births in 8 of the 13 cases. Neonatology management post-birth was necessary in 16% calls (3% births). 8% NB requiring neonatology management were transferred to the RPC. Calls to the neonatologist were largely for attendance at C/S for FTP, which were not associated with negative NB outcomes. In contrast, a small percentage (0.4%) of NB were born depressed at birth & this depressed status was not predicted in 0.25% babies.

CONCLUSIONS: We conclude that C/S for FTP are low-risk deliveries & that attendance by a neonatologist does not affect NB outcomes, therefore attendance of low-risk C/S by a DR nurse trained in neonatal resuscitation can occur without increasing the risk to the baby. This approach may simultaneously increase the cost-effectiveness of Neonatology services while better matching the use of highly specialized services to highly complicated problems, in a further effort to maintain value by minimizing costs without compromising quality.

133

Fellow

Can We Improve Neonatal Outcomes of Extremely Low Birth Weight Infants Born at Community Hospitals?

Nadine M. El-Khoury, Muhammad Zia, Sergio G. Golombek, Pediatrics - New York Medical College - Division of Newborn Medicine, Westchester Medical Center, Valhalla, NY.

BACKGROUND: In 1994 the NIH published their consensus report on the use of antenatal steroids for fetal maturation in preterm infants, concluding that a substantial decrease in neonatal morbidity & mortality, as well as substantial savings in health care costs could be achieved.Since that time, community Level II & III programs as well as neonatologists have proliferated; but the mother remains the best transport incubator.

OBJECTIVE: To determine if there is a significant difference in the outcome of ELBW neonates when comparing *inborn* deliveries (at an RPC) vs. *outborn* deliveries (community hospital), attended by a neonatologist, with regards to obstetrical use of antenatal steroids.

DESIGN/METHODS: A retrospective chart review of infants ≤ 1000g, born between June '98 & Dec '02, at Westchester Medical Center or at a community hospital in our network, was done.Groups were compared for demographic characteristics as well as for the total # of ventilator and O_2 days,CLD,NEC,ROP stage ≥ 3,sepsis,PVL,IVH grade ≥ 3,and mortality.

RESULTS: A total of 409 births were admitted to our NICU during this period (309 inborn/100 outborn).We evaluated 232 patient charts to date, excluding patients transferred after 7 days postnatal age (n=28) and patients who expired ≤7d of life (n=80). While there were no statistically significant differences between the two groups for mortality (97/309=31% vs. 29/100=29%), use of antenatal steroids and number of ventilator days did differ,as well as incidence of severe IVH. Outcome data are shown in the table as mean ± SEM

	Inborn (n=182)	Outborn (n=50)
BW (g)	773 ± 9.9	789 ± 21
Gest. age (wks)	26± 0.1	26 ± 0.2
Antenatal steroids§	92%	40%
Ventilator days§	17 ± 1.8	23 ± 3.5
O2 days	49 ± 3	55 ± 5.2
Chronic lung disease	21%	34%
IVH grade≥ 3§	8%	26%

§ p<0.05

CONCLUSIONS: We found no statistical differences in short-term outcomes or mortality rates, except for ↓ use of antenatal steroids and an apparent & attendant ↑in days on mechanical ventilation and in the incidence of severe IVH in the outborn group.Differences in steroid use may be attributed to: awareness of the obstetrician, availability of drug or timeliness of the birth. Further analyses of obstetrical circumstances should help explain these findings.We also plan to evaluate the effectiveness of a single dose of antenatal steroids.Finally, as a regional perinatal center, we will develop an educational program promoting the use of antenatal steroid therapy.

134

Barriers To Implementation of ADHD Guidelines in Inner City Primary Care Settings

Candace J. Erickson, Paola Carugno, David A. Perlstein, David H. Rubin, Pediatrics, St.Barnabas Hospital, Bronx, NY; Pediatrics, Columbia University College of Physicians and Surgeons, New York, NY; Pediatrics, Weill Medical College of Cornell University, New York, NY.

BACKGROUND: AAP Guidelines for evaluation/management of ADHD by primary care providers can be difficult to implement in inner city clinics. Managing ADHD requires ongoing communication between

family, teacher and doctor. Difficulties can arise from social, emotional and financial problems, language barriers, overwhelmed teachers, and physician time constraints.
OBJECTIVE: To assess inner city providers' use of the AAP ADHD guidelines and perceived barriers to implementing them.
DESIGN/METHODS: A questionnaire to ascertain providers' approach, attitudes, and perceived impediments to managing ADHD was distributed to all primary care providers at 10 inner city pediatric clinics.
RESULTS: 87% of 52 providers completed the survey. 87% were US graduates. Mean time since completing residency was 8.4 yrs. Respondents estimated that 15% of 6-12 year olds seen presented with symptoms of ADHD. 67% providers screened with questionnaires. 2% evaluated/treated ADHD. 40% referred to subspecialists.On 0-3 scale ("not at all" to "very much"), respondents rated the adequacy of their training re ADHD at 1.18, comfort with managing it at 1.05, belief that they should manage it at 1.34, and desire to manage it at 1.27. A subsample of 58% respondents were queried re their knowledge of the AAP guidelines. 73% knew they existed. 48% had read one. Those who had read one felt better trained (1.62) than those who had not (.79, p<.01). Years out of residency was not associated with attitudes re managing ADHD. On the same 0-3 scale, respondents rated 10 potential impediments to managing ADHD in their clincs. Time constraints, problems getting information from teachers, inability to diagnose comorbidities, and lack of experience with ADHD had means of 2.40, 1.96, 1.80 and 1.76 respectively. 5 of 6 remaining impediments were each endorsed by >55% respondents, but had means <1.50.
CONCLUSIONS: These providers do not evaluate/treat ADHD. Half have not read the guidelines. Self reported adequacy of training in, comfort with, belief that they should, and desire to manage ADHD were low. Reading the guidelines was associated with higher self-reported adequacy of training. Impediments to implementing the guidelines in this setting were identified and can provide the basis for interventions to improve primary care providers' ability to manage ADHD. Since in the inner city, the prevalence of ADHD is high and subspecialist are few, this is important.

135

Fellow

Perinatal Outcomes of Singletons Versus Twin Premature Newborns <1000g at Birth

Muhammad T. Zia, Ravi Mishra, Edmund F. LaGamma. Pediatrics, Divison of Neonatology, NY Medical College-Westchester Medical Center, Valhalla, NY.
BACKGROUND: Since 1980 the twin birth rate has risen 55% (CDC, 2002) and twining now accounts for a disproportional amount of preterm births. At term, twins have a higher mortality than singletons; however, the opposite is true between 30-to-37 weeks gestation, mortality is higher for singletons than for gestational age matched premature twin infants (Cheung et el, Am J Epidemiol 152:1107-16J 2000). Because of this, we hypothesized that improved management of perinatal and neonatal risk and disease factors (including use of surfactant, steroids and advances in ventilation) may also show advantages related to plurality in ELBW neonates.
OBJECTIVE: To compare the pre-discharge perinatal morbidity and mortality in ELBW premature newborns with respect to singleton versus twin gestation.
DESIGN/METHODS: This is an ongoing retrospective study of infants born between June 98 and December 02 with birth weight <1000g who were admitted to our NICU. Twins were compared to singletons with regard to demographics, antenatal factors and postnatal complications. A comparison of long-term neurological outcome is in progress.
RESULTS: 188 singletons have been compared to 27 sets of twins (n=54). Maternal complications including preeclampsia, and maternal fever were less for twins than singletons. Other comparisons are shown in the tables. Interestingly, no NEC was documented in 54 twins analyzed.The twins showed similar or better outcome than gestational age matched singletons in the weight group 500-1000 grams. Significant differences also exist for inborn vs transferred patients (see El-khoury, Peds Res, this meeting).
CONCLUSIONS: As with other more mature preterm twins, ELBW twins do not have more complications than gestational age matched singletons. This may result from perinatal management being provided under more controlled antepartum and intrapartum conditions due to the greater "anticipation" of risk.

Demographics of ELBW Singletons vs Twins

	n	Wt: Grams (Mean ± SEM)	Age: Weeks (Mean ± SEM)	Male n (%)	ROM>18hours n (%)	Antenatal Steroid n (%)	C/ Section n (%)
Singleton	188	758 ± 10	25.9 ± 0.1	94 (50%)	36 (19%)	148 (79%)	118 (63%)
Twins	54	783 ± 17	26.0 ± 0.2	20 (37%)	12 (22%)	42 (78%)	34 (63%)

Postnatal Complications in ELBW Singletons vs Twins

	Length of Stay, Days (Mean ± SEM)	NEC Stage 3 n (%)	Sepsis n (%)	BPD n (%)	ROP n (%)	3-4IVH Grade n (%)	Mortality n (%)
Singleton	74 ± 3	15 (8%)	59 (31%)	44 (23%)	3 (2%)	26 (14%)	35 (19%)
Twins	66 ± 5	0 (0%)	16 (30%)	15 (27%)	2 (4%)	6 (11%)	8 (15%)

136

Fellow

Longitudinal Changes of B-Type Natriuretic Peptide (BNP) in Preterm Neonates

Ralph L. da Graca, Denise C. Hassinger, Patrick A. Flynn, Mirjana Nesin, Peter A. M. Auld. Pediatrics, Weill Medical College of Cornell University, New York, NY.
BACKGROUND: BNP regulates physiologic vascular changes in response to fluid overload. BNP concentrations correlate with the severity of heart failure in adults. Bedside Triage BNP is a FDA approved device for the assessment of the severity of heart failure and left ventricular dysfunction in adults. The usefulness and normal values of BNP concentrations determined by Triage BNP has not been established in preterm neonates.
OBJECTIVE: To determine age-related concencentrations of BNP in preterm infants using bedside Triage BNP from birth to 2 months of age and correlate it to the presence or abscence of the patent ductus arteriosus (PDA).
DESIGN/METHODS: Serial serum BNP concentrations were measured in infants ≤ 32 weeks gestation during the first 2 months of life using bedside Triage BNP. Echocardiograms were performed every 4 days until closure of the PDA was documented by 2 consecutive echocardiograms. BNP concencentrations were correlated to the day of life, gestational age, and presence or absence of the PDA.
RESULTS: Seventeen preterm infants (GA 24-32 wks, BW 715-1670 g) were prospectively enrolled between 0-14 days of life. Serum BNP concentrations were determined on 159 samples and 79 echocardiograms were performed from enrollment until documented closure of the PDA. Median values were shown in Table.
Significant negative correlation was found between serum BNP concentrations and day of life (r =-0.43, p<0.0001) and remained significant when the subjects were stratified by gestational age: r=-0.44, p= 0.0017 for GA >28 wks and r=-0.434, p= 0.001 for GA ≤ 28 wks. Significantly lower BNP concentrations were found when the PDA was closed (median range: 6-134pg/ml), than when it was open (median range: 88-1280 pg/ml) p < 0.0001.
CONCLUSIONS: Similar to term infants BNP concentrations are age-related and decline during the first month of age. Low BNP values < 250 pg/ml in the first few days of life suggest a closed PDA. Triage BNP at the bedside might be a clinically useful tool for a neonatologist to assess physiologic cardiovascular changes in the premature infant.

Age-related changes of median serum BNP concentrations (pg/ml)

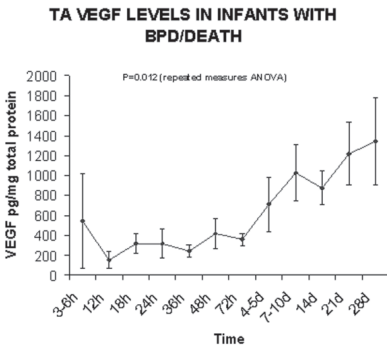
DOL	0-1	2-3	4-5	6-7	8-10	11-14	15-30
GA ≤ 28 wks	543.5	649.5	100	61	83	131	38
GA > 28 wks	209	91.5	1280	51.5	116	156	45
ALL pts	467	247.5	159	59.5	116	136	41
PDA OPEN	361.5	1145.5	1280	88	216	226.5	184
PDA CLOSED		134	23.5	22.5	22	42.5	39

137

Fellow

Interleukin (IL)-6 to Vascular Endothelial Growth Factor (VEGF) Ratio Predicts the Development of Brochopulmonary Dysplasia (BPD)/Death in Premature Infants

Jonathan H. Nedrelow, Vineet Bhandari. Pediatrics, Yale University, New Haven, CT; Pediatrics, Yale University, New Haven, CT.
BACKGROUND: Risk factors for bronchopulmonary dysplasia (BPD) include prematurity, respiratory distress syndorme (RDS) , and the host inflammatory response to various stimuli (hyperoxia, volutrauma, sepsis). Cytokine levels in the lung are an important measure of the inflammatory response.
OBJECTIVE: We hypothesized that an imbalance of cytokine release exists in the developing lung at risk for BPD/death.
DESIGN/METHODS: We collected tracheal aspirate (TA) samples (87) from 17 intubated and mechanically ventilated premature infants with RDS at 3-6, 12, 18, 24, 36, 48, 72 hours of life, and 4-5, 7-10, 14, 21, and 28 days of life. Demographic data were collected. Cytokines analyzed included IL-6 and VEGF using ELISA (R& D Systems). Statistical analyses included student's t-test and repeated measures ANOVA. Total protein content for each sample was measured by micro BCA (Invitrogen) and cytokine levels are expressed as pg/mg of total protein.



RESULTS: Clinical data is shown in the table. At 3-6 hours of life, IL-6/VEGF ratio was significantly lower in patients who went on to develop BPD or died (p=0.05). In addition, infants who developed BPD or died had a significant rise in the TA VEGF levels over 28 days (p=0.012).
CONCLUSIONS: Early, pronounced VEGF release (low IL-6/VEGF ratio) in neonates with RDS may be associated with the development of BPD/death.

Patient Demographics and Results

Patients n=17	No BPD n=6	BPD/death n=11	p value
Birth Weight, grams (mean)	866 (SD +/- 97)	838 (SD +/- 146)	p=0.12
Gestational Age, weeks (mean)	26.5 (SD +/- 2)	25.5 (SD +/- 1.4)	p=0.28
Oxygenation Index pre surfactant (mean)	2.8 (SD +/- 1.4)	4.7 (SD +/- 1.5)	p=0.01*
Length of Endotracheal intubation, days (mean)	14 (SD +/- 13)	43 (SD +/- 22)	p=0.01*
IL-6/VEGF ratio (pg/pg)	42 (SD +/- 28)	15 (SD +/- 14)	p=0.05*

A portion of the this work was funded by Dey Inc.

138

Fellow

Asialotransferrin as a Biochemical Marker for Subarachnoid-Pleural Fistula Diagnosis

Isaac Lazar, Carlos Knopf, Michael Halberthal, Gad Bar-Joseph. Pediatrics - Critical care, Rambam Medical Center and the Faculty of Medicine, Technion, Haifa, Israel; Clinical Chemistry - Section on Metabolic Diseases, Rambam Medical Center and the Faculty of Medicine, Technion, Haifa, Israel; Pediatrics - Critical Care, Yale University, New Haven, CT. (Sponsored by Clifford W. Bogue)
BACKGROUND: Subarachnoid Pleural Fistula (SPF) should be considered in patients with post traumatic pleural effusion and neurological deficit. When a fistula is formed between the spinal subarachnoid space and the pleural cavity, cerebrospinal fluid (CSF) tends to leak and accumulate, causing massive pleural effusion. Diagnosis of SPF is based on myelographic techniques that can potentially complicate the patient's condition. A biochemical diagnosis of the already drained pleural effusion, proving it to be CSF, would save the patient an unnecessary myelography. Asialotransferrin is a specific and sensitive marker for CSF, which is also present in serum of patients with Congenital Disorder of Glycosylationas (CDG) - a rare metabolic disease. We hypothesized that asialotransferrin could be used to diagnose SPF and exclude other etiologies of post traumatic pleural effusion.
OBJECTIVE: To show the presence of asialotransferrin in the pleural effusion of a 4 year old girl with post traumatic pleural effusion, thus confirming the clinical suspicion of SPF.
DESIGN/METHODS: We used Isoelectric Focusing of transferrin isoforms to study asialotransferrin presence in our patient's pleural effusion, and in samples from various patients' body fluids that might be accumulating in the pleural cavity after trauma. The fluid samples included: 1. A positive control - Serum from a patient diagnosed with CDG. 2. Our patient's pleural effusion suspected to be CSF. 3. A positive control - Normal CSF. 4. Pleural effusion (From a patient with graft versus host disease). 5. Peritoneal fluid (from a patient with severe viral disease and massive ascites). 6. A Negative control - Normal serum. 7. Pericardial fluid (from a patient with massive post pericardiotomy syndrome, following cardiac surgery).
RESULTS: The band that represents asialoreansferrin is present in our positive controls, normal CSF and the CSF suspected pleural effusion. It is absent in the peritoneal, pericardial, pleural and normal serum samples.
CONCLUSIONS: By detecting asialotransferrin in the pleural fluid from our patient, while showing its absence in other fluids that can accumulate in the pleural cavity after blunt chest trauma, we confirmed our hypothesis. Isoelectric focusing to detect asialotransferrin is a sensitive and non-invasive technique to detect CSF that can be used to diagnose SPF.

139

Pediatrician Knowledge of School Asthma Policies

Marian Larkin, Iman Sharif, Philip O. Ozuah. The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Children with asthma spend a significant amount of time in school and sometimes have symptoms there. However, several studies have suggested that schools may not always be able to meet the needs of children having acute asthma symptoms. The aim of this study was to assess what physicians know about New York City Board of Education policies regarding asthma medications in public schools.
OBJECTIVE: To test the hypothesis that pediatricians are not aware of policies regarding medication use in schools.

DESIGN/METHODS: We conducted a cross-sectional survey of pediatricians at a major academic medical center. Particpants were surveyed regarding knowledge of school policies regarding asthma management. Dieffernces in proportions were tested by Chi-square.This study was approved by Montefiore's Institutional Review Board.
RESULTS: Of 117 total respondents, 54 (46%) were pediatric attendings and 63 (54%) were residents or fellows. Nearly 85% reported that they "often" take care of children with asthma. Only 15.6% of respondents reported that they were "very familiar" with the NYC Board of Education's policy concerning use of asthma medications in school. Only 60.7% knew that students can carry and use a pump only if a physician completes a school medicationform, and a mere 14.5% knew that the physician can attach an "Asthma Action Plan" to the form. Attendings were significantly more likely to know that a medication form must be completed for a student to carry a pump (72% vs. 51% of housestaff, p=0.018). Overall, nearly 25% of respondents mistakenly believed that students are never allowed to carry their own asthma pumps in school, while 15.4% believed that a doctor's note is sufficient to allow a child to carry a pump in school. More than 86% reported having written such a note, but only 6.1% were "very confident" that their patients can access asthma medications while in school. While nearly 79% reported that they advise their teenage patients with asthma to carry a pump with them at all times in school, 21% reported telling these patients to keep their pump in the nurse's office. And when asked who is responsible for supervising the health of a child with asthma in the NYC public schools, more than 22% responded that they did not know.
CONCLUSIONS: Pediatricians in this study displayed a general lack of knowledge of school asthma policies.

140 Withdrawn

Cardiology II
Platform Session

Sunday, March 28 9:45am–12:00pm Mead C

141 Presentation Time 9:45 AM — Fellow

Strategy for Molecular Genetic Stratification of Familial Hypertrophic Cardiomyopathy

Sheila J. Carroll, Emerson Whittington, Daphne T. Hsu, Wendy K. Chung, Pediatric Cardiology, Columbia Presbyterian Medical Center, New York, NY; Pediatrics, Columbia Presbyterian Medical Center, New York, NY; Pediatrics-Molecular Genetics, Columbia Presbyterian Medical Center, New York, NY. (Sponsored by Bruce Gelb)

BACKGROUND: Familial hypertrophic cardiomyopathy (HCM) is a genetically heterogeneous disease with mutations in at least 12 large genes compromising the cardiac sarcomeres. The clinical course and prognosis vary according to the gene and specific mutation involved; identification of which would be useful in patient management and predicting other pre-symptomatic, susceptible individuals within families.
OBJECTIVE: Currently, no clinical genetic screening test is available for HCM. We have developed and applied an efficient, cost effective method of identifying mutations for HCM in families segregating the disease.
DESIGN/METHODS: Seventeen members of a single family with a strong family history of sudden death and HCM were analyzed by linkage analysis using a panel of polymorphic microsatellite markers selected because they flank three of the genes most commonly associated with HCM and sudden cardiac death. Coding exons of the linked gene were then amplified by the polymerase chain reaction and sequenced in a single unambiguously affected family member. Once the pathogenic mutation was identified, all family members were genotyped for the mutation.
RESULTS: We demonstrated linkage within the family to cardiac Troponin T (TNNT). Subsequent direct sequence analysis identified an Arg92Gln mutation that co-segregates with the clinical phenotype. This mutation is associated with aggressive disease within this family with six of 13 members dying from cardiac disease at a mean age of 35 and as young as 17. Of the seven carriers in the family, four demonstrated cardiac hypertrophy before the age of 30; the remaining three (ages 41-55) have experienced cardiac events in addition to having cardiac hypertrophy. We also definitively identified 10 genotype negative family members who are not at risk for familial HCM.
CONCLUSIONS: We describe a method for efficiently determining the genetic basis of HCM in families to allow identification of pre-symptomatic individuals and to provide prognostic information in order to develop individualized methods of surveillance and management. We demonstrate the utility in a family with a high incidence of sudden cardiac death.

142 Presentation Time 10:00 AM — Fellow

Doc-2, a Tumor Suppresor Protein Represses MAP Kinase Activation and Collagen Gene Expression in Cardiac Fibroblasts; Implications in Heart Failure

Mohamad K. Al-Ahdab, Deepa Chandrashekar, Rene A. Arcilla, Mahesh P. Gupta, Madhu Gupta, Pediatric Cardiology, The Heart Institute for Children, Hope Childrens Hospital, Oak Lawn, IL; Department of Cardiothoracic Surgery, The University of Chicago, Chicago, IL.

BACKGROUND: Cardiac remodeling in chronic heart failure is associated with increased collagen synthesis by fibroblasts where Ras signaling has been proposed to play a role. Previously, we have identified differential expression of DOC-2 in cardiac hypertrophy. DOC-2 is reported to inhibit Ras-signaling in other cells, however, its role in cardiac pathophysiology has never been explored.
OBJECTIVE: To test if inhibition of Ras signaling by DOC-2 will alter MAP kinase activation and collagen gene expression in cardiac fibroblasts and to understand cardiac remodeling induced by angiotensin II (A II) and phorbol esters (TPA).
DESIGN/METHODS: Primary cultures of neonatal rat cardiac fibroblasts were obtained by differential plating, grown in DMEM with 5% FBS for 48 hrs. Cells were infected with adenovirus backbone (Ad) or Ad-DOC-2 expression vector at a MOI of 20 for 72 hrs. After serum starvation for 24 hr, cells were treated with A II (1 uM) or TPA (0.1uM) for 2,5,10, and 20 min (Group1), for 15hr (Group2), or with MEK1/2 inhibitor PD98059 (10uM) for 8 hrs followed by A II treatment for 15 hr (Group3). Protein lysates were prepared and analyzed for phospho-ERK(Extracellular Signal- Regulated Kinase), total ERK and Type I collagen expression by Western analysis using specific antibodies. Total RNA was isolated from Group2 and analyzed by Northerns using Type I collagen and GAPDH cDNA probes.
RESULTS: GroupI: Treatment with TPA or A II resulted in increase in phospho-ERK (at 2 min) with maximal effect at 5 min (for A II) and 10 min (for TPA) returning to basal levels in 20 min. Ad-Doc-2 infection inhibited A II and TPA induced phospho-ERK activation without affecting total ERK. Ad-control had no effect on phospho-ERK. Group2: A II and TPA treatment for 15 hr increased typeI collagen expression by 66% and 20% respectively; Ad-Doc-2 infection inhibited collagen expression (both induced as well as basal) to almost undetectable levels, ad-control had no effect. Similar results were obtained by Northern analysis. Group3: PD98059 inhibited stimulatory effect of A II on collagen expression. PD98059 alone had no effect .
CONCLUSIONS: Inhibition of phospho-ERK represses collagen synthesis. DOC-2 inhibits growth factor-induced activation of phospho-ERK and represses collagen expression. DOC-2 may potentially modulate cardiac fibrosis during heart failure.

143 Presentation Time 10:15 AM — Fellow

Non-Invasive Localization of Mouse Embryos by Ultrasound Biomicroscopy (UBM)-Doppler Allows Genotype-Phenotype Correlation

Rui Ping Ji, Colin K. L. Phoon, Skirball Institute of Biomolecular Medicine; Pediatric Cardiology, NYU School of Medicine, New York, NY.

BACKGROUND: High-frequency UBM-Doppler allows study of cardiovascular physiology in the *in utero* mouse embryo from embryonic day (E) 8.25 onward (Phoon et al. *Physiol Genomics* 2003;14:3). However, in targeted genetic models, genotype-phenotype correlation has only been achieved using a "semi-invasive" imaging technique, whereby individual uterine sacs are exteriorized and identified while embryos remain *in utero* (Phoon et al. *Circulation* 2002; 106:II286).
OBJECTIVE: To localize mouse embryos via transabdominal, completely non-invasive imaging, using a new handheld 30 MHz transducer and techniques adapted from fetal echocardiography.
DESIGN/METHODS: Lacking aortic and pulmonary valves, *NFATc1* -/- embryos display a distinctive physiological phenotype of reversed diastolic aortic flow after the stages of anticipated valve development (> E12.5) and die *in utero*; *NFATc1* +/+ and +/- embryos show a normal phenotype. Timed-pregnant mice from heterozygote crosses (staged E12.5-14.5, 17.5) were anesthetized with IP pentobarbital. The bladder was used as a starting reference point, and each side of the abdomen was imaged in a craniolateral direction to follow the uterine horns. Dorsal aortic and intracardiac Doppler flows, and 4-chamber heart UBM views were attempted for each embryo. A UBM-derived map of the *in situ* intraabdominal litter was sketched and subsequently compared with a definitive map obtained after wide laparotomy. Genotyping was accomplished using standard PCR.
RESULTS: Of 10 mice imaged, 3 were correctly identified by UBM as non-pregnant. In the remaining 7 pregnant mice, all 28 living embryos were imaged and accurately localized. Litters of up to 7 non-resorbed embryos could be identified and localized. At E13.5, E14.5, and E17.5, all 4 embryos with reversed aortic flow and all 3 dead (but not yet resorbed) embryos imaged were *NFATc1* -/-. We were able to obtain aortic and intracardiac Doppler flow, and UBM cardiac images in all living embryos, although embryonic lie in especially E17.5 fetuses did not consistently allow a 4-chamber view of the heart. UBM was unable to identify all resorbing or resorbed embryos.
CONCLUSIONS: Non-invasive localization and multiparameter UBM-Doppler imaging of mouse embryos is highly feasible, providing genotype-phenotype correlation. Not only does this technique allow for more physiological imaging conditions, but non-traumatic serial imaging of a litter then becomes a possibility for the first time.

144 Presentation Time 10:45 AM — Fellow

Tfap2b Plays a Critical Role in the Development and Remodeling of the Mouse Ductus Arteriosus

Feng Zhao, Thomas Lufkin, Reinhard Buettner, Bruce D. Gelb, Pediatrics and Human Genetics, Mount Sinai School of Medicine, New York, NY; Molecular, Cell, and Developmental Biology, Mount Sinai School of Medicine, New York, NY; Institute of Pathology, University of Bonn, Bonn, Germany.

BACKGROUND: Char syndrome is an autosomal dominant disorder characterized by facial dysmorphism, 5th finger anomalies, and patent ductus arteriosus (PDA). We previously showed that this disorder results from dominant negative mutations in *TFAP2B*, which encodes an AP-2 class transcription factor. Others have shown that *Tfap2b* is expressed during murine embryogenesis in migrating neural crest, but expression in the cardiovascular system *per se* has not been examined. Targeted disruption of *Tfap2b* causes renal anomalies with early lethality.
OBJECTIVE: To study the role of Tfap2b in the development and remodeling of mouse ductus arteriosus.
DESIGN/METHODS: Whole mount and tissue section *in situ* hybridization was performed with C57B6 mouse embryos, harvested at different time points, using a 326-bp *Tfap2b* cRNA probe. *Tfap2b*$^{+/-}$ mice were intercrossed and newborn pups were sacrificed at 2 or 6 h *post partum*. Thoraces were fixed, paraffin embedded and sectioned serially. Ductal status was assessed with light microscopy after H&E staining. Genotyping of the pups was performed. Statistical analysis was performed with the Fisher exact test.
RESULTS: Expression of *Tfap2b* started at E8.5 in the neural tube where the neural crest cells originate. The pharyngeal arches were stained at E10.5. At E11.5, *Tfap2b* expression was detected in the fourth and sixth aortic arch arteries bilaterally. At E13.5, strong *Tfap2b* expression was detected in the arch of aorta and the ductus arteriosus. Ducts were generally closed at 2 h in wild type and *Tfap2b*$^{+/-}$ pups (8/8 and 7/8, respectively). In *Tfap2b*$^{-/-}$ pups, ducts were constricted but remained open at 2 h (0/8; $p<0.001$), a finding that persisted at 6 h among animals surviving that long. Additional novel findings included expression of *Tfap2b* in the limb buds starting at E10.5 and persisting in the tips of both fore- and hind limbs until E12.5 as well as polydactyly observed in all *Tfap2b*$^{-/-}$ pups and about 20% of *Tfap2b*$^{+/-}$ animals.

CONCLUSIONS: During murine embryogenesis, *Tfap2b* is expressed in the ductus arteriosus and its presursor, the left 6th aortic arch artery. Loss of Tfap2b impairs ductal closure. These findings suggest that PDA in Char syndrome results from loss of TFAP2B per se, not negative effects on other AP-2 factors, and that its pathogenesis need not involve abnormal neural crest tissue migration.

145 Presentation Time 11:00 AM

Neural Crest Cell Migration and Patterning in a Mouse Model of Persistent Truncus Arteriosus

Kathryn Maschhoff, Theresa Lubas, Paris Ward, Paul Anziano. Neonatology, Children's Hospital of Philadelphia, Philadlephia, PA; Pediatrics, University of Pennsylvania, Philadelphia, PA. (Sponsored by Susan Guttantag)

BACKGROUND: The Sox family of transcription factors plays a critical role in the regulation of embryonic development and in the determination of cell fate. One member of this family, Sox4, is required for normal conotruncal development. Deficiency of Sox4 in mice results in heart defects which are similar to those seen in patients with conotruncal defects. The endocardial cushions form but fail to fuse properly. Because the conotruncal septation defect in Sox4 -/- mice is reminiscent of that seen after neural crest ablation in chick embryos, one hypothesis for the function of Sox4 in conotruncal development is that it is involved in an inductive process between the endocardial ridges and neural crest cells that are migrating into the cushions.

OBJECTIVE: Determine the role of Sox4 in normal patterning of neural crest cells in the outflow tract.

DESIGN/METHODS: To determine the fate of neural crest cells in Sox4 null embryos., we utilized a lineage tracing strategy the Wnt-1 Cre mouse crossed with the R26R LacZ mouse that expresses beta galactosidase in any tissue expressing Cre. This mouse has been previously used to follow neural crest cells and their progeny as they migrate into the branchial arches and endocardial cushions. These mice were crossed with Sox4 KO mice. WT and Sox4 null embryos were harvested, and neural crest cells were visualized by LacZ staining. Apoptotic cells were detected by TUNEL staining.

RESULTS: As previously reported, many of the Sox4 null embryos exhibited persistent truncus arteriosus. Neural crest cell migration into the endocardial cushions of these embryos was initially normal. However, subsequent patterning of these neural crest cells is abnormal. In WT embryos, the neural crest cells become organized into rods of condensed mesenchyme which spiral around one another and ultimately fuse to form the conotruncal septum. After fusion, neural crest cells become restricted the aorticopulmonary septum. In the null embryos by contrast, the neural crest cells remain disorganized and continue to be seen throughout the conotruncus. The failure of normal remodeling of the neural crest cells in the conotruncus appears to be due in part to failure of these cells to undergo apoptosis at the proper time.

CONCLUSIONS: Sox4 is required for normal patterning of neural crest cells in the endocardial cushions of the outflow tract.

146 Presentation Time 11:15 AM

Calcium Regulation During Early Cardiac Development

George A. Porter, Jr., Ryan F. Makuck. Pediatrics, Yale University School of Medicine, New Haven, CT. (Sponsored by Scott A. Rivkees)

BACKGROUND: Although intracellular calcium signals play an essential role in cardiac physiology and modulate cardiac gene expression, the role of intracellular calcium homeostasis in early mammalian cardiac development is not clear.

OBJECTIVE: To determine the mechanisms of calcium regulation in the developing heart and to determine the role of altered calcium homeostasis on cardiac development.

DESIGN/METHODS: To address this issue, we used pharmacologic agents against proteins involved in calcium regulation in calcium imaging experiments and mouse embryo cultures.

RESULTS: First, in E8.5 embryos, blockade of the L-type calcium channel (nifedipine) and the sodium/calcium exchanger (KB-R7943), but not the ryanodine receptor (RyR, ryanodine) and sarco(endo)plasmic reticulum calcium ATPase (thapsigargin), altered intracellular calcium levels. However, at E9.5 the RyR and SERCA became active, indicating that the sarcoplasmic reticulum may be functional. Second, we determined the effects of these agents on cardiac morphogenesis and gene expression in cultured E8.5 embryos. Embryos cultured in the presence of all four reagents developed hearts that had a large left ventricle, lacked a right ventricle and had a long, thin outflow tract. These embryos demonstrated altered mRNA expression of the transcription factor Gata4, which was absent in the developing ventricles, and the sarcomeric protein Mylpc (myosin light chain 2V), which was decreased distal to the left ventricle and was absent at the site of the developing right ventricle. In contrast, the expression pattern of other cardiac transcription factors (Hand1, Hand2, Mef2c, Nkx2-5) and cytoskeletal proteins (Myhca, Tagln) mRNA did not change.

CONCLUSIONS: In conclusion, we have begun to define the mechanisms that regulate intracellular calcium levels in the early mammalian heart and demonstrate that proper intracellular calcium signaling is essential for normal cardiac gene expression and morphogenesis. Supported by grants from the NIH and from Pfizer, Inc.

Emergency Medicine Platform Session

Sunday, March 28 9:45am–11:30am Riverside

147 Presentation Time 9:45 AM Fellow

Serious Bacterial Infections (SBI) in Older Febrile Infants (FI); Incidence and Predictors

Allen L. Hsiao, Lei Chen, M. Douglas Baker. Pediatric Emergency Medicine, Yale University School of Medicine, New Haven, CT.

BACKGROUND: During the past 30 years, researchers have established the etiology and management of fever in young (<2 mo) infants, and in young (6-24 mo) pre-schoolers. However, little has been done to examine the etiology of fever in older (2-6 mo) infants, or to evaluate the usefulness of screening tests in this population.

OBJECTIVE: To determine the incidence of SBI in older (2-6 mo old) FI, and to evaluate potential clinical and laboratory predictors of SBI in these children.

DESIGN/METHODS: 12 month prospective consecutive cohort of 57-180 day old FI (rectal temp > 37.9°C) evaluated in an urban regional pediatric emergency department. A standard history and physical exam were performed on all FI. Clinical appearance was scored using the Yale Observation Score (YOS). From each infant, complete blood count (CBC) with differential, C-reactive protein (CRP), blood cultures (BC), catheterized specimen for urinalysis (UA) and urine culture (UC), and nasal swab for direct fluorescent antibody (DFA) for common viruses were obtained. Additional studies were performed at the discretion of the attending physician. Informed consent was obtained.

RESULTS: During the first 9 months of the study, 247 (94.7%) of 262 eligible FI were enrolled. UC and BC results were available for 242 FI. 34 Specimens (29 UC and 5 BC) from 33 FI were positive. One FI had concurrent UC and BC positive for the same pathogen (*E. coli*). DFAs were successfully obtained from 240 (97.1%) of enrolled FI; 61 (25.4%) were positive. Lumbar punctures from 46 FI revealed no cases of bacterial meningitis. Mean CRP was higher in FI with SBI (2.79 +/- 3.9) than in those without (1.09 +/- 1.76; $p < 0.001$). Mean WBC was higher in FI with SBI (17.0 +/- 8.7) than in those without (12.4 +/- 5.7; $p < 0.001$). 3 FI with UTI and 1 with bacteremia had otherwise negative testing. Of the FI with positive DFAs, 7 (11.5%) had concurrent SBI. Mean YOS did not differ between infants with SBI (9.05 +/- 3.6) and those without (8.15 +/- 3.9; $p < 0.18$).

CONCLUSIONS: Although the incidence of bacteremia (2%) is in-keeping with that of younger infants and older pre-schoolers, the incidence of UTI (11.7%) is higher than expected. Many (11%) 2-6 mo old FI with documented viral illness have concurrent bacterial diseases. While mean CRP and WBC are significantly higher in FI with SBI, neither is a reliable single predictor of either high or low risk for SBI. Clinical appearance does not distinguish infants with SBI.

148 Presentation Time 10:00 AM

Predictors of Pneumonia in Young Febrile Infants

S. Platt, D. Levine, N. Fefferman, P. Dayan, C. Macias, J. Zorc, W. Krief, J. Schor, D. Bank, K. Shaw, N. Kuppermann. Pediatrics and Emergency Medicine, New York Presbyterian Hospital/Weill Cornell Medical Center, New York, NY; The Multicenter RSV-SBI Study Group for the Pediatric Emergency Medicine Collaborative Research Committee of the AAP.

BACKGROUND: The decision to include chest radiographs(CXRs) in the evaluation of febrile infants is controversial, particularly in infants without evidence of respiratory disease.

OBJECTIVE: To identify predictors of pneumonia in young febrile infants.

DESIGN/METHODS: We conducted a multi-center prospective cross-sectional study from October-March,1997-2001, at any of 8 pediatric emergency departments of infants ≤ 60 days with fever ≥38° C. The infants with CXRs performed as part of the fever evaluation were the focus of this analysis. A single pediatric radiologist blinded to clinical information evaluated all CXRs for the presence of pneumonia, defined as a lobar infiltrate. We performed multivariable logistic regression on pre-determined variables to identify predictors of pneumonia. Variables included age, temperature, oxygen saturation, Yale Observation Scale score, upper respiratory tract infection (URI), respiratory rate (RR), retractions, flaring, rales, wheezing, white blood cell count, absolute band count (ABC), absolute neutrophil count and RSV status.

RESULTS: Of 1248 febrile infants evaluated, 482 (38.6%) had CXRs performed. Of these, 29 (6%) had lobar pneumonia. Only rales, RR and ABC were significant in the multivariable analysis.

Multivariable Logistic Regression

Variable	Pneumonia	No Pneumonia	Adjusted OR (95%CI)	*P*
Rales	44.4%(12/27)	11.3%(51/451)	3.1(1.2,8.1)	.02
RR≥60/minute	55.2%(16/29)	18.4%(83/452)	4.2(1.6,10.7)	<.01
ABC≥1.5x10^9/L	46.2%(12/26)	21.6%(90/417)	3.2(1.3,7.9)	.01

The presence of rales was documented in 478 (99%), RR in 481(99%) and ABC in 443 (92%). Of 194 patients with either rales, RR ≥60 or ABC≥1.5x10^9/L, 23 (11.9%, 95%CI: 7.7,17.3) had pneumonia. Of 253 infants with neither rales, RR ≥60 nor ABC≥1.5x10^9/L, 4 (1.6%, 95%CI:0.4,4.0) had pneumonia. The prediction model defined by the presence of any of the 3 variables versus none of the variables had the following accuracy: Sensitivity 85%(95%CI 66,96), Specificity 59%(95%CI 54,64) , PPV 12%(95%CI 8,17), NPV 98%(95%CI 96,100). The likelihood ratios (LR) were: LR positive 2.1, LR negative 0.25. Of the 4 patients with pneumonia not identified by rales, RR ≥60 or ABC≥1.5x10^9/L, none had wheezing, all had URI's and all were RSV negative.

CONCLUSIONS: The presence of rales, RR ≥60 or ABC≥1.5x10^9/L identifies 85% of febrile infants with lobar pneumonia.

Funded by Roche, MedImmune and Sanofi Laboratories

149 Presentation Time 10:30 AM Fellow

Urine Leukocyte Esterase as a Predictor of Urinary Tract Infections in Febrile Infants in the Emergency Department

Lei Chen. Section of Pediatric Emergency Medicine, Yale-New Haven Children's Hospital, New Haven, CT. (Sponsored by Karen Ann Santucci)

BACKGROUND: Previous studies have shown that under ideal laboratory conditions urine gram stain for bacteria has high positive and negative predictive values (PPV and NPV) for urinary tract infections (UTI) in febrile infants. It is unclear how these more operator-dependent tests compare with less technically demanding tests such as urine dipstick for leukocyte esterase (LE) in their respective predictive values for UTI in febrile infants.

OBJECTIVE: To compare the performances of various laboratory parameters in diagnosing urinary tract infections among febrile infants who present to an urban pediatric emergency department.

DESIGN/METHODS: A retrospective chart-review was conducted using the medical records of an urban pediatric emergency department during a nine-month period from 5/2002 to 1/2003. Data was collected from infants between the ages of one and 24 months from whom urine cultures were obtained as part of their fever workup. Results of urine analysis, urine microscopic analysis, urine gram stain, and urine culture were recorded. Specificity, sensitivity, predictive values of various laboratory tests were calculated.

RESULTS: Four hundred and sixty five children had urine culture performed during the study period. All had temperature higher than 38°C within 24 hours of the emergency department visit. Most of the samples (97%) were obtained via urethral catheterization. Sixty-two children were diagnosed to have UTI, defined as growth of a single organism at >10,000 CFU/ml. The overall incidence of UTI was 13%. Among diagnostic tests evaluated, trace or greater urine LE had a PPV of 69% and an NPV of 97%. Moderate or large LE had a PPV of 86%. Urine gram stain had a PPV of 82% and an NPV of 96%. Urine microscopy for pyuria, defined as >10 white blood cell (WBC) per high power field in a spun specimen, had a PPV of 86% and an NPV of 93%.

CONCLUSIONS: Urinary tract infections were common in our study population. Among diagnostic tests urine dipstick for LE appeared to be as reliable as more costly and labor-intensive tests such as urine microscopy and urine gram stain as performed at our institution. It could serve as a good screening test with an NPV of 97% in the population studied. In addition, the strength of the LE signal correlated with the likelihood of a UTI.

150 Presentation Time 10:45 AM Fellow

Utility of Bedside Bladder Ultrasound Prior to Urethral Catheterization in Infants

Lei Chen, Allen L. Hsiao, Christopher L. Moore, Karen A. Santucci. Section of Pediatric Emergency Medicine, Yale-New Haven Children's Hospital, New Haven, CT; Section of Emergency Medicine, Yale-New Haven Hospital, New Haven, CT.

BACKGROUND: Urethral catheterization (UC) is the method of choice in obtaining samples for urine culture and urine analysis in infants. Prior to the procedure, however, there is little certainty of the presence or the amount of urine in the bladder. Consequently this relatively invasive and uncomfortable procedure often needs to be repeated. The newly available technology of portable ultrasound may be useful in reducing the number of unsuccessful procedures.

OBJECTIVE: To investigate the utility of bedside ultrasound of the bladder performed by pediatric emergency medicine physicians prior to UC in order to reduce the number of unsuccessful procedures.

DESIGN/METHODS: A prospective convenience sample study was performed in the setting of an urban

pediatric emergency department. Infants aged 0 to 24 months were enrolled. During the observation phase UC was performed as usual and the amount of urine obtained was recorded. During the intervention period, a rapid bedside ultrasound of the bladder was performed by a pediatric emergency medicine physician immediately prior to UC. If sufficient amount of urine was seen, UC was carried out as usual. Otherwise UC was deferred and ultrasound was performed at 30-minute intervals until sufficient urine was identified. The amount of urine obtained was recorded.
RESULTS: During the observation phase 136 infants underwent UC. Among these the staff failed to obtain any urine on the first attempt in 10% (n=14) of the infants. In another 17% (n=23) of the subjects only sufficient quantity for urine culture was obtained. The overall rate of success, defined as obtaining greater than 2cc of urine, sufficient for culture, urine analysis, microscopy, and gram stain, was 72% (+/-3.9%). During the intervention period 45 infants were enrolled. Sufficient urine was identified on the first ultrasound in 76% (n=34) of the patients. Of the remainder, sufficient urine was identified on ultrasound within 60 minutes of the initial study. UC was successful on the first attempt in all study subjects. Compared with the success rate during the observation phase the difference was statistically significant (p<0.001).
CONCLUSIONS: The success rate of UC in infants was enhanced with the use of a rapid bedside ultrasound performed by pediatric emergency medicine physicians. Repeated attempts could be avoided with the proper use of this simple technique.

151 Presentation Time 11:00 AM — Fellow

Initial Fluid Resuscitation for Patients With Diabetic Ketoacidosis: How Dry Are They?

Michele J. Fagan, Jeffrey R. Avner, Hnin Khine. Pediatric Emergency Medicine, Children's Hospital at Montefiore, Bronx, NY.
BACKGROUND: Immediate and rapid fluid therapy is essential in the management of patients with diabetic ketoacidosis (DKA). Conventional management of these patients is to assume 10% dehydration at the time of initial presentation. However, recent concern regarding overhydration and its potential role in the development of cerebral edema in these patients has led to re-evaluation of this approach.
OBJECTIVE: To determine the actual percent loss of body weight (PLBW) in patients with DKA and to determine whether historical, clinical or laboratory parameters of dehydration are predictors of PLBW in patients with DKA.
DESIGN/METHODS: A prospective descriptive study was conducted in an inner city Pediatric ED. Eligible patients were those who presented with DKA (blood glucose>250 mg/dl, pH<7.3, HCO3<15 mEq/l, and moderate ketonuria or ketonemia). History of illness, clinical parameters, and laboratory data were collected on all patients at the time of enrollment. Treating physicians were asked to make a clinical assessment of degree of dehydration at initial presentation. Patients' weights were obtained at the time of presentation, inpatient discharge, and at the first clinic visit. PLBW was calculated using the following formula ((Discharge weight - Initial weight)/ Discharge weight) X 100. Degree of dehydration was classified as: mild < 4%, moderate 4 - 8%, and severe >8%.
RESULTS: Of the 36 patients enrolled, 29 were available for data analysis. Patients' age ranged from 5 to 20 years (median = 15). There was no significant difference between discharge and follow-up weight. PLBW ranged from 1.4 to 12.2% (median = 5.5%) and were classified as mild dehydration (n=11), moderate dehydration (n=15), and severe dehydration (n=3). Sensitivities of clinical assessment were 18% (95% CI: 5-48%) for mild dehydration, 27% (95%CI: 11-52%) for moderate dehydration, and 100% (95% CI: 44-100%) for severe dehydration. Clinicians overestimated the degree of dehydration in 19 of 29 (66%) patients. There were no historical data or laboratory data (pH, bicarbonate, glucose, Na, BUN) that predicted the degree of PLBW in these patients.
CONCLUSIONS: The majority of patients with DKA have moderate dehydration at the time of presentation. Clinical assessment, historical and laboratory data are poor predictors of PLBW. Based on these data initial fluid therapy for DKA should assume moderate dehydration with subsequent adjustment made according to clinical response.

152 Presentation Time 11:15 AM — Fellow

Patterns of Injury Associated With Routine Childhood Falls

Melanie L. Pitone, Magdy W. Attia. Department of Pediatrics, Division of Emergency Medicine, Alfred I. duPont Hospital for Children, Wilmington, DE and Thomas Jefferson University, Philadelphia, PA.
BACKGROUND: Falls are the leading cause of injury in children. Scant information exists on the pattern of injuries sustained following various types of routine childhood falls. Knowledge of the consequences of certain falls gives practitioners insight into potential injuries that their patients may sustain following a fall.
OBJECTIVE: To identify the pattern of injuries associated with routine childhood falls.
DESIGN/METHODS: A retrospective chart review of patients ≤12 years of age presenting over a 6 month period to a children's hospital emergency department (CHED) with a complaint of a fall. Patients were identified by ICD 9 E codes of 888.9 Fall NOS. Data were abstracted from dictated attending records by 2 individuals. Patients were classified into 3 age groups (<2 years, 2-4 years and 5-12 years of age) and analyzed for the type of fall and diagnosis.
RESULTS: 787 patients were enrolled. The mean age was 5.7 years (SD ±3.4 years). 56% were male. The types of falls reported were categorized as a fall down steps (13%), a fall from patient's own height (32%), a fall from an object (48%), and other (6%). In all three age groups the most common type of fall was from an object (50%, 50%, and 48% respectively). There were 91(12%) patients in the <2-year age group and 235(30%) in the 2-4 year age group. Both groups commonly fell from a bed/chair (35% and 25%, respectively). In the youngest children, the most frequent diagnosis was head injury (47%, odds ratio(OR) 4.8; 95%CI 3.1-7.6). One was a non-displaced skull fracture. None required neurosurgery. In children between 2-4 years of age no predominant injury was found (fracture 29%, head injury 28%). Children ages 5-12 years numbered 460(58%). Playground equipment was most commonly the object of their fall (26%). Their most frequent diagnosis was fracture (56%, OR 3.2; 95%CI 2.4-4.4). Of these, 80% were in the upper extremity (arm fracture OR 3.8; 95%CI 2.7-5.3).
CONCLUSIONS: In children who presented to a CHED with a fall, falling from an object was the commonest type of fall and was associated with more injuries. Those under 2 years of age most commonly fell from a bed/chair and sustained head injury. Children 5-12 years of age were likely to fall from playground equipment and fracture their upper extremity. Children 2-4 years of age did not have a specific pattern of injury. These findings are likely due to variation in developmental stages and body proportions among the groups and may be helpful to clinicians who evaluate routine childhood falls.

Endocrinology Platform Session

Sunday, March 28 9:45am–12:15pm Winthrop A-B

153 Presentation Time 9:45 AM — Fellow

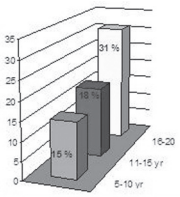
Vitamin D Deficiency in Obese Children

Ashutosh Gupta, Svetlana B. Ten, Golali Nejati, Neven Pesa, Amrit P. S. Bhangoo, Irina Kazachkova, Nicole A. V. Matthews, Henry Anhalt. Pediatrics, Maimonides Medical Center, Brooklyn, NY.
BACKGROUND: Vitamin D deficiency has been shown to be prevalent in all age groups including healthy children and adolescents, lean and obese adults and elderly. Calcitropic hormones have been postulated to be important regulators of glucose homeostasis in obese adults. Data regarding vitamin D status of obese pediatric subjects is not available.
OBJECTIVE: To determine the prevalence of vitamin D deficiency and its correlation to demographic and laboratory data in an obese pediatric population.
DESIGN/METHODS: After an overnight fast we measured 25-OH vitamin D, 1,25 $(OH)_2$ vitamin D_3, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, alkaline phosphatase, ALT, AST, TSH, total T4, glucose and insulin in 80 obese (BMI 33.3 ± 6.6 kg/m^2) children (40 male, 40 female; age 11.1 ± 3.3 yr., range 7-18 yr.). We defined vitamin D deficiency as 25-OH vitamin D level of <20 ng/ml and severe vitamin D deficiency as ≤10 ng/ml. QUICKI was used as the index of insulin sensitivity.
RESULTS: Overall 47.5% of all patients (n = 38; 19 boys, 19 girls) were vitamin D deficient and 12.5% (n = 10; 6 boys, 4 girls) were severely deficient. There was no correlation between 25-OH vitamin D levels and BMI, alkaline phosphatase, ALT, AST, total T4, total Cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, glucose, insulin and QUICKI. 25-OH vitamin D levels were weakly negatively correlated to age (r = -0.22, p = 0.05) and weight (r = -0.21, p = 0.05) and positively with TSH (r = 0.22, p = 0.05). 1, 25 $(OH)_2$ vitamin D_3 and total T4 showed a significant negative correlation (r = -0.70, p = 0.04).
CONCLUSIONS: About 15-20% of healthy children and adolescents are reported to be vitamin D deficient. We found that almost half of obese children were vitamin D deficient. Males and females were equally affected. Heavier and older the patients the more likely they were to be vitamin D deficient. Unlike adults, hypovitaminosis D did not confer insulin resistance in our patients, although the index used (QUICKI) is not very sensitive or specific for this purpose. Vitamin D endocrine system has been implicated in thyroid autoimmunity and glucose homeostasis in adults. More research is needed to understand the interaction of vitamin D and energy homeostasis in obese children and adolescents.

154 Presentation Time 10:00 AM — Fellow

Elevated Liver Transaminases Are a Frequent Complication of Obesity in Children Referred to the Kids Weight Down Program

Nicole A. V. Matthews, Irina Kazachkova, Shivinder Narwal, Graciela Wetzler, Golali Nejatii, Henry Anhalt, Svetlana Ten. Department of Pediatric Endocrinology, Maimonides Medical Center, Brooklyn, NY.
BACKGROUND: Fatty infiltration of the liver is a known complication of obesity in adults. Previous reports indicate that fatty liver affects 2.6% of children and up to 10-25% of obese adolescents. Serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) have been proposed as surrogate markers of hepatic fat accumulation.
OBJECTIVE: Primarily to identify the frequency of elevated liver enzymes among obese children involved in the Kids-Weight Down Program. Secondarily to seek correlations between elevated liver enzymes and other variables associated with insulin resistance.
DESIGN/METHODS: We screened liver function tests in 156 obese children (ages 5 to 20 yrs). Fasting lipid profiles, thyroid function tests, glucose and insulin levels were also obtained.
RESULTS: ALT and AST were elevated in 30/156 (19.2 %) children with obesity and normal glucose tolerance. In the group with elevated liver enzymes, HDL was significantly lower and triglycerides (TG) were significantly higher (P < 0.001). TG level correlated positively with ALT level (r=0.39, P< 0.001).



While HDL negatively correlated with ALT level (r= - 0.29, p < 0.001). Ratio TG/HDL correlated with ALT (r= 0.37, p < 0.001) and AST (r=0.27, p< 0.001). Frequency of elevated liver transaminases increases with age: from 15% at 5-10 years of age, to 18 % at 11 to 15 years and 31 % at 16- to 20 years of age (see Fig.). There were no differences in insulin resistance index (QUICKI), BMI or age between groups.
CONCLUSIONS: Elevated liver transaminases are a frequent complication of obesity in up to 19 % of our patients. Frequency of such complications increases with age. Elevated TG/HDL index can be a marker of abnormal liver enzymes, an important surrogate marker of fatty infiltration of the liver.

155 Presentation Time 10:15 AM

Is Microalbuminuria (MA) in Childhood Obesity Related to Glucose Toxicity?

Tania S. Burgert, Catherine Yeckel, William Tamborlane, Sonia Caprio. Section of Pediatric Endocrinology, Department of Pediatrics, Yale University, New Haven, CT.
BACKGROUND: Microalbuminuria (MA), often clustering with the metabolic syndrome, has emerged as a strong predictor of cardiovascular (CV) events even in non-diabetic adults. While the exact mechanism behind this association remains to be established, most studies suggest that MA is the result of increased vascular leakage denoting endothelial dysfunction associated with early atherogenesis. The Heart Outcome Prevention Evaluation (HOPE) trial furthermore demonstrated that the relationship between urinary albumin and CV events persisted even within the "normoalbuminuric" range.
OBJECTIVE: To prospectively study if the urine albumin creatinine ratio (UACR) is related to metabolic markers of cardiovascular risk in obese, non-diabetic children.
DESIGN/METHODS: The UACR (mg/mmol) was assessed for 155 obese (BMI: 35±8) children (age:13 ± 2). Abnormal UACR was defined as an abnormal UACR between 2.0-20. UACRs within the normalbuminuric range were separated into low normal (< 0.62mg/mmol) and high normal (0.62-1.99mg/mmol) values, based on the CV risk associations established by the HOPE trial. Analyses were performed between the UACR groups and other metabolic syndrome markers of increased CV risk, including glucose tolerance, insulin sensitivity (by HOMA and WBISI), insulin response to oral glucose, BMI, % body fat, blood pressure (BP) and lipid profile.
RESULTS: Even below the threshold for frank MA there was a strong positive correlation between the 2 hour blood glucose (BG) during OGTT and the UACR. In children with normal glucose tolerance the 2 hour glucose levels were: 108±16, 114±15, 116±15 in the low normal, high normal and abnormal groups respectively (p<0.05 low normal vs high/abnormal UACR). The relationship remained significant (p<0.001) after controlling for BMI, % body fat, age, insulin sensitivity, ethnicity and blood pressure. The relationship between glucose and UACR persisted even in those subjects classified as having impaired glucose tolerance (15% of the cohort) . MA was not associated with any other cardiovascular risk factors measured.
CONCLUSIONS: These data suggest that early glucose toxicity as reflected by mild elevations in plasma

glucose below the diagnostic cutoff for diabetes may contribute to chronic vascular inflammation leading to endothelial dysfunction. Whether a higher UACR is equally as predictive of CV disease in children as it is in adults, remains to be examined.

156 Presentation Time 10:30 AM

The Impact of Redefining Impaired Fasting Glucose in Children at Risk for Impaired Glucose Tolerance and Type 2 Diabetes Mellitus

Stasia Hadjiyannakis, Sarah E. Lawrence, Leanne M. Ward, Margaret L. Lawson. Pediatrics, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; Medicine, University of Ottawa, Ottawa, ON, Canada.

BACKGROUND: Current guidelines recommend a fasting plasma glucose (FPG) alone as the initial screening test for type 2 diabetes (T2DM) in childhood. The diagnosis of Impaired Glucose Tolerance (IGT) is also important, since several studies have demonstrated the ability to prevent or delay the onset of T2DM in these individuals. It has been shown that the sensitivity of a FPG alone in detecting IGT or T2DM is reduced compared to the oral glucose tolerance test (OGTT). Recently the definition for Impaired Fasting Glucose (IFG) has been lowered to improve sensitivity.

OBJECTIVE: To determine whether recent changes in the definition of IFG can improve the sensitivity in screening for IGT and T2DM in high risk pediatric patients.

DESIGN/METHODS: 62 patients (45 female) referred to our centre for evaluation of obesity, irregular menses, hirsutism, acanthosis nigricans and/or dyslipidemia underwent an OGTT with 1.75g/kg (maximum 75g) of Trutol® . The children were 5.2-17.9 yrs old with a mean age of 13.2 years. Blood Glucose levels were drawn at times 0 and 120 min. The results were reviewed using the following definitions:

IFG (ADA Guidelines, January 2003): FPG 110-125 mg/dl (6.1-7.0 mmol/l).

IFG (ADA Expert Committee, Diabetes Care, November 2003): FPG 100-125 mg/dl (5.6-6.9 mmol/l)

RESULTS: Using the old definition for IFG, 8 patients had abnormalities of glucose homeostasis. One patient had both IFG and IGT, 6 had IGT alone and 1 had T2DM. This resulted in a sensitivity and specificity in detecting IGT and or T2DM of 12.5% and 100% respectively. When the new definition for IFG was applied, 15 patients had abnormalities with glucose homeostasis. Seven had IFG alone, 2 patients had both IFG and IGT, 5 had IGT alone and 1 had T2DM. Therefore, using the new definition the sensitivity improved to 25% but was still suboptimal. The specificity was reduced to 87%.

CONCLUSIONS: Despite efforts to improve the sensitivity of screening by redefining IFG, the new definition resulted in recognition of only 1 additional patient with IGT but resulted in 6 new diagnoses of IFG. Five patients with IGT and the patient with T2DM would still have been missed without the 2-hPG. This may be further evidence that IGT and IFG are 2 distinct clinical entities. Therefore consideration should be given to using the 2-h OGTT when screening high risk pediatric patients.

157 Presentation Time 11:00 AM Fellow

Insulin and TSH Levels Can Predict Short-Term Response to Behavioral Intervention in Obese Children

Amrit Bhangoo, Golali Nejati, Lisa Altshuler, Susan Beren, Chaya Silverstein, Deborah DeSantis, Yanick Joseph, Henry Anhalt, Svetlana Ten. Division of Pediatric Endocrinology, Maimonides Medical Center, Brooklyn, NY; Kids Weight Down Program, Maimonides Medical Center, Brooklyn, NY.

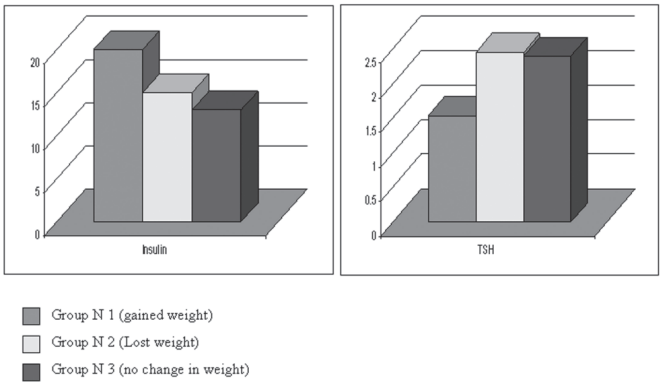
BACKGROUND: That insulin sensitivity can predict success in dieting and behavior modification is a new concept. Plasma levels of insulin and leptin are good predictors of successful intervention in adults.

OBJECTIVE: Identify biochemical markers in obese children that are predictive of response to lifestyle intervention.

DESIGN/METHODS: We evaluated cholesterol, LDL, HDL, TG, ALT, AST, TSH, T4, fasting glucose and insulin levels in 79 obese (BMI 35.5 ± 8.7 Kg/m^2) children (26 males, 53 females; age 13.3 ±4.1 yrs; 49 % White, 20 % black, 27 % Hispanic and 4 % Asian) who enrolled in the Kids Weight Down Program (KWD). KWD is a 12-week lifestyle modification program for obese children. It consists of an endocrinologist, behavioral and nutritional specialists. BMI's at the beginning and the end of the 3-months were calculated. Based on BMI participants were divided into 3 groups.Group N 1 (+ >1 kg/m^2),Group N 2 (- <1 kg/m^2),and Group N 3(=kg/m^2.)

RESULTS: 43 % patients lost weight, 43% didn't change BMI and 14 % gained weight at the end of 3 months. Only 5.2 % of children older than 15 yrs gained weight during the program compared to 18.7 % of children less than 10 yrs. TSH was lower in group 1 (1.54 ±0.52 mU/l)as compared to groups 2 (2.4 ± 1.8 mU/l, p=0.007) and 3 (2.4 ± 1.1 mU/l, p=0.05). Insulin levels although not significantly different (p< 0.06) were higher in group 1 (20.1 ± 1.1 uU/ml) compared with groups 2 (13.1 ± 8 uU/ml) and 3 (15.7 ± 6.5 uU/ml).

CONCLUSIONS: Elevated fasting insulin, predicts less success to lifestyle intervention. Lower TSH levels in group 1, may indicate complex influences of leptin on thyroid hormones to regulate REE and weight. Measuring biochemical markers may facilitate a more individualized approach during life-style intervention to children less than 10 years of age.



158 Presentation Time 11:15 AM Fellow

Childhood Obesity: Diabetes Risk in an Urban Hispanic Caribbean Population

Abeer Hassoun, Daisy Chin, Sadana Balachandar, Alexandra M. Manibo, Nicole Sherry, Phillip M. Pierorazio, Lenore S. Levine, Sharon E. Oberfield, Ilene Fennoy. Pediatric Endocrinology, Columbia University, New York, NY.

BACKGROUND: Childhood obesity is epidemic in pediatric populations with increased risk for diabetes in minority populations. The majority of studies in Hispanic children have been in those of Mexican-American heritage.

OBJECTIVE: Since prevalence of diabetes is known to vary by ethnic background, we sought to evaluate the risk of diabetes in obese children of primarily Dominican ancestry who attend the obesity clinic at Children's Hospital of Columbia University Medical Center.

DESIGN/METHODS: Over a 5 year period (1998-2003), 428 children were seen. Complete data was available on 352 who ranged in age from 2 to 20yrs, mean 11.25yrs (92.5% Hispanic with 56.2% of Caribbean ancestry, 6.7% South American, 20.1% unspecified Hispanic). Mean BMI-z was 2.63 (range =1.27 to 5.56). A two-hour glucose tolerance test, fasting glucose-insulin ratio (FGIR), and fasting lipid panel were obtained from 194/352 children.

RESULTS: Family history was positive for obesity (74.2%), diabetes (61.9%), hypertension (46.9%), and hyperlipidemia (12.4%). Using ADA criteria of FBS>109, impaired fasting glucose (IFG) was noted in 4 (2.1%). Impaired glucose tolerance (IGT) with glucose between 140 and 200 was seen in 7(6.1%). Seven of 11 children with abnormal glucose indices were in the 12+ age group, two in the 9-12 age group and one each age 7 and 8 yrs. Another 7 (3.6%) had FBS between 100 and 109 indicating IFG according to most recent guidelines (three age 12+, three age 9-12, and one age 8yrs). Although mean cholesterol and triglyceride were normal, children with IGT (177.29±31.0mg/dl and 130.86±61.81 mg/dl) or IFG (193.67±31.09 mg/dl and 151.33±55.97mg/dl) had the highest levels. FGIR <4 was present in 4 of 7 patients with IGT and 6 of the 11 with IFG, supporting insulin resistance.

CONCLUSIONS: Despite extraordinary family histories of obesity and diabetes, abnormalities of glucose and lipids were infrequent in this young, obese Hispanic Caribbean population. This is in contrast to previous reports (Sinha et al. NEJM, 2002; 346:802-10), potentially suggesting a different genetic susceptibility in our children.

Supported by funding from the Maxcor Foundation, Inc.

159 Presentation Time 11:30 AM Fellow

Oral Glucose Tolerance Test (OGTT) Findings in Minority Youth {African American (AA) and Caribbean Hispanic (CH)} at Risk for Type 2 Diabetes Mellitus (T2DM)

Mireya H. Garcia, Hadassa Nussbaum, Patricia Vuguin, Roy Grant, Joan Di Martino-Nardi. Pediatric Endocrinology and Diabetes, The Children's Hospital at Montefiore, Bronx, NY; The Children's Health Fund, The Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: The ADA recommends screening high risk children every 2 yrs with a fasting blood glucose (FBG) to diagnose T2DM and impaired glucose tolerance (IGT). The early detection of IGT is important in the prevention of T2DM. Recently, the ADA reduced the nl FBG to <100 mg% to permit the early identification of the pre-diabetic state/T2DM.

OBJECTIVE: To assess: 1) the prevalence of IGT and T2DM using the OGTT in minority youth meeting ADA criteria for "high risk"; 2) the reliability of the reduced FBG in detecting an abn OGTT; and, 3) the parameters most useful in identifying those at risk for an abn OGTT.

DESIGN/METHODS: OGTT was performed in obese CH or AA pubertal pts (BMI >85th %ile) 10-18 yrs of age, with a family history of T2DM and signs of insulin resistance. All pts had a nl random BG within 3 mos of testing. Parameters and insulin sensitivity {fasting Glucose/Insulin (G/I) and HOMA} were compared to lean minority controls matched for pubertal status.

RESULTS: 105 obese pts were studied (28 AA, 77 CH; 50M, 55F, 36 TII-III, 69 TIV-V). There were no significant differences according to sex or ethnic background. 11 had IGT; 1 CH male had T2DM. All 12 were TIV-V. 63% (7/11) with IGT had a nl FBG. Only 33% of pts with an abn OGTT (4/12) had an abn FBG. The pt with T2DM had a FBG 107mg%. HOMA and HgbA1c correlated with FBG and 120 min glucose (p<0.01), as well as BMI (p<0.05).

	Lean (n=15)	Obese Nl OGTT (n=93)	Obese Abnl OGTT (n=12)
Age (years)	14.3±1.1	13.6±2.3	15.7±1.1
BMI (kg/m^2)	20.4±3.3†¶	38±7.3†	42±7¶
Systolic blood pressure	103±12†¶	120±13†	123±7¶
Glucose 0 min (mg/dL)	82±9¶	84±8*	95±12¶*
HOMA	2.7±1.3†¶	5.5±4.1*†	13.2±11.9¶*
G/I ratio	8±4.3¶	5.7±5.5	3.6±3¶
Triglycerides	88±26‡¶¶	112±64‡	132±67¶¶
HDL	70±20†¶	47±11†	49±16¶
LDL	77±10†¶	93±27†	108±22¶
HgbA1c	5.3±0.14¶¶	5.3±0.3*	5.8±0.57¶¶*

Obese Nl OGTT vs. Obese Abn OGTT: *p<0.01; Lean vs. Obese Nl OGTT: †p<0.01, ‡p<0.05; Lean vs. Obese Abn OGTT:¶<0.01, ¶¶<0.05

CONCLUSIONS: 17% of late pubertal AA/CH teens have an abn OGTT. FBG ≥100mg% is not reliable in detecting IGT. Those minority youth most at risk for IGT/T2DM are T IV-V, have higher BMI, HgbA1c, LDL and lower HDL, and are more insulin resistant (higher HOMA, lower G/I). These teens should be screened more aggressively for IGT and T2DM.

General Pediatrics III
Platform Session

Sunday, March 28 9:45am–11:30am Mead A

160 Presentation Time 9:45 AM Fellow

Structured vs. Unstructured Data Entry: Measuring Attitudes and Comparing Documentation Completeness in Primary Care Pediatrics

Robert W. Grundmeier, Anthony A. Luberti, Susan E. Coffin, Curtis P. Langlotz, Kevin B. Johnson. Department of Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA; Department of Radiology, University of Pennsylvania, Philadelphia, PA; Department of Biomedical Informatics, Vanderbilt University, Nashville, TN.

BACKGROUND: Electronic health record (EHR) systems facilitate the capture of structured patient encounter data from clinicians at the point of care. Due to the unique challenges of delivering care to children, structured data entry may improve the quality of documentation and patient safety while preserving effective patient-clinician interactions.

OBJECTIVE: 1. Measure clinician attitudes toward structured data entry in an EHR

2. Compare data entry modalities for ease of use, time efficiency, and completeness of documentation

DESIGN/METHODS: Previously validated surveys with modifications were distributed to clinicians before and after implementation of an EHR. The surveys measured preferred documentation style, EHR priorities, and perceived impact on efficiency. Documentation completeness was compared by chart review. The population included attending pediatricians, nurse practitioners, and residents at four primary care centers. There were 199 clinicians during the 2-year pre-implementation interval and 157 during the 6-month post-implementation interval.

RESULTS: 134 clinicians returned pre-implementation surveys (response rate 67%). 85 (63%) preferred outline or structured documentation. 112 (84%) ranked "time efficiency" as a priority for the EHR.

115 clinicians returned post-implementation surveys (response rate 73%). 75 (62%) preferred outline or structured documentation. The majority felt documentation in the EHR was easier to find (82%), more efficient (61%), and more accurate (60%) than on paper. Results did not vary significantly based on gender, clinician type (resident vs. non-resident) or self-identified computer sophistication.

158 gastroenteritis encounters were reviewed for documentation completeness. Clinicians chose either a free text or a structured documentation tool in the EHR for each encounter. Presence or absence of documentation was tabulated for a total of 12 key history and physical elements. The average score was 8.6 for the free text group, compared to 10.7 for the structured documentation group ($p < .0001$).
CONCLUSIONS: The relatively high rate of preference for structured data suggests that providers are receptive to this modality. Clinicians preferred the EHR for availability of documentation, time efficiency, and accuracy. Documentation was more complete with structured data capture.

161 Presentation Time 10:00 AM — House Officer

Helping Teachers Breathe Easier: Improving Asthma Knowledge and Competencies Among Elementary School Teachers

Reva Snow, Sarah Kimball, Philip O. Ozuah. Pediatrics, The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Children with asthma spend a significant amount of time in school. We previously demonstrated low levels of knowledge about asthma among elementary school teachers in the Bronx, New York, an area with one of the highest rates of asthma hospitalization and death in the country. In collaboration with the Board of Education, we developed a targeted intervention for school staff. We hypothesized that this intervention would result in improved staff knowledge.
OBJECTIVE: To assess the impact of an intervention aimed at increasing elementary school teachers' knowledge of asthma and its management.
DESIGN/METHODS: We conducted an intervention study at four Bronx primary schools. The design included an inception cohort and historical controls. Baseline surveys of asthma knowledge were conducted in 2001; respondents from this survey served as historical controls. Then, a targeted intervention was developed based on the NHLBI and ALA recommended asthma knowledge areas for school staff, and included basic facts about asthma, recognizing an attack, recognizing triggers, promoting indoor air quality, identifying students with asthma, and standardizing in-school management of asthma and medications. The intervention was piloted and refined with a focus group of 20 elementary school teachers, resulting in a 15-minute PowerPoint presentation. Teachers at 4 Bronx primary schools received this intervention and were designated the inception cohort. A second survey was conducted following the intervention. Bivariate analyses compared asthma knowledge between the inception cohort and historical controls.
RESULTS: 107 teachers responded (75% response rate). In contrast to the low levels of asthma knowledge detected in the historical controls, the majority of teachers in the inception cohort displayed high levels of asthma knowledge post-intervention: Recognizing asthma (95% correct); School management (65%), Triggers (84%); Sports participation (84%); Use of inhalers (67%); Dosing of medications (69%); and Signs of asthma (95% correct).
CONCLUSIONS: Post intervention, the majority of teachers who particpated in this project showed substantially enhanced knowledge of asthma and its management. These findings have implications for efforts aimed at asthma management in schools.

162 Presentation Time 10:30 AM

The Vaccines for Children Program: A Difference-In-Difference Analysis of Changes in Immunization Status Disparities

Andrew D. Racine, Theodore J. Joyce. Pediatrics, Albert Einstein College of Medicine / Children's Hospital at Montefiore, Bronx, NY; National Bureau of Economic Research, New York, NY; Economics and Finance, Baruch College, City University of New York, New York, NY.
BACKGROUND: The Vaccines for Children Program (VFC) was created in 1994 to provide free vaccines to uninsured, Medicaid eligible, Alaskan Native, American Indian, and certain underinsured children under 18 years of age. Little is known about the VFC program's impact on immunization status disparities with respect to income, race/ethnicity or urban residence.
OBJECTIVE: To compare changes in income, race/ethnicity, and urban/non-urban immunization status disparities before and after the creation of the VFC program.
DESIGN/METHODS: We used 1995 and 1998 data from the National Immunization Survey (NIS), a nationally representative population based survey of over 30,000 households per year containing demographic and immunization-receipt information on 19-35 month-old children. Income categories were used to code children from poor (< 100 % of the Federal Poverty Level, FPL), near-poor (>= 100% FPL but < 250% of FPL) and non-poor (>= 250% of FPL) families. Analyses were restricted to 24-35 month olds vaccinated before VFC in 1995 and after VFC in 1998. Difference-in-difference analyses were used to compare pre-VFC (1995) to post-VFC (1998) changes in up-to-date (UTD) status in the 4:3:1:3:3 (DtaP, IPV, Measles containing vaccine, Hib, and HepB) vaccine series for poor/near-poor relative to non-poor children, for black and Hispanic relative to white children, and for urban relative to non-urban children.
RESULTS: From 1995, before the VFC program, to 1998 after its implementation, all children regardless of income, race/ethnicity, or urban residence category increased their likelihood of being UTD for the 4:3:1:3:3 series by statistically significant margins of between 13 and 23 percentage points. While the non-poor:poor/near-poor disparity in UTD status shrank from 9.8 to 6.6 percentage points ($p<0.08$) over this time, the white:black disparity in UTD status rose from 0 to 9.6 percentage points ($p<0.05$), and the white:Hispanic disparity rose from 2.3 to 4.8 percentage points (NS). For the same period, an initial urban:non-urban advantage in UTD status of 2.5 percentage points before VFC (NS), shifted to a non-urban:urban advantage of 7.3 percentage points ($p<0.05$) after VFC.
CONCLUSIONS: Introduction of the VFC program coincided with improved income-related disparities but exacerbated race/ethnicity and residence-related disparities in immunization status among 2-3 year olds. These trends merit further investigation.

163 Presentation Time 10:45 AM

Improving Residents' Competency in Pain Management

Sharon Calaman, Catherine C. Skae, Philip O. Ozuah. The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Effective pain management continues to be an elusive goal in medicine, particularly in pediatrics. It is important to teach pediatric house officers about pain management because behaviors learned during residency often become ingrained.
OBJECTIVE: To investigate the impact of an intervention aimed at increasing residents' competency in pain management.
DESIGN/METHODS: We conducted a Pre/Post Intervention study at a major children's hospital. The study design included a 3-month baseline observation period; followed by our intervention; followed by a 2-month post-intervention period. The intervention consisted of small group lectures about pain management; the development and distribution of a pocket guide to pain management; and daily rounds and 24-hour telephone coverage by three dedicated faculty members to answer questions and give feedback. Data were collected on pain assessments, the appropriateness of interventions, medical record documentation of pain, and patient demographic information. The appropriateness of interventions for given levels of pain was defined in accordance with WHO and AHCPR Guidelines. We tested differences in continuous and categorical variables using t-test and Chi-square respectively.
RESULTS: 5673 observations were analyzed (3026 pre- and 2647 post-intervention). The mean age was 11.3 years. 54% were medical diagnoses and 45% were surgical. Post-intervention, there was a substantial increase in the average number of assessments per patient (14.9 vs. 11.3). There was also a significant improvement in the appropriateness of pain management interventions (74% post-intervention vs. 66% pre-intervention, $p= .037$). This improvement was even greater for Pain Scores less than or equal to 4 (86% vs. 65%, $p= .003$). Also, there was a modest increase in the documentation of pain scores in house officers' daily notes (17% post-intervention vs. 11.5% pre-intervention, $p= 0.02$).
CONCLUSIONS: The results of this study show that a targeted intervention was sucessfully improved the appropriateness of pain interventions among pediatric house officers. Competency in pain mangement is an important facet of clinical practice.

164 Presentation Time 11:00 AM

Utility of 360-Degree Assessment of Competencies of Pediatric Residents

Sandra F. Braganza, Iman Sharif, Philip O. Ozuah. Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: The Accreditation Council of Graduate Medical Education (ACGME) requires that residency programs institute competency-based assessments. Traditionally, only faculty evaluate residents. However, the ACGME now recommends 360-degree assessments where colleagues, support staff, and patients also assess resident competencies. The usefulness of such assessments in pediatric education has not been tested.
OBJECTIVE: To 1) determine whether resident competency assessment by peers, support staff, and patients' parents differ from the assessment by faculty alone, and 2) identify particular competencies for which differences between faculty and peer/staff/parent assessments are most pronounced.
DESIGN/METHODS: We studied 14 pediatric residents (4 PL1s, 4PL2's, 4PL3's, 2PL4's) at an ambulatory site affiliated with a major academic center. We developed a questionnaire using the ACGME Outcomes Project website's sample questionnaires on Professionalism and Communication skills. The questionnaire assessed: Communication Skills, Empathy, Respect, and Integrity, on a 5-point Likert scale (1=Never a Problem, 5=Severe Problem). The questionnaire was administered anonymously to all faculty, resident peers, and support staff, and a consecutive sample of parents during 2 clinic sessions. Because virtually all responses were either "Never a Problem" or "Acceptable", we dichotomized responses between these two categories. Chi-square and Mann-Whitney U Tests compared differences in assessment.
RESULTS: 271 surveys were completed (68 faculty, 105 resident peers, 78 support staff, 20 parents). Chi-square analysis found differences between the faculty assessments and those of peers, support staff, and parents for all domains ($p=.000$). Compared to faculty, parents noted more problems with Empathy (63% vs. 19%, $p=.000$) and Respect (50% vs. 11%, $p=.000$). In contrast, parents noted fewer problems with Communication (0% vs. 22%, $p=022$). Resident peers were less likely to report problems with Communication (9% vs. 22%, $p=.018$) and Empathy (7% vs. 19%, $p=.033$). Support staff reported fewer problems with Empathy (3% vs. 19%, $p=.001$), Respect (1% vs. 11%, $p=.013$), Communication (1% vs. 22%, $p=.000$), and Integrity (0% vs. 11%, $p=.003$).
CONCLUSIONS: 360-degree assessment provided useful information about resident competencies that would not have been determined by faculty evaluations alone, particularly in the areas of Empathy and Respect. These findings have implications for resident competency assessment.

165 Presentation Time 11:15 AM — House Officer

Impact of Interventions Aimed at Compliance With New ACGME Resident Work Hour Regulations

Daniel Finkelstein, Philip O. Ozuah. The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: On July 1, 2003, new ACGME regulations went into effect limiting the time residents may work continuously to 30 hours. New York State has had a more stringent 27-hour limit in place since 1989. Residency programs across the country are struggling to implement daily schedules that adhere to work hours limitations while maintaining resident education.
OBJECTIVE: To assess the impact of serial changes to the daily schedule and responsibilities of pediatric residents on compliance with work hours regulations and attendance at educational activities.
DESIGN/METHODS: We performed a time series cohort analysis using self-administered surveys of pediatric residents at a major academic medical center. The questionnaire asked residents to document the times various scheduled activities took place, including their arrival and departure. The first questionnaire was administered in April 2002 prior to any interventions. Then, in October 2002, we reorganized the workday by combining two previously separate activities (resident work rounds and attending rounds) into one activity. We also designated these rounds to start at 7 a.m. (2.5 hours earlier than the previous attending rounds). A second survey was conducted in June 2003. Next, we made a second intervention by eliminating post-call note writing. A final work-hour survey was conducted in October 2003. Multivariate analysis of variance (MANOVA) for repeat measures tested mean differences in continuous variables.
RESULTS: A total of 76 resident-survey reports were analyzed. There was a decline in mean consecutive hours worked across the 3 study periods: 29.8 hrs (± 0.62) vs. 28.6 hrs (± 0.65) vs. 27.5 hrs (± 0.46). Using MANOVA, this was statistically significant at p=0.000. Also, the maximum reported consecutive hours worked declined across the 3 periods: 31 hrs vs. 29.8 hrs vs. 28.5 hrs; $p = 0.000$. Attendance at scheduled didactic sessions improved from 10-20% pre-intervention to >80-90% post-intervention.
CONCLUSIONS: The adoption of a system whereby attending rounds and didactic sessions are completed during the 1st 3 hours of the day significantly reduced the number of consecutive hours worked by on-call interns while enhancing attendance at educational sessions. Freeing interns from the responsibility for post-call note writing further reduced significantly the number of consecutive hours worked. These findings have implications for efforts aimed at compliance with ACGME resident workhour regulations.

Neonatology II
Platform Session

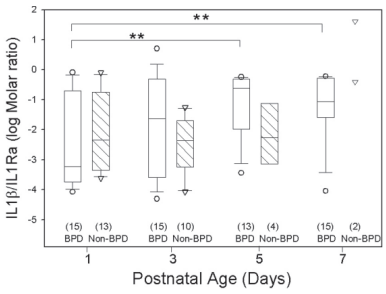
Sunday, March 28 — 9:45am–12:30pm — Mead B

166 Presentation Time 9:45 AM

Bronchopulmonary Dysplasia (BPD): Impaired Expression of Interleukin-1 Receptor Antagonist (IL1Ra)?

Deepika K. Kakkera, Mustafa M. Siddiq, Lance A. Parton. Pediatrics, Children's Memorial Hospital, Chicago, IL; Molecular and Cellular Biology, SUNY, Stony Brook, NY; Pediatrics, NY Medical College/ Children's Hospital of Westchester, Valhalla, NY. (Sponsored by Sergio Golombek)
BACKGROUND: Pulmonary expression of pro-inflammatory mediators has been detected as early as d1 in preterm infants.
OBJECTIVE: We tested the hypothesis that the IL-1 family of cytokines is an early marker for BPD, when measured in tracheal aspirates (TAs) obtained from premature infants being ventilated for RDS during the 1st wk of life.
DESIGN/METHODS: Serial TAs were collected on d1, 3, 5, and 7 from 35 infants, who were born < 30 weeks of gestation in the absence of chorioamnionitis, and who were being ventilated for RDS. TA wbc, IL-1α, IL-1β, and IL-1Ra ELISAs were performed. 16 infants required O_2 at 36 weeks postconceptional age

and were classified as BPD, 19 recovered from RDS (Non-BPD). Between and within group comparisons employed Mann-Whitney Rank sum test and Kruskal-Wallis One Way ANOVA on Ranks, respectively.
RESULTS: Maternal and infant demographics were comparable. TA IL-1α levels remained low in both groups throughout the 1st wk of life. TA IL-1β was significantly elevated in the BPD group above the Non-BPD group on d3 and 5 ($P<0.05$). TA IL-1Ra was significantly elevated in the BPD group for d1 ($P<0.001$), 3 ($P<0.01$), and 5 ($P<0.05$). Within the BPD group, TA IL-1β levels, IL-1Ra and the Molar ratio of IL-1β/IL-1Ra were all increased signficantly on d5 and 7 when compared to d1 ($P<0.01$), demonstrating that agonist expression outpaced antagonist expression during this time period.



CONCLUSIONS: While early (d1) agonist/antagonist molar balance favored protection, by d5 and 7 a threshold for IL-1Ra expression in the presence of increasing IL-1β favored pro-inflammation in the BPD group. We speculate that early (perinatal) stimuli provoke a strong (IL-1Ra) antagonist ex-pression that reaches a sub-optimal, non-protective threshold within the 1st wk of life in premature infants who develop BPD.
Funded by Children's and Women's Physicians of Westchester and Stony Brook Children's Foundation

167 Presentation Time 10:00 AM

Relationship Between Markers of Nitric Oxide Metabolism and Pulmonary Function in Infants at Risk of BPD

Andrew J. Gow, Philip L. Ballard, Michael Norberg, William E. Troug, Roberta A. Ballard. Pediatrics, Division of Neonatology, University of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, Philadelphia, PA; Pediatrics, University of Missouri-Kansas City School of Medicine, Children"s Mercy Hospital, Kansas City, MO.
BACKGROUND: The etiology of bronchopulmonary dysplasia (BPD) is not fully understood. However, nitric oxide (NO) and its metabolites have been implicated both as a preventative modality and markers of disease progression.
OBJECTIVE: To assess the status of nitrogen oxide metabolism, inflammation, and surfactant function in infants at risk of BPD.
DESIGN/METHODS: Tracheal aspirate and plasma samples were obtained from 16 premature infants at risk of BPD as defined by a requirement for respiratory support at 7 days of age. A surfactant pellet was prepared by centrifugation, in which minimum surface tension (ST) was measured by pulsating bubble surfactometer. Plasma and aspirate supernatant samples were measured for total nitrogen oxide content (NO_x) by reductive chemiluminesence. Aspirates were assessed for NO_2^-, nitrosothiol (SNO) by partial reduction chemiluminesence and cytokine content (epiPGF2a, IL-1b and IL-8) by ELISA.
RESULTS: Mean demographic data were: gestational age 25.6 weeks (range 24-28), age at sampling 15 days (range 6-22), and birthweight 738 g (range 502-1060). There were significant positive correlations between aspirate NO_x and severity score (as defined by FiO_2 times mean airway pressure) (r^2=0.24) and between both plasma and aspirate NO_x and ST (r^2= 0.26 & 0.16 respectively). In addition, there was a negative correlation between [$(NO_2^- + SNO)/NO_x$] with ST in aspirates, indicating that most NO produced was undergoing nitrative and oxidative metabolism. No association was seen for cytokines with either severity score or ST. ST values fell into two distinct groups above 10 mN/m (abnormal) and below 5 (normal). There were significant differences between the two ST groups for plasma and aspirate NO_x values as well as for metabolite ratios (Table).
CONCLUSIONS: We conclude that increased NO production and metabolism to higher oxides in the lung is associated with disease severity and surfactant dysfunction, consistent with inflammation as a component of BPD. We speculate that both altered NO production and metabolism are critical in the pathogenesis of BPD.

	Plasma NOx (μM)	Aspirate NOx (nm/mg protein)	$(NO_2^- + SNO)/ NO_x$
Abnormal ST	91 ± 20.8	19 ± 9.2	0.2 ± 0.05
Normal ST	39 ± 11.2	6 ± 2.6	0.4 ± 0.13

168 Presentation Time 10:15 AM Fellow

Natriuretic Peptide Clearance Receptor Is Downregulated in the Pulmonary Epithelium After Birth in Preterm and Full Term Lambs

Bobby Mathew, Christopher A. D'Angelis, Daniel D. Swartz, Vasanth H. Kumar, Peter A. Nickerson, Huamei Wang, Karen A. Wynn, Bruce A. Holm, Rita M. Ryan. Department of Pediatrics (Neonatology), SUNY-Buffalo and Women and Children's Hospital of Buffalo, Buffalo, NY; Department of Pathology, State University of New York at Buffalo School of Medicine, Buffalo, NY.
BACKGROUND: Factors regulating the maturation of the pulmonary epithelium to a fluid-absorbing, surfactant-releasing interface at birth are poorly understood. We have demonstrated previously that atrial natriuretic peptide (ANP) and its guanylyl cyclase linked receptor (NPR-A) are elevated in distal airway epithelial cells in fetal lambs, and decrease postnatally at term. The natriuretic peptide clearance receptor (NPR-C) is a second, non-guanylyl cyclase linked receptor for ANP and acts not only in the clearance of ANP but also in the inhibition of beta-adrenergic stimulated lung water clearance and surfactant release.
OBJECTIVE: To examine the developmental expression of NPR-C in the pulmonary epithelium of fetal and neonatal lambs, and to test the possible effect of premature delivery and ventilation on NPR-C expression.
DESIGN/METHODS: In order to define a possible role for NPR–C in transition, the developmental expression of NPR-C was examined using immunohistochemistry on lung sections from fetal lambs of 100 and 136 days gestation (term=145) and from postnatal 3 day and 4 week old lambs. In addition, to determine if NPR-C expression is exclusively developmentally regulated, or if early delivery would also downregulate NPR-C, the effect of preterm delivery on the pulmonary epithelial expression of NPR-C was assessed in 126-day preterm lambs ventilated for 24 hours compared to age matched fetal lambs.
RESULTS: At 100 days gestation NPR-C was confined to cuboidal epithelial cells lining the developing airways. By 136 days NPR-C was identified in type 2 alveolar pneumocytes and Clara cells. By 3 days and 4 weeks after delivery at term a dramatic reduction in NPR-C receptor expression was seen in distal lung epithelium. In premature lambs delivered at 126 days and ventilated (by necessity) for 24 hours, there was a similar significant reduction in NPR-C expression in the pulmonary epithelium compared to 126 day fetal lambs.
CONCLUSIONS: A dramatic reduction of NPR-C receptor expression is observed in the alveolar and bronchial epithelium in both term and significantly preterm lambs soon after birth. We speculate that NPR-C may have a role in modulating epithelial-mediated airway fluid clearance and surfactant secretion at birth.

169 Presentation Time 10:30 AM Fellow

Inhaled Carbon Monoxide Preserves Alveolarization and Improves Pulmonary Mechanics in Neonatal Murine Hyperoxia-Induced Lung Injury

Veniamin Ratner, Serguei V. Kishkurno, Maxim Fedarau, Richard A. Polin, David J. Pinsky, Vadim S. Ten. Pediatrics, Columbia University, New York, NY; Medicine, University of Michigan, Ann-Arbor, MI.
BACKGROUND: Low-dose inhaled carbon monoxide(CO) was shown to be protective against hyperoxia-induced lung injury in adult rats.
OBJECTIVE: To determine whether inhaled CO prevents/attenuates O_2 mediated lung injury in neonatal mice.
DESIGN/METHODS: C57bl/6J neonatal mice were exposed to 75% O_2 for 4 wks to induce lung injury(O_2LI). Beginning with the 2nd week of O_2 exposure, a subgroup received continuous CO inhalation(250 ppm) until the end of O_2 exposure (O_2LI+CO). Pulmonary function testing (PFT) followed by pulmonary histology was performed in naive and experimental mice. A separate cohort of mice with initially unknown heme-oxygenase-1 (HO-1) genotype was subjected to O_2LI. Outcome measures: Mortality within 4 wks of experiment, alveolarization (# of alveolar sacs/mm^2; radial alveolar count [RAC]) and PFT were compared between O_2LI, O_2LI+CO and age/strain-matched naive mice. Given that HO-1 mice were outbred from a different strain (129/J) HO-/- and HO+/+ mice were compared to each other.
RESULTS: O_2LI and O_2LI+CO mice exhibited a similar mortality. However, mortality was significantly higher (chi-square p=0.04) among HO-1 -/- compared to HO+/+ mice. Survived O_2LI HO-1-/- mice showed significantly higher ($p<0.01$) pulmonary resistance compared to O2LI HO+/+. Lung compliance (Cd), minute ventilation (MV/g), respiratory rates (RR), and lung histology were significantly altered in O_2LI mice compared not only to naive, but those treated with CO.

Mice	N	Cd (ml/cm H2O)	MV/g	RR	# Alv/mm2	RAC
Naive	**8**	.13±.06	1.05±.15	179±26	38.8±9.9	18±1
O2LI	11	.06±.04*	0.62±.15*	100±40*	22.7±2.8*	11±3*
O2 LI+CO	5	.10±.05	1.14±.22**	166±20**	31.4±4.7**	16±3**

*p < 0.01 compare to Naive mice, ** p < 0.05 compare to O2LI mice
CO-mediated PFT improvement significantly correlated (r=0.66. p=0.001) with preserved alveolarization and decreased elastin deposition.
CONCLUSIONS: Low dose inhaled CO during oxygen exposure significantly improves pulmonary mechanics, preserves alveolarization and decreases elastin deposition in developing murine lungs. Genetic deficiency of HO-1, the CO producing enzyme, increases mortality and worsens pulmonary mechanics in neonatal mice with hyperoxia-induced lung injury.
Partialy funded by Advancing Newborn Medicine Fellowship Grant , sponsored by Forest Pharmaceuticals

170 Presentation Time 11:00 AM Fellow

Effects of Surfactant (SF)-Augmented CPAP Therapy on Lung Structure and Inflammation

U. S. Nawab, T. Irwin-Sherman, S. M. Touch, T. J. Blackson, G. Zhu, T. H. Shaffer, M. R. Wolfson. Neonatol., Thomas Jefferson Univ, Phila., PA; Nemours Lung Ct, AI duPont Child Hosp, Wilm, DE; Physiol & Peds, Temple Univ Sch of Med, Phila, PA.
BACKGROUND: Failure to respond to CPAP can lead to intubation and SF treatment. While practice varies, intubation and pressure are required to alveolarize SF. Inadequate SF distribution and/or overdistension may lead to lung injury. Interaction between CPAP and SF effects on lung structure and inflammatory profiles has not been well described.
OBJECTIVE: To test the hypothesis that effects of SF (Survanta 100 mg/kg)-augmented CPAP on lung structure and inflammation are CPAP dose-dependent.
DESIGN/METHODS: Spontaneously breathing piglets (2.40 ± 0.70 kg) were anesthetized, instrumented, supported with CPAP 5 cm H_2O, injured (oleic acid: 0.08 mL/kg), and randomized to CPAP 2 or 5 alone (C2,C5) or with SF (C2S,C5S). F_IO_2 was titrated to SaO_2 95 ± 5% for 4 hrs. Arterial gases were measured hrly. Lung myeloperoxidase (MPO), IL8 and histomorphometry [EI=Expansion Index; EU=Exchange Unit], and interrelationships between 1 & 4hr time-averaged gas exchange/O_2 requirements, structure and inflammatory indices were assessed.
RESULTS: X ± SE; $p < 0.05$ vs C2 = *; C2S = ¥; C5 = §

Gr	n	P_aO_2 (mmHg)	$PaCO_2$ (mmHg)	MPO (U/gm)	IL 8 (pg/gm)	EI (%)	#EU (#)
C2	6	179 ± 27	39.3 ± 4.1	2.06 ± 0.19	5177 ± 879	20 ±0.09	579 ± 35
C2S	8	94 ± 12*	40.5 ±3.7§	2.70 ± 0.01*	5655 ± 349§	29 ± 1.7*	848 ± 20*
C5	8	180 ± 30	48.7 ± 2.9*	1.29 ± 0.09*¥	3397 ± 878*	28 ± 5.6*	783 ± 37*
C5S	8	129 ± 20	43.1 ± 1.9	2.00 ± 0.16§¥	4041 ± 814¥	33 ± 1.4*	811 ± 60*

There were no significant group differences in time-averaged F_IO_2 (0.73±0.02 SE). As a function of CPAP, EI, # open EU/field, and $PaCO_2$ increased; lung IL8 and MPO decreased. With SF, MPO increased and PaO_2 decreased; IL8 increased at C5 and EI increased at C2. CPAP and SF interaction resulted in lower MPO and IL8 at C5 vs C2S and greater EI at C5S vs C2. MPO was significantly and inversely related to EI with CPAP but not SF.
CONCLUSIONS: All groups could be weaned from F_IO_2 of 1 to 0.54 +/- 0.02 by 4 hrs, while maintaining SaO_2 > 90%. CPAP improved lung expansion and resulted in less inflammation. With equivalent expansion and SaO_2, inflammation increased and PaO_2 decreased following SF, notably at CPAP 2. It is unclear whether differences in inflammation are related to SF, delivery method, or CPAP level. Longer-term pre-clinical studies are required to elucidate mechanisms for these differences.
Nemours Found, Pa Dept Health

171 Presentation Time 11:15 AM Fellow

Gene Expression Profiling of Human Lung Type II Cell Differentiation

Kelly C. Wade, Linda W. Gonzales, John Gonzales, Susan H. Guttentag, Philip L. Ballard. Department of Pediatrics, Neonatology, Univ Penn and Children's Hospital of Philadelphia, Philadelphia, PA.
BACKGROUND: Differentiation of alveolar type II cells is a critical event in lung maturation. However, genes characteristic of mature type II cells and those regulating differentiation remain largely unknown.
OBJECTIVE: To identify genes up-regulated during hormone-induced differentiation of human lung epithelial cells *in vitro*.
DESIGN/METHODS: Enriched epithelial cells were isolated from 14-20 wk gestation lungs and cultured 4-72 h in serum-free medium alone or with dexamethasone and cAMP plus isobutylmethylxanthine (DCI) to induce type II cell differentiation. Gene expression was analyzed in 3 experiments with 6 lungs using 14 Affymetrix U133A chips and results were analyzed using Affymetrix Microarray Suite 5.0. Self organizing maps (SOM) of temporally related gene clusters were generated using GeneCluster 1.0. Gene expression was also examined by real time RT PCR and immunoblotting..
RESULTS: Gene expression profiling of differentiated cells compared to control cells indicated mRNAs for 399 proteins of known function and 98 hypothetical proteins up-regulated more than 2-fold. We further evaluated 2 clusters of genes identified by SOM analysis of time course data. One cluster contained 13 known genes that were slowly induced to high levels (>20 fold) at 72 h. This cluster included surfactant-related genes (SP-A/B/C, pepsinogen C, and lipoprotein lipase), regulatory molecules (Wnt inhibitory factor-1, hypoxia inducible factor 3α , nuclear receptor 4A2, and IGF2), an ion transporter (epithelial sodium channel-α), metabolic enzymes (monoamine oxidase, aldehyde dehydrogenase, alcohol

dehydrogenase) and the tight junction protein claudin 18. Up-regulation of these genes was confirmed by RT PCR. A second cluster contained early response genes that were maximally induced (2-10 fold) at early (4-8 h) time points. 4 members of this group (TTF-1, C/EBP-β /δ, and FOXA2) have known roles in type II cell differentiation, and induction was confirmed by immunoblotting. Other members are transcriptional inhibitors (ID 1/3) and regulators (DSIPI, TBX3, TCF8, SOX11).
CONCLUSIONS: Hormone-induced differentiation of type II cells involves up-regulation, with a variety of temporal patterns, of genes representing approximately 2% of the human genome. We speculate that early responding transcription regulatory factors are involved in the induction of a subset of slower responding genes that characterize the mature type II cell phenotype.

172 Presentation Time 11:30 AM — Fellow

SP-A Deficient Mice Exhibit a Biphasic Response to Bleomycin Induced Lung Injury

Jennifer H. Kaplan, John A. Casey, Yaniv Tomer, Francis R. Poulain, Samuel Hawgood, Michael F. Beers. Division of Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Pulmonary and Critical Care Division, University of Pennsylvania School of Medicine, Philadelphia, PA; Division of Neonatology, University of California, Davis, CA; Department of Pediatrics, University of California, San Francisco, CA. (Sponsored by Susan Guttentag)
BACKGROUND: Surfactant protein A (SP-A) is a 36-kDa member of the collectin family with well-documented antimicrobial function. However, SP-A's role in lung inflammation is less clear with *in vitro* studies suggesting either pro- or anti-inflammatory effects depending in part on the choice of model.
OBJECTIVE: To evaluate the role of SP-A in modulating inflammatory responses to a non-infectious pulmonary challenge *in vivo*, intra-tracheal bleomycin (ITB) or saline were administered to 7-9-week old C57/BL6 SP-A knockout (–/–) mice and syngeneic wild type (WT) controls.
RESULTS: SP-A (–/–) mice receiving ITB were protected from early mortality compared with WT mice. Kaplan Meier analysis demonstrated a ten-day survival of 100% for SP-A (–/–) mice receiving 3u/kg bleomycin vs. 73% survival for WT mice ($p<0.05$ by log rank analysis). In contrast, SP-D (–/–) mice receiving 2 u/kg ITB had 100% mortality by day 10 indicating early protection was collectin specific. At later time points following ITB (14-21 days), SP-A (–/–) mice experienced increased mortality (60% survival at 21 days) with no additional deaths in WT mice (73% survival at 21 days). By 21 days, when compared to all other groups, ITB SP-A (–/–) survivors exhibited greater weight loss and had histopathological evidence of increased lung fibrosis.
CONCLUSIONS: These data suggest that *in vivo* SP-A can impart both pro- and anti-inflammatory effects depending upon the underlying state of tissue activation.

Neurology Platform Session

Sunday, March 28 9:45am–12:00pm Putnam

173 Presentation Time 9:45 AM

C1q Gene-Deleted Neonatal (but Not Adult) Mice Are Protected Against Hypoxic-Ischemic Brain Injury

Vadim S. Ten, Sergei A. Sosunov, Sergei V. Kishkurno, Raymond J. Stark, Marina Botto, E. Sander S. Connoly, Jr., David J. Pinsky. Pediatrics and Neurosurgery, Columbia University, New York, NY; Medicine, University of Michigan, Ann Arbor, MI; Medicine, Royal Cllege of Medicine, London, United Kingdom. (Sponsored by Richard A. Polin)
BACKGROUND: We have reported that genetic deficiency of C1q(C1q-/-) is neuroprotective against HI in neonatal mice. However, in adult mice subjected to HI, C1q-/- did not result in neuroprotection.
OBJECTIVE: To determine whether neuroprotection observed in neonatal C1q-/- is blunted in adult C1q-/- mice secondary to maturation of complement pathways.
DESIGN/METHODS: HI was produced in neonatal (P-7), and adult (6-7wks) C57bl wild-type(WT) and C1q-/- mice by right carotid artery ligation followed by exposure to 8% O2 at 37C for 20(neonates) and 40(adult) minutes. Neuroprotection was defined by cerebral infarct volume (assessed by TTC staining) and mortality (maternal cannibalism was excluded). At 24 hr following HI brain sections were evaluated for infarct volume and stained by Nissl as well as for presence of C1q and C3 components of complement and microtubuli associated protein-2.
RESULTS: At 24hr following HI insult neonatal C1q-/- mice exhibited significantly decreased mortality (chi-square p=0.02) and cerebral infarct volume (p=0.0005) compare to WT pups. In sharp contrast adult C1q-/- were not protected (similar infarct volumes and mortality) compared to their WT counterparts. In WT mice of both neonatal and adult age, cerebral sections revealed significant immunostaining for C1q protein, which co-localized with the cytoplasm of nonviable neurons (as expected, sections from C1q-/- mice did not exhibit C1q immunoreactivity). C3, the first downstream common component of complement activation, was increased in the infarcted cerebral tissue of WT mice of both age groups. C3 was also increased in the affected hemisphere of adult C1q-/- mice, but remained unchanged in neonatal mice

	Neonatal		Adult	
Outcome	WT(n=20)	C1q-/-(n=16)	WT(n=4)	C1q-/-(n=4)
Mortality (%)	16.6	5.3*	37.5	37.5
Infarct volume (%)	55±5.4	22±6.1 **	29±7	32±7.9
C1q in brain (+)	+++	-	+++	-
C3 in brain (+)	+++	+	+++	+++

*chi-square p = 0.02 **p = 0.0005. n - is indicated for infarct volume = mean ± SEM
CONCLUSIONS: Genetic deletion of C1q offers neuroprotection against HI brain injury only in neonatal, but not in adult mice. Underdevelopment of the lectin or alternative pathways of complement in neonatal mice may explain the resistance of the developing brain to HI insult. Neuroprotection was lost in adult C1q-/- mice in which complement can be activated by non-classical pathways.

174 Presentation Time 10:00 AM

Multiple Periods of Hypoxic Preconditioning Prevents Hypoxic-Ischemic Energy Depletion and Expands Protection in Immature Rat Brain

Susan J. Vannucci, Robert M. Brucklacher, Robert C. Vannucci. Pediatrics, Columbia University/Children's Hospital of NY, New York, NY; Pediatrics, Hershey Medical Center/Penn State University, Hershey, PA.
BACKGROUND: In the immature rat, a period of systemic hypoxia provides preconditioning tolerance to a subsequent hypoxic-ischemic (HI) insult. We recently demonstrated PC-induced increase in brain glycogen stores which delays the depeletion of high energy phosphates during HI and prevents the secondary energy failure at 24 hrs of reperfusion.
OBJECTIVE: The purpose of these studies was to determine whether multiple periods of hypoxic preconditioning (PC) would further increase brain glycogen and provide greater neuroprotection.
DESIGN/METHODS: Wistar rats were culled to 10 pups/litter on the day of birth (P1). Each PC consisted of 3 hrs of 8% Oxygen/bal Nitrogen. Grp I: 1 PC on P5; Grp II : 1 PC on P5 & a PC on P6; Grp III : 1 PC on P5, 2 PC on P6, 12 hrs apart. Pups were subjected to 90 minutes of HI on P7. Brains were frozen for analysis pre HI, post HI (0 reperfusion), and at 24 hrs. Frozen brain from each hemisphere was processed for glycogen extraction/analysis or by perchloric acid. Metabolites were determined by enzymatic analysis and fluorometry.
RESULTS: Brain glycogen was increased in all three PC groups,with no difference among groups. Brain glucose increased in each PC group with no changes in blood glucose. Br/Bl ratios in II and III were elevated prior to HI, relative to control and I. ATP/PCr levels were partially depleted by 90 min of H/I in I but were fully recovered by 24 hours. In II, 5/14 pups had ATP/PCr depletion; again all recovered at 24 hrs. All pups in III tolerated 90 min of HI with full recovery at 24 hours.
CONCLUSIONS: This study demonstrates that brain glycogen reserves are not increased by multiple periods of preconditioning, but brain glucose is. The associated increase in brain/blood glucose ratio suggests a shift in the glucose transport capacity, which is normally quite low at P7 and limiting to cerebral glucose uptake and utilization during HI. In addition, even a 48 hour delay between the PC stimulus and HI provides a degree of protection and prevention of the secondary energy failure, whereas 3 periods of PC during the 48 hours before HI provides significant protection to 100 % of the animals. Although the mechanisms of preconditioning are complex, it is important to appreciate the extent to which the enhancement of endogenous energy reserves contributes to the observed protection.

175 Presentation Time 10:15 AM — House Officer

Renal Effects of Topiramate in Children With Seizures

Sarah M. Barnett, Anthony H. Jackson, Jane L. Garb, Herbert E. Gilmore, Beth A. Rosen, Dina H. Kornblau, Gregory L. Braden. Baystate Medical Center Children's Hospital, Springfield, MA; Tufts University School of Medicine, Boston, MA. (Sponsored by Edward O. Reiter)
BACKGROUND: Topiramate (TPM) effectively treats multiple types of seizures in children. Among its adverse effects is nephrolithiasis, estimated to occur in 1.5% of adults treated with TPM. However, the frequency of nephrolithiasis in *children* on TPM is unknown, and little is known about the frequency of nephrocalcinosis in children or adults.
OBJECTIVE: To investigate the link between TPM therapy and nephrocalcinosis/ nephrolithiasis, we posed these questions: 1) What is the incidence of nephrocalcinosis/ nephrolithiasis among a cohort of children on TPM? 2)Is hypercalciuria an effect of TPM therapy, or is it pre-existent in children with seizure disorders? 3) How will TPM affect serum bicarbonate levels and urine calcium/creatinine (Ca/Cr) ratios?
DESIGN/METHODS: Retrospective review of 40 consecutive children with epilepsy who were started on TPM between 1/1997 and 2/2003 and followed for a mean of 36 months with periodic measurements of serum electrolytes, urinary Ca/Cr ratios, and renal ultrasonography.
RESULTS: Nine of forty children (22.5%) had hypercalciuria, defined as urinary Ca/Cr ratio greater than or equal to 0.21, before TPM treatment began. Of these nine, three developed nephrocalcinosis and/or nephrolithiasis as demonstrated on ultrasonography; a fourth child without baseline data also developed nephrocalcinosis. There was a significant increase in mean urinary Ca/Cr ratio over time for all forty patients ($p<0.001$), as well as a significant decrease in mean serum bicarbonate over time ($p<0.01$). When the hypercalciuric group (n=9) was compared to the group with normal calcium excretion (n=14), the hypercalciuric group showed both a greater increase in the rate of change in urinary Ca/Cr ratios ($p<0.001$) and a greater decrease in the rate of change in serum bicarbonate levels ($p<0.05$).
CONCLUSIONS: Nephrocalcinosis and/or nephrolithiasis occurred in 10% (4/40) of this cohort: this is substantially higher than the 1.5% rate reported for adults on TPM. Pre-existent hypercalciuria was common in this population, and it appears to be a risk factor for nephrocalcinosis and/or nephrolithiasis. Our data demonstrated statistically-significant decreases in serum bicarbonate and increases in mean urinary Ca/Cr ratios over time. Before starting TPM therapy, children need baseline assessment of calcium excretion: hypercalciuric children merit careful renal surveillance during treatment with TPM.

176 Presentation Time 10:30 AM — Fellow

Delayed Rolling Over Skill Associated With Deformational Plagiocephaly

Dakshayani R. Guttal, Rami R. Grossman, Susana Rapaport. Pediatrics, Flushing Hospital Medical Center, Flushing, NY. (Sponsored by Susana Rapaport)
BACKGROUND: In June 1992 , the American Academy of Pediatrics started the back to sleep campaign.This campaign led to a reported increase in the incidence of infants with deformational plagiocephaly.This study is done to test the hypothesis that there is a relationship between deformational plagiocephaly and delay in rolling over skill.
This association can be partially explained by the fact that these infants with occipital flattening could have an exaggerated asymmetric tonic neck reflex which is known to prevent rolling over.
OBJECTIVE: To determine the relationship between delay in the skill of rolling over and occipital plagiocephaly as compared to the normal.
DESIGN/METHODS: This prospective study was conducted from September 2000 to November 2002. All infants with occipital plagiocephaly (N=41) and no other neurological deficits were selected for the study from our neurology clinic/office. A control group(N=42) matched for age and gender were selected from the Well Baby Clinic. DDST was administered to all these infants at every visit (q2-3 months). Each infant was followed for delay in rolling over skill until 18 months of age. Other variables like age sex ethnicity and confounding factors like type of delivery and birth weight were included in this study.
RESULTS: We had a mixed population, the Hispanics being the most and the African Americans being the least. Age of rolling over cases vs controls.

	<5mon	5-8mon	8mon
Cases	2	11	28
Controls	39	1	2

X2 = 0.001. There is no statistically significant difference between age of rolling over vs. birth weight and age of rolling over vs. type of delivery.
CONCLUSIONS: This study proves that there is a definite relation between delay in rolling over skill and deformational plagiocephaly and suggests not to be concerned about isolated delay in rolling over skill in an infant with deformational plagiocephaly.
Discussion- Deformational plagiocephaly can be easily prevented by changing position of the baby while sleeping. Infants can be kept prone when awake and while under supervision. Use of special pillows with beads or mustard seeds for the baby can prevent plagiocephaly. Special kind of helmets are being used to prevent or treat plagiocephaly

177 Presentation Time 11:00 AM — Fellow

Dietary Factors Influence Catecholamine Synthesis Via Second Messenger Pathways Converging on the CAMP-Response Element Binding Protein (CREB)

Parul V. Shah, Bistra B. Nankova, Edmund F. LaGamma. Division of Newbron Medicine, Pediatrics, Westchester Medical Center - NY Medical College, Valhalla, NY.
BACKGROUND: Rapid maturation of peripheral sympathoadrenal transmitter levels and function occur at 7-10 postnatal days in humans and in rats. Once enteral feeding is started, colonization of the gut, fermentation of carbohydrates and production of short chain fatty acids occur. We hypothesize that SCFA/ butyrate may act as an exogenous signal in establishing neuronal phenotype & function. Previous work in our lab (Peds Res 53:113,2003) suggested that butyrate can regulate the expression of the tyrosine hydroxylase gene (TH; rate-limiting enzyme in catecholamine biosynthesis) *in vitro* by activation of cAMP second messenger- and Mitogen Activated Protein Kinase (MAPK)-systems. Both signaling cascades have been

shown to transactivate CREB (cyclic AMP response element binding protein). We hypothesize that butyrate affects neurotransmitter gene expression via CREB.
OBJECTIVE: To determine whether butyrate treatment result in increased phosphorylation of CREB; and whether specific inhibitors of MAPK and PKA pathways can prevent CREB phosphorylation and induction of neurotransmitter gene expression.
DESIGN/METHODS: Rat pheochromocytoma cells (PC12), treated with physiological concentrations of butyrate (1 mM) were used. The extent of CREB phosphorylation was examined by Western blot analyses. The involvement of PKA and MAP kinase pathway was tested by using specific inhibitors: dideoxyadenosine (ddA, 100 uM) and U0126 (10 uM) resp. TH mRNA levels were determined by Northern blot.
RESULTS: Butyrate treatment of PC12 cells induces rapid phosphorylation of CREB lasting ~60 minutes in western blots using a phospho-CREB specific antibody. When the same blots were re-probed with CREB specific antibody, no change in relative amount of CREB protein was observed. Pre-treatment with specific inhibitors (U0126 and /or ddA) abolished the accumulation of TH mRNA, phosphorylation of ERK1/2 and CREB phosphorylation induced by butyrate.
CONCLUSIONS: The effect of butyrate on catecholaminergic neurotransmitter synthesis is dependent on increased phosphorylation of CREB via a PKA/MAP kinase signal-transduction mechanism(s). Since CREB is implicated in the regulation of complex processes ranging from development to plasticity, to disease and memory, we speculate that a dietary-derived environmental signal (butyrate), a clinicians feeding practices and their use of antibiotics can each modulate these processes.

178 Presentation Time 11:15 AM

Maturational Switch in Gene Expression of Blood Brain Barrier (BBB) Nutrient Transporters

Katherine V. Biagas, Ichha Sethi, Susan J. Vannucci. Pediatrics, Columbia University, College of Physicians and Surgeons, New York, NY. (Sponsored by Charles L. Schleien)

BACKGROUND: Delivery of glucose and monocarboxylic acids across the microvessels of the BBB requires specific transporter proteins - the GLUT1 and MCT1 transporters, respectively. Previous studies support a post-natal increase in BBB GLUT1 mRNA and protein in association with a comparable decrease in MCT1. The mechanisms for coordinated regulation of these genes in the BBB are unknown.
OBJECTIVE: The present study was designed to generate pure fractions of BBB RNA for measurement of specific gene expression and to investigate age-related and gender-based differences in gene expression in rats.
DESIGN/METHODS: BBB microvessels were prepared from whole brain homogenates from post-natal (P) 15 and P 28 day old rats. Brains were pooled from 6-8 rats of each sex. Microvessels were isolated by centrifugation in 17% dextran and final filtration through 40 μm nylon mesh. cDNA was synthesized using random hexamers from total RNA, which was extracted using TRIZOL reagent with on-column isolation and DNase treatment. Quantitative RT-PCR was performed using detection with SYBR Green. Data were normalized for each run and duplicate experiments were performed.
RESULTS: 2.8 ± 1.4 (Mean ± SD) fold increase in GLUT1 expression was demonstrated with a concomitant 4.9 ± 2.2 fold decrease in MCT1 expression with development (P28 vs. P15 rats). Greater than 2-fold difference in GLUT1 expression was seen in P28 female rats as compared with their male counterparts. MCT1 expression was similar in male and female rats of both ages.
CONCLUSIONS: This is the first investigation to measure gene expression in isolated microvessels of the BBB. The data confirm a maturational change in production of encoded mRNA for GLUT1 and MCT1 and suggests the possibility of transcriptional control of this process. This is also the first investigation of gender-based differences in gene expression of brain nutrient transporters. The difference in GLUT1 expression suggests a possible role of sex hormones in the control of such expression. Finally, this study establishes a system in which to study gene expression and regulation of the mammalian BBB under conditions of normal development and superimposed pathologic processes.
This work was supported by HD 30704 (SJV).

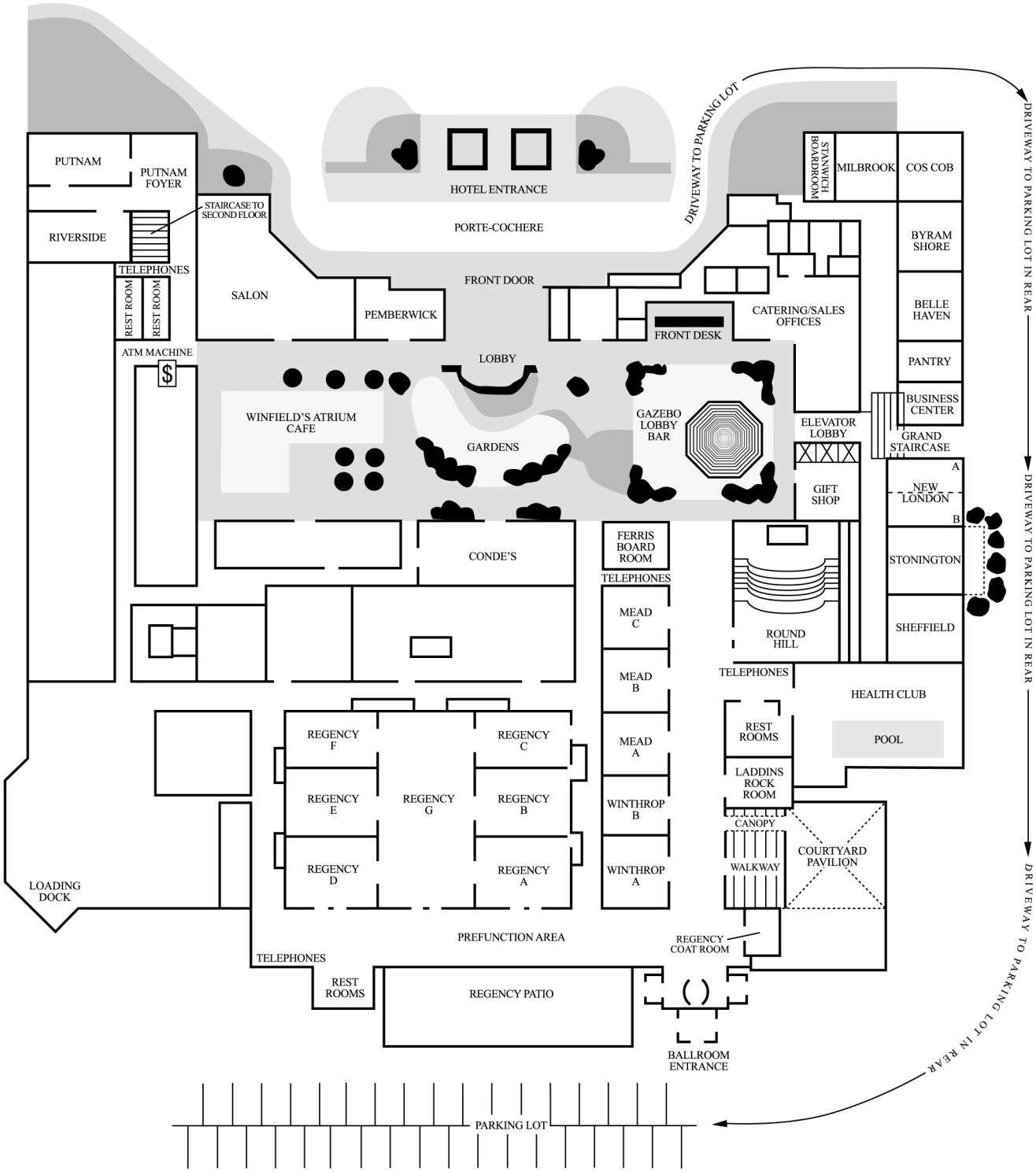
Index numerals refer to the abstract number.

Index numerals refer to the abstract number.

Index numerals refer to the abstract number.

Hyatt Regency Greenwich

1800 East Putnam Avenue
Old Greenwich, CT 06870
Phone: (203) 637 1234
Fax: (203) 637 2940



Rashmin C. Savani, M.B.Ch.B. *(Secretary-Treasurer)*
The University of Pennsylvania School of Medicine
Room 416F, Abramson Research Center
The Children's Hospital of Philadelphia
3516 Civic Center Boulevard
Philadelphia, PA 19104-4318
Phone: (215)590-5507
Email: Rsavani@mail.med.upenn.edu
URL: www.aps-spr.org/Regional_Societies/ESPR