Eastern Society for Pediatric Research 17th Annual Meeting

March 4–6, 2005
Hyatt Regency — Old Greenwich, CT

PROGRAM GUIDE

In cooperation with The Children's Hospital of Philadelphia

The Children's Hospital *of* Philadelphia®
A pediatric healthcare network

New for 2005

We are pleased to announce that we have engaged the services of The Children's Hospital of Philadelphia to run our 2005 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 Children's Hospital of Philadelphia will further enhance our meeting. This has already consisted of a secure website for membership/registration payments, timely announcements, enhanced room booking services and, for the meeting, will include improved informatics enabling presenters to load their presentations at a central station in advance.

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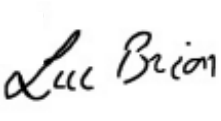
THE EASTERN SOCIETY FOR PEDIATRIC RESEARCH

Welcome to the 17th Annual Meeting!

Dear Colleagues:

Welcome to the 17th Annual Meeting of the Eastern Society for Pediatric Research (Eastern SPR)! 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 Eastern SPR Planning Committee and the other members of the Eastern SPR Council for their help. We appreciate the meeting planning and provision of CME accreditation by The Children's Hospital of Philadelphia, in particular Ann Hagan. 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 Eastern SPR 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.



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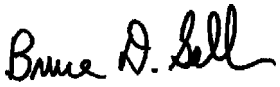

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David Valle, M.D.
Johns Hopkins University
Baltimore, MA

Meeting Services and CME Accreditation

Registration and CME Desk Hours

Registration will be held in the Round Hill Foyer of the Hyatt Regency. Registration hours are as follows:

Friday, March 4	4:30pm – 7:00pm
Saturday, March 5	7:30am – 7:00pm
Sunday, March 6	7:30am – 1:00pm

Abstract Publication

All abstracts being presented at the 2005 Eastern Society for Pediatric Research Annual Meeting are printed in this Program Guide, beginning on page 12.

Audio/Visual Information IMPORTANT!

All oral 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.

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 (i.e., Friday evening for Saturday morning presentations, Saturday morning for Saturday afternoon presentations, and Saturday afternoon for Sunday morning presentations). Please take your CD-ROM, ZIP drive or flash memory to the Registration Area located in the Foyer of the Round Hill Conference Room.

Business Center

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

CME Accreditation REQUIRED!

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 Children's Hospital of Philadelphia and the Eastern Society for Pediatric Research. The Children's Hospital of Philadelphia is accredited by the ACCME to provide continuing medical education for physicians.

The Children's Hospital of Philadelphia 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 hours of credit that he or she actually spent in the educational activity.

Disclosure

In accordance with Accreditation Council for Continuing Medical Education requirements on disclosure, information about relationships or presenters with commercial interests (if any) will be included in materials distributed in the Annual Meeting Registration Area.

Procedures for CME Credit

Physicians wishing to receive CME credits will need to report to the Annual Meeting Registration Area located in the Round Hill Foyer and sign the sign-in sheets. Those wishing credits for both Saturday and Sunday must sign in each day. The Poster Sessions are not designated for CME Credits.

CME Certificates will be mailed from the Continuing Medical Education Department at The Children's Hospital of Philadelphia within three to four weeks after the Annual Meeting concludes.

Sponsorship Honor Roll

The ESPR expresses its appreciation to all of our sponsors of the 2005 ESPR Annual Meeting

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Thomas R. Welch, M.D.
SUNY Upstate Medical University, Syracuse, NY

Friday, March 4

6:00pm–7:30pm

Poster Session I

Conde's

Saturday, March 5

8:15am–10:45am

Developmental Biology	Endocrinology	General Pediatrics I: Environmental Health	Hematology and Oncology	Neonatology I: Clinical	Pulmonary Medicine
FEATURED TALK Evolution, Diet and Human Developmental Biology	FEATURED TALK P53 and the IGF Axis		FEATURED TALK What Can the Pathophysiology of Alzheimer's Disease Teach Us About Chemotherapy-Induced Neurotoxicity?		FEATURED TALK Developmental Mechanisms To Regulate Inflammatory Cell Migration into the Lung
Winthrop A/B	**Stonington**	**Mead A**	**Mead C**	**Sheffield**	**Mead B**

11:00am–12:00pm

Plenary Session I

Announcement of the Mentor of the Year Award

Plenary Lecture: Postnatal Steroids — What Do the Data Really Show? ~ Ian Gross

Round Hill

12:00pm–1:00pm

Lunch with the Professors Educational Program	ESPR Business Meeting
Conde's	**Round Hill**

1:15pm–3:45pm

Plenary Session II

Plenary Lecture: Genetics, Genomics and the Promise of Individual Medicine ~ David Valle

Young Investigator Awards Finalists Presentations: Trainees and Faculty

Round Hill

4:00pm–6:00pm

Adolescent Medicine	Cardiac and Neonatal Outcomes Research	Emergency Medicine	General Pediatrics II: Quality of Care and Medical Education	Genetics	Neonatology II: Translational Research
FEATURED TALK Connect to Protect: A Population Level Adolescent HIV Prevention Trial					FEATURED TALK Neonatal Networks and Clinical Research
Mead C	**Winthrop A/B**	**Mead B**	**Mead A**	**Stonington**	**Sheffield**

6:00pm–7:30pm

Poster Session II

Conde's

Sunday, March 6

8:30am–9:30am

Plenary Session III

Announcement of the Young Investigator Awards

Plenary Lecture: Ins and Outs of Iron Transport ~ Nancy Andrews

Round Hill

9:45am–12:15pm

Cardiopulmonary Development	General Pediatrics III	Infectious Diseases	Neonatology III: Animal Models in Neonatology Research	Neurobiology
FEATURED TALK Development of Cardiac Left–Right Asymmetry	FEATURED TALK The Relationship Between Maternal Education and Child Health Status: Evidence from Immunization Rates	FEATURED TALK Investigation of HIV Pathophysiology and Novel HIV Therapeutics Using Transgenic Mouse Models	FEATURED TALK Blood–Brain Barrier: Structure, Function, Development and Perinatal Medicine	FEATURED TALK Stroke in Infants and Children: Progress and Challenges
Mead B	**Mead A**	**Mead C**	**Sheffield**	**Stonington**

6:00pm–7:30pm Conde's

Poster Session I

1 Association Between Marijuana Use and Asthma Severity in Adolescents
Sara B. Levine, Philip O. Ozuah. — *Abstract 1*

2 Rituximab in Treatment-Resistant Childhood-Onset Systemic Lupus Erythematosus (cSLE)
Deborah M. Levy, Philip J. Kahn, Lisa F. Imundo. — *Abstract 2*

3 Adverse Event Rates for Pediatric Cardiac Catheterization Procedures: Identification of High-Risk Populations
Lisa Bergersen, Alan Nugent, John F. Keane, Kimberlee Gauvreau, James E. Lock, Kathy J. Jenkins. — *Abstract 3*

4 Serum ß-Hydroxybutyrate Level Declines After Resuscitation in a Model of Pediatric Asphyxial Cardiac Arrest
Sandeep Gangadharan, George Ofori-Amanfo, Charles L. Schleien, Susan Vannucci. — *Abstract 4*

5 Susceptibility of Heme Oxygenase-1 Protein to Oxidation by Hemin
Guang Yang, Karen Szczepanski, Phyllis A. Dennery.— *Abstract 5*

6 The Role of Complement Activation in Preterm Labor Placentas
R. Markowitz, L. Bonifacio, A. Petrova, S. Han, B. Weinberger, D. Laskin, N. Hanna. — *Abstract 6*

7 Frequency of Gastrointestinal Disorders and Family History of Autoimmune Disease in Children with Autistic Spectrum Disorders and Controls
Maria R. Valicenti-McDermott, Kathryn McVicar, Herbert Cohen, Barry Wershil, Isabelle Rapin, Shlomo Shinnar. — *Abstract 7*

8 Characteristics of Toddlers with Autistic Spectrum Disorders Screened from High Risk and Low Risk Settings
Thyde M. Dumont-Mathieu, Jamie Kleinman, Deborah Fein. — *Abstract 8*

9 Predictors of Possession of a Carbon Monoxide Alarm in a Urban, Underserved, Low-Income, Pediatric Patient Population
Deborah M. Lopez, Kirsten Roberts-Butelman, Ellen J. Silver. — *Abstract 9*

10 Placebo Controlled Trials Are Well Received by Parents in Pediatric Research Regardless of Outcome
Nader N. Youssef, Maria Perez, Eric Lazar, Joel Rosh. — *Abstract 10*

11 Variation in Management of Common Inpatient Pediatric Illnesses: Hospitalists and Community Pediatricians
Patrick H. Conway, Christopher P. Landrigan, Sarah Edwards. — *Abstract 11*

12 Predictors of Multiple Pediatric Asthma Hospitalizations
Laura Dattner, Philip O. Ozuah. — *Abstract 12*

13 Predictors of Early Readmission for Asthma in Inner-City Children
Marina Reznik, Philip O. Ozuah. — *Abstract 13*

14 Knowldege of the Toxicity of Elemental Mercury in an Inner City Population
Jana E. Romm, Philip O. Ozuah. — *Abstract 14*

15 The Environment in Pediatric Practice: A Pilot Study of New York Pediatricians' Attitudes, Beliefs and Practices for Children's Environmental Health
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16 Parental Health Literacy: Can Parents Really Dose Liquid Medication Correctly?
Sarah Lo, Iman Sharif, Philip O. Ozuah. — *Abstract 16*

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Miriam Schechter, Robin Goldman, Andrew D. Racine. — *Abstract 20*

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Ramesh Vidavalur, Hussain Naveed, Barker Marta. — *Abstract 21*

22 The Predictive Ability of Predischarge End Tidal Carbon Monoxide (ETCOc) for Hyperbilirubinemia in Term and near Term Infants
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Scott A. Lorch, Anna M. Hibbs, Xianqun Luan, Phillip L. Ballard, Roberta A. Ballard, Jeffrey D. Merrill. — *Abstract 27*

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Aimee M. Barton, Kabir Abubakar, Jennifer Berg, Martin Keszler. — *Abstract 28*

29 Interaction of HO-1 with Cellular Proteins
Sean Levy, Qing Lin, Guang Yang, Shawndra Woodard, Phyllis Dennery. — *Abstract 29*

30 Sedation for Neurophysiology Tests
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31 Variations in IRB Interpretation of the Assent Requirement in Two Pediatric Placebo-Controlled Randomized Trials
K. Sarah Hoehn, Michael Kimberly, Chris Feudtner, Robert M. Nelson, Mark Schreiner. — *Abstract 31*

32 Scr Kinase Activation of the NAD(P)H Oxidase Mediates Ang II – Dependent Increase in Nitric Oxide Synthase Protein Expression in BPAEC
Xinmei Li, Susana Rapaport, Susan C. Olson, Michael S. Wolin. — *Abstract 32*

8:15am–10:45am Winthrop A/B

Developmental Biology

Moderator: Lewis P. Rubin, Brown University, Providence, RI

8:15 An Environmental Signal, Butyrate, Regulates Tyrosine Hydroxylase Gene Expression Via a Novel Promoter Element
Pranav Patel, Bistra Nankova, Kavitha Krishnan, Edmund LaGamma. — *Abstract 33*

8:30 Role of Antibiotics on the Production of Gut Derived Short Chain Fatty Acid (SCFA) and Its Effects on the Neurotransmitter Gene Expression in a Newborn Rat Model
Lawrence K. Fordjour, Pradeep V. Mally, Jie Xu, Anna-Maria Curatola, Karen Hendricks-Munoz. — *Abstract 34*

8:45 RNAi Screen for Shh Signaling Pathway Components in Mouse
Ting-Yi Lin, Steven Vokes, Andrew P. McMahon. — *Abstract 35*

9:00 The Effect of Hyperoxia on Reactive Oxygen Species (ROS) in Petrosal Ganglion Neurons in Organotypic Slice Culture
D. J. Kwak, S. D. Kwak, E. B. Gauda. — *Abstract 36*

9:15 Differential Effects of Androgen on ErbB Receptor and PLCg Expression and Phosphorylation in Fetal Rat Type II Cells
Sujatha M. Ramadurai, Soujanya L. Rallabandi, Lucia B. Pham, MaryAnn V. Volpe, Heber C. Nielsen. — *Abstract 37*

9:30 Break

9:45 Mechanism of SP-A-Stimulated Macrophage Chemotaxis: Role of TLR2, TGFß, RHAMM and Hyaluronan
Joseph P. Foley, Aisha Zaman, Theresa M. McDevitt, Akira Asari, Jo Rae Wright, Rashmin C. Savani. — *Abstract 38*

10:00 Surfactant Protein D: *S*-Nitrosylation and Effects on Inflammatory Functions
Changjiang Guo, Joseph P. Foley, Rashmin C. Savani, Andrew J. Gow. — *Abstract 39*

10:15 FEATURED TALK

Evolution, Diet and Human Developmental Biology
Lewis P. Rubin, Brown University, Providence, RI

8:15am–10:30am Stonington

Endocrinology

Moderator: Adda Grimberg, Children's Hospital of Philadelphia, Philadelphia, PA

8:15 Epigenetic Silencing of Pdx-1 in Growth Retarded (IUGR) Rats
Jun Park, Irina Suponitsky-Kroyer, Rebecca A. Simmons. — *Abstract 40*

8:30 Leptin Levels Decline Steadily During Prolonged Fasting in Lean Children
Lorraine E. Levitt Katz, Maire M. Abraham, Line Johansen, Abbas F. Jawad. — *Abstract 41*

8:45 Prevalence and Clinical Features of Double Diabetes in Children
Radhika Purushothaman, Neesha Ramchandani, Henry Anhalt, Svetlana Ten. — *Abstract 42*

9:00 Break

9:15 Reduced Caloric Intake in Early Life Prevents Obesity and Diabetes in Growth Retarded Rats
Irina Suponitsky-Kroyer, Hongshun Niu, Rebecca Simmons. — *Abstract 43*

9:30 Hyperglycemia in a Pediatric ICU
Alyssa J. Rake, Marybeth Roy, Christine McKiernan, Stephen Lieberman, Holley F. Allen. — *Abstract 44*

9:45 Late Rise of TSH in III Newborns Is Common and Not Dependent on Birthweight
Sharon J. Hyman, Fenella Greig, Arti Patel, Deborah Bowlby, Elizabeth Wallach, Ian Holzman, Robert Rapaport. — *Abstract 45*

10:00 FEATURED TALK

p53 and the IGF Axis
Adda Grimberg, Children's Hospital of Philadelphia, Philadelphia, PA

8:15am–10:15am Mead A

General Pediatrics I: Environmental Health

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

8:15 Social Costs of Mental Retardation Associated with Methylmercury Exposure in America
Leonardo Trasande, Philip J. Landrigan, Clyde Schechter, Karla A. Haynes. — *Abstract 46*

8:30 Awareness of Commercial Fish Mercury Advisory Among an Inner City Population
Jana E. Romm, Philip O. Ozuah. — *Abstract 47*

8:45 Sources of Fluoride Intake Among Inner City Children
Amy Lief, Philip O. Ozuah. — *Abstract 48*

9:00 Environmental Pollutants and Disease in New York State's Children: Estimates of Morbidity, Mortality and Costs for Lead Poisoning, Asthma, Cancer and Developmental Disabilities
Leonardo Trasande, Philip J. Landrigan, Clyde B. Schechter, Raphael Falk. — *Abstract 49*

9:15 Break

9:30 Does Media Exposure Impair School Performance?
Iman Sharif, James D. Sargent. — *Abstract 50*

9:45 Knowledge of Carbon Monoxide in a Low Income, Urban, Underserved Pediatric Patient Population
Deborah M. Lopez, Kirsten Roberts-Butelman, Ellen J. Silver. — *Abstract 51*

10:00 Interventions for Reduction of Diarrhea in Rural Guatemalan Children
Elizabeth A. Campbell, Cheryl D. Tierney, Barbara W. Stechenberg. — *Abstract 52*

8:15am–10:45am Mead C

Hematology and Oncology

Moderator: Peter Cole, University of Medicine and Dentistry of New Jersey, New Brunswick, NJ

8:15 Regulation of Mitogenic Signaling by Nerve Growth Factor (NGF) and Brain-Derived Neurotrophic Factor (BDNF) in Neuroblastoma Cells
Giselle L.S. Sholler, Charlotte M. Boney. — Abstract 53

8:30 Novel Chemotherapeutic Agent for High-Risk Neuroblastoma
Narasimha Swamy, Giselle L.S. Sholler. — Abstract 54

8:45 Nifurtimox Is Cytotoxic to Neuroblastoma Cells
Giselle L.S. Sholler, Boney Charlotte, Narashima Swamy. — *Abstract 55*

9:00 Break

9:15 Zinc Protoporphyrin IX Inhibits Cell Proliferation Via Suppression of Cyclin D1 Protein Synthesis in Hepatoma Cells
Zhi Wang, Guang Yang, Phyllis Dennery. — Abstract 56

9:30 Cranial Irradiation for Acute Lymphoblastic Leukemia (ALL): Effect on Growth and Endocrine Function in Indian Children
Umakanth A. Khatwa, P. S. Menon, Laxman S. Arya. — *Abstract 57*

9:45 Thrombopoietin and Platelet Response Following 10 vs 15 ml/kg of Transfused Platelets
Alex Kline, Amy Mackley, Scott Taylor, Steven McKenzie, David Paul. — *Abstract 58*

10:00 von Willebrand Factor Levels in Children with Sickle Cell Anemia
Dina M. DiMaggio, Iman Sharif, R. Labar, C. Bernstein, M. Mannix, M. Fagen, Paul T. Jubinsky. — *Abstract 59*

10:15 FEATURED TALK

What Can the Pathophysiology of Alzheimer's Disease Teach Us About Chemotherapy-Induced Neurotoxicity?
Peter Cole, University of Medicine and Dentistry of New Jersey, New Brunswick, NJ

8:15am–10:15am Sheffield

Neonatology I: Clinical

Moderator: Edmond LaGamma, New York Medical College, Westchester Medical Center, Valhalla, NY

8:15 Adequate First Week Protein and Calorie Intake Is Critical for 18 Month Developmental Outcomes in ELBW Infants
Rachel A. Vogt, Regina A. Gargus, Bonnie Stephens, Richard Tucker, Leslie McKinley, Martha Mance, Julie Nye, Betty R. Vohr. — *Abstract 60*

8:30 Intrauterine Infection Leads to the Delivery of Extremely Low Birth Weight Infants but Does Not Contribute to Their Death
Rita Verma, Cynthia Kaplan, Eugene Komaroff. — *Abstract 61*

8:45 Pulmonary Function and Weight Gain in Very Low Birth Weight (VLBW) Infants
A. M. Hibbs, S. A. Lorch, J. M. DiFiore, J. D. Merrill, E. C. Eichenwald, S. E. Courtney, A. Puri, R.A. Ballard, R. J. Martin. — *Abstract 62*

9:00 Break

9:15 The Role of Gastric and Tracheal Bacteria in Ventilator-Associated Pneumonia (VAP) in Premature Infants <1500gms
Mohamad T. El Abiad, Anne Marie Reynolds, Kirsten Blessing-Hanagan, Rita M. Ryan. — *Abstract 63*

9:30 Delayed Cord Clamping in Very Preterm Infants Reduces the Incidence of Intraventricular Hemorrhage (IVH) and Late Onset Sepsis (LOS)
Judith S. Mercer, Betty R. Vohr, William Oh. — *Abstract 64*

9:45 Vitamin A Supplementation in Preterm Infants: Vaccine Response
Vivien Carrion, Mark Ballow, Linda Duffy, Richard Browne. — *Abstract 65*

10:00 Familial and Genetic Susceptibility to Major Neonatal Morbidities in Premature Twins
Matthew Bizzarro, Anupama Shetty, Richard Ehrenkranz, Linda Ernst, Betty Vohr, Nirmala Desai, Henrietta Bada, Naveed Hussain, Ian Gross, Grier Page, Laura Ment, Jeffrey Gruen, Vineet Bhandari. — *Abstract 66*

8:15am–10:45am Mead B

Pulmonary Medicine

Moderator: Thomas B. Kinane, Harvard University, Boston, MA

8:15 Use of an Electronic Asthma Care Pathway Can Reduce Length of Stay and Improve Quality of Care
Pauline Fani, Beverley J. Sheares. — *Abstract 67*

8:30 Predictive Factors for the Use of Medications for Reactive Airways Disease (RAD) in Premature Infants After Hospital Discharge
Scott A. Lorch, Kelly C. Wade, Gabriel J. Escobar, Barbara Medoff-Cooper, Susan Bakewell-Sachs, Marla Gardner, John Greene, Orit Even-Shoshan, Jeffrey H. Silber. — *Abstract 68*

8:45 Asthma Educational Videoconferencing for Inner-City Immigrant Parents
Marina Reznik, Philip O. Ozuah. — *Abstract 69*

9:00 Improving Physician Prescription of Inhaled Corticosteroids for Asthma
Sandra F. Braganza, Iman Sharif, Philip O. Ozuah. — *Abstract 70*

9:15 Break

9:30 Pulmonary *Cryptococcus neoformans* Infection Increases Airway Responsiveness in a Rat Model
Jennifer A. Davis, Xuping Shao, Lewis P. Singer, David L. Goldman. — *Abstract 71*

9:45 Persistent Sodium Currents Play an Essential Role in the Ventilatory and Chemoreceptor Response to Hypoxia
E. Vincent Faustino, David Donnelly. — *Abstract 72*

10:00 HO-1 Regulates Postnatal Lung Alveolar Development
Sara Q. Lin, Rashmin C. Savani, Phyllis A. Dennery. — *Abstract 73*

10:15 FEATURED TALK

Developmental Mechanisms To Regulate Inflammatory Cell Migration into the Lung
Thomas B. Kinane, Harvard University, Boston, MA

Sponsored by an educational grant from INO Therapeutics, Inc.

11:00am–12:00pm Round Hill

PLENARY SESSION I

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

11:10 PLENARY LECTURE
Postnatal Steroids — What Do the Data Really Show?

Ian Gross
Yale University School of Medicine, New Haven, CT

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

12:00pm–1:00pm Round Hill

ESPR Business Meeting

12:00pm–1:00pm Conde's

Lunch with the Professors Educational Program

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

James F. Padbury
Women and Infants Hospital, Providence, RI

Sponsored by an educational grant from Mead Johnson Nutrionals

1:15pm–3:45pm Round Hill

PLENARY SESSION II

1:15 PLENARY LECTURE

Genetics, Genomics and the Promise of Individual Medicine

David Valle
Johns Hopkins University School of Medicine
Baltimore, MD

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

YOUNG INVESTIGATOR AWARDS FINALISTS

Trainees

2:15 Altered Signal Transduction from *PTPN11* Gain-of-Function Mutations in Noonan Syndrome
Kimihiko Oishi, Konstantin Gaengel, Kenichi Kamiya, Ursula Weber, Marek Mlodzik, Leslie Pick, Bruce D. Gelb. — *Abstract 74*

2:30 Astrocyte End-Feet in Germinal Matrix, Cerebral Cortex and White Matter in Developing Infants
Nadine El-Khoury, F. Hu, A. Braun, M. Nedergaard, E. LaGamma, P. Ballabh. — *Abstract 75*

2:45 Inter-alpha Inhibitor Protein (Ialp) Administration Improves Survival in Sepsis in Neonatal Mice
Kultar Singh, Kreso Bendelja, Ryan Heath, Yow-Pin Lim, James F. Padbury. — *Abstract 76*

Faculty

3:00 Wait and See Antibiotic Prescription for the Treatment of Acute Otitis Media: A Randomized, Controlled Trial
David M. Spiro, Khoon-Yen Tay, M. Douglas Baker, Donald H. Arnold, Eugene D. Shapiro. — *Abstract 77*

3:15 Depression Prevalence and Predictors in the Pediatric Emergency Department Adolescent Population
Sabina B. Singh, Sandra J. Nairn, Michael Franco, Edwin D. Boudreaux. — *Abstract 78*

3:30 Neurofibromin GAP-Related Domain Rescues Cardiovascular Defects of Nf1-Deficient Mice
Fraz A. Ismat, Min Min Lu, Jonathan A. Epstein. — *Abstract 79*

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

4:00pm–6:00pm Mead C

ADOLESCENT MEDICINE

Moderator: Jonathan Ellen, Johns Hopkins University, Baltimore, MD

4:00 "Energy Up!": Lifestyle Training and Weight Attenuation Among Inner-City Teens
Lynn Gettleman Chehab, Ileana Vargas, Betsy Pfeffer, Shaofu Chen. — *Abstract 80*

4:15 Double-Blind, Multicenter, Placebo-Controlled Trial of the Effect of ORTHO TRI-CYCLEN® on BMD in Pediatric Subjects with Anorexia Nervosa
Suzanne Riggs, Gary Strokosch, Debra Karvois, Andrew J. Friedman. — *Abstract 81*

4:30 Use of Marijuana by Adolescents with and Without Asthma
Sara B. Levine, Philip O. Ozuah. — *Abstract 82*

4:45 Inner City Adolescents and the Criminal Justice System
Delaney Gracy, Karen Soren, Shaofu Chen, Lindsay A. Thompson, Matilde Irigoyen. — *Abstract 83*

5:00 Residents' Knowledge, Attitudes, and Practices Regarding Emergency Contraception
Elizabeth Armstrong, Satoko Igarashi, Elizabeth Campbell, Laura Keonigs. — *Abstract 84*

5:15 Communication About Vaccines for Teenagers: A Qualitative Study with Teens and Their Parents
Andrea L. Benin, Ann C. Wu, Eric Holmboe, Eugene D. Shapiro, Walter Anyan. — *Abstract 85*

5:30 FEATURED TALK

Connect To Protect: A Population Level Adolescent HIV Prevention Trial
Jonathan Ellen, Johns Hopkins University, Baltimore, MD

4:00pm–5:45pm Winthrop A/B

CARDIAC AND NEONATAL OUTCOMES RESEARCH

Moderator: George Porter, Yale University, New Haven, CT

4:00 Marked Statewide Variation in Risk-Adjusted Hospital Charges for Congenital Heart Surgery
Jean A. Connor, Kimberlee Gauvreau, Kathy J. Jenkins. — Abstract 86

4:15 Medical Injuries and Congenital Heart Surgery
Oscar J. Benavidez, Kimberlee Gauvreau, Kathy J. Jenkins. — *Abstract 87*

4:30 Pediatric Interventional Catheterization: Development of a Risk Adjustment Model for Preventable Complications
Lisa Bergersen, Alan Nugent, John F. Keane, Kimberlee Gauvreau, James E. Lock, Kathy J. Jenkins. — *Abstract 88*

4:45 Time as an Influence on Parents' Decision Making About Research Participation for Their Neonates with CHD
K. Sarah Hoehn, Aruna Nathan, Susan Nicolson, Gil Wernovsky, Robert M. Nelson. — *Abstract 89*

5:00 Moderately Premature Infants at Kaiser Permanente Medical Care Program in California Are Discharged Home Earlier Than Their Peers in Massachusetts and the United Kingdom
Jochen Profit, Marie McCormick, John Zupancic, Douglas Richardson, Gabriel Escobar, Janet Tucker, William Tarnow-Mordi, Gareth Parry. — *Abstract 90*

5:15 High Incidence and Short Duration of Prescription Drug Use Among Premature NICU Graduates One Year After Discharge
Kelly C. Wade, Scott A. Lorch, Gabriel J. Escobar, Barbara Medoff-Cooper, Susan Bakewell-Sachs, Marla N. Gardner, John Greene, Orit Even-Shoshan, Jeffrey H. Silber. — *Abstract 91*

5:30 Racial Disparities and Low Frequency of Antibiotic Use Among Premature Infants After Hospital Discharge
Scott A. Lorch, Kelly C. Wade, Gabriel J. Escobar, Barbara Medoff-Cooper, Susan Bakewell-Sachs, Marla Gardner, John Greene, Orit Even-Shoshan, Jeffrey H. Silber. — *Abstract 92*

4:00pm–5:15pm Mead B

EMERGENCY MEDICINE

Moderator: To be determined

4:00 Sexual Assault and the Pediatric Emergency Department: Are We Prepared?
Kirsten Bechtel, Karen Santucci. — *Abstract 93*

4:15 A Randomized Trial To Assess the Efficacy of Point-of-Care Testing in Decreasing Length of Stay in a Pediatric Emergency Department
Allen L. Hsiao, Karen A. Santucci, Richard N. Shiffman, M. Douglas Baker. — *Abstract 94*

4:30 Bedside Ultrasound in the Diagnosis and Guided Reduction of Forearm Fractures in Children
Lei Chen, Christopher L. Moore. — *Abstract 95*

4:45 Attitudes and Preferences of Parents Toward Asthma Education in the Emergency Department
Jamal Harris, Kathryn Scharbach, Sarah Siegel, Melissa Tesher, Philip O. Ozuah. — *Abstract 96*

5:00 Parental Perception of the Passage of Time During a Stressful Event
Victoria Shulman, Christopher Kelly, Kelly Cleary, Jeffrey R. Avner. — *Abstract 97*

4:00pm–5:45pm Mead A

General Pediatrics II: Quality of Care and Medical Education

Moderator: Iman Sharif, Albert Einstein College of Medicine, Bronx, NY

4:00 Can Anticipatory Guidance Prevent Childhood Obesity?: Preliminary Results of a Randomized Controlled Trial
Katherine O'Connor, Iman Sharif, Harris Huberman, Philip O. Ozuah. — *Abstract 98*

4:15 Determining the Essential Components of Professionalism and Interpersonal/Communication Skills
Laura Dattner, Philip O. Ozuah. — *Abstract 99*

4:30 Parental Assessment of Quality of Ambulatory Care: How Do Attendings and Residents Compare?
Andrew D. Racine, Sheila Liewehr, Laura Weingart, Scott D. Krugman. — *Abstract 100*

4:45 Residents' Attitudes and Practices Regarding the Use of Analgesia and Sedation for Lumbar Puncture in Children
Vicky R. Breakey, Jonathan R. Pirie, Ran D. Goldman. — *Abstract 101*

5:00 Impact of a Modified Hospitalist System on the Quality of the Ward Experience for Residents and Attendings
Steve Paik, Matilde Irigoyen, Elizabeth Wedemeyer, Shaofu Chen, Frank Chimkin. — *Abstract 102*

5:15 Knowledge and Beliefs in School Nurses on Recurrent Abdominal Pain of Childhood. Opportunity for Therapeutic Alliance?
Nader N. Youssef, Thomas Murphy, Charlotte Intile, Joel R. Rosh. — *Abstract 103*

5:30 A Simple Intervention To Improve Parental Health Literacy: Writing Clearly
Iman Sharif, Sarah Lo, Philip O. Ozuah. — *Abstract 104*

4:00pm–5:30pm Stonington

Genetics

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

4:00 Pilot Study: *In Utero* Treatment of Osteogenesis Imperfecta (OI) Using Alendronate in a Mouse Model of OI
Edith A. McCarthy, Nancy P. Camacho, Roberto Garcia, Karen D. Hendricks-Munoz. — *Abstract 105*

4:15 Genetic Polymorphisms in Autism
John W. Harrington, Steven Colson, Sabrina Law, Ingrid Loma-Sanner, Ioana Godi, Sonya Strassberg, Lance Parton. — *Abstract 106*

4:30 Single Nucleotide Polymorphisms (SNPs) of Tumor Necrosis Factor (TNF) and Interleukin-1ß (IL-1ß) and the Risk of Bronchopulmonary Dysplasia (BPD) in Very Low Birth Weight Infants
Sonya S. Strassberg, Ioana Godi, Anita Shvarts, Lance A. Parton. — *Abstract 107*

4:45 Is There a Genetic Susceptibility to Broncho Pulmonary Dysplasia (BPD)?
Anupama H. Shetty, Matthew J. Bizzarro, Richard A. Ehrenkranz, Naveed Hussain, B. Jonsson, N. Desai, B. Vohr, Laura R. Ment, Jeffrey R. Gruen, Vineet Bhandari. — *Abstract 108*

5:00 Interleukin 8 (IL-8) Single Nucleotide Polymorphisms (SNPs) in Infants with Respiratory Syncytial Virus (RSV) Bronchiolitis: A Comparison of Full Term (FT) and Preterm (PT) Infants
John J. Welter, Dagne Assefa, Ioana A. Godi, Thomas Do, Sonya S. Strassberg, Nikhil Amin, Allen J. Dozor, Lance A. Parton. — *Abstract 109*

5:15 *PTPN11* Mutations Play a Minor Role in Isolated Congenital Heart Disease
Constance G. Weismann, Alfred Hager, Harald Kaemmerer, Cheryl Maslen, Rachel Bell, Dietmar Schranz, Joachim Kreuder, Bruce D. Gelb. — *Abstract 110*

4:00pm–6:00pm Sheffield

Neonatology II: Translational Research

Moderator: Roger Soll, University of Vermont College of Medicine, Burlington, VT

4:00 Effects of Labor on Neonatal Neutrophil Apoptosis and Inflammation
A. Bhattacharya, S. Murthy, M. Quizon, T. Choi, N. Hanna, J.D. Laskin, D.L. Laskin, B. Weinberger. — *Abstract 111*

4:15 Effects of Lipoxin A_4, an Anti-Inflammatory Lipid Mediator, on Neonatal Neutrophils
M. Quizon, A. Bhattacharya, T. Choi, N. Hanna, J.D. Laskin, D.L. Laskin, B. Weinberger. — *Abstract 112*

4:30 Viral Transfection of Endothelial Cells with Superoxide Dismutase Protects Against Hyperoxic Injury
Robert M. Angert, Yuchi Li, Hschi-chi Koo, Jonathan M. Davis. — *Abstract 113*

4:45 Altered Production of Pro- and Anti-Inflammatory Cytokines in Preterm Labor Placentas: Role of IL-10
L. Bonifacio, A. Bhattacharya, A. Petrova, D. Sorrentino, B. Weinberger, D. Laskin, S. Sharma, N. Hanna. — *Abstract 114*

5:00 Bilirubin Binding Capacity Is Directly Related to Gestational Age and Clinical Stability in Very Low Birthweight Neonates
Jesse Bender, William J. Cashore, William Oh. — *Abstract 115*

5:15 Circulating $CD34^+$ Stem Cells in the Premature Neonate and Their Possible Role in the Response to Lung Injury
Matthew J. Bizzarro, Vineet Bhandari, Diane S. Krause, Brian Smith, Ian Gross. — *Abstract 116*

5:30 FEATURED TALK

Neonatal Networks and Clinical Trials
Roger Soll, University of Vermont College of Medicine, Burlington, VT

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.

6:00pm–7:30pm Conde's

Poster Session II

1 Presenting Complaints in the PCOS Adolescent Female—Are Teen, Parent and Physician on the Same Page?
Michelle Adams, Marybeth Roy, Holley F. Allen. — *Abstract 117*

2 Does Asthma Written Action Plan Improve the Self Management of Asthma?
Uma Maikappan, Fernanda Kupferman, Won Baik-Han, Salima Walani, Susana Rapaport. — *Abstract 118*

3 Patient Characteristics Associated with Medical Injury Following Congenital Heart Surgery
Oscar J. Benavidez, Kimberlee Gauvreau, Kathy J. Jenkins. — *Abstract 119*

4 Cloning and Characterization of a Mouse Ap-2e Variant-1 with a Non-AUG Translation Start Site and Unique Function
Feng Zhao, Jian Zhang, Bruce D. Gelb. — *Abstract 120*

5 Antibody Inhibition of ErbB Receptors in Pulmonary Alveolar Type II Cell Lines
Sandra L. Murray, Washa Liu, Lucia D. Pham, Sujatha Ramadurai, MaryAnn V. Volpe, Christiane E.L. Dammann, Heber C. Nielsen. — *Abstract 121*

6 Butyrate, a Diet-Derived Short Chain Fatty Acid May Modulate the Immune Responses by Regulating Chromogranin A Gene Expression
Muhammad T. Zia, Bistra B. Nankova, Kavitha Krishnan, Edmund F. LaGamma. — *Abstract 122*

7 Hypoglycemia in Beckwith-Wiedemann Syndrome (BWS) Not Associated with Hyperinsulism (HI)
Preneet Brar, Robert Ferry, Audrey Iacobucci, Nadine Haddad, Laura Wanner, Charles A. Stanley, Lorraine Levitt Katz. — *Abstract 123*

8 A Comparison of Glutamine Content in Commonly Consumed Food Proteins Derived from Gene Sequencing vs. Biochemical Analysis
Carine M. Lenders, Simin Liu, Douglas Wimore, Laura Sampson, Lauren Dougherty, Donna Spiegelman, Walter Willett. — *Abstract 124*

9 Treatment Effectiveness of Gastroesophageal Reflux Disease in Infants: A Parental Satisfaction Survey
Yen P. Chen, Sheryl John, Rajeev Mehta, Anna Petrova. — *Abstract 125*

10 Alcohol Sclerotherapy of Low Flow Venous Malformations in Children
Dalya L. Chefitz, John Nosher. — *Abstract 126*

11 Determinants of Prolonged Hospitalization for Asthma in Inner-City Children
Marina Reznik, Philip O. Ozuah. — *Abstract 127*

12 Using GIS To Assess the Availability of Physical Activity Resources in an Inner City Community
Maida Galvez, Jessica Kobil, Cherita Raines. — *Abstract 128*

13 Trauma and Distress in Primary Care Pediatrics
Deborah P. Steinbaum, Laura Englander, Tara Balija, Alexi Tzavaras, Joseph Boscarino, Danielle Laraque. — *Abstract 129*

14 Mothers' Attitudes About Vaccination
Ann C. Wu, Daryl Wisler-Scher, Katherine Griswold, Eve Colson, Eugene D. Shapiro, Eric Holmboe, Andrea L. Benin. —*Abstract 130*

15 Transmission Rates of Perinatally Acquired (PNA) HIV Infection in Newborns with and Without Sickle Cell Hemoglobinopathy (SCH)
Rakesh B. Patel, Amy Palmieri, Echezona Ezeanolue, Patricia Wodi, Franklin Desposito, Arry Dieudonne, James Oleske. — *Abstract 131*

16 Transition of International Medical Graduates in an Inner-City Pediatric Residency Training Program
Vipin Agarwalla. — *Abstract 132*

17 "Dancing with Different Partners": The Impact of Restricted Work Hours on Learning in Continuity Clinic
Dorene Balmer, Angelo Giardino, Stephen Ludwig. — *Abstract 133*

18 Major Congenital Anomalies Place ELBW Infants at Higher Risk for Poor Growth and Developmental Outcomes
R. A. Vogt, S. C. Kandefer, W. K. Poole, B. J. Stoll, B. R. Vohr. — *Abstract 134*

19 Effects of Discordance in Birth Weight on Postnatal Catch-Up Growth in Very Low Birth Weight (VLBW) Multiple Birth Infants
Vinayak Govande, M. Roger Kim, Gunjeet M. Sahni, Michael A. Guiliano, Dominique Jean Baptiste. — *Abstract 135*

20 RSV Prophylaxis in a Second Season: How Effective Is It?
Sergio G. Golombek, Josephine Kelly. — *Abstract 136*

21 Role of Serum Transforming Growth Factor b 1 and Vascular Endothelial Growth Factor in the Prediction of Bronchopulmonary Dysplasia—A Pilot Study
Suhas M. Nafday, Melissa Scheiner, Luc P. Brion, Alfin G. Vicencio. — *Abstract 137*

22 Will an "Optimal FRC" Strategy Minimize Volutrauma-Associated Lung Injury?
Abdul Haleem, Ravi Mishra, Lance A. Parton, Ioana A. Godi, Sergio G. Golombek, Edmund F. LaGamma. — *Abstract 138*

23 Anemic Spleen, a Sentinel Sign of Perinatal Hemorrhage
Nenad Lilic, Sheila Laungani, Sukhvinder Ranu, Virginia M. Anderson. — *Abstract 139*

24 Butyrate Protects Lung Epithelial Cells from Pro-Inflammatory and Nitric Oxide-Mediated Damage
Ioana A. Godi, Edmund F. LaGamma, Lance A. Parton. — *Abstract 140*

25 Cardio-Respiratory Function of Preterm Infants Placed in Car Seats: Risk Factors and Outcomes
Vallier C. Ojadi, Rajeev Mehta, Anna Petrova. — *Abstract 141*

26 Effect of Recombinant Human Erythropoietin (rhEPO) on the Development of Retinopathy of Prematurity (ROP)
Nishant C. Shah, M. Roger Kim, Pushkaraj Jadav, Lourdes M. Cohen, Dominque Jean Baptiste, Jeremy Weedon. — *Abstract 142*

27 Use of Vinyl Bags in the Delivery Room Prevents Hypothermia in Preterm Very Low Birth Weight Infants
Bobby Mathew, Satyan Lakshminrusimha, Katherine Cominsky, Eileen Schroeder, Vivien Carrion. — *Abstract 143*

28 Tocolysis with High Dose Magnesium Sulfate ($MgSO_4$) Increases the Risk of Death in Extremely Low Birth Weight (ELBW) Infants
Rita Verma, Paul Ogburn, Eugene Komaroff. — *Abstract 144*

29 Phosphorus Initiative in a Pediatric Dialysis Program
Kimberly Serraro, Catherine Cahill, Evangeline Myrie, Mihail Subtirelu, Maya H. Doyle. — *Abstract 145*

30 Racial Background Has No Effect on the Characteristics of Primary Hypertension in Children
Tammy M. Brady, Joseph T. Flynn. — *Abstract 146*

31 Urinary Proteomic Arrays of Atherosclerotic Cytokines in Patients with Steroid-Resistant (SRNS) and -Sensitive Nephrotic Syndrome (SSNS)
Ibrahim F. Shatat, Robert P. Woroniecki, Katarina Supe, Frederick J. Kaskel. — *Abstract 147*

32 Short Bowel Syndrome: Incidence, Morbidity, Mortality and Predictive Factors for Survival
Parul Shah, Farida Nentin, Gustavo Stringel, Boriana Parvez. — *Abstract 148*

8:30am–9:30am Round Hill

PLENARY SESSION III

8:30 Announcement of the Young Investigator Award

8:40 PLENARY LECTURE
Ins and Outs of Iron Transport

Nancy Andrews
Harvard Medical School, Boston, MA

Sponsored by an educational grant from MedImmune, Inc.

9:45am–11:45am Mead B

CARDIOPULMONARY DEVELOPMENT

Moderator: Martina Brueckner, Yale University, New Haven, CT

9:45 Intracellular Calcium Signals in the Anterior Heart Field Affect Development of the Cardiac Outflow Tract
George A. Porter. — *Abstract 149*

10:00 Sox4 Is Required for Development of the Heart and Nervous System in the Zebrafish
Kathryn Maschhoff, Jeffrey Hannah, Alvin Chin. — *Abstract 150*

10:15 CEACAM6 in Human Fetal Lung Epithelial Cells: A Newly Identified TTF-1 Responsive Gene
Venkatadri Kolla, Linda W. Gonzales, Ping Wang, Sreedevi Angampalli, Kelly C. Wade, Philip L. Ballard. — *Abstract 151*

10:30 Break

10:45 Cathepsin H (CTSH) and Napsin A (NapA) Expression During Human Lung Development
Karna Murthy, Peggy Zhang, Kristin Ducrest, Amana Aktar, Susan H. Guttentag. — *Abstract 152*

11:00 Androgen Effect on ErbB Receptor and PLCγ Expression and Phosphorylation During Fetal Lung Maturation
Sujatha M. Ramadurai, Soujanya L. Rallabandi, Lucia D. Pham, Sandy L. Murray, Heber C. Nielsen. — *Abstract 153*

11:15 FEATURED TALK

Development of Cardiac Left–Right Asymmetry
Martina Brueckner, Yale University, New Haven, CT

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.

9:45am–12:00pm Mead A

GENERAL PEDIATRICS III

Moderator: Andrew Racine, Albert Einstein College of Medicine, Bronx, NY

9:45 Failure To Thrive in Infants with Gastroesophageal Reflux Disease
Yen P. Chen, Anna Petrova, Daniel Notterman, Soula Koniaris. — *Abstract 154*

10:00 Who Receives Appropriate Recommendations About Complementary and Alternative Medical Therapies?
Amy E. DeMattia, Harry Moskowitz, Kathi J. Kemper, Danielle Laraque. — *Abstract 155*

10:15 Variations in Pediatric Tuberculosis Screening in Connecticut Schools
Beth C. Natt, Juan C. Salazar. — *Abstract 156*

10:30 Break

10:45 The Feasibility and Effectiveness of an Exercise Prescription for Obese Children in the Primary Care Setting
Stephanie A. Carlin, Leif Nordstrom, Thomas Rowland. — *Abstract 157*

11:00 Clinical Correlates of Early Readmission for Sickle Cell Disease Vasoocclusive Crisis
Catherine C. Skae, Devika Brijlall, Mary McGuire, Philip O. Ozuah. — *Abstract 158*

11:15 Food Availability in an Inner-City Community: What's near Our Elementary Schools?
Maida Galvez, Cherita Raines, Jessica Kobil. — *Abstract 159*

11:30 FEATURED TALK

The Relationship Between Maternal Education and Child Health Status: Evidence from Immunization Rates
Andrew Racine, Albert Einstein College of Medicine, Bronx, NY

9:45am–12:00pm Mead C

INFECTIOUS DISEASES

Moderator: Harris Goldstein, Albert Einstein College of Medicine, Bronx, NY

9:45 A Rat Model of Neonatal Candidiasis
Lamia Soghier, David Goldman. — *Abstract 160*

10:00 Short Course of Fluconazole Prophylaxis in Very Low Birth Weight Infants
Smart Uko, Viral Dave, Lamia M. Soghier, Suhas Nafday, Gerald Reinersman, Lucille Herring, Luc P. Brion. — *Abstract 161*

10:15 Sexual Behaviors and Procreational Intentions of Adolescents and Young Adults with Perinatally Acquired Human Immunodeficiency Virus Infection
Echezona E. Ezeanolue, A. Patricia Wodi, Rakesh B. Patel, Arry Dieudonne, James M. Oleske. — *Abstract 162*

10:30 Influenza Vaccine: Immunization Rates, Knowledge and Attitudes of Resident Physicians in an Urban Teaching Hospital
Patricia Wodi, Sawsan Samy, Echezona Ezeanolue, Rytza Lamour, Rakesh Patel, Lawrence Budnick, Barry Dashefsky. — *Abstract 163*

10:45 Break

11:00 Differential Cytokine (CK) Responses in Cord vs. Adult Peripheral Blood Mononuclear Cells (PBMCs) Exposed to RSV and Hyperoxia In Vitro
Leonard R. Krilov, Thomas M. McCloskey, S. Hella Harkness, Paul J. Lee, Jonathan M. Davis. — *Abstract 164*

11:15 ***E. coli* O157:H7 Diarrhea and Hemolytic-Uremic Syndrome in an Urban Daycare Center**
Ryan M. Raffaelli, Don Weiss, Glenn J. Fennelly, Laura Kornstein, Heather Hanson, Sudha Reddy, Marc Paladini, Nathan Litman, Frederick Kaskel, Joseph Flynn. — *Abstract 165*

11:30 FEATURED TALK

Investigation of HIV Pathophysiology and Novel HIV Therapeutics Using Transgenic Mouse Models
Harris Goldstein, Albert Einstein College of Medicine, Bronx, NY

9:45am–12:00pm Sheffield

Neonatology III:

Animal Models in Neonatology Research

Moderator: Barbara Stonestreet, Women and Infants Hospital of Rhode Island, Providence, RI

9:45 Ontogeny and Regulation of Hyaluronan by Antenatal Corticosteroid, Ventilation and Hyperoxia in Non-Human Primate Models of BPD
Lindsay M. Johnson, Siddhartha Maru, Joseph P. Foley, Brad A. Yoder, Jacqueline J. Coalson, Anna Plaas, Rashmin C. Savani. — *Abstract 166*

10:00 Pulmonary Arterial (PA) Contractility in Neonatal Lambs Increases with 100% O_2 Resuscitation
Satyan Lakshminrusimha, Robin H. Steinhorn, Daniel D. Swartz, Sylvia F. Gugino, Rita M. Ryan, James A. Russell, Frederick C. Morin, Vasantha H. Kumar. — *Abstract 167*

10:15 Break

10:30 Aerosolized Prostacyclin [Ar-PGI_2] and Milrinone [Ar-MLR] Decrease Pulmonary Vascular Resistance [PVR] in Newborn Lambs with L-NAME Induced Pulmonary Hypertension [PHT]
N. Rashid, F. C. Morin, D. D. Swartz, K. A. Wynn, H. Wang, R. M. Ryan, V. H. Kumar. — *Abstract 168*

10:45 Surfactant Protein D Modifies the Response to Intratracheal Bleomycin
Jennifer H. Kaplan, John A. Casey, Elena N. Atochina, James H. Fisher, Yaniv Tomer, Helchem Kadire, Michael F. Beers. — *Abstract 169*

11:00 Activation of Natriuretic Peptide Receptor C Inhibits Adenylate Cyclase Mediated Relaxation in Juvenile Ovine Pulmonary Arteries (PA)
Bobby Mathew, Rita M. Ryan, Sylvia F. Gugino, James A. Russell, Frederick C. Morin, Lori C. Nielsen, Satyan Lakshminrusimha. — *Abstract 170*

11:15 Early Loss of HA in Association with Increased Peroxynitrite After Intratracheal Bleomycin in Rats
Rashmin C. Savani, Joseph P. Foley, Aisha Zaman, Bruno Flamion, Jeannine Martens, Anna Plaas. — *Abstract 171*

11:30 FEATURED TALK

Blood–Brain Barrier: Structure, Function, Development and Perinatal Medicine
Barbara Stonestreet, Women and Infants Hospital of Rhode Island, Providence, RI

9:45am–12:00pm Stonington

Neurobiology

Moderator: Rebecca Ichord, Children's Hospital of Philadelphia, Philadelphia, PA

9:45 Maturation and Antenatal Corticosteroids Reduce Apoptosis in the Fetal Brain
Shadi N. Malaeb, Grazyna B. Sadowska, Paul R. Monfils, Virginia Hovanesian, Barbara S. Stonestreet. — *Abstract 172*

10:00 Chronie Opiate Withdrawal in Neonatal Mice: Behavioral Analysis and c-Fos Expression
Anne-Lise J. Yohay, Ariel Mason, Megan Duffy, Debra Flock, Gabrielle McLemore, Frances Northington, Estelle B. Gauda. — *Abstract 173*

10:15 The Effects of Lipopolysaccharide Injection on Bax and Bcl2, Regulators of Apoptosis, in Neural Tissue of Newborn Mice
David F. Sorrentino, Morgan Peltier, Vallier Ojadi, Alexander Kusnecov. — *Abstract 174*

10:30 Effects of Single and Multiple Courses of Antenatal Corticosteroids on Apoptosis in the Brain of Preterm Ovine Fetuses
Shadi Malaeb, Grazyna B. Sadowska, Paul R. Monfils, Virginia Hovanesian, Barbara S. Stonestreet. — *Abstract 175*

10:45 Break

11:00 Novel Role of CREB in Butyrate-Induced Activation of Catecholaminergic Neurotransmission
Parul Shah, Bistra Nankova, Edmund LaGamma. — *Abstract 176*

11:15 Dose-Dependent Effects of Diet-Derived Signaling Factors (Butyrate) on Transcription of Catecholamine-Related Transmitter Genes: Tyrosine Hydroxylase
Santosh M. Parab, Bistra Nankova, Edmund F. LaGamma. — *Abstract 177*

11:30 FEATURED TALK

Stroke in Infants and Children: Progress and Challenges
Rebecca Ichord, Children's Hospital of Philadelphia, Philadelphia, PA

Sponsored by an educational grant from Advanced Imaging Research

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.

Poster Session I

Friday, March 4 6:00 PM-7:30 PM Conde's

1 Poster Board 1 — House Officer

Association Between Marijuana Use and Asthma Severity in Adolescents

Sara B. Levine, Philip O. Ozuah. Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Despite known effects of inhalational drugs on respiratory symptoms and lung function, there is a paucity of data describing patterns of marijuana use, specifically among adolescents with asthma. This study aimed to identify trends in marijuana and other substance use on the basis of severity of asthma.
OBJECTIVE: To examine the relationship between asthma severity and marijuana use by adolescents.
DESIGN/METHODS: We conducted a cross-sectional survey of adolescents (ages 13-19 years) in the inpatient and outpatient settings of an urban inner-city children's hospital. We designed a self-completion anonymous questionnaire based on questions adapted from the Youth Risk Behavior Surveillance System (YRBSS) and the National Heart Lung and Blood Institute guidelines for asthma. Substance use questions were modeled after the YRBSS, which has been validated in adolescents. Subjects were asked to answer multiple-choice questions about substance use (cigarettes, marijuana, and alcohol), frequency of cough, wheezing, or shortness of breath, and previous diagnosis of asthma. We used chi-square to test differences in dichotomous variables.
RESULTS: Of 207 participants, 60% were female, 80% were Black or Hispanic, and mean age was 16 years. 66 adolescents (32%) reported having ever been diagnosed with asthma by a healthcare provider, of whom 33% met the criteria for moderate to severe persistent symptoms based on NHLBI guidelines. Among all asthmatic adolescents, 35.9% had ever used marijuana, 36.4% had ever smoked cigarettes, and 50.0% had ever used alcohol. Adolescents with moderate to severe symptoms were less likely than their mild asthmatic peers to report having ever tried marijuana (32.4% vs. 40.0%) and cigarettes (35.3% vs. 37.5). Mild and severe asthmatic adolescents reported equally having ever used alcohol (50.0%). There were no differences in the age of initiation of substance use between the two groups.
CONCLUSIONS: Our findings suggest a trend toward less inhalational drug use among adolescents with severe asthma compared to their peers with mild asthma. National surveys of adolescent substance use consistently demonstrate clustering of behavior. Though previous studies have suggested that adolescents with asthma were using more marijuana and cigarettes than their nonasthmatic peers, within the group of adolescents with asthma these behaviors may be more common among those with mild symptoms.

2 Poster Board 2

Rituximab in Treatment-Resistant Childhood-Onset Systemic Lupus Erythematosus (cSLE)

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BACKGROUND: cSLE is an autoimmune disease with high morbidity, characterized by the production of multiple autoantibodies. Systemic immunosuppression is often required, however, patients may be resistant to multiple therapies and suffer significant side effects. Rituximab (RTX), an anti-CD20 monoclonal antibody, has a potential role in the treatment of autoimmune disease by selectively depleting B cells. RTX has been used in children primarily for autoimmune cytopenias and lymphoproliferative disease. RTX appears safe and efficacious in studies of adults with Rheumatoid Arthritis and SLE, but it has not been studied in cSLE.
OBJECTIVE: To examine the use of RTX in treatment-resistant cSLE.
DESIGN/METHODS: A retrospective review of cSLE patients recently treated with RTX at Children's Hospital of NY was conducted. RTX was prescribed for persistent lupus nephritis in 3 pts, and for persistent thrombocytopenia and myositis in Pt 4.
RESULTS: Four female cSLE patients were studied. The mean age at cSLE diagnosis was 14.75y(range 11-17y), and the duration of disease at initiation of RTX therapy was 4.5y (range 1-7y). All patients had failed treatment with oral high dose (2 mg/kg/day) and pulse IV steroids, IV cyclophosphamide (CXN), mycophenolate mofetil and azathioprine. Renal biopsy in Pts 1-3 confirmed persistent lupus nephritis, WHO Class IV±V, despite at least 6 mos of IV CXN (standard induction therapy). Bone marrow and muscle biopsies in Pt 4 confirmed non-malignant thrombocytopenia and inflammatory myositis. Laboratory studies demonstrated low C3 and C4, elevated ESR, anemia, and proteinuria ± hematuria with casts in Pts 1-3. Pt 4 had persistent thrombocytopenia (<40,000), anemia (£9), elevated CPK and aldolase with muscle weakness. RTX was dosed at 375 mg/m2/dose qwk for 4 weeks. All patients responded to one cycle of RTX, with improvement of C3/C4, proteinuria, anemia, and resolution of hematuria. IgG levels were followed after therapy without evidence of significant hypogammaglobulinemia. In Pt 4, the platelet count stabilized (>80), and muscle enzymes normalized with resolution of weakness. Pt 4 had one episode of herpes zoster treated with oral antivirals. No patient had an infusion reaction.
CONCLUSIONS: RTX may be considered in the management of treatment-resistant cSLE, but further randomized, controlled study is required.
Funded by Rituximab; childhood-onset systemic lupus erythematosus (cSLE).

3 Poster Board 3

Adverse Event Rates for Pediatric Cardiac Catheterization Procedures: Identification of High-Risk Populations

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BACKGROUND: Pediatric cardiac catheterization involves a complex patient population with different procedural objectives.
OBJECTIVE: We sought to determine the rate of adverse events and determine patient and procedural characteristics predictive of events.
DESIGN/METHODS: In January 2004, a prospective database was created to record patient and procedure characteristics and adverse events. Procedures were grouped into 5 categories based on anticipated risk. A committee reviewed events and determined seriousness according to pre-specified definitions. Patient and procedural characteristics associated with higher event rates were identified.
RESULTS: In 9 months, 791 procedures were performed and most involved at least one intervention (81%). Ages at procedures were: < 1 mo (4%); 1mo to 1 yr (16%); 1 to 2 yrs (14%); and > 3 yrs (66%). Procedures were electively scheduled in 78%, including 22% outpatient procedures, and performed with conscious sedation in 66%, general anesthesia in 33%, and with heart lung bypass support in 1%. In 38% of procedures an indicator of vulnerable hemodynamics was present including elevated pulmonary artery or right ventricular pressures > systemic, cyanosis (oxygen saturation <75%), or low cardiac index (< 2.0 L/min/m^2). The lowest anticipated procedural risk group comprised the largest proportion of procedures (group 1, 47%; 2, 32%; 3, 9%; 4, 9%; 5, 3%).
At least 1 adverse event occurred in 22.8% of procedures: serious life threatening events (2%), events requiring significant intervention (6 %), and minor events (17 %). Nearly half (45%) of minor events were blood transfusions. Adverse events were significantly more likely to occur in younger patients (37% < 3 yrs vs. 15% > 3yrs, p<0.001) and in those with an indicator of physiologic vulnerability (33% vs 14%, p <0.001). Adverse events were less common in outpatient procedures than inpatient and emergent procedures (8% vs 25% and 33%, p <0.001). Interventional procedures (25% vs 15%, p = 0.01) and higher procedural risk group were associated with increasing complication rates (11% in 1, 26% in 2, 39% in 3, 50% in 4, 44% in 5, p <0.001).
CONCLUSIONS: These data provide current estimates of adverse event rates in a referral center for pediatric cardiac interventions, and identify patient and procedural characteristics with a higher risk for adverse events.

4 Poster Board 4 — Fellow in Training

Serum ß-Hydroxybutyrate Level Declines After Resuscitation in a Model of Pediatric Asphyxial Cardiac Arrest

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BACKGROUND: Mortality from pediatric cardiac arrest remains high and the potential for meaningful neurologic outcome in survivors continues to remain dismal. During ischemia/reperfusion, metabolic alterations occur in the heart and brain and nutrient delivery may become limiting to energy metabolism. The immature brain utilizes glucose, lactate and ketone bodies. Glucose transport is low early in development. Ketone bodies, ß-hydroxybutyrate (ß-OH) and acetoacetate, are significant cerebral fuels. The utilization of ketone bodies may decrease reperfusion injury and improve neurologic outcome after cardiac arrest.
OBJECTIVE: We propose that endogenous ketone bodies decline in serum level after cardiac arrest. Supplementation of ketone bodies may decrease reperfusion injury and improve neurologic outcome after cardiac arrest.
DESIGN/METHODS: 17-20 day old Wistar rats were subjected to the asphyxial cardiac arrest protocol described by Clark et al in Pediatric Critical Care Medicine, 5(2); 139-44, with minor modification, for a period of 8 minutes. CPR was performed after reconnection to ventilator for 25-30 seconds or until return of spontaneous circulation. Blood was obtained prior to cardiac arrest and on return of spontaneous circulation for serum ß-OH, arterial blood gas and serum glucose.
RESULTS: Basal ß-OH was 0.53 mM ± SEM 0.10 (N=6). ß-OH levels significantly declined, to a mean of 0.35 mM ± SEM 0.11, demonstrating significant utilization of this fuel during ischemia and reperfusion. The serum glucose levels did not change significantly.
CONCLUSIONS: These results support the utilization of ketone bodies during and following asphyxial cardiac arrest and resuscitation. Additional supplementation with this nutrient may provide a valuable fuel to reduce reperfusion injury and improve patient outcome.

5 Poster Board 5

Susceptibility of Heme Oxygenase-1 Protein to Oxidation by Hemin

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BACKGROUND: Heme oxygenase-1 (HO-1) exerts cytoprotective effects and is induced by oxidative stress, such as hemin. The HO-1 protein has a c-terminal hydrophobic membrane-binding domain which can be cleaved by proteases. We have demonstrated that incubation of 3T3 cells with hemin was associated with nuclear localization of an immunoreactive HO-1 lacking the c-terminus. Because free heme catalyzes the formation of oxygen radicals via the Fenton reaction, and is geographically located near the HO protein (tightly sandwiched to the heme pocket), HO-1 protein may be susceptible to heme-mediated oxidation.
OBJECTIVE: To evaluate the susceptibility of HO-1 protein to oxidative modification by hemin in a cell free and a cellular systems.
DESIGN/METHODS: Full-length rat HO-1 (FLHO-1) cDNA was inserted into the pGEX/4T1 vector and expressed in E-coli. The GSTHO-1 fusion was purified on a Glutathione Sepharose 4B column with thrombin protease to cleave GST from HO-1. The recovered HO-1 protein was incubated with various concentrations of hemin for 2 h. In other experiments, NIH 3T3 cells were incubated with hemin for 8 h. The cell lysates were immunoprecipitated with HO-1 antibodies. In both experiments, the samples were subjected to protein carbonyl detection using Western analysis. Additionally, HisFLHO-1FLAG (FLHO-1 tagged with histidine at the N-terminus and FlAG at the c-terminus) cDNA was transfected into the 3T3 cells and incubated with hemin for 8 h. Collected cells were subjected to Western analysis using anti-His, anti-HO-1 and anti-FLAG antibodies.
RESULTS: Three HO-1 immunoreactive bands (32, 28 and 26 kDa) were detected in the GSTHO-1 system after thrombin protease digestion. The ratio of the 3 bands was 1:5:10 for 32:28:26 kDa as calculated by densitometry. When purified HO-1 was incubated with hemin, protein carbonyls were detected corresponding to all 3 bands with the highest increase seen on the 32 kDa band. In the 3T3 cells, incubation with hemin increased protein carbonyl content on the 28 kDa band. When the cells were transfected with HisFLHO-1FLAG, the FLAG signal was lost after hemin incubation.
CONCLUSIONS: Incubation of HO-1 protein with hemin increases protein carbonyl contents. The c-terminus is more susceptible to hemin-induced oxidation and this results in c-terminal cleavage of HO-1. We speculate that oxidative modification of HO-1 is important in mediating HO-1 cytoprotective effects.

6 Poster Board 6 — Medical Student

The Role of Complement Activation in Preterm Labor Placentas

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BACKGROUND: The role of complement activation in preterm labor has not been studied. We have previously shown that downregulation of the anti-inflammatory cytokine IL-10 in the placenta is associated with preterm labor. Complement components are known to be up-regulated in mice lacking IL-10, suggesting a possible link between IL-10 and complement activation.
OBJECTIVE: To determine whether complement is activated in placentas obtained from preterm deliveries and the possible role of IL-10 in suppressing such activation.
DESIGN/METHODS: Cultured placental explants from preterm (< 30 wks gestation) and term deliveries were cultured for 24 hours with or without IL-10, LPS or both. Complement activation products Bb (factor B cleavage product, alternative pathway), C3a (classical or alternative pathway), and SC5b-9 (non-lytic form of the terminal complement complex) were measured by ELISA. Using immunohistochemistry, localization and expression of the complement regulatory proteins CD46 (membrane cofactor protein), CD55 (decay accelerating factor) and CD59 (reactive lysis inhibitor) were compared in placentas from term and preterm deliveries and from second trimester placental samples from normal pregnancies after elective abortions.
RESULTS: Complement activation products were equally present in preterm, term and normal second trimester placentas and did not increase significantly after LPS stimulation. IL-10 treatment decreased the production of Bb only in preterm placentas. Both term and normal second trimester placentas showed

considerable expression of the complement regulatory proteins (CD46, CD55 and CD59) which was further upregulated by LPS treatment. Interestingly, expression of these proteins was significantly increased in preterm placentas. Immunohistochemistry confirmed the localization of placental complement regulatory proteins to the cytotrophoblast layer.
CONCLUSIONS: Complement regulatory proteins play a key role in controlling complement activation in placental tissues either in normal, LPS stimulated or preterm samples. Although IL-10 treatment decreased Bb activation in preterm placentas, the lack of IL-10 in those samples did not translate into higher Bb levels. Taken together, our data suggest a limited role of complement activation in the mechanism of preterm labor.

7 Poster Board 7 Fellow in Training

Frequency of Gastrointestinal Disorders and Family History of Autoimmune Disease in Children with Autistic Spectrum Disorders and Controls

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BACKGROUND: The reported frequency of GI symptoms in children with autistic spectrum disorders (ASD) is 9-46%. However, no comparison groups are available. A relationship has been postulated between GI disorders in children with ASD and autoimmune disorders. This has led to proposals for immune therapy of ASD.
OBJECTIVE: To assess lifetime prevalence of GI symptoms in children with ASD and its relationship to family history of autoimmune disorders.
DESIGN/METHODS: Cross sectional study with structured interview in 100 children with ASD and two control groups matched for age, gender and ethnicity, 100 with other developmental disabilities (DD) and 100 with normal development. Interview includes: Gastrointestinal Questionnaire, based on a Clinical Diagnostic Questionnaire for Pediatric Functional Gastrointestinal Disorders and Familial Autoimmune Questionnaire. Statistical analysis included paired t test and McNemar matched analysis test.
RESULTS: To date we have recruited 92 children with ASD, 53 with DD and 30 normal controls. Mean age was 9.6 yr. Of the 92 children with ASD, 59% had food selection, 14% complained of chronic vomiting, 15% of chronic abdominal pain, chronic diarrhea was present in 18%, bulky stools in 22%, fecal soiling in 23% and chronic constipation in 40%. Many had one or more symptoms. Children with ASD had a significant higher complaint of food selection ($p=0.041$). Chronic diarrhea ($p=0.003$), fecal soiling ($p=0.021$) and presence of bulky stools($p= 0.007$)compared to children with other DDs. They also had a higher rate of food selection ($p=0.001$) and other GI symptoms ($p<0.001$) than normal controls though to date there are few normal controls. Family history of autoimmune disease was present in 34 % of children with ASD, 32 % of DD controls and 43 % of normal controls. In children with ASD, there was no association between family history of autoimmune disorders and the presence of either overall or specific GI symptoms.
CONCLUSIONS: Children with ASD have a higher rate of GI symptoms, in particular food selectivity and chronic diarrhea, than children with other DD and normal controls. In this cohort, there is no association between family history of autoimmune disease and GI symptoms in children with ASD.

8 Poster Board 8

Characteristics of Toddlers with Autistic Spectrum Disorders Screened from High Risk and Low Risk Settings

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BACKGROUND: Autistic Spectrum Disorders (ASD) are estimated to affect between 1 in 250 and 1 in 1000 children. Early detection and intervention lead to improved outcomes. The Modified Checklist for Autism in Toddlers (M-CHAT) is a parent-report questionnaire consisting of 23 yes/no items designed to screen children 16 to 30 months old. Characteristics of the children with ASD detected by the M-CHAT have been reported for a combined sample of high and low risk children (Robins et. al, 2001).
OBJECTIVE: To assess whether there are differences in the children diagnosed with ASD when the M-CHAT is completed at primary care provider offices (low risk), as compared to early intervention sites (high risk).
DESIGN/METHODS: Parents complete the M-CHAT at either their child's primary care provider (PCP) or early intervention provider (EI) site. If the responses on the M-CHAT indicate a "fail," the family is contacted by phone for a scripted interview. If at the end of the phone interview it is determined that the M-CHAT is a "fail," the child is evaluated with the Mullen Scales of Early Learning, Vineland Adaptive Behavior Scales, Childhood Autism Rating Scale, Autism Diagnostic Interview-Revised, Autism Diagnostic Observation Schedule and the DSM-IV criteria.
RESULTS: Per procedure, those who remain a "fail" after the phone interview received an evaluation. Of the 38 children evaluated from the PCP sites, 18 [47%] were diagnosed with an ASD. From the EI sites, 152 evaluations yielded 115 [76%] children diagnosed with an ASD. Chi-square tests showed that the difference in proportion of ASD diagnoses is statistically significant ($p < .001$). Results from the evaluations revealed mean CARS scores of 33 and 32.86 for PCP and EI sites. Mean Vineland Communication standard scores were 62.615 and 64.531 for PCP and EI sites. Mean Vineland Socialization scores were 65.077 and 67.222 for PCP and EI sites. No statistically significant differences between groups were found for any of the assessment instruments.
CONCLUSIONS: The higher proportion of ASD diagnoses from the EI sample confirms its status as 'high risk.' However, the lack of statistical difference in the autistic symptoms, cognitive functioning and adaptive skills between the PCP and EI sites suggests that once identified, children from the two samples who are diagnosed with an ASD are very similar.

9 Poster Board 9

Predictors of Possession of a Carbon Monoxide Alarm in a Urban, Underserved, Low-Income, Pediatric Patient Population

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BACKGROUND: The silent killer carbon monoxide(CO) is the number one cause of poisoning deaths in the United States. CO is a colorless and odorless gas that accounts for an estimated 2,000 deaths per year. Those at highest risk include children and pregnant women. Morbidity and mortality from CO can be decreased with the use of CO alarms. It is estimated that the percentage of patients in a urban, underserved, low-income pediatric patient population possessing a CO monitor is very low. In addition, predictors of CO alarm possession are not known.
OBJECTIVE: To identify predictors of possessing a CO alarm in an urban, underserved, low-income pediatric patient populations.
DESIGN/METHODS: A 19 item questionnaire evaluating general knowledge of CO, the use of CO alarms and demographic data was administered to a convenience sample of the parents or guardians of children presenting for outpatient care at a hospital located in a low-income, urban, underserved area.
RESULTS: See Table.
415 questionnaires were completed. 64.8% participants reported the main language spoken in there home as English only, 14.5% were bilingual, and 20.7% were other, non-English.
CONCLUSIONS: Ownership of home, private insurance, the use of a smoke alarms and being worried about CO were associated with higher possession rates of CO alarm. Higher education level was also associated with having a CO alarm.

PREDICTORS OF HAVING A CO ALARM

Worried about CO	29.3% vs 17.1%	p<0.01
Have smoke alarm	22.6% vs 7.1%	p<0.01
Own home	44.6% vs 17.4%	p<0.01
Private insurance	36.2% vs 17.9%	p<0.01
Higher education	23.1% vs 7.1%	p<0.05

10 Poster Board 10

Placebo Controlled Trials Are Well Received by Parents in Pediatric Research Regardless of Outcome

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BACKGROUND: There is a paucity of randomized, placebo controlled trials (PCTs), the gold standard for research, in pediatric gastroenterology. Investigators and institutional review boards (IRBs) have concerns that parents will poorly perceive PCTs.
OBJECTIVE: To identify potential differences between parental perceptions in families who successfully completed (CO) a clinical trial compared to those who were non-completers (NC).
DESIGN/METHODS: Parents of both CO and NC children enrolled in 1 of 3 pediatric GI studies performed over the prior year were eligible for this study. Reasons for NC were screen failures, adverse events and treatment failures. 107 parents of 110 children were identified and sent a 26-item questionnaire eliciting their perception regarding participation in clinical research. Questionnaires were coded for anonymity, sent 6 months after their child's participation ended; and returned to investigators who had not met the family. Demographics, reasons for participation, risk/benefit perception, and consent process were assessed.
RESULTS: Of the 110 children, 104 (95%) were in PCTs. Seventy-eight (69%) parents returned the survey. Characteristics of parents included: maternal responders (98%), English as the primary language (97%), and education beyond high school (85%). Five parents (4.7%) had children involved in prior research trials. There were no significant differences in responses found between CO (n=49; 63%) and NC (n=29; 37%) (Table). Of 29 families who did not respond back, 7 (24%) were NC.

Percent Strongly Agree or Agree

	Completers	Non-Completers	
Research Important	100%	97%	p = .70
Minimal Risk To Child	94%	69%	p = .58
Perceived Benefit for Child	90%	72%	p = .13
Others May Benefit	100%	100%	
More Attention if in Study	59%	41%	p = .11
Reassuring Researcher	100%	90%	p = .15

CONCLUSIONS: PCTs are well received by parents who participate in research regardless of whether or not their children benefited from the study. Satisfaction from participation in research is not stratified by successful completion of a PCT. Positive perception may be due to understanding of the risks and benefits of the PCT and comfort with researchers. These results should encourage investigators and IRBs that if properly designed and conducted, pediatric PCTs can result in a high degree of parental satisfaction.

11 Poster Board 11 House Officer

Variation in Management of Common Inpatient Pediatric Illnesses: Hospitalists and Community Pediatricians

Patrick H. Conway, Christopher P. Landrigan, Sarah Edwards. Medicine, Children's Hospital Boston, Boston, MA.
BACKGROUND: Multiple studies have documented efficiency gains in pediatric hospitalist systems. Studies evaluating variability in care delivered by pediatric hospitalists (PHs) and community pediatricians (CPs) are lacking.
OBJECTIVE: To determine the variability in PHs and CPs management of inpatient illnesses, specifically comparing their adherence with evidence-based therapies and tests and use of therapies/tests of unproven benefit.
DESIGN/METHODS: PHs and CPs reported their frequency of use of diagnostic tests or therapies on a 5-point Likert scale (ranging from never to almost always) for six common inpatient pediatric illnesses: pneumonia, GERD, bronchiolitis, gastroenteritis, asthma, and first UTI. Responses of PHs and CPs were compared using univariate and multivariate logistic regression analyses to control for gender, race, years out of residency, days spent attending per year, and training background.
RESULTS: 213 PHs and 343 CPs responded to the survey. On univariate analyses, PHs and CPs were found to make significantly different management decisions for 37 of 49 (76%) tests and therapies evaluated ($p<.05$). On multivariate regression analyses, PHs were significantly more likely to use the following evidence-based therapies for asthma: albuterol (OR 4.2; 95% CI 1.3-13.4), atrovent in the first 24 hours of hospitalization (3.2; 1.7-5.9), and no atrovent after 24 hours of hospitalization (2.1; 1.1-3.9). There was no significant difference in the use of steroids in asthma (2.7; 0.7-10.6). After first UTI, PHs were more likely to obtain the AAP-recommended renal ultrasound (5.6; 1.5-21.2) and VCUG (4.9; 1.7-13.9). CPs were significantly more likely to utilize the following therapies not proven to be beneficial in bronchiolitis: xoponex (OR 6.6), inhaled steroids (6.3), oral steroids (6.4), and chest physiotherapy (1.9). There was no difference in the use of albuterol in bronchiolitis. CPs were also significantly more likely to use the following diagnostic tests unproven to change management in routine gastroenteritis: stool cultures (2.7) and rotavirus testing (3.6).
CONCLUSIONS: There is significant variability in the management of common inpatient pediatric illnesses. Overall, compared to CPs, PHs report greater adherence with evidence-based therapies to treat asthma. PHs also report less use of therapies and tests of unproven benefit in bronchiolitis and gastroenteritis.

12 Poster Board 12

Predictors of Multiple Pediatric Asthma Hospitalizations

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BACKGROUND: Although many children suffer from asthma, only a small percentage need to be admitted to the hospital multiple times per year. Little is known about these children with frequent admissions.
OBJECTIVE: To determine risk factors for children with three or more hospitalizations for asthma within a year.
DESIGN/METHODS: We conducted a case-control study of pediatric patients with multiple hospitalizations for asthma within a 365-day period. Computerized health records identified patients <21 years of age with 3 or more hospitalizations with a discharge diagnosis of asthma (ICD-9 493.0) within any 365-day period between 1/1/00 - 12/31/03. Each case was matched with 2 controls. Controls were patients with 2 or fewer hospitalizations, and were matched for age, gender and ethnicity. Data were abstracted for asthma history, medications, admissions, other medical problems, insurance, zip code of residence, and

environmental exposures. Multiple logistic regression analyses were used to control for confounders and to predict independent correlates of multiple hospitalizations.
RESULTS: 450 subjects were identified (150 cases, 300 controls). Cases and controls were matched (age 6.6 years, 60% male, 58% Hispanic, and 39% African American for both.) Mean hospitalizations were 3.6 for cases and 1.2 for controls.
Univariate analysis revealed that cases were more likely to have Medicaid or no insurance (64% vs 52%, p=0.026), to reside in zip codes with higher prevalence of poverty (p=0.006), to have a greater number of prior asthma hospitalizations (8.1 vs 2.4, p=0.000), to have been in the ICU for asthma (46% vs 21%, p=0.000), to be on inhaled steroids (92% vs 51%, p=0.000), to see a pulmonologist (67% vs 18%, p=0.000), and to have other chronic illnesses (54% vs 41%, p=0.010).
Multiple regression analyses revealed independent predictors of multiple hospitalizations to be: living in a zip code with higher prevalence of poverty (OR 2.2, p=0.029), taking inhaled steroids (OR 5.9, p=0.000), and consultation with a pulmonologist (OR 4.8, p=0.000). No significant influences were found for environmental exposures.
CONCLUSIONS: These findings suggest that economically disadvantaged children and those with more severe asthma are at increased risk for multiple hospitalizations. Poverty was an independent risk factor for multiple admissions, even after controlling for disease severity.

13 Poster Board 13 — Fellow in Training

Predictors of Early Readmission for Asthma in Inner-City Children

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. Some children with asthma will be readmitted with the same diagnosis within 30 days of discharge. Factors associated with early readmission have not been fully studied.
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 1/1/98 and 10/1/04. Computerized records identified children with a primary discharge diagnosis of asthma (ICD-9 493.0). Cases were children with asthma readmitted with the same diagnosis within 30 days of the index admission. For each case, we identified up to two controls which were children 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 abstracted from the medical records. Bivariate analyses (clogit, GEE statistics) were performed. Conditional logistic regression analysis determined the relative contribution of independent variables.
RESULTS: 458 subjects were analyzed (161 cases, 297 matched controls). Cases and controls were successfully matched (mean age for cases 6.4 years (SD 5.3) vs 6.4 years (SD 5.1) for controls; for both groups 64% were male, 61% Hispanic and 36% African American). Cases had a greater mean number of lifetime admissions for asthma (8.2 vs 3.3, p<.0001), were more likely to have received a pulmonary consultation prior to the index admission (OR 2.49, 95% CI 1.45-4.29) and to have a history of asthma ICU admission (OR 2.20, 95% CI 1.31-3.70). Using conditional logistic regression, history of multiple lifetime admissions 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 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: Our findings suggest that early readmission occurs among a subset of children with greater disease severity. History of multiple admissions, receipt of pulmonary consultation and prior ICU admission may identify children who are more likely to be readmitted and thus, guide inpatient and outpatient asthma management.

14 Poster Board 14 — Medical Student

Knowldege of the Toxicity of Elemental Mercury in an Inner City Population

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BACKGROUND: Published reports suggest that inner city populations may be exposed to elemental mercury via ritualistic usage. Inhalation of elemental mercury vapors can lead to toxicity. It is not known whether inner city residents are aware of the potential dangers arising from the use of mercury.
OBJECTIVE: To assess awareness of risks associated with the use of elemental mercury among an inner city population.
DESIGN/METHODS: We conducted a cross-sectional survey of subjects recruited from an inner city ambulatory clinic. The setting was the South Bronx, NY, a community in which reports suggest ritualistic use of elemental mercury may be prevalent. We developed a 23-item questionnaire that was pilot-tested and modified by a group of experts and lay people familiar with the cultural practices surrounding elemental mercury. The questionnaire was then administered by the same researcher to all subjects. Subjects were shown a mercury thermometer in order to indicate the substance in question. Then, we inquired about awareness of potential toxicity associated with different ritualistic uses of elemental mercury, knowledge of the routes of exposure that may cause toxicity, and methods to limit exposure.
RESULTS: 1000 subjects participated, of whom 43% were African American and 42% were Hispanic or Latino. Overall, 47% of participants did not know that boiling mercury in a pot may lead to poisoning, 44% did not know that burning mercury in a candle may lead to poisoning, and 40% were unaware that sprinkling mercury in the house may lead to poisoning. Similarly, 81% did not know that children breathe in more vapors than adults living in the same household, 71% did not know that mercury should not be flushed down the toilet, and 47% did not know that mercury vapors were harmful. 90% of subjects incorrectly thought that mercury poisoning could be caused by ingestion of liquid mercury and 88% of subjects incorrectly thought that most cases of mercury poisoning were caused by handling mercury with bare hands.
CONCLUSIONS: A substantial number of subjects did not know that practices associated with ritualistic uses of mercury may lead to toxicity. They did not know the route of exposure that leads to elemental mercury poisoning nor did they know proper disposal techniques. Further education is needed to limit the exposure of children to mercury in households where it may be used as a ritual object.

15 Poster Board 15 — Fellow in Training

The Environment in Pediatric Practice: A Pilot Study of New York Pediatricians' Attitudes, Beliefs and Practices for Children's Environmental Health

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BACKGROUND: Pediatricians can limit children's exposures to environmental hazards through education, identification of exposures, diagnosis, and advocacy for prevention. Unfortunately, physicians have little training in environmental health and usually limit their inquiry to lead and environmental tobacco smoke. Resources for children with environmental health concerns are also sparsely distributed across the nation.
OBJECTIVE: To assess attitudes and beliefs of New York State pediatricians about the role of the environment in children's health; and to obtain their opinion about the need for additional clinical resources for the evaluation of children with environmental health concerns.
DESIGN/METHODS: A four-page survey was sent to 1500 randomly selected members of the New York State American Academy of Pediatrics (500 from each District) in February 2004. A second mailing was sent six weeks later to nonrespondents. Descriptive data were tabulated and calculated using SPSS 11.0.
RESULTS: 20.9% response rate; 24 excluded because not currently in practice. 57% female; 78% primary care; respondents and nonrespondents did not differ in years of licensure or county. 93.5% reported seeing a patient in the past year significantly affected by environmnental exposure. Respondents agreed that history-taking would identify exposures causing symptoms (mean 4.07 on 1-5 Likert scale), and voiced high self-efficacy in history-taking, educating parents, and finding diagnostic and treatment resources for lead exposure (means 4.16-4.24). However, for pesticide, mercury and mold, self-efficacy was much lower (means 2.51-3.21; p<.001). Only 10.2% had heard of the existing Pediatric Environmental Health Specialty Unit, and 4.0% had referred patients. Respondents would make at least 2,477 hypothetical referrals/year to clinical centers in environmental pediatrics. 80.8% would like to learn more; 46.9% reported owning the AAP *Handbook of Pediatric Environmental Health.*
CONCLUSIONS: New York pediatricians agree that children are suffering preventable illnesses of environmental origin, but they feel ill-equipped to educate families about many common exposures. Significant demand exists for centers that can evaluate environmental health concerns, and for educational opportunities for pediatricians.

16 Poster Board 16 — House Officer

Parental Health Literacy: Can Parents Really Dose Liquid Medication Correctly?

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BACKGROUND: Health literacy, the ability to use health information to make appropriate health decisions, involves both reading and numeracy skills. While studies have shown that parents have difficulty reading medication instructions, none have adequately measured parental numeracy skills.
OBJECTIVE: To measure parental health literacy, including the numeracy skills required to dose liquid medication correctly.
DESIGN/METHODS: Cross-sectional survey of English-speaking parents of young children (< 5 yrs old)attending an inner-city health center. An investigator showed subjects a bottle of liquid medicine with a prescription label. First, subjects were asked to read the prescription label and answer two questions modeled after the Numeracy section of the Test of Functional Health Literacy in Adults: "How many times a day should you give this medicine?, and "When should you administer the next dose?" Subjects were then asked to use the medicine dropper to demonstrate how much medicine they should give. For each subject, a correct response to all questions was coded as correct Medication Dosing. An incorrect response to any question was coded as incorrect Medication Dosing.
To test for demographic predictors of health literacy, we used chi-square to compare Medication Dosing by immigrant status and education. We used Multiple logistic regression to adjust for confounders.
RESULTS: 326 subjects participated. The mean age of respondents was 32; 69% had completed high school, 72% were Medicaid recipients, and 76% were US born.
87% of subjects demonstrated incorrect Medication Dosing. Of these, 95% correctly stated the number of times per day to give the medicine. However, 83% stated a wrong time to give the next dose and 66% demonstrated the wrong amount of medicine to give.
Medication Dosing was less likely to be correct among immigrants and among subjects who had not completed high school. These differences persisted after logistic regression (immigrants: AOR 0.32; CI 0.11, 0.94; lack of high school education: AOR 0.09; CI .02, .40).
CONCLUSIONS: Most parents in this study could not dose a liquid medication correctly. Most errors occurred with determining the time to give the next dose, indicating deficient numeracy skills. Immigrant status and lack of high school education increased the risk of incorrect medication dosing.

17 Poster Board 17 — Fellow in Training

Use of a Psychosocial Screen To Detect Children with Post Traumatic Stress Disorder: Does Mother Know Best?

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BACKGROUND: Many screening tools are available to identify pediatric psychosocial problems, but it is unclear whether these adequately identify trauma related distress.
OBJECTIVE: To evaluate the sensitivity and specificity of the Pediatric Symptom Checklist (PSC), a general psychosocial screening tool, in recognizing children with symptoms of posttraumatic stress disorder (PTSD). PTSD symptoms were identified by the UCLA Post Traumatic Stress Reaction Index (PTSRI), which was used as a "gold standard" for PTSD in lieu of a clinical psychiatric interview.
DESIGN/METHODS: Ongoing, cross-sectional study of convenience sample of consecutive 8 to 10 year olds at a primary care pediatrics practice in East Harlem, New York City. Children complete the Youth PSC and the PTSRI with the assistance of a researcher; caregivers complete the Parent PSC and a demographic survey.
RESULTS: A total of 130 eligible children were approached between March and November 2004; 105 children (81%) enrolled and 103 completed all questionnaires. 23% of the children had positive screens on the Parent-completed PSC (cutoff score 28) and 33% had positive screens on the Youth-completed PSC (cutoff score 30). Overall, 43% of the children had a positive Parent and/or Youth PSC. On the PTSRI, 18% of the children scored at a level consistent with full PTSD (cutoff score 38). Ability of the PSC to detect PTSD is detailed below. In an attempt to improve sensitivity, the cutoff of the Youth PSC was lowered from 30 to 28. 43% of the children had positive Youth PSCs at this cutoff.

Comparison of Screening Tools' Ability to Detect PTSD

	Sensitivity	Specificity	LR + (CI)*	LR - (CI)*
Parent PSC	37%	80%	1.82 (0.88-3.76)	0.79 (0.55-1.13)
Youth PSC	68%	74%	2.61 (1.63-4.19)	0.42 (0.22-0.84)
Youth PSC lowered cutoff	84%	67%	2.53 (1.76-3.62)	0.24 (0.08-0.68)

*LR = likelihood ratio, CI = confidence interval

CONCLUSIONS: The Youth PSC, but not the Parent PSC, successfully identified inner city children with likely PTSD. The Youth PSC's sensitivity in detecting children with likely PTSD was increased to 84% when its cutoff was slightly lowered; this change decreased specificity to 67%. Of note, the children in East Harlem had a very high rate of positive screens on the Youth and Parent PSC, implying that they bear a high burden of psychosocial problems.

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Prevalence of Pulmonary Hypertension (PHTN) in Sickle Cell Disease (SCD) Adolescents with Pulmonary Complications

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BACKGROUND: Despite the high prevalence of PHTN in adults with SCD, the prevalence in the pediatric population with SCD is not known.

OBJECTIVE: We hypothesized that elevated pulmonary artery pressures may be found in SCD adolescents with history of pulmonary complications, such as acute chest syndrome (ACS), obstructive sleep apnea (OSA), asthma, and reactive airway disease (RAD).

DESIGN/METHODS: 30 such sickle cell disease adolescents were screened at Howard University and University of Michigan for PHTN with Doppler echocardiography. We defined PHTN as a tricuspid regurgitant jet velocity (TRV) of at least 2.5 m/sec (corresponding to a pulmonary artery systolic pressure greater than 35 mm Hg). PHTN was found in 16 SCD patients (53.3%) and 5 (16.7%) had TRV > 3.0 m/sec.

RESULTS: Clinical findings according to the presences or absence of PHTN are shown in the table 1.

CONCLUSIONS: Potential factors contributing to PHTN in patients with SCD include chronic hemolysis and chronic hypoxia. Early echocardiographic evaluation of patients with history of pulmonary disease and institution of therapy will decrease morbidity and mortality associated with PHTN. However, further studies are needed to clarify the prevalence and mechanisms of PHTN in adolescents with SCD.

Clinical and demographic data of 30 SCD adolescents who underwent echocardiography at Howard University Hospital or University of Michigan

	PHTN (N = 16)	No PHTN (N = 14)	P
Age in years (mean ± SD)	15.9 ± 3.2	17.4 ± 2.3	0.17
Females (no. and %)	5 (31.3)	7 (50)	0.5
Hemoglobin SS (no. and %)	14 (87.5)	11 (78.6)	0.5
HB concentration (mean ± SD)	8.0 ± 2.1	9.3 ± 1.9	0.11
WBC (mean ± SD)	10.9 ± 2.9	9.7 ± 3.7	0.4
Platelet (mean ± SD)	475 ± 172	364 ± 240	0.17
HbF percent (mean ± SD)	5.1 ± 3.5	6.4 ± 5.5	0.6
LDH (mean ± SD)	505 ± 162	264 ± 50	0.002
Total Bilirubin (mean ± SD)	4.1 ± 2.6	3.4 ± 2.6	0.5
Creatinine concentration (mean ± SD)	0.6 ± 0.2	0.7 ± 0.2	0.18
AST (mean ± SD)	48 ± 27	36 ± 16	0.18
ALT (mean ± SD)	51 ± 37	39 ± 20	0.3

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Regional Perinatal Forums as a Public Health Instrument

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BACKGROUND: New York State mandates that the Regional Perinatal Centers partner with community based organizations, county departments of health, insurance companies, and other stakeholders to approach perinatal public health in a multidisciplinary group or Perinatal Forum.

OBJECTIVE: To determine the impact of a Regional Perinatal Forum Conference (RPFC) on clinical and public health practice and whether this differs by occupation.

DESIGN/METHODS: A multiple choice survey was distributed to all 90 attendees of the 2004 RPFC at Westchester Medical Center. Email and phone follow up was used to maximize response. Chi square analysis was used for between group analyses.

RESULTS: The overall response rate was 61% (n=55), and by occupation included 22 nurses, 12 physicians, 3 health department officials, 9 members of community based organizations (CBO's), and 11 Others (including lactation consultants, administrators, and social workers). 98% of all responders deem the RPFC a helpful activity. 100% of physicians felt that they learned about regional perinatal public health which was significantly higher than nurses (58%) and CBO's (56%; $p<0.05$). Two thirds of all responders would change the way they teach their peers/staff after attending the RPFC. Interestingly, of the Others over 60% indicated that they would change their practice as a result of attending the RPFC.

CONCLUSIONS: The RPFC can serve as a powerful tool in disseminating public health and clinical practice guidelines to a diverse body of providers. For maximal efficacy in the future, breakout groups by occupation would allow for tailored information dispersal.

20 Poster Board 20

Snuglis and Car Seats and Nuks! Oh My! An Educational Program for Pediatric Residents To Demystify Childcare Merchandise

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BACKGROUND: The ever-increasing variety and quantity of childcare products marketed to parents presents a challenge to pediatric residents. They often lack personal familiarity with these items, and may be ill equipped to appropriately advise parents on the safety and utility of this merchandise. Pediatric residency training does not generally address this issue.

OBJECTIVE: 1) Assess resident knowledge of retail childcare merchandise 2) Develop a hands-on program to teach developmentally appropriate use of the products, raise awareness of marketing strategies and financial burden to parents, and stress the importance of these issues to pediatric practice and 3) Evaluate the usefulness of this program to trainees.

DESIGN/METHODS: A 25-item pretest was administered to a successive sample of 47 residents to assess knowledge in 4 domains: use of items with respect to 1) safety 2) nutrition 3)infant development, and 4) general familiarity with common childcare products. Included were questions on items like bike helmets, cribs, and high chairs. As part of the Developmental-Behavior rotation, small groups of residents went with a General Pediatric Attending to a major retail store where they explored areas such as car seats, safety, and newborn care products. Merchandise was extensively examined and discussed, with attention paid to pricing, marketing, safety, need and appropriate use. Relevant developmental topics covered included toilet training, infant feeding and toys. Residents completed a year-end program evaluation.

RESULTS: 47 residents completed the pretest. There were 19% PL-1s, 71% PL-2s, and 10% PL-3s. 17% were male. Scores ranged from 48%-96% correct with a mean of 72%. No differences in mean scores were noted by year of training, sex of resident, or among the 4 domains. Only 36% of residents could name 6 childproofing devices for the home, 57% knew bottles didn't require daily sterilization and 57% knew when to switch the positioning of a car seat. On the year-end evaluation this curricular module received a mean score of 5 on a five-point scale of educational relevance.

CONCLUSIONS: Significant gaps exist in pediatric residents' knowledge of childcare merchandise. Exposing residents to these products through a hands-on interactive program can address these gaps and is valuable in preparing residents to counsel families.

21 Poster Board 21 Fellow in Training

Serum Alkaline Phosphatase Levels in Premature Infants < 32 Weeks

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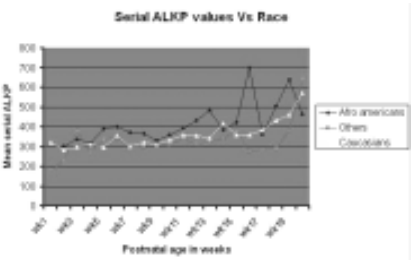
BACKGROUND: Premature infants born £ 32 wks of GA are at risk of developing metabolic bone disease.Serial total serum alkaline phosphatase (ALKP) measurements are considered to be a way of identifying premature infants with metabolic bone disease**.** Current literature states ALKP values for preterm infants as <5 times the adult normal limit as there are no baseline values in this population. However, the variations according to gestational age (GA) at birth, birth weight (BW), race and gender are unknown.

OBJECTIVE: The objective of this retrospective data analysis was to determine the mean and median serum ALKP values for infants born £ 32 weeks gestation. We also compared these values in relation to GA at birth, postnatal age, race, gender and BW.

DESIGN/METHODS: Data were reviewed from database at John Dempsey Hospital Level III NICU between January 1998 and December 2002. Based on 769 data points, the mean and median ALKP values were determined. Univariate analyses were performed to determine relationship of ALKP in relation to BW and GA. Multivariate analyses were utilized to determine the significance of gender, race, chronological GA, and weight gain on ALKP values.

RESULTS: The mean ALKP value is 346 ±113 IU/L and median is 308 IU/L . In univariate analyses, ALKP values demonstrated a negative linear relationship to both BW and GA at birth. ALKP values tended to - as chronological age -. Gender and Wt gain/day showed no significant association with ALKP values. Afro american infants were found to have significant higher mean ALKP values than Caucasian and other racial groups, even when adjusted to GA and gender.



CONCLUSIONS: In conclusion, major factors influencing ALKP values are GA, BW, race and postnatal age. Norms for ALKP values need to be based on GA, BW, race and postnatal age of infants.Further studies need to be done to elucidate key mechanisms for -ALKP in Afro american population.

22 Poster Board 22 Fellow in Training

The Predictive Ability of Predischarge End Tidal Carbon Monoxide (ETCOc) for Hyperbilirubinemia in Term and near Term Infants

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BACKGROUND: A major cause of neonatal hyperbilirubinemia is excessive bilirubin production, which can be monitored by measurements of end-tidal carbon monoxide (CO) corrected for ambient CO (ETCOc). Controversy exists on the utility of ETCOc measurements in the diagnosis and prediction of neonatal hyperbilirubinemia.

OBJECTIVE: To evaluate the ability of predischarge ETCOc measurements to predict neonatal hyperbilirubinemia.

DESIGN/METHODS: ETCOc is an index of bilirubin production and can provide non-invasive identification of hemolysis. We measured ETCOc prior to hospital discharge in term/near term neonates using the CO-Stat End Tidal analyzer and conducted a parental survey regarding neonatal jaundice on days 7 and 14 of life. Receiver operator characteristics (ROC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

RESULTS: Predischarge ETCOc readings were obtained in 73 term and near-term infants (4 were Coombs' +). Among these neonates, 33.3% developed jaundice (J+) after discharge. There were no significant differences in gestational age, birth weight, weight loss (%), age at discharge (hrs), Coombs' status and feeding among neonates with/without jaundice. Feeding, birth weight, weight loss and gestational age did not influence ETCOc levels. However, there was a negative correlation between ETCOc and age at measurement ($r = -0.49$, $P<0.001$). The age at measurement was similar for the (J+) and (J-) groups (45.6±17.3 hrs vs. 45.1±20.5 hrs, $P>0.05$). The age adjusted predischarge ETCOc was higher in (J+) as compared with (J-) group (1.8±0.8 ppm vs.1.3±0.4 ppm, $P= 0.008$). The area under the ROC curve was 0.645±0.071 with 95% CI 0.524-0.754 and threshold value of 1.4 ppm. The sensitivity, specificity, PPV and NPV of predischarge ETCOc for the prediction of neonatal jaundice were 66.7%, 57.1%, 53.9%, and 69.5%, respectively.

CONCLUSIONS: The high negative predictive value of predischarge ETCOc measurements permits identification of neonates at low risk of jaundice. ETCOc levels ^{3} 1.4 ppm can be used to support clinical decisions regarding post-discharge follow-up of neonates, which would be in compliance with the AAP guidelines that require predischarge identification of infants at risk for development of neonatal hyperbilribunemia.

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Extracellular Matrix (ECM) Modulation of Type 2 (T2) Cell Phenotype In Vitro

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BACKGROUND: The ECM plays a dynamic role in alveolar epithelial cell physiology and differentiation. Although the effects of individual matrix components have been investigated in animal models, there is a paucity of information in human type 1 (T1) and T2 cells.

OBJECTIVE: To examine the effects of fibronectin and laminin in an in vitro model of human T2 cell differentiation and T1 transdifferentiation.

DESIGN/METHODS: Human alveolar epithelial cells from 2nd trimester human fetal lung were cultured up to 7 d in 10 nM dexamethasone, 0.1 mM each of 8-Br-cAMP and IBMX (DCI) to establish T2 cell phenotype. Cells were cultured up to 7d on plastic (control), or plastic coated with 50 mg of either fibronectin or laminin. Alternately, DCI was removed after 4d, and cells were cultured for 3d without hormones to promote transdifferentiation to T1. Cells were analyzed by real time RT-PCR for T2 cell markers SP-B and Pepsinogen C (PGC), or the T1 marker PAI-1, normalizing results for 18S RNA. Results are expressed as mean± SE for 3 experiments and were analyzed by ANOVA.

RESULTS: DCI-induced in vitro differentiation resulted in a 3.3±0.7-fold induction of SP-B and 10.1±0.8-fold induction of PGC, as previously described. Cells plated on substrata exhibited similar induction of T2 markers (fibronectin: SP-B 7.8±3.8-fold, PGC 17.1±4.9-fold; laminin: SP-B 14.8±7.2-fold, PGC 25.2±10.5-fold). The trend towards increased SP-B and PGC expression on substrates compared to plastic alone did not reach statistical significance. Removal of hormones resulted in similar induction of PAI-1 in all conditions compared to cells treated with 4 d of DCI (plastic 33.8±21.3-fold, fibronectin 11.3±7.5-fold, laminin 19.9±16.9-fold).

CONCLUSIONS: ECM components fibronectin and laminin applied to the plating surface did not significantly alter the expression of T1 or T2 cell markers in our models of in vitro T2 differentiation and T1 transdifferentiation. The trend towards increased SP-B and PGC mRNA expression with ECM component-coated surfaces is in agreement with previous work by others and may foster a more stable in vitro culture environment.
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24 Poster Board 24 Fellow in Training

Inter-alpha Inhibitor Protein (IaIp) in Term and Preterm Infants at Birth

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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. They are produced by the liver and present in adult plasma in the range of 600-1200 mg/liter. A significant decrease of plasma IaIp levels occurs in sepsis. Our previous study has shown that IaIp are produced, independently, by the term as well as preterm newborn infants.
OBJECTIVE: The aim of this study is to establish the normal levels of IaIp in term and preterm infants at birth and to evaluate the effect of gender.
DESIGN/METHODS: On day of life 0, term and preterm infants, who had a blood sample taken in an EDTA container for any reason, decided by the admitting physician, were included in the study. Those infants with positive blood culture, chromosomal anomalies and significant congenital abnormalities were excluded. Residual blood samples were collected and plasma was extracted and frozen for later analysis. To measure plasma IaIp levels, a competitive ELISA was performed using MAb 69.31 antibody.
RESULTS: Plasma was analyzed from 294 infants. Their gestational age ranged from 22 weeks to 41 weeks. The mean IaIp level was 315 mg/liter with a 2 SD range of 237-393 mg/liter. There was no significant difference across the gestational age or gender.
CONCLUSIONS: IaIp is present in term and preterm infants' plasma at the levels of 237-393 mg/liter and there is no significant difference in its level at various gestations and gender.
Funded by ProThera Biologics.

25 Poster Board 25 Fellow in Training

The Effect of an Educational Campaign on Compliance Rates with Influenza Vaccination and Its Relationship to Gestational Age and Birthweight in Parents of Neonatal Intensive Care Unit (NICU) Patients

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BACKGROUND: The American Academy of Pediatrics recommends inactivated influenza vaccine for all close contacts (parents) of high-risk infants, a population encompassing all patients admitted to the NICU. However, compliance with influenza vaccination in the adult population is poor.
OBJECTIVE: To determine if education regarding new guidelines for vaccination would increase compliance among parents of lower birthweight and gestational age infants.
DESIGN/METHODS: For 14 weeks, during the 2003-04 influenza season, 92 parents of 56 NICU patients underwent an education program providing informed consent regarding influenza vaccine. Parents were then surveyed in June of 2004 to assess if they obtained the injection the previous winter. A financial analysis of cost savings based on average hospital admission rates for low income patients, seroconversion patterns for the vaccine and standardized outpatient visits was also conducted based on the questionannaire response data.
RESULTS: Eighty-Five parents (92%) indicated they intended to obtain the vaccine, however compliance equaled 32.6%. These parents were most motivated by their physician's recommendation to be immunized. Mothers were statistically twice as likely to obtain the vaccine ($p<0.05$ via paired t-test) and both sets of parents were statistically more likely to obtain the shot than one parent alone ($p<0.05$ via T- test). The two most common reasons for not receiving the flu vaccine were inconvenience and lack of availability. No correlation between compliance and patient birthweight, gestational age or length of stay. (Mann-Whitney Test) was seen. There was no correlation between level of parental education and compliance rates. Average per year savings for a large hospital network (NICU admission rate > 5000) totals 5 million dollars per year exclusive of indirect costs.
CONCLUSIONS: A directed educational program detailing the risk and benefits of influenza vaccine is effective in informing parents' decision to obtain vaccine. Neonatology departments should consider offering the vaccine in the NICU to overcome barriers parents face in complying with AAP influenza recommendations.

26 Poster Board 26 Fellow in Training

Correlations Between Gene Polymorphisms of Interleukin-1ß (IL-1ß), Interleukin-8 (IL-8) and Tumor Necrosis Factor (TNF-ζ) and Cytokine Concentrations in Cerebrospinal Fluid (CSF) of Term and Premature Neonates

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BACKGROUND: DNA polymorphisms in genes for different cytokines have been correlated with predisposition to fetal and neonatal diseases and conditions: premature labor, premature rupture of membranes, twining etc. Elevated concentrations of pro-inflammatory cytokines have been implicated in development of cerebral palsy, bronchopulmonary dysplasia, necrotizing enterocolitis.
OBJECTIVE: Objective of this study was to determine whether there is a relationship between polymorphisms in genes encoding cytokines and cytokine concentrations in CSF and correlate these findings with infants' gestational age at birth.
DESIGN/METHODS: DNA from buccal swabs (or from CSF) was obtained from 24 term and 52 premature infants who underwent clinically indicated spinal taps and had CSF available for analysis. Infants with CNS anomalies or confirmed infection were excluded. Polymorphisms were analyzed by polymerase chain reaction using specific primers for IL-1ß(+3953), TNF-ζ (-308) and IL-8. Concentrations of corresponding cytokines (IL-1ß, TNF-ζ and IL-8) in CSF were determined by automated chemiluminescent assay (Immulite).
RESULTS: Although buccal swabs are preferred method, DNA could be obtained from CSF for polymorphism analysis.
Correlation was found between TNF-ζ #genotype and concentration of TNF-a in CSF: infants who were heterozygous: TNF-ζ #1,2, had higher concentrations of TNF-ζ in CSF than infants who were homozygous: TNF-ζ #1,1, p=.069.
There were associations between IL-1ß allele 2 (IL-1b*2) carriage and prematurity (p=.002) and being singleton rather than twin (p=.004).
Correlations were found between CSF TNF-ζ concentration and birthweight: r=.38, p=.02. or prematurity p=.001. The median CSF IL-8 concentration was lower in premature than in term infants p=.007.
Other potential correlations (other genotypes, chorioamnionitis, premature birth, rupture of membranes, etc.) were not established.
CONCLUSIONS: Correlations were found between: TNF-ζ #genotype and concentration of TNF-ζ #in CSF and carriage of IL-1ß allele 2 and prematurity and singleton pregnancy.
TNF-ζ and IL-8 increase in CSF with gestational age.

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Early Peak Respiratory Severity Score (PRSS) as a Risk Factor for Bronchopulmonary Dysplasia (BPD)

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BACKGROUND: BPD is a major complication of prematurity, but the ability to predict which infants with a given birth weight (BW) or gestational age (GA) will experience this morbidity remains poor.
OBJECTIVE: To determine whether a physiologic marker of respiratory status between 4 and 10 days after birth, the PRSS (mean airway pressure x FiO_2), can also serve as an early predictor of BPD.
DESIGN/METHODS: We studied infants £32 wks GA requiring CPAP or mechanical ventilation who were enrolled in either the NO CLD trial (infants randomized to either postnatal nitric oxide or placebo at 20 centers) and the North American Thyrotropin-Releasing Hormone study (TRH) (Ballard RA, NEJM, 1998). PRSS was collected from bedside data. Logistic regression models were developed to determine the association of the PRSS between 4 and 10 days after birth and the development of death or BPD, defined as an oxygen requirement at 36 weeks postmenstrual age, after controlling for BW and GA in separate models.
RESULTS: 332 patients from the NO CLD trial and 194 from the TRH trial required CPAP or mechanical ventilation between days 4 and 10 after birth. The mean BW was 748 ± 124 g and mean GA was 25 ± 2.5 wks. 308 (59%) developed BPD. Logistic regression models including BW and PRSS showed that the PRSS between 4 and 10 days of age was significantly associated with BPD using thresholds of both 3.5 [Odds Ratio (OR) 1.96, 95% CI 1.37-2.80] and 4.0 [OR 2.10, 95% CI 1.46-3.02]. Although BW alone was significantly associated with BPD (p=0.03), when PRSS was added to the model, BW was no longer statistically significant. Both PRSS thresholds were significant when each trial was analyzed separately. When GA was substituted for BW, the PRSS between 4 and 10 days of age remained significant using thresholds of 3.5 [OR 1.77, 95% CI 1.21-2.57] and 4.0 [OR 1.83, 95% CI 1.25-2.67].
CONCLUSIONS: The PRSS that a ventilated infant reaches between 4 and 10 days after birth is a significant risk factor for development of BPD. This finding emphasizes the role of early postnatal lung disease in the development of BPD. PRSS may be a useful clinical and research tool to identify infants at increased risk for BPD.

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Effect of Arterial pH on Response to Inhaled Nitric Oxide (iNO) for Persistent Pulmonary Hypertension of the Newborn (PPHN)

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BACKGROUND: Many patients with PPHN fail to respond to iNO. In our nursery, we have noted that the well-known critical pH effect on oxygenation in infants with PPHN still occurs in infants receiving iNO.
OBJECTIVE: To explore the hypothesis that pH is an important determinant of responsiveness to iNO.
DESIGN/METHODS: Demographics, ventilator settings, arterial blood gases (ABG) and interventions for up to 96 hr. of life were extracted from the charts of 38 infants treated with iNO for PPHN from Jan. 2000 - Dec. 2004. The need for ECMO and survival to discharge were noted. Mean blood pressure (MBP) and mean airway pressure (MAP) were recorded at the time of each blood gas. The arterial/Alveolar (a/A) ratio was used as the primary outcome to account for the effect of $PaCO_2$ and FiO_2. Data were analyzed using simple linear and multiple linear regression analyses. In each infant, pH responsiveness was defined as a correlation coefficient (CC) of >0.45. Because pH sensitivity wanes as vasoconstriction subsides, further analysis was limited to the period of responsiveness.
RESULTS: Mean gestational age was 39.2 (36 - 41) weeks and a mean birth weight 3380 (2040 - 5178) g. PPHN was documented by echo in 36/38 infants; 25/38 infants were on high-frequency ventilation at the initiation of iNO. There was clear responsiveness to pH in 23/38 infants. Because the critical pH varied greatly between patients, the CC was much higher for individual patients (range 0.467 - 0.895, $p < 10^{-6}$ - $5x10^{-2}$) than for pH responders as a group (CC of 0.273 for a/A vs. pH, $p<10^{-6}$) during the responsive period. In 1 patient with limited data points CC=0.78, p=0.12. MAP also correlated with the a/A ratio in responders ($p<0.05$), while MBP was not correlated by multiple regression analysis. Critical pH in the responders ranged from 7.3 - 7.62 with 21/23 having a critical pH <7.55. Oxygenation dependence on critical pH waned over time. Of 7 patients requiring ECMO, only 2 exhibited pH responsiveness at any time in their course, and had critical pH >7.5. Among the 23 responders, only 2 required ECMO. All infants survived to discharge.
CONCLUSIONS: Failure to optimize pH may account for some of the observed unresponsiveness to iNO. Patients with a critical pH >7.55 are more likely to fail iNO therapy; due to the known risks of alkalosis marked hyperventillation should be avoided.
Funded by INO Therapeutics; Inhaled Nitric Oxide.

29 Poster Board 29 Undergraduate Student

Interaction of HO-1 with Cellular Proteins

Sean Levy, Qing Lin, Guang Yang, Shawndra Woodard, Phyllis Dennery. Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Pediatrics, University of Pennsylvania, Philadelphia, PA.
BACKGROUND: Heme oxygenase-1 (HO-1), the rate limiting enzyme in bilirubin production, is a cytoprotective protein in mammalian cells. This inducible enzyme may also play an important role in cellular signaling functions. A recent report demonstrates that HO-1 binds to its constitutive isoenzyme, HO-2. This serves to limit total cellular HO activity. Could HO-1 bind to other cellular proteins, and could HO-1 mediate its signaling effects through binding to key cellular proteins?
OBJECTIVE: To determine whether HO-1 binds to key cellular proteins under basal conditions
DESIGN/METHODS: A glutathione-Sepharose4B Microspin column (Amersham Biosciences, Piscataway, NJ) was linked with rat HO-1 protein. After centrifuging and washing with phosphate-buffered saline, mouse fibroblast cells (NIH-3T3) grown to 90% confluency were sonicated in phosphate-buffered saline and centrifuged at 3000 x g for 25 minutes at 4oC. The supernatant was transferred onto the column for 10 minutes at room temperature. The column was treated with 5 x 1 mL of glutathione elution buffer containing 20 mM reduced glutathione, The eluent was concentrated 10-fold and run on a 12% SDS polyacrylamide gel followed by staining of the gel with Coomasie blue.
In separate experiments, recombinant Y187 yeast cells (Matchmaker GAL4, Clontech, Palo Alto, CA) expressing HO-1 protein were used as the bait protein (GAL4 DNA-binding domain) for yeast cells expressing a mammalian cDNA library. Determination of HO-1-protein interaction was achieved by measuring LacZ reporter gene expression using ?-galactosidase activity with the colony-lift filter method

according to the manufacturer's (Clontech) protocol. Colonies were grown in LB medium. DNA from the colonies was then extracted and submitted for sequencing.
RESULTS: Eluents from the GST-HO-1 column demonstrated three bands on the SDS gel migrating at 36, 40 and 60 kD. Yeast two hybrid experiments revealed the presence of 8 positive clones that are being analyzed.
CONCLUSIONS: Under basal conditions, HO-1 protein interacts with proteins other than HO-2. We suspect that the 36 kD band represents HO-2 protein. Further analysis will determine the identity of the other protein bands.

30 Poster Board 30

Sedation for Neurophysiology Tests

Francis J. DiMario, Jr., Deborah Johnson, Cheryl Milone, Carol Leicher, Philip Brunquell. Pediatrics, Connecticut Children's Medical Center, Hartford, CT.
BACKGROUND: The performance and completion of neurophysiology procedures on children often requires the use of sedation / analgesia (conscious sedation). Such intervention is at times needed in order to minimize patient anxiety, secure electrodes, lessen muscle and movement artifacts onto test tracings, and assure a component of drowsiness and sleep recording. A number of guidelines have been advanced and modified over recent years by the American Academy of Pediatrics (AAP), the American Academy of Pediatric Dentistry (AAPD) and the American Society of Anesthesiologists (ASA), which advocate a systematic approach now required by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO).
OBJECTIVE: We report results from a prospective study determining the adverse effects and duration from conscious sedation with chloral hydrate (CH) used for EEG/BAER examination.
DESIGN/METHODS: All children undergoing EEG/BAER examination received standard pre-examination preparation instructions. Those children requiring conscious sedation were administered a standard dosage CH (50mg/kg po followed by 25mg/kg if needed to a max of 1500mg) and monitoring per protocol. At least three attempts by telephone were made to obtain a follow-up questionnaire within 72^0 on all sedated patients.
RESULTS: Over a period of 43 months (1997-2001), 5055 EEG/BAER examinations were performed. Sedation was administered in 15.5% (787/5055) and follow-up contacts were completed in 50% (391/787). Of these patients there were 224 boys (57%) and 156 (40%) were < 4 years old and 241 (62%) were 1-6 years old. A second dose of medication was needed in 3%. Sleep was achieved in 78% of attempts. Paradoxic agitation was initially encountered in 17%. Post sedation ataxia was noted in 41%. Forty percent of patients slept during their return home and 21.5% exhibited any behavioral change for $< 12^0$. Importantly, 96% of parents felt adequately prepared/informed prior to the procedure. Parents offered suggestions for improvement, which were incorporated into our procedure. No serious adverse effects were encountered in any of 787 sedated children.
CONCLUSIONS: Parental preparation and standard sedation protocol allowed for safe and effective CH sedation. Post sedation effects can be anticipated and prepared for.

31 Poster Board 31

Variations in IRB Interpretation of the Assent Requirement in Two Pediatric Placebo-Controlled Randomized Trials

K. Sarah Hoehn, Michael Kimberly, Chris Feudtner, Robert M. Nelson, Mark Schreiner. Anesthesiology and Critical Care Medicine, Children's Hospital of Philadelphia, Philadelphia, PA; Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA.
BACKGROUND: Previous studies have reported variability in IRB review and approval. Because federal regulations for research involving pediatric subjects do not specify when assent should be sought or how it should be documented, significant variability between IRB approvals for pediatric research may result.
OBJECTIVE: To systematically compare IRB responses to identical study protocols regarding consent and assent forms.
DESIGN/METHODS: Using a natural quasi-experimental study design whereby IRBs from 17 sites were exposed to one of two study protocols, we conducted a retrospective review of IRB letters and consent/assent forms from two different multi-institutional pediatric placebo-controlled randomized studies. One study randomized subjects to either placebo or inhaled nitric oxide for hypoxemic respiratory failure. The other study randomized children with breakthrough cancer pain to either oral transmucosal fentanyl citrate or placebo (3:1) after a dose finding and pharmacokinetic phase. The data abstracted from the IRB forms was the site-specific requirements for assent.
RESULTS: Inhaled nitric oxide study: Although the subjects in the inhaled nitric oxide study are critically ill and likely to be on mechanical ventilation, 4 of the 7 approved sites included the child's signature to indicate assent, with 2 of the 4 allowing investigator waiver. One site understood assent to be possible at the age of 7, another at the age of 12. None of the 4 centers addressed the feasibility of obtaining signed assent from a child in hypoxemic respiratory failure on a ventilator. The remaining 3 sites did not require assent. Fentanyl pain study: Of the 10 approved sites for the fentanyl pain study, all sites mentioned assent or waiver of assent. 9 out of the 10 sites required the child's signature. Only one site had simplified the key elements of the consent form for a separate assent form. The 9 remaining sites had additional lines on the parental permission form for signature of assent.
CONCLUSIONS: Significant variation exists in the implementation of the federal regulations regarding assent. The extent, underlying causes, and implications of this variability require further research and consideration.

32 Poster Board 32 Fellow in Training

Scr Kinase Activation of the NAD(P)H Oxidase Mediates Ang II – Dependent Increase in Nitric Oxide Synthase Protein Expression in BPAEC

Xinmei Li, Susana Rapaport, Susan C. Olson, Michael S. Wolin. Pedaitrics, Flushing Hospital and Medical Center, Flushing, NY; Biochemistry, New York Medical School, Valhalla, NY; Physiology, New York Medical School, Valhalla, NY.
BACKGROUND: Emerging evidence has demonstrated that reactive oxygen species (ROS) contribute to the pathogenesis disorders, such as respiratory distress syndrome, bronchopulmonary dysplasia, and asthma .Although the NAD (P) H oxidase has been well studied in the VSMCs, little is known about in endothelial cells.
Griendling et al first demonstrated that Ang II activates the NAD (P) H oxidase in vascular smooth muscle cells via the AT_1 receptor.On the other hand, Oeckler et al. have identified a role for Src in stretch activation of NAD (P) H oxidase in bovine coronary arteries. In pulmonary endothelium, Ang II stimulates an increase in nitric oxide synthase protein levels.Previous studies have demonstrated that activation of the NAD (P) H oxidase is required for H_2O_2-dependent increase in eNOS expression .
OBJECTIVE: The goal of the project is First, to determine Src tyrosine kinase mediates Ang II-dependent activation of the NAD (P) H oxidase in BPAECs. Secondely, determine Src activation of the NAD (P) H oxidase mediates Ang II-dependent increase in nitric oxide synthase protein expression .
DESIGN/METHODS: Cell Culture: BPAECs were isolated and cultured in DMEM (Gibco BRL).
Western Blot Analysis: for eNOS protein expression
Measurement of ROS in intact cells: Chemiluminescence counts(with 0.005mmol/L lucigenin prsent) will be obtained .
Src Kinase Assay: by Src kinase assay kit (UPSTATE co.)
Statistical Analysis: All statistical analysis will be performed by a Student's t–test . Statistical significance will be accepted at $P<0.05$.
RESULTS: 1. Src activity was maximal at 1 min (225+/-35% over basal, n=6 $P<0.05$) was prevented by Src kinase inhibitor, PP2 .
2. As determination, Ang II stimulated eNOS expression at 8 hours (2.75 ± 0.2 fold increase vs basal, $n = 7$, $P < 0.02$; that was completely blocked by PP2.
3. Stimulation of superoxide production was determined at 30 minutes
4. As determined by Western blot analysis, Ang II stimulated an increase in eNOS expression at 8 hours that was blocked by DPI and apocynin (data to be analyzed)
CONCLUSIONS: Scr Kinase Activation of the NAD(P)H Oxidase may Mediate Ang II - dependent Increase in Nitric Oxide Synthase Protein Expression in BPAEC

Developmental Biology Platform Session

Saturday, March 5 8:15 AM-10:45 AM Winthrop A/B

33 Presentation Time 8:15 AM Fellow in Training

An Environmental Signal, Butyrate, Regulates Tyrosine Hydroxylase Gene Expression Via a Novel Promoter Element

Pranav Patel, Bistra Nankova, Kavitha Krishnan, Edmund LaGamma. Deivision of Newborn Medicine, Maria Fareri Childrens Hospital- New York Medical College, Valhalla, NY.
BACKGROUND: Butyrate, a short chain fatty acid, is generated from fermentation of dietary carbohydrate in the lower intestines by symbiotic flora. Its role in genetic reprogramming of colonic epithelial cells, as a tumor suppressor agent, in apoptotic cell death and in gene regulation is well known. Actions are mediated through histone deacetylation & chromatin remodeling, by butyrate-dependent transcription factors, & by mRNA stabilization. We recently provided evidence for transcriptional regulation of the tyrosine hydroxylase gene (TH; the rate limiting enzyme in catecholamine biosynthesis) by butyrate at physiologic concentrations (*Ped Res*. 2003; 2004) in a PC12 cell model. Two key regions in the TH promoter were identified: an upstream butyrate responsive element (BRE) and proximal element containing the classical cAMP response motif (CRE).
OBJECTIVE: To confirm the involvement of BRE and CRE motifs of the TH promoter in the transcriptional effects of butyrate by site-directed mutagensis.
DESIGN/METHODS: PCR-based site-directed mutagenesis was used to introduce point mutations in desired promoter motifs in a plasmid containing a luciferase reporter gene under the control of the wild type TH promoter. Mutations were varified by sequence analysis. Wild type and mutated constructs were transfected into PC12 cells and the ability of butyrate to induce reporter gene activity was compared.
RESULTS: Two motifs, identical to the BRE previously identified in the enkephalin gene (Pediatr Res A2420, 2000) were found in the rat TH promoter by sequence homology and deletion studies.Point mutations were selected based on loss of DNA-protein interactions on a mobility shift assay. Single point mutation in the distal BRE motif lead to a decrease in butyrate-induced reporter gene activity by 25-to-48%. A mutation in the CRE site rendered the TH promoter unresponsive to butyrate.
CONCLUSIONS: Two functional elements mediating transcriptional responses to butyrate exist in the TH promoter. Thus, gut colonization, use of antibiotics and feeding practices may alter blood levels of diet-derived butyrate which in turn can affect sympathoadrenal catecholamine functions. These mechansism link exogenous nutritional signals to neuronal plasticity, cardiovascular function, stress adaptation and behavior.

34 Presentation Time 8:30 AM Fellow in Training

Role of Antibiotics on the Production of Gut Derived Short Chain Fatty Acid (SCFA) and Its Effects on the Neurotransmitter Gene Expression in a Newborn Rat Model

Lawrence K. Fordjour, Pradeep V. Mally, Jie Xu, Anna-Maria Curatola, Karen Hendricks-Munoz. Neonatology, New York University School of Medicine, New York, NY.
BACKGROUND: SCFAs are carboxylic acids that are produced in the colon by anaerobic bacteria. In PC-12 cell model SCFAs have been shown to induce tyrosine hydroxylase (TH), the rate limiting enzyme of catecholamine synthesis, and proenkephalin (ppENK) gene expression, suggesting a role in perinatal stress-adaptation (Mally, Pediatr Res 04). Use of broad-spectrum antibiotics is known to alter bacterial ecology of the colon and hence have an effect on the endogenous production of SCFA. In this project, we investigated the role of antibiotics on SCFA production and its effects on autonomic nervous system in a newborn rat model.
OBJECTIVE: To test the effects of antibiotics on: 1) Production of gut derived SCFAs; 2) Gene expression of TH and ppENK neurotransmitters.
DESIGN/METHODS: 52 newborn Sprague-Dawley rat pups were randomly assigned to four groups and for the first 7 days of life (DOL) were given: Group A-control (n=13) normal saline injections (10ml/kg/dose) intraperitoneally (IP) 2x a day. Group B (n=13) Ampicillin (100mg/kg/dose) 2x a day IP and Gentamicin (2mg/lb/dose) 1x day IP. Group C (n=13) Metronidazole (30mg/lb) 2x a day IP. Group D (n=13) Ampicillin (100mg/kg/dose) 2x a day IP, Gentamicin (2mg/lb/dose) 1x day IP and Metronidazole (30 mg/lb) 2x a day IP. On DOL 8 these pups were sacrificed, and adrenal tissue and blood samples were obtained. Total RNA was isolated from adrenals and RT-PCR reaction was performed with primers specific for TH and ppENK mRNA. Digital analysis of the PCR images was done by using DigiDoc system. SCFAs were quantified in blood samples by gas chromatography.
RESULTS: The following changes were observed in treated group when compared with control: Group B-increased expression of TH (2x), ppENK (2.5x) mRNA, $p<0.05$. Group C- decreased expression of TH (1.5x), ppENK (1.8x) mRNA, $p<0.05$. Group D- decreased expression of TH (1.6x) mRNA, $p<0.05$ and no change in ppENK mRNA. There was increased production of total SCFAs in plasma and 50% increase of plasma Byturate in Group B.
CONCLUSIONS: Antibiotic therapy alters normal gut colonization, production of gut derived SCFAs and expression of neurotransmitters. These effects may modify the rate of maturation and adaptive capacity of the sympathoadrenal system to common neonatal stressors.

35 Presentation Time 8:45 AM Fellow in Training

RNAi Screen for Shh Signaling Pathway Components in Mouse

Ting-Yi Lin, Steven Vokes, Andrew P. McMahon. Molecular and Cellular Biology, Harvard University, Cambridge, MA; Newborn Medicine, Children's Hospital, Boston, MA.
BACKGROUND: Sonic hedgehog (Shh) plays a pivotal role in multiple aspects of vertebrate development, including CNS, lungs, and limbs, among others. Mutations in Shh and components of its signaling pathway have contributed to a myriad of human congenital malformations. Haploinsufficiency for human SHH results in holoprosencephaly and associated craniofacial defects. Individuals with a defective Patched 1 (PTCH1) gene, which encodes the inhibitory receptor of Shh, develop Gorlin Syndrome with a range

of skeletal defects and predisposition to cancer. Mutations in Gli genes, transcription factors that mediate Shh activity, cause malformations in mice similar to those seen in human VACTERL. Although much is known about binding of Shh to Ptc and the subsequent de-repression of the activator Smo, little is known about the complex intracellular signal transduction that leads to the activation and repression of downstream targets.
OBJECTIVE: Our aim is to gain a better understanding of the molecular mechanism underlying the Shh signal transduction pathway by screening for and analyzing additional components of the pathway.
DESIGN/METHODS: In collaboration with the Perrimon lab, we initiated a targeted screen in mouse by RNAi knockdown of possible components of the Shh signaling pathway, utilizing the approximately 400 hits revealed in a genome-wide *Drosophila* screen. Our targeted screen focused on 3 major groups: transcription factors, membrane trafficking, and phosphatases/kinases. Mouse orthologs of the *Drosophila* hits were identified and siRNAs were generated using Dicer enzyme. The siRNAs were then transfected into NIH3T3 cells along with Hh-responsive luciferase construct. After Shh induction, luciferase activities were assayed for either up- or down-regulation of the Shh signaling pathway.
RESULTS: Among the 29 mouse genes targeted in our screen, knock down of 6 genes led to up-regulation and 7 genes to down-regulation of Shh activity, suggesting identification of both negative and positive regulators of the pathway.
CONCLUSIONS: We have optimized our assay to reliably analyze the gene function of potential components of the Shh signaling pathway in mouse. Analysis of where each of these genes fits in the pathway will lead to better understanding of the mechanism of Shh signal transduction, and may identify additional targets for pharmacological intervention.

36 Presentation Time 9:00 AM — Fellow in Training

The Effect of Hyperoxia on Reactive Oxygen Species (ROS) in Petrosal Ganglion Neurons in Organotypic Slice Culture

D. J. Kwak, S. D. Kwak, E. B. Gauda. Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD.
BACKGROUND: Infants with chronic lung disease have blunted chemoreceptors responses (*Pediatr Res 1994; 35:677-81).*Chronic hyperoxic exposure in newborn rats, results in life-long ablation of hypoxic chemosensitivity, hypoplasia of the carotid body and reduction in the number of chemoafferents. Hyperoxia is associated with increased production of reactive oxygen species (ROS) which can be cytotoxic. We hypothesized that hyperoxic exposure would increase ROS production in cell bodies of chemoafferents.
OBJECTIVE: Determine the effect of oxygen tension on the production of ROS in petrosal ganglion neurons using organotypic slice culture.
DESIGN/METHODS: The carotid bodies and petrosal-nodose ganglia from six 5 days old Sprague-Dawley rat pups were removed, embedded in 3% Agar and sectioned at 45mm. Tissue slices were incubated at 37° C (21% O_2/5% CO_2) over night. They were then exposed to hypoxia (8%O_2), normoxia (21% O_2) or hyperoxia (95% O_2) for 4 hours in the presence or absence of the ROS-sensitive fluorescent indicator, 2', 7'-dichlorodihydrofluorescein diacetate DCFDA; (2mM; Molecular Probes). Sections were then fixed in 2% parformaldehyde and mounted using Anti-Fade (Molecular Probes) on to glass slides. After subtracting for background fluorescence and normalization, gray level intensities for 200 petrosal ganglion neuorns were measured. A mean for each animal, for each oxygen exposure was determined and differences were determined by one-way ANOVA with posthoc analysis.
RESULTS: Increasing oxygen tension increased the level ROS production. Fluorescence intensity was 178±4 for hypoxia, 202 ±4 for normoxia, and 261 ±5 for hyperoxia, (mean ±SEM, P<0.000, ANOVA). Normoxic exposure increased ROS production by 13% from hypoxic exposure (P<0.01) with a further increase of 30% from normoxia to hyperoxia (P<0.001)
CONCLUSIONS: Using a novel technique of organotypic slices of the carotid body and petrosal ganglion, our data show a direct correlation between the level of oxygen tension in cell bodies of chemoafferent neurons and ROS production. Increased ROS production within chemoafferent cell bodies may account for evidence of cytotoxicity and ablation of hypoxic chemosensitivity in newborn animals that is life-long. Similar mechanisms may be operative in infants with chronic lung disease with blunted chemoreceptor responses. Supported by RO1 DA13940.

37 Presentation Time 9:15 AM

Differential Effects of Androgen on ErbB Receptor and PLCg Expression and Phosphorylation in Fetal Rat Type II Cells

Sujatha M. Ramadurai, Soujanya L. Rallabandi, Lucia B. Pham, MaryAnn V. Volpe, Heber C. Nielsen. Pediatrics, Tufts-New England Medical Center, Boston, MA.
BACKGROUND: Fetal lung type II cell ErbB receptor activity is important in responses to fibroblast communication controlling development of fetal lung maturation and surfactant synthesis. Our lab has shown that ErbB4 is the preferred dimer partner for the other ErbB receptors in fetal rat lung type II cells. Studies show male fetuses have delayed lung maturation due to androgen. Chronic in utero administration of Dihydrotestosterone (DHT), which delays fetal lung maturation, blocks fibroblast EGFR development and EGFR activation of PLCg phosphorylation. The effect of DHT on expression (*exp)* and phosphorylation *(phos)* of type II cell ErbB receptors and PLCg is not known.
OBJECTIVE: We hypothesized that chronic in utero androgen exposure alters type II cell ErbB receptor and PLCg *exp* and *phos.*
DESIGN/METHODS: Pregnant Sprague Dawley rats were implanted with DHT pellets on d11 of gestation. Primary fetal lung type II cell cultures were prepared from control and DHT-implanted dams on d17, d19, and d21, and grown to confluence with DHT (10^{-8}M) added to the media of cells from DHT animals. Cells were harvested as unstimulated or after EGF or NRG stimulation. Western blots were probed with antibodies to phosphotyrosine, each ErbB receptor, and to PLCg. Results were quantified by densitometry with actin as an internal standard.
RESULTS: DHT induced PLCg *exp* in d17 type II cells with no significant effect on *phos*. DHT induced the *exp* of ErbB2 on days 17, 19 and 21 and the expression of ErbB3 and B4 on days 17 and 21. The effect on *phos* differed between the receptors. DHT decreased EGF- and NRG-induced *phos* of ErbB2 and NRG-induced B3 *phos* on all 3 gestational days (19 and 21 > 17). DHT increased the NRG induced phosphorylation of ErbB4 on d19.
CONCLUSIONS: We found differences in ErbB receptor and PLCg *exp* and *phos* in fetal lung type II cells after chronic DHT exposure. These effects were opposite to what we have observed in fetal lung fibroblasts. Although DHT induced the expression of ErbB2, B3 and B4 in type II cells, it decreased the responsiveness of ErbB2 to EGF and NRG and B3 to NRG while increasing ErbB4 *phos* by NRG. DHT did not alter PLCg *phos* in type II cells. We speculate that androgen affects fetal lung type II cell maturation via alterations in stimulation of ErbB receptor *phos* but not in PLCg signaling.

38 Presentation Time 9:45 AM

Mechanism of SP-A-Stimulated Macrophage Chemotaxis: Role of TLR2, TGFß, RHAMM and Hyaluronan

Joseph P. Foley, Aisha Zaman, Theresa M. McDevitt, Akira Asari, Jo Rae Wright, Rashmin C. Savani. Div Neonatology, Dept Pediatrics, CHOP - Univ of Pennsylvania, Philadelphia, PA; Glycofunction Research Group, Seikagaku Corporation, Tokyo, Japan; Cell Biology, Duke Univ Medical Center, Durham, NC.
BACKGROUND: Surfactant Protein-A (SP-A) stimulates macrophage chemotaxis and phagocytosis of apoptotic neutrophils, mechanisms that result in production of Transforming Growth Factor-beta (TGFß). SP-A binds to several cell surface proteins including SIRPa, Calreticulin and Toll-Like Receptors (TLR) 2 and 4. Hyaluronan (HA), a glycosaminoglycan, promotes macrophage chemotaxis via interaction with the HA receptors RHAMM (Receptor for HA-Mediated Motility) and CD44.
OBJECTIVE: To define the role of HA and its receptors in SP-A-stimulated chemotaxis
DESIGN/METHODS: Chemotaxis of RAW 264.7 mouse macrophages to SP-A, TGFß and HA was examined. Blocking reagents included antibodies against RHAMM, CD44, SIRPζ, Calreticulin, TLR2/4 and HA-binding peptide (HABP) with appropriate controls. Cytoskeletal rearrangements were determined by phalloidin-FITC staining. Active TGFß content was measured by the luciferase reporter mink lung epithelial cell line (MLEC). HA content was determined by an ELISA-like assay. The activation of Cdc42 and Rac was determined using co-precipitation with p21-activated kinase (PAK1).
RESULTS: SP-A stimulated maximum chemotaxis at 100 mg/ml. This effect was completely blocked by anti-TLR2 antibody, but not by antibodies to TLR4, SIRPζ or Calreticulin. In addition, HA-binding peptide and an antibody to RHAMM blocked SP-A-stimulated chemotaxis, whereas anti-CD44 antibodies did not. Interestingly, anti-TGFß antibody blocked SP-A-stimulated migration and SP-A-stimulated HA production. Further, SP-A stimulated the production of TGFß in macrophages, an effect blocked by TLR2 antibody. TGFß-stimulated chemotaxis was blocked by anti-RHAMM antibody but not TLR2 antibody. Further, HA-stimulated chemotaxis was blocked by anti-RHAMM antibody and was independent of CD44, TLR-2, TLR-4 and TGFß. In association with filopodial extensions, HA stimulation resulted in activation of Cdc42, but not Rac, effects that were blocked by anti-RHAMM antibody.
CONCLUSIONS: SP-A:TLR2 interaction results in TGFß release from macrophages. TGFß, in turn, stimulates chemotaxis, a process that is dependent on RHAMM:HA interaction. HA & RHAMM regulate SP-A and TGFß-directed modulation of lung host defense.
Funded by Seikagaku Corporation Employee; Seikagaku Corporation, Tokyo, Japan.

39 Presentation Time 10:00 AM — Fellow in Training

Surfactant Protein D: *S*-Nitrosylation and Effects on Inflammatory Functions

Changjiang Guo, Joseph P. Foley, Rashmin C. Savani, Andrew J. Gow. Neonatology-Pediatrics, CHOP-University of Pennsylvania, Philadelphia, PA.
BACKGROUND: Surfactant protein-D (SP-D), a pulmonary collectin, exists as a multimer and is important in lung innate immunity. SP-D contains two conserved amino terminus cysteine residues that contribute to multimer formation. Post-translational modification of proteins at cysteines by nitric oxide (NO) forms *S*-nitrosothiol (SNO) and *S*-nitrosylation of proteins regulates both airway and vessel tone in pathophysiology. Since there are increased markers of NO production in pulmonary inflammatory diseases and SP-D alters the products of NO metabolism, we asked whether SP-D could be modified by NO.
OBJECTIVE: To determine whether S-nitrosylation could mechanistically alter SP-D function to affect macrophage cell functions both in vitro and in vivo.
DESIGN/METHODS: We induced acute lung injury by intratracheal administration of bleomycin. Bronchoalveolar lavage (BAL) was collected from bleomycin and saline-treated rats at days 2, 4, 7, 14 and 21 following administration. Lavage and recombinant SP-D were analyzed for multimeric state, nitrosylation, calcium signaling and chemotactic function.
RESULTS: BAL from bleomycin-treated rats showed increased SNO formation specifically on SP-D as early at 2 days and maximally at 4 days after injury. Concomitant with SNO formation, SP-D changed from multimer to trimer and dodecamer. *In vitro* nitrosylation of BAL from unmanipulated rats resulted in the same specific formation of SNO SP-D, alteration of conformational state and increased chemotactic function. *S*-nitrosylation of recombinant SP-D mimicked this effect. BAL from bleomycin-treated rats increased chemotaxis of macrophages (RAW264.7) and immunoprecipitation of SNO SP-D from this BAL abrogated the chemotactic effect. Further, *S*-nitrosylation of BAL from SP-D-/- mice produced no chemotactic response. Nitrosylated normal BAL and recombinant SP-D stimulated a significantly greater intracellular calcium influx in RAW264.7 cells than non-nitrosylated BAL and SP-D respectively, suggesting alteration of intracellular signaling with SNO modification.
CONCLUSIONS: We conclude that *S*-nitrosylation of SP-D results in an inability of this protein to form multimers, a gain of function in stimulating macrophage chemotaxis and intracellular calcium signaling. We speculate that SNO modification of SP-D promotes pulmonary inflammation after acute lung injury.
Funded By: NHLBI HL074115 and HL075930

Endocrinology Platform Session

Saturday, March 5 8:15 AM-10:30 AM Stoningham

40 Presentation Time 8:15 AM — Ph.D. Student

Epigenetic Silencing of Pdx-1 in Growth Retarded (IUGR) Rats

Jun Park, Irina Suponitsky-Kroyer, Rebecca A. Simmons. Pediatrics, UPENN, Children's Hosp. Philadelphia, Philadelphia, PA.
BACKGROUND: IUGR has been linked to later development of type-2 diabetes. Our model of intrauterine growth retardation in rats results in reduced ß-cell mass and onset of diabetes in adulthood. Transcription of Pdx-1, a critical ß-cell homeobox transcription factor, is decreased in fetal IUGR rats. Suppression of Pdx-1 expression persists after birth, implicating an epigenetic mechanism. ROS are increased in IUGR islets and Pdx-1 expression is decreased in ROS treated INS-1 cells (ß-cell line), suggesting that oxidative stress may underlie reduced Pdx-1 in IUGR's. The proximal promoter of Pdx-1 contains a highly conserved USF-1 binding site that is obligate for Pdx-1 transcription.
OBJECTIVE: To determine (1) if IUGR and (2) oxidative stress impairs USF-1 binding which in turn induces histone modifications, followed by DNA methylation, thereby locking in suppression of Pdx-1 transcription.
DESIGN/METHODS: Uterine artery ligation (n=10 rats) was performed on d19 gestation (term=22d). Controls were sham-operated animals (n=10). Islets were isolated from 1 and 7 week-old rats. INS-1 cells were cultured for 3 or 24h in rotenone (increases ROS production). Chromatin was immunoprecipitated

from islets or cells using antibodies to USF-1, acetyl-H3-lys9, dimethyl-H3-Lys4, or dimethyl-H3-Lys9. A 221 bp sequence of the proximal Pdx-1 promoter, incorporating the USF-1 binding site, was amplified and PCR products were separated and quantified.
RESULTS: USF-1 binding was markedly reduced in 1 and 7 week-old IUGR islets (50% and 20% of controls, 1 and 7 weeks, respectively) ($p< 0.05$). This was associated with blunted histone acetylation at Lys9 and histone dimethylation at Lys4, markers of chromatin silencing. Histone modifications progressed with age in IUGR rats (70% and 20% of controls at 1 and 7 weeks, respectively, ($p< 0.05$). In contrast, histone dimethylation at Lys9 (a marker of chromatin silencing) was only significantly increased at 7 weeks of age. 3 and 24h rotenone treatment of INS-1 cells decreased USF-1 binding, acetylation at H3-Lys9 and dimethylation at H3-Lys4. 24h rotenone treatment additionally increased dimethylation at H3-Lys9 (all $p<0.05$ vs control).
CONCLUSIONS: Our results show that IUGR via oxidative stress inhibits USF-1 binding which in turn induces histone acetylation followed by histone methylation of Pdx-1. This suggests that epigenetic programming can be induced by an adverse intrauterine milieu.

41 Presentation Time 8:30 AM

Leptin Levels Decline Steadily During Prolonged Fasting in Lean Children

Lorraine E. Levitt Katz, Maire M. Abraham, Line Johansen, Abbas F. Jawad. Endocrinology, Children's Hospital of Philadelphia, Philadelphia, PA; Biostatistics & Epidemiology, Children's Hospital of Philadelphia, Philadelphia, PA; UPenn School of Medicine.
BACKGROUND: Leptin, a hormone product of the OB gene, is released mainly by adipocytes and participates in the regulation of food intake and energy balance. In adults, leptin levels are influenced by BMI, exercise, and nutrient intake. The leptin response to prolonged fasting in children has not previously been studied.
OBJECTIVE: To evaluate the effects of fasting on serum leptin levels in healthy, lean children.
DESIGN/METHODS: Subjects: 19 children (11 female, 8 male), age 8.1±4.2 years (mean±SD), underwent standardized diagnostic fasting studies for suspected hypoglycemia. Subjects had a mean BMI of 16.9±2.7 kg/m^2 (range 13.8-23.0 kg/m^2, mean z-score 0.01±1.03). Blood was sampled at 6-hour intervals for glucose, insulin, C-peptide, leptin, free and total IGF-I, and IGFBP-1. Fasting studies were terminated for a glucose concentration <50 mg/dL (n=8) or completion of the allotted fasting duration (n=11). Nine children had ketotic hypoglycemia, 8 had no disorder, and 2 had steroid-induced adrenal suppression.
RESULTS: The subjects' fasting periods ranged from 15-40 hours. By longitudinal mixed effects model, leptin declined significantly over time ($p<0.001$). Fasting leptin levels correlated with total IGF-I ($r=0.7$, $p<0.001$), insulin ($r=0.6$, $p<0.001$), and C-peptide ($r=0.6$, $p<0.001$) and had a strong negative correlation with IGFBP-I ($r=-0.6$, $p<0.001$). Significant correlations were also seen between leptin and glucose ($r=0.5$, $p<0.001$), BMI ($r=0.5$, $p<0.001$), age ($r=0.4$, $p=0.001$) and free IGF-I ($r=0.4$, $p<0.001$). Of the patients who had leptin levels measured at the start of fasting (n=12), leptin dropped significantly from an initial mean±SEM during the first 6 hours of 15.3±5.6 ng/mL to 3.1± 0.9 ng/mL at the end of the fast ($p=0.03$, paired t-test). Prolonged fasting in this population also resulted in significant declines in glucose, insulin, C-peptide, total and free IGF-I, and an increase in IGFBP-1.
CONCLUSIONS: After 6 hours, leptin levels steadily decline during prolonged fasting in lean children. The decline is likely related to the suppression of insulin secretion. While baseline leptin levels were related to BMI and age, in the final fasting sample, leptin levels showed minimal variation in this pediatric cohort encompassing a wide age range.

42 Presentation Time 8:45 AM House Officer

Prevalence and Clinical Features of Double Diabetes in Children

Radhika Purushothaman, Neesha Ramchandani, Henry Anhalt, Svetlana Ten. Pediatrics, Maimonides Medical Center, Brooklyn, NY; Pediatric Endocrinology and Metabolism, Maimonides Medical Center, Brooklyn, NY; Pediatric Endocrinology, Saint Barnabas Medical Center, West Orange, NJ.
BACKGROUND: Diabetes had been classified as type 1A, type 1B and type 2. Double diabetes involving immune mediated b cell failure and insulin resistance, has been recently described.
OBJECTIVE: Cross-sectional study to find the prevalence of double diabetes in our clinic.
DESIGN/METHODS: Islet cell, thyroid and celiac antibodies, BMI, lipid profile, blood pressure were analyzed in 119 diabetic children. Those with positive islet cell autoantibodies (ISA) and BMI<85% were defined as type 1A diabetics. Type 1B diabetics were those who had negative ISA and BMI<85%. Double diabetes was defined by positive ISA and BMI > 85% and/or acanthosis nigricans (AN). Type 2 diabetes was defined as negative ISA and BMI>85 % and/or AN. There were no cases of MODY or atypical diabetes as per family history.
RESULTS: Double diabetes was present in 11.8% of all diabetics and 53.8 % of children with obesity. Of 119 patients, 93 (age 7.8 ± 3.8 yrs., 54.8% boys, BMI 19.2 ± 3.3 kg/m^2) had type 1 diabetes (type 1 group), 14 (age 9.7 ± 6 yrs., 42.9% boys, BMI 29.6 ± 5.7 kg/m^2) had double diabetes (DD group) and 12 (age 14.2 ± 1.8 yrs.,75 % boys, BMI 38.4 ± 8 kg/m^2) had diabetes type 2 (type 2 group). ISA were positive in 72.3 % of children with diabetes type 1. Age of diagnosis, BMI, LDL, total cholesterol, systolic and diastolic blood pressure increased from type 1 to DD to type 2 groups ($p<0.05$). The HDL decreased from type 1 to DD to type 2 groups ($p< 0.05$). Only type 1 group had positive celiac antibodies (36.1%). **T**hyroid antibodies did not vary significantly between the 3 groups (28.6% in type 1; 18.2% in DD and 33.3% in type 2). Total insulin dose was lower in double diabetes group than in type 1 group. Positive family history of diabetes in first-degree relatives was in 16.3 % in type 1,30.8 % in DD and 30 % in type 2 group.
CONCLUSIONS: Double diabetes is highly prevalent in obese children. In case of combination of diabetes with elevated BMI and/or acanthosis nigricans, islet cell antibodies screening is necessary to differentiate between diabetes type 2 and double diabetes. Double diabetics have elevated BMI, acanthosis nigricans, higher blood pressure and LDL, lower HDL and insulin requirement than diabetes type.

43 Presentation Time 9:15 AM

Reduced Caloric Intake in Early Life Prevents Obesity and Diabetes in Growth Retarded Rats

Irina Suponitsky-Kroyer, Hongshun Niu, Rebecca Simmons. Pediatrics, UPENN, Children's Hosp. Philadelphia, Philadelphia, PA.
BACKGROUND: Intrauterine growth retardation (IUGR) has been linked to the later development of a number of diseases. After birth, a disproportionately faster rate of recovering weight may increase the risk for development of obesity and type 2 diabetes. We have developed an animal model of IUGR in the rat. IUGR rats display accelerated growth and increased fat mass in early life, and by 6 months of age they develop diabetes.
OBJECTIVE: To determine: (1) if caloric restriction during early life can prevent the development of obesity and diabetes in IUGR rats, and (2) if there is a critical window for dietary intervention.
DESIGN/METHODS: Bilateral uterine artery ligation (n=10 dams) was performed on d19 gestation (term=22d). Sham-operated animals served as controls (n=10 dams). Litters were culled to 8 at birth. Maternal rats were fed ad-lib or fed 50% of ad-lib intake throughout lactation (21 days). The 4 suckling pup study groups were: calorie restricted (CR) controls, CR IUGR's, ad-lib controls, and ad-lib IUGR's. To determine whether caloric restriction at an older age will prevent obesity and diabetes, IUGR and control rats were nursed from ad-lib fed moms, and then at weaning rat pups were calorie restricted (50% of ad lib) or fed ad-lib for 3, 6, or 9 weeks. Body composition (by Dexa Scanning), GTT's, and ITT's were measured at 3, 6, 9, and 36 weeks of age.
RESULTS: Caloric restriction during suckling significantly reduced weight gain in both IUGR and control rats ($p<0.05$). Fat mass was also reduced in CR IUGR and CR controls ($p<0.05$) at 3 weeks of age and this reduction persisted through 36 weeks of age. Glucose tolerance and insulin sensitivity were markedly improved in CR IUGR and CR controls compared to the ad-lib groups at all ages examined ($p<0.05$). None of the CR IUGR's developed diabetes by 36 weeks of age, compared to 65% of ad-lib IUGR's. Calorie restriction after weaning did reduce weight gain and fat mass in controls and IUGR's, but not permanently. Regardless of length of calorie restriction after weaning, there was only a transient improvement in glucose tolerance and insulin sensitivity, and the development of diabetes was not prevented in IUGR rats.
CONCLUSIONS: Our results suggest that reduced caloric intake and prevention of accelerated weight gain during a critical period of development can prevent obesity and diabetes in IUGR individuals.

44 Presentation Time 9:30 AM House Officer

Hyperglycemia in a Pediatric ICU

Alyssa J. Rake, Marybeth Roy, Christine McKiernan, Stephen Lieberman, Holley F. Allen. Pediatrics, Baystate Medical Center Children's Hospital, Springfield, MA.
BACKGROUND: Critically-ill patients have relative insulin resistance and hyperglycemia. Dramatically improved outcomes in non-diabetic adults with tight glucose control with insulin have been reported. Other studies have confirmed these findings and insulin therapy has become common practice in many adult ICUs. In children, stress hyperglycemia is described and associated with poor outcomes in children with near drowning, sepsis, and cystic fibrosis and in one previous study in the PICU.
OBJECTIVE: The goal of this study was to evaluate the extent of hyperglycemia in non-diabetic children admitted to a community Pediatric Intensive Care Unit using a minimally invasive continuous blood glucose monitor (CGMS).
DESIGN/METHODS: 18 PICU patients were enrolled from May 2002 to October 2004. Inclusion criteria were ages 1-20 years, non-diabetic, and with central lines. Eligible patients/guardians were sequentially approached and consented. Using a continuous blood glucose monitor (Medtronic MiniMed) BG levels were collected for 72 hours. The monitor was calibrated and values confirmed with laboratory blood glucose levels drawn every 6 hours. If the patient remained eligible, the CGMS was removed and re-inserted for a second 72 hour period. Data on length of time in the PICU, total hospital time, ventilatory status, and medications/drips were collected. A follow-up phone interview was done one month after discharge. The study was Institutional Review Board approved.
RESULTS: Data from 17 patients revealed an average BG of 111. One patient was excluded because of sensor malfunction. No patients remained normoglycemic (< 126). 9 patients had BG >200, all 17 had BG >140. Percent of total patient time (all patients) spent hyperglycemic was 16.5% with BG 126-139, 25.6% with BG 140-199, and 2.2% with BG >200. 14 peaks of hyperglycemia were missed by the lab BG. Diagnoses of the patients with BG >200 were, pneumonia(3), status asthmaticus(1), head injury(2), malignancy(2), and intestinal perforation(1).
CONCLUSIONS: There is significant hyperglycemia in pediatric critical care patients. The CGMS revealed more extensive hyperglycemia then seen with the lab values alone. It would be beneficial for patient care to have a continuous monitor which allows real time monitoring, as the CGMS only allowed retrospective data collection. Insulin therapy to improve outcomes in critically ill children requires further study.
Funded by CGMS (Medtronic Minimed); CGMS is FDA approved for use in diabetic children. Our off-label use was in critically-ill non-diabetic children.

45 Presentation Time 9:45 AM Fellow in Training

Late Rise of TSH in Ill Newborns Is Common and Not Dependent on Birthweight

Sharon J. Hyman, Fenella Greig, Arti Patel, Deborah Bowlby, Elizabeth Wallach, Ian Holzman, Robert Rapaport. Pediatrics (Endocrinology & Newborn Medicine*), Mt Sinai School of Medicine, New York, NY.
BACKGROUND: Controversy continues from database screening studies about the need for repeat screening or testing of newborns to identify late rise in TSH (LRT). We previously recommended continued thyroid monitoring in very low birth weight (VLBW) and other sick newborns.
OBJECTIVE: To determine from case reviews the frequency of LRT, and describe characteristics of affected infants.
DESIGN/METHODS: Data were analyzed from infants evaluated for abnormal thyroid tests over a 13 month period at one hospital. Repeat thyroid tests were performed by filter paper screen if hospital care > 4 wks or by serum if thyroid dysfunction was clincially suspected. LRT was defined as serum TSH >10 uU/ml after normal TSH on initial newborn screen. Serum TSH, T4, T3 and urine iodine were measured by standard assays.
RESULTS: LRT was identified in a total of 14 infants. Of 736 admissions to NICU, 10/15 consultations with normal initial TSH screen had LRT (1.4 %). Four additional cases of LRT occurred in other ICU settings. TSH elevation resolved in 6/14 (group A); TSH elevation persisted in 8/14 and were treated (group B) (Table). Concurrent medical features included surgery 10 (A4, B6); dopamine use 6 (A1, B5); gastrointestinal disease 6 (A4,B2); congenital heart disease (CHD) 4 (A2, B2). Urine iodine was elevated (> 350 mcg/L) in 6/11 measured (A 2/4, B 4/7). Group B included 3 with TSH >40 uU/ml; all had elevated urine iodine (1 Down Syndrome, CHD, surgery; 1 CHD, multiorgan disease, surgery; 1 VLBW, surgery).
CONCLUSIONS: 1. LRT was demonstrated in 14 infants. In 10 infants this comprised 1.4% of NICU admissions. Thyroxine therapy was used in 8/14 (57%); TSH >40 occurred in 3/14 (21%). 2. Of 14 cases of LRT half were not VLBW. 3. Groups A and B had wide overlap in clinical features. Dopamine use was greater in Group B (A 1/6; B 5/8). 4. We recommend ongoing thyroid evaluation of ill newborns regardless of birthweight.

	A (No Rx); N=6	B (Rx); N=8
Birth wt (g); range (# <1500g)	910-3100 (3)	489-3750 (4)
Gest. age (wk); range (# <30 wk)	25-40 (2)	24-40 (4)
Age evaluated (day); range (mean)	6-85 (40)	7-99 (41)
Initial TSH uU/ml; range (mean)	10.6-20.6 (12.9)	10.5-1326.0 (234.8)
Age resolved/Rx (day); range (mean)	10-105 (62)	11-104 (52)

General Pediatrics I: Environmental Health Platform Session

Saturday, March 5 8:15 AM-10:15 AM Mead A

46 Presentation Time 8:15 AM Fellow in Training

Social Costs of Mental Retardation Associated with Methylmercury Exposure in America

Leonardo Trasande, Philip J. Landrigan, Clyde Schechter, Karla A. Haynes. Department of Community and Preventive Medicine, Mount Sinai School of Medicine, New York, NY; Department of Family Medicine, Albert Einstein College of Medicine, New York, NY.

BACKGROUND: Methylmercury (MeHg) is a fetal neurotoxicant. Exposure results principally from consumption by pregnant women of fish and seafood contaminated by anthropogenic and natural mercury (Hg) . The Environmental Protection Agency made steady progress in the 1990s in reducing Hg emissions from power plants, but recently proposed to slow this progress. The costs of failing to prevent exposure to this neurotoxicant have not been quantified.

OBJECTIVE: To estimate the social burden of mental retardation (MR) that results from MeHg exposure in the 2000 U.S. birth cohort, and to identify the portion of this burden that is attributable to Hg emissions from coal-fired power plants.

DESIGN/METHODS: To estimate the loss in cognition associated with MeHg exposure in the 2000 U.S. birth cohort, we applied two models (log model: a .85-2.4 point decrease in IQ per doubling of Hg concentration >5.8 µg/L; linear model: .59-1.24 point decrement per µg/L increase >5.8 µg/L. We assumed that MeHg exposure is not correlated with native intelligence (and normally distributed with SD 15), and used an environmentally attributable fraction model. We relied upon previously published per case cost estimates for MR, and estimated that 13-26% of MeHg exposure is attributable to anthropogenic sources, of which 5.7-11.1% are attributable to American power plants.

RESULTS: Each year 637,233 children are born in the U.S. with cord blood Hg levels >5.8 µg/L, and suffer loss of IQ ranging from 0.76-3.21 points. This IQ loss is associated with 2237 (range 536-20417) cases of MR, and health care, special education and other costs amounting to $1.9 billion (range $.7-24.7B) each year. American coal fired power plants account for 90 cases which cost $109 million (range 42-820 cases, $26M-1.9B/yr). This analysis suggests that .4% of cases of MR (range .04-3.2%) may be attributable to American coal-fired power plants, while 3.1% (range .8-29.2%) are attributable to MeHg exposure from all anthropogenic emissions.

CONCLUSIONS: Toxic injury to the fetal brain caused by Hg emitted from coal-fired power plants exacts a significant human and economic toll on American children. These costs should be considered in the debate on Hg controls.

47 Presentation Time 8:30 AM Medical Student

Awareness of Commercial Fish Mercury Advisory Among an Inner City Population

Jana E. Romm, Philip O. Ozuah. The Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Methyl mercury, a known neurotoxin, is found primarily in fish. The developing nervous system of young children and fetuses are particularly susceptible to the toxic effects of methyl mercury. In order to prevent toxicity from methyl mercury ingestion, federal and state agencies have published fish consumption advisories aimed at young children, nursing mothers, pregnant women, and women who may become pregnant. No prior studies have investigated inner-city residents' awareness of these guidelines.

OBJECTIVE: To determine knowledge of the federal commercial fish mercury advisory among an inner city population.

DESIGN/METHODS: A cross-sectional survey of subjects recruited from the waiting rooms of an inner city clinic. We developed a 14-item questionnaire that was pilot-tested and modified by a group of experts and then administered by the same researcher to all subjects. We inquired about awareness of the source of methyl mercury toxicity, at-risk populations for mercury toxicity, and knowledge of the types of fish that should be both avoided and limited in the diets of the at-risk population. Descriptive statistics were performed.

RESULTS: 1000 subjects participated, of whom 85% were women,73% were women of childbearing age (defined as younger than age 40), 43% were African American, and 42% were Hispanic/Latino. Overall, 44% of participants did not know that children should limit fish intake, 42% did not know that mercury was found in high levels in certain fish, and 40% did not know that nursing mothers should limit fish intake. When asked about young children, nursing mothers, pregnant women, and women who may become pregnant, 52% of subjects were unaware about limiting the consumption of tuna, 50% did not know the guidelines for swordfish, and 42% did not know the advisory for shark. Similarly, 53% of subjects did not know the recommendations for consumption of shrimp.

CONCLUSIONS: A substantial number of subjects were unaware of the federal recommendations for commercial fish consumption. The majority of participants were women of childbearing age, a target population for the advisories. Also, participants in this study were inner city residents. Inner city children have been shown to be at increased risk for developmental delays and thus, may be more vulnerable to mercury toxicity. Our findings suggest a need for further education targeted to this at-risk population.

48 Presentation Time 8:45 AM House Officer

Sources of Fluoride Intake Among Inner City Children

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

BACKGROUND: Dietary fluoride can inhibit dental caries, but an excess of fluoride during tooth development can cause dental fluorosis. In children, sources of fluoride include water, beverages made with water and unintentional ingestion of dentrifice. The American Academy of Pediatrics (AAP) recommends that pediatricians assess each child's fluoride intake in order to assure optimal fluoride exposure. However, there is no prior literature evaluating the sources of fluoride of inner-city children.

OBJECTIVE: To investigate the sources of fluoride intake among inner-city children.

DESIGN/METHODS: We conducted a cross-sectional survey of parents/guardians of children aged 0-8 years at an inner-city children's hospital located in the Bronx, New York. We created an interviewer-administered questionnaire by adapting and modifying a validated instrument used in the Iowa Fluoride Study (IFS). Parents/guardians were surveyed about their children's water consumption, beverage consumption and dentrifice use (based on published data regarding major sources of fluoride). Data were analyzed using descriptive statistics.

RESULTS: We enrolled 110 children in this study, of whom 22.7% were less than 1 year old, 41.9% were between 1-4years, and 19.2% were between 5-8 years. Overall, 96% drank water daily (mean of 15 oz./day), while 74% drank juice daily (mean of 20 oz./day). Bottled water was the main source of water intake for 41% of all children. Infants £1 year drank an average of 6 oz. of water and 6 oz. of juice per day. Children 1-4 years drank an average of 17 oz. of water and 13 oz. of juice per day. Children 5-8 years drank a daily average of 20 oz. of water, 20 oz. of juice, and 11 oz. of soda. Seventy-one percent of all children were regularly exposed to toothpaste, of which 81% used more than the recommended pea-sized amount while tooth brushing. For children aged 1-4 years, 75% used more than the recommended amount of toothpaste, and of those aged 5-8 years, 96% used more than the recommended amount.

CONCLUSIONS: Participants in this study drank substantial amounts of bottled waters, juices and sodas with varying quantities of fluoride. Also, we found that the majority of children in this study used more than the recommended amount of toothpaste while brushing their teeth. These findings have implications for inner-city pediatricians attempting to adhere to the AAP recommendations regarding fluoride counseling.

49 Presentation Time 9:00 AM Fellow in Training

Environmental Pollutants and Disease in New York State's Children: Estimates of Morbidity, Mortality and Costs for Lead Poisoning, Asthma, Cancer and Developmental Disabilities

Leonardo Trasande, Philip J. Landrigan, Clyde B. Schechter, Raphael Falk. Department of Community and Preventive Medicine, Mount Sinai School of Medicine, New York, NY; Department of Family Medicine, Albert Einstein College of Medicine, New York, NY.

BACKGROUND: Knowing the incidence, prevalence and economic costs of environmental disease in children can help guide preventive efforts and put into perspective arguments that exclusively focus on the costs of preventing pollution. Direct comparison with the costs of other categories of illness can be useful in the setting of priorities and allocation of resources.

OBJECTIVE: To estimate the incidence, prevalence, mortality and costs of four categories of pediatric illness in New York State that may be attributable to chemical pollutants in the ambient environment.

DESIGN/METHODS: We applied an environmentally attributable fraction (EAF) model. Expert review panels judged EAFs to be 100% for lead poisoning, 30% for asthma (range 10-35%), 5% for cancer (range 2-10%), and 10% for neurobehavioral disorders (range 5-20%). For prevalence and incidence data, we used New York State data whenever possible. When State data were not available, we applied national rates. To develop estimates of costs, we relied on data from the U.S. Environmental Protection Agency, Centers for Disease Control and Prevention, National Center for Health Statistics, the Bureau of Labor Statistics, the Health Care Financing Agency, and the Practice Management Information Corporation.

RESULTS: The environmentally attributable cost of lead poisoning, asthma, pediatric cancer and neurobehavioral disorders in New York State's children in 2000 is estimated to be $4.65 billion (range $4.13-$5.53 billion, 2000 dollars). Lead poisoning contributes the majority of this cost at $3.66 billion, followed by neurobehavioral disorders at $0.83 billion (range $0.42-1.66 billion).

CONCLUSIONS: Diseases of toxic environmental origin make an important and insufficiently recognized contribution to total health care costs among children in New York State. As Medicaid costs and lost economic productivity contribute much of this social cost, an investment in additional clinical resources to prevent and treat environmental exposures and diseases of environmental origin is likely to be cost-effective.

50 Presentation Time 9:30 AM

Does Media Exposure Impair School Performance?

Iman Sharif, James D. Sargent. Pediatrics, Children's Hospital at Montefiore/AECOM, Bronx, NY; Pediatrics, Dartmouth Medical School, Lebanon, NH.

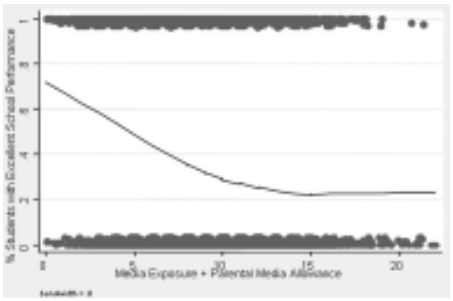
BACKGROUND: Studies of the relationship between media exposure and school performance have yielded conflicting results.

OBJECTIVE: To test whether media exposure is associated with poor school performance.

DESIGN/METHODS: We surveyed randomly selected middle-school students in the Northeastern US, and collected data on school performance and media exposure.

The main outcome was self-report of excellent school performance ("How would you describe your grades last year?" Excellent/Good/Average/Below average). Responses to questions about home media availability (television, cable, satellite) and quantity of media viewing were summed to create a Media Exposure index (0-11). We measured parental Media Allowance(0-3) by response to the following question: "How often do your parents let you watch R-rated videos/movies?"(never, once in a while, sometimes, all the time).

First we summed the Media Exposure and Media Allowance indices, and plotted a lowess curve to determine the relationship with school performance. Logistic regression tested the independent effects of Media Exposure and parental Media Allowance, and adjusted for demographics, child personality, and parenting style.



RESULTS: 5,394 subjects participated; 51% girls, mean age=12. Overall, 35% reported "Excellent" grades. The lowess plot showed a strong negative correlation between Media Exposure/Allowance and school performance. Multivariate analysis revealed a decreased odds of excellent school performance for each 1-point increase on both the Media Exposure index (AOR=0.92; CI 0.90, 0.95) and parental Media Allowance (AOR=0.89; CI 0.84, 0.95).

CONCLUSIONS: Media exposure has a linear association with poor school performance, independent of several confounding influences. Parental media restriction is positively associated with school performance, independent of media exposure and general measures of parenting style.

51 Presentation Time 9:45 AM

Knowledge of Carbon Monoxide in a Low Income, Urban, Underserved Pediatric Patient Population

Deborah M. Lopez, Kirsten Roberts-Butelman, Ellen J. Silver. Pediatrics, Albert Einstein College of Medicine - Jacobi Medical Center, Bronx, NY; Pediatrics, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Carbon monoxide(CO) is the number one cause of poisoning deaths in the United States. CO is a colorless and odorless gas that accounts for an estimated 2,000 deaths per year. Those at highest risk include children and pregnant women. Little is known about the level of knowledge of CO among the low income, urban, underserved pediatric patient population. In addition, the percentage of patients in this population with CO alarms is unknown.

OBJECTIVE: To determine general knowledge of CO in a low income, urban, underserved pediatric patient population as well as to determine the percentage of families in this patient population that possess a CO alarm.

DESIGN/METHODS: A 19 item questionnaire evaluating general knowledge of CO was administered to a convenience sample of the parents or guardians of children presenting for outpatient care at a hospital

located in a low-income, urban, underserved area. Data was analyzed via Pearson Chi-Square.
RESULTS: 415 questionnaires were completed. See *Results table.
Awareness of CO varied within different sub-groups based upon primary language spoken at home. In homes where English is the primary language, 92.2% stated that they had heard of CO. In bilingual homes, 66.7% stated that they had heard of CO. In non-English speaking homes, 60.5% stated that they had heard of CO ($p<0.05$). Those surveyed that correctely identified a source of CO were more worried about carbon monoxide ($p<0.05$). Only 21% of the population reported having a CO alarm.
CONCLUSIONS: General awareness of CO was reasonably high among this targeted population. However specific knowledge about carbon monoxide in this urban, underserved, low-income pediatric patient population was poor, less than half of those surveyed could correctly identify a source of CO. Primary language spoken at home is a predictor of having heard of CO. Most important, despite the dangers of CO, only 37.8% of those surveyed reported being worried about it and even fewer (21.7%) eported having a CO alarm. This data suggests that in this population knowledge about CO is limited.

*RESULTS

Stated that they heard of CO	81.9%
Stated that they know what CO is	63.4%
Correctely identify what causes CO	45.5%
Worried about CO	37.8%
Have CO alarm	21.7%

52 Presentation Time 10:00 AM — House Officer

Interventions for Reduction of Diarrhea in Rural Guatemalan Children

Elizabeth A. Campbell, Cheryl D. Tierney, Barbara W. Stechenberg. Pediatrics, Baystate Medical Center - Tufts University, Springfield, MA.

BACKGROUND: Many organizations in developing countries choose water and/or sanitation interventions based on monetary cost or feasibility rather than considering ultimate effectiveness in decreasing diarrheal illness.
OBJECTIVE: To investigate the most effective water and sanitary interventions for reducing childhood diarrheal illness.
DESIGN/METHODS: Secondary data analysis of the 1995 Guatemalan Survey of Family Health (EGSF), a study of women aged 18-35 from rural villages in four departments of Guatemala. Women were interviewed via standardized questionnaire about household characteristics, pregnancy history, and illness in their children during a 2-week period prior to the survey.
RESULTS: Of 1984 households with children under 5 years, 34% had any diarrheal illness during the survey period. Household drinking water came from village tap water systems of unknown origin, wells, and from other locations (i.e. river, rain water, etc). Chi square analysis revealed that tap water and well water yield similar reductions in diarrhea, and are significantly better than other water sources ($p = 0.0008$). Households also used various elimination locations: Toilet in or near house, latrine, and other locations (forest, pit, etc). Among these locations only toilets reduced childhood diarrhea ($p = 0.02$).
CONCLUSIONS: Organizations interested in decreasing childhood diarrheal illness should choose either piped tap water systems or deep borehole wells to improve drinking water, and should provide toilets in or near households, rather than latrines. Sanitation via toilets may be more costly, but will have a greater reduction in childhood diarrheal illnesses than other sanitation interventions.

Hematology and Oncology Platform Session

Saturday, March 5 8:15 AM-10:45 AM Mead C

53 Presentation Time 8:15 AM — Fellow in Training

Regulation of Mitogenic Signaling by Nerve Growth Factor (NGF) and Brain-Derived Neurotrophic Factor (BDNF) in Neuroblastoma Cells

Giselle L.S. Sholler, Charlotte M. Boney. Department of Pediatrics, Brown University/Hasbro Childrens Hospital, Providence, RI.

BACKGROUND: Neuroblastoma has been shown to have distinct subtypes characterized by differences in Trk receptor expression, which may affect aggressiveness and prognosis. Although TrkA and TrkB receptors have been shown to activate the same signaling pathways (MAPK and AKT), we hypothesized that regulation and downstream action of these pathways by the Trk receptors are distinct.
OBJECTIVE: To elucidate differences in mitogenic signaling downstream of NGF-activated TrkA versus BDNF-activated TrkB in three neuroblastoma cell lines.
DESIGN/METHODS: Cell lines with varying Trk receptor expression (IMR32, SMSKCN, SMS KCNR) were stimulated with 100 ng/ml NGF or BDNF and total cell lysates were analyzed by western blot for phosphorylated and total MAPK, AKT and ShcA. NGF or BDNF-stimulated proliferation was analyzed by immunohistochemistry for BrDU incorporation. Apoptosis was measured using TUNEL assay. Western blots of cell lysates were performed to confirm the presence of TrkA and TrkB receptors in each cell line.
RESULTS: Western blots using anti-TrkA, anti-TrkB and "pan"Trk antibodies confirmed that IMR32 cells express TrkA, SMSKCN cells express both TrkA and TrkB, and SMSKCNR cells express TrkB. NGF activation of MAPK peaked at 5 minutes and was back to baseline at 30 minutes, whereas BDNF activated MAPK at 5 minutes and was still active at 90 minutes. Phosphorylation of ShcA paralled MAPK activation by NGF and BDNF. Activation of AKT by NGF peaked at 5 minutes and rapidly diminished, but activation by BDNF peaked at 5 minutes and was still active at 90 minutes. BrDU incorporation increased ~3-4 fold with NGF but ~8 fold with BDNF. The MEK inhibitor PD098059 inhibited NGF and BDNF-stimulated BrDU incorporation and MAPK activation to basal levels. LY294002 inhibition of AKT/PI3K pathway resulted in significant apoptosis that was reversed partially by BDNF.
CONCLUSIONS: MAPK and AKT are stimulated by NGF and BDNF. MAPK has a clear role in mitogenesis, whereas the PI3K/AKT pathway is important for cell survival. However, BDNF activation of both pathways is sustained, and BDNF appears to be a more potent activator of cell proliferation and survival. These results indicate that regulation of mitogenic signaling by NGF and BDNF is different, suggesting distinct roles for NGF and BDNF in neuroblastoma cell growth.

54 Presentation Time 8:30 AM

Novel Chemotherapeutic Agent for High-Risk Neuroblastoma

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BACKGROUND: Neuroblastoma (NB) is the most common heterogeneous and malignant tumor of childhood. They grow aggressively, metastasize, induce angiogenesis and remain resistant to multimodal therapy. Eradication of refractory microscopic disease has remained a significant challenge. The severity of NB calls for development of novel therapeutic strategies. In order to improve the outcome for patients with this disease, there is an urgent need for development of new drugs. Our past efforts have lead to the development of bromoacetoxycalcidiol (B3CD) as a cytotoxic agent for NB. Our Long-term goals are understand molecular mechanism of action of B3CD and to develop it as a chemotherapeutic agent for NB.
OBJECTIVE: To determine the cytotoxic/apoptotic activities of B3CD and its effect on TrkB, AKT and MAPK signaling in NB cells.
DESIGN/METHODS: NB cells were treated with B3CD for 48 hours. Proliferation was measured by MTS and BrdU incorporation assays. Apoptosis was assessed by DNA fragmentation and caspase-3 assays. Effect of B3CD on TrkB signaling by BDNF was assessed by western-blot analysis of AKT and ERK phosphorylation. Effect on angiogenesis was determined by chick chorioallantoic membrane (CAM) assay. B3CD was injected to mice to test toxicity.
RESULTS: B3CD inhibited the proliferation SK-N-SH, SH-SY5Y, SMS-KCN and SMS-KCNR neuroblastic cells in a dose dependent manner. At 0.5 μM, B3CD inhibited > 50% ($p<.035$) and >90% at 1.0 μM ($p<.01$) viability and proliferation respectively. B3CD activated caspase-3 and induced apoptosis. It inhibited phosphorylation of ERK1/2 and AKT demonstrating the role of MAPK and AKT pathways. B3CD also inhibited TrkB signaling by BDNF indicating that B3CD suppresses BDNF mediated chemoprotection generally observed in NB. In addition, B3CD inhibited proliferation of endothelial cells and angiogenesis in CAM assay. Administration of B3CD to mice did not cause hypercalcemia or weight loss indicating a lack of apparent toxicity.
CONCLUSIONS: B3CD is a potent antiproliferative and apoptotic agent in NB. AKT and MAPK signaling was inhibited by B3CD. It suppressed the BDNF mediated chemoprotection by inhibiting TrkB signaling. In addition, B3CD inhibited angiogenesis. B3CD can be potentially developed as a chemotherapeutic agent for NB.

55 Presentation Time 8:45 AM — Fellow in Training

Nifurtimox Is Cytotoxic to Neuroblastoma Cells

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BACKGROUND: Childhood neuroblastoma presents with aggressive disease and a high relapse rate, most of which do not survive. Well tolerated new treatments are needed. We treated a patient with Stage IV Neuroblastoma who acquired Chagas Disease from a transfusion. The neuroblastoma appeared to be sensitive to the Chagas treatment, Nifurtimox (a nitroheterocyclic compound). Nitrofurans have shown chemotherapeutic efficacy especially when combined with other anti-tumor drugs such as alkylating agents. Nifurtimox leads to cellular damage of T. Cruzi as well as mammalian tissue by formation of free radicals and redox cycling. Free radicals interacting with macromolecules lead to cellular damage and cell death of sensitive cells and organisms. The lipophilic NO_2 group is also vital for tissue penetration, including that of tumors.
OBJECTIVE: To determine the effect of Nifurtimox on Neuroblastoma cell lines.
DESIGN/METHODS: Neuroblastoma cell lines were cultured in complete RPMI media and treated with 1 to 20 ug/ml Nifurtimox for 4-6 days. Cell viability was assessed by MTS formazan reduction and proliferation by BrdU incorporation assays. Apoptosis was assessed by TUNEL assay and caspase-3, 8, and 9 activity. Signaling pathways were elucidated by western blot.
RESULTS: Nifurtimox was cytotoxic to neuroblastoma cell lines. Cell viability decreased from ~80% at day 4 to ~60% at day 6 with 1ug/ml of Nifurtimox. With the same incubation of 4 to 6 days, cellular proliferation decreased from ~80% to 50% with 1ug/ml of Nifurtimox and from ~60% to 20% with 10ug/ml of Nifurtimox. After a 4 day incubation with Nifurtimox, cells showed and increase in caspase activity. Incubating these cells with Nifurtimox for 90 minutes resulted in a decrease in basal AKT phosporylation, then adding BDNF shows a decrease in TrkB stimulation of AKT phosporylation.
CONCLUSIONS: Nifurtimox decreased viability of Neuroblastoma cell lines most likely due to apoptosis. There is also a significant decrease in cellular proliferation. The observed decrease in AKT phosphorylation may result in these cells being more susceptible to chemotherapy. Nifurtimox is well tolerated in children and cytotoxic to Neuroblastoma cells which may make this a novel adjunctive therapy in the treatment of Neuroblastoma.
Funded by Nifurtimox; Neuroblastoma.

56 Presentation Time 9:15 AM — Fellow in Training

Zinc Protoporphyrin IX Inhibits Cell Proliferation Via Suppression of Cyclin D1 Protein Synthesis in Hepatoma Cells

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BACKGROUND: Zinc protoporphyrin IX(ZnPP) is an endogenous competitive inhibitor of heme oxygenase (HO), the rate limiting enzyme in bilirubin production. Recently, ZnPP was shown to inhibit splenic, liver and lung tumor progression in animal models. This was attributed to inhibition of HO activity. However, we found that ZnPP also suppressed lymphoma B cell growth in mice through increased apoptosis.
OBJECTIVE: To further understand the mechanism by which ZnPP suppresses tumor cell growth, and to evaluate the effects of ZnPP on cell cycle regulation.
DESIGN/METHODS: Cultured hepatoma cells (HepG2) were incubated with 1, 5, 10, 25 and 50 mM of ZnPP or vehicle control for 48 hours. The cells then were subjected to BrdU pulse labeling. Incorporation of BrdU into DNA (an index of cell proliferation) was analyzed by enzyme-linked immunosorbent assay (ELISA), using HRP as well as the In Vitro Imaging System (IVIS) to quantify light emission.
In other experiments, HepG2 cells were treated with 25 mM of ZnPP for 12, 24, 36 and 48 hours, and the cell lysates were subjected to SDS-PAGE (12%) followed by Western blotting to detect cyclin D1 protein levels.
Double strand oligonucleotides (5'gcccgcccccgccccc3') synthesized from the human cyclin D1 gene promoter region were labeled with a-32P by fill-in reaction, and incubated with ZnPP. Electrophoretic mobility shift assay was performed to detect whether ZnPP causes conformational changes in DNA fragments from the cyclin D1 gene promoter.
RESULTS: After ZnPP incubation at 10, 25 and 50 mM, cell proliferation was inhibited to 71%, 68% and 77% compared to vehicle treated values ($p<0.05$). Cellular cyclin D1 protein levels were nearly undetectable 12 hours after ZnPP incubation, in contrast to vehicle controls. Incubation of ZnPP with an SP1 consensus sequence from the cyclin D1 promoter resulted in a concentration dependent differential migration of the ZnPP –oligonucleotide complex.
CONCLUSIONS: In a tumor cell model, ZnPP inhibits cell proliferation and suppresses cyclin D1 gene expression. Furthermore, ZnPP forms a complex with the SP1 consensus sequence on the cyclin D1 gene promoter. We hypothesize that inhibition of cell proliferation by ZnPP results from complexation of ZnPP with specific G¤C rich regions on the cyclin D1 gene promoter, leading to suppression of cyclin D1 gene transcription.

57 Presentation Time 9:30 AM Fellow in Training

Cranial Irradiation for Acute Lymphoblastic Leukemia (ALL): Effect on Growth and Endocrine Function in Indian Children

Umakanth A. Khatwa, P. S. Menon, Laxman S. Arya. Pediatrics, Lincoln Hospital, Bronx, NY; Pediatrics, All India Institute of Medical Sciences, New Delhi, India.

BACKGROUND: The adverse effects of CNS irradiation (CRT) on growth and endocrine function in survivors of childhood ALL are a concern. While studies have demonstrated a varying degree of growth retardation and growth hormone (GH) deficiency in western children, studies in Indian children are lacking.

OBJECTIVE: Determine the effects of CRT on linear growth and endocrine function in Indian children treated for ALL.

DESIGN/METHODS: 28 children attending the pediatric oncology clinic at All India Institute of Medical Sciences, New Delhi who completed MCP 841 protocol for ALL and were in continuous first remission for $^{3}2$ years were enrolled. Mean age at enrollment was 9.7 years (SD=3.2). CNS prophylaxis consisted of intrathecal methotrexate and CRT. Duration of treatment (chemotherapy plus radiotherapy) was 22 months. Mean age of receiving CRT was 6.1 years (SD=2.9). CRT was administered as 9 daily doses of 200 rads each (total dose: 1800 rads). Growth parameters were measured at 6 month intervals: height, weight and upper/lower body segment ratio. Bone age X-ray was done at study entrance and repeated at the end. GH stimulation test with clonidine was done at the end of the study. GH, thyroid stimulating hormone (TSH), follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels were measured.

RESULTS: 53% of children were growth retarded at study enrollment (height >1 SD below population mean) at a mean of 3.3 years after receiving CRT. 35% were growth retarded at study completion, indicating catch-up growth in some. None had skeletal disproportion, and growth velocity was normal during the study. 50% were GH deficient by the GH stimulation test (peak GH level <7 ng/ml). TSH was low (<0.5 mU/L) in 22.2%, indicative of hypothalamic or pituitary dysfunction, and elevated in 11% (>5.0 mU/L), indicative of primary thyroid failure. 18.5% had combined GH and TSH deficiency. FSH and LH were normal in all. Bone age was more retarded in GH deficient children compared to non-GH deficient children.

CONCLUSIONS: While some patients had catch-up growth, those with GH deficiency are likely to be growth retarded on final height. Thyroid function should be monitored in these patients. The effect of malnutrition and parasitic infestation on growth in oncology patients in developing countries should also be considered.

58 Presentation Time 9:45 AM Fellow in Training

Thrombopoietin and Platelet Response Following 10 vs 15 ml/kg of Transfused Platelets

Alex Kline, Amy Mackley, Scott Taylor, Steven McKenzie, David Paul. Neonatology, Thomas Jefferson Univ., Philadelphia, PA; Neonatology, Christiana Care Health Services, Newark, DE; Cardeeza Foundation,Hematology, Thomas Jefferson Univ., Philadelphia, PA.

BACKGROUND: Thrombocytopenia is common, affecting up to 25% of NICU admissions, but the optimal volume of platelet transfusion remains unknown. Thrombopoietin (Tpo) is known to be the central regulator of platelet production in adults. The role of Tpo in neonatal platelet regulation is not well understood. Studies in animals and adults have shown a decrease in Tpo following platelet transfusion. Platelet factor 4 (PF4), a marker of platelet activation, has not been measured in neonates in response to platelet transfusion.

OBJECTIVE: To determine the safety and efficacy of 10 vs 15 ml/kg of transfused platelets and analyze the change in Tpo and PF4 following platelet transfusion.

DESIGN/METHODS: After informed consent, preterm neonates undergoing platelet transfusion were randomized to either 10 or 15 ml/kg of platelets. Blood was obtained for Tpo and PF4 pre-transfusion, one, and 24 hours post-transfusion. Tpo and PF4 were measured using a standard ELISA technique. The study was powered to show a decrease in Tpo of 50%, with a b of 0.8 and a of .05. Statistical analysis was performed using repeated measures ANOVA, a $p<0.05$ was considered significant.

RESULTS: The gestational age of study infants was 27.2 ± 3.0 wks, and birth weight was 977 ± 614 g, and did not differ between the 10 (n=10) and 15 (n=10) ml/kg groups. There were no differences between the 10 and 15 ml/kg groups in platelet count pre (54.8 ± 25 vs 58.6 ± 21 x1000/mm^3, p=0.73), 1-hour (136.6 ± 44.4 vs 184.1 ± 64 x1000/mm^3, p=0.08), and 24 hours (144 ± 42.3 vs 172 ± 64 x1000 /mm^3, p=0.32) post-transfusion respectively. Tpo and PF4 did not differ between groups at any of the study time points. As platelet counts did not differ pre or post transfusion, the groups were also combined for analysis. In the combined groups, Tpo dropped 43% (95% confidence 37-49%, p=.01) 1-hour post compared to pre-transfusion. Both transfusion volumes were equally well tolerated.

CONCLUSIONS: Although well tolerated, there was no clinical or statistical rise in platelets following an increased transfusion volume of 15 ml/kg compared to standard volume. PF4 was not affected by transfusion. Tpo decreased following platelet transfusion, suggesting that Tpo kinetics in neonates are similar to adults following transfusion.

59 Presentation Time 10:00 AM House Officer

von Willebrand Factor Levels in Children with Sickle Cell Anemia

Dina M. DiMaggio, Iman Sharif, R. Labar, C. Bernstein, M. Mannix, M. Fagen, Paul T. Jubinsky. Pediatric Heme/Onc, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Sickled erythrocytes are known to damage the vascular endothelium, which can lead to the release of von Willebrand factor (vWF). Elevated levels of vWF have been observed in adults with HbSS disease(SSD) and they increased further during vaso-occlusive crisis.[1] In contrast, a report of vWF levels in children with SSD showed lower vWF levels than the control group.[2]

OBJECTIVE: To determine if there is a relationship between vWF levels and clinical status in pediatric patients with SSD.

DESIGN/METHODS: vWF levels in patients 1-21 years old, with confirmed SSD, were measured (Asserchrom vWF; Diagnostica Stago). Patients who received transfusions within the previous 3 months were excluded. Samples were drawn from inpatients in SSD crisis, and from asymptomatic outpatients with SSD. Each sample was assayed in quadruplicate. The patient's medical history was obtained and was later confirmed by chart review. The clinical data collected included number and type of hospital admissions (pain/acute chest syndrome/fever), number of SSD related admissions in the previous two years, medications, and laboratory results. We used the independent samples t test to compare vWF levels between clinical status groups.

RESULTS: To date, the vWF levels for 43 of a targeted 180 samples have been measured. Levels of vWF were normally distributed, with a mean of 150.7±51.6 IU/dl, which is 1.5 times higher than that reported for unaffected controls. vWF levels were higher for subjects admitted with vaso-occlusive crisis, fever, or acute chest syndrome as compared to asymptomatic subjects (154.9 IU/dl ± 41.8 vs 144.9 IU/dl±63.5). The highest vWF levels occurred in patients with acute chest syndrome compared to all other crises (201 IU/dl±20 vs 157.4 IU/dl±41, p=0.31). Patients with > 5 hospitalizations over the previous two years had higher vWF than those with fewer hospitalizations (167.9 IU/dl± 31.2 vs 139.6 UI/dl±59.6, p=.087).

CONCLUSIONS: Our findings suggest that levels of vWF are elevated in children with SSD, and increase further during acute manifestations of the disease. These results are similar to those observed in adult patients. Analysis of the remaining patient samples is necessary to determine if vWF levels correlate to other clinical variables or have prognostic significance.

[1]Blood Coag Fibr 1995;6:93-99.
[2]Turk J. Ped 1999;41:323-7.

Neonatology I: Clinical Platform Session

Saturday, March 5 8:15 AM-10:15 AM Sheffield

60 Presentation Time 8:15 AM Fellow in Training

Adequate First Week Protein and Calorie Intake Is Critical for 18 Month Developmental Outcomes in ELBW Infants

Rachel A. Vogt, Regina A. Gargus, Bonnie Stephens, Richard Tucker, Leslie McKinley, Martha Mance, Julie Nye, Betty R. Vohr. Department of Pediatrics/Neonatology, Women and Infants Hospital/Brown Medical School, Providence, RI.

BACKGROUND: Literature suggests that better nutrition in ELBW infants leads to better long term growth, which correlates with better developmental outcomes.

OBJECTIVE: The purpose of this study was to evaluate early protein and calorie intake and subsequent developmental outcomes of ELBW infants. The hypothesis was that infants receiving higher intakes in the first week of life would have higher Bayley scores at 18m.

DESIGN/METHODS: Charts were reviewed for 150 ELBW survivors born at WIH from 2000-2001. Mean birthweight was 797g; Mean GA was 26w. Daily protein and calorie intake for the first four weeks of life was collected. Socioeconomic/maternal and neonatal morbidity data was also recorded. 125 infants (83%) returned for follow up at 18m and were included in the analysis. Bivariate analysis tested correlations between protein and kcal intake during wks 1, 2, 3, 4, and Bayley scores at 18m. Separate regression models were used to evaluate the contributions of 1st week protein g/kg/d and kcal/kg/d to development. Independent variables for the model were BW, SNAPPE II scores at 24h, AGA/SGA, maternal age and education, and mean g pro/kg/d or kcal/kg/d in week 1. Models were run for MDI and PDI at 18m.

RESULTS: Only week one intakes correlated with outcomes: Mean kcal/kg/d correlated with Bayley MDI (r=0.3, p=0.0005) and PDI (r=0.3, p=0.0007) at 18 m, while mean g pro/kg/d correlated with Bayley MDI (r=0.24, p=0.0071) and PDI (r=0.22, p=0.0181) at 18m. After adjusting for confounding variables, kcal/kg/d in 1st wk had independent effects on MDI (B=0.61, p=0.0009) and PDI (B=0.54, p=0.0009); Mean g pro/kg/d in 1st wk had independent effects on MDI (B=11.0, p=0.013) and PDI (B=9.3, p=0.02). For every 10 kcal/kg/day (mean) in the first week there was a 6 point increase in MDI and 5 point increase in PDI scores. An increase of 1 g/kg/day (mean) in the first week correlated with an 11 point increase in MDI and 9.3 point increase in PDI scores.

CONCLUSIONS: Higher protein and calorie intake in the first week is associated with higher Bayley scores at 18m in ELBW infants. Increased emphasis needs to be focused on providing adequate nutrition in week one for all ELBW infants.

61 Presentation Time 8:30 AM

Intrauterine Infection Leads to the Delivery of Extremely Low Birth Weight Infants but Does Not Contribute to Their Death

Rita Verma, Cynthia Kaplan, Eugene Komaroff. Pediatrics, SUNY School of Medicine, Stony Brook, NY; Pathology, SUNY School of Medicine, Stony Brook, NY; Preventive Medicine, SUNY School of Medicine, Stony Brook, NY.

BACKGROUND: Adverse intra-uterine events may precipitate preterm labor (PTL) and delivery of an ELBW infant (birth weight < 1000 gm). The nature and pathogenesis of these events are not well understood. However, these events may result in placental histopathological changes which may in turn serve as marker of PTL and perinatal complications in ELBW neonates.

OBJECTIVE: To investigate the placental histopatholgy and placental markers for intrauterine events leading to PTL and neonatal mortality (death before DOL 28) in ELBW infants

DESIGN/METHODS: We examined placental histopathlogy in 105 ELBW infants admitted to the NICU of SUNY Hospital for the presence of chorioamnionitis (CHO), abruption (AB), ischemia (IS), infarction (IN), calcification (CA), cord vascular thrombosis (TH) and cord inflammation (INF). Placental histopatholgy was studied by a pathologist blinded to the study population. We also noted birth weight (BW), sex and gestational age (GA) in each infant. The infants were further divided and compared under 2 groups: survivors (S) and non survivors (N). Statistical calculations used the Student t test, chi square test, Fisher's exact test and ANOVA. P value was set at .05 for significance. Data are presented as mean (SD) for continuous and % for categorical variables.

RESULTS: 41 infants were studied in S and 64 in N. Only 7 placenta were normal (6.6%), of which 9% were normal in S and 4% in N (p .3). The frequency of abnormalities in all 105 infants were: CHO 62.8%, IS 45.7%, INF 36.2%, AB 23.8%, CA 20%, TH 19% and IN 17.1 %. Some placenta showed multiple findings.

CONCLUSIONS: Intrauterine infection and placental ischemia are the commonest placental findings in preterm labor leading to the delivery of an ELBW infants. However, neither is associated with neonatal death, which in turn is predicted by BW and GA.

Placental histopathology in ELBW infants

variable	Survivors	Non survivors	p
BW(g)	738 (131)	620(124)	.003
GA(week)	25.5(1.3)	24.1(1.3)	.001
male (%)	46	48	.9
CHO(%)	58	65	.4
AB(%)	26	21	.5
IS(%)	48	43	.6
IN(%)	17	17	.9
TH(%)	14	20	.4
CA(%)	19	18	.9
INF(%)	36	35	.9

62 Presentation Time 8:45 AM Fellow in Training

Pulmonary Function and Weight Gain in Very Low Birth Weight (VLBW) Infants

A.M. Hibbs, S. A. Lorch, J. M. DiFiore, J. D. Merrill, E. C. Eichenwald, S. E. Courtney, A. Puri, R. A. Ballard, R. J. Martin. Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Neonatology, Rainbow Babies and Children's Hospital, Cleveland, OH; Neonatology, Brigham and Women's Hospital, Boston, MA; Neonatology, Schneider Children's Hospital, New Hyde Park, NY; Neonatology, Cedars Sinai Medical Center, Los Angeles, CA.

BACKGROUND: Lung disease in VLBW infants is known to affect weight gain.

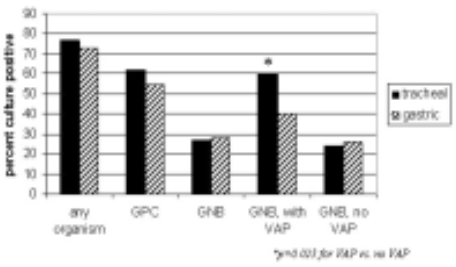
OBJECTIVE: We hypothesize that a baseline pulmonary function test (PFT) in the first weeks of life can predict an infant's future weight at 36 weeks post-menstrual age (Wt_{36}).

DESIGN/METHODS: We studied conventionally ventilated infants with GA Ω32 weeks and BW <1250g enrolled at 7-21 days of age in the NO CLD multicenter randomized trial of inhaled nitric oxide who had a baseline PFT prior to study drug. PFTs were obtained with the CO2SMO plus! Respiratory Profile Monitor and Analysis Plus! Software. Dynamic compliance (C_{dyn}) and expiratory airway resistance (R_{exp}) were calculated via a least squares technique using a single compartment linear model. Linear regression models were generated to assess the association of Wt_{36} with C_{dyn} and R_{exp} after controlling for confounding factors including weight at the time of PFT (Wt_{PFT}). Treatment with iNO remained blinded.
RESULTS: 54 infants with mean GA 25.4 wks (range 23-28) and BW 739g (range 500-1105) had a PFT performed at a mean age of 15 days (range 7-21). Mean C_{dyn} was 0.39 cc/cmH_2O (range 0.20-0.66), and R_{exp} 226 cm $H_2$0/L/sec (range 53-349). Mean Wt_{36} was 1847g (range 1267-2350). In univariate analysis, C_{dyn} was significantly ($p<0.001$) associated with Wt_{36}. When Wt_{PFT} was added to this model, the effect size on C_{dyn} dropped by 29%, but C_{dyn} remained significant ($p=0.027$). In contrast, R_{exp}, duration of parenteral nutrition, days to enteral feedings of 100kcal/kg, days on ventilator, and ventilation status at 36 wks were not significantly associated with Wt_{36} in univariate models. In a multivariate linear regression model (R^2=0.55), C_{dyn} remained significant (coefficient 686 g/cc/cmH20, $p=0.008$) after controlling for Wt_{PFT} ($p<0.001$) and GA ($p<0.001$).
CONCLUSIONS: In VLBW infants, baseline C_{dyn} predicts Wt_{36}. This highlights the effect of lung disease on growth in VLBW infants, and may reflect work of breathing or overall severity of illness. Confounding due to a treatment with iNO cannot be evaluated.

63 Presentation Time 9:15 AM — Fellow in Training

The Role of Gastric and Tracheal Bacteria in Ventilator-Associated Pneumonia (VAP) in Premature Infants <1500gms

Mohamad T. El Abiad, Anne Marie Reynolds, Kirsten Blessing-Hanagan, Rita M. Ryan. Pediatrics (Neonatology), Women & Children's Hosp of Buffalo - SUNY Buffalo, Buffalo, NY.
BACKGROUND: Aspiration of gastric contents is believed to be a risk factor for ventilator-associated pneumonia (VAP) in adults and may be due to gastric bacteria. Gastric colonization and aspiration may predispose premature infants to VAP.
OBJECTIVE: To study gastric and tracheal colonization and their association with VAP.
DESIGN/METHODS: We cultured prospectively weekly gastric (G) and tracheal (T) aspirates in ventilated infants <1500 gms until extubation or 8 weeks of age. VAP was diagnosed based on a need for increased ventilatory support, X-ray changes, and + T culture (cx). Univariate analysis was done using STATA (State College, TX).
RESULTS: There were 111 TCxs and 67 GCxs from 27 patients born at a mean gestation of 26.2 wks and mean birthweight of 878 gms. The average age at sampling was 22 days. Microorganisms were present in 78% of TCxs and 73% of GCxs. Gram + cocci (GPC) were present in 62% TCxs and 55% GCxs, most commonly coag neg Staph and Enterococcus. Gram (-) bacilli (GNB) were present in 27% of TCxs and 28% of GCxs, most commonly E. coli, Klebsiella, Enterobacter and Stenotrophomonas. Yeast were present in 4% of TCxs and 8% of GCxs. In instances in which simultaneous G and T samples were available (n=66), 44 (67%) were both positive, 8 were both negative, 4 were G + and T (-), and 10 were G (-) and T + ($p=0.002$, Fisher exact test). When simultaneous G and T samples were both positive, there was at least one organism in common in 34/44 (77%). There was a significant correlation of mean age and TCx results; the mean age at sampling was 24.5 days for positive TCxs and 13.0 days for negative TCxs ($p=0.0002$, t-test). Of the 27 infants enrolled, 25 (92%) had at least one positive TCx and 24 (89%) had at least one positive GCx. Nine (33%) babies had 10 episodes of VAP: 5 had a TCx positive for both GPC and GNB, 4 had a TCx positive for GPC alone, and 1 had a TCx positive for GNB alone. GNB were present in 60% of TCx at the time of VAP compared with 24% at the time of no VAP ($p=0.023$, Fisher exact test).
CONCLUSIONS: Recovery of bacteria from both gastric and tracheal aspirates is common in ventilated preterm infants. When simultaneous cultures from both sites are positive, over 75% of the time there is at least one organism in common suggesting a possible role for aspiration in the development of VAP.



64 Presentation Time 9:30 AM

Delayed Cord Clamping in Very Preterm Infants Reduces the Incidence of Intraventricular Hemorrhage (IVH) and Late Onset Sepsis (LOS)

Judith S. Mercer, Betty R. Vohr, William Oh. College of Nursing, University of Rhode Island, Kingston, RI; Pediatrics, Brown University & Women & Infants Hospital, Providence, RI.
BACKGROUND: The current prevailing obstetrical practice at the birth of the very preterm infant is to immediately clamp the umbilical cord.
OBJECTIVE: The aim of this study was to compare the effects of immediate (ICC) and delayed (DCC) cord clamping on infants born between 24 to 32 weeks on two primary variables: bronchopulmonary dysplasia (BPD) defined as oxygen use at 36 weeks and suspected necrotizing enterocolitis (NEC). Secondary outcome variables were blood pressure, hematocrit, LOS, IVH, and various respiratory variables. The hypothesis was that DCC would result in decreased incidence of BPD and suspected NEC.
DESIGN/METHODS: This was an unmasked randomized controlled trial in which women in labor with infants between 24 and 32 weeks gestation were randomized to ICC (cord clamped at 5 to 10 seconds) or DCC (30 to 45 seconds) groups. Based on our previous pilot data and using BPD as our primary outcome variable, sample size to detect a 30% absolute difference and a power of .80 required 31 infants in each arm. DCC infants were held at 10 inches below the introitus whenever possible. The exact time of cord clamping was measured. All care of study infants throughout their NICU stay was at the discretion of the attending physicians.
RESULTS: Intention-to-treat analyses revealed no differences in maternal variables, birth weights, gestational age, Apgar scores, initial temperature, and peak serum bilirubin levels.
There were no significant differences in the incidence of BPD (20% vs. 18%, p = 0.76), or suspected NEC (53% vs. 32%, p = 0.086), and any of the respiratory variables. Significant differences in IVH, sepsis, and hematocrit were found between the ICC and DCC groups.

Groups/p value	IVH	Sepsis	Hematocrit
ICC n = 34	14 (41%)	9 (27%)*	45.9 + 6.2**
DCC n = 35	4 (11%)	2 (6%)*	48.9 + 6.1**
p value	0.008	0.03	0.05

*n (%); **mean (SD)

In the ICC group 13 (38%) had grade 1-2 IVH compared to 4 (11%) in the DCC group. One ICC infant had grade 4 IVH.
CONCLUSIONS: In addition to a higher hematocrit, delayed cord clamping appears to protect very low birth weight preterm infants from IVH and late onset sepsis. DCC is an easy to implement perinatal intervention.

65 Presentation Time 9:45 AM

Vitamin A Supplementation in Preterm Infants: Vaccine Response

Vivien Carrion, Mark Ballow, Linda Duffy, Richard Browne. Division of Neonatology, Women & Children's Hospital of Buffalo.
BACKGROUND: Preterm infants have suboptimal antibody responses to hepatitis B vaccine. Vitamin A and its metabolites have a wide range of effects on immunologic functions including augmentation of immunoglobulins.
OBJECTIVE: The present study was undertaken to determine the effects of Vitamin A supplementation in very low birth weight infants on the antibody response following immunization with Hepatitis B (HB) vaccine.
DESIGN/METHODS: This randomized clinical trial enrolled infants <32 weeks GA between 700-1500gm, and divided these into 2 groups: "Low" L-LBW (700-1100gms) and "High" H-LBW (1101-1500gms). Infants were randomized to receive Vitamin A 5000 IU by IM injection 3x/week or sham injection (control) for 4 weeks from enrollment. Plasma vitamin A (retinol) levels were measured. Preterm babies born to hepatitis B antigen negative mothers were immunized at 2, 4 and 6 months of age with HB vaccine. Blood was collected at 9 months of age, and the plasma tested for IgG antibodies to hepatitis B surface antigen Abbott Laboratories, Abbott Park, IL) and tetanus toxoid by enzyme immunoassay. A level of anti-HB IgG antibodies < 10 mIU/ml and to tetanus toxoid < 0.1 IU/ml were considered to be non-protective.
RESULTS: 184 infants were enrolled. 94/184 were Vitamin A treated and 90/184 were control. The serum retinol levels at birth were lower in L-LBW babies compared to the H-LBW babies, e.g.0.49 mmol/L vs. 0.53 mmol/L. With Vitamin A therapy, there was an increase in plasma retinol levels both in the L-LBW and H-LBW babies with the highest level seen at 2 weeks and 1 month after birth. The highest plasma retinol levels were seen at 2 weeks after birth, e.g. 0.71 mmol/L. Among L-LBW infants, the proportion of infants who responded to HB vaccine (∅10 mIU/ml) was similar between the control and the Vitamin A treatment groups, e.g. 69% and 67%, respectively. Among the H-LBW preterm infants, the Vitamin A treatment group had a higher proportion of responders (65%) vs. the control group (44%; $p=0.059$). No differences were seen for IgG antibody responses to tetanus toxoid in any of the treatment groups.
CONCLUSIONS: Our study suggests a possible beneficial effect of Vitamin A therapy on enhancement of hepatitis vaccine responses in higher birthweight (1101-1500 grams) preterm infants.Targeting the LBW preterm infants for vitamin A supplementation warrants further studies.
Supported by NIH grant HD3726303.

66 Presentation Time 10:00 AM — Fellow in Training

Familial and Genetic Susceptibility to Major Neonatal Morbidities in Premature Twins

Matthew Bizzarro, Anupama Shetty, Richard Ehrenkranz, Linda Ernst, Betty Vohr, Nirmala Desai, Henrietta Bada, Naveed Hussain, Ian Gross, Grier Page, Laura Ment, Jeffrey Gruen, Vineet Bhandari. Pediatrics, Yale University School of Medicine, New Haven, CT; Pediatrics, Brown University School of Medicine, Providence, RI; Pediatrics, University of Kentucky School of Medicine, Lexington, KY; Pediatrics, University of Connecticut School of Medicine, Farmington, CT; Biostatistics, University of Alabama at Birmingham, Birmingham, AL.
BACKGROUND: Intraventricular hemorrhage(IVH), necrotizing enterocolitis(NEC), and bronchopulmonary dysplasia(BPD) remain significant causes of morbidity and mortality in premature newborns. We propose that, in addition to environmental factors, there is a significant genetic contribution to the development of these conditions.
OBJECTIVE: To conduct a multicenter retrospective study of premature twins to evaluate the familial tendency and genetic contribution of 3 major morbidities.
DESIGN/METHODS: In a multicenter retrospective study of twins born at Ω32 weeks of gestation, we collected data on IVH, NEC, and BPD. Logisitic regression(LR) was used to assess the influence of several independent covariates on the development of these conditions. A zygosity analysis was performed to estimate the genetic contribution.
RESULTS: Data were obtained on 348 twin sets with a mean gestational age of 29 weeks and birth weight of 1262 grams. LR analyses showed that respiratory distress syndrome(RDS) ($p=0.005$), treating institution ($p=0.001$), and twin with IVH ($p=0.001$) were significant independent variables for IVH; the same was true for BPD ($p=0.008$, $p=0.02$, and $p<0.0001$, respectively). For NEC, only an affected twin was signficant ($p=0.002$). Zygosity data (based on placental examination) were obtained on 160 monzygotic (MZ) and dizygotic (DZ) twin sets. The analyses revealed that the observed concordance for BPD, but not for IVH and NEC, was significantly higher ($p<0.0001$) than the expected concordance in MZ twins. These results show that BPD has a genetic component; the estimated heritability was 48.7%.
CONCLUSIONS: Our twin analyses reveal that IVH, NEC, and BPD are familial in origin. The data also show that there is a strong genetic susceptibility to the development of BPD in preterm infants.

Pulmonary Medicine Platform Session

Saturday, March 5 8:15 AM-10:45 AM Mead B

67 Presentation Time 8:15 AM — Fellow in Training

Use of an Electronic Asthma Care Pathway Can Reduce Length of Stay and Improve Quality of Care

Pauline Fani, Beverley J. Sheares. Pediatrics, Columbia University, New York, NY.
BACKGROUND: Studies have shown that asthma clinical pathways, when properly designed and implemented can result in improved patient care and reduced length of stay.
OBJECTIVE: To improve the quality and efficiency of inpatient asthma care, we developed and implemented an electronic asthma care pathway (ACP) designed to promote state-of-the-art asthma care while reducing length of stay (LOS) and re-admission rates.
DESIGN/METHODS: The ACP utilizes the Eclypsis system for electronic charting and orders, and focuses on standardizing patient assessment and treatment, family education, discharge criteria, referral to continuing primary care and expeditious discharge planning. Use of ACP templates increase the likelihood that salient features of the asthma history are obtained, proper medications and medication delivery devices are prescribed, and all patients receive a standard set of educational messages. Children ∅12 months of age admitted with a primary diagnosis of asthma and no respiratory co-morbidity are eligible for inclusion. Process measures include (LOS), percent of patients discharged with written treatment plans (WTP), long-term controllers (LTC), and valve holding chambers. Outcome measures include readmission rates. Children with a primary diagnosis of asthma admitted during the same period last year prior to instituting the ACP served as a comparison group.

RESULTS: During the first 3.5 months of ACP 80 patients, mean age 7 years, were admitted with a primary diagnosis of asthma, compared with 159 patients from the previous year. Overall LOS for asthma has decreased from 2.9 days (comparison group) to 1.8 days for children on the ACP (P<0.0001). The overall readmission rate to date has declined to 2.5% compared with 7% for the comparison group (P<0.081). Use of valve holding chambers increased from 36% to 60% (P<0.0001). LTC use remained stable at 84% and primary care follow-up appointments remained at 40%. WTP use (27%) has not changed.
CONCLUSIONS: Use of the ACP has increased efficiency and quality of asthma care resulting in decreased hospital LOS and readmission rates. We anticipate that WTP use and referrals to primary care pediatricians for follow-up care will increase as the ACP is further integrated into the residency training and physicians incorporate state-of-the-art asthma care into practice.

68 Presentation Time 8:30 AM

Predictive Factors for the Use of Medications for Reactive Airways Disease (RAD) in Premature Infants After Hospital Discharge

Scott A. Lorch, Kelly C. Wade, Gabriel J. Escobar, Barbara Medoff-Cooper, Susan Bakewell-Sachs, Marla Gardner, John Greene, Orit Even-Shoshan, Jeffrey H. Silber. Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA; Perinatal Research Unit, Kaiser Permanente, Oakland, CA.
BACKGROUND: Premature infants are at increased risk for the development of RAD, but the use and appropriateness of RAD medications in these infants are not known.
OBJECTIVE: To determine predictive factors for the use of oral and inhaled RAD medications in premature infants enrolled in a managed care system.
DESIGN/METHODS: The Infant Functional Study (MCHB R40MC00236) studied all surviving infants born at Ω32 wks gestational age (GA) among 6 Northern California Kaiser Permanente hospitals between 1998-2001 (N=893) along with a random sample of 541 infants of 33-34 wks GA. We excluded infants with congenital anomalies, home ventilation, or who were lost to follow-up. The study tracked prescriptions for albuterol, steroids, and other asthma medications filled within one year of hospital discharge. Use of oral albuterol and oral steroids without inhaled steroids were collected as markers of inadequate treatment. Logit models determined prognostic factors for use of these medications after controlling for socioeconomic status (SES) and medical conditions.
RESULTS: 275 infants (19.2%) received albuterol: 210 received inhaled and 127 received oral albuterol. 116 (8.1%) received steroids: 73 received inhaled and 83 received oral steroids. After controlling for SES, the use of inhaled albuterol was increased by lower GA, prior history of a ductus arteriosis (odds ratio (OR) 1.70, 95% CI 1.09-2.63), black race (OR 2.11, CI 1.31-3.39), and male sex (OR 1.37, CI 1.00-1.87), but not bronchopulmonary dysplasia (BPD). The prescription of oral albuterol without a subsequent inhaled albuterol prescription was strongly associated with black race (OR 3.39, CI 1.60-7.19) and lower SES class. While the use of oral steroids was more common only with GA Ω30 wks, the use of inhaled steroids was increased in infants of both lower GA and with BPD (OR 2.37, CI 1.18-4.76). No risk factor was associated with use of oral steroids alone.
CONCLUSIONS: Regardless of BPD status, younger GA infants are more likely to use RAD medications. Black race and lower SES class are independently associated with increased use of oral albuterol alone, which may be a marker of inadequate treatment.
Funded by MCHB R40MC00236.

69 Presentation Time 8:45 AM Fellow in Training

Asthma Educational Videoconferencing for Inner-City Immigrant Parents

Marina Reznik, Philip O. Ozuah. Pediatrics, The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Videoconferencing has been increasingly used for health education in rural areas. However, little is known about the effectiveness of videoconferencing in the delivery of health education to a population of inner-city immigrant parents.
OBJECTIVE: To determine the effectiveness of educational videoconferencing for inner-city immigrant parents.
DESIGN/METHODS: A prospective case-control, pre-post study of immigrant parents attending a class on English as a Second Language (ESL) in the Bronx, New York. A 60-minute videoconference was used to deliver an asthma education curriculum that we had previously developed. Cases were parents who participated in the videoconference. Controls attended their regularly scheduled ESL classes but did not have the videoconferencing experience. To test knowledge gain, we employed a before-after study design. For cases, we administered a 10-item true/false questionnaire at the beginning and end of the videoconference. For controls, we administered the same questionnaire at the beginning and end of their ESL class. Each correct answer to a true/false statement scored one point, so the maximum total knowledge score was 10. Bivariate analyses (paired t-test, McNemar test) compared the two groups.
RESULTS: 90 subjects participated (47 cases, 43 controls). Cases and controls were similar in their demographic characteristics, including gender (82% female in the case group vs 86% in the control group), Hispanic/Latino ethnicity (62% vs 74%) and median residence in the US (7 years for cases vs 10 years for controls). The majority of the subjects were immigrants from the Dominican Republic, Mexico and Puerto Rico. Controls showed no significant post-test improvement in knowledge scores (6.6 for pre-test vs 6.4 for post-test, p=.38). In contrast, cases demonstrated significant knowledge gain post-videoconference (7.3 vs 8.3, p<.0001). For example, cases were significantly more likely to answer the following items correctly at post-test: "Children who take asthma medicine every day become addicted to it" (53% vs 73%, p=.035); "Coughing can be a sign of asthma" (75% vs. 89%, p=.039).
CONCLUSIONS: Our findings suggest that educational videoconferencing was an effective tool for delivering health education to a population of inner-city immigrant parents. As compared to controls, the asthma-related knowledge of participants improved after the videoconference.

70 Presentation Time 9:00 AM

Improving Physician Prescription of Inhaled Corticosteroids for Asthma

Sandra F. Braganza, Iman Sharif, Philip O. Ozuah. Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: We have shown that physician documentation of asthma severity improves the use of inhaled corticosteroids (ICS) by children with asthma.
OBJECTIVE: To test the effectiveness of an intervention to increase 1)physician documentation of asthma severity, and 2)prescription of ICS for children with persistent asthma.
DESIGN/METHODS: Pre-post intervention study at an academic health center. Intervention: we placed a 2x3" sticker on visit forms for all patients with asthma. The sticker listed the National Asthma Education and Prevention Program (NAEPP) criteria for asthma severity classification, and highlighted the criteria for which ICS were indicated.
We reviewed charts of all patients treated for asthma for 1 week before (baseline) and 1 week during the intervention, and abstracted data about documentation of asthma severity and physician prescription of ICS. After each physician encounter, we interviewed the patient about asthma symptoms to determine asthma severity.
Main outcomes: Physician documentation of asthma severity, prescription of ICS for subjects with persistent asthma. We used chi-square to compare outcomes between baseline and intervention. Multivariate regression adjusted for potential confounders, including age, gender, asthma severity, physician level of training, and presence of an asthma action plan in the chart.
RESULTS: We reviewed 185 charts (95 baseline; 90 intervention). The mean age was 7.3 years; 56% were males. Physicians were more likely to document asthma severity for subjects treated during the intervention (67% vs. 100%, p<.001). Subjects for whom severity classification was documented were more likely to be prescribed ICS (48% vs. 20%, p=.005).
We interviewed 138 subjects (75 baseline; 63 intervention). The baseline and intervention groups were as likely to have persistent asthma (83% vs. 71%, p=0.115). Physicians were more likely to prescribe ICS for subjects with persistent asthma treated during the intervention (42% vs. 62%, p=.04).
The impact of the intervention on ICS use persisted after adjusting for potential confounders. The intervention significantly increased the odds of ICS use (AOR=2.14, CI: 1.01, 4.53).
CONCLUSIONS: This simple intervention increased physician documentation of asthma severity and prescription of ICS for children with asthma.

71 Presentation Time 9:30 AM Fellow in Training

Pulmonary *Cryptococcus neoformans* Infection Increases Airway Responsiveness in a Rat Model

Jennifer A. Davis, Xuping Shao, Lewis P. Singer, David L. Goldman. Pediatrics, Children Hospital at Montefiore, Bronx, NY; Benin.
BACKGROUND: In a recent study, we found that the majority of NYC children older than 2 years had serologic evidence for *Cryptococcus neoformans* infection. Infections in this cohort are likely to be subclinical, but may have important health implications. Given the known propensity of this organism to elicit TH2 polarized inflammation, together with the high incidence of asthma in urban areas, we hypothesized that this subclinical infection may influence the development of asthma.
OBJECTIVE: To determine the effects of *C. neoformans* pulmonary infection on airway reactivity using a rat model.
DESIGN/METHODS: Brown Norway (BN) and Fischer rats were intratracheally infected with *C. neoformans* (ATCC strain 24067) or PBS. Rats were sensitized by intraperitoneal injections of 1mg ovalbumin in Aluminum Hydroxide (1.3%) on days 14 and 24. Following exposure to aerosolized ovalbumin on days 28 and 29, rats were challenged with doubling doses of aerosolized methacholine. In separate experiments, infected, non-sensitized rats and control rats were challenged with methacholine 28 days after infection. Anesthetized rats were tracheotomized and mechanically ventilated. A whole body plethysmograph (Buxco) was used to measure esophageal and tracheal pressures and changes in flow. The dose of methacholine at which airway resistance doubled was determined for each rat and an average calculated.
RESULTS: For BN rats, baseline airway resistance was not different for infected animals compared with non-infected animals. For sensitized animals, the average dose of methacholine needed to induce doubling of airway resistance was lower for infected rats compared to non-infected rats (4.36 ± 2.6 mg/ml vs. 12.05 ± 5.5 mg/ml, $p < .05$). This effect was observed in non-sensitized rats as well. Baseline transpulmonary pressures were increased in infected sensitized rats versus non infected sensitized rats. Overall, Fischer rats exhibited less airway responsiveness to methacholine and infection was not associated with increased responsiveness.
CONCLUSIONS: Infection with *Cryptococcus neoformans* increased airway responsiveness in a rat model. This effect was rat strain dependent. Based on these findings, together with the high prevalence of subclincal infection among immunocompetent, urban children and the high prevalence of asthma in this cohort, we suggest that additional human studies are warranted.

72 Presentation Time 9:45 AM Fellow in Training

Persistent Sodium Currents Play an Essential Role in the Ventilatory and Chemoreceptor Response to Hypoxia

E. Vincent Faustino, David Donnelly. Pediatrics, Yale University School of Medicine, New Haven, CT.
BACKGROUND: Acute hypoxia elicits a hyperventilatory response via carotid body chemoreceptors. Persistent sodium current (INaP) which is inhibited by riluzole (Ril), an anti-spasticity drug for ALS, has been implicated to play a role in the generation of carotid body afferent activity. We, therefore, hypothesized that Ril reduces the ventilatory and carotid body neural responses to acute hypoxia.
OBJECTIVE: To determine the effect of Ril on the hypoxic ventilatory response of unanesthetized rats and the neural discharge activity of isolated rat chemoreceptors
DESIGN/METHODS: Ventilatory recordings were obtained from unanesthetized 2-week old rats using whole-body plethysmography during room air breathing and acute hypoxia (O_2 12%), before and following treatment with DMSO (vehicle) or Ril at 1 (Ril1) or 2 mg/kg (Ril2). Rise in respiratory rate (RR), tidal volume (TV) and minute ventilation (MV) during hypoxia pre- and post-drug treatment were compared using paired t-tests.
To measure chemoreceptor afferent activity, peripheral chemoreceptor complexes (carotid body/sinus nerve/glossopharyngeal nerve/petrosal ganglia) were harvested, intact, from 2-week old rats. Single axon activity was recorded from a petrosal soma, during superfusion with normoxic saline (pO_2»150 mmHg) and during acute hypoxia (pO_2»90 mmHg), before and during exposure to DMSO or increasing dosages of Ril. The frequency and amplitude of the discharge activity were analyzed using Student's t-test and 1-way ANOVA, respectively.
RESULTS: Both Ril doses ablated the rise in RR, TV and MV observed during hypoxia (Ril1: RR p=0.004, TV p=0.002, MV p=0.008; Ril2: RR p=0.01 TV p=0.04 MV p=0.02). In contrast, DMSO did not significantly alter the respiratory response to 12% O_2.
In isolated peripheral chemoreceptors, Ril, at increasing drug concentrations, caused a persistent drop in the spontaneous discharge frequency during normoxia and hypoxia compared to DMSO. Suppression of spontaneous activity was significant at doses >/= 5 µM (normoxia, p=0.03; hypoxia, p=0.02). In contrast, Ril caused no significant change in action potential amplitude.
CONCLUSIONS: Riluzole caused a large reduction in the ventilatory response to acute hypoxia of the unanesthetized animal and a significant decrease in activity from isolated peripheral chemoreceptors. Thus, we speculate that INaP is critically important in the function of peripheral chemoreceptors.

73 Presentation Time 10:00 AM

HO-1 Regulates Postnatal Lung Alveolar Development

Sara Q. Lin, Rashmin C. Savani, Phyllis A. Dennery. Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA.
BACKGROUND: Postnatal lung maturation requires proper alveolar development. In neonatal mice, daily subcutaneous injection of Dexamethasone (Dex) at doses that did not significantly alter somatic growth resulted in severe disruption of lung septation, whereas intraperitoneal injection of Retinoic Acid (RA) resulted in numerous and small alveoli. Combined injection of RA and Dex rescued the Dex phenotype, resulting in near-normal alveolar development. Heme oxygenase 1 (HO-1), the rate limitng enzyme in bilirubin formation is expressed at high levels in the murine lung in the prenatal and immediate postnatal period. HO-1 is also protective against oxidative stress and enhances cell proliferation in vivo.
OBJECTIVE: We hypothesize that HO-1 is important to postnatal lung development and that alteration of HO-1 protein expression by Dex/RA contributes to the protection against lung injury.
DESIGN/METHODS: To determine whether Dex can transcriptionally regulate HO-1 expression, Dex/

RA was injected into transgenic HO-1-luc mice. These mice express a transgene incorporating the 15kb HO-1 promoter sequence fused with the luciferase reporter. The mice were injected with Dex (3mg/Kg) or/and RA(500ug/Kg) for 14 days after birth and monitored with the In Vitro Imaging System (I.V.I.S, Xenogen). This method allows us to monitor photon emission as an index of the HO-1 promoter activity in the same transgenic animal during the entire experimental time course. HO1 promoter activity was compared in littermates injected with Dex, RA or Dex/RA as well as sham-injected controls. In some animals, lung samples were harvested at various time points for histology and protein analysis.
RESULTS: In the lungs of Dex-injected mice, immunoreactive HO-1 protein was increased five fold as compared with controls. The increased expression was first detected after 5 days of daily Dex injection. Injection with RA alone did not alter lung HO-1 protein levels. The elevated HO-1 protein levels observed with Dex returned to normal when the neonates were injected with Dex/RA, consistent with the reversal of lung morphological changes.
CONCLUSIONS: These results demonstrate that HO-1 is regulated by factors which influence alveolarization and suggest that HO-1 plays an important role in postnatal lung alveolar development. Further analysis with the HO-1-luc mice will shed light on the effects of Dex and RA on transcriptional regulation of HO-1 during the process.

Plenary Session II
Platform Session

Saturday, March 5 1:15 PM-3:45 PM Round Hill

74 Presentation Time 2:15 PM Fellow in Training

Altered Signal Transduction from *PTPN11* Gain-of-Function Mutations in Noonan Syndrome

Kimihiko Oishi, Konstantin Gaengel, Kenichi Kamiya, Ursula Weber, Marek Mlodzik, Leslie Pick, Bruce D. Gelb. Pediatrics, Human Genetics, and Molecular, Cell & Developmental Biology, Mount Sinai School of Medicine, New York, NY; Entomology, University of Maryland, College Park, MD.
BACKGROUND: Noonan syndrome (NS) results from mutations in *PTPN11*, encoding the protein tyrosine phosphatase SHP-2. SHP-2 mutants have gain-of-function (gof) with increased phosphatase activity. SHP-2's fruitfly homologue, corkscrew (csw), acts through receptor tyrosine kinases (RTKs). Previously, we generated transgenic flies expressing wild type (wt) or NS mutant csw. Ubiquitous expression of strong mutants was lethal while allele N308D resulted in ectopic wing veins, consistent with Egfr gof.
OBJECTIVE: To characterize the effects of csw gof mutants on signal transduction.
DESIGN/METHODS: Transgenic flies expressing A72S, N308D and wt *csw* driven by *tub-Gal4* were analyzed. Other mutants were obtained from Bloomington Stock Center. Immunohistochemistry was performed with anti-dpErk and anti-trachea antibodies. A *tll* cRNA probe was used for *in situ* hybridization.
RESULTS: Probing of Ras signaling downstream of Egfr in N308D flies revealed that loss-of-function (lof) alleles of positive regulators (*downstream of receptor kinase, son of sevenless, Ras, rolled* (Mapk), *pointed, Hsp83*) resulted in suppression of ectopic veins while lof alleles of negative regulators (*sprouty, Gap1*) enhanced the phenotype. Lof alleles of *Egfr*, its ligand (*vein*) and positive extracellular regulators (*Star, rhomboid*) suppressed while lof alleles for *argos*, a negative regulator, enhanced the wing phenotype. Epistatic analysis for other pathways showed enhancement with reduced Notch signaling and suppression with reduced Bmp and Jak/Stat signaling; the latter did not affect normal wing development. Anti-dpErk immunostaining showed equivalently increased Erk activation for csw wt and mutant transgenics compared to wt flies. Torso pathway signaling assessed with *tll* expression and trachea development (Fgfr pathway) were normal in A72S embryos.
CONCLUSIONS: In the fly, N308D engenders ectopic wing veins through gof effects requiring ligand stimulation of Egfr as well as an intact Ras-Mapk cascade. There are epistatic relationships to other pathways including noncanonical Jak/Stat signaling. Increased Ras-Mapk signaling in NS is necessary but not sufficient to alter development dependent on RTK signal transduction.

75 Presentation Time 2:30 PM Fellow in Training

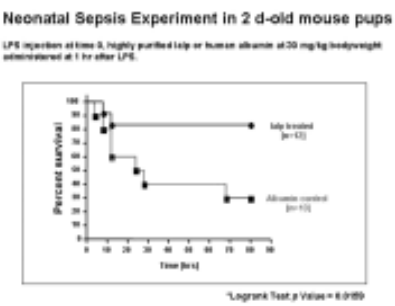
Astrocyte End-Feet in Germinal Matrix, Cerebral Cortex and White Matter in Developing Infants

Nadine El-Khoury, F. Hu, A. Braun, M. Nedergaard, E. LaGamma, P. Ballabh. Newborn Medicine, Cell Biology, Maria Fareri Children's Hospital-NY Med Coll, Valhalla, NY.
BACKGROUND: Astrocyte end-feet ensheathe blood vessels in the brain and are believed to provide structural integrity to the cerebral vasculature. We sought to determine in the developing human whether the fragility of the germinal matrix (GM) vasculature (compared to cortex and white matter) is due to decreased coverage of the blood vessels by astrocyte end-feet
OBJECTIVE: To catalogue the perivascular coverage by astrocyte end-feet in the GM compared to cortex and white matter in developing humans of 16 to 40 wk gestational age(GA)
DESIGN/METHODS: Human brain samples were obtained at autopsy from subjects of GA 16 to 40 wks, at <18 h postmortem interval. We performed double immunolabeling for Glial Fibrillary Acidic Protein (GFAP) and Aquaporin-4 (AQ-4) with a vascular marker, Laminin. Images were acquired by confocal microscopy on coronal sections from brains of 5 fetuses and 8 premature infants. Sets of 45-75 images per subject yielding 2104 blood vessels for AQ-4 and 1742 blood vessels for GFAP immunostaining were analyzed for their co-localization with Laminin using Metamorph software
RESULTS: Perivascular coverage by GFAP+ astrocyte end-feet increased consistently as a function of GA in cortex and white matter from 16 to 40 wks (ANOVA P<0.001). In contrast, in the GM, GFAP+ end-feet coverage increased only between 16 and 20 wk GA (P<0.01) then plateaued. In addition, coverage by GFAP+ end-feet was consistently less in the GM compared to cortex or white matter from 24 to 34 wks (P<0.01). Unlike GFAP expression, AQ-4+ astrocyte end-feet were already developed in GM at 16-17 wks ensheathing ~60 % of blood vessels and coverage did not change with advancing GA from 16 to 40 wks. Vascular coverage by AQ-4+ end-feet was <5% in cortex and white matter at 16-17 wks, increased to ~60% by 19-20 wks, then plateaued. There was no significant difference in % coverage of blood vessels by AQ-4+ end-feet among GM, cortex and white matter for 20-40 wk GA
CONCLUSIONS: The water channel molecule AQ-4 matures earlier in gestation than GFAP and thus, is reliable for identification of astrocyte end-feet for premature brain. The lesser degree of GFAP expression in astrocyte end-feet in GM compared to cortex and white matter may reflect a cytoskeletal structural difference that contributes to the fragility of GM vasculature and propensity to hemorrhage.

76 Presentation Time 2:45 PM Fellow in Training

Inter-alpha Inhibitor Protein (IaIp) Administration Improves Survival in Sepsis in Neonatal Mice

Kultar Singh, Kreso Bendelja, Ryan Heath, Yow-Pin Lim, James F. Padbury. Pediatrics, Women & Infants' Hospital, Providence, RI; Hematology/Oncology, Rhode Island Hospital, Providence, RI.
BACKGROUND: IaIp are group of serine proteases inhibitors found in a relatively high concentration in plasma. 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.
OBJECTIVE: The aim of this study is to evaluate the effects of parenterally administered IaIp in LPS induced sepsis in neonatal mice.
DESIGN/METHODS: Sepsis was induced in 2 days old BALB/c mice with a subcutaneous injection of 25 micrograms of E. Coli derived LPS. An LPS dose response curve of lethality was determined. In 2 days old mice, 25 micrograms of LPS injected subcutaneously had a survival rate of 30% after 80 hours. In the subsequent experiment, two day old animals (n=22) were injected with this dose of LPS and then randomized into two groups. The treatment group (n=12) received an intraperitoneal injections of 60 micrograms of highly purified human IaIp one hour after the infection. The control group (n=10) received equal amount of human albumin.



RESULTS: Only 30% pups in the control group survived 80 hours after the infection of LPS in contrast to a 83% survival in the treatment group (Longrank test p value=0.0159). This data is reprentative of multiple experiments.
CONCLUSIONS: These results suggest that administration of IaIp offers a beneficial effect in septic newborn mice and warrant further investigation.
This study is supported by the NICHD/NIH Grant#1 R21 HD047600-01.
Funded by NICHD/NIH Grant#1R21 HD047600-01; ProThera Biologics.

77 Presentation Time 3:00 PM

Wait and See Antibiotic Prescription for the Treatment of Acute Otitis Media: A Randomized, Controlled Trial

David M. Spiro, Khoon-Yen Tay, M. Douglas Baker, Donald H. Arnold, Eugene D. Shapiro. Pediatrics, Yale University School of Medicine, New Haven, CT; Emergency Medicine, Vanderbilt University School of Medicine, Nashville, TN.
BACKGROUND: Resistance to antibiotics is a major public health concern. Acute otitis media (AOM) is the most common diagnosis for which antibiotics are prescribed for children in the United States, yet the vast majority of AOM infections resolve spontaneously without antimicrobial therapy.
OBJECTIVE: To determine whether treatment of AOM using a wait and see prescription (WASP) significantly reduces use of antibiotics compared with a standard treatment prescription (STP) and to evaluate whether beliefs of parents related to the use of antibiotics are affected by use of WASP.
DESIGN/METHODS: The study is an ongoing randomized controlled trial. We are enrolling consecutive patients aged 6 months to 12 years diagnosed with AOM in the pediatric emergency department. Patients with a coexistent bacterial infection, perforation of the tympanic membrane, poor access to medical care, or who either were toxic in appearance or had used antibiotics in the previous 7 days were excluded. Parents in the WASP group were given instructions not to fill the prescription unless "symptoms worsen or do not improve after 48 hours." Parents in the STP group were encouraged to begin antibiotic therapy as soon as possible. All enrolled patients received both ibuprofen suspension and topical otic analgesic drops. A research assistant blinded to group assignment conducted structured phone interviews at 4-6 days, 11-14 days, and 30-40 days after enrollment.
RESULTS: A total of 103 patients were randomized either to the WASP group (n= 49; median age 31 months) or to the STP group (N= 54; median age 34 months; p= NS). Significantly more parents in the WASP group did not fill the antibiotic prescription (59% vs. 4%, p< .01). There were no significant differences between the groups in duration of fever, otalgia, use of ibuprofen, use of analgesic otic drops, days of school/work missed, or return visits for medical care. At the 30-40 day follow-up, substantially more families in the WASP group were willing to withhold antibiotics for future episodes of AOM (55% vs. 30%, p< .05).
CONCLUSIONS: The WASP model may significantly reduce unnecessary use of antibiotics in children and may alter parental expectations related to antibiotic treatment of future episodes of acute otitis media.

78 Presentation Time 3:15 PM

Depression Prevalence and Predictors in the Pediatric Emergency Department Adolescent Population

Sabina B. Singh, Sandra J. Nairn, Michael Franco, Edwin D. Boudreaux. Department of Emergency Medicine, UMDNJ-RWJMS, Camden, NJ; Department of Psychiatry, UMDNJ-RWJMS, Camden, NJ.
BACKGROUND: There is a paucity of information regarding depression in adolescents presenting to the Pediatric Emergency Department (PED). Prevalence rates of depression in teenagers are 20%. Adolescents often seek healthcare in the weeks preceding a suicide attempt. The PED is often their only source of healthcare. A retrospective study found PED physicians did not adequately screen adolescents for depression.
OBJECTIVE: To determine prevalence and predictors of depression among adolescents presenting to the PED, and association of depression with somatic chief complaints.
DESIGN/METHODS: A prospective consecutive enrollment of adolescents (13-18y) presenting to the PED between 10am-10pm over 11 weeks. Non-verbal, altered mental status or severely ill patients were excluded. The Harvard Department of Psychiatry Scale was used to screen for depression. Demographic factors and presenting complaint were noted.
RESULTS: Interim analysis for the first 156 of the 206 enrolled patients was conducted. Average age 15y (SD 1.35); 51.9% were females; 28% White, 38% Black and 31% Hispanic; 45% lived with the mother only. The most frequent chronic illness noted was asthma in 23% patients.
Positive depression screening was noted in 10.3%(16) patients. The percentage positive screening among Whites was 7%, Blacks 14%, Hispanics 10% p=0.5. Females had a prevalence rate of 17% and males 4% P<.01. Positive screen for depression was 3% in adolescents with no prior ED visit, 10% with 1 visit, 22% with 2 or more visits p<.01; 18% adolescents with chronic illness screened positive screen as compared to 6% without chronic illness p=.2; prior psychiatric history 37% screened positive as compared to 3% with no prior psychiatric history p<.01. Obese adolescents were more likely to be depressed. No significant difference was noted in positive screening among patients presenting with (11%) or without (9%) somatic complaints.
CONCLUSIONS: The predictors for positive depression screening were female sex, frequent PED visits and history of prior psychiatric treatment. Black race, chronic illness and obesity were associated with higher positive depression screening although this did not reach significance, this could be due to our small sample size. Somatic presenting complaints were not associated with an increase in positive screening.

79 Presentation Time 3:30 PM

Neurofibromin GAP-Related Domain Rescues Cardiovascular Defects of Nf1-Deficient Mice

Fraz A. Ismat, Min Min Lu, Jonathan A. Epstein. Division of Cardiology, The Children's Hospital of Philadelphia, Philadelphia, PA; Division of Cardiology, University of Pennsylvania School of Medicine, Philadelphia, PA.

BACKGROUND: Neurofibromatosis type I (von Recklinghausen's disease) is a common autosomal dominant condition, characterized by pathology of neural crest-derived tissues, but also causes cardiovascular abnormalities in affected patients. The gene responsible for this disease, NF1, encodes neurofibromin, a large molecule that in part acts as a ras GTPase activating protein (GAP). A mouse model homozygous for a null allele of the murine homologue (Nf1) has a set of embryonic lethal cardiovascular defects reminiscent of common forms of congenital heart disease. In particular, Nf1-/- embryos have overgrowth of the developing endocardial cushions, malrotation of the outflow tract, and thinned myocardium.

OBJECTIVE: We postulate that neurofibromin ras-GAP function is critical for normal cardiovascular development.

DESIGN/METHODS: The isolated GRD domain demonstrably down-regulates ras activity. We have successfully targeted the murine Rosa locus such that GRD is expressed upon cre-mediated recombination.

RESULTS: Expression of this Rosa-GRD, under the regulation of a ubiquitously expressed cre, is able to rescue the cardiac defects in Nf1-/- mice. These defects, uniformly lethal by mid-gestation, are rescued to birth with GRD expression. Rescued newborn pups interestingly show overgrowth of neural crest-derived tissues, such as dorsal root ganglia and adrenal medulla.

CONCLUSIONS: Modulation of ras, while critical in cardiovascular development, may not be the only function of Nf1 relevant to tumor formation. We are currently evaluating the effects of more tissue-restricted GRD expression, including endothelial, smooth muscle, and neural crest.

This work is supported by a Young Investigator Award from the National Neurofibromatosis Foundation.

Adolescent Medicine Platform Session

Saturday, March 5 4:00 PM-6:00 PM Mead C

80 Presentation Time 4:00 PM Fellow in Training

"Energy Up!": Lifestyle Training and Weight Attenuation Among Inner-City Teens

Lynn Gettleman Chehab, Ileana Vargas, Betsy Pfeffer, Shaofu Chen. Division of General Pediatrics, Columbia University, New York, NY.

BACKGROUND: Weight attenuation in adolescence can aid in the prevention of adult obesity and its complications. Most prior studies of adolescent school-based nutrition and exercise programs fail to demonstrate significant, long-term effects on weight attenuation.

OBJECTIVE: To evaluate the effect of a lifestyle training program on weight attenuation in adolescent girls.

DESIGN/METHODS: Students of an inner-city, parochial high school participated in Energy Up, a weekly, voluntary after-school program, led and designed by a lifestyle coach. Rooted in theories of empowerment and self-efficacy, this program used psycho-educational skills building and non-stigmatizing language to focus on nutrition, exercise, and self-esteem. Each session consisted of 15-30 minutes of education, followed by an hour of aerobic exercise, and concluded with healthy food tastings. The program used positive affirmations and incentives. Physicians were on-site for participation and educational input. Study measurements included level of participation and changes in weight and body mass index (BMI) over the 9 month program.

RESULTS: From 9/03-6/04, 44 Latina girls, aged 12-18 participated in Energy Up. 43 were post-menarchal. Of the 39 participants whose weights and heights were measured, 9 (23%) had BMI<85 %, 19 (49%) were overweight (BMI 85-95 %), and 11 (28%) were obese (BMI >95%). Girls with BMIs <85% experienced a mean weight gain of 2.9 lbs (median 2.4 lbs, range –1.8 to +7.8 lbs), overweight girls had a mean weight loss of 2.9 lbs (median 0 lbs, range –45 to +26 lbs), and the obese girls had a mean weight loss of 12.9 lb (median 7.8 lbs, range –35 to +1 lbs). For those participants with BMI ∅85 %, the correlation between percent of classes attended and weight loss was 0.6 ($p < .01$). One-fifth of the participants chose to continue the program for the 2004-2005 school year: 2 continued to lose weight and 5 were able to maintain their weight over the summer when Energy Up was not in session.

CONCLUSIONS: A lifestyle-focused weekly after-school program showed long-term weight attenuation among inner city adolescent girls. Further studies are necessary to identify effective components and the longer-term impact of this program.

81 Presentation Time 4:15 PM

Double-Blind, Multicenter, Placebo-Controlled Trial of the Effect of ORTHO TRI-CYCLEN® on BMD in Pediatric Subjects with Anorexia Nervosa

Suzanne Riggs, Gary Strokosch, Debra Karvois, Andrew J. Friedman. Pediatrics, Rhode Island Hospital, Providence, RI; Rush Presbyterian - St. Luke's Medical Center, Chicago, IL; Women's Health Care, Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ; Internal Medicine, Johnson & Johnson Pharmaceutical R&D, Raritan, NJ.

BACKGROUND: Females with anorexia nervosa are estrogen-deficient. Adolescent females with anorexia nervosa often fail to accrue bone normally and may not achieve maximal peak bone mass. These females are also at risk for osteoporosis. However, because multiple factors affect bone development, it is unknown if estrogen deficiency is the predominant cause of the osteoporosis/osteopenia in anorexia nervosa patients. In other states of estrogen deficiency, estrogen replacement therapy is protective in preventing further bone loss. There has been no clear consensus on whether oral estrogen can increase bone mass in adolescent females with anorexia nervosa.

OBJECTIVE: Evaluate the effect of ORTHO TRI-CYCLEN® on lumbar spine (LS) (L1-L4) BMD in pediatric subjects with anorexia nervosa (AN).

DESIGN/METHODS: 123 females, post-menarcheal through age 17 with AN, were enrolled and randomized (1:1) to ORTHO TRI-CYCLEN or placebo for 13 consecutive 28-day cycles. 123 subjects were enrolled; 88 subjects completed at least 12 treatment cycles (completer population). Treatment groups were similar for age (overall mean: 15.1 yrs) and Body Mass Index (BMI) (overall mean: 17.77 kg/m^2).

RESULTS: In a completer population, the ORTHO TRI-CYCLEN group had a significantly greater increase in mean LS BMD compared with placebo at Cycle 13 (0.0374 g/cm^2 and 0.0218 g/cm^2; p=0.018). There was no significant difference in mean increase in total hip BMD in subjects treated with ORTHO TRI-CYCLEN compared with placebo at Cycle 13. The incidence of adverse events for subjects in the ORTHO TRI-CYCLEN group (N=61 [78.7%]) was similar to the placebo group (N=62 [79.0%]) except for worsening of AN (ORTHO TRI-CYCLEN: 2; placebo: 11).

CONCLUSIONS: In a completer population, the ORTHO TRI-CYCLEN group had a significantly greater increase in mean LS BMD compared with placebo at Cycle 13. There was no significant difference in mean increase in total hip BMD between the groups. The results of this study suggest that ORTHO TRI-CYCLEN may benefit adolescent females with AN by increasing LS BMD and potentially reducing future fracture risk.

Funded by Ortho-McNeil Pharmaceutical, Inc.; Ortho Tri-Cyclen; Treatment of bone mineral density in pediatric anorexia nervosa patients; Johnson & Johnson Pharmaceutical R & D.

82 Presentation Time 4:30 PM House Officer

Use of Marijuana by Adolescents with and Without Asthma

Sara B. Levine, Philip O. Ozuah. Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: There is a paucity of data describing patterns of marijuana use, specifically among adolescents with asthma or other severe respiratory symptoms. We hypothesized that marijuana may be used preferentially by asthmatic adolescents given its purported immediate bronchodilator action.

OBJECTIVE: To test the hypothesis that marijuana use will be more prevalent in adolescents with asthma

DESIGN/METHODS: We conducted a survey of adolescents (13-19 years) at an urban children's hospital, using a self-completion anonymous questionnaire. The questionnaire was adapted from the national Youth Risk Behavior Surveillance System (YRBSS) and the NHLBI asthma guidelines. Adolescents were asked about substance use (cigarettes, marijuana, and alcohol), frequency of cough, wheezing, or shortness of breath, and previous diagnosis of asthma. Substance use questions were modeled after the YRBSS, which has been validated with adolescents. Lifetime substance use and age of initiation were compared on the basis of diagnosis of asthma. Chi-square was used for univariate analyses.

RESULTS: Of 207 participants, 60% were female, 80% were Black or Hispanic, and mean age was 16 years. 66 adolescents (32%) reported having ever been diagnosed with asthma by a healthcare provider, but an additional 34 without asthma reported moderate to severe respiratory symptoms, measured in accordance with NHLBI guidelines. Overall, 28.8% had ever used marijuana, 33.5% had ever smoked cigarettes, and 51.0% had ever used alcohol. Adolescents with a diagnosis of asthma, however, were more likely than their nonasthmatic peers to report having ever tried marijuana (35.9% vs. 25.6%) and cigarettes (36.4% vs. 31.7%). Asthmatic and nonasthmatic adolescents reported equally having ever used alcohol (51.1% vs. 50.0%). Compared to their nonasthmatic peers with significant respiratory symptoms, moderate to severe asthmatic adolescents were more likely to report having ever used marijuana (32.4% vs. 15.6%), or cigarettes (35.3% vs. 27.3%,), but equally likely to report having ever used alcohol (50.0% vs. 52.9%). There were no differences in age of initiation of marijuana, tobacco, or alcohol between the groups.

CONCLUSIONS: Our findings suggest that asthmatic adolescents are using more marijuana than their nonasthmatic peers, and this difference is significantly larger than differences in other substance use behaviors. Reasons for these differences are unclear.

83 Presentation Time 4:45 PM Fellow in Training

Inner City Adolescents and the Criminal Justice System

Delaney Gracy, Karen Soren, Shaofu Chen, Lindsay A. Thompson, Matilde Irigoyen. General Pediatrics, Columbia University, New York, NY.

BACKGROUND: In certain inner city communities, the rates of arrest and incarceration are very high. Little is known about the effects of the interaction of inner city adolescents with the police and the courts (criminal justice system) and how this affects their lives and well-being.

OBJECTIVE: To assess the level of personal and indirect exposure to the criminal justice system among inner city adolescents, their perceptions the police and court system, and the effects of these exposures on their lives.

DESIGN/METHODS: We conducted a cross-sectional survey of a convenience sample of 13-19 year-olds at an adolescent primary care practice in an inner city minority community in New York City. 85% of patients attending this clinic have medicaid. Patients completed an anonymous questionnaire assessing experience, both personal and indirect, with the criminal justice system, the impact of the experience on their lives, and subsequent unmet needs.

RESULTS: 147 adolescents participated, 35 declined. Of the participants, 67% were female, 77% Latino, 12% African American. 5% reported personal arrest and 2% personal incarceration. Most (70%) knew one or more individuals who had been arrested(9% knew 1, 14% knew 2, 47% knew 3 or more). 26% had visited someone in jail. A quarter (23%) reported being treated unfairly by police; a fifth (21%) reported that they had been harassed by police when they felt they were doing nothing wrong. Adolescents were divided in their impressions of the police: a third regarded police as trustworthy and fair, a third unfavorably, and a third were ambivalent. 40% reported being helped by police and 95% felt police security at schools was a good idea. A third (32%) knew someone working in the criminal justice system, and of these, half were family members. 40% would not consider working for the criminal justice system, 24% would, and 36% were unsure. Of those who knew someone who had been arrested, a third (28%)reported consequent stress; 32% associated sadness and, of these, 20% were interested in counseling or social work services.

CONCLUSIONS: Adolescents at an inner city practice reported a high level of contact with the criminal justice system, both negative and positive. This interaction can be a source of social stress for some and support for others and reveals an area where targeted screening tools developed for pediatricians working with inner city youth may be beneficial.

84 Presentation Time 5:00 PM House Officer

Residents' Knowledge, Attitudes, and Practices Regarding Emergency Contraception

Elizabeth Armstrong, Satoko Igarashi, Elizabeth Campbell, Laura Keonigs. Medicine-Pediatrics, Baystate Medical Center, Springfield, MA.

BACKGROUND: There are numerous barriers to the effective use of emergency contraception (EC), including lack of patient education on EC, difficulty obtaining EC in a limited time frame, and physician discomfort prescribing EC.

OBJECTIVE: To assess the knowledge, attitudes, and prescribing practices of EC among medicine, pediatric, and combined medicine-pediatric residents at Baystate Medical Center (Springfield, MA).

DESIGN/METHODS: A self-administered survey was distributed to 109 pediatric, med-peds, and internal medicine residents in Jan-Feb 2004. Respondents reported their sex, resident year, specialty, religion, beliefs on abortion, and exposure to formal education on EC.

Outcomes included ability to name at least one form of EC and dosing, timing, and side effects of that method. Other outcomes included beliefs about adverse effects of EC, attitudes on making EC available over-the-counter, and awareness of state policy on EC and minors.

RESULTS: 66/109 surveys were returned, representing 41% of medicine, 76% of pediatric and 76% of med-peds residents. There was a significant difference in ability to correctly prescribe EC based on specialty (P=0.03), with 68% of pediatric, 73% of med-peds, and 38% of medicine residents correctly answering questions on EC dosing. 84% of pediatric, 100% of med-peds, and 63% of medicine residents identified common side effects of EC (P=0.004). Among all respondents, barriers to prescribing EC included concerns that other birth control would not be used (62%) or that EC would be used incorrectly (44%), possible teratogenicity (36%), and uncertainty as to laws on treatment of minors (17%). Patient's or physician's religion was not a major barrier.

CONCLUSIONS: There was a significant difference between the knowledge and practices of residents based on their specialty. These data may have been limited by sample size and by the lower percentage of internal medicine respondents. Pediatric and med-peds residents were more likely to answer questions on EC correctly, perhaps owing to more exposure to EC use in adolescent rotations. However, at least 27% of all residents had difficulties with EC dosing, and many cited misconceptions (teratogenicity, non-adherence) as barriers preventing them from prescribing EC. This suggests that all residents would benefit from further education on EC, with particular attention to the medicine curriculum.

85 Presentation Time 5:15 PM — Fellow in Training

Communication About Vaccines for Teenagers: A Qualitative Study with Teens and Their Parents

Andrea L. Benin, Ann C. Wu, Eric Holmboe, Eugene D. Shapiro, Walter Anyan. Pediatrics, Yale, New Haven, CT; American Board of Internal Medicine, Philadelphia, PA.

BACKGROUND: New vaccines are being targeted for teenagers. Because of both the developmental tasks of adolescence and the growing publicity about real and perceived risks of vaccination, learning to communicate about vaccines with teens and their parents is important. Teens need to understand about vaccines not only for their own health but also because they are the next generation of parents; their attitudes to vaccines for their own children will be shaped by their personal experiences with vaccination.
OBJECTIVE: To understand attitudes of parents and teens about vaccination.
DESIGN/METHODS: We used qualitative methodology to conduct and analyze private, open-ended interviews of mothers and of teens receiving well-child care .
RESULTS: We interviewed 25 mothers and 25 11-14 year-olds from suburban and inner-city areas. There were 2 main categories of themes: understanding of concepts related to vaccination and decision-making about vaccination. (1)Understanding of concepts: Both mothers and teens had trouble understanding the ideas of risks, benefits, prevention, and what vaccines are. Adults and teens frequently mistook depo-provera or phlebotomy as vaccinations. (2)Decision-making: Mothers accepted vaccination as a routine part of life - not as something about which they had a choice. Many saw it as an opportunity for an educational time with the teen, a time to begin to help teen have some responsibility and to develop skills for transition to adulthood. Teens felt that decision-making should be in the realm of the adults but expressed concerns that they were being deceived or lied to about vaccines. Being told that "it won't hurt" reinforced their sense of deception, and they consistently worried about the physical pain or the size of the needle. Despite acceptance of their disenfranchised state, teens expressed a developing awareness of why vaccines were important.
CONCLUSIONS: There is substantial room for improved education/knowledge regarding vaccination; even the very basic concepts about vaccination cannot be taken for granted but must be explained to both adults and teens. The teenage period represents a time when both adults and children recognize the need for learning responsible decision-making; discussion regarding the risks and benefits of vaccines can be part of transitioning to adult decision-making.

Cardiac and Neonatal Outcomes Research Platform Session

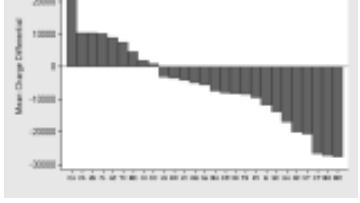
Saturday, March 5 4:00 PM-5:45 PM Winthrop A/B

86 Presentation Time 4:00 PM — Fellow in Training

Marked Statewide Variation in Risk-Adjusted Hospital Charges for Congenital Heart Surgery

Jean A. Connor, Kimberlee Gauvreau, Kathy J. Jenkins. Cardiology, Childrens Hospital Boston, Boston, MA.

BACKGROUND: Selected referral to institutions with low mortality rates has been proposed as a strategy to improve outcomes for congenital heart surgery; the impact of such strategies on medical costs is not known.
OBJECTIVE: To examine whether hospital charges for congenital heart surgery varies across geographic regions.
DESIGN/METHODS: Cases of congenital heart surgery (<18y) were identified from the Health Care Utilization Project KID 2000 database using ICD-9-CM codes. To adjust for baseline case mix differences, patient characteristics independently associated with higher log transformed charges were identified. Procedures were grouped into RACHS-1 risk categories. Differences between observed and expected mean charges were examined for each state. Predictors of these differences were explored, including ratio of state volume of congenital heart surgery cases to number of institutions performing congenital heart surgery and the proportion of each state's caseload at children's and teaching hospitals, and with specific insurance types (Medicaid, private/HMO, other).
RESULTS: Among the 9,406 cases of congenital heart surgery for which a RACHS-1 risk category could be assigned, mean charges were $ 54,725. RACHS-1 risk category, age, prematurity, major non-cardiac structural anomaly, multiple surgical procedures, chromosomal abnormality and weekend admission were associated with higher charges. Among the 27 states examined, risk adjusted charges varied by $ 51,912 (See Figure). States with children's hospitals had a $12,572 higher charge differential (p=0.009). Other case mix descriptors were not associated with mean dollar charge differential.
CONCLUSIONS: States varied considerably in risk adjusted hospital charges for congenital heart surgery procedures. States containing 1 or more children's hospital were found to have a higher charge differential.



87 Presentation Time 4:15 PM — Fellow in Training

Medical Injuries and Congenital Heart Surgery

Oscar J. Benavidez, Kimberlee Gauvreau, Kathy J. Jenkins. Cardiology, Children's Hospital, Boston, Boston, MA.

BACKGROUND: Complex pediatric patients have been identified as being a vulnerable group for medical injury. Comprehensive assessment of the prevalence of injury events among children undergoing congenital heart surgery has not been performed.
OBJECTIVE: We examined 1) the prevalence of medical injury codes and 2) the relationship of reported medical injury codes to mortality among pediatric cases of congenital heart surgery.
DESIGN/METHODS: Data were obtained from the Healthcare Cost and Utilization Project Kids' Inpatient Database 2000. We identified inpatient discharges of congenital heart surgery cases using ICD-9-CM codes. A previously validated algorithm was used to identify codes indicating medical injury. Medical injury codes were categorized as related to: 1) procedure, 2) device, implant or graft, 3) drug or biologic, or 4) radiation.
RESULTS: Among the 12,717 cardiac surgical cases identified, 4014 (32%) had at least one medical injury code; there were a total of 6650 codes of medical injury (523 injuries per 1000 cases). Procedure related injury codes were the largest category and represented 75% of all reported injury codes and occurred with a frequency of 392 per 1000 cases. Device, implant, or graft related injuries: 21% of reported injury codes and occurred with a frequency of 111 per 1000 cases. Drug/biologic related injuries: 4% of reported injury codes and occurred with a frequency of 20 per 1000 cases; there were no reported radiation injury codes.
Among the procedure related injury codes, respiratory complications represented 18% of all injury codes (94/1000 cases); cardiac complications 17% of all injury codes (87/1000 cases); Hematoma/hemorrhage complications 9 % (48/1000 cases); vascular complications 7% (36/1000 cases); and infectious complications 4% of all injury codes (20/1000cases).Patients who died had a greater rate of medical errors (505/1000 cases vs. 306/1000 cases, p<0.001).
CONCLUSIONS: Medical injury codes are frequently reported among congenital heart surgery cases and are associated with mortality. The most common type of medical injury is procedure related. Additional work is needed to identify patient factors predictive of medical injuries or setting in which injury was more likely to occur.

88 Presentation Time 4:30 PM

Pediatric Interventional Catheterization: Development of a Risk Adjustment Model for Preventable Complications

Lisa Bergersen, Alan Nugent, John F. Keane, Kimberlee Gauvreau, James E. Lock, Kathy J. Jenkins. Cardiology, Children's Hospital, Boston, MA.

BACKGROUND: A risk adjustment method is necessary to account for the complexity of case mix in pediatric catheterization.
OBJECTIVE: To develop a risk adjusment method for pediatric catheterization procedures so valid comparisons of outcomes can be determined.
DESIGN/METHODS: Using a prospective database, we identified patient and procedural characteristics predictive of preventable serious or somewhat serious complications. A committee reviewed events and categorized according to seriousness and preventability. Creation of 2 diagnosis groups and 5 procedural risk groups allowed classification according to the complexity of the diagnosis and anticipated relative risk of the procedure. An indicator of physiologic vulnerability was developed to account for hemodynamic conditions considered high risk, including elevated pulmonary artery or right ventricular pressure, cyanosis, and low cardiac output. Variables that were both statistically significant and increased the area under the receiver operator characteristic (ROC) curve were chosen for the final model. Expected complication rates and standardized complication ratios (SCR) were then determined for practitioners.
RESULTS: Of 791 procedures, 26 (3.3%) had possibly or definitely preventable, serious or somewhat serious events. Event rates tended to increase as procedural risk category increased (0.5% in 1, 4.4% in 2, 4.2% in 3, 11.1% in 4, 8.0% in 5, p <0.001). Higher event rates were observed in younger patients (11.4% age < 1 month vs 2.9% ∅1 month, p<0.001) and those with physiologic vulnerability (4.7% vs 2.1%, p=0.04). These 3 factors remained independent predictors of higher event rate in multivariate analysis (area under ROC = 0.787); no other factors contributed significantly. Among 7 cardiologists, significant case-mix differences were identified. Application of the risk adjustment yielded SCR's ranging from 0.5 to 1.7, and risk adjusted complication rates ranging from 1.6% to 5.6%. Although statistically significant differences in complication rates were not detected, there was a trend towards higher risk adjusted rates for less experienced interventionalists.
CONCLUSIONS: Further development and future validation of this risk adjustment method for pediatric cardiac catheterization will allow valid assessment of risk-adjusted performance of both practitioners and institutions.

89 Presentation Time 4:45 PM

Time as an Influence on Parents' Decision Making About Research Participation for Their Neonates with CHD

K. Sarah Hoehn, Aruna Nathan, Susan Nicolson, Gil Wernovsky, Robert M. Nelson. Anesthesiology and Critical Care Medicine, Children's Hospital of Philadelphia, Philadelphia, PA; Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Parents of neonates with congenital heart disease (CHD) often need to make decisions about research participation in the short time frame between delivery and surgery. This study examines how time affects parents' decision making regarding research participation for their critically ill neonate.
OBJECTIVE: The objective was to assess the impact of time on parental decision making for research participation with neonates with CHD.
DESIGN/METHODS: Two investigators conducted interviews with parents of neonates with CHD who were eligible to participate in three different research studies (MRI, Heart rate variability, Genetics) within 1 – 7 days of the neonates' surgery (mean post-operative day 5). All parents were asked to give a yes/no answer to the two following questions. (1) Did you have adequate time to make a decision about research participation? (2) Did you feel pressured to participate in research studies?
RESULTS: Thirty-seven parents of 24 neonates diagnosed with CHD were interviewed, of which 15 received the diagnosis prenatally and 22 postnally. Of those parents whose neonates were diagnosed prenatally, 14/15 (93%) participated in at least one study; of those diagnosed postnatally, 19/22 (86%) participated in at least one study. Despite the short time frame, 22/37 (59%) of the parents stated that they had adequate time to make the decision. However, many parents expressed concern regarding the limited time to decide. Those parents who declined participation in at least one study suggested that they may have made a different decision if they had more time. There was a significant relationship between the parental perception of adequate time and agreement to be in each research study (MRI: p=0.002; HR: p=0.03; Gen:p=0.009). Only 3 parents reported feeling pressure to participate in the studies offered to them.
CONCLUSIONS: Those parents who reported having inadequate time to make a decision generally refused research participation, although most parents decided to participate in at least one of several studies offered to them. Future directions include quantifying parental understanding of the parental permission process and exploring the appropriate time frame to make decisions about research participation.

90 Presentation Time 5:00 PM — Fellow in Training

Moderately Premature Infants at Kaiser Permanente Medical Care Program in California Are Discharged Home Earlier Than Their Peers in Massachusetts and the United Kingdom

Jochen Profit, Marie McCormick, John Zupancic, Douglas Richardson, Gabriel Escobar, Janet Tucker, William Tarnow-Mordi, Gareth Parry. Harvard Newborn Medicine Program, Boston, MA; Harvard School of Public Health, Boston, MA; Deceased; Kaiser Permanente Medical Care Program, Oakland, CA; University of Aberdeen, Aberdeen, United Kingdom; University of Sydney at Westmead Hospital, Wentworthville, NSW, Australia; School of Health and Related Research, University of Sheffield, Sheffield, United Kingdom.

BACKGROUND: Comparison of neonatal outcomes between health delivery models and across national borders may yield information on optimally efficient care. Moderately premature infants are an ideal

group of infants to study such variation in medical management because readiness for discharge depends on a predictable pattern of developmental maturation consistent with gestational age.
OBJECTIVE: To compare gestational age at discharge between infants born at 30 to 34 6/7 weeks gestational age, who were admitted to neonatal intensive care units (NICUs) with three different delivery models: a managed care model in California, a mixed payer model in Massachusetts and a national health service model in the United Kingdom (UK).
DESIGN/METHODS: Prospective observational cohort study.
Setting: 54 UK, 5 California and 5 Massachusetts NICUs.
Subjects: 4359 infants who survived to discharge home following admission to a NICU.
Main outcome measures: Gestational age at discharge home.
RESULTS: The median (interquartile range) postmenstrual age at discharge of the infants in California, Massachusetts and the UK were 35.7 (35-36.4), 36.0 (35.4-36.9), and 36.1 (35.4-36.9) weeks respectively (p=0.001). Compared to the UK, discharge of infants (adjusted for illness acuity) occurred 3.9 (95% CI 1.4, 6.5) days earlier in California, and 0.9 (95% CI –1.2, 3.0) days earlier in Massachusetts.
CONCLUSIONS: Infants of 30 to 34 6/7 weeks gestation at birth admitted and cared for in the hospitals in California have a shorter length of stay compared to those in Massachusetts and the UK. We speculate that certain characteristics of the integrated healthcare approach pursued by the health maintenance organization of the NICUs in California may foster earlier discharge. The California system may provide opportunities for identifying practices for reducing the length of stay of moderately premature infants in Massachusetts and the UK.

91 Presentation Time 5:15 PM

High Incidence and Short Duration of Prescription Drug Use Among Premature NICU Graduates One Year After Discharge

Kelly C. Wade, Scott A. Lorch, Gabriel J. Escobar, Barbara Medoff-Cooper, Susan Bakewell-Sachs, Marla N. Gardner, John Greene, Orit Even-Shoshan, Jeffrey H. Silber. Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; Perinatal Research Unit, Kaiser Permanente, Oakland, CA.
BACKGROUND: After discharge, many premature infants require treatment for acute and chronic conditions such as bronchopulmonary dysplasia (BPD). Use of prescription medications (Rxs) in these infants is unknown.
OBJECTIVE: To determine the frequency, duration, and risk factors for Rx use in premature infants in a managed care system for one year after discharge.
DESIGN/METHODS: The Infant Functional Study (MCHB R40MC00236) studied all surviving infants born ≤32 wks gestational age (GA) among 6 Kaiser Permanente hospitals between 1998-2001 (N=896) along with a random sample of 541 infants 33-34 wks GA. Patients were excluded with congenital anomalies, home ventilation, VP shunt, or loss to follow-up. This study tracked Rxs filled within one yr of hospital discharge, excluding topical, over-the-counter, and nutritional medications. Logit and Cox models were used to determine prognostic factors for (1) use of all Rx and (2) duration of chronic Rx use including H_2 blockers, prokinetics, diuretics, and caffeine.
RESULTS: 575 infants received Rx at an average cost of $79.72/pt/yr. Among those infants, 4.82 Rxs/pt/yr were prescribed. Antibiotics were the most common Rx (35%) followed by inhalers, H_2 blockers, prokinetics, diuretics, and caffeine. Need for Rx was inversely related to GA and BW (P=0.004); 52% of infants ≤26 wks GA and 59% of infants with BW≤750g required Rx. After controlling for GA or BW, need for any Rx was associated with BPD (OR 1.78, 95% CI 1.16-2.71), history of ductus arteriosis (PDA) (OR 1.46, CI 1.01-2.10), and black race (OR 1.77, CI 1.22, 2.60). 103 infants (7%) had a Rx at the time of hospital discharge. Rx use at discharge was associated with GA<30 wks and BPD. 46% of infants were off these Rx within 2 mo post discharge, 58% by 4 mo, 71% by 6 mo, 90% by 10 mo post discharge. GA and BW were associated with a longer need for these chronic Rxs whereas BPD and other neonatal morbidities were not.
CONCLUSIONS: Lower GA, black race, BPD, and history of PDA are all risk factors for increased Rx use in the first year after discharge. Even though the youngest infants require chronic medications, over half are off within 4 mo of discharge.
Funded by MCHB R40MC00236.

92 Presentation Time 5:30 PM

Racial Disparities and Low Frequency of Antibiotic Use Among Premature Infants After Hospital Discharge

Scott A. Lorch, Kelly C. Wade, Gabriel J. Escobar, Barbara Medoff-Cooper, Susan Bakewell-Sachs, Marla Gardner, John Greene, Orit Even-Shoshan, Jeffrey H. Silber. Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA; Perinatal Research Unit, Kaiser Permanente, Oakland, CA.
BACKGROUND: Antibiotics are commonly prescribed medications to children, averaging 1.6-3.7 antibiotic courses/patient/year (ARx/pt/yr) in 3-36 month infants (Finkelstein, Pediatrics 2001). Antibiotic Rx patterns in premature infants are unknown.
OBJECTIVE: To define the incidence and risk factors for oral antibiotic use in the first year after discharge among premature infants enrolled in a managed care system.
DESIGN/METHODS: The Infant Functional Study (MCHB R40MC00236) studied all surviving infants born at ≤32 wks gestational age (GA) among 6 Northern California Kaiser Permanente hospitals between 1998 and 2001 (N=893) along with a random sample of 541 infants of 33-34 wks GA. Infants were excluded with congenital anomalies, home ventilation, VP shunt, or loss to follow-up. Data were collected on all oral antibiotic use in the first year after discharge. Logit models were used to identify prognostic factors for use.
RESULTS: Among the 1434 infants, the mean frequency of antibiotic courses was 0.69 ARx/pt/yr. 32% (463 infants) had at least one antibiotic course. Most antibiotics (70%) were given 6-12 months after discharge, with amoxicillin accounting for 60% of antibiotics received over the year. GA and neonatal morbidities such as bronchopulmonary dysplasia were not associated with the use of an antibiotic after discharge. When controlling for these factors, black race (odds ratio (OR) 1.58, 95% CI 1.07-2.34), hispanic ethnicity (OR 1.43, CI 1.07-1.92), and male gender (OR 1.23, CI 1.04-1.63) were associated with an increased odds of receiving antibiotics. Black males had the highest antibiotic frequency (1.25 ARx/pt/yr) followed by hispanic males (0.87), white males (0.67), black females (0.67), hispanic females (0.59), and white females (0.54).
CONCLUSIONS: Preterm NICU graduates in a managed care setting receive fewer antibiotics in the first yr after discharge than prior estimates. Black race, hispanic ethnicity, and male gender, not the extent of prematurity or neonatal morbidities, are associated with increased odds for antibiotics. Socioeconomic status or environmental exposures may contribute to these observed racial differences.
Funded by MCHB R40MC00236.

Emergency Medicine Platform Session

Saturday, March 5 4:00 PM-5:15 PM Mead B

93 Presentation Time 4:00 PM

Sexual Assault and the Pediatric Emergency Department: Are We Prepared?

Kirsten Bechtel, Karen Santucci. Pediatrics, Yale University School of Medicine, New Haven, CT.
BACKGROUND: Nearly 700,000 rapes occur in the United States yearly. The majority of victims are females under the age of 18 years. Previous studies have documented that personnel in some adult emergency departments often do not have the expertise or training to evaluate victims of sexual assault.
OBJECTIVE: The purpose of this study was to evaluate the preparedness of pediatric emergency departments in the US and Canada to evaluate children and adolescents who have been sexually assaulted.
DESIGN/METHODS: A 2-page survey was sent to Pediatric Emergency Medicine Fellowship directors in the United States and Canada. The survey included questions related to: number of sexual assaults evaluated in each Pediatric Emergency Department on a yearly basis; which ED personnel performed the examination and collection of forensic evidence; whether ED personnel had received previous training in the evaluation of sexual assault; whether a child abuse evaluation service was available at the institution to perform the examination and evidence collection; whether STD, HIV and pregnancy prophylaxis was provided; whether a social worker was available to support patients.
RESULTS: Seventy-two percent (36/50) of programs responded to the survey. In 81% and 86% of programs, either the pediatric ED attending or fellow performed the evaluation and collected evidence. In 42% of programs, a Sexual Assault Nurse Examiner (SANE) was available to perform the examination and evidence collection. In 75% and 89% of programs did the attendings and fellows have previous training in the evaluation of sexual assault. In 94% of programs, STD, pregnancy and HIV chemoprophylaxis was provided. In 97% of programs, there was a child abuse evaluation team at the institution, but in only 58% of programs did the service perform the examination and in only 53% of programs did the service provide training to emergency department personnel. In 94% of programs was a social worker available to support the patient.
CONCLUSIONS: Medical staff in pediatric emergency departments surveyed are well informed in the evaluation of pediatric sexual assault. In some institutions the child abuse evaluation service performs the assessment, but only engaged in acute forensic cases in about half of surveyed programs. Pediatric patients in the surveyed programs nearly always receive appropriate medical evaluation, proper chemoprophylaxis and social work support after sexual assault.

94 Presentation Time 4:15 PM Fellow in Training

A Randomized Trial To Assess the Efficacy of Point-of-Care Testing in Decreasing Length of Stay in a Pediatric Emergency Department

Allen L. Hsiao, Karen A. Santucci, Richard N. Shiffman, M. Douglas Baker. Pediatric Emergency Medicine, Yale University School of Medicine, New Haven, CT; Yale Center for Medical Informatics, Yale University, New Haven, CT.
BACKGROUND: Utilization of emergency services around the country has increased substantially during the past decade, with increasing numbers of medically fragile patients and greater burdens of the underinsured. At many hospitals, supportive service and facility improvements have been unable to keep pace with increasing demand. In many circumstances, a large proportion of emergency department (ED) length of stay results from waiting for results of diagnostic tests, including laboratory results.
OBJECTIVE: To compare the effect of "point-of-care" (POC) analysis of blood work with traditional laboratory methods on length of stay in a pediatric emergency department (PED).
DESIGN/METHODS: A prospective, randomized controlled study of patients presenting to an urban ED of a tertiary care hospital during peak patient volume hours. The study was conducted over a 6 month period, enrolling 225 patients who required blood work that could be performed by a POC device. After informed consent, 114 patients were randomized to the POC group, 111 to routine laboratory analysis. Exact times of critical phases of management and patient flow were recorded by dedicated research assistants. Medical management decisions were made at the discretion of the supervising physicians.
RESULTS: Similar waiting periods were noted in both groups for time spent in the waiting room, time waiting for first physician contact, and time waiting for blood draw. Significantly less time was required for results to become available to physicians when POC testing was used (70.1 minutes, $p < 0.001$). Significant decrease in overall length of stay was also noted, with patients randomized to the POC group spending 36.01 minutes ($p < 0.001$) less time in the ED.
CONCLUSIONS: POC use can significantly decrease the length of stay in select pediatric patients in an emergency department setting. POC devices may prove to facilitate patient flow during busiest periods of service demand.
Funded by i-Stat Corporation for research assistants, materials also donated for study use. No financial support, incentive, or payment made to any of the authors, including the primary investigator.

95 Presentation Time 4:30 PM Fellow in Training

Bedside Ultrasound in the Diagnosis and Guided Reduction of Forearm Fractures in Children

Lei Chen, Christopher L. Moore. Pediatrics, Yale University School of Medicine, New Haven, CT; Emergency Medicine, Yale University School of Medicine, New Haven, CT.
BACKGROUND: Forearm fractures are common injuries in children. Displaced and angulated fractures usually require reduction. These are often performed in the Emergency Department (ED). Proper anatomic alignment is sometime difficult to assess during reduction. A common method to evaluate the adequacy of reduction is with a portable fluoroscopy unit. Ultrasound guidance during reduction attempt offers several potential advantages: 1) The procedure does not involve ionizing radiation; 2) Compared with fluoroscopy units, the newer ultrasound units are more portable; 3) Repeated studies can be obtained easily and quickly.
OBJECTIVE: To investigate the reliability of ED physician-performed ultrasound in the diagnosis and guided reduction of forearm fractures in children.
DESIGN/METHODS: Children suspected of having forearm fractures were enrolled prospectively in an urban pediatric ED from 6/2004 to 11/2004. A bedside ultrasound of the forearm bones was performed by a Pediatric Emergency Medicine (PEM) physician while blinded to x-ray results. Routine plain radiographs were obtained. Ultrasound findings were compared against the x-ray findings. Reductions were performed as usual by orthopedic surgeons. Ultrasound was used to guide the reduction procedure. The injury was splinted or casted. Post-reduction radiographs were performed. Any need for further reduction was recorded.
RESULTS: During the study period 68 patients were enrolled. Radiographs revealed forearm fractures in 48 patients. Twenty-nine subjects had fractures of the radius alone; 17 had fractures of both the radius and the ulna; 2 had fractures of the ulna alone. Ultrasound revealed the correct type and location of the fracture in 46 patients. The sensitivity for the detection of forearm fractures was 97% (95% C.I. 89%-

100%) using ultrasound. The specificity was 100% (95% C.I. 83%-100%). Twenty-six subjects underwent reduction of their fractures in the ED. Only 2 subjects required re-reduction following the initial reduction. The initial success rate of ultrasound-guided reduction was 92% (95% C.I. 75%-99%).
CONCLUSIONS: Bedside ultrasound performed by PEM physicians is a reliable and convenient method of diagnosing forearm fractures in children. It is also useful in guiding the reduction of these fractures.

96 Presentation Time 4:45 PM House Officer

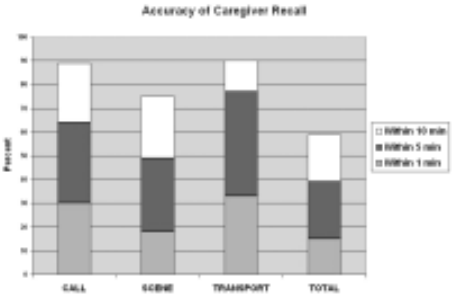
Attitudes and Preferences of Parents Toward Asthma Education in the Emergency Department

Jamal Harris, Kathryn Scharbach, Sarah Siegel, Melissa Tesher, Philip O. Ozuah. The Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: For many inner city families, the emergency department (ED) serves as a frequent source of acute and chronic asthma management. Asthma education may improve clinical outcomes for children with asthma and ED visits are potential educational opportunities. However, few studies have evaluated parental attitudes and preferences toward asthma education while in the ED with a child for an acute asthma exacerbation.
OBJECTIVE: To examine parental attitudes and preferences toward receiving asthma education while in the ED with a child for an acute asthma exacerbation.
DESIGN/METHODS: We conducted a cross-sectional study of parents of children in the asthma treatment room of an inner-city pediatric ED. We developed a 15-item questionnaire to assess preferences/attitudes toward asthma education. The questionnaire was administered to study subjects in English or Spanish while their child was receiving treatment in the asthma room. Subjects were asked about duration of asthma diagnosis in the index child, prior experiences with asthma educational materials, and future preferences for asthma education. Chi- Square was used to test differences in dichotomous variables.
RESULTS: Parents or guardians of 52 children (range 1-18 years old) participated in the study. Mean age of children was 6.9 years (SD 4.5), 21% had asthma for less than 1 year, 44% for 1-5 years, and 35% for more than 5 years. Overall, 90% of participants had received some prior asthma education. Of those who had experienced specific educational media, 100% found group education very helpful as compared to 81% who found one-on-one education very helpful ($p = .029$). Also, 93% found computer-based education very helpful, but only 61% and 54% found written materials and videos very helpful ($p = .014$). Overall, 89% of participants expressed a desire for asthma education while in the ED. 94.2% of participants wanted written material and 92.3% wanted one-on-one education from a health professional.
CONCLUSIONS: Despite high levels of previous exposure to asthma education, a majority of participants expressed interest in receiving asthma education in the ED. These findings suggest that many parents visiting the ED for asthma treatment would take advantage of asthma education if offered. Our data shed some light on approaches that families have found helpful in the past.

97 Presentation Time 5:00 PM

Parental Perception of the Passage of Time During a Stressful Event

Victoria Shulman, Christopher Kelly, Kelly Cleary, Jeffrey R. Avner. Pediatric Emergency Medicine, Children's Hospital at Montefiore/AECOM, Bronx, NY.
BACKGROUND: Many management decisions in pediatric emergency medicine are based on a caregiver's recollection of the duration of specific events such as a seizure or loss of consciousness. However, the accuracy of the caregiver's recollection is unknown.
OBJECTIVE: To determine whether a caregiver is accurate in their recollection of the passage of time related to a stressful event.
DESIGN/METHODS: A convenience sample of caregivers who arrived to a Pediatric ED by ambulance were administered a brief questionnaire before the physician began the history of the child's illness that included their recollection of the following time intervals: calling the ambulance to arrival at the scene (CALL), arrival of the ambulance at the scene until departure (SCENE) and from the scene until arrival in the ED (TRANSPORT). The TOTAL time was the addition of the 3 intervals. The caregiver's recalled times were then compared to the ACTUAL times from the ambulance run sheets.
RESULTS: 61 caregivers recalled all 3 time intervals. The mean ACTUAL CALL time was 6 minutes (range 1-25) and the mean ACTUAL TOTAL time was 33 minutes (range 12-72). The time interval closest to the stressful event, the CALL time, was underestimated by the caregiver in 11 cases (18%), was exact in 8 cases (13%) and was overestimated in 42 cases (69%). Caregiver accuracy of ACTUAL time is shown on the graph. There was no association of caregiver accuracy with time of day, triage level, stress self-assessment, caregiver age or whether a clock was checked at anytime.



CONCLUSIONS: Caregivers recollection of the ambulance time intervals during their child's illness was generally unreliable. If used as a marker for the caregiver's perception of the passage of time during a stressful event, these data suggest that interval estimates alone, should not be used to guide management.

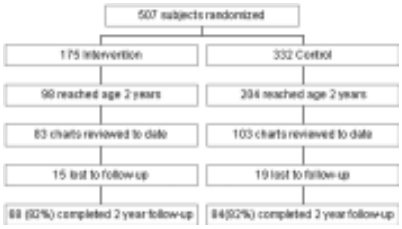
General Pediatrics II: Quality of Care and Medical Education Platform Session

Saturday, March 5 4:00 PM-5:45 PM Mead A

98 Presentation Time 4:00 PM House Officer

Can Anticipatory Guidance Prevent Childhood Obesity?: Preliminary Results of a Randomized Controlled Trial

Katherine O'Connor, Iman Sharif, Harris Huberman, Philip O. Ozuah. Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Few studies document effective strategies for preventing childhood obesity. Anticipatory guidance(AG) by physicians improves child outcomes in: parent-infant interactions, language development, sleep, and injury prevention. No studies have tested whether AG around nutrition prevents childhood overweight.
OBJECTIVE: To test the effectiveness of AG about nutrition on preventing childhood obesity.
DESIGN/METHODS: We conducted a randomized controlled trial at an inner-city academic health center. We assigned infants (4-6 months old) to one of three groups that received AG at each routine health maintenance visit. Intervention group: At each visit, subjects received AG about iron rich foods;at 9-18 months, subjects were counseled to reduce milk consumption to no more than 16 ounces per day. Two control groups recieved AG about reading to infants.
The main outcome was body mass index(BMI) at age 24 months, calculated using the chart documented weight and height. We used chi-square analysis to compare the incidence of overweight (BMI>85th percentile for age) in the intervention and control groups. Multivariate analysis was used to adjust for demographic differences.
RESULTS: 507 subjects were enrolled and randomized. 85% Medicaid recipients; 53% male, 50% Latino. 152 subjects have completed 24 months follow-up (68 intervention, 84 controls). Intervention subjects were less likely to be overweight (21% vs. 32%, p=.11). Logistic regression results indicated a significantly decreased odds of overweight in the intervention group (AOR=0.38, CI 0.15, 0.70). Data collection is ongoing.



CONCLUSIONS: Physician AG about nutrition appears to be an effective means to prevent overweight at 24 months of age. Preliminary findings support the inclusion of AG about nutrition during routine health maintenance visits.

99 Presentation Time 4:15 PM

Determining the Essential Components of Professionalism and Interpersonal/Communication Skills

Laura Dattner, Philip O. Ozuah. Pediatrics, SUNY Downstate Medical Center, Brooklyn, NY; Pediatrics, The Children's Hospital at Montefiore, Bronx, NY.
BACKGROUND: The ACGME has introduced six core competencies for medical training, including professionalism and interpersonal/communication skills. Little is known about what pediatric patients and their parents consider to be essential components of these competencies.
OBJECTIVE: To determine what pediatric patients and their parents consider to be essential components of professionalism and interpersonal/communication skills.
DESIGN/METHODS: We designed an anonymous web-based survey for hospitalized patients and their parents. A questionnaire was developed based on the ACGME Outcomes Project sample questionnaires. Respondents were asked 8 questions about the professionalism and interpersonal/communication skills of residents, using a 5-point Likert scale. We used univariate analyses as appropriate and multiple logistic regression to determine independent predictors of an excellent rating in professionalism and interpersonal/communication skills.
RESULTS: 253 resident evaluation surveys were completed by pediatric patients and their parents. Overall, residents received very positive evaluations. Mean score was 4.8 (with 5 being highest) for questions about friendliness, respectfulness, understanding/compassion, listening, and clear communication, 4.7 for questions about informing about care and inclusion in decision-making, and 4.6 for overall evaluation. Multiple regression analyses revealed that 3 of the 7 questions independently predicted a global score of 5 (excellent) for the general evaluation of professionalism and interpersonal/communication skills. For all respondents, questions which predicted a global score of 5 were: "Does Dr. X speak to you in ways that are clear and easy to understand?" ($p=0.000$), "Does Dr. X include you in decisions and planning of care?" ($p=0.002$), and "Does Dr. X listen to your concerns?" ($p=0.013$). These findings were consistent for junior and senior residents, male and female residents, and for parents as well as patients.
CONCLUSIONS: Essential components of professionalism and interpersonal/communication skills which independently predicted an excellent global score were: listening to concerns; including families in decisions and planning of care; and clear communication. These findings have implications for the design of assessment tools for professionalism and interpersonal/communication skills.

100 Presentation Time 4:30 PM

Parental Assessment of Quality of Ambulatory Care: How Do Attendings and Residents Compare?

Andrew D. Racine, Sheila Liewehr, Laura Weingart, Scott D. Krugman. Pediatrics, Albert Einstein College of Medicine / Children's Hospital at Montefiore, Bronx, NY; Pediatrics, Franklin Square Hospital Center, Baltimore, MD.
BACKGROUND: Many children at academic medical centers in the U.S. receive primary care from pediatric residents yet very little is known about how the quality of that care compares to care delivered by experienced attending clinicians.
OBJECTIVE: To compare the quality of pediatric ambulatory care reported by parents of children with resident versus attending primary care providers (RPCPs vs APCPs) at two inner-city academic medical center practices.
DESIGN/METHODS: Families at two urban academic practices were surveyed using a modified version of The Parents Perception of Primary Care© (P3C) during a two week interval as part of a multicenter observational study. RPCP and APCP scores were compared cross-sectionally in five domains using 21 items: 2 for access, 4 for communication, 4 for comprehensiveness, 6 for contextual knowledge and 5 for longitudinal coordination. Chi square and student t tests were used for bivariate comparisons, OLS and logistic regressions for multivariate analyses.
RESULTS: 473 surveys were returned: 99 from patients of 50 different RPCPs and 374 from patients of 28 different APCPs. Patients were 45% Latino, 28% black, 7% white, and 20% other. Over 67% were on Medicaid and 71% were reported in excellent or very good health. Bivariate comparisons revealed no differences between RPCP and APCP patients in aggregate scores for any of the five quality domains but on two individual items: does the doctor explain things to your satisfaction, and can the doctor arrange for referrals, APCP scores exceeded RPCP scores. In multivariate comparisons controlling for patient age, maternal education, insurance status, race/ethnicity, site of care and child's health status, RPCP scores were less than APCP scores for the overall P3C ($p=0.016$) and for the longitudinal coordination component ($p=0.030$). Individual items that differed significantly included: does the doctor explain things to your satisfaction (OR 0.33, $p<=0.006$) and does the doctor talk with you about your child's growth (OR 0.5, $p=0.047$).
CONCLUSIONS: Parental assessment of the overall quality of care delivered by pediatric residents compares favorably to that delivered in similar settings by attending pediatricians. Perceived quality differences in communication and follow-up merit more study.

101 Presentation Time 4:45 PM — House Officer

Residents' Attitudes and Practices Regarding the Use of Analgesia and Sedation for Lumbar Puncture in Children

Vicky R. Breakey, Jonathan R. Pirie, Ran D. Goldman. Department of Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada; Division of Pediatric Emergency Medicine, The Hospital for Sick Children, Toronto, ON, Canada.

BACKGROUND: Although analgesia and sedation for painful procedures in children have been proven to be safe and effective, it was suggested that pain management during lumbar puncture (LP) in children is sub-optimal.
OBJECTIVE: To document factors influencing residents' decisions to use analgesia and sedation during a LP and to compare practices of Pediatric Residents (PR) and Emergency Medicine Residents (ER).
DESIGN/METHODS: Residents from training programs across Canada responded to a mailed survey regarding practices in the use of analgesia and sedation for LP in children. Student t-test and Chi-squared test were used to compare the two resident groups using SPSS statistical software.
RESULTS: 245/374 (67%) residents completed the survey. 57% and 1% of PR and ER respectively reported frequently doing LPs with no local anesthetic ($p< 0.005$). PR reported more frequent use of EMLA (64% vs. 27%, $p<0.005$) whereas PR reported less frequent use of lidocaine (29% vs. 94%, $p<0.005$). The factors that PR cited significantly more often as deterrents to using local anesthesia included age, prolonged procedure, pain of injection and adverse effects. Adverse effects of local anesthesia occured at a low rate in both groups(3 vs. 5%). 78% of PR reported using sedation at least once for LP versus 60% of ER ($p<0.005$). 35% of PR reported frequent use of benzodiazepines, compared to 20% of ER ($p<0.05$), but there was no significant difference in the reported use of Ketamine (11% vs. 9%). 19% of PR witnessed adverse effects of sedation versus only 5% of ER ($p<0.05$). 39% of PR and 57% of ER reported formal education during residency in the use of sedation ($p<0.05$). Significantly more PR were responsible for teaching trainees (75% vs. 44%, $p<0.005$). PR were less likely to recommend the use of local anesthetic when teaching the LP ($p<0.005$).
CONCLUSIONS: Most PR report infrequent use of local anesthesia for LP in children but use more sedation, when compared to ER. PR indicate less education in sedation than their ER colleagues and higher incidence of adverse effects of sedation. These findings should initiate development of an educational curriculum to improve procedural competency and ensure PR are capable teachers, as they have greater responsibilities in educating trainees.

102 Presentation Time 5:00 PM — Fellow in Training

Impact of a Modified Hospitalist System on the Quality of the Ward Experience for Residents and Attendings

Steve Paik, Matilde Irigoyen, Elizabeth Wedemeyer, Shaofu Chen, Frank Chimkin. Division of General Pediatrics, Columbia University, New York, NY.

BACKGROUND: The role of the pediatric attending physician at academic medical centers has evolved in the past decade. In response to increasing patient complexity and acuity, most pediatric hospitals have expanded the role of the inpatient attending, others have increased the hours attendings work, and some have shifted to using hospitalists as inpatient experts. Limited data are available about the impact of these changes on the quality of the ward experience for residents and attendings.
OBJECTIVE: To examine the effect of changing from a traditional half day attending model to a modified hospitalist system on the quality of the ward experience for residents and attendings.
DESIGN/METHODS: In June 2004, we implemented a modified hospitalist system at a children's hospital, by extending the generalist attending coverage from part time to full time. Prior to implementation, and prospectively, we surveyed participating general pediatric attendings (n=45), interns (n=49), and residents (n=57) at the end of every rotation. The survey involved self-ratings on the ward experience, and the level of supervision, teaching and teamwork, using a five-point Likert scale.
RESULTS: By mid-year, 92% of interns, 77% of residents, and 71% of attendings had completed surveys. Since implementation, residents perceived the attendings to be more readily accessible, (mean pre= 4.2 to post= 4.4, $p<.05$), and to make more timely decisions (4.1 to 4.5, $p<.05$). Residents perceived increased efficiency of patient care and improvements with discharge, but these findings were not significant. Residents reported no significant change in the level of autonomy or involvement in decision making. Attendings reported increased time to counsel patients (3.9 to 4.9, $p<.05$) and to discuss patient care with residents (3.5 to 4.6, $p<.05$) with nurses and social workers (2.9 to 4.4, $p<.01$). Attendings also felt more informed about changes in patient status (3.0 to 4.3, $p<.05$) and felt that patient care had improved.
CONCLUSIONS: The implementation of a modified hospitalist system at a children's hospital led to improved satisfaction for residents and attendings, with perceived improvements in patient care. Importantly the new system appears not to affect resident's level of autonomy and decision making.

103 Presentation Time 5:15 PM

Knowledge and Beliefs in School Nurses on Recurrent Abdominal Pain of Childhood. Opportunity for Therapeutic Alliance?

Nader N. Youssef, Thomas Murphy, Charlotte Intile, Joel R. Rosh. Pediatric Gastroenterology, Goryeb Children Hospital /Atlantic Health System, Morristown, NJ.

BACKGROUND: Recurrent abdominal pain (RAP) affects up to 20% of children. RAP carries social consequences often leading to school absence and frequent physician evaluation. Initial assessment of RAP is often made at the school nurse (SN) level.
OBJECTIVE: The aim of this study is to determine what knowledge and beliefs SNs have regarding RAP.
DESIGN/METHODS: SNs selected from the New Jersey School Nurses Association Directory. SNs were sent a 21-item questionnaire eliciting their perceptions regarding RAP. The definition of RAP was 3 episodes of abdominal pain interfering with activity for 3 months in the past year. Questionnaires were coded for anonymity. Experience, knowledge on RAP, disease perception, knowledge of medicines, and need for education were assessed.
RESULTS: There were 131 of 425 (31%) questionnaires returned. Over 98% reported seeing children with RAP. More than 10 visits/ month for RAP was reported by 31% of SNs. Of respondents, 77% felt that an extensive evaluation by an MD is needed but only 23% believed that medication would help RAP. Communication with MDs about RAP was considered poor by 84% of SNs. SNs reported that 70% of children with RAP were faking the pain or seeking attention. Children with RAP were considered sad (35%) or lazy (38%) by SNs. SNs recommendations for RAP included: rest (94%), go to bathroom (90%), back to class (68%) and sent home (48%). Mean total nursing experience was 26.1 ± 14 years with a mean school nurse experience of 11.1 ± 21 years. There was no significant differences found between SNs with > 10 years experience vs. SNs with less experience.

	10 years experience or less	More than 10 years experience	
RAP Severity			
Serious	3%	5%	p =ns
Minor	33%	24%	p =ns
Don't Know	64%	71%	p =ns
Medication			
Good Knowledge	12%	10%	p =ns
Some Knowledge	75%	64%	p =ns
No Knowledge	12%	14%	p =ns
Education			
Lacking	77%	88%	p =ns
Enough	20%	9%	p =ns
Too Much	0	0%	p =ns

CONCLUSIONS: Experienced SNs have negative views of children with RAP and are unclear about disease severity. SNs may inadvertently contribute to increased social stigmata felt by children with RAP who may feel their complaints are not taken seriously. Education of SNs and better communication from MDs may allow for enhanced partnerships and strategies to reduce associated costs and school absenteeism seen in children with RAP.

104 Presentation Time 5:30 PM — House Officer

A Simple Intervention To Improve Parental Health Literacy: Writing Clearly

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

BACKGROUND: Health literacy is the ability to use health information to make appropriate health decisions. Interventions to improve parental health literacy can focus either on parental education or systemic improvements in the way health information is provided. One intervention suggested by experts in health literacy is to write prescriptions using metric units. This practice has been shown to reduce medication errors on inpatient pediatric units; however, the effectiveness of this practice in the outpatient setting has not been tested.
OBJECTIVE: To measure the effectiveness of a simple systemic intervention on improving parental health literacy.
DESIGN/METHODS: We conducted a case-control study among English and Spanish-speaking parents of young children(<5 years old) attending an inner-city pediatric health center. Each subject served as her own control. At baseline, we showed subjects a bottle of liquid medicine with a prescription label "give one dropperful two times a day."(Label1) We asked subjects to read the label and use the medicine dropper to demonstrate the amount they should give.
Intervention: We showed subjects a second prescription label for the equivalent intended dose of medicine: "give 0.6ml two times a day."(Label 2) Subjects were again asked to demonstrate the amount of medicine they should give. Both labels were shown in English to English-speakers, and in Spanish to Spanish-speakers.
Analyses: The main outcome measure was correct medication dosing. We used a standardized scoring sheet to record whether subjects correctly or incorrectly demonstrated the amount of medicine to give for Label 1(baseline) and for Label 2 (intervention).
RESULTS: 491 subjects participated. The mean age was 34; 73% were Medicaid recipients, 64% had completed high school, 48% were immigrants, and 35% spoke primarily Spanish.
Overall, the intervention significantly increased the odds of correct medication dosing (OR= 9.85; CI 2.4, 86.0). 38% of subjects dosed the medicine correctly after reading Label 1. 93% dosed the medicine correctly after reading the metric label.
CONCLUSIONS: A simple change in the way we wrote a prescription resulted in a substantial improvement in parental health literacy. The findings suggest that writing prescriptions clearly, by specifying the dose in metric units, improves parents' ability to understand and administer the intended dose.

Genetics Platform Session

Saturday, March 5 — 4:00 PM-5:30 PM — Stoningham

105 Presentation Time 4:00 PM

Pilot Study: *In Utero* Treatment of Osteogenesis Imperfecta (OI) Using Alendronate in a Mouse Model of OI

Edith A. McCarthy, Nancy P. Camacho, Roberto Garcia, Karen D. Hendricks-Munoz. Pediatrics-Neonatology, New York University School of Medicine, New York, NY; Research Division, The Hospital for Special Surgery, New York, NY.

BACKGROUND: Treatment of osteogenesis imperfecta (OI) with alendronate as early as 2 weeks of age appears to be effective in reducing fractures and increasing bone properties in the *oim/oim* mouse model of OI. (McCarthy, *Pediatr Res* 52:1-11, 2002)) Since many of the more severe forms of OI result in fractures *in utero*, these severely affected infants may benefit from treatment initiated prior to birth. Treatment of mothers pre-conception may have benefit as well since bisphosphonates are retained in the bone long term and may be gradually re-released over time.
OBJECTIVE: To evaluate the transplacental effects of bisphosphonate treatment on fetal bone quality in the oim mice and to determine if treatment would be tolerated by OI-affected mothers and their nursing pups.
DESIGN/METHODS: Alendronate (0.03 mg/kg/day) or saline was administered to adult female *oim/oim* mice via weekly subcutaneous injection for 1 month prior to conception and/or throughout pregnancy. Offspring were sacrificed at 14 weeks of age and bones dissected and analyzed for fracture count, bone density and geometry, histology, weight gain and long bone growth.
RESULTS: Maternotoxicity was noted in the alendronate treatment groups; several mice suffered spontaneous abortions, stillbirths, or preterm delivery. Of the surviving pups, alendronate treatment pre-conception or both pre- and post-conception had no adverse effect on weight gain but was significantly detrimental to long bone growth (femur length = $14.3\text{mm} \pm 0.9$ *vs*. $15.4\text{mm} \pm 0.7$ in controls; $p=0.02$), as well as vertebral height and width. There was no change in bone density or cortical thickness. Fracture count was unchanged. Histological evaluation of tibiae and spines showed increased osteopenia and thinning of cortical bone but improved organization of the growth plate.
CONCLUSIONS: *In utero* treatment with alendronate in *oim/oim* mice showed decreased survival of offspring, did not decrease fracture incidence, resulted in shorter limb length and vertebral height, had no positive effect on bone density, and caused osteopenia and thinning of cortical bone. Only at the level of the growth plate did alendronate treatment *in utero* seem to have a positive effect.

106 Presentation Time 4:15 PM

Genetic Polymorphisms in Autism

John W. Harrington, Steven Colson, Sabrina Law, Ingrid Loma-Sanner, Ioana Godi, Sonya Strassberg, Lance Parton. Pediatrics, New York Medical College, Valhalla, NY; Neonatology, New York Medical College, Valhalla, NY.

BACKGROUND: Autism is a neurological developmental disorder of both genetic and non-genetic origin. Activation of the inflammatory response system-mediated through increased production of pro-inflammatory cytokines-has been proposed to be associated with the manifestations of autism. Variable cytokine expression may be genetically controlled by single nucleotide polymorphisms (SNPs), which may trigger an exaggerated level of cytokine mediator expression.
OBJECTIVE: The purpose of this pilot study was to determine SNP frequencies for pro-inflammatory cytokine genes of TNFa (-308) and IL8 (-251) in patients with autistic spectrum disorders (ASDs)
DESIGN/METHODS: A buccal swab was obtained on family cohorts of ASD patients over the age of two (unaffected parents, unaffected sibling over the age of three). DNA was isolated followed by PCR SNP analysis. ASD was diagnosed by a developmental specialist utilizing the DSM-IV criteria and/or an autism screening test (CARS or ADOS). Each subject also completed a brief questionnaire that inquired

about: sex, age, ASD type, overall health, illnesses, hospitilizations, medications, and ethnicity.
RESULTS: 45 subjects and 43 controls underwent PCR analysis. Subjects represented 33 males and 12 females with a mean age of 7.1 years (range 2-17). 73% were Caucasian, 9% African American, and 18% Asian, Latino, Middle Eastern, or mixed. ASD diagnoses were 13/45 with classic autism, 8/45 with aspergers, 1/45 with Retts, and 23/45 with PDD-NOS. Genotype frequency for TNF-alpha-308 and stratification were not significant p=0.99 and 0.79 respectively. Genotype frequency and stratification for IL8 (-251) are shown in tables.
CONCLUSIONS: IL8 (-251) polymorphism has a significantly higher genotype frequency in this population of ASD patients. Overall health, illnesses, and hospitilizations did not have any predictive value with mutations.

IL-8 (-251) SNP

ASD	AT	AA	Total
0	39	3	42
1	11	2	13
2	5	3	8
3	1	0	1
4	15	8	23

p= 0.042; IL8 (-251) SNP, stratified by ASD category

IL8 (-251), Genotype Frequency

ASD	AT	AA
Absent	39	3
Present	32	13

p=0.019

Funded by Children's and Women's Physician's of Westchester, LLP.

107 Presentation Time 4:30 PM

Single Nucleotide Polymorphisms (SNPs) of Tumor Necrosis Factor (TNF) and Interleukin-1ß (IL-1ß) and the Risk of Bronchopulmonary Dysplasia (BPD) in Very Low Birth Weight Infants

Sonya S. Strassberg, Ioana Godi, Anita Shvarts, Lance A. Parton. Pediatrics (Neonatology), New York Medical College: Westchester Medical Center, Valhalla, NY.
BACKGROUND: The progression to BPD following premature birth is associated with elevation of proinflammatory mediators in the infants' airways such as TNFζ and IL1ß. The release of these mediators has been associated with peri- and neo- natal triggers, but the magnitude and duration of this inflammatory response may be programmed through SNPs within the genes of these mediators.
OBJECTIVE: The aim of this study is to examine the association between the risk and severity of BPD and the following SNPs: TNFζ (-308, -238, -1031, -863, -857), TNFß (+250), and IL1ß (+3953, -511, -31).
DESIGN/METHODS: Infants weighing <1kg were enrolled. DNA was isolated from buccal swabs and subjected to polymerase chain reaction utilizing specific primers. BPD was defined as the need for oxygen to maintain saturations above 88% when infants achieved 36 weeks postmenstrual age (PMA). The severity of BPD was classified as follows: first, the diagnosis of BPD was made if supplemental oxygen was administered for at least 28 days, plus: infants with mild BPD were in room air by 36 weeks PMA; those with moderate BPD needed < 30% oxygen at 36 weeks PMA; and infants with severe BPD required ∅30% oxygen and/or positive pressure at 36 weeks PMA.
RESULTS: 40 BPD and 65 non-BPD patients were enrolled with birth weights of 748±17g and 805±17g, and gestational ages of 25±0.2 wks and 26±0.2 wks, respectively. Infants were similar in maternal and patient demographics. TNFζ-308 SNP was associated with increased severity of BPD ($p<0.05$). The frequency of subjects who carried at least one variant allele in the haplotype TNFζ-1031/-857 was significantly higher among BPD patients than in preterm infants without BPD ($p<0.05$). The IL1ß-511 SNP was carried in an increased number of BPD versus non-BPD patients ($p=0.05$). There was no significant increase in the number or severity of BPD patients carrying the SNPs of TNFζ (-238, -863), TNFß (+250), or IL1ß (+3953, -31).
CONCLUSIONS: The SNP TNFζ-308 is associated with increased severity of BPD and therefore may help to distinguish the degree of BPD. The haplotype TNFζ-1031/-857 and the SNP IL1b-511 are associated with increased risk of BPD. We speculate that these genetic factors increase the susceptibility of preterm infants to BPD.
Funded by Children's and Women's Physicians of Westchester.

108 Presentation Time 4:45 PM — Fellow in Training

Is There a Genetic Susceptibility to Broncho Pulmonary Dysplasia (BPD)?

Anupama H. Shetty, Matthew J. Bizzarro, Richard A. Ehrenkranz, Naveed Hussain, B. Jonsson, N. Desai, B. Vohr, Laura R. Ment, Jeffrey R. Gruen, Vineet Bhandari. Neonatal Perinatal Medicine, Dept of Pediatrics, Yale University School of Medicine, New Haven, CT; Neonatal Perinatal Medicine, University of Connecticut Health Center, Farmington, CT; Neonatal Medicine, Karolinska Hospital, Stockholm, Sweden; Neonatal Medicine, University of Kentucky, Lexington, KY; Neonatal Medicine, Brown University, Providence, RI.
BACKGROUND: BPD remains a significant problem despite advances in the management of the sick premature newborn. It has been postulated that sepsis *in-utero*, locally in the lung or systemic, along with ventilator-induced trauma as well as hyperoxia initiates an inflammatory cascade. These may act on the immature lung, predisposing the infant to develop BPD
OBJECTIVE: We hypothesized that in addition to the environmental factors there is a genetic component to the development of BPD, defined as a need for oxygen at 36 weeks of corrected gestational age.
DESIGN/METHODS: First, we analyzed by logistic regression the influence of several independent covariates to the development of BPD in twin pairs = 32 weeks and born between the years of 1994 - 2003. We then analyzed zygosity data based on placental examination and compared the expected to observed concordance rates between monozygotic and dizygotic twins to isolate the genetic component of BPD
RESULTS: There were a total of 836 infants (418 twin sets) from 5 centers. Logistic regression analysis demonstrated that presence of BPD, birth weight and RDS in the covariate twin were highly significant predictors for BPD in the subject twin. This suggests a familial tendency to the development of BPD. Zygosity analysis was then conducted on 41 sets of monozygotic (MZ) and 133 sets of dizygotic (DZ) twin pairs from 2 centers. One or both of 13 of the MZ and 28 of the DZ twin pairs had BPD, with an overall rate of 24%. The observed concordance rate for BPD in MZ twins was almost 4-fold, while that of DZ twins was 1.4-fold over the expected concordance rate ($p<0.001$). These remained significant over a range of BPD rates from 25% ($p<0.02$) to 40% ($p<0.001$).
CONCLUSIONS: The significant increase in the concordance rates of BPD in MZ twin pairs, which share 100% of their genomic information, shows a genetic susceptibility to the development of BPD.

109 Presentation Time 5:00 PM — Fellow in Training

Interleukin 8 (IL-8) Single Nucleotide Polymorphisms (SNPs) in Infants with Respiratory Syncytial Virus (RSV) Bronchiolitis: A Comparison of Full Term (FT) and Preterm (PT) Infants

John J. Welter, Dagne Assefa, Ioana A. Godi, Thomas Do, Sonya S. Strassberg, Nikhil Amin, Allen J. Dozor, Lance A. Parton. Pediatric Pulmonology, Maria Fareri Children's Hospital at Westchester Medical Center and New York Medical College, Valhalla, NY; Neonatology, Maria Fareri Children's Hospital at Westchester Medical Center and New York Medical College, Valhalla, NY; New York Medical College, Valhalla, NY.
BACKGROUND: A wide range of illness severity is seen in infants with RSV bronchiolitis, and some of this may be due to intrinsic genetic differences. The heightened inflammatory response seen in the airways of infants with RSV bronchiolitis is in part related to high levels of IL-8. The IL-8 haplotype (-251A/ +396G/ +781T/ +1238delA/ +1633T/ +2767T) is associated with increased disease severity in FT infants as well as increased transcription in human respiratory epithelial cells. It is unknown whether these genetic differences are related to the increased frequency of lower airway disease seen in PT infants infected with RSV.
OBJECTIVE: To compare the prevalence of IL-8 genetic polymorphisms in PT and FT infants hospitalized with RSV bronchiolitis.
DESIGN/METHODS: DNA samples of infants admitted with their first episode of RSV bronchiolitis were isolated from buccal swabs and subjected to polymerase chain reaction utilizing specific primers. Prematurity was defined as gestational age Ω36 weeks.
RESULTS: We enrolled 24 PT and 39 FT infants, mean gestational ages of 32 ± 4 and 39 ± 1 weeks respectively. Demographics were similar for both groups.

IL8 Polymorphism	FT Allele Frequency	PT Allele Frequency	Difference (95% CI)
-251A	0.50	0.42	0.08 (-0.19 to 0.33)
+781T	0.59	0.57	0.02 (-0.29 to 0.34)
+1633T	0.46	0.38	0.08 (-0.21 to 0.34)
+2767T	0.33	0.22	0.09 (-0.23 to 0.33)
Overall	0.62	0.54	0.08 (-0.06 to 0.22)

CONCLUSIONS: The IL-8 SNPs associated with severity of RSV bronchiolitis in full term infants tend to occur less frequently in preterm infants with RSV bronchiolitis. Funded by MedImmune.

110 Presentation Time 5:15 PM — House Officer

PTPN11 Mutations Play a Minor Role in Isolated Congenital Heart Disease

Constance G. Weismann, Alfred Hager, Harald Kaemmerer, Cheryl Maslen, Rachel Bell, Dietmar Schranz, Joachim Kreuder, Bruce D. Gelb. Pediatric Cardiology, Giessen University, Giessen, Germany; Pediatric Cardiology, Deutsches Herzzentrum Muenchen, Munich, Germany; Human Genetics, Oregon Health Science University, Portland, OR; Pediatrics, Mount Sinai School of Medicine, New York, NY; Human Genetics, Mount Sinai School of Medicine, New York, NY.
BACKGROUND: *PTPN11* missense mutations cause »50% of Noonan syndrome (NS), an autosomal dominant disorder that is associated with various types of congenital heart disease (CHD), most commonly valvar pulmonary stenosis and hypertrophic cardiomyopathy. Atrioventricular septal defects (AVSD) and coarctation of the aorta (CoA) occur in 15% and 9%, respectively.
OBJECTIVE: The aim of this study was to determine whether *PTPN11* mutations contribute to the etiology of relevant forms of non-syndromic CHD.
DESIGN/METHODS: The 15 coding *PTPN11* exons and their intron boundaries were PCR amplified from genomic DNAs of patients with AVSD (n=24) and CoA (n=157). Amplimers were analyzed using denaturing high-performance liquid chromatography and sequenced if abnormal. No coding region polymorphisms were identified in 100 controls.
RESULTS: We found two exonic changes, one being synonymous and one non-synonymous. A non-dysmorphic AVSD patient with no other known medical problems had a C-to-T transition at nucleotide 127 in exon 2, predicting a Leu43Phe substitution that affects the phosphotyrosine binding region (PTBR) in the N-SH2 domain. It is in close proximity to an NS mutation (Thr42Ala). Preliminary biochemical analysis support gain-of-function effects similar to those observed with other NS SHP-2 mutants. An otherwise healthy CoA patient had a silent mutation at position 540 in exon 5 corresponding (Asp180Asp). The change was identified in his father who did not have a history of CHD and was not predicted to alter an exonic splice enhancer.
CONCLUSIONS: Our study identified the first example of isolated CHD associated with a *PTPN11* mutation. Such events are rare, being observed in 1/181 cases or 0.55% (95% CI: 0.014-2.97%). The Leu43Phe mutation belongs to a rare class of *PTPN11* mutations altering the N- or C-SH2 PTBR. These defects should not alter the autoinhibition of the *PTPN11* protein product, SHP-2, which is the mechanism for the vast majority of NS mutations. Future studies will be directed towards understanding these rare PTBR mutants. Funded by Mount Sinai School of Medicine.

Neonatology II: Translational Research Platform Session

Saturday, March 5 4:00 PM-6:00 PM Sheffield

111 Presentation Time 4:00 PM

Effects of Labor on Neonatal Neutrophil Apoptosis and Inflammation

A. Bhattacharya, S. Murthy, M. Quizon, T. Choi, N. Hanna, J.D. Laskin, D.L. Laskin, B. Weinberger. Pediatrics/Neonatology; Env/Commun Med, UMDNJ-RWJ Med School; Pharm Tox, Rutgers Univ., New Brunswick, NJ.
BACKGROUND: We have previously shown that apoptosis is reduced in neonatal PMN relative to adults and that this is associated with impaired expression of caspase-3 and TNF-family receptors. Neonatal diseases such as BPD are associated with prolonged inflammation, which is promoted by cytokines that further reduce PMN apoptosis. The process of labor may be triggered by inflammatory signals in the fetus and placenta that activate PMN and delay clearance of these cells by apoptosis.
OBJECTIVE: We hypothesize that normal labor primes neonatal PMN. Thus, the rate of apoptosis is reduced in PMN after labor, and this is associated with specific alterations in expression of inflammatory and apoptotic mediators. Labor may also be related to changes in the production of, or response to, anti-inflammatory eicosanoids.
DESIGN/METHODS: PMN from umbilical blood following labor or elective cesarean section (CS) were cultured ± LPS (100 ng/ml). PMN apoptosis (24 h) was measured using Annexin V/flow cytometry. TNF-ζ, monocyte chemoattractant protein-1 (MCP-1), and inhibitor of apoptosis protein-2 (IAP-2) mRNA expression were quantified by PCR. Caspase-3 activity was measured using a colorimetric assay. Expression of 5-lipoxygenase protein was quantified by western blot.
RESULTS: PMN apoptosis decreased by 18% following labor compared with CS. This was associated with decreased caspase-3 activity. In contrast, IAP-2, which antagonizes apoptosis through inhibition of caspases, was strongly expressed in adult but not neonatal PMN, and labor had no effect. LPS-induced expression of TNF-ζ, a pro-inflammatory cytokine, and MCP-1, a chemokine mediating leukocyte trafficking, were significantly increased after labor. Moreover, 5-lipoxygenase expression and lipoxin A_4 (LXA_4) receptor density were decreased after labor, suggesting reduced production or responsiveness to LXA_4, an anti-inflammatory eicosanoid.

CONCLUSIONS: Labor is associated with reduced PMN apoptosis, which may be related to increased exposure to TNF-ζ and MCP-1 and reduced production of caspase-3. Decreased responsiveness to LXA_4 may also contribute to impaired apoptosis after labor. Priming of PMN by labor, and impaired clearance of these cells from tissues by apoptosis, may exacerbate inflammatory tissue injury in compromised infants following normal delivery.

112 Presentation Time 4:15 PM — Fellow in Training

Effects of Lipoxin A_4, an Anti-Inflammatory Lipid Mediator, on Neonatal Neutrophils

M. Quizon, A. Bhattacharya, T. Choi, N. Hanna, J.D. Laskin, D.L. Laskin, B. Weinberger. Pediatrics/Neonatology; Environ and Commun Med, UMDNJ-RWJ Med School; Pharm-Toxicol, Rutgers Univ, New Brunswick, NJ.

BACKGROUND: Knowledge of the mechanisms that govern the resolution of inflammation—different from inhibition of inflammation—is limited. It has recently been shown that lipoxin A_4 (LXA_4) is generated from arachidonic acid through the actions of 5- and 15-lipoxygenases. LXA_4 is thought to serve as an endogenous "stop signal". Thus, eicosanoid "class-switching" from inflammatory (prostanoids, leukotrienes) to anti-inflammatory (LXA_4) may be instrumental in triggering the resolution of inflammation. This process may be impaired in neonates, as indicated by delayed apoptosis of neonatal PMN relative to adult cells.

OBJECTIVE: We hypothesize that LXA_4 exerts anti-inflammatory effects in adult PMN by blocking chemotaxis and inducing apoptosis, and that these responses are reduced in neonatal cells. Differences in the response to LXA_4 may be due to reduced expression of FPRL1 and LXA_4R receptors on neonatal PMN.

DESIGN/METHODS: PMN were isolated from adult and umbilical cord blood. Apoptosis after 24 h, in the presence or absence of LXA_4 (100 nM) and LPS (100 ng/ml), was measured using Annexin V/flow cytometry. The effects of pre-incubation (30-120 min) of the cells with LXA_4 on fMLP-induced chemotaxis was measured using a modified Boyden chamber. Expression of FPRL1 was quantified by immunofluorescence, and LXA_4R by PCR. Expression of 5-lipoxygenase protein was quantified by western blot.

RESULTS: Treatment of adult PMN with LPS + LXA_4 markedly increased apoptosis. LXA_4 alone did not affect the rate of apoptosis. In contrast, LXA_4, as well as LXA_4 + LPS, reduced apoptosis in neonatal PMN. LXA_4 also significantly reduced the chemotactic response of adult, but not neonatal, PMN. Whereas FPRL1 receptor expression was greater in neonates, LXA_4R expression was similar on adult and neonatal cells. Expression of 5-lipoxygenase was also comparable in adult and neonatal PMN.

CONCLUSIONS: Neonatal PMN are less sensitive to the apoptotic and anti-chemotactic effects of LXA_4 than adult cells. Altered response to LXA_4 is not associated with impaired expression of the FPRL1 or LXA_4R receptor proteins in neonatal cells. Developmental changes in the response to LXA_4 in neonatal PMN may contribute to deficiency in the resolution phase of inflammation, increasing the risk of chronic inflammatory conditions.

113 Presentation Time 4:30 PM

Viral Transfection of Endothelial Cells with Superoxide Dismutase Protects Against Hyperoxic Injury

Robert M. Angert, Yuchi Li, Hschi-chi Koo, Jonathan M. Davis. Pediatrics and the CardioPulmonary Research Institute, Winthrop University Hospital/SUNY Stony Brook School of Medicine, Mineola, NY.

BACKGROUND: Newborns exposed to hyperoxia have increased production of reactive oxygen species (ROS), a contributing factor to bronchopulmonary dysplasia. Undervascularized lungs are a prominent pathologic finding in these patients. Efforts utilizing antioxidant gene transduction have been developed for pulmonary epithelial cells.

OBJECTIVE: We tested the hypothesis that adenovirus, genetically engineered to deliver Mn superoxide dismutase (SOD) DNA to epithelial cells, would also transfect endothelial cells, conferring increased SOD activity and preventing hyperoxia-induced cellular damage.

DESIGN/METHODS: Human Vein Endothelial Cells (HUVEC) were grown in the appropriate medium and transduced with recombinant adenovirus containing SOD at 150 multiplicity of infection (MOI), as well as 150 MOI adenovirus containing Lac Z as a control. Lac Z transduced cells were stained with X-Gal and visualized under light microscopy to determine transduction efficiency. SOD transduced cells were assayed for SOD activity as a functional measure. Transduced cells and controls were then exposed to 95% oxygen for 5 days with daily cell counts and microscopic examination.

RESULTS: Lac Z containing adenoviruses successfully transduced the HUVEC cells when stained and analyzed by light microscopy. SOD activity was increased by 2.1 fold compared to Lac Z controls. Cell morphology showed marked swelling and large nuclei in the Lac Z controls (early signs of hyperoxic injury), while the SOD transfected cells retained a more normal appearance. There were no significant differences in the cell survival rate between the two groups.

CONCLUSIONS: Adenovirus can be successfully used to deliver SOD genes to cells with resultant overexpression of the gene. Unlike epithelial cells where growth inhibition under hyperoxia is reversed by similar levels of SOD overexpression, there is no evidence that endothelial cell are similarly protected. There are substantial morphological differences between hyperoxia and control cells, suggesting resistance to hyperoxia. Continuing the experiments for longer than 5 days might yield differences in survival, following the morphologic changes. Further increases in SOD activity in transduced cells may also enhance their survival.

114 Presentation Time 4:45 PM — Fellow in Training

Altered Production of Pro- and Anti-Inflammatory Cytokines in Preterm Labor Placentas: Role of IL-10

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BACKGROUND: There is a growing recognition that placental cytokines play a fundamental role in the mechanisms of immunologically mediated preterm labor. We have previously shown that preterm labor is associated with decreased production of the anti-inflammatory cytokine IL-10. However the role of IL-10 in regulating other placental cytokines is not well characterized.

OBJECTIVE: The purpose of this study is to determine whether altered production of placental pro- and anti-inflammatory cytokines is associated with preterm labor and whether this process can be reversed by IL-10 treatment.

DESIGN/METHODS: Cultured placental explants from preterm (< 32 weeks gestation) and term deliveries were cultured for 24 hours with or without IL-10, LPS or both. Production of pro-inflammatory (IL-1b, TNF-ζ and IFN-ν) and anti-inflammatory cytokines (IL-13 and IL-4) were measured in supernatants by ELISA. Cytokine mRNA was quantified by Q-RT-PCR. Using immunohistochemistry, cytokine localization and expression was compared in placental tissue sections from preterm deliveries and second trimester placental samples from normal pregnancies after elective abortions.

RESULTS: Expression of IFN-ν, TNF-ζ, IL-1ß and IL-4 was increased in preterm compared to normal second trimester and term placentas. In contrast, the anti-inflammatory cytokine IL-13 expression was significantly decreased in preterm placentas. These cytokines were produced by cultured placental explants with or without treatment with LPS. Interestingly, preterm placental explants treated with IL-10 significantly increased IL-13 while decreased production of IL-4, IFN-ν, TNF-ζ, IL-1ß both in standard culture conditions and after LPS stimulation. Immunohistochemistry confirmed the localization of placental cytokines to the cytotrophoblast layer.

CONCLUSIONS: Decreased production of the anti-inflammatory cytokines IL-10 and IL-13 may contribute to inappropriate expression of inflammatory cytokines that can trigger the onset of preterm labor. IL-10 treatment abrogated changes in inflammatory and anti-inflammatory cytokines associated with preterm labor pointing to a potential role of IL-10 in treatment of preterm labor.

115 Presentation Time 5:00 PM — Fellow in Training

Bilirubin Binding Capacity Is Directly Related to Gestational Age and Clinical Stability in Very Low Birthweight Neonates

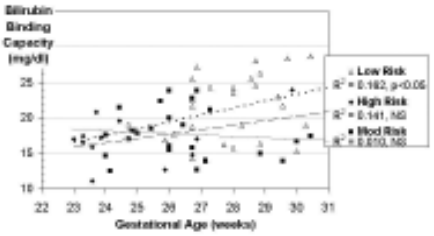
Jesse Bender, William J. Cashore, William Oh. Pediatrics, Brown Medical School, Women & Infants' Hospital, Providence, RI.

BACKGROUND: Unbound, unconjugated bilirubin (UB) is most likely the toxic fraction responsible for neonatal encephalopathy due to hyperbilirubinemia. Serum levels of UB are dependent on the bilirubin binding capacity (BBC) of albumin. BBC has been described for neonates over 28 weeks gestational age (GA) (Cashore 1977), but not for the less mature infants at increased risk for bilirubin encephalopathy.

OBJECTIVE: To determine the ontogeny of in-vitro serum BBC and affinity in VLBW neonates, stratified by physiologic risk.

DESIGN/METHODS: Ninety-two neonates (23-30 weeks GA, 440-1300g) were enrolled prospectively. Day 5 TB and UB were measured with the UB-A1 analyzer (Arrows Co, Tokyo, Japan) and albumin with the bromocresol purple method. Nonlinear regression of saturation curves formed by bilirubin titration generated binding affinity and capacity data. Clinical status for each infant was rated as high, moderate, or low risk using a modified SNAP-PE model. Low risk was considered clinically stable.

RESULTS: As shown in the figure, BBC has a direct relationship to gestational age in the low risk (R^2 = 0.162, $p<0.05$) but not moderate or severe risk groups. BBC is significantly higher (ANOVA, $p<0.001$) in the low risk group (21.3 ± 4.6 mg/dl) than in moderate (17.7 ±3.4 mg/dl) or high (17.0 ±3.43 mg/dl) risk groups. The affinity of the primary bilirubin binding site on albumin, K_1 ($11.5 \pm 5.65 \times 10^7$) does not differ by clinical risk status or gestational age. Secondary binding at K_2 ($2.5 \pm 1.43 \times 10^7$) and K_3 ($1.1 \pm 0.7 \times 10^7$) differ ($p<0.001$) from K_1. Unbound bilirubin has a significant, direct correlation to total bilirubin (R^2 = .316, $p<0.001$), and is higher in unstable than in stable neonates.



CONCLUSIONS: In clinically stable very preterm VLBW infants, BBC is directly proportional to gestational age, and is higher than in unstable neonates.

116 Presentation Time 5:15 PM — Fellow in Training

Circulating $CD34^+$ Stem Cells in the Premature Neonate and Their Possible Role in the Response to Lung Injury

Matthew J. Bizzarro, Vineet Bhandari, Diane S. Krause, Brian Smith, Ian Gross. Pediatrics; Division of Perinatal Medicine, Yale University School of Medicine, New Haven, CT; Laboratory Medicine and Pathology, Yale University School of Medicine, New Haven, CT; Laboratory Medicine and Internal Medicine, Yale University School of Medicine, New Haven, CT.

BACKGROUND: Preterm neonates have higher levels of circulating $CD34^+$ stem cells than term infants and adults. Clinical studies suggest that fetal stem cells have multilineage potential. Animal data indicate that $CD34^+$ cells home to the alveoli of injured lung tissue. We hypothesize that $CD34^+$ stem cells play a role in the recovery of injured lung in the premature neonate.

OBJECTIVE: To measure circulating $CD34^+$ stem cell levels in premature neonates and to determine if there is a correlation between the initial $CD34^+$ counts and measures of pulmonary function.

DESIGN/METHODS: In neonates of gestational ages (GA) 24-32 weeks, peripheral $CD34^+$ stem cell counts were measured using FACS and flow cytometry at 0-2, 6-8, 13-15, and 20-22 days of life. Data pertaining to prenatal care, neonatal demographics, and short-term outcomes were collected. Pulmonary function tests were also performed to coincide with CD34+ sampling.

RESULTS: 22 subjects with mean GA of 25.6 weeks and birth weight of 783 grams were analyzed. A mean of 115.0 $CD34^+$ cells/ul were observed in the 1st week of life with a decline to 52.2 cells/ul at the 4th. A significant inverse correlation was observed between initial $CD34^+$ count and gestational age ($p < 0.05$). In a subset of intubated subjects (n=6), a statistically significant correlation was observed between initial $CD34^+$ stem cell count and lung compliance at 4 weeks ($p<0.05$), and a significant inverse relationship with days in oxygen ($p < 0.001$). The latter correlation was not observed in the entire population.

CONCLUSIONS: Premature neonates have extremely high levels of circulating $CD34^+$ cells in their peripheral blood at birth. These levels decline over the first 4 weeks of life, but remain higher than those previously reported in umbilical cord blood (40 cells/ul), the peripheral blood of more mature preterm (37 cells/ul) and term neonates (32 cells/ul), and adults (2 cells/ul). Premlinary data indicate that there may be a correlation between higher initial $CD34^+$ stem cell count and improvement in lung compliance, although this finding is currently limited to a small number of subjects.

Poster Session II

Saturday, March 5 — 6:00 PM-7:30 PM — Conde's

117 Poster Board 1 — House Officer

Presenting Complaints in the PCOS Adolescent Female — Are Teen, Parent and Physician on the Same Page?

Michelle Adams, Marybeth Roy, Holley F. Allen. Pediatrics, Baystate Medical Center, Springfield, MA.

BACKGROUND: Polycystic Ovary Syndrome begins to develop in adolescence. Although previous studies confirm that adolescent girls with PCOS have specific concerns regarding symptoms of PCOS and that these symptoms have a negative affect on their quality of life, there have been no studies to date examining whether adolescents with PCOS share the same concerns as their parents regarding their PCOS symptoms nor examining doctors' perceptions of adolescent patients' concerns. Awareness of differences in perceived severity of presenting symptoms should help doctors focus their management of PCOS to better address the patient and the parents' needs.

OBJECTIVE: This study aims to evaluate potential differences between concerns of adolescents with PCOS, their parents concerns and the doctors' perception of the adolescents' concerns regarding their PCOS symptoms.

DESIGN/METHODS: Participants were recruited from the Pediatric Endocrinology Clinic and the Pediatric Weight Management Clinic at Baystate Medical Center. Eligible patients were female, ages 13

to 18, with at least one symptom of PCOS, completed a questionnaire rating their degree of concern regarding their symptoms. They were asked to rank their concerns on a 5 pt Likert scale ranging from 1- not at all to 5- extremely concerned. In separate confidential questionnaires parents and doctors rated their perception of the adolescents' degree of concern. These were compared with findings on PE and testosterone levels.
RESULTS: In our population, teens with PCOS were most concerned about their weight (73.3%), followed by acne (30.5%), irregular menses (26.3%), and hirsutism (20.7%). Significantly more patients had a higher degree of concern about their acne and weight than their doctors perceived their degree of concern($p<0.005$ and $p=0.02$ respectively). In 24.3% of patients with acne, their doctors underestimated the patients' level of concern. Non-obese (BMI<35) adolescents with PCOS rated their weight concerns higher than their doctors ($p=0.05$). There was a suggestion that parents were more concerned than they perceived their daughters' concern about irregular menses($p=0.07$).
CONCLUSIONS: Doctors underestimated patients degree of concern in regards to their acne and weight. Parents' own concerns were consistent with those of their daughters. Adolescents with PCOS overall were most concerned about their weight.

118 Poster Board 2 — House Officer

Does Asthma Written Action Plan Improve the Self Management of Asthma?

Uma Maikappan, Fernanda Kupferman, Won Baik-Han, Salima Walani, Susana Rapaport. Pediatrics, Flushing Hospital Medical Center, Flushing, NY.
BACKGROUND: Current guidelines recommend the use of written action plans as a key component of asthma care. It is controversial whether written action plans do have a large impact on outcomes when applied to the general population of asthmatics. However, these interventions may have a beneficial effect, like reducing emergency-room visits and hospitalizations, when applied to selected populations, particularly patients with high baseline utilization.
OBJECTIVE: To estimate the knowledge of asthma self management in parents of asthmatic children and to assess the effectiveness of asthma written action plan for the self management of asthma in children and adolescents.
DESIGN/METHODS: This is a prospective, case-control, six-month-study undertaken in a primary care setting at a community hospital in Queens, NY. Parents of asthmatic children were given a questionnaire which included 15 questions that assessed their knowledge about symptoms, self-management and complications of asthma. After completing the questionnaire, they were randomly divided into 2 groups: the study group received a written action plan and the control group, was given the same information but only verbally. The same survey was repeated 4-5 weeks later to both groups. The answers of both surveys were scored and analyzed statistically.
RESULTS: Ninety-two parents of asthmatic children participated in the study: 46 in the study group and 46 in the control group. Age ranges of patients were 6-20 yrs (mean: 9.7 yrs). 65% were male. 38% were Hispanics, 30% were Asian, 20% were African-American, 11% were Caucasians and 1% others. Both groups scored higher after the intervention. However, the written action plan group scored higher than the control group. The mean score difference between survey 1 and survey 2 for the written action plan group was 2.44 ($p = 0.00$) and for the control group was 0.64 ($p = 0.00$). The most common mistakes included knowledge about treatment of exercise induced asthma, use of peak flow meter and preventive and rescue medications.
CONCLUSIONS: Written action plans are effective tools to educate caregivers about asthma management. Thus, we believe that the quality of asthma care can be improved with appropriate asthma education programs.

119 Poster Board 3 — Fellow in Training

Patient Characteristics Associated with Medical Injury Following Congenital Heart Surgery

Oscar J. Benavidez, Kimberlee Gauvreau, Kathy J. Jenkins. Cardiology, Children's Hospital, Boston, Boston, MA.
BACKGROUND: We have identified a high frequency of diagnosis codes for medical injury following congenital heart surgery.
OBJECTIVE: To identify clinical characteristics that place patients at risk for reported medical injury.
DESIGN/METHODS: Cases of congenital heart surgery were identified from the Healthcare Cost and Utilization Project Kids' Inpatient Database 2000. A previously validated algorithm identified ICD-9-CM codes indicating medical injury. To quantify surgical complexity, we used Risk Adjustment of Congenital Heart Surgery (RACHS-1) category and number of procedure codes as categorized into low (1-2 procedures), medium (3-5) and high (>=6). Generalized estimating equation models examined gender, age, prematurity and non-cardiac structural anomalies as possible predictors of injury.
RESULTS: Among the 12,717 cardiac surgical discharge cases, 4014 (32%) reported at least one medical injury code. In unadjusted analyses, females OR 0.9, $p=0.004$ and premature infants OR 0.6, $p<0.001$ were less likely to have a reported medical injury code. Patients with greater procedure complexity had greater odds for reported injury: category 1 OR 1.0; 2 OR 1.8; 3 OR 2.9; 4 OR 3.0; 5 OR 4.7; category 6 OR 4.1, $p<0.001$. Patients undergoing more procedures were also at greater risk for injury: low OR 1.0; medium OR 1.8; high OR 5.0, $p<0.001$. Age < 1 year and major non-cardiac anomalies were not associated with reported injury. After adjusting for risk category and number of procedures, gender and non-cardiac structural anomalies were no longer significant. Prematurity and age < 1 year remained independently predictive of lower injury risk: prematurity OR 0.4, $p<0.001$; age < 1 OR 0.8, $p<0.001$. The area under the ROC curve for the final model was 0.692.
CONCLUSIONS: Congenital heart surgical case complexity, number of procedures, older age at surgery and non-prematurity are predictive of increased likelihood of reported medical injury codes. Further study is needed to determine ways to reduce medical injury in this complex population.

120 Poster Board 4

Cloning and Characterization of a Mouse Ap-2e Variant-1 with a Non-AUG Translation Start Site and Unique Function

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BACKGROUND: AP-2 transcription factors (a, b, g, d and e) are sequence-specific DNA-binding proteins that play important roles in embryonic development. Many genes have variantly spliced forms, which can possess unique roles depending on expression pattern and function.
OBJECTIVE: To characterize a variantly spliced form of mouse Ap-2e.
DESIGN/METHODS: An Ap-2e variant EST clone was sequenced. RT-PCR was performed to verify the existence in nature. Subcellular localizations were determined using a C-terminal FLAG tag. Mutants were generated and expressed *in vitro* using reticulocyte lysates. EMSAs were performed to document DNA binding. Transactivation was assayed by co-transfection into NIH3T3 cells along with a CAT reporter construct.
RESULTS: Clone E1B30217C16 from a murine eye library contained a variant cDNA that matched the published Ap-2e cDNA except the EST lacked 156 bp in exon 2 where an alternative splicing site was found. RT-PCR found that the variant existed at low-copy in nature. While the wild type Ap-2e localized to the nucleus, the variant localized to the cytoplasm. *In vitro* translation produced two proteins, sized at about 40 and 45 kDa, suggesting two translation start sites. The 40 kDa protein concurred with predicted translation from the first or second ATG (24 bp apart). However, there was no upstream ATG in the open reading frame that could account for the 45 kDa protein. Truncation of the cDNA at position –98 suggested that the 45 kDa protein was translated from a non-AUG start site. Mutational analysis demonstrated that the 40 kDa protein was translated from the second ATG and the non-AUG translation start site of the 45 kDa form could not be used alone. EMSA showed shifted bands. Co-expression of both 40 and 45 kDa proteins in cell culture resulted in transactivation, while the expression of the 40 kDa protein alone had dominant-negative effects on other AP-2 proteins.
CONCLUSIONS: A variant transcript of Ap-2e exists in mouse embryonic tissues and possesses two translation start sites, of which one is a non-AUG start site. The variant proteins can bind the AP-2 consensus sequence. The larger variant protein can transactivate gene expression, while the 40 kD form has dominant negative behavior, providing a novel mechanism for AP-2 regulation. Its subcellular localization in the cytoplasm suggests yet another level of transcriptional control.

121 Poster Board 5

Antibody Inhibition of ErbB Receptors in Pulmonary Alveolar Type II Cell Lines

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BACKGROUND: Fetal lung maturation involves fibroblast-type II epithelial cell communication through erbB receptors (erbB1, erbB2, erbB3, erbB4). ErbB ligands (EGF; neuregulin, (NRG)) stimulate this process. Ligand binding induces ErbB homo- and heterodimer formation and phosphorylation, activating multiple signal transduction cascades. Specific dimers involved in fetal lung surfactant synthesis are unknown. We showed that erbB receptor blocking antibodies (Abs) reduced ligand-induced DSPC synthesis (a measure of surfactant synthesis) in the human lung epithelial carcinoma line, A549. Anti-erbB Abs alone or in combination differentially decreased synthesis induced by EGF, NRG or fibroblast conditioned media (FCM).
OBJECTIVE: We hypothesize that erbB receptor dimer formation necessary for DSPC synthesis differs between tumor-derived vs non-transformed lung cell lines.
DESIGN/METHODS: MLE12 cells (derived from SV40 transgenic mouse pulmonary tumors) and L2 cells (non-transformed cells derived from normal adult rat lung) were preincubated with inhibitory Abs directed against extracellular epitopes of the erbB receptors, individually or in combination. Cells were then treated overnight with EGF (10ng/ml), NRG(10nM) or FCM, and ^{3}H-choline to measure DSPC synthesis.
RESULTS: Anti-erbB3 decreased DSPC synthesis in all ligand-treated MLE12 cells by 25-35%. Anti-erbB1+anti-erbB4 affected only FCM-treated cells (40% decrease); anti-erbB2+anti-erbB4 reduced DSPC in all ligand-treated cells by 65%. NRG and FCM stimulated DSPC in L2 cells by 50%. Preincubation with anti-erbB3 or 4 further stimulated incorporation by 200% (NRG) and 300% (FCM).
CONCLUSIONS: A549, MLE12 and L2 cells have all been used as pulmonary type II cell models. Inhibitory erbB Abs differentially affect surfactant synthesis in these different cell lines. Inhibitory Abs against NRG-binding receptors B3 and B4 are particularly effective, alone or in combination with anti-erbB2, in tumor-derived lines. In contrast, the same Abs were stimulatory in non-transformed L2 cells from normal adult lung, particularly in the presence of FCM. We speculate that effects on surfactant synthesis are signaled through different ErbB dimers depending on the cell line used. NIH HL37930, HL04436, Hood and Peabody Foundations.

122 Poster Board 6

Butyrate, a Diet-Derived Short Chain Fatty Acid May Modulate the Immune Responses by Regulating Chromogranin A Gene Expression

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BACKGROUND: Chromogranin A (CgA) is a member of the "granin" family of acidic soluble secretory proteins that are co-stored and co-released with a wide range of neuropeptides including classical neurotransmitters such as adrenal catecholamines. CgAs are believed to be prohormones producing peptides with an array of biologically active functions. For example, CgA fragments exert bacteriolytic and antifungal effects which may play a role in stress-related situations or act as an immediate protection against pathogens (NEJM 348:1134,2003). Butyrate, a diet-derived, short chain fatty acid can modulate gene transcription and steady-state mRNA levels of tyrosine hydroxylase (TH), the rate-limiting enzyme in catecholamine biosynthesis and the neuropeptide enkephalin in PC12 cells only when both a cAMP (CRE) & butyrate response elements exist (BRE; Peds Res 55:847, 2004). In contrast, dopamine beta-hydroxylase and PNMT catecholaminergic genes do *not* have both elements and are *not* induced.
OBJECTIVE: To determine whether: 1) butyrate changes CgA mRNA levels in PC12 cells and 2) this effect is dose and time dependent?
DESIGN/METHODS: Wild type PC12 (rat pheochromocytoma) cells were used in these experiments. Cells were treated with 1mM, 1.5mM and 6 mM of butyrate for 24 hours and 48 hours. Total RNA was extracted and subjected to northern blot analyses for CgA expression. Ribosomal 18S rRNA levels were analyzed as a loading control.
RESULTS: Steady-state CgA mRNA levels were detectable at baseline by northern blot analysis and as early as 24 hours after exposure to1.5 mM butyrate ($p = ns$). However, after 48 hours exposure, CgA mRNA levels were more than doubled ($n = 5$, $p < 0.05$). No differences were seen on 18S rRNA levels under any of these conditions.
CONCLUSIONS: Butyrate elevates CgA mRNA levels in a time-dependent fashion similar to effects on TH & enkephalin (see 3 abstracts by Shah, Parab, & Patel, PAS 2005). Since the CgA promoter has at least one CRE, our data suggests a BRE must also exist. The coordinate regulation of CgA with other stress-adaptive hormones like catecholamines and opiate peptides, portends a significant biological role in adaptation. We speculate that by affecting chromogranin A gene expression, diet-derived butyrate can also modulate immune responses shortly after birth.

123 Poster Board 7 — Fellow in Training

Hypoglycemia in Beckwith-Wiedemann Syndrome (BWS) Not Associated with Hyperinsulism (HI)

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BACKGROUND: BWS results from an imprinting imbalance of critical genes at 11p15 (IGF-2,WT1,P57). Hypoglycemia in BWS has been presumed to be caused by HI.Alternatively,the mechanism for the hypoglycemia may be IGF-II overexpression.
OBJECTIVE: To evaluate insulin provocative studies and IGF axis parameters in 2 patients with hypoglycemia and BWS.
DESIGN/METHODS: Patient 1 presented with hypoglycemia at 11 mos of age.After failure of diazoxide and octreotide, he intially attained glycemic control on growth hormone (rhGH) 0.25mg/kg/day sc.
Patient 2 presented with hypoglycemia at DOL1.She failed octreotide and diazoxide therapies.Patients

underwent fasting studies and acute insulin response tests (AIRs) with tolbutamide,glucose,calcium and L-leucine as insulin secretagogues.Serum growth factors were assessed by commercial RIAs.
RESULTS: Both children showed no evidence of HI based on fasting studies and AIRs.Fasting hypoglycemia occurred at 2-4 hours in both patients with serum insulin levels less than<3 muU/l.AIRs revealed no response to calcium or leucine stimulation in patient 2 and suppressed insulin levels in (<3 muU/l) in patient 1 in response to calcium,leucine and glucose.
Growth Factors:Patient 1:*Pre GH Rx* IGF-II=102 (336-642ng/ml);IGF-I =13 (15-101ng/ml) ; IGFBP-3= 0.5 (.5-2.4mg/l).
Patient 2 : *Pre GH Rx* IGF-II= 205 (334-642ng/ml);IGF- I <1 (23-101ng/ml); IGFBP-3= 0.2 (0.4-2.1mg/l). Stimulation with arginine and propanolol induced peak GH level of 34.1ng/ml.
Patient 1 had labile blood sugars on GH (0.25 mg/kg week) but responded to continuous NG dextrose.Patient 2 on GH (0.45 mg/kg/week)maintained normoglycemia during a fast of 10 hours .
CONCLUSIONS: Hypoglycemia in these 2 patients with BWS cannot be attributed to HI.Both had suppressed IGF-I and IGFBP-3 levels compatible with suppression of GH secretion by IGF-II.One case responded to treatment with high dose GH.These observations suggest that hypoglycemia in BWS may be due to overexpression of IGF-II exacerbated by low IGFBP-3.Further investigations should evaluate levels of high molecular as well as processed IGF-II.

124 Poster Board 8 Ph.D. Student

A Comparison of Glutamine Content in Commonly Consumed Food Proteins Derived from Gene Sequencing vs. Biochemical Analysis

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BACKGROUND: Glutamine is the most prevalent amino acid in the body and is commonly converted in glutamate. There is increasing evidence that glutamine plays a key role in the transfer of carbon and nitrogen between tissues, partitions energy, regulates glucose oxidation of the brain, and protects tissues from oxidative damages. Including glutamine in a nutrient database is the first step to understanding the health effects of dietary glutamine.
OBJECTIVE: To determine the content of glutamine in major food proteins.
DESIGN/METHODS: A validated 131-food items food frequency questionnaire was used to identify the 30 foods that contributed the most to protein intake in the Nurses' Health Study (1984). We estimated the content in proteinogenic amino acids of foods based on protein fractions generated from genetic sequencing methods compiled by the Swiss Institute of Bioinformatics and compared this data to that generated from chemical methods compiled by the USDA. Spearman and Pearson correlations coefficient were calculated.
RESULTS: Glutamine content varied from 0.06-to 2.97-g/100g of food in orange juice and dark bread and contributed to 1-to 33%-g/100g of protein in bean and dark bread. The proportion of glutamine in beef protein was 4.75% using the gene sequencing method and 4.36% based on the revised chemical analysis proposed by Kuhn et al. The Spearman correlation coefficients for each of the 30 foods' composition in amino acids varied from 0.62 to 0.99 between the two methods. The nurses' daily mean (SD) glutamine intake was 7.16(2.41) g/day. The Pearson correlation coefficient between intake of glutamine and total protein by nurses was 0.84. We also calculated the correlation coefficicents for each of the 16 amino acid consumed by the nurses in g/day and in g/100 g protein between the two methods, which ranged from 0.93 to 0.99 and from -0.04 to 0.82.
CONCLUSIONS: These data suggest that: 1) Glutamine content can be estimated from gene sequencing methods; 2) There is a wide variation in glutamine intake allowing for exploration of glutamine consumption and disease independently from that of protein.

125 Poster Board 9

Treatment Effectiveness of Gastroesophageal Reflux Disease in Infants: A Parental Satisfaction Survey

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BACKGROUND: Treatment of children with gastroesophageal reflux disease (GERD) continues to garner great attention. Comparison of parental satisfaction with clinical outcomes can be useful for improving disease management strategies.
OBJECTIVE: To assess the effectiveness of the therapeutic intervention in children with GERD by comparing parental satisfaction with clinical outcome.
DESIGN/METHODS: A satisfaction survey of 49 parents of children with GERD was conducted. Parental satisfaction with different types of conservative (positioning, thickened feeding and pharmacological) treatments of their children was measured using a satisfaction scale. The level of satisfaction with each type of GERD treatment was identiifed as significant, moderate, minimal or no improvement, or worsening of symptoms. Measurements of clinical outcome included the child's monthly growth (normal/poor) and intensity of discomfort (mild/moderate/severe). The association between the level of parental satisfaction with treatment and clinical outcome was determined.
RESULTS: Among the 49 parents, 25 (51.0%) reported use of antireflux precautions (positioning, thickened feeds, or antacids) for the management of GERD in their children. H-2 blockers were used in 81.7% of cases and, less frequently, proton pump inhibitors (32.7%) or prokinetic agents (4%), p<0.01. Approximately 40% parents reported moderate satisfaction when using antireflux precautions, thickened feeds or antacids as treatment. However, 77.5% of the parents were of the opinion that treatment with medication especially H-2 blockers significantly improved clinical presentation of GERD in their children. Among infants with and without poor growth, parental satisfaction with the lifestyle modification and/or pharmacological treatment was not different (69% vs.44.3% and 75% vs.78%, respectively). Discomfort associated with GERD decreased gradually during the first 6 months of life (from 51.0% to 14.5%, P<0.01). We found that the degree of parental satisfaction was significantly associated with the reduction of infant discomfort.
CONCLUSIONS: Parental satisfaction with GERD treatment is unrelated to the child's growth outcome but is associated with improvement of the child's symptoms of discomfort and, therefore, may have limited applicability to affirming the efficacy of the therapeutic management.

126 Poster Board 10

Alcohol Sclerotherapy of Low Flow Venous Malformations in Children

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BACKGROUND: Venous malformations (VMs) in childhood are caused by congenitally defective vascular smooth muscle and endothelium. VMs occur in the skin and muscle but can also involve nerves and bone. They can be disfiguring and disabling and are unresponsive to drugs used for hemangiomas. Treatment consists of surgery and sclerotherapy, but data on sclerotherapy in children is limited. Pediatricians seeing children with these lesions may be unaware of this treatment option and of its safety.
OBJECTIVE: To demonstrate alcohol sclerotherapy as an appropriate option for treatment in children with VMs.
DESIGN/METHODS: We conducted a prospective analysis of patients referred for VMs in 2004. Patients were evaluated with MRI and color flow Doppler and for complicating medical diagnoses. Under general anesthesia children had contrast venography followed by percutaneous instillations of acohol into the vascular lesion. All were observed overnight.
RESULTS: Six patients were evaluated for extremity VM (4-17yrs). Data is summarized in the table.

Summary of Patients with VMs

Age/ Gender	Location	Previous Interventions	Presenting Problems	Sclerotherapy Y	Outcome Good
15y/M	L upper thigh	sclerotherapy complic by compartment syndrome	pain, bleeding, unable to exercise		
14y/F	R forearm	no	severe pain, unable to exercise	Y	Good
8y/F	L lower thigh	surgical excision with skin grafting	pain, unable to exercise	Y	Good
17y/F	L thigh	no	pain, periosteal thickening of femur	-	-
7y/F	L thigh	no	pain, bleeding	-	-
4y/F	R lower ext	no	leg length discrepency,pain, diff. ambulating	-	-

All patients were characterized as low flow venous lesions with one having a varient of Klippel Trenaunay. Three of the 6 have received treatment to date. Duration of procedure ranged from 45-90 minutes, with maximum 0.3 ml/kg of 98% alcohol (range 0.05 to 0.3 ml/kg). Intraoperative monitoring included SaO2, ETCO2, blood pressure, pulse, and urinalysis. No adverse effect was observed. Mild post-operative pain was managed with NSAID and opiate analgesia.
CONCLUSIONS: Alcohol sclerotherapy is an option for children with low-flow venous malformations. All treated children had complete thrombosis (no flow on Doppler) of treated area of the lesion and no procedure-related complications. Further data is required to evaluate its immediate safety and long-term efficacy.

127 Poster Board 11 Fellow in Training

Determinants of Prolonged Hospitalization for Asthma in Inner-City Children

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BACKGROUND: Asthma hospitalization rates are higher among inner-city minority children. A number of these children will have a longer and costlier hospital stay. Identifying the factors associated with prolonged asthma hospitalizations for this population may help to decrease length of stay and reduce hospital costs.
OBJECTIVE: To identify the determinants of prolonged hospitalization in inner-city minority children with asthma.
DESIGN/METHODS: A retrospective chart review of a cohort of children hospitalized with asthma at a Children's Hospital between 1/1/98 and 10/1/04. Long-stay group was defined as children hospitalized with the primary diagnosis of asthma for more than 3 days. Short-stay group were children hospitalized with asthma for 3 days or less. Bivariate analyses (t-test, chi-square test) compared the two groups. Logistic regression analysis identified variables associated with prolonged hospital stay.
RESULTS: 479 subjects were analyzed, of whom 60% were Hispanic, 36% African American, 64 % male and the mean age was 6.6 years (SD 5.3). Mean length of stay was 3.1 days (SD 1.7). 30% of subjects were hospitalized for longer than 3 days. Subjects in the long-stay group were older (7.6 years vs 6.1 years, p=.006), had a greater mean number of lifetime asthma admissions (8.2 vs 3.8, p=.002) and were more likely to receive a pulmonary consultation during the index hospitalization (OR 4.2, 95% CI 2.6-6.9). Subjects in the long-stay group were also more likely to be admitted to the ICU (OR 2.6, 95% CI 1.6-4.2) and to require oxygen supplementation (OR 3.2, 95% CI 2.1-4.9) during the index hospitalization. Using logistic regression, oxygen requirement during the hospitalization, history of multiple asthma admissions, and receipt of a pulmonary consultation during the index admission were found to be independent predictors of prolonged hospitalization. We found no significant differences between the two groups on exposure to environmental triggers, mean number of days with worsening asthma symptoms and home management prior to admission.
CONCLUSIONS: Our findings suggest that inner-city minority children with more severe asthma have longer hospital stay. Early recognition of factors associated with prolonged hospitalization may help identify such children and optimize their inpatient management to decrease length of stay.

128 Poster Board 12 Fellow in Training

Using GIS To Assess the Availability of Physical Activity Resources in an Inner City Community

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BACKGROUND: Childhood overweight is epidemic in the US, especially among African American and Latino children. This suggests that East Harlem (EH), NYC, a predominantly minority community is at greater risk for childhood overweight. Factors unique to the urban environment may influence physical activity levels including lack of outdoor play spaces, scarcity of organized activities and concerns for safety.
OBJECTIVE: To characterize the availability of physical activity resources in the urban environment of East Harlem, NYC.
DESIGN/METHODS: A comprehensive walking survey of EH zip codes 10029 and 10035 was performed. Physical activity resources were classified into: parks, playgrounds, sports fields, pools, recreation centers, afterschool programs, private facilities, and facilities at religious institutions. Data were cross referenced with data from city/state agencies. Information was verified by telephone when needed. The geographic information systems (GIS) software package ArcGIS 8.3 was used to convert database files into geographic files. Physical activity resources were geocoded by address. Base maps of EH were created using data from the NYC Department of City Planning. Maps were then generated depicting physical activity resources in EH.

RESULTS: 81% of elementary schools surveyed in EH have either extracurricular activities or outdoor play areas available. 90% of EH housing projects have playgrounds on site.
CONCLUSIONS: GIS is a useful research tool to assess the availability of physical activity resources. Physical activity resources are widely available at EH schools and housing projects. Access, quality of resources and safety concerns may limit use of these resources. Addressing environmental influences on physical activity for inner city children provides an opportunity to combat childhood overweight at the community level.

129 Poster Board 13 Fellow in Training

Trauma and Distress in Primary Care Pediatrics

Deborah P. Steinbaum, Laura Englander, Tara Balija, Alexi Tzavaras, Joseph Boscarino, Danielle Laraque. Pediatrics, Mount Sinai Medical Center, New York, NY.

BACKGROUND: Studies have found high rates of post traumatic stress disorder (PTSD) in adults and adolescents in primary care practices in the inner city and in school-aged children in the inner city. No published study has examined the prevalence of PTSD in a general pediatric setting.

OBJECTIVE: To describe patients at an inner city pediatrics practice with symptoms of PTSD.

DESIGN/METHODS: Ongoing, cross-sectional convenience sample of consecutive English-speaking 8 to 10 year olds at a primary care practice in East Harlem, New York City. PTSD symptoms were measured via the UCLA Post Traumatic Stress Reaction Index (PTSRI). A PTSRI score of 38 or above is consistent with a preliminary diagnosis of PTSD (sensitivity of 95%, specificity of 87%).

RESULTS: Complete information was obtained for 103 children (80% of 130 approached) of whom 19 children (18%) had scores consistent with a diagnosis of PTSD. 96% of the children were exposed to at least one trauma type and 39% were exposed to 3 or more trauma types; 4% reported no trauma exposure. 33% of the sample had experienced family violence, and 51% community violence. 25% of the total sample reported being bullied by their peers while only 2 of these New York City children reported the events of 9/11 as a trauma. 4 children reported a history of sexual abuse. Children meeting criteria for PTSD reported a higher mean number of trauma types (3.11 vs 2.13)* and were more likely to report family violence* or community violence* as the type of trauma experienced. The mean PTSRI score for the sample was 24.48 (SD of 13.93). Mean scores were lower for children identified as gifted and talented*, and were higher for children reporting bullying* and those whose parent reported the child had an emotional or behavioral problem.* PTSRI scores did not differ by sex, child age, race/ethnicity, history of foster care or domestic violence, owning cat/dog, or having ever seen a mental health professional.

CONCLUSIONS: Children in this primary care practice report high rates of trauma exposure, with a large proportion experiencing multiple traumas as reflected in the high rates of likely PTSD in the sample. Of note, "gifted and talented" was associated with lower mean symptom scores. Many children spoke of bullying while few mentioned sexual abuse or the events of 9/11 as significant stressors.

*$p<0.05$

130 Poster Board 14 Fellow in Training

Mothers' Attitudes About Vaccination

Ann C. Wu, Daryl Wisler-Scher, Katherine Griswold, Eve Colson, Eugene D. Shapiro, Eric Holmboe, Andrea L. Benin. Pediatrics, Yale, New Haven, CT; Pediatrics, Columbia, New York, NY; Northwestern, Chicago, IL; American Board of Internal Medicine, Philadelphia, PA.

BACKGROUND: Adverse publicity has led many parents to develop heightened concerns about vaccination.

OBJECTIVE: To describe mothers' attitudes about vaccination shortly after the birth of their child.

DESIGN/METHODS: We administered a questionnaire to English- or Spanish-speaking women 2-5 days post-partum. The 56 questions used Likert scales or were multiple choice and were derived from our prior qualitative study of attitudes about vaccines. Since our prior study showed that a trusting relationship with a pediatrician is the strongest determinant of positive attitudes about vaccination, we used multivariable linear regression to identify less trustful mothers

RESULTS: Of 296 mothers approached, 228 (77%) participated; 39% were primiparous, 23% received WIC, 75% planned to breastfeed. Twenty-nine percent felt worried about vaccinating their baby; and 4% reported that their child would get none or only some of the recommended childhood vaccinations. Eighty-nine percent felt that benefits of vaccination outweighed risks; 78% felt that the pediatrician's recommendation was a reason to vaccinate. When mothers ranked reasons to vaccinate, the most important was to prevent disease in the baby (74%). Mothers who were planning to breastfeed (P=.04), were having their first baby (P=.02), or had an income <$40,000 but did not receive WIC (P=.01) were less trusting. Mothers were not knowledgeable; e.g., only 15% knew that hepatitis B vaccine prevented liver cancer, 16% answered "not sure" when asked to choose from a list of side effects (fever, soreness, redness), and 10% chose autism as a side effect. Ninety-eight percent wanted information on diseases that vaccines prevent, names of vaccines, and side effects. For 70%, the best time to get such information about vaccines was during their pregnancy, yet only 18% received it during their prenatal care.

CONCLUSIONS: Even though the majority of mothers vaccinate their infants, mothers have concerns about vaccines. Special attention should be given to primiparous mothers, mothers with low family incomes who do not qualify for WIC, and breast feeding mothers. All mothers would like and would benefit from additional knowledge regarding the risk and benefits of vaccines, particularly during pregnancy.

131 Poster Board 15 Fellow in Training

Transmission Rates of Perinatally Acquired (PNA) HIV Infection in Newborns with and Without Sickle Cell Hemoglobinopathy (SCH)

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BACKGROUND: Worldwide, perinatal transmission has long been the predominant mode of acquiring pediatric HIV infection. Anecdotal observations suggest that PNA HIV infection is uncommon among children with SCH. Perhaps a selective advantage associated with SCH confers relative protection against PNA HIV infection similar to that enjoyed vis-à-vis malaria by persons with sickle cell trait (SA) living in malaria-endemic regions.

OBJECTIVE: To compare transmission rates of PNA HIV infection in HIV-exposed neonates with and without sickle cell disease (SS) or SA.

DESIGN/METHODS: All neonates perinatally exposed to HIV who were born at University Hospital (UH) [Newark, NJ] from 1997 through 2003 and followed at the François-Xavier Bagnoud HIV Screening Clinic were retrospectively identified from Clinic logs and cross matched with a list of contemporaneous UH neonates with SS or SA compiled from newborn screening test results maintained by the NJ Department of Health and Senior Services. Medical records were reviewed to determine ultimate HIV status and to verify SCH status. Transmission rates of PNA HIV infection by SCH status were calculated.

RESULTS: Overall, 44 of 324 neonates perinatally exposed to HIV were infected (transmission rate = 13.5%). Of exposed neonates with SS or SA, 4 of 48 (8.3%) were infected, whereas, of exposed neonates without SS or SA, 40 of 276 (14.5%) acquired HIV infection ($p = 0.36$).

CONCLUSIONS: Although lacking statistical significance, the transmission rate of PNA HIV infection was lower in subjects with SCH than in those without it. Studies with greater statistical power are needed to further explore this suggested association; potential protective mechanisms also await elucidation.

132 Poster Board 16

Transition of International Medical Graduates in an Inner-City Pediatric Residency Training Program

Vipin Agarwalla. Department of Pediatrics, Brookdale University Hospital Medical Center, Brooklyn, NY.

BACKGROUND: International medical graduates (IMGs) represent an increasing proportion of residents in pediatric residency training programs. Teaching IMGs presents important challenges to these programs. A paucity of literature exists on the topic of adjusting curriculum or programs to facilitate IMGs' adaptation to their new medical and personal situation.

OBJECTIVE: The objective of this curriculum is to facilitate the transition of IMG resident so that he/she will be able to competently deliver pediatric care to a diverse patient population in an inner city setting.

DESIGN/METHODS: Based on needs assessment and literature review, a four unit curriculum was designed with goals, objectives and instructional strategies to facilitate the transition of the IMG residents. The first unit was piloted and evaluated. An expert in curricular design and two educators and expert in cultural competency and IMG matters evaluated the entire curriculum.

RESULTS: Experts found the curriculum to be well designed and consistent. Residents found the pilot unit to be well designed and effective. Learner evaluation data from the pilot test indicated that this curriculum can increase resident's knowledge and skills.

CONCLUSIONS: With the increasing number of IMGs in U.S. residency programs the faculty must make a commitment to address their special needs and training requirements.

The implementation of a formal curriculum will enhance the process of transition for these residents. This might ease some of the identifiable problems faced by this substantial sector of health care providers. This will also lead to better performance of these physicians and result in improved patient care and satisfaction.

Four Units of the Curriculum

Aim of the Curriculum:To facilitate the transition of IMG pediatric residents enabling them to competently deliver pediatric care to a diverse patient population in an inner city setting

Unit 1. Introduction to Cultural Competency: Development of positive attitude and awareness of the knowledge and skills required in developing cultural competence in healthcare delivery

Unit 2. Personal adjustment: Adjust to daily living in the U.S

Unit 3. Professional adjustment: Adjust to the U.S. health care system with special reference to the needs of the patients from inner city neighborhood

Unit 4. Development of communication and language skills: Communicate well with patients

133 Poster Board 17 Ph.D. Student

"Dancing with Different Partners": The Impact of Restricted Work Hours on Learning in Continuity Clinic

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BACKGROUND: ACGME's work hour standard (WHS) has had far-reaching effects on GME. In continuity clinic, residents ideally attend the same afternoon clinic and are supervised by the same preceptors throughout their training. Rescheduling continuity clinic to comply with WHS may impact the longitudinal learning relationship between residents and continuity clinic preceptors (CCP).

OBJECTIVE: To explore residents' perceptions of the impact of the WHS on their continuity experience and on what they learn from CCPs.

DESIGN/METHODS: 3rd year pediatric residents (n=10) assigned to one community-based clinic, supervised by 10 CCPs, participated in qualitative interviews. 3rd year residents were purposefully selected because they could reflect on clinic experiences before and after WHS. Interviews were ivalidated by the respondents, inductively coded and thematically analyzed.

RESULTS: All residents identified the elimination of post-call clinic, described as *dreaded*, *painful* and *embarrassing*, as the *real difference* in their continuity experience since the implementation of WHS. Unsolicited comments about the effects of eliminating post-call clinic on learning were related to readiness to learn (*attentive*, *receptive to learning*) and discontinuity in the resident-CCP relationship (*harder to build on what you know, having to start back at square one with a different CCP*). A few mentioned that care provided by well-rested pediatricians was fairer to families; none said it was safer.

Residents offered a range of responses when asked about the effect of WHS on what they learned from CCPs. For some residents, learning was *about the same* because each CCP taught the basics of primary care. For others, learning had *absolutely changed* because variation in clinical management and expertise among CCPs increased the *depth and detail* of what they learned. All residents mentioned that seeing *different perspectives* and *different ways of doing things* was benefical because it helped them *figure out which style works best* for them.

CONCLUSIONS: WHS has generally improved pediatric residents' perceptions of their continuity experience and what they learn from CCPs because residents come to clinic ready to learn and because *dancing with different partners* exposes them to a panoply of practice styles.

134 Poster Board 18 Fellow in Training

Major Congenital Anomalies Place ELBW Infants at Higher Risk for Poor Growth and Developmental Outcomes

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BACKGROUND: Studies of growth & neurodevelopmental impairment (NDI) in ELBW infants often exclude infants w/ major congenital anomalies; thus, there is little outcome data available on these infants.

OBJECTIVE: To compare growth & NDI outcomes of ELBW infants w/ major anomalies/syndromes to ELBW infants w/o these findings. It is hypothesized that infants w/ anomalies will have worse growth & NDI.

DESIGN/METHODS: A retrospective cohort analysis of all ELBW infants born at 19 Neonatal Network Centers between 1993-2001 (n=13,611) was performed. 2,049 were excluded (1,985 died before 12h of life, 64 had missing information). 2,821 died before d/c. 52% of infants w/ anomalies (n=147) died before or shortly after d/c. Of survivors, 138 (1.6%) had major anomalies/syndromes. 81% of survivors (104 infants w/ anomolies & 6,896 control infants) underwent neurodevelopmental & growth evaluation at 18-22m CA. Socioeconomic/maternal & neonatal morbidity data was collected. Outcome variables were Bayley scores, NDI, CP, visual/hearing impairment, Wt, Lt, & HC. Wilcoxon & chi square tests were used to evaluate for significant differences between groups. Logistic regression models were used to explore associations between test group & outcomes.

RESULTS: Infants w/ anomalies were more likely than controls to have MDI<70, PDI<70, NDI, Wt<10th%, Lt<10%, HC<10th. Differences in rates of visual/hearing impairment & CP were not significant. After adjusting for center, neonatal, & SES variables, logistic regression models revealed increased risks for poor outcomes in test group:

Outcome	MDI < 70	PDI < 70	NDI	Wt < 10%	Lt < 10%	HC < 10%
OR(95% CI)	3.0(1.9,4.7)	2.6(1.6,4.2)	2.5(1.6,3.9)	2.0(1.2,3.2)	2.6(1.7,4.0)	1.9(1.2,3.0)
p value	< 0.0001	<0.0001	0.0001	0.0043	<0.0001	0.0031

CONCLUSIONS: ELBW infants born w/ major anomalies/syndromes have 2-3 times greater risk of poor growth & NDI compared to ELBW infants w/o anomalies. This is valuable information when counseling parents of & obtaining appropriate support services for ELBW infants w/ major anomalies.

135 Poster Board 19 House Officer

Effects of Discordance in Birth Weight on Postnatal Catch-Up Growth in Very Low Birth Weight (VLBW) Multiple Birth Infants

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BACKGROUND: With an increasing trend of multiple births the incidence of small for gestation age (SGA) discordant infant is rising (10% with twin and 47% with triplet pregnancies). Postnatal catch up

growth has been reported in term discordant twin infants (Marie P et al.). However, postnatal growth charecteristics of preterm SGA discordant multiple birth infants are not known.
OBJECTIVE: To evaluate the effect of intra-pair BW discordance on the postnatal catch-up growth of very low birth weight (VLBW) multiple birth infants in NICU.
DESIGN/METHODS: Of 50 sets of VLBW multiple birth infants (BW£1500g) born at two institutions and discharged between 1/1/95 and 9/1/04, 26 sets had more than 8% discordance in BW (Difference in BW/ /BW of larger infant) (Table 1.) Gender, gestational age (GA), birth and discharge weight (DW), length of stay (LOS), weight gain/day, and weight gain/kg of birth weight/day were compared between the smallest and largest infants using paired t-test.
RESULTS: The mean BW and GA of 26 pairs of discordant multiple birth infants were 1142±250g and 29±3wk respectively. The intra-pair BW difference varied from 70-714g (8.5-48%). The catch-up growth characteristics of the smallest and the largest VLBW multiple birth infants are in Table 2.
CONCLUSIONS: Despite of the lower DW and shorter LOS the smallest discordant VLBW multiple birth infant shows a significantly higher postnatal catch up growth than the lagest one. We speculate that SGA VLBW multiple birth infant with intrauterine growth restriction may have adaptive metabolic programing for rapid postnatal catch up growth.

Table 1. The type and number of sets of VLBW multiple birth infants born, discharge, and discordance(N=50)

Type	# of sets born	# of sets discharged	# of sets with discordance
Quadruplet	2	1	1
Triplet	10	10	9
Twins	38	28	16
Total	50	39	26

Table2. The comparison of growth characteristics

Variables	Largest discordant infants	Smallest discordant infants	P value
Birth Weight(g)*	1280±221	1004±198	<0.0001
Male/Female	14/12	9/17	0.15
DW(g)*	2302±276	2181±212	0.034
LOS(d)*	56±20	62±19	0.049
Weight gain(g/d)	19.1±3.3	19.4±3.3	0.65
Weight gain/kg of BW/day*	15.4±3.6	19.0±1.2	<0.0002

136 Poster Board 20

RSV Prophylaxis in a Second Season: How Effective Is It?

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BACKGROUND: RSV causes acute respiratory tract illness in patients of all ages, and is the leading cause of LRTI in infancy and childhood. RSV hospitalization costs are substantial, and higher for patients with lower gestational age, lower BW, BPD and younger age. Palivizumab prophylaxis has been shown to reduce hospitalizations for infants at-risk. The AAP recommends palivizumab prophylaxis for infants Ω2 yrs old with chronic lung disease (CLD/BPD), hemodynamically significant congenital heart lesions or other serious conditions that compromise pulmonary or immune functions (other than prematurity).
OBJECTIVE: To describe the results of infants receiving their 2nd season of palivizumab RSV-prophylaxis
DESIGN/METHODS: Prospective F/U of all infants receiving RSV-prophylaxis, either at home or at the pediatricians' office during the 2003-04 season.
RESULTS: A total of 582 patients were followed from November 2003 through April 2004, 394 (68%) receiving their doses at home, and 188 (32%) receiving them at the MD office. Data is shown as mean±SD(median).There were no differences between both groups: GA 30.5±4(31) wk, BW 1545±718(1446) gr. The distribution of population by GA was: <28wk=110 infants;28-31 wk= 169;32-35 wk=193;>35 wks=53;no GA available= 57. A total of 2321 injections were given (home=1687; office=634), with an average of 3.9/patient. The age at the beginning of the season was 403±153(343) days. Neither RSV cases nor RSV hospitalizations were reported in either population. No significant adverse effects were noted.
CONCLUSIONS: Children receiving palivizumab prophylaxis for a second season tolerated the injections without problems and had no RSV hospitalizations. Several bigger premature infants received palivizumab prophylaxis during the season. Although the results are encouraging, more education seems to be necessary in our area regarding the appropriate indications for the 2nd season prophylaxis. Because health care budgets are limited, economic analyses are needed to optimize the allocation of resources in health care.
Funded by MedImmune; Curative Health Services.

137 Poster Board 21

Role of Serum Transforming Growth Factor b 1 and Vascular Endothelial Growth Factor in the Prediction of Bronchopulmonary Dysplasia—A Pilot Study

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BACKGROUND: Increasing survival of extremely low birth weight (VLBW) infants has contributed to an increased incidence of bronchopulmonary dysplasia (BPD). While standardized care of these infants continues to evolve, the basic mechanisms leading to the development of BPD remain elusive. Furthermore, there are no reliable methods to predict the development, severity and progression of BPD.
Infants with BPD have increased expression of lung specific TGF-b 1 (a key cytokine in controlling repair) and low levels of vascular endothelial growth factor (VEGF, a cytokine required for angiogenesis and lung development), in tracheal aspirates (TA's).
OBJECTIVE: This IRB approved study was designed to determine preliminary data for serial serum levels of TGF-b 1and VEGF and to correlate serum levels with the development and severity of BPD
DESIGN/METHODS: Preterm neonates less than 32 weeks had serum specimens drawn at birth, and on day 7 for analyses of TGF-b 1 and VEGF. We used average value of the cytokines drawn on these two days, in each patient. Clinical data including patient demographics, clinical risk index for babies (CRIB score) and data on possible risk factors for BPD such as gestational age, prenatal steroids, ventilation, oxygen requirement, patent ductus arteriosus, sepsis etc were recorded. BPD was defined as continued oxygen requirement and /or need for continuous positive pressure ventilation at 36 weeks post menstrual age with radiological changes suggestive of BPD.All samples were analyzed using ELISA techniques. Data were statistically analyzed using SPSS 12.We used discriminant analysis with a step-wise entry, using only variables known during the first week of life.
RESULTS: A total of 18 patients were recruited into the study – 6 patients developed BPD and 11 did not. Of the variables studied, three variables differentiated BPD (n=6) vs. non-BPD (n=12): CRIB score (6.2 ± 5.3 vs. 1.1 ± 1.2), log VEGF (2.8 ±1.8 vs. 4.5 ± 2.0) and C-section (100 % vs. 42 %). The Wilk's lambda was 10.73, p = 0.001.Predicted BPD vs. non-BPD on a small sample using this model was correct in 17/18 patients.
CONCLUSIONS: Serum levels of VEGF in the first week of life in VLBW could be utilized as a marker for prediction of BPD. Larger sample size is needed to arrive at a meaningful predictive model.

138 Poster Board22 Fellow in Training

Will an "Optimal FRC" Strategy Minimize Volutrauma-Associated Lung Injury?

Abdul Haleem, Ravi Mishra, Lance A. Parton, Ioana A. Godi, Sergio G. Golombek, Edmund F. LaGamma. Neonatology, Maria Fareri Children's Hospital, Valhalla, NY.
BACKGROUND: A "*lung protective strategy*" (ventilating above & below the compliance inflection points) reduces local and systemic cytokines levels in ARDS patients(JAMA 281:54,1999). Using our similar *Optimal FRC* approach, any pCO_2 is allowed as long as the pH is > 7.20 and the base deficit is < -5 meq/L (AmJPerinatol 20:453,2003).
OBJECTIVE: To determine whether using similar blood gas targets an *Optimal FRC* ventilation strategy (on-line ventilator graphics) is associated with lower levels of inflammatory mediators compared to conventional management (without graphics) .
DESIGN/METHODS: All infants were managed on assist-control (AC) ventilation (VIP-Bird) with termination sensitivity at 5%. Subjects had birth weights <1000g, clinical or radiological evidence of HMD & required mechanical ventilation on postnatal day1. Exclusion criteria: Early onset sepsis, major congenital anomalies or anticipated need for < 24h of ventilatory support. During the first postnatal week demographic data were recorded as was IL-6 & IL-8 levels in tracheal aspirates and serum using ELISA. Sequential comparisons were performed using a two-way ANOVA or t-test where appropriate.
RESULTS: The average weight of patients in the"loop-seen" was(n=27; 738 ± 26 g) vs. (n=20; 704 ± 32 g) in the "loop-not seen" group. No significant differences were noted in either achieved ventilator settings or in cytokines levels observed between the two groups. Aggresssive weaning of pressure by our clinicians resulted in a decrease in the mean airway pressure and oxygenation index in both study groups. The incidence of O_2 requirement after 36 weeks was identical in both groups (40% vs 29%, NS).
CONCLUSIONS: Targeted blood gas values were as effective as using lung mechanics in minimizing volutrauma while on AC ventilation since our clinicians are entrained to this approach. This expensive ventilator option may not be necessary as there appears to be other causes of CLD independent of VILI.
DEMOGRAPHIC AND LUNG FUNCTION DATA

X±SEM (range)	n	GA	Birth Wt.(g)	PIP at start	PIP at 48hr	TV at start ml/kg	TV at 48hr ml/kg
Loop seen	27	26±0.3 (23,29)	738±26 (475,960)	12.4±0.2 (10,14)	10.6±0.5 (8,16)	6.3±0.6 (4.2,12.2)	4.8±0.7 (2,8.4)
Loop covered	20	26±0.3 (24,29)	704±32 (420,950)	13±0.5 (11,16)	11±0.4 (8,13)	6.2±0.7 (2.4,9.6)	4.4±0.7 (1.6,8.2)

Funded by Forest Laboratories.

139 Poster Board 23 Fellow in Training

Anemic Spleen, a Sentinel Sign of Perinatal Hemorrhage

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BACKGROUND: Perinatal hemorrhage is a common cause of morbidity and mortality. A bloodless spleen is a frequent histologic finding.
OBJECTIVE: Our study compares microscopic findings in the spleen where perinatal hemorrhage was present and in cases where the cause of death was unrelated to perinatal hemorrhage.
DESIGN/METHODS: Spleens from 64 consecutive perinatal autopsies performed at Kings County Hospital Center were reviewed. Stillborn and liveborn cases were included. Gestational age ranged from 21 weeks of gestation to 7 days after delivery. Clinical charts were reviewed for signs and symptoms of perinatal hemorrhage, including placental abruption, retroplacental hematoma, pulmonary and intraventricular hemorrhage. Twenty-three cases without perinatal hemorrhage were taken as controls. Twenty-one autopsies with hemolytic disease and infectious conditions such as pneumonia, splenitis, and ingestion of infected amniotic fluid were excluded. Morphologic analysis of the spleen sections evaluated the capsule trabeculae and red pulp. In addition, the weight and gross appearance were compared between perinatal hemorrhage cases and controls.
RESULTS: At autopsy anemic spleens had depleted red pulp with prominent trabeculae, wrinkled capsule, and visible hematopoiesis. The cord literal of cells appears prominent and islands of nonreactive white pulp are easily seen. In control cases white pulp is less evident, trabeculae are absent and the capsule smooth.

Anemic spleen morphology and perinatal hemorrhage

	Anemic spleen	Normal spleen
Perinatal hemorrhage	19	1
No perinatal hemorrhage	0	23

Anemic spleen morphology is a reliable indicator of perinatal hemorrhages.
Prevalence of perinatal hemorrhage in all cases reviewed was 20% (13/64). Sensitivity and specificity of anemic spleen findings were 95% and 100%, respectively. The weight and gross appearance were not affected grossly.
CONCLUSIONS: The microscopic findings of an anemic spleen on light microscopy have a 95% chance to be seen in a case of perinatal hemorrhage. However, if not seen, that reliably excludes the presence of perinatal hemorrhage. Histologic sections of the spleen frame the case as death from catastrophic hemorrhage by rapidly targeting the immediate cause of death.

140 Poster Board 24 Fellow in Training

Butyrate Protects Lung Epithelial Cells from Pro-Inflammatory and Nitric Oxide-Mediated Damage

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BACKGROUND: Sodium butyrate (NaB) is a short chain fatty acid that is produced by intestinal flora following the initiation of feedings in the neonate. It inhibits histone deacetylase, and modulates the balance among proliferation, differentiation and apoptosis. The potential beneficial effects of NaB include the repression of iNOS expression, and anti-inflammatory effects on lung cells. Previously we have reported that elevated airway pro-inflammatory cytokines are present in ELBW infants who progress to BPD as early as the 1st week of life. Since ELBW infants may have delayed initiation of enteral feedings during this period, we wanted to determine whether NaB could offer protection from airway pro-inflammatory mediated damage that is being activated during this same period.
OBJECTIVE: To evaluate the response of lung epithelial cells to NaB in the presence of the pro-inflammatory mediator Interleukin-8 (IL8) and following Nitric Oxide (NO) exposure.
DESIGN/METHODS: A549 cells (human lung adenocarcinoma cells) were either treated with 1mM NaB or pretreated (30min) with 1mM NaB (PRE NaB) followed by exposure to the pro-inflammatory agent IL8 (300ng/ml) or to the NO donor DETANONOate (0.4mM). Apoptosis was quantified at 0, 2, 4 and 6h using cell death detection ELISA. Necrosis was assessed at 0, 2, 4 and 6h by lactate dehydrogenase (LDH) release into the supernatant. ANOVA was used to compare the 3 groups exposed to IL8 or NO. A *P* value < 0.05 was statistically significant.

RESULTS: Pretreatment with NaB for 30 min significantly decreased the rate of apoptosis (Table) and the release of LDH (Table) from these lung cells following exposure to both IL8 and a supraphysiologic level of NO for 4h (P<0.001).

LDH Released

	Control*	IL8*	NO*
4h-No NaB	0	0.06±0.001	0.17±0.001
4h-NaB	0.16±0.006	0.19±0.006	0.19±0.003
4h-PRE NaB	0	0	0

Mean±SD, *P<0.001

Apoptosis

	Control*	IL8*	NO*
4h-No NaB	6.9±0.5	68.7±1.3	83.8±0.6
4h-NaB	84.4±2.6	63.7±2.5	76.6±6.4
4h-PRE NaB	5.4±0.2	4.4±0.8	4.4±1.0

Mean±SD, *P<0.001

CONCLUSIONS: Pretreatment with NaB significantly reduced both apoptosis and necrosis following exposure to IL8 and NO-donor in this *in vitro* lung epithelial model. We speculate that intestinal-derived butyrate may offer protection from ELBW lung inflammation.

141 Poster Board 25

Cardio-Respiratory Function of Preterm Infants Placed in Car Seats: Risk Factors and Outcomes

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BACKGROUND: Little is known about factors that predispose to the occurrence and severity of cardio-respiratory dysfunction during placement of prematurely born infants in a car seat.

OBJECTIVE: To investigate the impact of gestational age, weight at discharge and the infant's pre-existing cardio-respiratory dysfunction (in the supine position) on the cardio-respiratory function during placement in the car seat (semi-upright position).

DESIGN/METHODS: Forty-two preterm neonates with gestational age 24 to 35 weeks and discharge weight 1790 to 2570 grams were monitored (prior to discharge from the NICU) for the detection of cardio-respiratory function abnormalities before, during, and after placement in a car seat (45 minutes in each position). The occurrence of periodic breathing, apnea, bradycardia, oxygen desaturation or any combination of these symptoms was analyzed with respect to gestational age, weight at discharge, and pre- and post-testing abnormalities.

RESULTS: We found that during car seat placement, periodic breathing, oxygen saturation<90%, heart rate< 80 per minute, or a combination of these symptoms occurred in 59.6, 78.2, 33.3, and 83.3% of these infants, respectively. For infants with and without pre-existing cardio-respiratory dysfunction, the probability for developing cardio-respiratory events during placement in the car seat was similar (80% vs. 83.3%, respectively). Increased episodes of oxygen desaturation alone or a combination of cardio-respiratory symptoms that occurred during placement of these infants in the car seat were associated with the weight at discharge (<2,000 grams) but not gestational age (Ω28 weeks or >28<37 weeks). Repositioning from the car seat to the supine position showed normalization of cardio-respiratory function in the majority (83%) of the tested infants. None of the tested clinical factors were associated with the severity of the cardio-respiratory symptoms.

CONCLUSIONS: Pre-discharge cardio-respiratory testing during placement of preterm infants in a car seat is important for the prevention of cardio-respiratory dysfunction during their transportation. However, the high risk for the development of cardio-respiratory symptoms will require an alternative mode of safe transportation for preterm infants, especially those with a discharge weight <2,000 grams .

142 Poster Board 26 House Officer

Effect of Recombinant Human Erythropoietin (rhEPO) on the Development of Retinopathy of Prematurity (ROP)

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BACKGROUND: Non-hematopoietic effects of erythropoietin on the increased release of endothelin-1 and the stimulation of angiogenesis has been reported (Carlini R et al.).

OBJECTIVE: To determine the effect of rhEPO on the development ROP in very low birth weight (VLBW) infants.

DESIGN/METHODS: Retrospective case control analysis was done for 85 VLBW infants born with gestation age(GA)Ω32 wks at 2 institutions between 1/1/02 and 12/1/04. The rhEPO dose was 200-250 unit/kg/dose every alternate day. Ophthalmologic examinations were done at the age of 5 to 6 wks and followed by 1-4 wks interval. The data were analyzed using SPSS by chi-square test, logistic regression analysis and Spearman rank order correlation (rs).

RESULTS: Out of 85 VLBW infants, 38(45%) were male and 47(55%) were female. 56(66%) infants received rhEPO while 29(34%) infants did not receive rhEPO. In the rhEPO and non-rhEPO groups, the mean birth weights were 1000 and 1010 gram, mean GA were 28.3 and 27.9, ROP was 12(21%) and 11(38%) respectively. The rate of ROP was not significantly different(P=0.10). Logistic regression analysis adjusted by gestation age, oxygen dependency at 28 days of life and sepsis also showed no significant difference in ROP(P=0.18). Among the infants who received rhEPO, there was no correlation between the exposure or duration of rhEPO and stage of ROP, plus disease, threshold disease and surgery required for ROP. However, there was a significant weak positive correlation between the duration of rhEPO treatment and development of prethreshold disease.

CONCLUSIONS: The study showed no significant difference in the rate of ROP between rhEPO and non-rhEPO group. However, a significant tendency of prethreshold disease associated with the duration of rhEPO therapy warrants further studies in rhEPO on the growth and development of retinal vessels in preterm infants.

Correlation between duration of rhEPO treatment and severity of ROP (n=56)

Severity of ROP	Spearman(rs)	P value
Staging	0.37	0.36
Plus disease	0.21	0.11
Pre-threshold disease*	0.29	0.03
Threshold disease	0.24	0.07
Surgery required	0.21	0.11

143 Poster Board 27 Fellow in Training

Use of Vinyl Bags in the Delivery Room Prevents Hypothermia in Preterm Very Low Birth Weight Infants

Bobby Mathew, Satyan Lakshminrusimha, Katherine Cominsky, Eileen Schroeder, Vivien Carrion. Pediatrics, The Women and Children's Hospital of Buffalo, Buffalo, NY.

BACKGROUND: Significant evaporative heat loss occurs in newborn infants in the delivery room (DR). Previous studies have shown that the use of polyethylene bags in the DR reduces hypothermia and mortality in low birth weight infants Ω32 weeks gestation age (GA).

OBJECTIVE: This study evaluated the use of vinyl bags (Vi-Drape® isolation bag) in very low birth weight infants Ω28 weeks GA in the DR and its effect on admission temperature, morbidity and mortality.

DESIGN/METHODS: Twenty four infants Ω28 weeks GA were allocated to the Vi drape bag group or standard care before delivery. Eleven infants were placed in Vi drape bags immediately following delivery without drying. Thirteen control infants received standard care with drying and placement under a radiant warmer. Vital signs including axillary temperature were taken on admission to the neonatal unit. Patient characteristics such as GA, birth weight, sex, race, prenatal care, antenatal steroids, maternal infection, worst pH and base deficit in the first 6 hours, intraventricular hemorrhage (IVH), time to regain birth weight and mortality at 30 days were evaluated.

RESULTS: There were no significant differences in the baseline characteristics such as GA, birth weight, cord pH and base deficit or time for transfer to the neonatal unit. No infant in the Vi drape group had a temperature less than 35°C on admission compared to 5 infants in the standard treatment group (p<0.05 by Fisher exact test). The average temperature in Vi drape group was significantly higher (35.9 ± 0.17 vs. 35.1 ± 0.19°C, p < 0.005 by unpaired 't' test). One infant in the Vi drape group and 3 infants in the standard treatment group died in the first 30 days. Mean worst pH and base deficit in the first 6 hr were 7.3/-5 in the Vi drape group and 7.2/-7 in the standard care group. None of these parameters reached statistical significance. There was no significant difference in incidence or severity of IVH.

CONCLUSIONS: This study demonstrates that admission temperatures are significantly better when extremely premature babies are placed in vinyl bags without drying. There is a tendency towards less mortality in this group although statistical significance was not reached due to small sample size. We conclude that this simple intervention is effective in maintaining temperature in very low birth weight infants.

144 Poster Board 28

Tocolysis with High Dose Magnesium Sulfate ($MgSO_4$) Increases the Risk of Death in Extremely Low Birth Weight (ELBW) Infants

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BACKGROUND: Mothers in preterm labor with ELBW fetus (weight < 1000 gm) are aggresively tocolyzed to increase the gestational age (GA) and decrease postnatal mortality and morbidity. This, and improved postnatal care have decreased the GA limit of neonatal viability and less mature infants are resuscitated and treated in NICU. It is possible that mortality and its predictors have changed in ELBW infants.

OBJECTIVE: To determine the risk factors for death in ELBW infants

DESIGN/METHODS: All ELBW infants born during a 2-year study period were studied as survivors (S) and non-survivors (D, death before DOL 28). Standard maternal variables including PROM, delivery mode, any tocolysis, multiple tocolytics, $MgSO_4$ tocolysis and dose, labor duration, steroid and antibiotics use; neonatal variables including birth weight (BW),GA, race, sex, Apgar score at 1 and 5 minutes (Ap 1 and 5), DR resuscitation, surfactant use, degree of ventilatory support, need of inotropes (IN) and fluid intake/output during DOL 0-7, PDA, IVH (≥ grade3), antibiotics days, postnatal steroid, BPD (O_2 need on DOL 28); and placental histopathology were analyzed. Wilcoxon Rank Sums, chi square and Fisher's exact tests were done for group comparisons. Data are expressed as mean (SD), median (range) and ratio and proportion. P value ≤.05 indicated significance.

RESULTS: 59 infants were studied of which 11 died (18%). D infants had lower BW (658 ±144 vs. 778±158 gm, p.02) and Ap 5 (median and range, 6 and 5-8 vs. 7 and 2-9, p.01). D required higher PIP (16±5.4 vs.12±2.5 cm H_2O, p.02) and FiO_2 on DOL 3 (58±29 vs. 37±13 %, p.03). 44% in D received IN compared to 0% in S (p.0001). 40% in D and 12% in S received only $MgSO_4$ for tocolysis (p.04). Use of mutiple tocolytics did not differ (38% vs.18 %, p.2). Total dose of $MgSO_4$ was higher in D (33.2 ±28 vs. 10.2 ±23 gm, p.01). 50% infants in D and 10% in S received $MgSO_4$ in cumulative doses > 10 gm (p.008).

CONCLUSIONS: Tocolysis with $MgSO_4$ in high doses is associated with a greater risk of neonatal death in ELBW infants. Infants who die are also smaller, depressed at birth, and require inotropic and higher ventilator support for hypotension and respiratory distress during the immediate neonatal period.

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Phosphorus Initiative in a Pediatric Dialysis Program

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BACKGROUND: Hyperphosphatemia contributes toward renal osteodystrophy ("ROD") in pediatric hemodialysis patients with resulting impairment of growth. Phosphate binders are a key treatment for ROD. A multidisciplinary team developed a short-term phosphorus initiative to increase patients' awareness and control of phosphorus, with three components: teaching, participation, and incentive, as a quality improvement project.

OBJECTIVE: To evaluate patient understanding of phosphorus levels, diet and binders; to find interventions which encourage compliance with prescribed binders; and to assess outcome of intervention as evidenced by phosporus levels.

DESIGN/METHODS: An age-appropriate teaching tool was created to supplement standard intervention (dietitian review of diet and monthly "report card"). Intensive, individual evaluation and teaching was done by child life specialist and nursing staff during hemodialysis. Each child decorated a paper "bone" placed on a wall graph in yellow (low), green (target), or red (high) range each month, as visual reinforcement. Target range for phosphorus was 3.5-5.5, following the K/DOQI guideline for patients with kidney failure. Patients achieving target levels received incentive movie tickets.

RESULTS: Eight patients undergoing chronic hemodialysis were entered into the initiative. Four had normophosphatemia and four had hyperphosphatemia during the four months prior to the intervention; all were treated with CaCO3 (1g-2.4g TID with meals). The doses were not changed during the initiative. Overall phosphorus levels were lower, and the percent of values within the target range were higher, during the intervention period. Serum calcium levels were normal throughout. Three out of four patients with high phosphorus levels prior to the intervention achieved normoophosphatemia during the intervention.

CONCLUSIONS: A initiative that increased patients awareness of phosphorus levels, diet and binders resulted in short-term improvement of phosphorus levels. The child life specialist played a major role within the multidisciplinary team in creating a teaching tool and visual reference to encourage patient participation in the initiative. Patients demonstrated retention in talking with the team and each other about their lab values. A finer assessment of teaching tools and outcome measures for this initiative is in progress.

146 Poster Board 30 Fellow in Training

Racial Background Has No Effect on the Characteristics of Primary Hypertension in Children

Tammy M. Brady, Joseph T. Flynn. Pediatrics, Johns Hopkins School of Medicine, Baltimore, MD; Pediatric Nephrology, Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: Many studies have shown that normal blood pressure (BP) differs in children of different races, with non-white children generally felt to have higher BP than white children. However, it is unknown whether children with confirmed hypertension (HTN) exhibit similar differences.

OBJECTIVE: To determine whether the characteristics of children with primary HTN vary by race.

DESIGN/METHODS: Children referred for evaluation of elevated BP and diagnosed with primary HTN at the Children's Hospital at Montefiore, Bronx, NY between 2001-2004 and at the University of Michigan between 1995-2000 were studied retrospectively. Characteristics at the time of initial evaluation were examined for differences by racial group.

RESULTS: 137 children were diagnosed with primary HTN. Of these, 92 (67%) were male and 45 (33%) were female. 26 (19%) were African American, 73 (53%) Caucasian, 10 (8%) Caucasian-Hispanic, 25 (18%) Caribbean-Hispanic, and 3 other races. For this analysis, children were grouped as either white (n=73) or nonwhite (n=64). There was no difference in age at first visit among white/nonwhite (both 13.3 yrs, p=NS) and there was no significant difference in mean systolic or diastolic BP index (BP/95th percentile BP; SBP 1.11 vs 1.10, p=NS, DBP 0.94 vs 0.90, p=0.09). Lipid profiles (total cholesterol, LDL, HDL and triglycerides) were also similar among the two groups, as were fasting insulin and glucose. 85.5% of whites reported a family history of hypertension compared to 93.4% of nonwhites (p=0.15). LVH was found in 25.4% of whites and 34.2% of nonwhites (p=NS). Characteristics found to differ significantly between the two groups were BMI (whites vs nonwhites: 27.2 vs 32.1kg/m2, p=0.003) and serum sodium (whites vs nonwhites: 141 vs 140 mEq/dL, p=0.01).

CONCLUSIONS: In this cross-sectional study of children with primary HTN seen at referral centers, few characteristics varied significantly between white and non-white children at time of diagnosis of HTN. BMI was significantly higher in nonwhites, which is consistent with other data independent of hypertension. Serum sodium was significantly higher in white children, a finding that warrants further investigation

147 Poster Board 31 Fellow in Training

Urinary Proteomic Arrays of Atherosclerotic Cytokines in Patients with Steroid-Resistant (SRNS) and -Sensitive Nephrotic Syndrome (SSNS)

Ibrahim F. Shatat, Robert P. Woroniecki, Katarina Supe, Frederick J. Kaskel. Pediatric Nephrology, Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: Patients with SRNS have an increased risk of progression to end stage renal disease (ESRD) and atherosclerotic complications. Statin therapy may delay progressive loss of renal function. It is unclear if patients with SRNS have different urinary excretion of atherosclerotic cytokines during the course of their disease compared to patients with SSNS.

OBJECTIVE: We hypothesized that urinary excretion of cytokines associated with atherosclerosis is greater in patients with SRNS, before the onset of ESRD, as compared to SSNS and controls.

DESIGN/METHODS: We obtained clinical data and used the proteomic approach to analyze the urine in 8 patients with new onset SRNS, SSNS, and in controls (CTR). We arrayed 20 urinary cytokines linked to atherosclerosis. The subjects' age ranged from 5-18 years old. To account for steroid effects on cytokine expression, we used control subjects that were treated with high dose steroids for chronic asthma, and had no proteinuria. The experiment was performed in duplicate for reproducibility.

RESULTS: Our subjects were divided into three groups: 3 patients with SRNS, 3 patients with SSNS, and 2 CTRs. Blood pressure in all three groups was <90% for age and height. Mean body mass index was 23.13 in patients with SRNS, 23.16 in patients with SSNS, and 26.85 in the CTR group. There was no difference in the mean urine protein/ creatinine ratio between the SRNS group and SSNS group (p=0.26). Average serum cholesterol (mg/dl) was 191 in the SRNS group, and 291 in the SSNS group (p=0.44). Mean serum creatinine (mg/dl) was 0.76 in both SRNS and SSNS groups, and 0.45 in the CTR group (p=0.51). Overall, there was increased urinary expression of cytokines associated with atherosclerosis in patients with nephrotic syndrome (NS) compared to the CTR group. However, comparing to the CTR group, the level of MCP-1 expression was increased in both SRNS and SSNS patients. RANTES expression was increased in SRNS as compared to SSNS and CTR group.

CONCLUSIONS: Measurement of urinary cytokines proved to be a reproducible and sensitive test. We identified differentent cytokine expression among SSNS, SRNS and CTR groups. These differences may permit early identification of a subgroup of patients with NS that have an increased risk for atherosclerotic disease and deterioration of renal function.

Funded by Emerald Foundation Inc.

148 Poster Board 32 Fellow in Training

Short Bowel Syndrome: Incidence, Morbidity, Mortality and Predictive Factors for Survival

Parul Shah, Farida Nentin, Gustavo Stringel, Boriana Parvez. Pediatrics, NYMC, Maria Fareri Children's Hospital at WMC, Valhalla, NY; Surgery, NYMC, Maria Fareri Children's Hospital at WMC, Valhalla, NY.

BACKGROUND: Short bowel syndrome (SBS) is defined as malabsorptive state, occuring after intestinal resection. Majority of the patients present in the neonatal period, following NEC, intestinal volvulus or atresia, gastroschisis or Hirschsprung's disease. These patients receive TPN for an extended period of time, which leads to multiple morbidities, including cholestasis, central line sepsis and liver failure.

OBJECTIVE: To determine the incidence, morbidity and mortality of SBS, following NEC and to identify predictive factors for mortality of SBS at our Regional Perinatal Center.

DESIGN/METHODS: We performed retrospective chart review of SBS patients, following surgical NEC, from January 2000 to December 2003, as part of an ongoing project for establishing a SBS database and multi-disciplinary SBS team. SBS was defined as TPN dependence for > 90 days. Statistical analysis was done using two-sample Wilcoxon test. p value of <0.05 was considered statistically significant.

RESULTS: Out of the 50 patients with NEC, 12 (24%) developed SBS. The mortality was 41% (5/12). Survivors achieved full enteral feeds at 138 ± 53 days compared to non-survivors, who never reached full feeds. All SBS patients had at least one episode of sepsis (3 ± 3). Survivors were discharged home at 45 ± 3 weeks corrected age (CA). Although they were all appropriate for GA at birth, at discharge 85% of them had failure to thrive, with weights in 5 being < 5% and head circumference in 6 < 5% for their CA. As shown in the table, non-survivors had higher peak conjugated bilirubin, longer duration of TPN and longer length of stay.

CONCLUSIONS: SBS in neonates is associated with a high mortality and multiple morbidities. High conjugated bilirubin is predictive of mortality. Most SBS patients demonstrate failure to thrive at discharge. We speculate that strict management protocol by a multi-disciplinary SBS team would reduce the mortality and morbidities of neonatal SBS.

	Survivors N=7	Non-survivors N=5	p
TPN duration (days)	115±13(99-131)	171±73(99-294)	0.09
Peak D bilirubin (mg/dl)	8±6(1-20)	25±14(10-42)	0.02*
LOS (days)	130±22(108-162)	176±75(100-295)	0.33

mean±SD(range)

Cardiopulmonary Development Platform Session

Sunday, March 6 9:45 AM-11:45 AM Mead B

149 Presentation Time 9:45 AM

Intracellular Calcium Signals in the Anterior Heart Field Affect Development of the Cardiac Outflow Tract

George A. Porter. Pediatrics, Yale University School of Medicine, New Haven, CT.

BACKGROUND: The anterior heart field generates myocytes for much of the cardiac outflow tract, which is a major site of congenital heart lesions. We have previously demonstrated that altered intracellular calcium signaling causes abnormal development of the cardiac outflow tract. Conversely, others have shown that hearts of embryos with abnormal outflow tract development also have abnormal intracellular calcium signaling.

OBJECTIVE: Our objective was to determine the effects of altered calcium signals on the differentiation and migration of myocytes from the anterior heart field into the cardiac outflow tract.

DESIGN/METHODS: Outflow tracts and anterior heart fields from E9.5 mouse embryos were cultured on collagen plugs for up to one week in the presence of vehicle or experimental agents and harvested for immunolabeling and gene expression analysis. To examine differentiation and migration, samples were stained with antibodies to myosin heavy chain. Quantitative RT-PCR was performed to compare the expression levels of a number of genes expressed in differentiating cardiac myocytes and normalized to the expression of the housekeeping gene Rpb1.

RESULTS: The differentiation and migration of anterior heart field cells toward the cardiac outflow tract was inhibited by the calcium channel blocker, nifedipine, in a concentration dependent manner. For example, 100 nM nifedipine had little effect, while in specimens treated with 10 and 100 uM nifedipine, no differentiation or migration was seen. Conversely, adding the calcium channel agonist, BayK8644, or increasing extracellular calcium in the media dramatically increased the number of differentiated cardiac myocytes as well as the migration of these cells toward the developing outflow tract. In contrast, ryanodine and dantrolene, which alter the activity of the ryanodine receptor, did not inhibit differentiation and migration of myocytes.

CONCLUSIONS: Altering intracellular calcium signals derived from the extracellular fluid via L-type calcium channels affects the development of the cardiac outflow tract by decreasing the differentiation and migration of cells from the anterior heart field. These results suggest that intracellular calcium signals are an important modulator of cardiac development, especially in the outflow tract.

150 Presentation Time 10:00 AM

Sox4 Is Required for Development of the Heart and Nervous System in the Zebrafish

Kathryn Maschhoff, Jeffrey Hannah, Alvin Chin. Neonatology, Children's Hospital of Philadelphia, Philadlephia, PA; Cardiology, Children's Hospital of Philadelphia, Philadlephia, PA; Pediatrics, University of Pennsylvania, Philadelphia, PA.

BACKGROUND: The Sox family of conserved transcription factors plays a critical role in the regulation of embryonic development. One member of this family, Sox4, is required for normal cardiac development. Sox4 deficiency results in abnormal patterning of neural crest cells and in defects in septation of the outflow tract, inculding persistent truncus arteriosus. Sox4 deficiency also leads to dysplasia of the semilunar valves. Because of its rapid embryonic development and ability to be experimentally manipulated, the zebrafish, Danio rerio, is a useful tool for studying the role of genes in cardiac development. In contrast to higher vertebrates, the zebrafish outflow tract remains unseptated. Thus, this experimental system allows us to study the role of Sox4 in valvulogenesis seperately from its role in outflow tract septation.

OBJECTIVE: Compare the protein sequence and expression pattern of zebrafish Sox4 with that of its mouse and chicken counterparts. Use antisense morpholinos to determine the function of Sox4 in zebrafish cardiac development.

DESIGN/METHODS: Sox4 expression was detected by in situ hybridization. Zebrafish embryos were injected with Sox4 antisense morpholinos. The resulting morphants were analyzed by HE staining, whole mount in situ hybridization, and TUNEL staining.

RESULTS: As in the mouse and chicken, Sox4 is present in the nervous system, heart, and branchial arches in the zebrafish embryo. In particular, we detected expression in structures populated by neural crest cells. 48 hours after injection of anti-Sox4 morpholinos, the majority of morphants showed clear evidence of cardiac failure with a prominent pericardial effusion. Close examination of these embryos revealed regurgitation of blood within the heart with little circulation of blood throughout the embryo. In addition, the heart rate was markedly decreased in most morphants. Abnormalities of the brain were evident as well, with the brain appearing necrotic in many morphants.

CONCLUSIONS: In the zebrafish, Sox4 is required for the development of valve function, even prior to the onset of endocardial cushion formation. Our studies of Sox4 in zebrafish have also revealed a role for this gene in neural development.

151 Presentation Time 10:15 AM

CEACAM6 in Human Fetal Lung Epithelial Cells: A Newly Identified TTF-1 Responsive Gene

Venkatadri Kolla, Linda W. Gonzales, Ping Wang, Sreedevi Angampalli, Kelly C. Wade, Philip L. Ballard. Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; School of Medicine, University of Pennsylvania, Philadelphia, PA.

BACKGROUND: Thyroid transcription factor-1 (TTF-1) is essential for both early fetal lung morphogenesis and *in vitro* surfactant protein (SP) gene expression by epithelial cells, but the TTF-1 responsive target genes have not been largely identified.

OBJECTIVE: To further investigate the role of TTF-1 in epithelial cell maturation, by identifying and confirming genes previously unrecognized as TTF-1 responsive genes.

DESIGN/METHODS: Undifferentiated epithelial cells were isolated from human fetal lung (15-20 wk) and cultured with DCI [Dex (10 nM) + 8-Br-cAMP (0.1 mM) + IBMX (0.1 mM)] to promote type II cell differentiation. Some cells were transduced with adenovirus expressing rTTF-1 (CMV-12A2, 1-10 pfu/cell) in the absence of hormones. RNA was analyzed by DNA microarray (Affymetrix) and real time RT-PCR and Western analysis were employed to confirm RNA and protein changes, respectively. Cells and explants were stained by immunofluorescence.

RESULTS: By DNA microarray analysis, a variety of genes, both surfactant related and unrelated, were identified as reproducibly induced during both hormone treatment and by overexpression of rTTF-1 *in vitro*. The most highly induced (10-fold vs control) gene was CEACAM6 (Carcino Embryonic Antigen Cell Adhesion Molecule), a member of a family of membrane glycoproteins expressed in a variety of epithelial cells and associated with adenocarcinomas. By Real time RT-PCR and Western analysis CEACAM6 mRNA and protein were increased at 48h after DCI exposure, reaching 5-fold and 7±1 fold, respectively (n=4) after 72 h. Transduction of cells with CMV-12A2, similarly increased both mRNA (12±1 fold, n=3) and CEACAM6 protein (13±1 fold, n=4) at 72 h. Hormone-induced CEACAM6 expression

was reduced by ~50% by TGFß (10 nM). By immunofluorescence little endogenous CEACAM6 was present in undifferentiated HFL cells, but staining was intense in epithelium of explants treated with hormones, colocalizing with SP-B. The alveolar epithelium of uncultured lung expressed CEACAM6 at >32 wk gestation but not at <24 wk.
CONCLUSIONS: We conclude that CEACAM6 expression is developmentally and hormonally regulated and may play a role in maturation of the undifferentiated lung epithelium during normal fetal development.

152 Presentation Time 10:45 AM — Fellow in Training

Cathepsin H (CTSH) and Napsin A (NapA) Expression During Human Lung Development

Karna Murthy, Peggy Zhang, Kristin Ducrest, Amana Aktar, Susan H. Guttentag. Pediatrics, University of Pennsylvania, Philadelphia, PA.
BACKGROUND: CTSH and NapA have been implicated in the proteolytic processing surfactant protein B (SP-B). Mature SP-B is absent when either enzyme is inhibited or down-regulated. Our laboratory has shown that SP-B processing is developmentally regulated, suggesting that these enzymes are similarly controlled.
OBJECTIVE: To examine developmental and hormonal regulation of CTSH and NapA during human gestation.
DESIGN/METHODS: We examined by real time RT-PCR: 1. ontogeny using 2nd trimester human fetal lung, 2. time course (NapA only) during in vitro T2 cell differentiation using 10 nM dexamethasone (Dex), 0.1 mM 8-bromo-cAMP and 0.1 mM IBMX (DCI), 3. individual hormone responsiveness in T2 cells, and 4. expression in A549 and H441 cells in response to 50 nM Dex for 3 days.
RESULTS: In 2nd trimester human fetal lung, CTSH mRNA increased from 12 weeks gestation through 21 wk (6.4 ng ± 0.5 at 12 wk to 41.9 ng ± 13.0 at 21 wk; n=3, mean ± SE), as did Napsin expression (0.0 ng ± 0.0 at 12 wk to 2.1 ng ± 1.4 at 21 wk, n=3). As previously shown for CTSH, NapA expression increased during DCI-mediated in vitro T2 cell differentiation (0.3 ng ± 0.2 at 0 h to 3.0 ng ± 1.7 by 96 h, n=3), mimicking the developmental increase in NapA in vivo. CTSH induction in vitro was enhanced with DCI treatment (22 ng ± 6.8 Way, vs. 55 ng ± 16.7 DCI) with no dominant effect from the individual hormones. In contrast, the effect of DCI on NapA expression was dominated by the effect of cAMP (1.3 ng ± 0.7 Dex, vs. 3.0 ng ± 1.0 cAMP/IBMX, vs. 3.3 ng ± 2.0 DCI, n=3). CTSH and NapA were both detectable in A549 and H441 cell lines. There was no significant effect of Dex on CTSH or NapA expression in A549 cells (6.2 ng ± 0.1, Con vs. 9.2 ng ± 2.0 Dex, n=3; NapA: 7.3 ng ± 0.7 Con vs. 9.7 ng ± 3, Dex, n=3). H441 cell CTSH expression was also unresponsive to Dex (16.4 ng ± 4.0 Con vs. 12.0 ng ± 0.8), whereas NapA expression in H441 cells was robust and down-regulated by Dex (860 ng ± 30, Con vs. 485 ng ± 51, Dex).
CONCLUSIONS: CTSH and NapA gene expression are under developmental and hormonal regulation during the 2nd trimester of human gestation, consistent with induction of expression in maturing T2 cells.
Supported by HL59959.

153 Presentation Time 11:00 AM

Androgen Effect on ErbB Receptor and PLCγ Expression and Phosphorylation During Fetal Lung Maturation

Sujatha M. Ramadurai, Soujanya L. Rallabandi, Lucia D. Pham, Sandy L. Murray, Heber C. Nielsen. Pediatrics, Tufts-New England Medical Center, Boston, MA.
BACKGROUND: ErbB receptors (EGFR, ErbB2, ErbB3, ErbB4) control cell proliferation, differentiation and survival. EGF and Neuregulin (ligands for EGFR and ErbB3/4 respectively) are important in development of fetal lung fibroblast-type II cell communication leading to surfactant synthesis. Delayed fetal lung maturation occurs in males. Androgens enhance fetal lung growth and delay the onset of fibroblast-type II cell communication. Chronic in utero Dihydrotestosterone (DHT) exposure blocks fetal lung EGFR development and EGFR-stimulated PLCg phosphorylation (*phos*). Effects of DHT on the other ErbB receptors are unknown.
OBJECTIVE: We hypothesized that DHT differentially regulates fetal lung fibroblast ErbB receptor expression (*exp*) and *phos*, altering development of PLCγ signaling.
DESIGN/METHODS: Pregnant Sprague Dawley rats were implanted with DHT pellets on d11 of gestation. Sex-specific fetal lung fibroblast cultures were prepared from control (CON) and DHT-implanted dams on d17, 19, 21, and grown to confluence with DHT (10^{-8} M) added to the media of DHT animals. Confluent cells were harvested as unstimulated or after EGF or NRG stimulation. Western blots were probed with antibodies to phosphotyrosine, each ErbB receptor, and to PLCγ, then quantified by densitometry with actin as an internal standard.
RESULTS: PLCγ *exp* and EGF- and NRG-stimulated *phos* were increased in d19 vs d17 CON; males increased > females. DHT treatment abolished the changes. DHT affected ErbB receptor *exp* and *phos* diversely. DHT decreased ErbB2, B3 and B4 *exp* in d17 and d19 female and d19 male cells. NRG stimulated ErbB2 *phos* in d19 CON and DHT-treated male, and d19 DHT-treated female cells. NRG stimulated ErbB3 *phos* in CON female d17 and d19, and male d19. DHT abolished NRG stim in females but not in males. NRG stimulated ErbB4 *phos* in d17 and d19 female CON, and both EGF and NRG stimulated ErbB4 *phos* in male CON. DHT abolished NRG stim of ErbB4.
CONCLUSIONS: In utero DHT exposure makes PLCγ *phos* unresponsive to NRG. DHT induced differential effects on ErbB receptor *exp* and *phos*. DHT increased NRG-induced *phos* of ErbB2 and decreased *phos* of ErbB3 and 4 during development of fibroblast-type II cell communication. We speculate that DHT delays lung maturation by shifting the NRG-stimulated prefered ErbB heterodimer so that PLCγ is not activated.
Support: NIH HL37930

General Pediatrics III Platform Session

Sunday, March 6 — 9:45 AM-12:00 PM — Mead A

154 Presentation Time 9:45 AM

Failure To Thrive in Infants with Gastroesophageal Reflux Disease

Yen P. Chen, Anna Petrova, Daniel Notterman, Soula Koniaris. Pediatrics, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.
BACKGROUND: Gastroesophageal reflux disease (GERD) is frequently observed in infants and children. The majority of children receiving a diagnosis of GERD have no associated morbidity. Some children with GERD display failure to thrive (FTT) but the risk factors and incidence of this complication have not been comprehensively studied.
OBJECTIVE: To identify risk factors and outcomes associated with poor growth in children with GERD.
DESIGN/METHODS: Forty-nine subjects with GERD were enrolled in the study. The diagnosis of GERD was based upon clinical history, when necessary to confirm the diagnosis, children also underwent for a pH probe study. GERD symptoms, family history, social history, and growth (weight and length) were evaluated initially and at monthly intervals. GERD severity was assessed by a symptom scorecard that documented the frequency and volume of regurgitation, intensity of crying, feeding and sleep difficulty, back arching, and other extraesophageal symptoms. A diagnosis of FTT was established if weight was below the 5th percentiles (for age and gender), or if the growth curve crossed two major percentile lines in a short time (less than 3 months).
RESULTS: FTT was diagnosed in 10 (20.5%) of the children with GERD. There were no significant differences between FTT+ and FTT- subjects with respect to gender, race, parental educational level, or complication during pregnancy. Family history of hiatal hernia and peptic ulcer disease was more frequent in children with FTT than in those growing normally (6/10 vs.7/39, p=0.001 and 7/10 vs. 14/39, p= 0.01, respectively). Although GERD symptoms appeared in both the FTT+ and FTT- groups at the same post-natal age (2 months), symptoms persisted until 18 months in higher proportion of infants with FTT+ (3/10 vs. 2/39, p=0.02). Severity of GERD symptoms as determined by a symptom scorecard did not differ between FTT+ and FTT- subjects. Replacement of breast-feeding by formula occurred earlier in infants with FTT than in those who grew normally (at second month 8/10 in FTT+ vs. 13/39 in FTT-, respectively, p=0.01). Four of 10 patients with FTT were neurodevelopmentally delayed compared with 2/39 without FTT (p<0.004).
CONCLUSIONS: GERD associated FTT is associated with duration rather than severity of GERD symptoms. FTT in infants with GERD is also associated with neurodevelopmental delay and earlier cessation of breast-feeding.

155 Presentation Time 10:00 AM — Fellow in Training

Who Receives Appropriate Recommendations About Complementary and Alternative Medical Therapies?

Amy E. DeMattia, Harry Moskowitz, Kathi J. Kemper, Danielle Laraque. Pediatrics, Mount Sinai School of Medicine, New York, NY; Public Health Sciences and Family Medicine, Wake Forest University School of Medicine, Winston-Salem, NC.
BACKGROUND: Most children and families who use complementary and alternative medical (CAM) therapies do so without consulting a licensed provider (pediatrician/CAM practitioner). To date, no studies have examined recommendations made by CAM retailers to children, nor compared recommendations based upon socioeconomic status (SES).
OBJECTIVE: To compare the content, quality and cost of recommendations for children made by unlicensed CAM retailers within two New York City neighborhoods of divergent SES.
DESIGN/METHODS: Posing as consumers, culturally concordant researchers sought recommendations from CAM retailers for two clinical scenarios describing a six-week-old febrile infant, and a toddler with an upper respiratory infection. Scenarios were scripted, memorized and pre-tested. All retailers selling CAM products without the direction of a licensed provider in the neighborhoods of East Harlem (EH), a racially diverse and largely low-income area, and the Upper East Side (UES), a high-income area, were eligible, identified and mapped on Arcview 8.0 (N=26). Scenarios were posed at sites still in business in March (N=23) and April (N=20) of 2004.
RESULTS: In response to the scenario describing a febrile infant: 33% of UES retailers referred the child to a MD, 0% to the emergency department (ED), and 40% to over-the-counter products – of which 25% were not indicated for age. In EH, 50% of retailers referred the child to a MD, 5% to the ED, and 0% to over-the-counter products. Both UES and EH retailers made other recommendations. The mean price of UES recommendations was $9.66 while that of EH was $2.33 (p=.04). In response to the scenario describing a toddler with an upper respiratory infection: 14% of UES retailers referred the child to a MD, 0% to the ED, and 93% to over-the-counter products. In EH 0% of retailers referred the child to a MD or ED, and 83% to over-the-counter products. The mean price of UES recommendations was $10.55 while that of EH was $4.26 (p=.002).
CONCLUSIONS: CAM retailers in this study made numerous and varied recommendations for children. EH retailers tended to refer an infant with a potentially serious condition to the ED or MD, and made less expensive recommendations than their UES counterparts.

156 Presentation Time 10:15 AM — House Officer

Variations in Pediatric Tuberculosis Screening in Connecticut Schools

Beth C. Natt, Juan C. Salazar. Pediatrics, Connecticut Children's Medical Center, Hartford, CT; Pediatric Infectious Diseases, Connecticut Children's Medical Center, Hartford, CT.
BACKGROUND: The State of Connecticut Department of Public Health (DPH) recommends that at each mandated school health assessment, children should be assessed for their risk of exposure to tuberculosis. Those deemed at risk for having latent tuberculosis infection (LTBI) according to American Thoracic Society and the Centers for Disease Control and Prevention (CDC) criteria are required to undergo tuberculin skin testing. Likewise tuberculin skin testing is discouraged for children at low-risk for LTBI. Connecticut municipalities are ultimately responsible for implementing these guidelines within their own school district.
OBJECTIVE: To determine how well Connecticut school districts adhere to DPH school age targeted tuberculin testing guidelines.
DESIGN/METHODS: School districts in Connecticut were contacted by letter, telephone or in person to evaluate their tuberculosis screening policy. The responsible public health officer at each school district was asked if they utilized a risk based assessment to recommend tuberculin skin testing at school entry and/or for repeat testing. Their written or stated tuberculosis screening policies were then compared to stated DPH guidelines.
RESULTS: From the 123 (80%) school districts that responded, only 41% follow current DPH risk assessment guidelines, 32 % overscreen and 27% underscreen children at mandated school physical examinations. For those who underscreen, 15% require a risk assessment only at school entry and 85% require no screening at all. In many instances the policy is left at the discretion of the school nurse and/or local pediatrician.
CONCLUSIONS: Our findings reveal that the majority of Connecticut school districts are not following DPH tuberculosis screen guidelines. Current policies therefore lead to expensive investigations for children with false positives tuberculin skin tests. Even more concerning, children with LTBI may be missed if not screened in a timely fashion.

157 Presentation Time 10:45 AM — House Officer

The Feasibility and Effectiveness of an Exercise Prescription for Obese Children in the Primary Care Setting

Stephanie A. Carlin, Leif Nordstrom, Thomas Rowland. Pediatrics, Baystate Medical Center Children's Hospital, Springfield, MA.
BACKGROUND: There is a strong correlation between physical inactivity and childhood obesity. Pediatricians need an effective approach to address this important aspect of health care maintenance.
OBJECTIVE: To determine the feasibility and effectiveness of an exercise prescription for obese children and adolescents in the primary care office setting.
DESIGN/METHODS: 30 children and adolescents, aged 10-15 without co-morbidities or medications that would limit exercise, were identified in the primary care office setting as having a BMI of greater than or equal to the 85%ile. Subjects were counseled by their pediatrician on the importance of an active lifestyle and given basic instruction on the program. They were provided with an exercise booklet and pedometer and asked to formulate their own individualized exercise plan to be performed over the 4 month study period. At 1 week follow-up, the individualized exercise plan was reviewed and subjects were instructed to increase their average number of steps by 1,000 steps/week to a goal of 14,000 steps/

day. Subjects were to keep a daily log of their activities and step counts. Monthy follow-up visits were planned. Questionnaires were distributed to staff involved in the study.
RESULTS: Out of 23 subjects, 43% were not enrolled secondary to lack of interest or parental refusal. Of the remaining 13, only 1 subject completed the study. 31% of the enrollees had 1-2 follow-up office visits but were not successful in completing the program. 46% of them had no office follow-up visits since study start. 15% of enrolled subjects admittedly dropped out of the program at or after 1 month. Data from the subject who completed the study revealed an average of 10,763 steps/day during the study period as compared to 12,735 steps/day prior to study start. 4 exercise logs and 2 pedometers were returned at study conclusion.
CONCLUSIONS: The findings in this study suggest that individualized exercise prescriptions using pedometers may not be feasible or effective in the setting of a busy pediatric primary care office. However, study presentation and organization, parental support, and motivation of the participants are factors that may have contributed to the lack of this study to produce positive results.

158 Presentation Time 11:00 AM

Clinical Correlates of Early Readmission for Sickle Cell Disease Vasoocclusive Crisis

Catherine C. Skae, Devika Brijlall, Mary McGuire, Philip O. Ozuah. The Children's Hospital at Montefiore/ Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: A subset of patients admitted for sickle cell vasoocclusive crisis (VOC) are readmitted with the same diagnosis within 14 days of discharge. For this subset of patients, we wondered whether there were differences between those patients with frequent admissions/year versus those without. Understanding these differences may lead to better disease management and prevention of early readmission for VOC.
OBJECTIVE: To identify the clinical correlates of patients with early readmission for sickle cell VOC.
DESIGN/METHODS: We conducted a case-control study of a cohort of children hospitalized for VOC at a children's hospital between 1/1/2000 and 12/1/2004. Computerized records identified children with a primary/secondary diagnosis of VOC (ICD-9 282.62). Computer-derived records were verified by review of medical charts. Cases were defined as children with VOC readmitted with the same diagnosis within 14 days of index admission, but who did not have frequent yearly admissions for VOC. Controls were defined as children who were readmitted within 14 days of index admission and who had 5 or more admissions for VOC in a given calendar year. Cases and controls were matched for age, gender, and ethnicity. Data were abstracted from the medical records. Bivariate analyses were performed and conditional logistic regression analysis determined the relative contribution of independent variables.
RESULTS: 132 early readmissions were identified and analyzed, of which 44 were cases and 88 were matched controls. Cases and controls were successfully matched (mean age for cases 13 yrs vs. 14.8 yrs for controls; for both groups 50% were male, 92% African American). Cases were significantly more likely to have higher pain scores in the 24 hours preceding discharge, including maximum pain score/24 hours (3.6 for cases vs. 2.4 for controls; p = .048), and average pain score/24 hours (2.9 vs. 1.7; p = .018). No significant differences were found between the groups in mean length of stay for index admission (6.1 for cases vs. 5.4 for controls), admission hemoglobin (8.5 vs. 9.5), days to readmission (5.1 vs. 6.4), mean LOS for readmission (6.5 vs. 6.0), and discharge hemoglobin (8.7 vs. 9.3).
CONCLUSIONS: Early readmission for VOC in patients without frequent admissions for VOC was associated with higher pain scores in the 24 hours preceding discharge.

159 Presentation Time 11:15 AM — Fellow in Training

Food Availability in an Inner-City Community: What's near Our Elementary Schools?

Maida Galvez, Cherita Raines, Jessica Kobil. Community and Preventive Medicine; Pediatrics, Mount Sinai School of Medicine, New York, NY.
BACKGROUND: "Growing Up Healthy in East Harlem," a community based participatory research project is examining environmental determinants of childhood overweight, including access and availability of foods in the inner city, predominantly minority community of East Harlem (EH), NY. We hypothesize that the density and proximity of unhealthy food resources and limited availability of healthy foods may influence children's diets and risk of overweight.
OBJECTIVE: To assess the density of healthy and non-healthy food resources in East Harlem, NYC and proximity to elementary schools.
DESIGN/METHODS: A comprehensive walking survey of EH zip codes 10029 and 10035 was performed. Names and addresses of all food resources were collected and compared to data from the NYS Department of Agriculture. Food stores were classified into: supermarkets, grocery stores, bodegas, restaurants, fast food stores, and specialty stores (e.g., fruit market, ice cream shop, bakery). Maps were generated depicting the EH food environment using the geographic information systems software package, ArcGIS 8.3.

RESULTS: Unhealthy foods are abundant in EH. 99% of elementary schools have unhealthy food stores within a 125 meter radius. 57% have 3 or more unhealthy food resources in the same vicinity. Unhealthy food resources far outnumber healthy food resources by nearly 6:1. Within EH, there are disparities in the availability of fresh fruits and vegetables, with stores selling fresh fruits and vegetables in zip code 10029 outnumbering 10035 by 3:1. This figure exceeds the population differential between the two zip codes of 2.3:1.
CONCLUSIONS: East Harlem elementary schools have many unhealthy food stores in close proximity. In combating the rising epidemic of childhood overweight, there is a need to address community level changes in food availability of the urban environment.

Infectious Diseases Platform Session

Sunday, March 6 9:45 AM-12:00 PM Mead C

160 Presentation Time 9:45 AM — Fellow in Training

A Rat Model of Neonatal Candidiasis

Lamia Soghier, David Goldman. Pediatrics, Albert Einstein College of Medicine, Children's Hospital at Montefiore, Bronx, NY.
BACKGROUND: *Candida albicans* causes a disproportionate number of infections among premature newborns. These infections are associated with significant morbidity and mortality. The basis for the enhanced susceptibility of premature neonates to candidal infection is poorly understood and difficult to study.
OBJECTIVE: The aim of this study was to develop a rat model of neonatal candidiasis without immunosuppression and to characterize the susceptibility of neonatal rats to systemic and gastrointestinal candidiasis relative to adult rats.
DESIGN/METHODS: Sprague Dawley rats (age 2-3 days and 2 months) were infected intravenously (i.v.) or intragastrically with a clinical strain of *C. albicans*, BSMY 212. The course of experimental infection was determined by survival experiments. In other experiments, enumeration of organ fungal burden and histologic examination were done.
RESULTS: Following i.v. inoculation of 1 x 10^7 organisms, pups died earlier compared to adults (median survival times 32 and 11 days, respectively (p=0.05). Similar trends were observed for different inocula of *C. albicans* (i.e., 5 x 10^7). At 30 days, all pups but no adults exhibited liver involvement (p=0.01). Pups remained systemically infected at 60 days with progression of renal disease ($\log_{10}$ 3.5 ± 2.70 colonies/ g) (mean ± SD), renal enlargement and loss of renal tissue. Pups also exhibited enhanced susceptibility to gastrointestinal infection and developed early systemic dissemination to the liver, lung and kidney. Systemic spread was not present in adults. More prolonged gastrointestinal infection with persistent stool shedding (up to 5 weeks) was observed in pups. Adults and pups exhibited different patterns of gastrointestinal involvement. Gastric infection was present in pups, but not in adults and correlated with a higher stomach pH relative to adults (5.2 ± 0.6 vs. 2.8 ± 0.3, p = 0.003). Cecal infection was consistently present for adults, but appeared later in the course of infection for pups.
CONCLUSIONS: Rat pups exhibited enhanced susceptibility to *C. albicans* infection following both systemic and gastric infection. These findings suggest both local and systemic defects in the pup response to infection, similar to what has been described in premature human neonates. This includes higher gastric pH. The rat neonatal model provides a useful system for the study of neonatal candidiasis.

161 Presentation Time 10:00 AM — Fellow in Training

Short Course of Fluconazole Prophylaxis in Very Low Birth Weight Infants

Smart Uko, Viral Dave, Lamia M. Soghier, Suhas Nafday, Gerald Reinersman, Lucille Herring, Luc P. Brion. Pediatrics, Albert Einstein Coll. Med, Child. Hosp Montefiore, Bronx, NY.
BACKGROUND: Fungal sepsis is common in very low birth weight (VLBW) infants and is associated with several risk factors including broad spectrum antibiotics. A Cochrane review (McGuire et al) has shown that a 4-6-week fluconazole course significantly reduces the risk for fungal sepsis, relative risk (RR) 0.20 (95% confidence interval 0.07,0.64). One potential risk of such prophylaxis is the development of fungal resistance.
OBJECTIVE: To determine feasibility and efficacy of fluconazole prophylaxis during periods of prolonged antibiotic administration in VLBW infants.
DESIGN/METHODS: Observational study of 2 subsequent 15-month cohorts, before and after starting routine fluconazole prophylaxis in march 2003. Fluconazole prophylaxis (3mg/kg q48hrs) was administered to any infant with GA $\leq$ 32 weeks or birth weight $\leq$ 1500 grams, in whom a decision was made to administer broad spectrum antibiotics for > 3 days. The duration of prophylaxis was the same as that of antibiotic therapy. In both cohorts, patients with suspected (thrombocytopenia or cutaneous yeast infection associated with clinical deterioration) or proven fungal sepsis received amphotericin for 5 days pending cultures. Patients dying within 3 days of birth were excluded from the study.
RESULTS: Among 178 infants in the pre-fluconazole group, 8 died during the first 3 days, 56 (33%) were treated with amphotericin for symptoms or signs suggestive of fungal sepsis, and 16 (9%) had confirmed fungal sepsis. Among 140 infants in the fluconazole group, 7 died during the first 3 days, 24 (18%) were treated with amphotericin and 1 (0.8%) had confirmed fungal sepsis.The median duration of fluconazole prophylaxis was 8 days (range 2-60, quartiles of 4-16). The estimated RR of confirmed fungal sepsis associated with short-courses of fluconazole prophylaxis was 0.08 (0.01,0.6), similar to that with a 4-6-week course (Cochrane review).
CONCLUSIONS: Short courses of fluconazole prophylaxis during antibiotic therapy may be as efficacious as a 4-6-week course in reducing the risk of fungal sepsis in VLBW infants. In the absence of a control group, other factors may have contributed to the low frequency of fungal sepsis in our study; this will be assessed by multivariate analysis. A multicenter randomized trial could compare efficacy and toxicity of this mode of prophylaxis with a 4 to 6-week course.
Funded by Fluconazole used as prophylaxis for fungal infection in very-low-birth-weight infants.

162 Presentation Time 10:15 AM — Fellow in Training

Sexual Behaviors and Procreational Intentions of Adolescents and Young Adults with Perinatally Acquired Human Immunodeficiency Virus Infection

Echezona E. Ezeanolue, A. Patricia Wodi, Rakesh B. Patel, Arry Dieudonne, James M. Oleske. Division of Pediatric Infectious Diseases, University of Medicine & Dentisty of New Jersey-New Jersey Medical School, Newark, NJ.
BACKGROUND: Increasingly, children with perinatally acquired (PNA) human immunodeficiency virus (HIV) infection survive to adolescence and become sexually active. Understanding their sexual behaviors and procreational intentions could help inform designing reproductive health and secondary prevention programs.
OBJECTIVE: To assess the sexual knowledge, behaviors and procreational intentions of adolescents and young adults with perinatally-acquired HIV infection using descriptive epidemiologic techniques.
DESIGN/METHODS: A cross-sectional survey of adolescents and young adults aged 13-24 years with perinatally- acquired HIV infection followed at an urban teaching hospital was conducted from June 2003 through September 2004. Participants completed a questionnaire that inquired about sexual knowledge and behaviors. Participants aware of their diagnoses also completed items regarding disclosure and procreational intentions. Statistical analyses were done using chi-square.

RESULTS: 57 of 77 (74%) eligible participants completed the survey. Among all respondents aware of their diagnoses, 35 of 50 (70%) expressed intentions to have children. 12 of 15 (80%) respondents with acquired immunodeficiency syndrome expressed intentions to have children. A majority of those aware of the risk of maternal to child(MTC) transmission (71.1%) expressed a desire to procreate. Frequency of this intention did not differ by ethnicity (p=0.785), age (p=0.482) or gender but was higher among those who perceived MTC transmission as low when compared to those believing the risk to be high (p=0.025). 19 of 57 (33%) respondents reported having had penile-vaginal or oral sex, 89.4% of them after learning of their HIV status. Five of 19 (26%) sexually active respondents initiated sex prior to age 15 years. Five of 28 (17.9%) female respondents had been pregnant.
CONCLUSIONS: Despite awareness of their HIV diagnoses and perceived high risk of MTC transmission of HIV infection, adolescents with perinatally acquired HIV infection express intentions to have children. Programs providing comprehensive care to HIV-infected youth should offer early, age appropriate education regarding reproductive health, including procreational choices and considerations.

163 Presentation Time 10:30 AM — Fellow in Training

Influenza Vaccine: Immunization Rates, Knowledge and Attitudes of Resident Physicians in an Urban Teaching Hospital

Patricia Wodi, Sawsan Samy, Echezona Ezeanolue, Rytza Lamour, Rakesh Patel, Lawrence Budnick, Barry Dashefsky. Department of Pediatrics, University of Medicine & Dentistry (UMDNJ)-New Jersey Medical School(NJMS), Newark, NJ; School of Public Health, UMDNJ-NJMS, Newark, NJ; Occupational Medicine Service, Department of Medicine, UMDNJ-NJMS, Newark, NJ.
BACKGROUND: Reported compliance with guidelines urging voluntary annual influenza immunization (II) for health care workers is low (<37%), thus potentially subjecting patients to unnecessary risk of infection. Resident physicians (RP) specific II rates at our institution are unknown.
OBJECTIVE: To determine RP (1) rates of II, (2) knowledge of and attitudes towards II, (3) reasons for electing or declining II: and to determine if rates of II differ between primary care (PC) and non-PC trainees.
DESIGN/METHODS: An anonymous, self-administered questionnaire survey to randomly selected convenience samples of 150 PC and non-PC RP. II status in 2003-04 and previous seasons (by retrospective report), factors influencing their choices, and answers to a 20-item test of knowledge about influenza vaccine, was elicited.
RESULTS: 205/ 300 (68.3%) distributed (196 evaluable) questionnaires were returned. No difference in response rates between PC and non-PC [p=0.79]. Overall II rate for all RP in 2003-04 was 38.3%(n=75); rates did not differ between PC (38.9%) and non-PC (37.6%), [p=0.63]. 68 (34.7%) had never received II and 38.3% (n=75) did not intend to elect II next season. RP most often cited "self-protection" as reason for electing (93.3%) and "lack of time" for declining (47.1%) II. Concern of vaccine safety was expressed by 26.4% (32/121) of RP not vaccinated in 2003-04 and 31% of all RP falsely identified influenza as an adverse effect of II. RP varied greatly in their ability to correctly answer factual questions about II; mean knowledge score (KS) =13.7(perfect KS=20). PC and non-PC trainees did not differ by KS (p=0.43). Although "ever vaccinated" RP had higher KS than "never vaccinated" (p=0.01), among the "ever vaccinated" II status in 2003-04 did not differ by KS (p=0.08).
CONCLUSIONS: Most RP, both PC and non-PC trainees, decline recommended annual II. RP decisions regarding II do not consistently correlate with factual knowledge, which on average is only moderate. Misconceptions about vaccine safety occur significantly among RP.

164 Presentation Time 11:00 AM

Differential Cytokine (CK) Responses in Cord vs. Adult Peripheral Blood Mononuclear Cells (PBMCs) Exposed to RSV and Hyperoxia In Vitro

Leonard R. Krilov, Thomas M. McCloskey, S. Hella Harkness, Paul J. Lee, Jonathan M. Davis. Pediatrics, Winthrop University Hospital, Mineola, NY; Immunology, North Shore-LIJ Research Institute, Manhasset, NY.
BACKGROUND: RSV causes marked inflammation with mononuclear cell infiltrate in the lower respiratory tract in infants. Hyperoxia (=O_2) is used in the treatment of RSV infection but may also cause inflammatory changes in the small peripheral airways. CK expression may contibute to these inflammatory changes.
OBJECTIVE: To assess the effects of RSV and =O_2 on cord vs. adult-derived PBMCs.
DESIGN/METHODS: PBMCs from healthy adults or cord blood (n=3 of each) were separated over Ficoll and $2x10^6$ cells were exposed to RSV-Long (MOI=1) or media (mock). After 24 h, cells were maintained in room air (RA) or 95% O_2 up to 6 days. Aliquots were collected at 24 h intervals and assayed for CKs by flow cytometry using a Cytometric Bead Array Kit (IFNv, TNFζ , IL2, IL4, IL6, and IL10).
RESULTS: RSV induced marked =in IFNvand IL6 at 24, 48, 72 and 144h in the adult PBMCs. This effect was inhibited by =O_2 for IFNv but not IL6. =O_2 alone ⇐d IFN ℘secretion but not IL6. IFNv responses to RSV in cord PBMCs were markedly lower while the IL6 responses were similar to the adult cells. IL10 and IL2 were detected at lower concentrations and with modest =/s in response to RSV. TNFζ and IL4 were not detected in significant conentrations.
CONCLUSIONS: These experiments suggest that alterations in CK responses with exposure to RSV and =O_2 may contribute to inflammatory changes in the lung. The diminished IFNv responses to RSV in cord cells could contribute to the severity of RSV infection in young infants.

	IFNg - ADULT	IFNv- CORD	IL6 - ADULT	IL6 - CORD
48h RA mock	6 - 559 pg/ml	0 - 16	175 - 2453	210 - 1411
48h RA RSV	462 - >2,5000	65 - 126	2028 - >5000	>2500 - >5000
48h O2 mock	0 - 93	12 - 75	185 - 1719	317 - 1143
48h O2 RSV	170 - 2250	0 - 50	2112 - >5000	>2500 - >5000
72h RA mock	0 - 85	0 - 44	58 - 209	276 1210
72h RA RSV	1079 - >5000	0 - 306	2112 - >5000	2446 - >5000
72h O2 mock	159 - 216	11 - 48	21 - 2028	110 - 786
72h O2 RSV	8 - 721	0 - 72	2025 - >5000	>2500 - >5000

n=3 adult and 3 cord bloods

165 Presentation Time 11:15 AM — House Officer

E. coli O157:H7 Diarrhea and Hemolytic-Uremic Syndrome in an Urban Daycare Center

Ryan M. Raffaelli, Don Weiss, Glenn J. Fennelly, Laura Kornstein, Heather Hanson, Sudha Reddy, Marc Paladini, Nathan Litman, Frederick Kaskel, Joseph Flynn. Pediatrics, Albert Einstein College of Medicine - Children's Hospital at Montefiore, Bronx, NY; New York City Department of Health and Mental Hygiene, New York, NY; Lewis M. Fraad Department of Pediatrics, Jacobi Medical Center and Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: We present five patients admitted with bloody diarrhea with 40% progression to hemolytic-uremic syndrome (HUS). All attended the same urban daycare center.
OBJECTIVE: The importance of determining relationships among patients is paramount to diagnosing and managing this disease pattern in the future.
DESIGN/METHODS: An urban daycare center in Bronx, NY with 36 patients known to have diarrheal illnesses between June 1-July 1, 2004. Ten (28%) had positive stool cultures for E.coli O157:H7 and one other had a positive shiga toxin test. Eight (73%) were in the same classroom and 5 (63%) were hospitalized.
RESULTS: All five hospitalized patients were 2-3 years old and without significant past medical history. Patients 1, 2, 4 and 5 had positive stool cultures. Patient 3 had a positive shiga toxin test. All had diarrhea (>3 stools/day) for greater than or equal to two days prior to admission. Patient 2 was initially treated with intravenous antibiotics. Patients 2 and 3 had HUS. Patient 2 was transferred to the Pediatric ICU (PICU) on hospital day 2 whereas patient 3 was admitted, after 10 days of bloody diarrhea, directly to the PICU. Neither required dialysis. Patients 4 and 5 had uneventful courses (Patient 5 lab data unavailable).

Hematocrit and creatinine trends for hospitalized patients with bloody diarrhea

Patient	Hct (Day 1)	Hct (Low)	Hct (D/C)	Cr (Day 1)	Cr (High)	Cr (D/C)	Transfusion (RBC)
1	38.9	37.3	37.3	0.5	0.5	0.2	No
2	39.8	18.5	31.2	0.5	1.2	0.3	Yes
3	17.7	13.5	21.8	1.7	1.7	0.7	Yes
4	36.6	36.6	36.6	0.5	N/A	N/A	No

Cr=Creatinine (mg/dl), Hct=Hematocrit (%), N/A=Not Applicable, RBC=packed red blood cells

CONCLUSIONS: Because of the nature of E.coli O157:H7 to occur in outbreaks, and the potential to develop HUS as a complication, rapid diagnostic and management decisions are required. Therefore, when patients present with bloody diarrhea, close evaluation of possible exposures, such as daycare centers, should be made and the diagnosis of enterohemorrhagic E.coli infection entertained.

Neonatology III: Animal Models in Neonatology Research Platform Session

Sunday, March 6 — 9:45 AM-12:00 PM — Sheffield

166 Presentation Time 9:45 AM

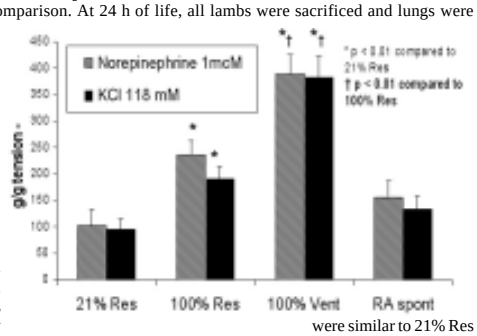
Ontogeny and Regulation of Hyaluronan by Antenatal Corticosteroid, Ventilation and Hyperoxia in Non-Human Primate Models of BPD

Lindsay M. Johnson, Siddhartha Maru, Joseph P. Foley, Brad A. Yoder, Jacqueline J. Coalson, Anna Plaas, Rashmin C. Savani. Neonatology-Pediatrics, CHOP-Univ of Pennsylvania, Philadelphia, PA; Pathology, UTHSC, San Antonio, TX; Rheumatology-Internal Medicine, Univ Southern Florida, Tampa, FL.
BACKGROUND: Bronchopulmonary Dysplasia (BPD) is characterized by inflammation, interstitial fibrosis and a lack of alveolization. Ventilated preterm baboon models recapitulate both "Old" and "New" BPD. Elevated lung hyaluronan (HA) is found in human lung diseases and in animal models of lung injury. We have previously shown that HA-binding peptide is able to limit inflammation and fibrosis after bleomycin injury in rodents.
OBJECTIVE: We hypothesize that hyaluronan (HA) is critical to inflammation in the pathogenesis of BPD. This study examines the expression of HA in baboon BPD models.
DESIGN/METHODS: HA was localized by immunofluorescence using a biotinylated HA-binding probe and content was determined using an ELISA-like assay. Ontogeny studies examined controls between 90d and 185d of gestation (n=8-11). Animals with preterm delivery and ventilation for 10-14 days were examined both at 125d (new BPD, n=6-8) and 140d (old BPD, n=6-8). The effect of antenatal corticosteroids was examined in the 125d model (n=3-4).
RESULTS: At 90 days, intense HA staining was seen exclusively in mesenchyme. With advancing gestation, HA was increasingly restricted to the subepithelial matrix of large airways with little to no HA in the distal lung by term. Lavage HA content confirmed this decrease in HA. Preterm baboons in the 125d, 14d PRN model were compared to appropriate controls. Prenatal exposure to corticosteroids uniformly decreased HA in the lungs of both control and ventilated animals. Ventilation resulted in increased HA staining in distal thickened septae and a maximum 2.5-fold increase in lavage at 6 days of ventilation. Preterm baboons delivered at 140 days gestation and allowed to develop RDS for 24 hours had intense staining for HA in large patchy areas of the lung. Animals ventilated with 100% oxygen showed increasing parenchymal HA staining throughout the lung with time.
CONCLUSIONS: Lung HA decreases with gestational age and antenatal corticosteroid exposure. Preterm birth, RDS, ventilation and exposure to 100% oxygen all result in increased HA in distal airspaces and lavage. HA may be a good marker for the development of BPD.

167 Presentation Time 10:00 AM

Pulmonary Arterial (PA) Contractility in Neonatal Lambs Increases with 100% O_2 Resuscitation

Satyan Lakshminrusimha, Robin H. Steinhorn, Daniel D. Swartz, Sylvia F. Gugino, Rita M. Ryan, James A. Russell, Frederick C. Morin, Vasantha H. Kumar. Pediatrics & Physiology, SUNY, Buffalo; Pediatrics, Northwestern University, Chicago.
BACKGROUND: The optimal FiO_2 in the gas used during resuscitation is a subject of controversy. The effect of O_2 on PA contractility is not known.
OBJECTIVE: To study differences in PA contractility following ventilation with 21% O_2 or 100% O_2 for 30 min in term neonatal lambs.
DESIGN/METHODS: Term lambs were delivered by C-section, intubated and mechanically ventilated. Two groups of 6 lambs were ventilated with 100% O_2 (100% Res) or 21% O_2 (21% Res) for the first 30 minutes of life ('resuscitation'). Subsequently, the ventilator FiO_2 was adjusted to maintain a PaO_2 between 45 - 70 mmHg for 24h. The 100% Res group was weaned to 21-25% O_2 by 4-6 hours of life. Five lambs ventilated continuously with 100% O_2 (100% Vent) and 2 spontaneously breathing newborn lambs (RA Spont) were studied for comparison. At 24 h of life, all lambs were sacrificed and lungs were harvested. Fifth generation PA rings were isolated and constricted with norepinephrine (1 mcM) and KCl (118 mM) in standard tissue baths bubbled with 94% O_2 and 6% CO_2. Constriction force was expressed as g per g PA weight.



RESULTS: PAs isolated from 100% Vent lambs and 100% Res lambs constricted significantly more to norepinephrine and potassium chloride than PA from 21% Res lambs. Constriction responses in PA from lambs breathing room air spontaneously were similar to 21% Res lambs.

CONCLUSIONS: Exposure to 100% O_2 during mechanical ventilation increases PA contractility to NE and KCl. This effect is observed even after relatively brief exposures to hyperoxia during a 30-minute resuscitation. In contrast, normoxic resuscitation and ventilation do not alter PA contractility. We speculate that reactive oxygen species generated during resuscitation with 100% O_2 may affect pulmonary vascular resistance.
Funded by American Academy of Pediatrics #1040244-32665.

168 Presentation Time 10:30 AM — Fellow in Training

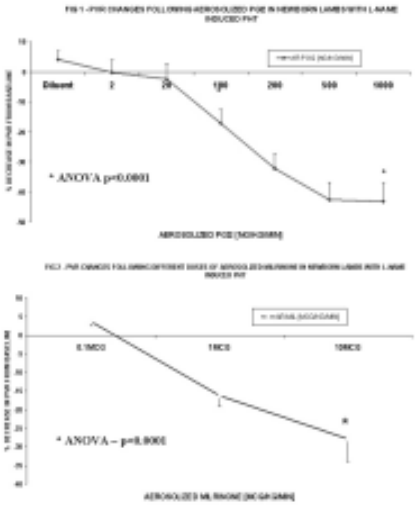
Aerosolized Prostacyclin [Ar-PGI_2] and Milrinone [Ar-MLR] Decrease Pulmonary Vascular Resistance [PVR] in Newborn Lambs with L-NAME Induced Pulmonary Hypertension [PHT]

N. Rashid, F. C. Morin, D. D. Swartz, K. A. Wynn, H. Wang, R. M. Ryan, V. H. Kumar. Women & Children's Hospital of Buffalo, Buffalo, NY.

BACKGROUND: PGI_2 increases cAMP by stimulating adenylate cyclase within smooth muscle cells resulting in vasodilation. MLR increases cAMP in smooth muscle cells by inhibiting the enzyme phosphodiesterase3.

OBJECTIVE: To study the dose-response effects of Ar-PGI_2 and Ar-MLR on pulmonary hemodynamics in newborn lambs with L-NAME induced PHT.

DESIGN/METHODS: Near term lambs [N=6] at 139 days gestation [term=145 days] were delivered by C-section. Thoracotomy was done for ductal ligation and instrumentation. PHT was induced by L-NAME [bolus-25mg/kg then infusion - 10mg/kg/hr] & Indomethacin [2mg/kg bolus] starting at delivery. Lambs were ventilated in 100% O_2. Baseline pulmonary artery pressures were 58.7 [± 3.7] mm Hg. PGI_2 was administered at random doses followed by milrinone with sequentially increasing doses via the Aerogen nebulizer over 10 min with a 30 min interval between doses. PVR was calculated before and after each dose.



RESULTS: PVR decreases significantly with 100, 200, 500 & 1000ng/kg/min of Ar-PGI_2 [ANOVA - $p<0.0001$] and 1 & 10m/kg/min of Ar-MLR [ANOVA - $p<0.0001$].

CONCLUSIONS: Ar-PGI_2 and Ar-MLR are effective pulmonary vasodilators in newborn lambs with L-NAME induced PHT. These agents may offer an alternative therapy in PHT unresponsive to nitric oxide.

169 Presentation Time 10:45 AM — Other (indicate)

Surfactant Protein D Modifies the Response to Intratracheal Bleomycin

Jennifer H. Kaplan, John A. Casey, Elena N. Atochina, James H. Fisher, Yaniv Tomer, Helchem Kadire, Michael F. Beers. Div. of Neonatology, Children's Hospital of Phila., Phila., PA; Pulm & Critical Care Div., U. of PA School of Med, Phila., PA; Div Pulm Sciences and Critical Care, Denver Health Medical Center, Denver, CO.

BACKGROUND: Surfactant protein D (SP-D) is a 43-kDa member of the collectin family with well-documented antimicrobial function. However, SP-D'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-D in modulating non-infectious lung injury, we employed the bleomycin model of lung injury in mice deficient in or over-espressing SP-D.

DESIGN/METHODS: Intra-tracheal bleomycin (ITB) was administered to 7-9-week old SP-D over-expresser (SP-DOE) mice, littermate (WT) controls, and SP-D knockout (SP-DKO) mice. SP-DOE mice demonstrate a 6-fold elevation in constitutive levels of BAL SP-D.

RESULTS: Following 3U/kg ITB, SP-DOE mice had a 21 day survival of 100% versus 42% survival for WT. In contrast to the protective effect in SP-DOE, SP-DKO had 100% mortality by day 10 at smaller doses of ITB (2U/kg). Despite protection from mortality, 21 days after ITB SP-D OE exhibited equivalently elevated BAL protein (2991±396 mg SP-DOE vs. 1416±567 mg WT, p=0.063) and increased BAL cells (332±34 X103 vs. 214±29 X 103, p=0.026). In contrast to WT or SP-DKO, cytospin analysis demonstrated a predominance of small, non-activated macrophages in SP-DOE mice receiving ITB, however by trichrome staining patchy lung fibrosis occurred in all 3 models.

CONCLUSIONS: These data indicate a dissociation between early and late events in bleomycin induced lung injury and suggest that in vivo over-expression of SP-D protects mice from early mortality following ITB but via mechanisms distinct from the recruitment of inflammatory cells.

Funded by Forest Pharmaceuticals Advancing Newborn Medicine.

170 Presentation Time 11:00 AM — Fellow in Training

Activation of Natriuretic Peptide Receptor C Inhibits Adenylate Cyclase Mediated Relaxation in Juvenile Ovine Pulmonary Arteries (PA)

Bobby Mathew, Rita M. Ryan, Sylvia F. Gugino, James A. Russell, Frederick C. Morin, Lori C. Nielsen, Satyan Lakshminrusimha. Pediatrics, Physiology and Biophysics, SUNY, Buffalo, NY.

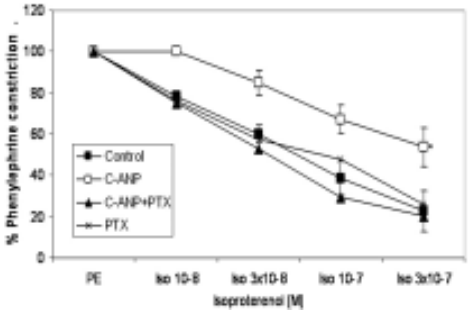
BACKGROUND: Natriuretic peptides (ANP, BNP and CNP) bind to natriuretic peptide receptor C (NPR C) with equal affinity. Stimulation of the NPR C receptor leads to inhibition of cAMP production in some biological systems by activation of the Gi subunit of adenyl cyclase (AC). Pertusis toxin (PTX) blocks activation of the Gi subunit. C-ANP is a selective agonist of NPR C receptor.

OBJECTIVE: To evaluate the expression, localization and function of NPR-C receptors in juvenile ovine PA.

DESIGN/METHODS: 6 week old lambs (n= 6) were sacrificed and 5th generation PAs were isolated and studied using standard tissue bath techniques. PAs were constricted with phenylephrine and relaxed with a ß adrenergic agent, is oproterenol or AC agonist, forskolin. Some PAs were pretreated with C-ANP 10^{-9}M (NPR-C agonist) with or without PTX (0.5mg/ml).

RESULTS: Isoproterenol relaxed PA and pretreatment with C- ANP significantly inhibited this relaxation (figure 1 - * $p < 0.05$ by ANOVA repeated measures for the curve compared to control). Addition of PTX to vessels treated with C-ANP reversed this inhibition. Forskolin (3 mcM) alone relaxed PA by 79.5 ± 8.5%. Pretreatment with C-ANP significantly impaired forskolin relaxation by 35.3 ± 12.7%. Following pretreatment with C-ANP and PTX, forskolin relaxed PA by 68.5 ± 18.1%. NPR-C mRNA was demonstrated in PA by RT-PCR. Immunohistochemistry revealed NPR-C staining in smooth muscle of PA.

CONCLUSIONS: NPR-C receptor is localized and expressed in juvenile ovine PA. Stimulation of this receptor results in inhibition of AC mediated relaxation of PA by activation of the inhibitory Gi subunit of AC. These results indicate that natriuretic peptides can inhibit the effect of various cAMP dependent pulmonary vasodilators by binding to NPR-C receptors.



171 Presentation Time 11:15 AM

Early Loss of HA in Association with Increased Peroxynitrite After Intratracheal Bleomycin in Rats

Rashmin C. Savani, Joseph P. Foley, Aisha Zaman, Bruno Flamion, Jeannine Martens, Anna Plaas. Neonatology-Pediatrics, CHOP-Univ of Pennsylvania, Philadelphia, PA; F.U.N.D.P., Univ of Namur, Namur, Belgium; Rheumatology-Internal Medicine, Univ of Southern Florida, Tampa, FL.

BACKGROUND: High molecular weight hyaluronan (HMW HA) has structural functions in the lung. LMW HA has been implicated in inflammation after bleomycin injury. Depolymerization of HMW to LMW HA occurs either by enzymatic action of hyaluronidases or by superoxide & peroxynitrite-mediated chemical degradation. Peroxynitrite, the product of superoxide and nitric oxide, causes 3-nitrotyrosine (3-NT) modifications on proteins.

OBJECTIVE: To determine the depolymerization of HA by oxidative and ntirative stresses after bleomycin injury.

DESIGN/METHODS: Polyacrylamide gel electrophoresis and Fluorescence Assisted Carbohydrate Electrophoresis (FACE) were used to determine the relative sizes of HA. Immunofluorescence double labeling for HA and peroxynitrite was accomplished using a biotinylated HA-binding probe and an antibody to 3-NT. Expression and activity of Hyaluronidases 1 and 2 (Hyal-1/2) were determined using real time RT-PCR, immunolocalization and by HA gel zymography.

RESULTS: Both hyaluronidase and peroxynitrite exposure of HMW HA (1 x 10^6 Da) resulted in LMW HA (200 Da). Two hours after intratracheal bleomycin in rats, there was almost complete loss of HA from the subepithelial matrix of larger airways. At the same time, serum HA was increased, but lavage HA was not. Bleomycin-injured lung sections examined by dual-label immunofluorescence showed decreased HA in association with increased 3-nitrotyrosine staining. No expression of Hyal-1 was noted in the lung under any condition. Hyal-2 was expressed in vascular smooth muscle and in macrophages, but expression by real time RT-PCR was similar in control and injured conditions. Further, gel zymography for hyaluronidase activity showed no differences between conditions suggesting that the disappearance of HA two hours after bleomycin was likely due to peroxynitrite degradation.

CONCLUSIONS: We conclude that there is a profound early loss of HMW HA from the lung after actue lung injury. We speculate that oxidative and nitrative stresses depolymerize HA to produce LMW HA that promotes homing of activated inflammatory cells to the lung. Strategies to limit HA depolymerization and sequestration of LMW HA are appropriate therapeutic goals in lung injury.

Neurobiology Platform Session

Sunday, March 6 — 9:45 AM-12:00 PM — Stoningham

172 Presentation Time 9:45 AM — Fellow in Training

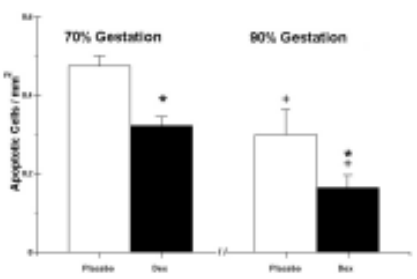
Maturation and Antenatal Corticosteroids Reduce Apoptosis in the Fetal Brain

Shadi N. Malaeb, Grazyna B. Sadowska, Paul R. Monfils, Virginia Hovanesian, Barbara S. Stonestreet. Pediatrics, Brown University and Women & Infants' Hospital of Rhode Island, Providence, RI; Core Research Laboratories, Rhode Island Hospital, Providence, RI.

BACKGROUND: Apoptosis plays an important role during brain development. Antenatal corticosteroids reduce the incidence of intraventricular hemorrhage and white matter damage in premature infants. A decreased rate of apoptosis may be one of the mechanisms by which endogenous and exogenous corticosteroids provide beneficial maturational effects to the premature brain.

OBJECTIVE: To test the hypotheses that the rate of apoptosis decreases with maturation and after antenatal treatment with corticosteroids in the ovine fetus.

DESIGN/METHODS: Ovine fetuses at 107 days (70%) of gestation were examined 18 h after last of four 6 mg dexamethasone (Dex, n=8) or placebo (PL, n=8) injections were given every 12 h over 48 h to the ewes, or same course of Dex (n=10) or PL (n=9) given at 136 days (90%) of gestation. Cerebral cortices were snap frozen and apoptotic nuclei per mm^2 counted on 6-micron sections using Apoptag® assay to detect in situ nuclear DNA fragmentation. Fetal cortisol levels were measured.



RESULTS: The number of apoptotic cells was lower at 90 than 70% gestation, and in fetuses exposed to Dex than PL at both ages, and similar between the 70% Dex and 90% PL groups (Fig, M±SEM,*P=0.02 vs PL, †P<0.05 vs 70%). Fetuses at 90% had higher plasma cortisol levels than at 70% gestation (16.8±2.2 vs 7.7±0.7 ng/ml, P=0.01).

CONCLUSIONS: Apoptosis in the fetal brain decreases with advancing gestation. This decline is associated with an increase in fetal cortisol concentrations. Maternal antenatal corticosteroid treatment reduces the rate of apoptosis in the fetal cerebral cortex. We speculate that modulation of apoptosis by endogenous and exogenous corticosteroids is one of the mechanisms of hormonal regulation of brain maturation in the fetus.

173 Presentation Time 10:00 AM Fellow in Training

Chronie Opiate Withdrawal in Neonatal Mice: Behavioral Analysis and c-Fos Expression

Anne-Lise J. Yohay, Ariel Mason, Megan Duffy, Debra Flock, Gabrielle McLemore, Frances Northington, Estelle B. Gauda. Pediatrics - Neonatology, Johns Hopkins University, Baltimore, MD; Morgan State University, Baltimore, MD.

BACKGROUND: Studies in human infants and neonatal rats have defined developmentally regulated behaviors of opioid withdrawal (OW) . Research in genetically manipulated adult mice has described genes that modify the development and expression of opioid dependence and OW and alter the cellular and behavioral signs of naloxone-precipitated (NP) OW. Lack of a neonatal mouse model hinders similar investigations into the roles of these genes during development. The c-Fos gene and protein are used in adult models to identify neuronal groups activated in response to NP-OW and correlations between c-Fos expression and behavioral signs of NP-OW are done.

OBJECTIVE: To determine the behavioral signs of OW and correlate these with c-Fos expression in the midbrain (Mb) and brainstem (Bs) of neonatal mice.

DESIGN/METHODS: Mouse pups were exposed to methadone (M, 14mg/kg/day of maternal weight) or Saline (S) tranplacentally and via breastmilk from gestational day 15 to postnatal day (PND) 7 via mini-osmotic pumps. At PND 7, the animals were treated with Naloxone (N, 5mg/kg) or S. A blinded observer scored videotaped behaviors for each group (SS, n=6; SN, n=7; MS, n=8; MN, n=7). Scoring was based on that described for the neonatal rat (Jones KL, Barr GA, 1995). Behaviors were grouped as quiet and active. The Mb and Bs were processed for c-Fos expression using Western blot. Behavioral score differences amongst the 4 groups were determined by ANOVA and post hoc analysis.

RESULTS: Myoclonus, head moves, moving paws, walking, quiet and straub tail were commonly observed behaviors. The frequency of active and quiet behaviors was similar among the 4 groups. c-Fos expression increased by 23% and 14% in the Mb and Bs, respectively, of MN mice compared to SS controls. c-Fos expression was similar among SS, SN and MS.

CONCLUSIONS: Unlike the PND 7 rat, there are no characteristic OW behaviors for PND 7 mice. The increase in c-Fos expression in the MN group suggests that Mb and Bs neurons are altered by prenatal exposure to opioids in immature mice. Behavioral signs cannot distinguish OW in newborn mice. However, c-Fos expression in the brain is a cellular marker of OW in this newborn model. This data is useful for future investigations of OW in genetically manipulated neonatal mice.

174 Presentation Time 10:15 AM

The Effects of Lipopolysaccharide Injection on Bax and Bcl2, Regulators of Apoptosis, in Neural Tissue of Newborn Mice

David F. Sorrentino, Morgan Peltier, Vallier Ojadi, Alexander Kusnecov. Pediatrics, UMDNJ, New Brunswick, NJ; Obstetrics, UMDNJ, New Brunswick, NJ; Psychology, Rutgers University, Piscataway, NJ.

BACKGROUND: Newborn sepsis is associated with poor neurologic outcomes and increased rates of periventricular leukomalacia. The inflammatory mediators present in sepsis have been shown to cause spontaneous neurodegeneration. This may occur through intrinsic apoptotic pathways that are regulated by the Bcl-2 family of proteins. Two regulators in this family of proteins are Bax (proapoptotic) and Bcl-2 (antiapoptotic) which inhibits Bax activity.

OBJECTIVE: The present study tests the hypothesis that exposure to LPS alters the mRNA and protein content of Bax and Bcl-2 in neural tissue in newborn mice.

DESIGN/METHODS: 5 day old mice were injected intraperitoneally with LPS, to simulate sepsis, or saline. 6 hours later they were sacrificed and brain tissue was harvested for protein and RNA isolation. Bax and Bcl-2 mRNA was quantified using Q-RT-PCR. Protein content of Bax and Bcl-2 was quantified by western blot analysis. The data was analyzed using the Mann Whitney U Test.

RESULTS: There was no statistically significant difference in mRNA content after LPS treatment vs control for Bax (mean: 3.34 vs. 4.59, p=0.063) or Bcl-2 (mean:4.18 vs. 4.21, p=0.75). There was a significantly altered ratio of Bax to Bcl-2 mRNA in LPS treated mice vs. control (mean:1.25 vs. 0.77, p=0.048). The alteration was likely due to increased Bax mRNA as this approached significance while Bcl-2 production was essentially unchanged. In contrast, there was no difference in the protein content of Bax or Bcl-2 6 hours after LPS exposure.

CONCLUSIONS: We conclude that, 6 hours after LPS exposure, there are altered ratios of mRNA for Bax and Bcl-2, leading to a predominance of antiapoptotic mechanisms but no alterations in existing protein in neural tissue in newborn mice. We speculate that this is an early response to prevent apoptosis in neural tissue of newborns after infectious insult. Further studies will be necessary to determine the specific cell type responsible for this altered expression. Microglia and astrocytes are the cells most likely to be responsible for this finding since it is well recognized that inflammatory mediators prevent apoptosis in these cells. We anticpate that at later time points we will see an increase in Bax protein content relative to Bcl-2.

175 Presentation Time 10:30 AM Fellow in Training

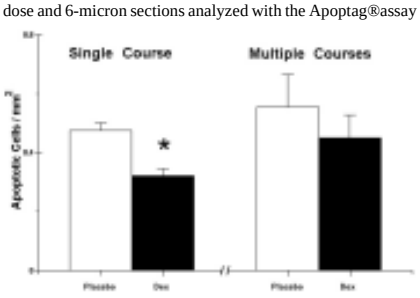
Effects of Single and Multiple Courses of Antenatal Corticosteroids on Apoptosis in the Brain of Preterm Ovine Fetuses

Shadi Malaeb, Grazyna B. Sadowska, Paul R. Monfils, Virginia Hovanesian, Barbara S. Stonestreet. Pediatrics, Brown University and Women & Infants' Hospital of Rhode Island, Providence, RI; Core Research Laboratories, Rhode Island Hospital, Providence, RI.

BACKGROUND: Although a single course of antenatal corticosteroids is associated with beneficial effects on brain maturation, multiple courses are associated with reduced brain weight at birth in premature infants, and potentially cause neuronal and white matter injury in animal studies.

OBJECTIVE: To determine the effects of single and multiple courses of antenatal corticosteroids on the rate of apoptosis in cerebral cortices of ovine fetuses at 70%gestation.

DESIGN/METHODS: Catheterized ovine fetuses at 107 days of gestation were examined after a single course of four 6 mg dexamethasone (n=8) or placebo (n=8) injections given every 12 h over 48 h to the ewes, or same course of dexamethasone(n=14) or placebo(n=11) given weekly for 5 weeks. Cerebral cortex was snap frozen 18 hours after last dose and 6-micron sections analyzed with the Apoptag®assay to detect *in situ* nuclear DNA fragmentation. Apoptotic nuclei per mm^2 were counted by a microscopist unaware of group assignments.



RESULTS: The number of apoptotic cells was significantly lower in fetuses of ewes exposed to a single course of dexamethasone than placebo (Fig, M±SEM, *P=0.001 vs Placebo) and did not differ between fetuses of ewes exposed to multiple courses of dexamethasone or placebo, or between fetuses of ewes exposed to single or multiple courses of dexamethasone.

CONCLUSIONS: Single, but not multiple courses, of maternally administered antenatal corticosteroids are associated with a significant decrease in the number of apoptotic cells in cerebral cortices of ovine fetuses at 70% gestation.

Funded NIH HD34618.

176 Presentation Time 11:00 AM Fellow in Training

Novel Role of CREB in Butyrate-Induced Activation of Catecholaminergic Neurotransmission

Parul Shah, Bistra Nankova, Edmund LaGamma. Devision of Newborn Medicine, Maria Fareri Children's Hospital-New York Medical College, Valhalla, NY.

BACKGROUND: Butyrate is a short chain fatty acid (SCFA) produced by bacterial fermentation of dietary carbohydrates that act *locally* on epithelial cell maturation, differentiation and apoptosis as well as *systemically* to regulate gene expression (i.e hemoglobin synthesis). We previously demonstrated that butyrate could induce tyrosine hydroxylase (TH; the rate limiting enzyme in catecholamine biosynthesis) and enkephalin gene expression at physiologic blood levels (1mM; Peds Res 53:113, 2003). Activation of both, PKA/cAMP & MAPK second messengers systems were required. Since both cascades converge on the cAMP response element binding protein (CREB), we hypothesized that CREB may be involved in mediating the effects of butyrate.CREB is a ubiquitous transcription factor implicated in complex processes ranging from development to plasticity to disease and memory,

OBJECTIVE: To determine whether butyrate interacts with CREB phosphorlyation-dependent mechanisms.

DESIGN/METHODS: Rat pheochromocytoma (PC12) cells were used as a model. Western blot analyses were performed to detemine whether butyrate effects on CREB require activation of adenylate cyclase or MAPK pathways. Transfection experiments with wild type & dominant-negative CREB expression vectors and a plasmid containing the TH promoter controling a luciferase reporter gene were done to test involvement of CREB.

RESULTS: Butyrate-induced phosphorylation of CREB was evident at10 & ^{3} 60 min as revealed by western blots with phospho-CREB-specific antibody. When the same blots were re-probed with CREB-specific antibody, no change in the relative amount of CREB protein was observed. Pre-treatment with the MAPK-specific inhibitor (U0126) or the adenylate cyclase inhibitor dideoxyadenosine abolished the: accumulation of TH mRNA, phosphorylation of ERK1/2 & CREB phosphorylation that were induced by butyrate. Co-expression of dominant-negative CREB greatly reduced the ability of butyrate to activate the TH promoter.

CONCLUSIONS: P-CREB is a necessary mediator of the molecular effects of butyrate. Speculation: at physiologic blood levels, diet-derived SCFA's can activate catecholaminergic and neuropeptide biosynthetic pathways. Thus, a clinician's feeding practice and use of antibiotics can alter the sympahtoadrenal adaptive responses to neonatal stress (e.g.hypoglycemia, hypoxia, hypotension, cold).

177 Presentation Time 11:15 AM Fellow in Training

Dose-Dependent Effects of Diet-Derived Signaling Factors (Butyrate) on Transcription of Catecholamine-Related Transmitter Genes: Tyrosine Hydroxylase

Santosh M. Parab, Bistra Nankova, Edmund F. LaGamma. Maria Ferrari Childrens Hospital, NYMC, Valhalla, NY.

BACKGROUND: Butyrate (SB), a short chain fatty acid (SCFA) regulates transcription of a variety of genes including tyrosine hydroxylase (TH), the rate limiting enzyme in catecholamine biosynthesis. Our previous work revealed delayed accumulation of TH & enkephalin mRNA in butyrate-differentiated PC12 cells at physiological concentrations (1mM). However, at high concentration (6mM), TH mRNA levels were lower than control suggesting that concentration-dependent control mechanisms may differ at the transcriptional or post-transcriptional level.

OBJECTIVE: To determine a) the time course of changes in TH & ppEnk mRNA levels compared to endogenous transcription rates of TH & ppEnk genes and b) whether synthesis of new protein is required for these effects.

DESIGN/METHODS: PC12 cells were exposed to 1 or 6 mM SB. The relative TH & ppEnk mRNA levels and rate of transcription were determined at different time intervals by Northern blot analysis & run-on assays. The ability of SB to modulate neurotransmitter gene expression was compared in control, vehicle treated cells & cells exposed to the protein synthesis inhibitor cycloheximide (CH).

RESULTS: At the lower concentration of SB (1 mM) the gradual accumulation of TH & ppEnk mRNA was associated with an increased rate of transcription for both genes. Moreover, inhibition of protein synthesis by CH did *not* affect the ability of SB to elevate TH & ppEnk mRNA levels. Similalry, at the higher dose (6 mM), the rate of transcription of both genes was upregulated. However, while ppEnk mRNA levels *increased* under these conditions, the relative TH mRNA levels were significantly *decreased*. The effect on lowering TH mRNA levels required *de novo* protein synthesis.

CONCLUSIONS: SB has dose-dependent effects on TH mRNA levels operating by different molecular mechanisms. **Speculation:** SB may act as a molecular switch *in vivo* to regulate steady-state levels of TH mRNA depending on the plasma concentration. In turn, this may affect the production of catecholamines and neonatal adaptive responses to stress. For example, down-regulation of TH mRNA levels by SCFA may contribute to the blunted epinephrine responses characteristic of hypoglycemia associated autonomic failure. These findings may have additional clincial significance during states of high circulating levels of SCFA (i.e. ketoacidosis, starvation).

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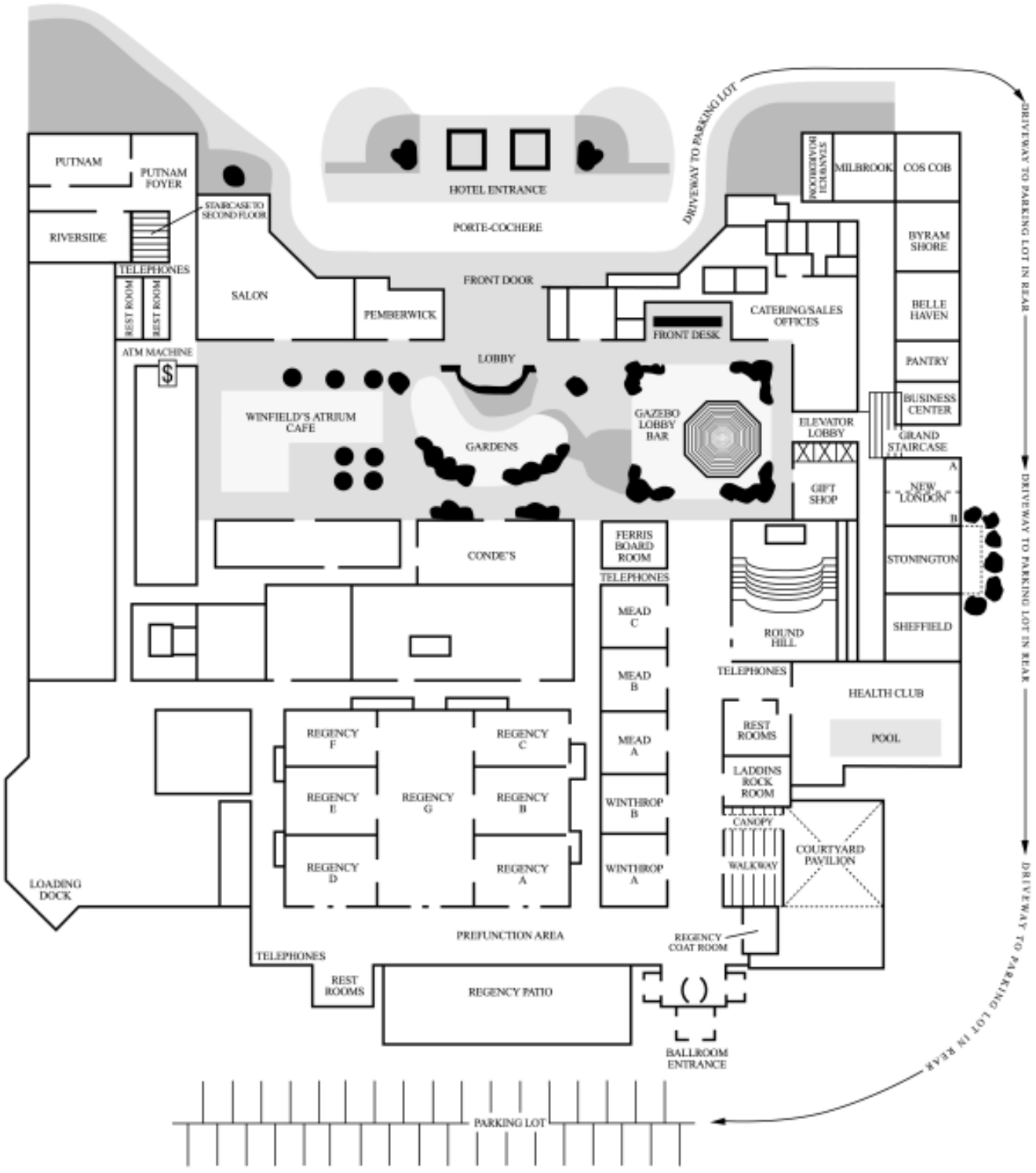

Notes

SAVE THE DATES!

ESPR 18th Annual Meeting

March 17-19, 2006
Hyatt Regency, Old Greenwich, CT

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