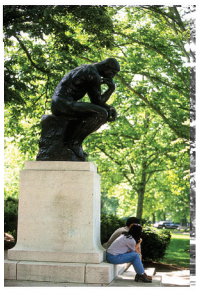
Program Guide

March 25-27, 2011 • Doubletree Hotel • Philadelphia, PA





THE EASTERN SOCIETY FOR PEDIATRIC RESEARCH

23rd Annual Meeting

Jointly Sponsored By:
The Center for Continuing Education,
Tulane University Health Sciences Center

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Contents

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The ESPR would like to express appreciation to the following companies for their support:

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Help Support our exhibitors by visiting their booths during these hours:

Friday	6:00 pm - 7:30 pm
Saturday	7:30 am - 8:30 am
	10:30 am - 10:45 am
	4:00 pm - 4:15 pm
	6:00 pm - 7:30 pm
Sunday	7:45 am - 8:30 am
	9:30 am - 9:45 am

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Boston, MA

Dear Colleagues,

Welcome to the 23rd Annual Meeting of the Eastern Society for Pediatric Research (ESPR) and to our host city of Philadelphia, the Cradle of Liberty!

The Eastern Society for Pediatric Research Council and Planning Committee are confident that you will enjoy our exciting program. Highlights include State-of-the-Art Plenary Talks and the highly popular Lunch with the Professor educational program for trainees, which has been expanded to cover two pertinent topics. High-quality original research is presented in subspecialty platform sessions with leading clinical and scientific authorities moderating the presentations and in two poster sessions.

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

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

ACKNOWLEDGEMENTS: The organization of this meeting would not have been possible without the help of the administrative offices of the American Pediatric Society (APS) and the Society for Pediatric Research (SPR). We are especially grateful to: Debbie Anagnostelis (Executive Director), Kathy Cannon, Belinda Thomas, Jesse Osman and Lisa Thompson. We also recognize the energetic efforts of the Eastern SPR Planning Committee and Council Members for their guidance and vision in selecting this new venue and the efforts of Tulane University in New Orleans as our 2011 sponsor for the CME program. In addition, we thank various members of the regional pediatric community for reviewing the submitted abstracts and for moderating our platform sessions. Lastly, our corporate and leading academic sponsors were instrumental in making this meeting possible.

Most of all, we want to thank you for attending and for contributing your wisdom and experience in the pursuit of excellence. We hope that you enjoy and profit from the meeting, and look forward to your continued participation in future meetings!

Lawrence Nogee, MD
President

Edmund F. La Gamma, MD, FAAP
Secretary

George Porter, Jr. MD, PhD
Chair, Planning Committee

THE EASTERN SOCIETY FOR PEDIATRIC RESEARCH

RECOGNITION OF NEW MEMBERS

The Council of the Eastern Society for Pediatric Research would like to recognize the following new members who have joined the society within the last year.

Membership in the Society reflects not only peer recognition of research achievements in pediatrics, but continuing commitment to pediatric research and fostering the career development the next generation of pediatric researchers. The Council and Society members welcome active participation in the organization. Like our parent organization, the Eastern SPR seeks to promote the generation of new knowledge, the professional growth of the current and next generation of academic pediatricians, and the translation of research discoveries into treatments that will benefit children worldwide. We believe that membership and active participation in the Eastern Society for Pediatric Research can meaningfully contribute to professional success as an academic pediatrician.

To celebrate this achievement, new members will be recognized at the Opening Reception on Friday, March 25, 2011. Once again, congratulations and welcome to the Eastern Society for Pediatric Research.

Marc Auerbach, M.D., Yale University School of Medicine
Timothy Baba, M.D., Ph.D., Floating Hospital for Children at Tufts Medical Center
Helen Christou, M.D., Brigham and Women's Hospital, Harvard Medical School
Caroline Chua, M.D., Geisinger Medical Center
Diva De Leon, M.D., The Children's Hospital of Philadelphia
Roberta DeBiasi, M.D., Children's National Medical Center
Gary Emmett, M.D., Thomas Jefferson University Hosptial
Evan Fieldston, M.D., MBA, MSHP, The Children's Hospital of Philadelphia
Joanna Floros, Ph.D., Penn State College of Medicine
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Maida Galvez, M.D., MPH, Mount Sinai School of Medicine
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Lisa Saiman, M.D., MPH, Columbia University
Samir Shah, M.D., MSCE, The Children's Hospital of Philadelphia
Charles Stanley, M.D., The Children's Hospital of Philadelphia
Alfin Vicencio, M.D., Cohen Children's Medical Center of New York
Clyde Wright, M.D., The Children's Hospital of Philadelphia

Meeting Services & CME Accreditation

Registration and CME Desk Hours

Registration will be held on the 3rd floor. Registration hours are as follows:

Friday, March 25	4:00pm – 7:00pm
Saturday, March 26	7:30am – 7:30pm
Sunday, March 27	7:30am – 1:00pm

Abstract Publication

All abstracts being presented at the 2011 Eastern SPR Annual Meeting are printed in this Program Guide, beginning on page 15.

Audio/Visual Information

All oral presentations must be made using PowerPoint. Computers and LCD projectors will be provided. Presenters should have submitted their presentations in advance, are still required to check in at Speaker Ready.

Speaker Ready (Chamber Board Room-4th floor)

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

Business Center

The Business Center at the Doubletree Philadelphia is located on the 3rd floor.

Statement Of Need

Research and technology are changing rapidly in medicine and it is important for physicians and healthcare professionals to critically evaluate the emerging developments. Physicians and healthcare professionals in pediatrics need to increase their competence in discerning which of the emerging research and technologies are applicable to their patient populations. Discussions and debates on these emerging data stimulate the development of new guidelines, appropriateness criteria and evidence-based changes in medical practice.

The ESPR annual meeting provides a forum for young investigators to share their translational and clinical research with mentors and senior investigators. This gives the junior investigators important feedback in a non-threatening environment, provides for critiques and opportunities to improve the presentation before presenting on a national stage, and fosters mentoring from senior investigators.

The senior investigators benefit from this educational format by engaging in discussions on how to translate the research into practice, debates on how the new information supports or discredits the "old" information, and assists in the design of possible new research options and extensions.

The Eastern Society for Pediatric Research Annual Meeting addresses a three-fold need:

1. Young investigators need to increase their competence and performance in presenting their research in a structured yet relaxed atmosphere.
2. Regional clinicians need to increase their competence in evaluating and designing strategies to incorporate cutting edge clinical and basic science into practice.
3. Trainees need to increase their competence and performance in establishing collaborative relationships with mentors to address the barriers which may be interfering with research development.

Target Audience

Physicians within the pediatric specialties, internal medicine, family medicine.

Non-physicians: Scientific researchers in both translational and clinical research in pediatrics. Healthcare professionals engaged with the pediatric population.

Overview And Objectives

The overall goal of this meeting is to improve patient care by increasing learner competence in evaluating the emerging translational and clinical research in pediatrics and determining parameters for expansion and modification of promising research developments while fostering the preliminary research of young investigators.

Learner Objectives: At the conclusion of this educational activity, the participant should be better able to:

- Critically evaluate the emerging translational and clinical research.
- Discuss new developments in pathophysiology of human disease with colleagues.
- Identify new areas of investigation which will inform research and improve patient care.
- Develop optimal strategies for clinical investigation and transmission of clinical research results.
- Develop relationships with mentors and peers to address the barriers which interfere with research development.

Predicted Outcomes:

- Determine whether appropriate changes need to be recommended in patient protocols as indicated in the emerging research data.
- Implement new tools for teaching, research and medical practice.
- Apply appropriate evidence based recommendations in my research, teaching and/or medical practice.
- Present research in a national forum.
- Establish collaborations to expand or address barriers which are identified

Accreditation:

Physicians

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

Tulane University Health Sciences Center designates this live activity for a maximum of 11.50 AMA PRA Category 1 CreditsTM. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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

Tulane Disclosure Policy

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

How To Obtain Your *AMA PRA* Category 1 Credits™

Tulane and the Eastern Society for Pediatric Research are now using a secure electronic format for evaluation and credit verification. The evaluation remains anonymous but the link does allow you to give us your contact information which will be incorporated into the Certificate of Credit.

At the conclusion of the conference on Sunday, you will be sent a link to an electronic evaluation and credit verification form. If you do not receive this in your inbox on Sunday afternoon, check your spam/junk mailbox. You can contact cme@tulane.edu if you did not receive it and Tulane will send you another link for claiming your credits.

You will receive your certificate of credit by Wednesday, April 29, 2011. If you do not receive it by then, please notify Tulane University at cme@tulane.edu.

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Eastern SPR Schedule-at-a Glance

Doubletree Philadelphia
March 25-27, 2011

Friday, March 25

6:00pm–7:30pm

Poster Session I & Reception
— Symphony Ballroom - 3rd Floor —

Saturday, March 26

7:30am–8:30am

Continental Breakfast
— Symphony Ballroom - 3rd Floor —

8:15am–10:30am

Neonatology - Pulmonary I
— Overture - 3rd Floor —

Neonatology - Infectious Diseases
— Aria A - 3rd Floor —

GI/Hematology - Oncology/Nephrology/Nutrition
— Maestro B - 4th Floor —

General Pediatrics I
— Concerto - 3rd Floor —

General Pediatrics - Vulnerabilities
— Maestro A - 4thFloor —

Pulmonary & Asthma
— Minuet - 4th Floor —

10:30am–10:45am

Coffee Break
— Symphony Ballroom - 3rd Floor —

10:45am–11:45am

Plenary Session I

PLENARY LECTURE
Gary Freed, MD, MPH
Pediatric Workforce: Can Research Impact Policy?
— Overture - 3rd Floor —

12:00pm–1:00pm

Meet the Professor Lunch
Gary Fleisher, MD and Gary Freed, MD, MPH
— Aria A - 3rd Floor —

Iman Sharif MD
Nuts and Bolts of Writing an IRB Proposal
— Concerto - 3rd Floor —

Eastern SPR Business Meeting
— Rhapsody - 4th Floor —

1:10pm–4:00pm

Plenary Session II

MENTOR OF THE YEAR
Gary Fleisher, MD
Fevers, Fellows, and Positive Cultures
— Overture - 3rd Floor —

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

4:00pm–4:15pm

Coffee Break
— Symphony Ballroom - 3rd Floor —

4:15pm–5:45pm

Cardiovascular & Critical Care
— Minuet - 4th Floor —

General Pediatrics - Medical Education & Quality Improvement
— Maestro A - 4thFloor —

Infectious Diseases & Immunology
— Aria A - 3rd Floor —

Neonatology - Clinical Studies I
— Overture - 3rd Floor —

Neonatology - Epidemiology and Follow Up
— Concerto - 3rd Floor —

Neurobiology I
— Maestro B - 4th Floor —

6:00pm-7:30pm

Poster Session II & Reception
— Symphony Ballroom - 3rd Floor —

Sunday, March 27

7:45am–8:45am

Continental Breakfast
— Symphony Ballroom - 3rd Floor —

8:30am–9:30am

Plenary Session III

PRESENTATION OF THE YOUNG INVESTIGATOR AWARDS

PLENARY LECTURE
Hal Dietz, MD
Marfan Syndrome and Related Disorders; From Molecules to Medicines
— Overture - 3rd Floor —

9:30am–9:45am

Coffee Break
— Symphony Ballroom - 3rd Floor —

9:45am–12:00pm

General Pediatrics II
— Aria A - 3rd Floor —

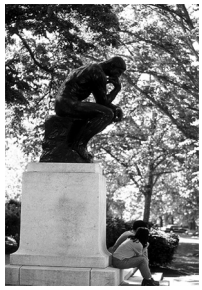
Emergency Medicine
— Maestro A - 4th Floor —

Neonatology - Clinical Studies II
— Overture - 3rd Floor —

Neonatology - Pulmonary II
— Concerto - 3rd Floor —

Endocrinology & Obesity
— Minuet - 4th Floor —

Neurobiology II
— Maestro B - 4th Floor —



□□□ Friday, March 25, 2011 □□□

Poster Session I

General Pediatrics

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

1 **The Association of Vitamin D Deficiency and Asthma Severity in Children**
Archana Mehta, Janelle Sher, Mary J. Ward, Melanie Wilson-Taylor. – Abstract 1

2 **The Impact of Teaching Metered-Dose Inhaler Administration to Residents and Medical Students**
Sharyn H. Miskovitz, Jason Fletcher, Sandra F. Braganza. – Abstract 2

3 **Edinburgh Postpartum Depression Scale Score among Mothers of Infants in the NICU**
Cynthia O. Isedeh, Emily Valentino, Emelynn J. Fajardo, Sandra Rudnitzky, Ben H. Lee. – Abstract 3

4 **Postpartum Depression Screening Program – The Attitudes and Acceptance of Pediatric Care Providers**
Sandeep K. Sadashiv, Kerry Kauffman, Andy C. Wang, Michael Janeczko. – Abstract 4

5 **What Is My Neighborhood? Using Travel Patterns by Urban Minority Children and Their Families To Define Neighborhood**
Leigh S. Goldstein, Maida P. Galvez, Susan Teitelbaum, Kathleen McGovern, Mary S. Wolff, Barbara Brenner. – Abstract 5

6 **Can Postnatal Weight Loss Predict Early Onset Neonatal Hyperbilirubinemia?**
Nidhi Agarwal, Rusly Harsono, Fernanda Kupferman, Lourdes Cohen, Shirley Pinero, Louis Primavera, Susana Rapaport. – Abstract 6

7 **Perceptions of English and Spanish-Speaking Caregivers about the Role of Pediatricians in Community Violence Prevention Counseling**
Mario Cruz, Raphael Rom, Saskia Spiess, Salman Farsi, Daniel Taylor. – Abstract 7

8 **Relationship between Health Literacy and Body Mass Index**
Roopa Chari, Joel Warsh, Tara Ketterer, Adam Badaczewski, Iman Sharif. – Abstract 8

9 **Performance of the NVS and STOFHLA in Children**
Iman Sharif, Laurie Bauman, Debra Roter, Tara Ketterer, Roopa Chari, Deepa Rastogi, Sandra Braganza, Mary Ann Abrams, Katherine Freeman, Arthur E. Blank, Ruth E.K. Stein, Benard P. Dreyer. – Abstract 9

10 **Preliminary Validation of the Newest Vital Sign in School-Aged Children**
Joel Warsh, Adam Badaczewski, Iman Sharif. – Abstract 10

11 **Clearing the Air: Outdoor Fine Particulate Matter and Costs of Infant Bronchiolitis Hospitalizations**
Perry E. Sheffield, Angkana Roy, Kendrew Wong, Leonardo Trasande. – Abstract 11

12 **Using Audience Response Systems To Determine Gaps in Pediatric Environmental Health Knowledge**
P. Sheffield, S. Balk, S. Braganza, M. Chitkara, J. Forman, M. Galvez, A. Miodovnik, S. Palevsky, A. Roy, H. Brumberg. – Abstract 12

13 **Developing a Best Practices Algorithm To Minimize Infant Risk of Bilirubin Encephalopathy**
Melissa A. Schneider, Claire Hoppenot, Gary A. Emmett. – Abstract 13

14 **Are We Communicating with Primary Care Providers? – Assessment after Initiation of a Pediatric Hospitalist Program**
Sheila Liewehr, Lindsey Douglas. – Abstract 14

15 **Pre-Menarchal Girls' and Parents' Perceptions about Urogenital Symptoms: Causes and Associations**
Cynthia W. DeLago, Carmen V. Vasquez, Claudia Clarke, Esther Deblinger, Martin Finkel. – Abstract 15

16 **Health, Obesity, and Environment in East Harlem, NY**
Maida Galvez, Lawrence C. Kleinman, Carol Horowitz, Nita Vangeepuram, Michelle Ramos, Thalia MacMillan. – Abstract 16

17 **Mexican Children in East Harlem, NY Have Distinct Diet and Activity Behaviors Compared to Other Hispanic Children**
Nita Vangeepuram, Maida P. Galvez, Thalia L. MacMillan, Michelle Ramos, Carol R. Horowitz, Lawrence C. Kleinman. – Abstract 17

18 **A Comparison of Dietary and Physical Activity Behaviors in New York City Children from Different Ethnic Minority Subgroups**
Nita Vangeepuram, Nancy Mervish, Susan L. Teitelbaum, Maida P. Galvez, Barbara Brenner, Mary S. Wolff. – Abstract 18

Cardiovascular & Critical Care

19 **Duration of Central Venous Line Is Not Associated with Increased Deep Venous Thrombosis in Critically Ill Children**
E. Vincent S. Faustino, Sheila J. Hanson, Karla A. Lawson, Renee A. Higgerson. – Abstract 19

20 **Coronary Complications in Children with Kawasaki Disease in Association with Time of IVIG Treatment**
Deepa Prasad, Aswine Bal, Maria UmaliPamintuan, Elizabeth MammenPrasad, Anna Petrova. – Abstract 20

21 **Cardiac Effects of CNS Stimulants in Patients with ADHD: Comparing the Recommendations of the American Heart Association with the American Academy of Pediatrics**
Deepak Patel, Karen Carpenter, Robert Escalera. – Abstract 21

22 **Mitochondrial Function Is Limited in the Early Embryonic Heart Due to a Dysfunction in Complex I**
David L. Hoffman, Jennifer R. Hom, George A. Porter. – Abstract 22

Neurobiology

23 **Src Kinase-Mediated Mechanism of CREB Protein Phosphorylation during Hypoxia in Neuronal Nuclei of Newborn Piglets**
Cindy Soon, Simran Ahluwalia, Anli Zhu, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 23

24 **Effect of Hypoxia on Caspase-3 Activation Following Src Kinase Inhibition in the Newborn Piglet Brain**
Amit M. Mukhia, Kirstie Marcello, Lynn Fuchs, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 24

25 **Mechanism of Increased Expression of CaM Kinase IV during Hyperoxia in the Neuronal Nuclei of the Cerebral Cortex of Newborn Piglets**
Leslie A. Ridall, Qazi Ashraf, Amit Mukhia, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 25

26 **Effect of Neuronal Nitric Oxide Synthase (nNOS) Inhibition during Hyperoxia on Expression of CaM Kinase IV in Neuronal Nuclei of the Cerebral Cortex of Newborn Piglets**
Janice Hobbs, Lynn Fuchs, David Fralinger, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 26

27 **Effect of Neuronal Nitric Oxide Synthase (nNOS) Inhibition during Hyperoxia on Expression of CaM Kinase-Kinase in Neuronal Nuclei of the Cerebral Cortex of Newborn Piglets**
Janice Hobbs, Jarle Stone, Qazi Ashraf, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 27

28 **Mechanism of Tyr^{99} Phosphorylation of Calmodulin during Hyperoxia in the Newborn Brain**
Justin R. Buland, Kirstie Marcello, Nicholas Obiri, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 28

29 **Effect of Chronic Postnatal Inflammation on Somatic and Brain Growth in Mice**
Shadi N. Malaeb, Jonathan M. Davis, Olaf Dammann, Maribel Rios. – Abstract 29

30 **Hypothermia Attenuates Hypoxic Neuronal Insults in C Elegans**
Saima Aftab, Robert Kalb. – Abstract 30

31 **Amplitude EEG (aEEG) Response during Surgical Ligation (SL) of a Patent Ductus Arteriosus (PDA) in Preterm Infants (PI) Is a Potential Measure of Pain Control**
Ericalyn Kasdorf, Murray Engel, Jeffrey M. Perlman. – Abstract 31

32 **Evaluation of Use and Parental Perception of Improvement in Disease Symptoms with Complementary and Alternative Medication in Patients with Attention Deficit Hyperactivity Disorder Currently Undergoing Conventional Treatment**
Monideep Dutt, Jose Serruya, Arati Reddy, Louis Primavera, Fernanda Kupferman, Rusly Harsono, Kanchana Roychoudhury, Susana Rapaport, Partha Chatterjee. – Abstract 32

Pulmonary & Asthma

33 **Traditional Pulmonary Function Testing Interpretation Understimates Obstructive Airway Disease by Ignoring the Small Airway**
Patricia Visbal Edmondson. – Abstract 33

34 **Younger Infants with RSV Bronchiolitis: Should We Admit Them?**
Gaston I Zylberg, Ramkumar Natarajan, Fernanda Kupferman, Lily Q. Lew, Susana Rapaport, Rusly Harsono. – Abstract 34

Infectious Diseases & Immunology

35 **Novel Use of the Audience Response System To Improve Adherence to Transmission Precautions**
Lisa Saiman, Lauren D. Rosenberg. – Abstract 35

36 **Severity of Illness and Use of the 'Medical Home' during the First vs. Second Waves of 2009 Influenza a (H1N1) in a Pediatric Healthcare Facility**
Saul R. Hymes, Amanda Buet, J. Scott Baird, Jonathan Sury, Patricia DeLaMora, Lisa Saiman. – Abstract 36

37 **Increased LDL-Cholesterol (LDL-C) in HIV-Infected Children on Highly Active Antiretroviral Therapy (HAART)**
Prabi Rajbhandari, Sudershan Subedi, Stefan Hagmann, Murli Purswani, Milred Maldonado. – Abstract 37

38 **Racial Variation in RSV Immunoprophylaxis**
Erika F. Dennis, Corrine Fager, Scott A. Lorch. – Abstract 38

39 **Role of CXCR2 and Heparan Sulphate Proteoglycan in CXCL5-Regulated Chemokine Clearance and Lung Inflammation**
Junjie Mei, Ning Dai, Yuhong Liu, Samithamby Jeyaseelan, Janet S. Lee, G. Scott Worthen. – Abstract 39

Neonatology

40 **Less Is More: Cost Savings of Fluid Restriction in Transient Tachypnea of the Newborn**
Annemarie Stroustrup, Leonardo Trasande, Ian R. Holzman. – Abstract 40

41 **Effect of Perinatal Prophylaxis for Group B Streptococcus on Severity of Transient Tachypnea of the Newborn**
Annemarie Stroustrup, Roxane Perez, Elissa DeLorenzo, Ian R. Holzman. – Abstract 41

42 **The Development of a Decision-Aid To Guide Counseling of Parents Facing Imminent Extreme Premature Delivery**
Ursula Guillen, Sanghee Suh, David Munson, Michael Posencheg, Elissa Truitt, John Zupancic, Amiram Gafni, Haresh Kirpalani. – Abstract 42

43 **Placental Transfusion Strategies in Preterms <1000 g BW: Meta-Analysis of Short and Long Term Outcomes**
Sarvin Ghavam, Dushyant Batra, Heike Rabe, Mercer Judith, Kugelman Amir, Hosono Shigeharu, Haresh Kirpalani. – Abstract 43

44 **Age Dependent Inter-alpha Inhibitor Protein (IAIP) Concentration in Plasma and Expression in Ovine Liver, Kidney and Heart**
Mariya Spasova, Grazyna B. Sadowska, Yow-Pin Lim, Barbara S. Stonestreet. – Abstract 44

45 **Transient In Utero Knockout (TIUKO) of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Gene Results in Gut Immaturity and Inflammation in Adult Sprague-Dawley Rats**
John J. Tadros, Shetal I. Shah, Craig Cohen. – Abstract 45

46 **Real-Time Cerebral, Splanchnic, and Renal Near-Infrared Spectroscopy (NIRS) in Very Low Birthweight Neonates: An Analysis of Baseline Variability**
Jonathan P. Mintzer, Joseph Dayan, Monique Gardner, Michelle Master, Michael Chelala, Gad Alpan, Edmund F. LaGamma, Boriana Parvez. – Abstract 46

47 **Complications Associated with Peripherally Inserted Central and Non-Central Catheters in the Newborn Intensive Care Unit**
Kathryn E. Colacchio, Yanhong Deng, Veronika Northrup, Matthew Bizzarro. – Abstract 47

48 **Developmental Outcome in Late Preterm Infants at 24 to 30 Months of Age**
Vinay Sharma, Fernanda Kupferman, Susana Rapaport, Esmil Perez, Lourdes Cohen, Harsono Rusly, Louis Primavera, Kanchana Roychoudhury. – Abstract 48

49 **Breastmilk Science: Critical Review of Publications over the Last 30 Years**
Angela Mukherjee, Celia Thomas, Sheila Mak, Nancy Mejias-Cepeda, Ben H. Lee. – Abstract 49

50 **Increased Odds of Mechanical Ventilation at 36 Weeks Gestation: Gestational Age Paradox**
Romal K. Sekhon, Amy B. Mackley, David A. Paul. – Abstract 50

51 **Red Blood Cell Storage Time and Morbidities of Prematurity**
Jonathan R. Swanson, Elias Matta, Catherine Sawtell, Charles Matarazzo, Ben Lee. – Abstract 51

52 **Late Preterm Infants' Skill at First Oral Feeding Predicts Length of Hospital Stay**
Kiran Bhat, Chantal Lau, Richard J. Schanler. – Abstract 52

53 **Enhancement of Accuracy of the Umbilical Vein Catheter Tip Localization: Using Echocardiography and X-Rays**
Anoop Pulikal, Pradeepkumar Charlagorla, Sbestian Tume, Ali Nadroo, Manoj Chabra. – Abstract 53

54 **Thyroid Function in Late Preterm Infants in Relation to Respiratory Morbidity and Mode of Delivery**
Renee M. Behme, Amy B. Mackley, Louis Bartoshesky, David A. Paul. – Abstract 54

55 **Premature Infants Conceived Via Artificial Reproductive Technology (ART) Are More Immature Than Naturally Conceived (NC) Infants of Similar Gestational Age (GA)**
Melissa Scala, Jennifer Berg, Martin Keszler, Kabir M. Abubakar. – Abstract 55

56 **Role of 4G/5G Single Nucleotide Polymorphism in the Spontaneous Closure of Patent Ducutus Arteriosus?**
Divya Chhabra, Johanna M. Calo, Edel Mendoza, Kristen Aland, Lance A. Parton. – Abstract 56

57 **Association of Placental Inflammatory Changes with Maternal Fever and Elevated Neonatal CRP: A Guide To Initiate Antimicrobial Therapy**
P. Charlagorla, C. Abban, C. Salafia, S Van Horn, D. Hoang, B. Dygulska, P. Narula. – Abstract 57

58 **Urinary Biomarkers of Acute Kidnew Injury (AKI) in Critically Ill Neonates**
Suma B. Hoffman, An N. Massaro, Angel Soler Garcia, Sofia Perazzo, Patricio Ray. – Abstract 58

□□□ Saturday, March 26, 2011 □□□

Neonatology - Pulmonary I Platform Session

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

Moderator: Phyllis Dennery, MD

8:15 AM **Generation of Mice with Lung-Specific Expression of Nuclear Heme Oxygenase-1**
Fumihiko Namba, Ping La, Amal P. Fernando, Guang Yang, Phyllis A. Dennery. – Abstract 59

8:30 AM **VEGF Heparin-Binding Isoform Attenuates Hyperoxia Via Neuropilin-1 in Explanted Embryonic Lung**
Americo E. Esquibies, Alia Bazzy-Asaad, Lloyd G. Cantley. – Abstract 60

8:45 AM **S-Nitrosylation of Surfactant Protein-D Upregulates C-C Chemokine Ligand 2 (CCL-2) Expression in Macrophages**
Rania El-Khawam, Changjiang Guo, Andrew Gow. – Abstract 61

9:00 AM **Neonatal Hyperoxia Restricts Somatic Growth, Induces Chronic Lung Disease (CLD) & Pulmonary Hypertension (PH) in Adult Mice**
Vasanth H. Kumar, Huamei Wang, Daniel D. Swartz. – Abstract 62

9:15 AM **NFκB Is Essential in Regulating Rev-erbα Promoter Activity in Hyperoxia**
Guang Yang, Haiyan Xiao, Maurice D. Hinson, Ping La, Qing S. Lin, Clyde J. Wright, Phyllis A. Dennery. – Abstract 63

9:30 AM **Angiogenesis in Neonatal Hyperoxic Lung Injury**
Anne Chetty, Gong-jie Cao, Heber C. Nielsen. – Abstract 64

9:45 AM **miR-221 and miR-130 Regulate Hox Genes Controling Vascular and Epithelial Morphogenesis in Developing Lung**
Sana Mujahid, Heber C. Nielsen, MaryAnn V. Volpe. – Abstract 65

10:00 AM **Neonatal Hyperoxia Leads to Arrested Lung Development with Absent Compensatory Lung Growth in Adult Mice as Measured by Radial Alveolar Count (RAC)**
Vasanth H. Kumar, Huamei Wang, Rita M. Ryan. – Abstract 66

10:15 AM **Hox Control of Vasculogenesis in Developing Mouse Lung**
Thanhxuan Vong, Sana Mujahid, Heber C. Nielsen, MaryAnn V Volpe. – Abstract 67

Neonatology - Infectious Diseases Platform Session

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

Moderator: Rita Ryan, MD

8:15 AM **Lipases as Virulence Factors in Candida Albicans and Parapsilosis Infection in a Neonatal Rat Model of Invasive Candidiasis**
David Tofra, Lamia M. Soghier, Christina Long, Joshua D. Nosanchuk, Atilla Gacser, David L. Goldman. – Abstract 68

8:30 AM **Prolonged Antibiotics in the First Week of Life Increase the Odds of Chronic Lung Disease (CLD) in Very Low Birth Weight Infants**
Alexandra Novitsky, Deborah Tuttle, Robert G. Locke, Lisa Saiman, Amy Mackley, David A. Paul. – Abstract 69

8:45 AM **The Role of Nitrated Fatty Acids in Modulating Inflammation in Neonates**
Sharada H. Gowda, Faith E. Archer, Debra L. Laskin, Andrew Gow, Anna M. Vetrano, Barry I. Weinberger. – Abstract 70

9:00 AM **Usefulness of Urinary Immune Biomarkers in Evaluation of Neonatal Sepsis: A Pilot Project**
Sukumar Suguna Narasimhulu, Karen D. Hendricks-Munoz, William Borkowsky, Pradeep V. Mally. – Abstract 71

9:15 AM **Enhanced Neonatal Cord Blood (CB) Natural Killer (NK) Cell Activation Following Stimulation with Genetically Engineered K562 Cells: Potential for CBNK Amplification for Neonatal Adoptive Cellular Immunotherapy (ACI)**
Michele A. Levin, Janet Ayello, Jessica Hochberg, Carmella Vandeven, Frances Zhao, Mitchell S. Cairo. – Abstract 72

9:30 AM **Inflammation in Neonatal Bacterial Meningitis: The Role of Novel Biomarkers**
Lakshmi Srinivasan, Laurie Kilpatrick, Soraya Abbasi, Mary C. Harris. – Abstract 73

9:45 AM **Docosahexaenoic Acid (DHA) Upregulates the Innate Immune Response in Neonatal Cord Blood**
Michael M. Espiritu, Jeffrey M. Perlman, Susanna Cunningham-Rundles. – Abstract 74

10:00 AM **Reference Ranges for Cerebrospinal Fluid (CSF) Parameters in Non-Infected Preterm and Term Infants in the NICU – A Multicenter Prospective Study**
Lakshmi Srinivasan, Samir S. Shah, Michael A. Padula, Soraya Abbasi, Karin L. McGowan, Mary C. Harris. – Abstract 75

10:15 AM **Efficacy of Als3p-Specific Monoclonal Antibody in a Mouse Model of Neonatal Candidiasis**
Nancy Y. Tsai, Sonia S. Laforce-Nesbitt, Lois L. Hoyer, Joseph M. Bliss. – Abstract 76

GI / Hematology - Oncology / Nephrology / Nutrition Platform Session

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

Moderator: Susan Furth, MD, PhD

8:15 AM **Changes in Vitamin D Status in Incident Pediatric Crohn Disease**
Aaron R. Prosnitz, Mary B. Leonard, Justine Shults, Babette S. Zemel, Bruce W. Hollis, Robert N. Baldassano, Meena Thayu. – Abstract 77

8:30 AM **Preliminary Results of Phase I/II Study of Clofarabine (CLO) in Combination with Cytarabine (ARA-C) and Total Body Irradiation (TBI) Followed by Allogeneic Stem Cell Transplantation (AlloSCT) in Children, Adolescents and Young Adults (CAYA) with Poor-Risk Acute Leukemia**
Angela Ricci, Mark Geyer, Lauren Harrison, Dierdre Duffy, Monica Bhatia, James Garvin, Diane George, Prakash Satwani, Alexa Cheerva, Julie Talano, M. Fevzi Ozkaynak, Theodore Moore, Joseph Schwartz, LeeAnn Baxter-Lowe, Mitchell S. Cairo.
– Abstract 78

8:45 AM **Are Children with Elevated Body Mass Index at Increased Risk for Gastroesophageal Reflux? A Community-Based Study**
Sowmya Angusamy, Babu Bangaru, Louis Primavera, Rapaport Susana, Fernanda Kupferman. – Abstract 79

9:00 AM **Thyroid Dysfunction in Children with Immune Thrombocytopenia (ITP)**
Jennifer Hughes, Zoltan Antal, James Hurley, Mary J. James, James Bussel. – Abstract 80

9:15 AM **Bone Mineral Metabolism in Pediatric Kidney Transplant Recipients**
PJ Galutira, S. Beste, N. Samtani-Gaffney, M. DelRio, B. Goilav.
– Abstract 81

9:30 AM **Coordinated Synthesis of Heme and Iron-Sulfur Clusters in Mammalian Cells: Implications for Cell Function**
Ping La, Phyllis A. Dennery. – Abstract 82

9:45 AM **Pediatric Pharmacokinetics (PK) of IV Busulfan (Bu) in Allogeneic Stem Cell Transplantation (AlloSCT) Recipients: Dosing q12 Hours Schedules Are Safe and Comparable to q6 Hours Schedules**
John LeGall, Michael Milone, Ian Waxman, Les Shaw, Lauren Harrison, Deirdre Duffy, Olga Militano, Monica Bhatia, Prakash Satwani, Diane George, James H. Garvin, M. Brigid Bradley, Carmella van de Ven, Mitchell S. Cairo. – Abstract 83

10:00 AM **GA101, a Type II Glycoengineered Antibody Against CD20 Induces Significant InVitro Cell Death of PreB-ALL (PBALL) and PreB Lymphoblastic Lymphoma (PBLL)**
Christina Cho, Janet Ayello, Andrew Stier, William Quish, Mitchell S. Cairo. – Abstract 84

10:15 AM **Vitamin D Levels and Bone Density of Children with IBD: Experience of a Pediatric Digestive Disease Center in Northern Virginia**
Vahe Badalyan, Stacie Townsend, Samantha Fish, Ian Leibowitz.
– Abstract 85

General Pediatrics I Platform Session

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

Moderator: Karen Carpenter, MD

8:15 AM **Effectiveness of a Brief Health Education Intervention To Address Chronic Malnutrition in Quito, Ecuador**
Preetha J. Iyengar, Kathryn Scharbach, Sandra F. Braganza.
– Abstract 86

8:30 AM **Which Visual Formats of Complex Data Best Help Patients Make Informed Health Decisions?**
Sanghee Suh, Ursula Guillen, Haresh Kirpalani. – Abstract 87

8:45 AM **Does Umbilical Cord Length — An Indirect Measure of Fetal Activity — Predict Hyperactivity in Grade School Children?**
Andrew Adesman, Jennifer K. Leung, Ruth Milanaik, Sarah A. Kiem.
– Abstract 88

9:00 AM **Pretesting Health Reform: Impact of State Laws Extending Parents' Health Insurance Coverage to Young Adults**
Alexander B. Blum, Joseph S. Ross, Lawrence C. Kleinman.
– Abstract 89

9:15 AM **Do Questions about Parent Concerns Provide Adequate Surveillance?**
Emily N. Neger, Shela Merchant, Brandi S. Henson, R. Christopher Sheldrick, Ellen C. Perrin. – Abstract 90

9:30 AM **Comparison of Anthropometric Measures in the Longitudinal Assessment of Fat Mass**
Thao-Ly T. Phan, Michelle M. Maresca, Hossain Jobayer, George A. Datto. – Abstract 91

9:45 AM **Improving Response Rate for Mailed Pediatric Questionnaires: Effect of Cover Letter Tone and Literacy Level**
Andrew Adesman, Alison Cohn, Nina Kohn, Helen Papaioannou, Ruth Milanaik. – Abstract 92

10:00 AM **Development and Initial Validation of the Preschool Pediatric Symptom Checklist (PPSC)**
Shela Merchant, Brandi S. Henson, R. Christopher Sheldrick, Ellen C. Perrin, J. Michael Murphy. – Abstract 93

10:15 AM **Doing the FDA's Bidding: Off-Label Pediatric Drug Studies in the Medical Literature**
Douglas Nassif, Luis Gamboa, Priya Bhasker, Susannah Olnes, Karen Carpenter. – Abstract 94

General Pediatrics - Vulnerabilities Platform Session

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

Moderator: David Listman, MD

8:15 AM **Urine STD Screening of Pediatric Patients Presenting to the Emergency Department with Behavioral/Psychiatric Complaints. Are They at High Risk of Infection?**
David A. Listman, Ashmita Monga, Jennifer Goodrich. – Abstract 95

8:30 AM **Impact of Shared Decision Making on Behavioral Impairment among US Children with Special Health Care Needs**
Alexander Fiks, Russell Localio, Stephanie Mayne, Evaline Alessandrini, James Guevara. – Abstract 96

8:45 AM **Utilization of Onsite Domestic Violence Services at a Pediatric Hospital: A 4-Year Review**
Mario Cruz, Patricia B. Cruz, Ryan McGorty, Maria D. McColgan.
– Abstract 97

9:00 AM **Association of Shared Decision Making with Health Care Expenditures and Utilization among US Children with Special Health Care Needs**
Alexander G. Fiks, Stephanie Mayne, James P. Guevara, Evaline Alessandrini, Russell Localio. – Abstract 98

9:15 AM **Cervical Dysplasia in Immunocompromised vs. Immunocompetent Adolescents**
Amanda M. Jacobs, Melissa J. Fazzari, Susan M. Coupey.
– Abstract 99

9:30 AM **Suicidal Ideation and Intent in a Community Sample of Preadolescent Youth: A Case-Control Study**
Mariel Giannetta, Nancy Brodsky, Laura Betancourt, Matthew B. Wintersteen, Hallam Hurt. – Abstract 100

9:45 AM **Maternal Factors Associated with Medicaid/SCHIP Renewal for Low-Income, Minority Children**
Omolara A. Thomas, Melissa S. Stockwell, Dodi Meyer.
– Abstract 101

10:00 AM **Improving Teacher Knowledge of Safety in Preschoolers**
Michael A. Ferguson, Nancy Miller, Jennifer Friderici, Margaux Frank.
– Abstract 102

10:15 AM **Swaddling and Safe Sleeping Practices in an Inner City Population**
Barbara A. Kelly, Monique Mondesir, Natalia A. Isaza, Matilde M. Irigoyen. – Abstract 103

Pulmonary & Asthma Platform Session

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

Moderator: Alfin Vicencio, MD

8:15 AM **An Intronic ABCA3 Mutation Responsible for Respiratory Disease**
Amit Agrawal, Aaron Hamvas, F. Sessions Cole, Daniel Wegner, Carl Coghill, Keith Harrison, Lawrence Nogee. – Abstract 104

8:30 AM **Cryptococcus Neoformans-Specific IgA in Bronchoalveolar Lavage Fluid from Children with Poorly-Controlled Asthma**
Alfin G. Vicencio, Kalliope Tsirilakis, Xiaoxiao Lee, Arturo Casadevall, David L. Goldman. – Abstract 105

8:45 AM **Corticosteroid Timing and Length of Stay for Children with Asthma in the ED**
Stephanie Davis, Georgia Burke, Emily Hogan, Sharon R. Smith. – Abstract 106

9:00 AM **Composite Clinical Respiratory Disease Scoring Tool: Does It Predict the Need for Hospitalization in Children with RSV Bronchiolitis?**
Gaston I Zylberg, Ramkumar Natarajan, Fernanda Kupferman, Susana Rapaport, Lily Q. Lew, Rusly Harsono. – Abstract 107

9:15 AM **Inhaled Corticosteroids Improve Short-Term Symptoms after a Pediatric Emergency Visit for Asthma: A Randomized Clinical Trial**
Esther M. Sampayo, Joey Mechak, Amber Chew, Richard Scarfone, Joseph Zorc. – Abstract 108

9:30 AM **Relationship between Parental Health Literacy and Self-Efficacy with Managing Child Asthma**
Iman Sharif, Debra Roter, Laurie Bauman, Roopa Chari, Tara Ketterer, Mary Ann Abrams, Katherine Freeman, Arthur E. Blank, Benard P. Dreyer, Ruth E.K. Stein. – Abstract 109

9:45 AM **The Role of Pre-Operative Pulmonary Function Testing as a Screening Tool in Patients with Adolescent Idiopathic Scoliosis**
Gina T. Coscia, Joshua P. Needleman, Lisa S. Ipp, Mary J. Ward. – Abstract 110

10:00 AM **Exercise Improves Lung Function & Habitual Activity in Children with Cystic Fibrosis**
Shruti M. Paranjape, Laura A. Barnes, Kathryn A. Carson. – Abstract 111

10:15 AM **Intrauterine Growth Restriction Alters Lung Morphology and Function during Postnatal Growth in Rats**
Catalina Bazacliu, Melissa F. Carmen, Satyan Lakshminrusimha, Julie Basu-Ray, Rita M. Ryan, Daniel D. Swartz. – Abstract 112

10:30 AM **Break**

Plenary Session I

10:45AM-11:45AM **Overture**

10:45AM **Plenary Lecture - "Pediatric Workforce: Can Research Impact Policy?"**
Gary Freed, MD, MPH, University of Michigan Health System, Ann Arbor, MI

Meet the Professor Lunch

12:00PM-1:00PM **Aria A**
Gary R. Fleisher, MD and Gary L. Freed, MD, MPH

12:00PM-1:00PM **Concerto**
Nuts and Bolts of Writing an IRB Proposal
Iman Sharif, MD, MPH

Eastern SPR Business Meeting

12:00PM-1:00PM **Rhapsody**

Plenary II & Mentor of the Year & Young Investigator Presentations

1:10PM-4:00PM **Overture**

1:10PM **Mentor of the Year Presentation**
Fevers, Fellows, and Positive Cultures
Gary R. Fleisher, MD, Children's Hospital Boston, Boston, MA

Young Investigator Presentations

2:00 PM **Validation of a Pediatric Resident Disaster Triage Evaluation Tool**
Mark X. Cicero, Antonio Riera, Veronika Northrup, Fangyong Li, Marc Auerbach, Carl R. Baum. – Abstract 113

2:15 PM **Reiterated Roles for Jun in the Second Heart Field and Neural Crest during Heart Development**
Jason Z. Stoller, Tao Zhang, Eldhose B. Thekkethottiyil, Julie De Mesmaeker, Shoumo Bhattacharya, Jue Zhang, Fen Wang. – Abstract 114

2:30 PM **Cell Death after Oxidant Stress Is Determined by Inhibitory Proteins of the NF-κB Activation Cascade**
Clyde J. Wright, Fadeke Agboke, Manasa Muthu, Phyllis A. Dennery. – Abstract 115

2:45 PM **Break**

3:00 PM **Epidemiology of Refractory Kawasaki Disease: Analysis of 42 US Pediatric Hospitals from 2005 to 2008**
Sunil J. Ghelani, Kavita Parikh. – Abstract 116

3:15 PM ***Staphylococcus aureus* Infections in Women and Neonates Following Late Pregnancy Anovaginal Colonization**
Karina A. Top, Amanda Buet, Jiang Yao, Susan Whittier, Adam J. Ratner, Lisa Saiman. – Abstract 117

3:30 PM **Blood Cultures in the Emergency Department Evaluation of Childhood Pneumonia**
Maria H. Dugan, Joshua P. Metlay, Louis M. Bell, Robert W. Grundmeier, Todd Florin, Elizabeth Hines, Samir S. Shah. – Abstract 118

3:45 PM **Superoxide Anions Mediate Increased Pulmonary Arterial Contractility in 100% O_2 Resuscitated Asphyxiated Lambs**
Jayasree Nair, Stephen Wedgwood, Bobby Mathew, Robin Steinhorn, Satyan Lakshminrusimha. – Abstract 119

4:00 PM **Break**

Cardiovascular & Critical Care Platform Session

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

Moderator: Fraz A Ismat, MD

4:15 PM **Outcomes of Tight Glycemic Control in Critically Ill Children**
Sarah B. Kandil, E. Vincent S. Faustino. – Abstract 120

4:30 PM **Spontaneous and Pharmacological Closure of PDAs in ELBW Infants Is Influenced by Thrombocytopenia**
Kiran Dwarakanath, Narendra R. Dereddy, Divya Chabra, Christine Schabacker, Johanna Calo, Lance A. Parton. – Abstract 121

4:45 PM **Developmental Expression of Pepsinogen C in a Gene Trap Mouse Model**
Maria V. Fraga, Brittany Perry, Peggy Zhang, Susan H. Guttentag. – Abstract 122

5:00 PM **Mutation of Ryanodine Receptor Type 1 Causes Fetal Heart Failure and Demise**
Matthew R. Kaufmann, Meier Olivia, Shey-Shing Sheu, George A. Porter, Jr. – Abstract 123

5:15 PM **The Embryonic Mitochondrial Permeability Transition Pore Controls Cardiac Myocyte Mitochondrial Maturation and Differentiation**
Jennifer R. Hom, Rodrigo A. Quantanilla, David L. Hoffman, Karen L. de Mesy Bentley, Jeffery D. Molkentin, Shey-Shing Sheu, George A. Porter. – Abstract 124

5:30 PM **Prostaglandin E2 Receptor Gene Polymorphisms Are Associated with Reduced Spontaneous Closure of Ductus Arteriosus in ELBW Infants**
Kristen Aland, Kiran Dwarakanath, Johanna M. Calo, Lance A. Parton. – Abstract 125

General Pediatrics - Medical Education & Quality Improvement Platform Session

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

Moderator: Marina Reznik, MD, MS

4:15 PM **Framework for Quantifying & Matching Workload & Workforce in Healthcare Settings**
E. Fieldston, L. Zaoutis, P. Hicks, D. Geiger, E. Sladek, P. Agosto, L. Bell. – Abstract 126

4:30 PM **Qualitative Analysis of Student Attitudes towards Teaching and Counseling: Three Student Profiles Emerge**
Judith A. Turow, Amy Rothkopf, Stacy Henderson, Lindsey Lane. – Abstract 127

4:45 PM **New Pediatric Interns' Infant Lumbar Puncture Skills**
David O. Kessler, Todd P. Chang, Joshua M. Sherman, Nikhil B. Shah, Geetanjali B. Srivastav, Christopher G. Strother, Kajal Khanna, Michael Holder, Stephen J. Cico, Renuka S. Mehta, Matei Petrescu, Jennifer Reid, Kiran B. Hebbar, Noel S. Zuckerbraun, Martin B. Pusic , Marc Auerbach. – Abstract 128

5:00 PM **Resident Medication Reporting Errors during Pre-Rounding**
Misha Bhat, Kathleen M. Donnelly, Swati Agarwal. – Abstract 129

5:15 PM **Reliability of Parental Self-Report of Inhaled Corticosteroid Adherence in Inner-City Children with Persistent Asthma**
Marina Reznik, Philip O. Ozuah. – Abstract 130

5:30 PM **Do Caregivers of Children with Persistent Asthma Know How To Use Metered Dose Inhaler Plus Spacer Device?**
Yu Cao, Jacquelyn Dorsky, Marina Reznik. – Abstract 131

Infectious Diseases & Immunology Platform Session

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

Moderator: Elijah Paintsil, MD

4:15 PM **The Etiology of Respiratory Infection and Severity of Illness**
Therese Canares, Paul Chambers, Kathryn Scharbach. – Abstract 132

4:30 PM **Time to and Predictors of CD4+ T-Lymphocytes Recovery in HIV-Infected Children Initiating Antiretroviral Therapy in Ghana**
Meghan Prin, Lorna Renner, Fang-Yong Li, Bamenla Goka, Veronika Northrup, Elijah Paintsil. – Abstract 133

4:45 PM **Simulation of Nosocomial and Occupational Risks of Hepatitis C Virus Transmission**
Elijah Paintsil, Brett D. Lindenbach, Robert Heimer. – Abstract 134

5:00 PM **The Utility of Rapid RSV and Influenza Testing Versus a Multiplex PCR Viral Assay in Cohorting Hospitalized Patients**
Therese Canares, Kathryn Scharbach. – Abstract 135

5:15 PM **Distribution of Respiratory Syncytial Virus (RSV) Subtypes A and B among Infants Presenting to the Emergency Department (ED) with Lower Respiratory Tract Infection (LRI) or Apnea**
Hasan S. Jafri, Kelly J. Henrickson, Xionghua Wu, Doris Makari, Hanaa Elhefni. – Abstract 136

5:30 PM **Genetic Variation in Antimicrobial Peptide, Human-β-Defensin-1 (DEFB1) Is Associated with Recurrent Staphylococcus aureus Skin Infection in Children**
Hitesh S. Deshmukh, Howard R. Faden, Lucy C. Holmes, Steven R. Gill. – Abstract 137

Neonatology - Clinical Studies I Platform Session

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

Moderator: Bobby Mathew, MBBS, MRCP (UK)

4:15 PM **Low Vagal Tone Is Associated with Impending Necrotizing Enterocolitis in the Preterm Infant**
Kim Kopenhaver Haidet, Charles Palmer. – Abstract 138

4:30 PM **Intrauterine Growth Restriction Alters Vascular Reactivity in Adult Female Rats**
Melissa F. Carmen, Catalina Bazacliu, Bobby Mathew, Sylvia Gugino, Satyan Lakshminrusimha, Daniel D. Swartz. – Abstract 139

4:45 PM **Location of Spontaneous Intestinal Perforation (SIP) – Role of Initial Peristalisis**
Bobby Mathew, Jayasree Nair, Melissa F. Carmen, Daniel D. Swartz, Sylvia F. Gugino, Satyan Lakshminrusimha. – Abstract 140

5:00 PM **Randomized Controlled Trial of Early Total Parenteral Nutrition (TPN) Cycling To Prevent Cholestasis in VLBW Infants (VLBWI)**
Agnes Salvador, Michael Janeczko, Rachel Porat, Romal Sekhon, Anja Mowes, David Schutzman. – Abstract 141

5:15 PM **Enteral Feeding and Antenatal Betamethasone Alter Mesenteric Vascular Reactivity in Late Preterm Lambs**
Jayasree Nair, Bobby Mathew, Melissa Carmen, James Russell, Satyan Lakshminrusimha. – Abstract 142

5:30 PM **The Proinflammatory Role of Serotonin in a Murine Model of Necrotizing Enterocolitis**
Maria M. Talavera, Kara Gross, Sam Li, Korey Stevanovic. – Abstract 143

Neonatology - Epidemiology & Follow Up Platform Session

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

Moderator: Jane E. McGowan MD

4:15 PM **Variation in NICU Late Preterm Admisison Rates without Identifiable Cause**
Kathryn Ziegler, David A. Paul, Matthew Hoffman, Jonathan Cohn, Robert Locke. – Abstract 144

4:30 PM **Very Early Language Skills of Late Preterm Compared to Term Infants at Birth and 44 Weeks Corrected Age**
Katharine Johnson, Bonnie Stephens, Richard Tucker, Betty Vohr. – Abstract 145

4:45 PM **Adult-Infant Conversations in the NICU Are Associated with Higher Cognitive and Language Scores at 7 Months in Very Preterm Infants**
Melinda A. Caskey, Bonnie Stephens, Richard Tucker, Betty Vohr. – Abstract 146

5:00 PM **Can Prenatal Steroids Be a Risk Factor for Preterm Delivery?**
Claudia Halaby, Ellen Gurzenda, Yuko Arita, Morgan Peltier, Nazeeh Hanna. – Abstract 147

12

5:15 PM **Longitudinal Neurodevelopmental (ND) Outcome in Congenital Diaphragmatic Hernia (CDH) Survivors during the First 3 Years of Life**
Enrico Danzer, Marsha Gerdes, Jo Ann D'Agostino, Casey Hoffman, Judy Bernbaum, Michael W. Bebbington, Jennifer Siegle, Natalie E. Rintoul, Holly L. Hedrick. – Abstract 148

5:30 PM **The Increase in Neonatal Morbidity Associated with Cesarean Birth Varies with Gestational Age among Full Term Neonates**
Shaon Sengupta, Vivien Carrion, Rita Ryan, James Shelton, Ralph Wynn, Satyan Lakshminrusimha. – Abstract 149

Neurobiology I
Platform Session

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

Moderator: Jeffrey Pearlman, MB Ch B

4:15 PM **Notch Receptors and Their Ligands in Intraventricular Hemorrhage**
Sabrina Malik, G. Vinokunda, F. Hu, P. Ballabh. – Abstract 150

4:30 PM **The Effect of Src Kinase Inhibition and EGFR Inhibition on Caspase 9 Activity Following Post-Hypoxic Recovery**
Kirstie Marcello, Jarle Stone, Anli Zhu, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 151

4:45 PM **Overexpression of Extracellular Superoxide Dismutase (EC- SOD) Has a Protective Role Against Hyperoxia Induced Brain Injury in Neonatal Mice**
Nahla Zaghloul, Mansour Nassim, Hardik Patal, Champa Codipilly, Philippe Marambaud, Stephen Dewey, Mohamed Ahmed. – Abstract 152

5:00 PM **Hyperthermia Following Hypoxia-Ischemia in the Neonatal Rat Has a Biphasic Response: Increased Infarct or Selective Hippocampal Damage**
Matthew A. Rainaldi, Susan J. Vannucci, Jeffrey M. Perlman. – Abstract 153

5:15 PM **DNA Methyl-Transferase Activity during Hypoxia in Neuronal Nuclei of Newborn Piglets**
Amit Mukhia, David Fralinger, Anli Zhu, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 154

5:30 PM **Behavioral and Neurodevelopmental Changes in a Neonatal Rat Model of Inflammation and Global Hypoxia – "Dual Hit Model"**
Lamia M. Soghier, Solomon Moshe, Aristea Galanopoulou. – Abstract 155

Poster Session II
General Pediatrics

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

1 **Teaching Airport Personnel about Children with Autism**
Yahaira I. Marquez, Rebecca B. Jackel, Roger Ideishi, Angela Jones, Clara E. Notredame, Matilde M. Irigoyen, Wendy J. Ross. – Abstract 156

2 **Development and Initial Validation of the Baby Pediatric Symptom Checklist (BPSC)**
Shela Merchant, Brandi S. Henson, R. Christopher Sheldrick, Ellen C. Perrin, J. Michael Murphy. – Abstract 157

3 **Exploring the Risks, Trends, and Opportunities for Improvement Regarding Security for Hospitalized Children at Baystate Children's Hospital**
Jackcy Jacob, Karine Issa-El-Khoury, Linda George, Jennifer Friderici, Nancy Miller. – Abstract 158

4 **Exploring Opportunities for Improving Security in Children's Hospitals: Focus Groups**
Nancy H. Miller, Karine Issa-El-Khoury, Jackcy Jacob, Terry Kuta. – Abstract 159

5 **Nonresident Fathers and Fatherhood: A Needs Assessment**
Lysette Ramos, David Jones, Tanya White-Davis, Peter Sherman. – Abstract 160

6 **Accessing Sources and Knowledge of Reproductive Health in 14-21 Year-Old High School Students in the Bronx**
Ravi Saksena, Molly Broder, Laura Polizzi, Peter Sherman. – Abstract 161

7 **Effect of Time Management Training on the Efficiency of Pediatric Residents in Training**
Khadijah Abdurrazaq, Kenneth Etokhana, Ayoade Adeniyi, Ronald Bainbridge, Richard Neugebauer, Toby Gafny. – Abstract 162

8 **NYC Girls Are Steps Away from Growing up Healthy: Patterns of Activity Behaviors in an Inner City Minority Cohort**
Caroline Gluck, Maureen Miller, Maida P. Galvez, Kathleen McGovern, Jessica Montana, Nancy Mervish, Susan L. Teitelbaum, Mary S. Wolff, Barbara Brenner. – Abstract 163

9 **Does Bedside Nursing Presence during Family-Centered Rounds Decrease the Number of Pages to Ward Interns?**
Samantha Fish, Bridget Allard, Kathleen Donnelly. – Abstract 164

10 **Release Planning for Juveniles in Detention in New Jersey**
Lisa L. Park, Ben H. Lee. – Abstract 165

11 **Pediatric Medication Dosing Errors**
Kathryn M. Scharbach, Philip O. Ozuah. – Abstract 166

12 **Maternal Factors Associated with Intention to Exclusively Breastfeed or Breast and Formula Feed among Urban Minority Women**
Shilpa G. Hundalani, Stefan Mandakovic Falconi, Ramesh Matam, Matilde Irigoyen. – Abstract 167

13 **Intent to Breastfeed and Successful Breastfeeding in an Inner City Population: Does Obesity Matter?**
Shilpa G. Hundalani, Ramesh Matam, Stefan Mandakovic Falconi, Matilde Irigoyen. – Abstract 168

14 **Impact of Delivery Type and Maternity Care Practices on Initiation of Breastfeeding in an Inner City Population**
Shilpa G. Hundalani, Stefan Mandakovic Falconi, Ramesh Matam, Matilde Irigoyen. – Abstract 169

15 **Teaching Pediatric Code Leadership Skills: Integrated vs. Stand Alone Curriculum**
Ian S. Goodman, Gerard Langois, Blake Spirko, Howard Smithline, Fidela Blank, Gladys L. Fernandez. – Abstract 170

16 **The Influence of Military Bases and Public University Campuses on Chlamydia Rates in Florida Counties: A Spatial Analysis Using a Geographic Information System (GIS)**
James J. Burns, Lela A. Hobby, Alex Husserl, John Lanza. – Abstract 171

17 **Identifying Patient Characteristics That Influence a Mandated Reporter's Decision To Report Child Abuse**
Erin Rawson, Kadija Toor, William Hauda, Riva Kamat. – Abstract 172

Emergency Medicine

18 **Pediatric Residents' Procedural Experience: How Much Is Enough?**
Michelle J. Alletag, David O. Kessler, Marc A. Auerbach. – Abstract 173

19 **Impact of BASE Camp: Simulation-Based Multidisciplinary Team Training for Pediatric Emergency Medicine Fellows**
Kevin Ching, Marc Auerbach, Frank Overly, Linda Brown, Chaoyan Dong, Colleen Gillespie, Michael Falk, David Kessler. – Abstract 174

20 **Communication Malfunction: Utilizing Electronic Order Systems To Improve Communication and Reduce Radiation Exposure for Children with Ventricular Shunts**
Emily A. Spengler, Jennifer Anders, Mahadevappa Mahesh. – Abstract 175

Endocrinology & Obesity

21 **"Missing" Mutations: Post-Zygotic Mosacism in Congenital Hyperinsulinism**
Katherine Lord, Kara Snider, Courtney MacMullen, Susan Becker, Arupa Ganguly, Charles A. Stanley. – Abstract 176

22 **Markers of Body Composition as Predictors of Total and Undercarboxylated Osteocalcin in Healthy Children**
David R. Weber, Andrea Kelly, Rita Herskovitz, Mary B. Leonard, Virgina A. Stallings, Babette S. Zemel. – Abstract 177

23 **Nature and Nurture: Multifactoral Rickets in Two Pre-School Aged Children**
Jeffrey D. Roizen, Michael A. Levine. – Abstract 178

24 **Association of Serum Sphingolipids and Serum Adipocytokines with Insulin Resistance in Adolescents at Risk for Metabolic Syndrome**
Indrajit Majumdar, Lucy D. Mastrandrea. – Abstract 179

25 **Vitamin D Supplementation Improves Metabolic Parameters in Obese African American Adolescents**
Shobhit Jain, Kiran K. Yelakanti, Santosh Mukka, Vinod Kumar, Laura Dunkley, Rich Dunlop, Yogendra Saxena, Ninad Desai, Svetlana Ten, Lee Waldmann, Amrit P.S. Bhangoo. – Abstract 180

26 **Pituitary Volume by MRI Is Associated with IGF-1 in Children with Growth Failure**
Andrew Tenore, Molly O. Regelmann, Bradley N. Delman, Robert Rapaport. – Abstract 181

27 **Knowledge, Attitudes and Clinical Practices of Pediatric Residents in a Community Hospital Regarding Vitamin D: Pre- and Post-Intervention Analysis**
Shipra Bansal, Fernanda Kupferman, Rusly Harsono, Susana Rapaport, Louis Primavera, Lily Lew. – Abstract 182

28 **Novel Presentations of Congenital Hyperinsulinism Due to Mutations in Hepatocyte Nuclear Factor 1 and 4 Alpha**
Diana E. Stanescu, Nkecha Hughes, Bernard Kaplan, Charles A. Stanley, Diva D. De Leon. – Abstract 183

29 **Adherence to 2008 Vitamin D Suplementation Recommendations in Infants**
Cecilia P. Damilano, Inna Polyakov, Gail S. Rose-Green, Robert Karch, Matilde Irigoyen. – Abstract 184

30 **FKBP4 Causing Glucocorticoid Resistance (GR) Is a Novel Reason for Premature Adrenarche**
S. Ghanny, L. Nie, D. Tan, F. Lacbawan, J. Michl, A. Bhangoo, S. Ten. – Abstract 185

31 **Weight Loss and Metabolic Benefit with the Addition of Glucagon-Like Peptide Agonists and Pioglitazone to Type 2 Diabetes Mellitus Adolescent Treatment**
Nouhad Raissouni, Sheila Perez, Oxana Lazareva, Fatma Ahmed, Sonal Bhandari, Amrit Bhangoo, Svetlana Ten. – Abstract 186

GI/Nutrition/Hematology & Oncology

32 **Novel Coagulopathy and Severe Hemorrhage with Epstein-Barr Virus-Associated Disease**
John S. Baird, Pooja Kulkarni, Thyyar M. Ravindranath, Prakash Satwani. – Abstract 187

33 **Etiology of Kidney Disease and Kidney Transplant Outcome in Pediatric Minorities**
S. Beste, P. J. Galutira, N. Samtani-Gaffney, M. DelRio, B. Goilav. – Abstract 188

34 **Use of Screening Urine Dipsticks in Well-Child Care To Detect Asymptomatic Proteinuria without Proper Interpretation Leads to Unnecessary Referral of Pediatric Patients**
Alexa Calero, Stephen P. Katz, Preethi Thomas, Jacob Rosenberg Rosenberg, David Fagan. – Abstract 189

Neonatology

35 **Early Fortification of Expressed Breast Milk (EBM) Improves Calcium (Ca) and Phosphorus (P) Intake and Reduces Peak Alkaline Phosphatase (AlkP) Level in Premature Neonates**
Jayasree Nair, Maria Janina U. Pabalan, Nancy Garrison, Rita Ryan, Vivien Carrion, Satyan Lakshminrusimha. – Abstract 190

36 **Tidal Volume Needed for Normocapnia in Infants with Meconium Aspiration Syndrome**
Saumya Sharma, Shane Clark, Kabir M. Abubakar, Martin Keszler. – Abstract 191

37 **Mechanical Ventilation at Postnatal Day 7 and Bronchopulmonary Dysplasia among Extremely Preterm Infants**
Munish Gupta, Abigail Bushman, Richard B. Parad, Michelle Starr, Michele Phillips, Linda J. Van Marter. – Abstract 192

38 **IFN-γ and IP-10 in Tracheal Aspirates from Premature Infants: Relationship with Bronchopulmonary Dysplasia**
Zubair H. Aghai, Kartik Mody, Judy G. Saslow, Riva Eydelman, Vishwanath Bhat, Gary E. Stahl, Kee H. Pyon, Vineet Bhandari. – Abstract 193

39 **Impact of Histological Chorioamnionitis on Tracheal Aspirate Cytokines in Premature Infants**
Zubair H. Aghai, Jeanette Camacho, Kartik Mody, Judy G. Saslow, Riva Eydelman, Vishwanath Bhat, Gary E. Stahl, Kee H. Pyon, Vineet Bhandari. – Abstract 194

40 **Screening for Autism in Former Preterm Infants**
Raja R. Senguttuvan, Jordan S. Kase. – Abstract 195

41 **Status of Neonatal Resuscitation Efforts in Resource-Poor Countries: Challenges and Opportunities**
Judson Heugel, Joy Lawn, Erin Mack, Stephen Wall. – Abstract 196

42 **Late-Onset LipopolySaccaride (LPS) Challenge Alters the Serum and Pulmonary Inflammatory Response in Three-Week Old Sprague-Dawley Rat Pups Preconditioned with Birth Hyperoxia**
Surabhi Jain, Pavan Vasa, Avinash Chander, Shetal Shah. – Abstract 197

43 **Localization of Sirtuin 1 in Fetal Membranes: Possible Role in Perinatal Inflammation**
Kartik Mody, Neena Singh, Judy G. Saslow, Riva Eydelman, Vishwanath Bhat, Gary E. Stahl, Kee H. Pyon, Jeanette Camacho, Zubair H. Aghai. – Abstract 198

44 **Contaminant or Pathogen: Predictors of Coagulase Negative Staphylococcal Bacteremia in the NICU**
Kathleen A. Gibbs, Betsy C. Herold, Robert S. Green. – Abstract 199

45 **Racial Differences in the Effects of Maternal Age on NICU Admission Rates**
Beatriz de Jongh, David Paul, Katie Zeigler, Mathew Hoffman, Robert Locke. – Abstract 200

46 **Short-Term Hyperoxia Alters Lung Levels of T-Lymphocytes in Newborn Gram-Negative-Infected Sprague-Dawley Rat Pups**
Simran Buttar, Shetal Shah, Avinash Chander. – Abstract 201

47 **Short-Term Hyperoxia Alters Lung Levels of Pro-Inflammatory Cytokines Tumor-Necrosis Factor Alpha (TNF-a) and Interleukins 2 and 8 (IL-2, IL-8) in Newborn Gram-Negative-Infected Sprague-Dawley Rat Pups**
Kimberly Dao, Shetal Shah, Avinash Chander. – Abstract 202

48 **Clinical Characteristics, Demographics and Outcomes of Neonates with Fetomaternal Hemorrhage, 1993-2008**
Annemarie Stroustrup, Leonardo Trasande. – Abstract 203

49 **Protein Binding at 5'UTR mRNA in Surfactant Protein A Splice Variants**
Faizah N. Bhatti, Patricia Silveyra, Joanna Floros. – Abstract 204

50 **Risk Factors for Surgical Necrotizing Enterocolitis in VLBW Infants Admitted to a Tertiary Care Neonatal Unit**
Faizah N. Bhatti, Coleen P. Greecher, Sol Rodriguez-Colon, Umar Farooq, David Stewart, Mitchell Kresch. – Abstract 205

51 **Overexpression of Extracellular Superoxide Dismutase (EC-SOD) Preserves Macrophage Function in Neonatal Mice Exposed to Hyperoxia**
Kanchan Mishra, Champa Codipilly, Lin Mantell, Mohamed Ahmed. – Abstract 206

52 **Morbidity and NICU Admissions among Early Term (37-38 wk) and Term (39-41 wk) Neonates in Erie County (NY)**
Shaon Sengupta, Alyssa Herrmann, Priya Singhal, James Shelton, Vivien Carrion, Ralph Wynn, Rita M. Ryan, Kamal Singhal, Satyan Lakshminrusimha. – Abstract 207

53 **Increased Methemoglobin (MHb) Levels Predict Response to Inhaled Nitric Oxide (iNO) in Persistent Pulmonary Hypertension of the Newborn (PPHN)**
Rita Dadiz, Jayasree Nair, Linda Reubens, Carl T. D'Angio, Rita M. Ryan, Satyan Lakshminrusimha. – Abstract 208

54 **The Role of Manganese Superoxide Dismutase in the Pathogenesis of Neonatal Lung Disease and Other Newborn Ailments**
Edward Hurley, Kristen Aland, Johanna M. Calo, Divya Chhabra, Edel Mendoza, Sonya Strassberg, Lance A. Parton. – Abstract 209

55 **Omegaven™ (O) a Novel Omega-3 Fatty Acid Emulsion Reverses Parenteral Nutrition Associated Cholestasis (PNAC) in Infants Requiring Prolonged PN without Side Effects**
Michael M. Espiritu, Jeffrey M. Perlman. – Abstract 210

56 **Lipopolysaccaride and Hyperoxia Effects on Alveolar Development and Surfactant Protein B in Newborn Rats**
Fiona Yuen, Liji B. Chacko, Shetal Shah, Avinash Chander. – Abstract 211

57 **Selective Fluconazole Prophylaxis for Very Low Birth Weight (VLBW) Infants Colonized with Candida**
M. Roger Kim, Praveen Chandrasekharan, Munmun Rawat, Dominique Jean-Baptiste, Myron Sokal. – Abstract 212

58 **SNIPPV vs. NIPPV: Does Synchronization Matter?**
Vikramaditya Dumpa, Karol Katz, Veronika Northrup, Vineet Bhandari. – Abstract 213

Sunday, March 28, 2010

Plenary Session III & Presentation of The Young Investigator Awards

8:30AM-9:30AM **Overture**

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

8:40AM **Plenary Lecture - Marfan Syndrome and Related Disorders; From Molecules to Medicines**
Hal Dietz, MD, Johns Hopkins University School of Medicine, Baltimore, MD

9:30 AM **Break**

General Pediatrics II Platform Session

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

Moderator: Roberta DeBiasi; E Fieldston, MD, MBA, MS

9:45 AM **Construction of a Flavonol and Lignan Database for Assessing Phytoestrogen Intake in an Inner City Minority Cohort of Girls**
Eliza W. Gardiner, Nancy Mervish, Susan L. Teitelbaum, Maida P. Galvez, Kathleen McGovern, Mary S. Wolff. – Abstract 214

10:00 AM **Efficacy of Primary Care Clinics Offering Increased Influenza Vaccine Delivery**
Daniel M. Fein, Andrew D. Racine. – Abstract 215

10:15 AM **Family Centered Rounds in Theory and Practice: An Ethnographic Case Study**
Anupama Subramony, Patricia Hametz, Dorene Balmer. – Abstract 216

10:30 AM **Limited Impact of Reducing Length of Stay on Daily Peak Census at a Children's Hospital**
Evan Fieldston, Bhuvaneswari Jayaraman. – Abstract 217

10:45 AM **Implementation and Outcome Analysis of an Institutional Pediatric Acute Hematogenous Osteomyelitis (AHO) Diagnosis and Management Pathway**
Kavita Parikh, David Hyun, Wendy Hoffner, Caroline Rassbach, Roberta L. DeBiasi. – Abstract 218

11:00 AM **Communication between Families and Physicians: A Comparison Study of Family Centered Rounds**
Anupama Subramony, Talia Schwartz, Susan Waitzkin, Patricia Hametz. – Abstract 219

11:15 AM **Practice Differences of Hospitalists vs Non-Hospitalists in Bronchiolitis: A Multi-Center Study**
Russell McCulloh, Sarah Smitherman, Solomon Adelsky, Morgan Congdon, Jamie Librizzi, Kristin Koehn, Brian Alverson. – Abstract 220

11:30 AM **Repeat Lab Testing from the Emergency Department: How Often and How Important?**
Evan S. Fieldston, David F. Friedman. – Abstract 221

11:45 AM **Urogenital Symptom-Reporting after Sexual Abuse vs. Genital Irritant Contact in Pre-Menarchal Girls**
Cynthia DeLago, Esther Deblinger, Martin Finkel. – Abstract 222

Emergency Medicine Platform Session

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

Moderator: Lei Chen, MD

9:45 AM **Fever: What Is an Effective Way of Educating Parents?**
David M. Pinter, Carolina M. Cuba, Fernanda E. Kupferman, Lily Lew, David DiJohn, Rusly Harsono, Louis Primavera, Susana Rapaport, Gagan J. Gulati. – Abstract 223

10:00 AM **Multiple Critically Ill Children in the Pediatric Emergency Department Impacts Quality of Care as Indicated by Prolonged Length of Stay**
Alexandra E. Remus, Sharon Smith, Christopher Carroll, Adam M. Silverman. – Abstract 224

10:15 AM **Draining Ears and Tympanostomy Tubes: A Survey of Pediatric Otolaryngologists and Pediatric Emergency Medicine Physicians**
Shira L. Schwartz, Vahe Badalyan, Peter S. Roland, Richard H. Schwartz. – Abstract 225

10:30 AM **Does the IVC Diameter Correlate with Central Venous Pressure (CVP) in the Assessment of Intravascular Volume in Children?**
Lorraine Ng, Benjamin Taragin, Jeffrey Avner, Michael Ushay, Denise Nunez. – Abstract 226

10:45 AM **Little Fingers, Big Trouble: Child Self-Unbuckling**
Lilia B. Reyes. – Abstract 227

11:00 AM **Training Experiences of Pediatric Emergency Medicine Fellows before Fellowship**
Kevin Ching, Marc Auerbach, Frank Overly, Linda Brown, Chaoyan Dong, Colleen Gillespie, Michael Falk, Nikhil Shah, Eric Weinberg, David Kessler. – Abstract 228

11:15 AM **Analgesia Use for Infant Lumbar Puncture by Interns after an Educational Intervention**
Daniel M. Fein, Jeffrey R. Avner, Marc O. Auerbach, Eileen J. Klein, Geetanjali Srivastava, Elizabeth B. Seelbach, Joshua A. Rocker, Christopher Strother, David O. Kessler. – Abstract 229

11:30 AM **Electrocardiograms in Children with Lyme Meningitis: Should We Screen for Lyme Carditis?**
Elizabeth J. Welsh, Keri A. Cohn, Lise E. Nigrovic, Amy D. Thompson, Elizabeth M. Hines, Samir S. Shah. – Abstract 230

11:45 AM **Just in Time Simulation-Based LP Training: A Qualitative Evaluation**
Gunjan Kamdar, Lindsey Tilt, David Kessler, Kajal Khanna, Geetanjali Srivastava, Todd Chang, Amanda Krantz, Stephen Cico, Mike Holder, Jennifer Reid, Martin Pusic, Kevin Ching, Marc Auerbach. – Abstract 231

Neonatology - Clinical Studies II Platform Session

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

Moderator: Haresh Kirpalani, MD

9:45 AM **Prospective Randomized Controlled Trial of Restrictive Fluid Management in Transient Tachypnea of the Newborn**
Annemarie Stroustrup, Ian R. Holzman. – Abstract 232

10:00 AM **Quality of Reporting in Neonatal Clinical Trials**
Sara B. DeMauro, Annie Giaccone, Haresh Kirpalani, Barbara Schmidt. – Abstract 233

10:15 AM **Reciprocal Vocalizations between Female Caregivers and Their Infants Surpass Those of Male Caregivers in the First Months of Life**
Katharine Johnson, Bonnie Stephens, Richard Tucker, Betty Vohr. – Abstract 234

10:30 AM **A Novel Murine Model of Preterm Birth Based on the Genetic Ablation of Decorin and Biglycan**
Megan Calmus, Elyse E. Macksoud, Renato V. Iozzo, Richard Tucker, Beatrice E. Lechner. – Abstract 235

10:45 AM **Effects of Bilirubin on Neutrophil Inflammatory Responses in Newborn Infants**
Suganya Kathiravan, Faith E. Archer, Anna M. Vetrano, Daniel S. Hirsch, Barry I. Weinberger, Thomas Hegyi. – Abstract 236

11:00 AM **Elevated Blanket Temperatures during Whole Body Cooling with Servo-Controlled Blanketrol III**
Mario Zichella, Dorothy McElwee, Susan Adeniyi-Jones. – Abstract 237

11:15 AM **Yield of Surveillance Cultures for Infants Transferred to the NICU**
Theodore Macnow, Dana O'Toole, Lisa Saiman, Jennifer Duchon. – Abstract 238

11:30 AM **Gas Exchange in the First Minute of CPR Following Asphyxial Cardiac Arrest in Newborn Piglets**
Bobby Mathew, Daniel D. Swartz, Melissa Carmen, Sylvia F. Gugino, Jayasree Nair, Rita M. Ryan, Satyan Lakshminrusimha. – Abstract 239

11:45 AM **Maternal Microchimerism in the Fetus**
Arlene E. Balubayan, Rakhi Mehrotra, Heber C. Nielsen, Christiane E.L. Dammann. – Abstract 240

Neonatology - Pulmonary II Platform Session

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

Moderator: Christiane Dammann, MD

9:45 AM **Effect of FiO_2 and NO on Oxygenation and Pulmonary Vascular Resistance at Birth**
Satyan Lakshminrusimha, Daniel D. Swartz, Bobby Mathew, Sylvia F. Gugino, Stephen Wedgwood, Robin H. Steinhorn. – Abstract 241

10:00 AM **Age-Dependent *In Vitro* Mouse Lung Type II Cell Behavior**
Rony O. Dey Hazra, Cristina Scapin, Oya Guengoeze, Katja Zscheppang, Heber C. Nielsen, Christiane E.L. Dammann. – Abstract 242

10:15 AM **How Accurate Are Measures of Tidal Volume, Compliance and Resistance on Neonatal Ventilator Displays?**
Soraya Abbasi, Emidio Sivieri, Robin Roberts, Haresh Kirpalani. – Abstract 243

10:30 AM **Intravenous Sildenafil Improves Oxygenation and Suppresses PDE5 Activity in Lambs with PPHN**
Satyan Lakshminrusimha, Stephen Wedgwood, Kathryn N. Farrow, Sylvia F. Gugino, James A. Russell, Robin H. Steinhorn. – Abstract 244

10:45 AM **Effect of Inspired Oxygen and Inhaled Nitric Oxide (iNO) on Oxygen Uptake from the Lung and Arterial Oxygen Content in Newborn Lambs and Lambs with Persistent Pulmonary Hypertension of the Newborn (PPHN)**
Melissa F. Carmen, Bobby Mathew, Sylvia Gugino, Jayasree Nair, Daniel D. Swartz, Satyan Lakshminrusimha. – Abstract 245

11:00 AM **Vascular Endothelial Growth Factor in Tracheal Aspirates from Preterm Infants: Effect of Surfactant Therapy**
Avinash Purohit, Rajeev Mehta, Anna Petrova. – Abstract 246

11:15 AM **Hyperoxia Modulates Bacterial Lipopolysaccharide-Induced Inflammation and Nitric Oxide Synthase**
Mohammed Rashed Shareef, Tudevdagva Gerelsaikhan, Pavan Vasa, Joseph DeCristofaro, Avinash Chander. – Abstract 247

11:30 AM **Antenatal Betamethasone Improves Pulmonary Transition in Late Preterm Lambs Delivered by Elective Cesarean Section**
Pritha Nayak, Daniel D. Swartz, Bobby Mathew, Sylvia F. Gugino, Karen A. Wynn, Stephen Wedgwood, Robin H. Steinhorn, Satyan Lakshminrusimha. – Abstract 248

11:45 AM **Inhibition of Pro-Inflammatory Cytokine Release from Macrophages of the Newborn: Insensitivity to Glucocorticoids Compared to Interleukin-10**
Olena Predtechenska, Hardik Patel, Ivana Vancurova, Dennis Davidson, Kavita Kasat. – Abstract 249

Endocrinology / Obesity Platform Session

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

Moderator: Diva D De León-Crutchlow, MD

9:45 AM **Is There a Different Relationship between Vitamin D 25-OH and Parathyroid Hormone in Children with Type 1 Diabetes (T1D)?**
Emily Frydman, Crystal Wittcopp, Holley F. Allen, Paul Visintainer, Edward O. Reiter, Nancy S. Dunbar. – Abstract 250

10:00 AM **Effects of the GLP-1 Receptor Antagonist Exendin-(9-39) on Postprandial Hypoglycemia after Fundoplasty**
Andrew Calabria, Stephanie Givler, Paul Gallagher, Diva De Leon. – Abstract 251

10:15 AM **Screening Patients with Type 1 Diabetes for Celiac Disease and Hypothyroidism**
Irena E. Glick, Kathleen M. Link, Patrick W. Mason, Karen R. Carpenter. – Abstract 252

10:30 AM **Sex Steroids: Better Indices of Pubertal Suppression Than Gonadotropins in Histrelin Treated Patients?**
Michelle Klein, Molly Regelmann, Elizabeth Chacko, Sharon Hyman, Dennis Chia, Elizabeth Wallach, Robert Rapaport. – Abstract 253

10:45 AM **Vitamin D Deficiency Is Associated with Cardiovascular Disease Risk Factors but Not Obesity in Pediatric Type 1 Diabetes**
Chelsea Gordner, Chrystal Wittcopp, Nancy Dunbar, Elsina E. Hagan, Holley Allen, Paul Visintainer, Edward O. Reiter. –Abstract 254

11:00 AM **Counter-Regulatory Hormonal Responses to Single vs Recurrent Hypoglycemia and Its Effect on Catecholamine Synthesis**
Necla Kirtok, Bistra Nankova, Owen Chan, Edmund F. La Gamma. – Abstract 255

11:15 AM **IGF-BP3 Is a Good Predictor of Response to GH and Increlex in Non-GHD Patients with Low IGF1**
O. Lazareva, I. Predescu, S. Malik, A. Bhangoo, S. Ten. – Abstract 256

11:30 AM **BP/Height Ratios: Simple and Accurate Method of Detecting Elevated Blood Pressure in Children**
Minu M. George, Sudhakar Basetty, Iuliana Predescu, Anil Mongia, Svetlana Ten, Amrit Bhangoo. – Abstract 257

11:45 AM **HNF1A Is a Frequent Reason of Insulin Dependant Diabetes in Children with and without Islet Cell Antibodies with Good Response to Sulfonylurea Therapy**
Steven Ghanny, Lina Nie, Dujuan Tan, Sheila Perez, Sonal Bhandari, Felicitas Lacbawan, Amrit Bhangoo, Svetlana Ten. – Abstract 258

Neurobiology II
Platform Session

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

Moderator: Barbara Stonestreet, MD

9:45 AM **Mechanism of Ca^{2+}-ATPase Activation during Hyperoxia in Neuronal Nuclei of the Cerebral Cortex of Newborn Piglets**
Nicholas Obiri, Kirstie Marcello-Donnelly, Meredith Monaco, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 259

10:00 AM **The Effect of a Common Hemochromatosis Gene Mutation in the Survival of Mice Exposed to Hypoxia**
Asha Ittoop, Elizabeth Neely, Wint Nander, Charles Palmer, James Connor. – Abstract 260

10:15 AM **Effect of Nitric Oxide Synthase Inhibition on Activation of Caspase-9 during Hyperoxia in Newborn Piglets**
Meredith L. Monaco, Altina T. Phaire, R. Kirkland Sallas, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 261

10:30 AM **Tract Based Spatial Statistics Diffusion Tensor Imaging Shows Anatomic Differences in White Matter Tracts in Subjects with Ornithine Transcarbamylase Deficiency (OTCD)**
Nathaniel Robbins, Kyle Shattuck, John vanMeter, Andrea L. Gropman. – Abstract 262

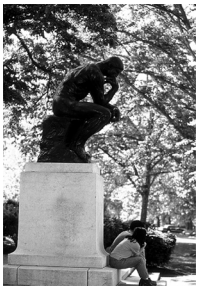
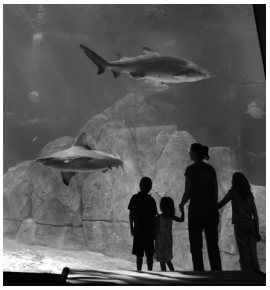
10:45 AM **Necrostatin-1 Modulates BDNF Levels in Forebrain Following Neonatal Hypoxia-Ischemia**
Raul Chavez-Valdez, Lee J. Martin, Devin Mack, Sheila Razdan, Debbie L. Flock, Estelle B. Gauda, Frances J. Northington. – Abstract 263

11:00 AM **Effect of Hyperoxia on Increased Expression of Bax Protein in the Cerebral Cortex of Newborn Piglets**
Erica W. Mandell, Qazi Ashraf, Simran Ahluwalia, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 264

11:15 AM **Head Growth and Neurodevelopmental Outcome (ND) in Infants Treated with Head Cooling (SHC)**
Raquel Gomez, Marcy Gringlas, Susan Adeniyi-Jones. – Abstract 265

11:30 AM **Interleukin-6 Reduces the Expression of the Tight Junction Protein Occludin in Isolated Cerebral Microvessels from Young and Adult Sheep**
Susan S. Cohen, May Min, Erin E. Cummings, Xiaodi Chen, Grazyna Sadowska, Surendra Sharma, Barbara S. Stonestreet. – Abstract 266

11:45 AM **Effect of Epidermal Growth Factor Receptor (EGFR) Kinase Inhibition during Hypoxia on Phosphorylation of Ca^{++}/Calmodulin-Dependent Protein Kinase IV (CaM Kinase IV) in Neuronal Nuclei of Newborn Piglets**
Mark Michael, R. Kirkland Sallas, David Fralinger, Om P. Mishra, Maria Delivoria-Papadopoulos. – Abstract 267


2011 ESPR Abstracts

General Pediatrics
Poster Session

Friday, March 25, 2011
6:00 PM-7:30 PM

1

House Officer

The Association of Vitamin D Deficiency and Asthma Severity in Children

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BACKGROUND: Asthma is a major public health problem in the United States affecting approximately 10% of children and 150,000 pediatric hospitalizations annually. Researchers have proposed that vitamin D plays a role in modulating the immune response in asthma by inhibiting pulmonary inflammatory responses and enhancing innate defense mechanisms against pathogens. The role of vitamin D modulation of asthma severity in children is currently unknown.

OBJECTIVE: Describe the association between asthma severity and vitamin D deficiency in children. Hypothesis: More severe asthma is associated with vitamin D deficiency.

DESIGN/METHODS: Unrestricted, public data were obtained from the National Health and Nutritional Examination Survey (NHANES 2005-6). Subjects were selected for age between 2 and 18 years. The following variables were included in this analysis: (1)serum 25(OH) D level (deficient = level <11 ng/ml; sufficient = level >30), (2)asthma severity (derived from annual number of asthma attacks, ER visits, unexpected asthma visits and nighttime symptoms), (3)age, (4)family income.

RESULTS: The sample included 616 subjects. Figure 1 has descriptive data.

Variable	Mean	s.d.	Range
Age (y)	11.2	5.0	2.5-18.9
Age at asthma dx (y)	4.6	4.1	1-17
25 (OH)D (ng/dL)	20.8	8.0	2-59
Asthma prevalence	% of sample		
Mild intermittent	6		
Mild persistent	2		
Moderate persistent	1		
Severe persistent	2		
Past asthma	5		
Wheezing	5		

Prevalence of asthma was 11%; mild intermittent was the most common form. 5% of the sample experienced periodic wheezing but did not have asthma. Prevalence of vitamin D deficiency was 10%; 11% of the sample was vitamin D sufficient.

Vitamin D deficiency was significantly less likely in children with moderate to severe asthma than in those with milder asthma (35% vs. 64%, p<.05; OR=1.8, p<.05). Vitamin D was negatively correlated with age and positively correlated with annual family income (p's < .001). Age, vitamin D level, and family income were not associated with asthma severity.

CONCLUSIONS: The data show a significant negative correlation between vitamin D deficiency and asthma severity. Children with milder forms of asthma had lower vitamin D levels. These initial results will be tested against a larger set of NHANES data to assess the role of vitamin D in asthma pathogenesis.

2

The Impact of Teaching Metered-Dose Inhaler Administration to Residents and Medical Students

Sharyn H. Miskovitz, Jason Fletcher, Sandra F. Braganza.
Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY; Department of Family and Social Medicine, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: For optimal asthma care, the National Heart, Lung and Blood Institute (NHLBI) recommends that clinicians teach their patients proper metered-dose inhaler (MDI) technique. Despite these guidelines, pediatric healthcare provider knowledge and skill of MDI and spacer administration crucial to the treatment partnership is often lacking. Several studies have demonstrated healthcare professionals' lack of knowledge and skill involving MDIs and residency training programs often do not incorporate MDI administration education as part of their curriculum.

OBJECTIVE: 1) To establish current medical student and resident (pediatric and family medicine) baseline knowledge regarding the use of MDIs, 2) to evaluate the effect of a training curriculum on medical student and resident knowledge of MDI use, and 3) to determine the change in confidence in discussing asthma management and teaching MDI administration technique.

DESIGN/METHODS: We created a unique one-hour educational curriculum that included a presentation, video demonstration, and interactive tool that involved role-playing. This curriculum was taught to medical students, pediatric residents, and family medicine residents. Each participant completed pre- and post-intervention surveys. Participant knowledge on MDI administration was assessed by nine multiple choice questions. Participant confidence on discussing asthma management and teaching MDI administration technique was assessed by three five-point Likert scale questions. Changes were examined using paired groups t-tests.

RESULTS: Forty-six subjects (67% pediatric residents, 11% family medicine residents, and 22% medical students) completed the surveys. Resident average knowledge score increased from 44% to 86% (p<0.001). Medical student average knowledge score increased from 48% to 90% (p<0.001). Participant average confidence score on discussing asthma management and teaching MDI administration technique increased from 3.3 to 4.3 (p<0.001).

CONCLUSIONS: Medical students and pediatric and family medicine residents lack adequate knowledge regarding the administration of MDIs to properly treat their patients with asthma. However, a brief curriculum can help remedy this by improving knowledge of MDI use and confidence in discussing asthma management and teaching MDI administration technique. Education on MDI administration should be formally incorporated into training programs so providers will be more effective in educating their patients with asthma.

3

Edinburgh Postpartum Depression Scale Score among Mothers of Infants in the NICU

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BACKGROUND: Postpartum depression affects 10-20% of women after giving birth. Recent studies report that mothers of preterm infants in the NICU have a higher incidence of postpartum depression with a rate of 28-70%. Since 2007, the Edinburgh Postpartum Depression Scale (EPDS) has been implemented at Morristown Memorial Hospital to identify mothers who have an increase risk of postpartum depression and therefore require psychiatric consultation. The hypothesis is that mothers with infants admitted to the NICU will have higher EPDS scores when compared to mothers who have newborns admitted to the well baby nursery.

OBJECTIVE: The purpose of this study is to investigate if mothers with infants admitted to the NICU have higher EPDS scores when compared to mothers with infants admitted to the well baby nursery.

DESIGN/METHODS: We collected the documented EPDS scores of mothers who gave birth to infants that were directly admitted to the NICU and well baby nursery at Morristown Memorial Hospital from March 2007 to August 2009. Key variables such as infant's birth weight, infant's gestational age, maternal age, maternal insurance, maternal marital status and maternal parity were obtained from chart review. Mothers were excluded if death of the infant occurred and if maternal scores were unknown. The data was analyzed using Statistical Program for the Social Sciences 15.0 software.

RESULTS: The sample was composed of 211 infants admitted to the NICU and 722 infants admitted to the well baby nursery. Of the 211 NICU infants, 28% of the mothers' EPDS score (score >9) were significant for risk of postpartum depression. Of the 211 NICU infants, 72% of the mothers scored less than 9. Of the 722 infants in the well baby nursery, 8% of the mothers' score were significant for risk of postpartum depression. The NICU mothers had a mean EPDS score of 6.40 with standard deviation of 5.217. The well baby mothers had a mean EPDS score of 3.54 with standard deviation of 3.303.

CONCLUSIONS: The study reveals that there is a significant difference in EPDS scores between the study groups. A large percentage of mothers with infants in the NICU group had EPDS score less than 9. This may be due to inaccuracy of EPDS to identify mothers at risk for postpartum depression. Therefore, a better assessment specifically targeted to mothers with infants in the NICU is needed in order to accurately determine when psychiatric consultation is necessary.

4

House Officer

Postpartum Depression Screening Program – The Attitudes and Acceptance of Pediatric Care Providers

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BACKGROUND: Identifying postpartum depression (PPD) is an important component of postpartum maternal care, as well as infant health and safety. Universal screening for PPD prior to discharge using Edinburgh Postnatal Depression Scale (EPDS) was initiated in the post partum unit of our hospital. It was unclear how this initiative was perceived and influenced subsequent pediatric care.

OBJECTIVE: This study was designed to 1) evaluate documentation of PPD screening in the postpartum unit and in the pediatric clinic and 2) determine both the primary care pediatrician's attitudes toward and knowledge of PPD screening, and willingness to further identify mothers and children requiring interventions.

DESIGN/METHODS: 1) We identified 194 neonates discharged from the nursery from 2/1/10 until 2/28/10 and conducted retrospective chart review for documentation of the PPD screening in the postpartum unit and the pediatric clinic.

2) We also conducted an anonymous 16-question survey of 41 pediatric providers regarding their knowledge of PPD, familiarity with screening tools and attitudes about screening for PPD.

RESULTS: Screening was documented in 97% of maternal records indicating 4% in high risk (EPDS score >14) and 5% in intermediate risk (EPDS score 10-13) for PPD. By contrast, only 4%

of newborn records at discharge had a documented EPDS. Of the 59 infants seen at the pediatric clinic 17% had documentation of PPD screening (post partum EPDS score or other screening). Most pediatric providers (97%) considered detection of PPD important. Two thirds of the providers discussed symptoms of PPD with mothers in the clinic and the remaining one third did not routinely screen for PPD. About 14% were uncomfortable discussing about PPD or screening for PPD in the clinic. The majority (75%) had never used EPDS screening tool and a further 19% were not aware of EPDS. A fifth (19%) felt it was not their responsibility for providing information to mothers with PPD.
CONCLUSIONS: Pediatric care providers acknowledge the importance of identifying PPD and intervening with those families to optimize child health, safety and development. However, many feel uncomfortable, unprepared and poorly equipped to play an active role. Development of guidelines, training for providers and knowledge of locally available resources are key strategies to improve screening in the pediatric outpatient setting.

5

Medical Student

What Is My Neighborhood? Using Travel Patterns by Urban Minority Children and Their Families To Define Neighborhood

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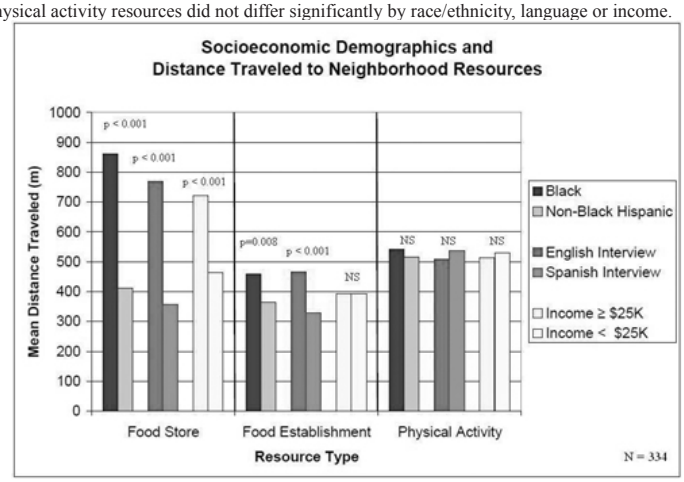
Mount Sinai School of Medicine, New York, NY; Department of Preventive Medicine, Mount Sinai School of Medicine, New York, NY; Department of Pediatrics, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: The role of neighborhood in children's health has been a growing area of research. Distances traveled to neighborhood resources may help elucidate definition of neighborhood. Little is known about socioeconomic influences on travel patterns, particularly for urban, minority families who are at high risk for health disparities.
OBJECTIVE: Describe differences in neighborhood travel patterns by race/ethnicity, primary language and income based on most frequently used food stores, food establishments (restaurants and fast food) and physical activity resources.
DESIGN/METHODS: Distances traveled by East Harlem, NY children (n=334) and their families to frequently used neighborhood resources were calculated using ArcGIS. Differences in distances according to race/ethnicity (Black or non-Black Hispanic), interview language (English or Spanish) and annual income (< or ≥ $25K) were assessed using t-tests.
RESULTS: Mean distances traveled by Blacks and by English interview were significantly farther than Hispanics and Spanish interview respectively for both food stores and food establishments. Those with a family income ≥$25K traveled farther to food stores than those earning <$25K; this relationship was not seen for food establishments. Distances traveled by children to neighborhood physical activity resources did not differ significantly by race/ethnicity, language or income.



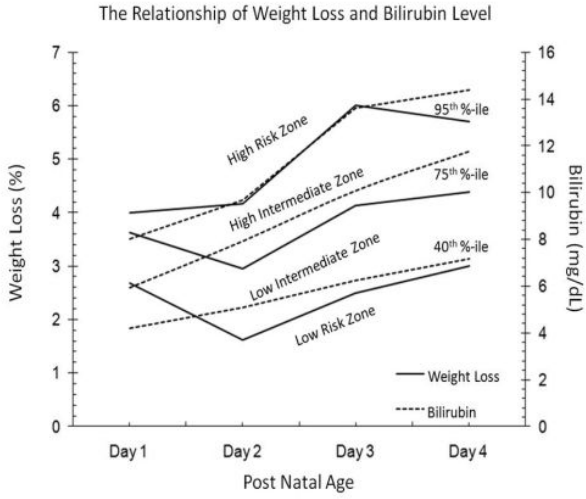
Geographical clustering did not appear to account for these associations. Neighborhood defined by resource use was far smaller than researcher-defined neighborhood for this project, 6 vs 10 blocks.
CONCLUSIONS: These data suggest that race/ethnicity, primary language and income are associated with children's families' choice of food store and food establishment within their community but not with choice of child's physical activity resource. Further research is needed to assess how differences in travel patterns influence dietary behaviors and physical activity levels.

6

Can Postnatal Weight Loss Predict Early Onset Neonatal Hyperbilirubinemia?

Nidhi Agarwal, Rusly Harsono, Fernanda Kupferman, Lourdes Cohen, Shirley Pinero, Louis Primavera, Susana Rapaport.
Pediatrics, Flushing Hospital Medical Center, Flushing, NY; Psychology, Touro College, New York, NY.

BACKGROUND: Neonatal bilirubin nomogram (BN) is currently used to follow trends in bilirubin levels (BL), assess risks, and time interventions. Studies have shown weight loss to be an independent risk factor in predicting early-onset neonatal hyperbilirubinemia (EONH). Little is known about the correlation between percent weight loss (PWL) and BL to predict EONH.
OBJECTIVE: To determine the correlation between PWL and BL in EONH.
DESIGN/METHODS: We reviewed medical records of healthy infants (gestational age ≥ 36 weeks) born and followed at our hospital from Jul to Sep 2010. Birth and subsequent weights, age, and BL (determined by transcutaneous or serum measurements or by clinical estimates) were recorded. BL were categorized into their corresponding BN risk groups (G1 <40, G2 40-75, G3 75-95 and G4 >95 %ile). A positive PWL test was defined as any PWL above the upper limit 95 % confidence interval (CI) for mild hyperbilirubinemia (G1). We computed sensitivity and specificity for EONH requiring close followup and/or intervention. Comparisons among groups were done using Tukey test.
RESULTS: Of the 220 infants, we obtained 281 paired measurements of PWL and BL in the first 4 days of life and categorized them into the following risk groups, 111 in G1, 77 G2, 22 G3 and 10 G4. G1 had a mean PWL of 1.96, (95% CI 0.7-3.5, $p < 0.01$). Using a cut-off PWL of 3.5%, we predicted that 49.5% of infants fell into high-risk groups (sensitivity 70%, specificity 67%). Linear regression analysis showed a significant relation between BL and PWL (R^2 of 0.3, 95% CI 0.2 – 0.4). Trends of PWL paralleled those of BL.



CONCLUSIONS: Increases in PWL increased the risk of severity of hyperbilirubinemia. A PWL as low as 3.5 significantly predicted a likelihood of placement in a higher (G2-G4) risk group. Our average PWL graph predicted an analogous trend when plotted against average BL. A novel PWL graph is a reliable alternative to BN in predicting EONH.

7

Perceptions of English and Spanish-Speaking Caregivers about the Role of Pediatricians in Community Violence Prevention Counseling

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General Pediatrics, St. Christopher's Hospital for Children, Philadelphia, PA; Drexel University College of Medicine, Philadelphia, PA; School of Public Health, Drexel University, Philadelphia, PA.

BACKGROUND: Community Violence (CV) remains a recognized threat to the health and well-being of children. In response the AAP has called for pediatricians to screen for CV and provide anticipatory guidance during well-child visits. Little is known about caregiver opinions about the role of pediatricians in discussing CV during well child visits. Less is known about how these perceptions may differ by culture and ethnicity.
OBJECTIVE: The objectives were: 1) to examine caregivers' perceptions of the role of pediatricians in CV prevention counseling during well-child visits; and 2) to identify differences in these perceptions between English and Spanish-speaking caregivers.
DESIGN/METHODS: During the 2-month study period self-administered surveys were completed by English and Spanish-speaking caregivers of children ages 0-21 who presented to an inner-city primary care clinic. The survey assessed perceptions about: the pediatrician's role in CV prevention counseling, interest in discussing CV prevention with the pediatrician, neighborhood safety, risk and protective factors for CV exposure, and strategies to avoid CV exposure.
RESULTS: 276 out of 306 caregivers participated. 46% identified as Black, 43% as Latino, 5% as multi-racial. 57% of Latinos were Puerto Rican, 23% Dominican, and 20% Mexican, Central American or South American. 56% of Latinos were predominantly English-speaking. 82% of caregivers identified as the patients' mother, 11% as the father. 59% were unaware that their pediatrician could advise them about CV prevention. 30% were interested in discussing CV prevention with their pediatrician. Spanish-speaking caregivers were more interested in discussing CV-related topics with their pediatrician when compared to English-speaking caregivers (67% vs 24% for CV prevention, 62% vs 29% for discipline techniques, 68% vs 33% for appropriate television programming)[all $p<0.01$].
CONCLUSIONS: The majority of caregivers at an inner-city clinic did not want to discuss CV prevention with their pediatrician. Most did not recognize their doctor as a CV prevention resource. Spanish-speaking caregivers were more interested in discussing CV with the doctor than were English-speaking caregivers. Acculturation and differences in the perceived scope of physician's practice may explain these findings. Future research should quantitatively assess caregiver barriers to discussing CV with their pediatrician.

8

Medical Student

Relationship between Health Literacy and Body Mass Index

Roopa Chari, Joel Warsh, Tara Ketterer, Adam Badaczewski, Iman Sharif.
General Pediatrics, Nemours/A.I. duPont Hospital for Children, Wilmington, DE.

BACKGROUND: In a previous published study of **overweight** children, we reported a relationship between child's own health literacy and child's body mass index (BMI). No studies have explored the relationship between either child literacy or parental health literacy and body mass index amongst a general population of normal weight and overweight/obese children and adults.
The Newest Vital Sign (NVS), is a commonly used screen for health literacy in adults. Because the NVS tests the subject's ability to read and interpret a nutrition label, we hypothesized that it may

be a particularly useful correlate of BMI as a health outcome.
OBJECTIVE: To test the relationship between child and parental health literacy and child BMI.
DESIGN/METHODS: We conducted a cross-sectional survey amongst a convenience sample of child-parent dyads in the outpatient waiting areas of a pediatric hospital. To measure literacy, we administered the Newest Vital Sign (NVS) to each child and parent.
Anthropometric measurements on the child and parent were taken, and demographic data collected. We calculated child BMI and BMI percentile for age/gender, as well as parental BMI. We used the NVS as an ordinal scale (0-6). We used spearman correlations to compare NVS scores with BMI and other variables. For sub-analyses, we categorized weight into one of three categories using accepted standards for children and adults: normal weight, overweight, and obese. Three children with bmi < 5th percentile were excluded from the analyses.
RESULTS: We surveyed 91 child-parent dyads. Child bmi ranged from 13.9-43.4; 45(49%) were normal weight, 16(18%) were overweight, and 30(33%) were obese. Parental BMI ranged from 10 to 49; 62% were overweight/obese.
There was no relationship between either child or parental literacy and child bmi percentile across the study population. There was no relationship between parental and child BMI.
Amongst 46 overweight/obese chidren, higher child BMI was associated with lower parental NVS (rho=-0.48, p=0.001) and lower child NVS (rho=-0.37, p=0.01). Parental BMI and child BMI percentile were associated (rho=0.36, p=0.03).
CONCLUSIONS: The relationship beween literacy and BMI appears to be limited to the overweight/obese population. A larger sample size will enable adjusted analyses. Whether low health literacy is a predictor or result of increased bmi will need to be evaluated in a prospective trial.

9

Performance of the NVS and STOFHLA in Children

Iman Sharif, Laurie Bauman, Debra Roter, Tara Ketterer, Roopa Chari, Deepa Rastogi, Sandra Braganza, Mary Ann Abrams, Katherine Freeman, Arthur E. Blank, Ruth E.K. Stein, Benard P. Dreyer.
Pediatrics, Nemours/A. I. duPont Hospital for Children, Wilmington, DE; Pediatrics, Albert Einstein College of Medicine/Children's Hospital at Montefiore, Bronx, NY; Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; Pediatrics, NYU School of Medicine, New York, NY; Iowa Health System, Des Moines, IA.
BACKGROUND: Health literacy is critical to the effective management of childhood asthma, but no validated measures of child health literacy are available. We piloted the use of two widely used adult measures, the Newest Vital Sign (NVS) and the Short Test of Functional Health Literacy (STOFHLA) in school-aged children.
OBJECTIVE: To test whether the NVS and STOFHLA are feasible and valid in children with asthma, as evidenced by a) higher scores with age, b) correlation with each other, and c) correlation with better disease management.
DESIGN/METHODS: We analyzed baseline data from an ongoing cohort study of children with asthma, ages 8 and up. Children completed the NVS (6 items interview) and the STOFHLA (36 item, timed). Using a MicroLoop Spirometer, we measured lower area obstruction (% predicted FEV1/FVC for age, sex and body composition) at 2 weeks follow-up. Parental literacy(TOFHLA) and years of education were also measured.
Literacy measures were used as ordinal scores, as well as literacy categories according to adult criteria: NVS (limited, 0-1; possibly limited, 2-3; adequate, 4-6); STOFHLA (inadequate, 0-16; marginal, 17-22; adequate, 23-36). We used spearman correlation to test the relationship between the two tests, and between each test with other variables.
RESULTS: We collected data for 40 children. Mean age was 9.4(SD 1.8); 62% were male.
The NVS was completed by 38 children; 25(66%) scored limited; 11(29%) possibly limited; and 2(5%) adequate literacy. On the STOFHLA, 21(52%) scored inadequate, 9(23%) marginal, and 10(25%) adequate. Older age was associated with higher NVS(rho=0.37, p=0.02) and STOFHLA (rho=0.68, p<0.00001).
NVS and STOFHLA was not significantly correlated (rho=0.28, p=0.10).
Higher NVS (rho=0.38, p=0.03) and STOFHLA (rho=0.40, p=0.02) were related to better % predicted FEV1/FVC. There was no relationship between airway obstruction and parental literacy(rho=-0.15, p=0.42), or education(rho=0.21, p=0.24).
CONCLUSIONS: The NVS and STOFHLA were feasible to administer. Scores were concentrated in the low literacy categories, suggesting the need to add or revise some items to improve the distribution. With these preliminary data, the measures show promising validity in children.With modest revisions and formal validation studies, these scales may prove suitable to measure health literacy in children.

10

Medical Student

Preliminary Validation of the Newest Vital Sign in School-Aged Children

Joel Warsh, Adam Badaczewski, Iman Sharif.
Division of General Pediatrics, Nemours/A.I. duPont Hospital for Children, Wilmington, DE.
BACKGROUND: Studies in adults have demonstrated positive associations between health literacy and health outcomes. In children, similar studies have been hampered by lack of measures of child health literacy. The ability to measure the association between child health literacy and disease outcomes can aid the design of interventions to improve self-management of common chronic childhood diseases such as asthma and obesity. We piloted the Newest Vital Sign (NVS), a commonly used screen for health literacy amongst adults, in school-aged children.
OBJECTIVE: To obtain estimates of the relationship between children's performance on the NVS and the Gray Silent Reading Test (GSRT), a test of reading comprehension that has established reliability and validity between ages 7-25.
DESIGN/METHODS: We surveyed a convenience sample of school-aged children in the pediatric outpatient clinics of a children's hospital. Children were administered the NVS, followed by the Gray Silent Reading Test.
For the NVS, children looked at a food label, while a trained interviewer asked them 6 questions that measure reading comprehension and numeracy skills. We scored the NVS according to adult standards: Limited (0-1); possibly limited(2-3); adequate (4-6) literacy.
For the GSRT, children read a series of 13 passages, each followed by 5 reading comprehension questions. We used the raw score (0-65) in all analyses.
We used spearman correlation to test the relationship between the NVS and the GSRT raw score. We used analysis of variance to compare the GSRT score for limited/possibly limited/adequate literacy on the NVS.
RESULTS: We surveyed 38 children; mean age 11.2(SD 2.3); 58% male.
On the NVS, 39% scored limited literacy, 39% scored possibly limited literacy, and 21% scored adequate literacy. GSRT scores ranged from 1 to 51, with a mean of 21(SD 14). Older age was associated with better performance on the NVS (rho=0.34; p=0.04) and GSRT (r=0.77, p<0.0001).
The NVS and GSRT were correlated (rho=0.64, p<0.00001).
Mean(SD) GSRT for each category of NVS was: Limited: 11(10) vs. Possibly Limited: 26(13) vs. Adequate: 31(11), p=0.0004.
CONCLUSIONS: The NVS has good correlation with the GSRT in children. The NVS may be prove a useful tool for measuring health literacy in children. Additional data may enable the identification of appropriate age-related categorization of NVS scores for use in children.

11

Clearing the Air: Outdoor Fine Particulate Matter and Costs of Infant Bronchiolitis Hospitalizations

Perry E. Sheffield, Angkana Roy, Kendrew Wong, Leonardo Trasande.
Pediatrics and Preventive Medicine, Mount Sinai School of Medicine, New York, NY; General Pediatrics, Erie Family Health Center, Chicago, IL.
BACKGROUND: Increasing evidence supports an association of chronic outdoor air pollution and bronchiolitis hospitalization in infants. However, there are no nationally representative studies that include data on economic burden of air pollution and bronchiolitis. We hypothesize that higher lifetime fine particulate matter (PM2.5) exposure is associated with increased severity of bronchiolitis and consequently higher costs among hospitalized infants.
OBJECTIVE: To examine the association of lifetime, or chronic, PM2.5 and bronchiolitis hospitalization length of stay (LOS), charges and costs in a nationwide sample.
DESIGN/METHODS: We merged bronchiolitis hospitalization discharge data for infants (age 1-12 months) from the 1999-2007 Nationwide Inpatient Sample and ambient air pollutant data from the Environmental Protection Agency. Hospitals with no air quality data within 10 miles were excluded. Our predictor was the average concentration of PM2.5 over the lifetime of the infant. We used multivariate linear regression for outcomes of bronchiolitis hospitalization LOS and log-transformed charges and costs, controlling for ozone and nitrogen dioxide during the month of hospitalization, patient demographics, hospital characteristics, and month of admission. Separate analysis examined gastroenteritis as an outcome. Other air pollutants were excluded due to high autocorrelation (Pearson rho>.3).
RESULTS: Compared to the entire sample of infants hospitalized for bronchiolitis, our subsample includes only those with available air pollutant data. This subsample includes more urban (99.6 vs 55%) and teaching (69 vs 30%) hospitals, as well as more black (15 vs 7%) and Hispanic (36 vs. 3%) patients. In multivariable analyses (n=42,617 unweighted), a 1-unit (microgm/m3) increase in lifetime PM2.5 was not significantly associated with LOS but was associated with a $285 increase in charges (95% CI: $25-734, p=.028) and a $127 increase in costs (95% CI: $28-302, p=.0041). Including LOS in the cost and charge models decreased the effect of lifetime PM2.5, indicating that the association is partly mediated by LOS. For gastroenteritis charges, no association was seen with PM2.5
CONCLUSIONS: In urban areas, ambient lifetime PM2.5 exposure is associated with increased costs for infant bronchiolitis hospitalizations. The economic burden caused by air pollutants on healthcare utilization needs to be considered by environmental policymakers.

12

Using Audience Response Systems To Determine Gaps in Pediatric Environmental Health Knowledge

P. Sheffield, S. Balk, S. Braganza, M. Chitkara, J. Forman, M. Galvez, A. Miodovnik, S. Palevsky, A. Roy, H. Brumberg.
AAP District II, Chapter 3, Committee on Environmental Health, New York, NY; General Pediatrics, Erie Family Health Center, Chicago, IL.
BACKGROUND: General pediatricians are often called upon by families to interpret pediatric environmental health (PEH) messages that appear in the media. The use of audience response systems (ARS) in educational workshops has not been tested as a way to assess pediatricians' knowledge about or skills in interpreting such messages.
OBJECTIVE: To use the ARS to measure providers' knowledge regarding 3 current PEH concerns (bisphenol A (BPA), teens' UV radiation exposure from tanning booths, and hazards from cell phone use).
DESIGN/METHODS: We presented a multi-media workshop using an ARS in different venues: 1) a pediatric grand rounds at an academic medical center; 2) a workshop at the New York Academy of Medicine, and 3) a workshop at PAS 2010. The presentation entitled "What Gets Said: Deconstructing Media Messages About Pediatric Environmental Health Concerns" included questions on baseline knowledge, opinions on relative importance of PEH issues, case scenario responses, and likelihood of using the information presented. Workshop participants responded anonymously to multiple-choice questions with ARS devices.
RESULTS: Participants' responses from the 3 sessions were pooled. The majority of participants (n=96) were pediatricians. Participant responses indicated knowledge gaps in all three topic areas: 93% (88/92) of respondents were unaware of the specific human health effects associated with BPA exposure; 74% (29/39) were unaware of the extent of tanning booth use by 17 year old females; 66% (38/58) were unaware of the current evidence regarding cell phone exposure. Although most participants (73%, (n=90)) reported receiving clinical questions occasionally or frequently about PEH issues presented in the media, 66% (n=89) reported feeling uncomfortable or unsure of how to respond to those queries. From a list of potential PEH concerns, the primary concern was secondhand smoke for >50% of participants. Throughout the sessions, the percentage of electronic responses was maintained (95-100%). Feedback on using the ARS technology was positive.
CONCLUSIONS: ARS technology helped to identify gaps in PEH knowledge. Adult learners stayed engaged demonstrated by consistent responses throughout the workshop. ARS systems can be further adapted for targeted pediatrician training in PEH.

13

Medical Student

Developing a Best Practices Algorithm To Minimize Infant Risk of Bilirubin Encephalopathy

Melissa A. Schneider, Claire Hoppenot, Gary A. Emmett.

Pediatrics, Thomas Jefferson University, Philadelphia, PA; Nemours Foundation, Wilmington, DE.

BACKGROUND: About 5% of newborns develop serum bilirubins (TSBs) high enough to require medical intervention. Following TSBs prevents the catastrophic outcome of bilirubin encephalopathy. Observation of newborns is not sufficient to safely monitor jaundice in the Well Baby Nursery. Many nurseries perform a transcutaneous bilirubin (TcB) early on the 2nd day of life. If the TcB is high, a TSB is drawn at the same time as the newborn screen. TcB has been shown to be an adequate screening test for the TSB, but exact negative predictive values (NPV) have not been reported. What TcB level cutoff for drawing a TSB gives the best combination of less blood draws while protecting the newborn?

OBJECTIVE: To find the TcB level that minimizes phlebotomy, thus pain and suffering to the newborn, yet does not miss potential cases of bilirubin encephalopathy.

DESIGN/METHODS: All available TcB (Minolta JM103) and TSB measurements from newborns (≥ 37 weeks gestation) born between July 13, 2009-July 12, 2010 were analyzed during a retrospective chart review of the Thomas Jefferson University Hospital Well Baby Nursery electronic medical records. All charts with both a TcB ≥ 6.0 (mg/dL) and a TSB drawn immediately after were selected and then stratified into groups based on TcB level. These charts were then analyzed for their NPV for High Intermediate or High Risk based on the "bilitool.org" nomogram.

RESULTS: Between July 13, 2009-July 12, 2010, 1216 infants ≥ 37 weeks gestation were discharged from the Well Baby Nursery. Of those, 1016 (83.6%) had a recorded TcB level. TcB levels ranged from 0-15.6 (mean = 6.6, median = 6.6). 510 infants were male (50.2%). Using the TcB as a cutoff level, each group (6.0-6.9, 6.0-7.9, 6.0-8.9, 6.0-9.9, and ≥ 6.0) was analyzed for its NPV. The NPV was noteworthy for both the TcB levels 6.0-6.9 with 5 High Intermediate Risk and no High Risk infants (96.1%) and 6.0-7.9 with 17 High Intermediate Risk and 1 High Risk infants (94.25%). Using the TcB level 6.0-8.9 resulted in 30 High Intermediate Risk and 3 High Risk infants (91.99%).

CONCLUSIONS: Infants ≥ 37 weeks gestation with a TcB below 8 may be discharged from the Well Baby Nursery without a follow-up TSB safely with the understanding that about 1/1000 infants may be at High Risk for developing severe hyperbilirubinemia and that all infants should be seen by their primary pediatrician within 24-48 hours of discharge.

14

Are We Communicating with Primary Care Providers? – Assessment after Initiation of a Pediatric Hospitalist Program

Sheila Liewehr, Lindsey Douglas.

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BACKGROUND: The communication between hospitalists and primary care providers (PCPs) is essential to the care of patients. There is little data in the pediatric literature on PCP satisfaction and needs regarding communication with hospitalists as well as on interventions to improve communication between pediatric inpatient and outpatient providers. PCP communication needs and satisfaction at the Children's Hospital at Montefiore (CHAM) have not been assessed since the initiation of the pediatric hospitalist program in 2007. Over the last three years CHAM has relied heavily on a written discharge summary as the means of communication with PCPs.

OBJECTIVE: Anonymously survey pediatric PCPs at Montefiore Medical Center to assess: 1). Current satisfaction with communication regarding hospitalized patients and 2). Preferences of communication regarding hospitalized patients.

DESIGN/METHODS: A survey comprised of 18 questions was distributed via e-mail link to an online survey system to all pediatric PCPs at the Montefiore Medical Group (MMG) practices and to all private pediatricians who have admitting privileges to CHAM, 133 in total. The survey was comprised of 4 parts: 1) Demographic information, 2) PCPs access to a hospital-based email system and an electronic medical record alert system, 3) PCPs experience with timing, frequency and method of communication on admission and discharge and 4) PCPs overall satisfaction and preferences.

RESULTS: Thus far we have received 34 completed surveys (26%). 47% of PCPs were rarely or never notified of their patient's admission and 68% were rarely or never notified of their patient's discharge from the hospital. 74% of PCPs rarely or never received a written discharge summary. However, when PCPs did receive a written discharge summary 92% found it useful. Only 26% of PCPs in our survey were satisfied with communication with the hospitalists. The preferred mode of communication amongst PCPs at CHAM is email (80%).

CONCLUSIONS: The survey results indicate that PCPs are not satisfied with present communication. This baseline data will aid in constructing an intervention to improve communication between pediatric PCPs and hospitalists. Further research could assess the impact of such communication on patient satisfaction and outcomes.

15

Pre-Menarchal Girls' and Parents' Perceptions about Urogenital Symptoms: Causes and Associations

Cynthia W. DeLago, Carmen V. Vasquez, Claudia Clarke, Esther Deblinger, Martin Finkel.

Pediatrics, Albert Einstein Medical Center, Philadelphia, PA; Pediatrics, University of Medicine and Dentistry of New Jersey School of Osteopathic Medicine, Stratford, NJ.

BACKGROUND: Pre-menarchal girls often present with urogenital symptoms (dysuria, genital soreness, pruritus, bleeding or vaginal discharge). Once trauma, skin disorders, infections and foreign bodies are excluded, chemical/physical irritants are considered. Little information is published about associations between these irritants and urogenital symptoms in a well population.

OBJECTIVE: Describe prevalence of parent /girl-reported urogenital symptoms, perceived causes and associations with genital irritants in pre-menarchal girls.

DESIGN/METHODS: We consecutively enrolled 5-12 y/o pre-menarchal girls arriving for well-child visits at an urban, hospital-based pediatric office and a suburban pediatric office. Parents/girls were separately asked about girls' prior urogenital symptoms and perceived causes. Next, parents were asked about girls' exposure to genital irritants (tight-fitting clothes, nylon underwear/tights, bike or horseback riding, bubble baths, soap, shampoo, genital hygiene and trauma). Medical records were reviewed for Tanner stage, BMI, and medical conditions.

RESULTS: We surveyed 191 parent/pre-menarchal 5-12 y/o girl dyads (91 urban, 100 suburban; 45% Black, 41% White, 72% Tanner 1; mean age 8 yrs). 40% of parents reported their girls had histories of urogenital symptoms vs. 50% of girls. Of these, 29% of parents attributed symptoms to poor hygiene vs. 14% of girls, 20% vs. 20% soap products, 13% vs. 2% UTIs, but 24% vs. 53% could not identify a cause. Analysis of symptoms vs. associated irritant exposures showed poor hygiene was associated with dysuria, soreness, and pruritus; tight underwear/pants, soap, or shampoo were associated with dysuria and genital soreness; and bubble baths were associated only with parent-reported genital soreness (all ps<0.05). No associations were found with nylon underwear/tights, bike or horseback riding. No irritants were associated with a vaginal discharge. Race, ethnicity, eczema, obesity/overweight were not associated with symptoms.

CONCLUSIONS: Urogenital symptoms are very common in pre-menarchal girls. When parents/girls cannot identify a cause or infections are excluded, physicians should focus on improving genital hygiene and eliminating exposures to soap products and tight-fitting clothing. Elimination of bike/horseback riding or nylon underwear/tights is not indicated. Persistent symptoms despite treatment or a vaginal discharge warrants further evaluation.

16

Health, Obesity, and Environment in East Harlem, NY

Maida Galvez, Lawrence C. Kleinman, Carol Horowitz, Nita Vangeepuram, Michelle Ramos, Thalia MacMillan.

Mount Sinai School of Medicine, New York, NY; Communities IMPACT Diabetes Center, New York, NY.

BACKGROUND: Obesity is prevalent in urban minority communities. The Sector of Excellence for the Elimination of Disparities (SEED) is a 2 census tract area of East Harlem, NY (EH).

OBJECTIVE: As part of baseline assessement for a community-partnered project to reduce diabetes-related disparities in the SEED, we combined multiple assessments of the health and environment of children.

DESIGN/METHODS: We administered surveys (English/Spanish) at community sites in the SEED to 117 adults regarding their children and to 291 adults regarding social capital and collective efficacy (SC/CE). We oversampled at schools and after school programs. We also performed a block by block assessment of the neighborhood, including food stores, restaurants, green spaces, and sidewalks.

RESULTS: Most respondents (83%) were mothers. The average child was 7 years (range 3-15). Parents reported the health of 36% of children as only good, fair, or poor. Asthma was prevalent (31%) but did not explain these low health scores. 55% of children were overweight or obese (O/O) by BMI. Mean screen time was 2.0 hours daily (IQ range 1-3) and median time walking or running 2.0 hours/day. There was an average of 1 park or playground every 7 blocks: parks were used more frequently than playgrounds. Parents report low (0.3) median intake of soda, no diet soda, 2.0 servings of milk (49% whole or chocolate), 1.0 of juice, and only 0.4 servings of salad or green vegetables daily. 63% agreed that the family often watched TV while eating, and only 39% averaged at least one family meal per day. A typical child had 1 fast food meal and one food purchase from a bodega per week. Favorite purchases included pizza, fries, chips, and ice cream. A minority of food stores surveyed carried healthy foods- 43% had apples, 38% tomatoes, and 19% fat-free milk. Of 21 restaurants surveyed, 52% were either national fast food chains, pizza, or Chinese take out. Most (67%) of restaurants had at least one healthy item (usually salad). Sidewalks were not always easily walkable, with 51%% in disrepair and 21% obstructed. The number of trees per block face varied widely, with mean=3.9 and SD=4.2. Measures of SC/CE varied widely block to block.

CONCLUSIONS: Even in a 2 census tract area of EH, environment varies from block to block. Children's health status is concerning, as are rates of O/O. Multiple aspects of the food, built, and behavioral environments may combine to produce high rates of local childhood O/O.

17

Mexican Children in East Harlem, NY Have Distinct Diet and Activity Behaviors Compared to Other Hispanic Children

Nita Vangeepuram, Maida P. Galvez, Thalia L. MacMillan, Michelle Ramos, Carol R. Horowitz, Lawrence C. Kleinman.

Mount Sinai School of Medicine, NY, NY; Lighthouse International, NY, NY.

BACKGROUND: Low-income minority children have high rates of obesity. While studies have examined racial differences in diet and physical activity, no studies have looked at differences in Hispanic subgroups.

OBJECTIVE: To examine racial/ethnic differences in diet and physical activity in children from an ethnic minority community.

DESIGN/METHODS: Community and academic partners administered a field survey in English or Spanish to parents/guardians of children residing in the Sector of Excellence for the Elimination of Disparities, a two census tract area in East Harlem, NY, identified for targeted interventions to decrease diabetes related disparities. Diet and physical activity behaviors and perceived health were compared using Chi Square and T-tests.

RESULTS: The 116 children had a mean age of 7 years (range 3-15), 48% were female, 26% non-Hispanic Black, 29% Puerto Rican, 26% Mexican, and 19% other/mixed Hispanic. The only difference in behaviors between Hispanic and Black children was higher mean daily servings of green vegetables among Black children (0.7 servings vs. 0.2 servings, p=0.006). However, there were many significant differences between Mexican and non-Mexican Hispanic children.

Compared to non-Mexican Hispanic respondents, Mexican respondents reported their children participate less frequently in organized after school activities (40% versus 61%, p=0.07) and rated their children's overall health less favorably (20% vs. 43% reported their child's health as excellent and 27% vs. 7% as fair or poor, p=0.01). However,

Mexican respondents reported their children had healthier behaviors, including less screen time and fewer servings of sweetened beverages (Table reports mean values):

	Mexican	Non-Mexican Hispanic	P value
Daily TV hours	1.3	1.9	0.009
Daily computer hours	0.2	1.1	0.0003
Daily servings of sweetened beverages	0.4	1.2	0.004
Daily servings of milk	2.2	1.6	0.03
Daily servings of fruit juice	1.2	2.2	0.02
Daily servings of green vegetables	0.1	0.3	0.01
Weekly purchases of food/drink at bodega	1.1	2.1	0.03

CONCLUSIONS: Among Hispanics, Mexican parents rated their child's health lower, but reported healthier behaviors. Awareness of differences between Mexican and other Hispanic children may help in development of targeted interventions to improve health.

18

A Comparison of Dietary and Physical Activity Behaviors in New York City Children from Different Ethnic Minority Subgroups

Nita Vangeepuram, Nancy Mervish, Susan L. Teitelbaum, Maida P. Galvez, Barbara Brenner, Mary S. Wolff.

Mount Sinai School of Medicine, NY, NY.

BACKGROUND: Low-income minority children have high rates of obesity. While studies have examined racial differences in diet and physical activity, no studies to date have included Hispanic subgroups.

OBJECTIVE: To examine racial/ethnic differences in diet and physical activity in mixed ethnic minority New York City (NYC) children.

DESIGN/METHODS: Cross-sectional data from a community based study of 505 6-8 year old NYC children were used. Dietary intake was obtained by 24-hour diet recalls using the Nutrition Data System for Research. Physical activity was assessed via questionnaire. Diet and activity were compared across groups using Chi Square and ANOVA tests.

RESULTS: Mean ages and gender distribution were similar across racial/ethnic groups. Obesity rates were lowest in non-Hispanic Black children (18%) and among Hispanics were lowest in Mexican children (25%). There were racial/ethnic differences in mean daily servings of certain food groups (healthiest groups in bold and unhealthiest underlined):

	Mexican	Dominican	Puerto Rican	Other/mixed Hispanic	Black
Total N	98	33	72	49	91
Fruits (not including juice)	**1.2**	**1.3**	0.6	1.0	0.8
Whole grains	**1.1**	0.5	0.5	0.7	0.6
Refined Grains	2.6	3.7	4.7	3.6	4.2
Low fat dairy	**1.2**	1.2	1.0	0.9	0.9
Regular meats	**1.3**	**1.5**	2.5	2.1	2.6
Regular Oils	1.3	1.6	2.3	1.6	1.9
Sweetened beverages	0.5	0.6	1.2	0.9	1.0
Diet beverages	1.9	1.7	1.5	1.8	1.3
Total calories	**1193**	1423	1691	1460	1581

Mean total sedentary hours were lower in Mexican children (3.3) compared to Dominican (4.3), Puerto Rican (4.6), and Black (4.8) children, p<0.05. There were other activity differences:

	Mexican	Dominican	Puerto Rican	Other/mixed Hispanic	Black	P value
Total N	143	41	100	68	133	
%Participating in Organized Recreational Activities(n=485)	21.7	31.7	34.7	41.8	39.1	0.01
%Playing Video games>1 hour daily(n=484)	6.3	4.9	18.0	3.0	9.7	0.005
%Daily computer use outside school(n=435)	12.4	39.5	27.6	31.7	29.8	0.001
%Watching>2 hours television daily(n=484)	26.8	31.7	38.0	23.9	38.8	0.11

CONCLUSIONS: Dietary and physical activity behaviors varied across racial/ethnic subgroups among NYC children, and may in part contribute to obesity disparities. Targeted interventions in different ethnic subgroups might be warranted to address specific behaviors.

Cardiovascular & Critical Care Poster Session

Friday, March 25, 2011
6:00 PM-7:30 PM

19

Duration of Central Venous Line Is Not Associated with Increased Deep Venous Thrombosis in Critically Ill Children

E. Vincent S. Faustino, Sheila J. Hanson, Karla A. Lawson, Renee A. Higgerson.

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BACKGROUND: Presence of a central venous line (CVL) is a known risk for deep venous thrombosis (DVT) in children. CVL insertion damages the endothelium and initiates thrombus formation. Other factors may be important in the development of CVL-related deep venous thrombosis (DVT) in critically ill children.

OBJECTIVE: To determine risk factors in the development of symptomatic CVL-related DVT in critically ill children.

DESIGN/METHODS: We performed a nested case control study involving children previously enrolled in a multicenter study on symptomatic venous thromboembolism (VTE). Patients less than 18 years old with CVL inserted during the admission who developed a CVL-related DVT were classified as cases. Each case was matched by age, gender and hospital of origin to 4 control patients who did not have any VTE. Bivariate and multivariate comparisons were performed using conditional logistic regression analysis.

RESULTS: Symptomatic CVL-related DVT was diagnosed in 29 patients. The majority (n=17, 58.6%) of the DVT was detected within 1 week of CVL insertion. Patients with symptomatic CVL-related DVT were appropriately matched to control patients, with similar characteristics. Compared to the 116 control patients, duration of CVL (OR: 1.02; 95% CI: 0.98, 1.06; *P*=.352) and severity of illness (OR: 1.15; 95% CI: 0.89, 1.49; *P*=.274) were not associated with CVL-related DVT. There was a trend towards increased DVT in children with trauma (odds ratio [OR]: 8.64; 95% confidence interval [CI]: 0.87, 86.23; *P*=.066) but decreased DVT in patients with acyanotic congenital heart disease (OR: 0.27; 95% CI: 0.06, 1.11; *P*=.069). Other factors not associated with CVL-related DVT include race and ethnicity, operative status, use of mechanical ventilation, and presence of cancer, cyanotic congenital heart disease or sepsis.

CONCLUSIONS: The lack of association between duration of CVL use and CVL-related DVT and the early development of DVT suggest that insertional factors (e.g. number of venous puncture and size of the CVL) or patient characteristics (e.g. age, underlying illness and co-morbidities but not its severity, and presence of coagulation disorders) may be more important in the development of CVL-related DVT. The use of early thromboprophylaxis in critically ill children with CVL should be further investigated.

20

Coronary Complications in Children with Kawasaki Disease in Association with Time of IVIG Treatment

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Pediatrics, Jersey Shore University Medical Center, Neptune, NJ.

BACKGROUND: Kawasaki disease is the leading cause of acquired heart disease in children in developed countries.Approximately 20-25% of untreated children develop coronary aneurysm (CA).Treatment with IVIG within 10 days of onset of fever reduces the risk to 2-4%.Currently there are no studies indicating the effectiveness of IVIG therapy after 10 days of onset of fever.

OBJECTIVE: To determine the risk of CA lesions in children with KD treated with IVIG after 10 days. Impact of demographics, clinical and laboratory presentation of disease on development of cardiac complications in children with KD was analyzed.

DESIGN/METHODS: Medical charts and ECHO (at time of admission, 3, 6, 9 weeks, and 6-12 months) of children with KD were reviewed. The association between CA lesions at 3 weeks and administration of IVIG within and after 10 days was statistically analyzed.

RESULTS: Among 71 children with KD, 11 (15.5%) developed CA lesions at 3 weeks. IVIG therapy after 10 days was more likely to be associated with CA lesions (54.6% vs. 11 .7%, P<0.01). The significant association between the development of CA lesions and IVIG administration after 10 days was confirmed in the regression model that included patients age,WBC, platelet counts and IVIG administration as dichotomous variable (*Wald Statistics* 3.9, P<0.05). We found higher mean leukocyte and platelet counts in patients with CA complications.However, no significant association was observed between the time of IVIG administration and time for normalization of coronary complications. All patients with coronary complications were detected by echocardiogram between 1-3 weeks of onset of the fever. 81.8% (9 out of 11) of children with coronary abnormality had normalization of coronary aneurysm by 3 months. The two children who had residual coronary abnormality beyond 3 months had giant, saccular coronary aneurysm which got significantly smaller by one year.

CONCLUSIONS: Late (after 10 days) treatment of KD with IVIG results in more CA lesions at 3 weeks after KD onset but is not associated with longer resolution of CA pathology. Treatment with IVIG on or before 10 days is an independent factor that impact better coronary outcome in children with KD. This study shows that patients with KD treated with IVIG after 10th day of illness may still benefit in terms of the time to normalization of coronary abnormality. A large prospective study will be beneficial to address this issue.

21

House Officer

Cardiac Effects of CNS Stimulants in Patients with ADHD: Comparing the Recommendations of the American Heart Association with the American Academy of Pediatrics

Deepak Patel, Karen Carpenter, Robert Escalera.

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BACKGROUND: Attention deficit/hyperactivity disorder (ADHD) is a common disorder affecting up to 8 to 10 percent of all school-aged children. Stimulant drugs are effective in improving behavior in these patients. Reports of sudden unexpected deaths (SUD) among patients taking stimulant drugs have led to a debate between the AHA and the AAP concerning the safety of CNS stimulants in children with undiagnosed at-risk congenital heart disease and/or arrhythmias prior to starting stimulant medications.

OBJECTIVE: To examine patients with ADHD referred to a pediatric cardiologist for the prevalence of 1) cardiac abnormalities identified via cardiovascular screening (CVS) and 2) cardiac abnormalities identified that preclude the initiation of stimulant medication.

DESIGN/METHODS: A retrospective chart review was undertaken of 271 pediatric patients referred to a pediatric cardiologist for CVS either prior to initiating or while on CNS stimulants. Data extracted from charts included age, sex, type of stimulant, dose, symptoms (chest pain, palpitations, shortness of breath, exercise intolerance, dizziness and syncope), family history SUD, and results of CVS (BP, auscultation, EKG, ECHO, Holter Monitor and stress test).

RESULTS: A total of 271 EKG's were reviewed. There were 164 patients evaluated by EKG only and no contraindications to stimulant medication were found. There were 107 patients evaluated with EKG and formal consultation. In the pre-medication group, 2/43 (5%) were symptomatic and in the on-medication group, 22/64 (34%) were symptomatic (p = 0.001). There were 2/23 (8.7%) patients found to have a contraindication to stimulant medication (SVT, prolonged QTC) and both were in the symptomatic group of patients on medication (p = 0.045). Both patients with a contraindication were taking dexmethylphenidate; however, dextroamphetamine was most commonly prescribed (54%).

CONCLUSIONS: There is no value in performing a routine EKG patient prior to starting a CNS stimulant. In those patients who are symptomatic (symptoms and/or family history of SUD), cardiology consultation is indicated. Stimulant medication significantly increases the prevalence of cardiac symptomatology. We recommend patients with cardiac symptoms be referred for a cardiology evaluation. Patients on stimulant medication need to be requestioned by their physician regarding cardiac symptomatology at each follow-up visit.

22

Fellow in Training

Mitochondrial Function Is Limited in the Early Embryonic Heart Due to a Dysfunction in Complex I

David L. Hoffman, Jennifer R. Hom, George A. Porter.

Division of Pediatric Cardiology, University of Rochester Medical Center, Rochester, NY.

BACKGROUND: Proper cardiac function is crucial to ensure embryonic survival. The heart is the first organ to become functional during embryonic development, with the onset of beating at 8 days post fertilization (E8). Within two days of this (E10.5), blood begins to circulate providing nutrients to the developing embryo. Early defects in the embryonic heart can result in embryonic death or severe deformities leading to death during or shortly following birth. Although structural cardiac anomalies rarely cause demise, functional cardiac defects are much more devastating in utero.

In the adult heart, mitochondria play an important role in proper function. Mitochondrial dysfunction can result in cardiac dysfunction and eventually death. While mitochondrial function is well studied in the adult heart, which relies on complex I as its primary source of electron entry, little is known about mitochondrial function in the developing embryonic heart.

OBJECTIVE: This study employs established bioenergetic and mitochondrial proteomic techniques, which have been adapted and applied in whole embryonic hearts and cardiomyocytes during cardiac organogenesis (E9.5, E11.5, E13.5) to support the hypothesis that at early stages of embryonic cardiac development, mitochondrial function is limited due to an immature complex I, thus resulting in decreased $\Delta\Psi m$ and increased potential for oxidative stress. The primary objective of this study is to determine the cause for the complex I dysfunction observed in E9.5 hearts, and determine its role in cardiac development.

DESIGN/METHODS: This study utilizes novel and established methods in mitochondrial bioenergetics to assay complex I functionality in primary embryonic heart culture, and whole hearts. These methods include: Clear Native PAGE, Blue Native PAGE (one and two dimensional), Epifluoresence microscopy, and spirometry using the Seahorse Bioscience XF24 Extracellular Flux Analyzer.

RESULTS: Data generated in this lab show that at the early stages of embryonic development (E9.5) mitochondrial membrane potential ($\Delta\Psi m$) is low, and the potential for increased oxidative stress is high. A minimal change in $\Delta\Psi m$ is observed at E9.5 upon the addition of the complex I inhibitor rotenone. This observation is contrasted in E13.5 myocytes, which exhibit a higher sensitivity of $\Delta\Psi m$ to rotenone.

CONCLUSIONS: In concert, data presented suggest that at E9.5 complex I of the mitochondrial electron transport chain is non-functional.

Neurobiology
Poster Session

Friday, March 25, 2011
6:00 PM-7:30 PM

23

House Officer

Src Kinase-Mediated Mechanism of CREB Protein Phosphorylation during Hypoxia in Neuronal Nuclei of Newborn Piglets

Cindy Soon, Simran Ahluwalia, Anli Zhu, Om P. Mishra, Maria Delivoria-Papadopoulos.

Dept. of Pediatrics, Drexel University and St. Christopher's Hospital for Children, Philadelphia, PA.

BACKGROUND: Previously we have shown that hypoxia results in increased phosphorylation of cyclic-AMP response element binding (CREB) protein in the cerebral cortex of newborn piglets. It is known that intranuclear Ca^{++} regulates nuclear functions such as Ca^{++}-dependent CREB protein mediated transcription of apoptotic proteins. We have also shown that Src kinase inhibitor PP2 blocks the hypoxia-induced increase in Calcium/calmodulin dependent protein kinase IV(CaM Kinase IV) activity, which is responsible for phosphorylation of CREB protein at $Serine^{133}$.

OBJECTIVE: The present study tests the hypothesis that hypoxia-induced increased CREB protein phosphorylation is mediated by Src Kinase in the neuronal nuclei of newborn piglets.

DESIGN/METHODS: Piglets were divided into: normoxic (Nx, n=3), hypoxic (Hx, n=3) and hypoxic-treated with Src inhibitor (Hx+PP2, n=3) groups. We administered the highly selective Src kinase inhibitor PP2 [4-amino-5-(4-chlorophenyl)-7-(t-butyl) pyrazolol (3-,4-pyrimidine, IC_{50} 5nm] to prevent the CREB protein phosphorylation during hypoxia. Hypoxia was induced by FiO_2 of 0.07 for 60 min. PP2 was administered (0.4 mg/kg, i.v.) 30 min prior to hypoxia. Neuronal nuclei were isolated and nuclear proteins were probed with $Serine^{133}$ specific phosphorylated anti-CREB antibody using Western blot analysis. The bands were detected by chemiluminiscence, analyzed by imaging densitometry and expressed as absorbance.

RESULTS: Brain tissue ATP (µmoles/g brain) was 4.4±0.4 in Nx, 1.5±0.3 in Hx and 1.7±0.4 in Hx+PP2. PCr (µmoles/g brain) was 3.5±0.2 in Nx, 1.3±0.3 in Hx and 1.2±0.3 in Hx+PP2. Density of CREB protein phosphorylation ($ODxmm^2$) was 651.85±8.73 in Nx, 988.38±70.49 in Hx ($p<0.05$ vs Nx) and 722.63±27.66 in Hx+PP2 ($p<0.05$ vs Hx). The data show that pretreatment with Src kinase inhibitor prevents the hypoxia-induced increased CREB protein phosphorylation.

CONCLUSIONS: The increased phosphorylation of CREB protein at $serine^{133}$ during hypoxia is Src kinase-mediated. Src kinase mediated tyrosine phosphorylation of calmodulin the activator of CaM kinase IV and CaM Kinase IV leads to increased activation of CaM kinase IV due to increased interaction between phosphorylated calmodulin and CaM kinase IV. The increased activity of CaM kinase IV results in increased phosphorylation of CREB protein at $serine^{133}$, triggering apoptotic protein expression in the hypoxic brain. (Funded by NIH-HD 20337).

24

House Officer

Effect of Hypoxia on Caspase-3 Activation Following Src Kinase Inhibition in the Newborn Piglet Brain

Amit M. Mukhia, Kirstie Marcello, Lynn Fuchs, Om P. Mishra, Maria Delivoria-Papadopoulos.

Dept. of Pediatrics, Drexel University and St. Christopher's Hospital for Children, Phila, PA; Dept. of Pediatrics, Albert Einstein Medical Center, Phila, PA.

BACKGROUND: Caspase-3, activated by caspase-9, executes cell death by cleaving numerous intracellular proteins and enzymes. Previously we have shown that cerebral hypoxia results in increased caspase-9 and caspase-3 activity in the cerebral cortex of newborn piglets. We have also demonstrated that hypoxia results in increased Src kinase activity, a protein tyrosine kinase, known to mediate cell proliferation and cell death in the brain via tyrosine phosphorylation of specific proteins.

OBJECTIVE: The present study tests the hypothesis that hypoxia-induced activation of caspase-3 in the cerebral cortex of newborn piglets is mediated by Src kinase.

DESIGN/METHODS: Piglets were divided into: normoxic (Nx, n=4), hypoxic (Hx, n=4) and hypoxic-pretreated with a selective Src kinase inhibitor (Hx +PP2) groups. Hypoxia was induced by decreasing FiO_2 from 0.21 to 0.07 for 60 min. PP2 [4-amino-5-(4-chlorophenyl)-7-(t-butyl) pyrazolol (3-,4-pyrimidine, IC_{50} 5nm] was administered (0.4 mg/kg, i.v.) 30 min prior to hypoxia. ATP and phosphocreatine (PCr) were determined biochemically to document cerebral energy status. Cerebral cortical cytosol fractions were isolated and the activity of caspase-3 determined spectrofluorometrically at 37°C for 500 seconds using a specific fluorogenic substrate for caspase-3 (Ac-DEVD amino-methyl-coumarin).

RESULTS: ATP (µmoles/g brain) was 4.4±0.8 in the Nx group, 2.2±0.38 in the Hx group and 3.5±1.5 in the Hx+PP2. PCr (µmoles/g brain) was 3.7±0.3 in the Nx group, 1.1±0.14 in the Hx group, and 1.8±0.79 in the Hx+PP2 group (p=NS). Caspase-3 activity (nmoles/mg protein/hr) was 1.84±0.29 in Nx, 2.81±0.75 in Hx ($p<0.05$ vs Nx) and 1.66±0.25 in Hx+PP2 ($p<0.05$ vs. Hx) group. The data show that hypoxia results in increased activity of caspase-3 in the cytosolic fraction of the cerebral cortex of newborn piglets and pretreatment with Src kinase inhibitor PP2 prevents the hypoxia-induced increased caspase-3 activity.

CONCLUSIONS: Hypoxia-induced activation of caspase-3 is mediated by Src kinase. Src kinase mediated tyrosine phosphorylation of anti-apoptotic proteins, such as Bcl-2 and Bcl-xl leads to increased activation of caspase-9 and subsequent activation of caspase-3. Therefore, Src kinase inhibitor would prevent caspase-3 activation by preventing tyrosine phosphorylation of anti-apoptotic proteins, and thereby decreasing the pro-apoptotic potential of the cell. (NIH-HD-20337)

25

House Officer

Mechanism of Increased Expression of CaM Kinase IV during Hyperoxia in the Neuronal Nuclei of the Cerebral Cortex of Newborn Piglets

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BACKGROUND: Previous studies have shown that hyperoxia results in increased calcium/calmodulin-dependent protein kinase IV (CaM kinase IV) activity and increased phosphorylation of cyclic-AMP-response element binding (CREB) protein in neuronal nuclei of the cortex of newborn piglets. We have also shown that hyperoxia results in increased generation of nitric oxide free radicals as demonstrated by increased nitration of neuronal proteins.

OBJECTIVE: The present study aims to investigate the mechanism of increased CaM kinase IV expression during hyperoxia in the cerebral cortex of newborn piglets and tests the hypothesis that the hyperoxia-induced increased CaM kinase IV expression is mediated by neuronal nitric oxide synthase (nNOS)-derived nitric oxide.

DESIGN/METHODS: Piglets were assigned to normoxic (Nx, n=3), hyperoxic (Hyx, n=3) and hyperoxic pretreated with a highly selective inhibitor of nNOS, 7-nitro-indazole-sodium salt (Hyx+7-NINA, n=3) groups. The Nx group was exposed to an FiO_2 of 0.21 for 1 hour. The Hyx groups were exposed to an FiO_2 of 1.0 and maintained at a PaO_2 > 400 mmHg for 2 hours. Cerebral tissue levels of ATP and phosphocreatine (PCr) were measured biochemically to determine cerebral tissue energy statues. Neuronal nuclei were isolated and separated by Western blot analysis and probed with a specific CaM Kinase IV antibody. Protein bands were detected by enhanced chemiluminescence, analyzed by imaging densitometry and band density expressed as ($ODxmm^2$).

RESULTS: ATP (µmoles/g brain) was 4.9±1.1 in Nx, 5.1±0.5 in Hyx (p=NS), and 4.8±0.7 in Hyx+7-NINA (p=NS). PCr (µmoles/g brain) was 3.3±0.6 in Nx, 3.2±0.5 in Hyx (p=NS), and 3.1±0.4 in Hyx+7-NINA (p=NS). The density of CaM Kinase IV was 387.92±101.17 in Nx, 680.58±62.59 in Hyx ($p<0.05$) and 373.98±21.95 in Hyx+7-NINA ($p<0.05$ vs. Hyx). The data show that administration of 7-NINA prior to hyperoxia prevents the hyperoxia-induced increase of CaM Kinase IV expression.

CONCLUSIONS: The hyperoxia-induced increased expression of CaM Kinase IV is mediated by nitric oxide derived from nNOS. NO mediates modification through lipid peroxidation of neuronal nuclear membrane high affinity Ca^{2+}-ATPase leading to increased nuclear Ca^{++}-influx and activation of CaM Kinase IV. CaM Kinase IV results in increased phosphorylation of CREB protein that in turn further increases the expression of CaM Kinase IV protein. (NIH-HD 20337)

26

House Officer

Effect of Neuronal Nitric Oxide Synthase (nNOS) Inhibition during Hyperoxia on Expression of CaM Kinase IV in Neuronal Nuclei of the Cerebral Cortex of Newborn Piglets

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BACKGROUND: We have shown that nitric oxide (NO) free radicals generated either in vivo or in vitro result in increased nuclear Ca^{++}-influx. Calcium/calmodulin dependent protein kinase IV (CaM kinase IV), located in the nucleus, is activated by increased Ca^{++}-influx in the neuronal nuclei of piglets. We have also shown that hyperoxia results in increased CaM kinase IV activity in neuronal nuclei.

OBJECTIVE: The present study tests the hypothesis that hyperoxia-induced increased activation of CaM kinase IV in the neuronal nuclei of the cerebral cortex of newborn piglets is mediated by NO.

DESIGN/METHODS: Piglets were divided into normoxia (Nx, n=5), hyperoxia (Hyx, F_iO_2 of 1.0, PO_2 >400mmHg for 2 hrs, n=5), hyperoxia-pretreated with a non-specific NOS inhibitor, N-nitro-L-arginine, to demonstrate if CaM kinase IV activation is NO mediated (Hyx+NNLA, 40 mg/kg i.v., 60 min prior to hyperoxia, n=3) and hyperoxia pretreated with a highly selective neuronal, NOS inhibitor 7-nitro-indazole-Na, to determine if NO is derived from nNOS (Hyx+7-NINA, 1mg/kg, i.v., 60 min prior to hyperoxia, n=3) groups. ATP and phosphocreatine (PCr) were determined to document cerebral tissue energy. Cortical neuronal nuclei were isolated and CaM kinase IV activity was determined by incorporation of radioactive ^{33}P from ATP into a specific substrate (syntide-2) at 37°C for 2 minutes.

RESULTS: ATP (µmoles/g brain) was 4.9±1.1 in the Nx, 5.1±0.5 in the Hyx (p=NS), 4.6±0.9 Hyx+NNLA and 4.8±0.7 in Hyx+7-NINA (p=NS). PCr (µmoles/g brain) was 3.3±0.6 in Nx, 3.2±0.5 in Hyx group (p=NS), 3.32±0.5 in Hyx+NNLA and 3.1±0.4 in the Hyx+7-NINA (p=NS). The activity of CaM kinase IV (pmoles/mg protein/hr) was 2117±91 in Nx, 2821±85 in Hyx (p< 0.05 vs Nx), 2332±99 in Hyx+NNLA (p<0.05 vs Hyx, p=NS vs Nx) and 2026±100 in Hyx+7-NINA (p<0.05 vs Hyx, p=NS vs Nx). The data show that a non-specific NOS and neuronal NOS inhibitors prevent the hyperoxia-induced increased activity of CaM kinase IV in neuronal nuclei.

CONCLUSIONS: The mechanism of activation of CaM kinase IV during hyperoxia is mediated by NO derived from neuronal nitric oxide synthase. NO-mediated Src and EGFR tyrosine kinase-dependent tyrosine phosphorylation of calmodulin (CaM kinase activator) at Tyr^{99} may increase interaction with calmodulin binding domain of CaM Kinase IV resulting in its activation during hyperoxia. (NIH-HD 20337)

27

Fellow in Training

Effect of Neuronal Nitric Oxide Synthase (nNOS) Inhibition during Hyperoxia on Expression of CaM Kinase-Kinase in Neuronal Nuclei of the Cerebral Cortex of Newborn Piglets

Janice Hobbs, Jarle Stone, Qazi Ashraf, Om P. Mishra, Maria Delivoria-Papadopoulos.

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BACKGROUND: We have previously shown that hyperoxia results in increased activity of CaM Kinase-IV, that phosphorylates CREB protein, leading to the transcription of apoptotic proteins. Previous studies have also shown hyperoxia results in increased generation of nitric oxide free radicals that lead to programmed cell death. CaM Kinase-kinase activates CaM Kinase IV by phosphorylation.

OBJECTIVE: The present study tests the hypothesis that the increased expression of CaM Kinase-kinase during hyperoxia in the neuronal nuclei of newborn piglets is mediated by nitric oxide.

DESIGN/METHODS: Nine newborn piglets were assigned to: normoxic (Nx, n=3), hyperoxic (Hyx, n=3), and hyperoxic+7-NINA (Hyx+7-NINA, n=3) groups. Hyperoxia was induced with an FiO_2 of 1.0 for 2 hours. The PaO_2 was maintained at >400 mmHg. A selective neuronal nitric oxide synthase inhibitor, 7-NINA, was administered (1mg/kg i.v., 30 min prior to hyperoxia). Cerebral energy metabolism was measured by determining ATP and phosphocreatine (PCr) levels. Neuronal nuclei were isolated and CaM Kinase-kinase expression was measured using Western blot analysis using a specific CaM Kinase-kinase antibody. The protein bands were analyzed using imaging densitometry.

RESULTS: ATP levels (µmoles/g brain) were 4.9±1.1 in the Nx, 5.1±0.5 in the Hyx, 4.8±0.4 Hyx+7NINA (p=NS). PCr (µmoles/g brain) was 3.3±0.6 in Nx, 3.2±0.5 in Hyx group and 3.1±0.4 in Hyx+7-NINA (p=NS). The expression of CaM Kinase-kinase is measured as absorbance (OD x mm^2). CaM Kinase-kinase expression was 78.4±0.72 in the Nx group, 120.33±4.74 in the Hyx group, and 80.5±19.1 in the Hyx+7-NINA group. The data demonstrate that administration of NOS inhibitor 7-NINA prevented the hyperoxia-induced increase in CaM Kinase-kinase expression.

CONCLUSIONS: The increased expression of CaM Kinase-kinase following hyperoxia is mediated by nitric oxide. Nitric oxide increased, resulting in nuclear Ca^{2+}-influx by modifying nuclear high affinity Ca^{2+}-ATPase leading to the activation of CaM-Kinase IV. This results in increased expression of CaM Kinase-kinase protein via CREB-transcription pathway. The increased expression of CaM Kinase-kinase activating CaM-Kinase IV may be a nitric oxide-mediated mechanism, leading to increased expression of apoptotic proteins during hyperoxia. (NIH-HD 20337)

28

House Officer

Mechanism of Tyr^{99} Phosphorylation of Calmodulin during Hyperoxia in the Newborn Brain

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BACKGROUND: Studies have shown that calmodulin, a Ca^{++} binding protein, activates enzymes including neuronal nitric oxide synthase (nNOS). We have shown that hyperoxia results in increased Tyr^{99} phosphorylation of calmodulin. Calmodulin is an activator of nNOS. Tyrosine phosphorylation of calmodulin occurs at Tyr^{99}. We have also shown that hyperoxia results in increased nitration of neuronal proteins indicating generation of nitric oxide (NO) free radicals in the cerebral cortex.

OBJECTIVE: The present study aims to investigate the mechanism of calmodulin modification during hyperoxia and tests the hypothesis that hyperoxia-induced increase in Tyr^{99} phosphorylation of calmodulin in the cortex of newborn piglets is mediated by NO derived from nNOS.

DESIGN/METHODS: Piglets were divided into normoxic (Nx, n=3), hyperoxic (Hyx, n=5) and hypoxic-pretreated with a highly selective nNOS inhibitor 7-nitro-indazole sodium salt (Hyx+7-NINA, 1 mg/kg i.v., prior to hyperoxia, n=3) groups. Hyperoxia was induced by exposure to FiO_2 of 1.0 to maintain PaO_2 >400 mmHg for 2 hrs. ATP and phosphocreatine (PCr) were determined to document cerebral tissue energy status. Nuclei were isolated and tyrosine phosphorylation of calmodulin was determined by Western blot analysis using anti-phospho-($pTyr^{99}$)-calmodulin antibody. Protein bands were detected, analyzed by densitometry and expressed as absorbance.

RESULTS: ATP (µmoles/g brain) was 4.9±1.1 in the Nx group, 5.1±0.5 in the Hyx group (p=NS), and 4.8±0.7 in the Hyx+7-NINA group (p=NS). PCr (µmoles/g brain) was 3.3±0.6 in the Nx group, 3.2±0.5 in the Hyx group (p=NS) and 3.1±0.4 in the Hyx+7-NINA group (p=NS). The density of $pTyr^{99}$ calmodulin (ODxmm^2) was 460.50±52.47 in Nx, 669.99±13.05 in Hyx and 449.02±39.56 in Hyx+7-NINA. The data show that administration of nNOS inhibitor 7-NINA prior to hyperoxia prevented the hyperoxia-induced increased Tyr^{99} phosphorylation of calmodulin.

CONCLUSIONS: The hyperoxia-induced Tyr^{99} phosphorylation of calmodulin is mediated by NO derived from nNOS. NO free radicals generated during hyperoxia lead to inactivation of protein tyrosine phosphatases SH-PTP1 and SH-PTP-2 resulting in increased tyrosine phosphorylation of calmodulin. Tyr^{99} phosphorylated calmodulin, as compared to the non-phosphorylated moiety, binds with a higher affinity at the calmodulin binding domain of nNOS leading to increased activation of nNOS and increased generation of NO.(NIH-HD 20337)

29

Effect of Chronic Postnatal Inflammation on Somatic and Brain Growth in Mice

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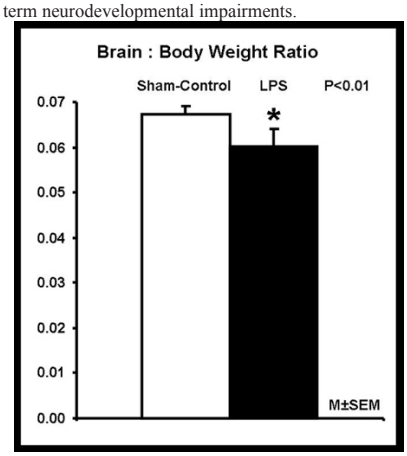
BACKGROUND: Perinatal systemic inflammation is associated with damage to the developing brain. Intraperitoneal (IP) Lipopolysaccharide (LPS) administration to newborn mice pups has been used as a model for systemic inflammation. There is paucity of data to show the effect of postnatal systemic inflammation on brain growth in newborn mice.

OBJECTIVE: Test the hypothesis that daily IP administration of LPS for 10 days significantly affects body and brain weights in juvenile mice pups.

DESIGN/METHODS: C57BL6/J mice pups in the experimental (LPS; N=22) group received daily IP injections of 0.3 µg/gram LPS (E. coli 055:B5; Sigma-Aldrich) between day 3 and day 13 of life. Pups in the control group (N=26) received equivalent volumes of vehicle solution IP. Three litters were included in each group. The pups were sacrificed under isoflurane anesthesia on day 14. Total body weight, wet brain weight, and brain to body weight ratios were compared between the 2 groups by t-test.

RESULTS: A total of 13 pups in the LPS group, and 19 pups in the control group survived to day 14 (59% vs. 73%; P=NS). Pups in the LPS group weighed 5.98±0.45g and pups in the control group weighed 5.71±0.22 g at day 14 (M±SEM; P=NS). Pups in the LPS group had an average daily weight gain of 0.22±0.01 g/g/day, and pups in the control group had an average daily weight gain of 0.15±0.01 g/g/day (M±SEM; P<0.03). The average brain weight was 0.34±0.007 g for pups in the LPS group, and 0.38±0.007 for pups in the control group (M±SEM; P<0.01). The brain to body weight ratio was 10.5% less in pups in the LPS compared to pups in the control group (P<0.01; Figure).

CONCLUSIONS: Chronic postnatal systemic inflammation was associated with an increased rate of somatic growth and reduced brain weight at two weeks of age in mice. This has important implications in newborn infants with sepsis or other conditions associated with inflammation and could explain longer term neurodevelopmental impairments.



30
Fellow in Training

Hypothermia Attenuates Hypoxic Neuronal Insults in C Elegans

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BACKGROUND: The neonatal brain is extremely vulnerable to hypoxia. Previous human and animal studies have demonstrated that hypothermia decreases the severity of brain injury after a hypoxic ischemic insult. Hypothermia is a therapeutic modality now used to limit the severity of brain injury in neonatal hypoxic ischemic encephalopathy. The effect of hypothermia on the individual neuron specifically at a time point remote from the initial hypoxic insult is not well characterized. The soil nematode Caenorhabditis elegans (C. elegans) has several useful features that enable investigation of neuroprotective affects of hypothermia after a hypoxic insult.

OBJECTIVE: To study the effect of hypothermia on the degree and severity of hypoxic neuronal injury in C. elegans.

DESIGN/METHODS: In our previous work we have demonstrated that C. elegans neurons are selectively vulnerable to hypoxic insults. We obtained worm strains in which green fluorescent protein (GFP) was expressed in the neurons known to be most vulnerable to hypoxia. These were AFD, ADE and PDE neurons .We subjected synchronized larval stage L4 worms to 48 hrs of anoxia (FiO2<0.5%) at 20º C followed by return to normoxia at either 20º C or at a hypothermic temperature 15 º C. The integrity of individual neurons was examined at these two different temperatures at 24 and 72 hr time points. The degree of neuronal injury was graded from normal to severe injury in each of the individual neurons.

RESULTS: We noted an overall similar survival in the groups at the two different temperature conditions. Examination of the morphology of neurons revealed a difference in the severity of axonal injury between the hypothermia group and the group that recovered at normal temperature. At 24 hrs all three neuron types showed a significantly less severe degree of neuronal injury for the worms placed in a hypothermic environment after the anoxic insult than the worms that were left at normothermic conditions (p<0.05). This protective effect of hypothermia was sustained when these neurons were again examined at the 72 hrs time point.

CONCLUSIONS: Hypothermia attenuates the degree of hypoxic neuronal injury in C. elegans, and the worm is a unique model system to study mechanisms and pathways effecting hypoxic neuronal injury.

31
Fellow in Training

Amplitude EEG (aEEG) Response during Surgical Ligation (SL) of a Patent Ductus Arteriosus (PDA) in Preterm Infants (PI) Is a Potential Measure of Pain Control

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BACKGROUND: Recent studies have demonstrated increased risk of neurodevelopmental impairment following SL of a PDA, the mechanisms of which are unclear. Intra-operative stress as a consequence of inadvertent pain may be a contributing factor. Hypothesis: Pain, as evidenced by an ↑ in heart rate (HR) and blood pressure (BP), during surgical PDA ligation will be accompanied by an elevation in aEEG voltage (μV).

OBJECTIVE: To characterize changes in aEEG signal in preterm neonates undergoing surgical PDA ligation, and to determine whether these changes are accompanied by ↑ in HR and BP.

DESIGN/METHODS: A prospective, observational, cohort study of preterm infants with PDA requiring SL. Cerebral function monitoring was used to obtain aEEG for ~ 40 min. prior to, during surgery, and for two hours post-op. HR and mean BP were similarly recorded. All patients were paralyzed and administered fentanyl. Data were analyzed using Student's t-tests.

RESULTS: PI (n=14) of GA 26.4 ± 2.6 weeks, BW 840 ± 266 grams were studied at postnatal age 25.3 ± 13.3 days. HR and BP both ↑ significantly intra-op (Table). Maximum HR occurred during skin closure in 8/14 infants. BP remained significantly ↑ post-op compared to pre-op. Following anesthetic induction aEEG became suppressed, with a significant ↑ in aEEG μV during maximum HR. This was seen as upward shift in aEEG amplitude, especially well-visualized as aEEG had been maximally suppressed from administration of anesthesia. Post-op aEEG returned to this suppressed state. Mean fentanyl dose administered was 16.4 mcg/kg (range 3.7- 47).

	Intra vs. Pre-op	Post vs. Intra-op	Post vs. Pre-op
Mean Δ HR BPM	↑ 18.1 ± 12.5**	↓ 20.9 ± 7.9**	↓ 2.8 ± 9.8 NS
Mean Δ BP mm Hg	↑ 5.4 ± 5.6**	↓ 1.6 ± 4.1 NS	↑ 3.8 ± 4.9*

BPM= beats per minute; NS = non-significant

	Intra vs. Pre-op	Δ intra-op at Max HR	Post vs. Pre-op
Mean Δ aEEG μV	↓ 4.3 ± 3**	↑ 1*° [IQR 1.5]	↓ 4.1± 3.3**

*p <0.05; **p<0.005; °median difference; IQR=interquartile range

CONCLUSIONS: HR and BP ↑ significantly during SL of a PDA in PI. The aEEG became suppressed with anesthesia, however at maximum heart rate there was a concurrent elevation in the aEEG. In many cases maximum HR occurred during skin closure, suggesting a response to pain. The aEEG may be a powerful adjunct in optimizing pain control during surgical procedures such as PDA ligation. Local anesthetic should be considered for skin closure.

32
House Officer

Evaluation of Use and Parental Perception of Improvement in Disease Symptoms with Complementary and Alternative Medication in Patients with Attention Deficit Hyperactivity Disorder Currently Undergoing Conventional Treatment

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BACKGROUND: Attention deficit hyperactivity disorder (ADHD) affects 3-12% of school-aged children and up to 30% of patients treated with stimulant medications experience side effects. Parental concern with long-term use of these controlled substances may make them seek complementary and alternative medication (CAM) that are "more natural and safer." Literature review shows usage of CAM in ADHD but more knowledge is needed.

OBJECTIVE: To understand and evaluate use of CAM and parental perception on improvement in symptoms in patients with ADHD.

DESIGN/METHODS: This was a descriptive prospective study. A questionnaire was offered to parents of children between 6-18 years with ADHD. Demographic data, source of information for specific CAM, its providers and reasons for use were obtained. Perceptions of improvement in symptoms were recorded. Data were analyzed using percentages for descriptive statistics and Pearson's Chi square (p<0.05 being significant) for comparisons between CAM use and the independent variables recorded.

RESULTS: Of 68 children, 82.4% used CAM and 73.2% used more than one CAM. Only 37.5% informed their primary doctor of CAM use. Usage of CAM was more prevalent when ADHD diagnosis was made by subspecialists, namely neurologists and developmental specialists (p<0.04). No significant difference was noted between use of CAM and ADHD subtypes, time since diagnosis, type of conventional medication; patient age, gender, country of descent; parental education, duration of stay in US, income, health insurance; child's educational proficiency, class placement and disciplinary actions (p>0.05). Conventional medication was discontinued by 30.4% of subjects, of which 88.2% used only CAM. Among those, 76.5% used CAM because of parental beliefs and 53% used it because the parents themselves did. Up to 41% of parents feared side effects of conventional medication. The parental perception of improvement in symptoms were between 20-100% using different CAM.

CONCLUSIONS: CAM was widely used among ADHD patients. Parents perceived significant improvement in symptoms with CAM. A minority of parents share information on CAM with the primary doctor and CAM was more likely to be used in patients diagnosed by subspecialists.

Pulmonary & Asthma
Poster Session

Friday, March 25, 2011
6:00 PM-7:30 PM

33

Traditional Pulmonary Function Testing Interpretation Understimates Obstructive Airway Disease by Ignoring the Small Airway

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BACKGROUND: Reduction in forced expiratory flow between the 25%-75%(FEF 25-75)of the forced vital capacity(FVC),reflecting small airway obstruction has been almost completely ignored in pulmonary function testing(PFT) literature. Despite recent emphasis on the importance of the small airway, the historical definition of obstructive airway disease (OAD) -a reduction in forced expiratory flow in 1 sec (FEV1) & reduction of the FEV1/forced vital capacity ratio (FEV1/FVC)- continues to be used, & FEF25-75 remains ignored, leading to OAD underdiagnosis. We have noted this trend in our own institution where PFTs are read by 2 adult pulmonologists(APs).

OBJECTIVE: To analyze pediatric PFT data at FHMC from 1/03-9/10, and compare official interpretations by APs vs the pediatric pulmonologist (PP)[PVE] who re-interprets data on the patients seen in our pediatric out and in-patient departments, and determine the incidence of missed diagnosis of OAO.

DESIGN/METHODS: 110 patients, age range 6 to 18 yrs with a history of (hx/o) or possible asthma, performed 118 PFTs, (spirometry, lung volume measurement, and diffusion capacity). 6 were excluded due to incomplete studies, 112 PFTs were analyzed for the difference between the AP and PPs' diagnosis of OAD. OAD was defined as one or more of:1.<80% predicted 1.FEV1, 2.FEV1/FVC, 3.FEF25-75, 3.Normal but disporpotionately reduced FEF25-75 vs 1. or 2., 4.increased RV.

RESULTS:

PFT Diagnosis, AP vs PP

PFT Diagnosis	Read by AP	Read by PP
OAD	12 (11%)	85 (76%)
Incorrectly read as NL	73 (65%)	0
Correctly read as NL	20 (18%)	23 (20%)

Out of 112 PFTs: 85(76%) were read as OAD by PP vs only 12(11%)by AP. 73(65%)were erronously read as normal(NL) by ignoring the presence of decreased FEF25-75 and/or increased RV, & 10(1%)as limited vs 0 by PP. Only 36(32%)were correctly interpreted as NL (20[18%]),OAD (12[11%])or limited(4[4%]) by AP. 23(20%) were NL by PP. Further, 16(14%) were errornously read as limited but read as OAD(13[11%]),& NL (3[.03]).
CONCLUSIONS: The majority of pediatric PFTs were erronously read as NL by APs yielding the wrong diagnosis in 70 patients. It is likely that the historical tradition of ignoring abnormal FEF25-75, which is present in the majority of our patients, continues to understimate the presence of OAD. The pediatric practitioner must be aware of this deficit by interpreters of PFTs and review the data themselves to aid in their diagnosis, treatment and follow-up of patients with OAD.

34

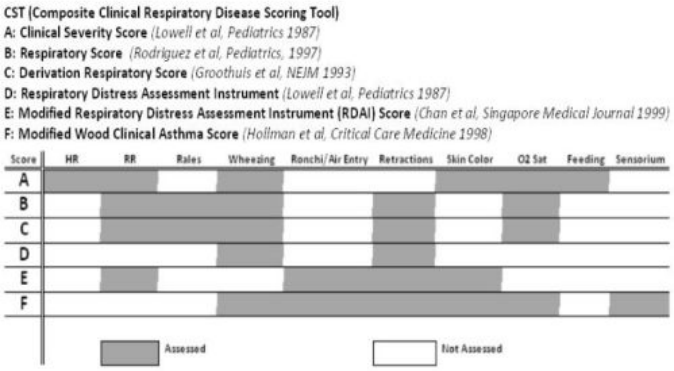
House Officer

Younger Infants with RSV Bronchiolitis: Should We Admit Them?

Gaston I Zylberg, Ramkumar Natarajan, Fernanda Kupferman, Lily Q. Lew, Susana Rapaport, Rusly Harsono.

Pediatrics, Flushing Hospital Medical Center, Flushing, NY.

BACKGROUND: Studies have shown that infants < 3 months of age are at risk for severe respiratory syncytial virus (RSV) infection. Although RSV infection is often mild and self-limited, the clinical course for infants with mild or severe disease is difficult to predict at onset. As a result, practitioners hospitalize infants less than 3 months of age with RSV regardless of their respiratory symptom severity.
OBJECTIVE: To identify the relationships between chronological age and clinical severity, the need for hospitalization in children ≤2 years of age admitted for RSV infection.
DESIGN/METHODS: We reviewed medical records of previously healthy children ≤ 2 years of age with confirmed RSV infection that were admitted to our hospital for 2 consecutive RSV seasons (Oct'08 - Apr'10). Clinical severity was done using 6 different composite clinical respiratory disease scores (CST).



The need for hospitalization (HOSP) was defined as: oxygen therapy, positive pressure ventilation, apnea, feeding problem or frequent bronchodilator nebulization. We also collected length of hospital stay (LOS). Children were grouped according to their corrected age into: < 8 weeks (G1), 8 weeks to < 6 months (G2), 6 months to < 1 year (G3) and 1 to 2 years of age (G4). Comparisons among groups were done with $\chi 2$ and ANOVA (significant: $p < 0.05$).
RESULTS: We included 101 children (mode gestational age of 39 weeks and median corrected age of 23.3 weeks). There were 22 (G1), 36 (G2), 23 (G3) and 20 (G4). Of the 4 age groups, there were 82% in (G1), 64% (G2), 74% (G3) and 80% (G4) with moderate to severe CST ($p>0.14$). Among all age groups, there was no difference in HOSP (45% - 69%, $p >0.07$) and LOS (3 - 5 days, $p >0.05$).
CONCLUSIONS: Chronological age does not necessarily determine severity of RSV respiratory disease. Age does not serve as single determinant to admit children with RSV infection. Composite clinical respiratory disease score may help identify children potentially having more than mild disease.

Infectious Diseases & Immunology Poster Session

Friday, March 25, 2011
6:00 PM-7:30 PM

35

Novel Use of the Audience Response System To Improve Adherence to Transmission Precautions

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BACKGROUND: Interventions to improve adherence to transmission precautions in acute care settings are needed.
OBJECTIVE: To improve adherence to transmission precautions in our PICU with an educational intervention using the audience response system (ARS) to improve adult learning by facilitating audience attention and participation. We hypothesized [1] knowledge of transmission precautions would exceed actual implementation and [2] adherence would improve following education.
DESIGN/METHODS: This pilot study was performed from Jun-Aug 2010. Using a pre-post test design, we performed 20 hours of observation of adherence to transmission precautions followed by the education intervention followed by 20 hours of observation. Observations focused on availability and appropriate use of personal protective equipment (PPE). Education posed questions based on case vignettes were answered by the interdisciplinary team using ARS. The $\chi 2$ test was used to compare observations in the pre- vs. post-intervention period.
RESULTS: We performed observations in 66 (pre-) and 58 (post-) sessions; correct PPE supplies were noted in nearly 100% of sessions. Pre-intervention, when entering an isolation room, 66% and 70% of healthcare workers (HCWs) donned gloves and gowns, respectively, but only 21% and 22% tied their gown at the neck and waist, respectively. 100 members of the interdisciplinary team (including 63 nurses and 30 physicians) attended 14 educational sessions. Most (78%) knew the appropriate transmission precautions for an infant with lower respiratory tract infection (droplet and contact) and the PPE needed (gowns and gloves) for a multi-drug resistant organism (83%) and for hospital-onset diarrhea (97%). Adherence improved post-intervention; 75% of HCWs donned gloves ($p=.012$) and 81% donned gowns ($p=.003$), while 43% and 32% tied gowns at the neck ($p<.001$) and waist ($p=.023$). Knowledge of transmission precautions was higher (87%) than overall adherence both pre- (58%) and post- (67%) intervention.
CONCLUSIONS: We speculate that our intervention provided booster education to more experienced HCWs and more effective education to newly-hired HCWs. However, post-intervention, < 50% of HCWs tied their gowns, confirming the benefit of using gowns that do not need tying. ARS should be studied in other settings.

36

Severity of Illness and Use of the 'Medical Home' during the First vs. Second Waves of 2009 Influenza a (H1N1) in a Pediatric Healthcare Facility

Saul R. Hymes, Amanda Buet, J. Scott Baird, Jonathan Sury, Patricia DeLaMora, Lisa Saiman.

Department of Pediatrics, Columbia University College of Physicians & Surgeons, NY, NY; National Center for Disaster Preparedness, Mailman School of Public Health, Columbia University, NY, NY; Department of Pediatrics, Weill Cornell Medical College, NY, NY; Department of Infection Control & Prevention, New York-Presbyterian Hospital, NY, NY.

BACKGROUND: We previously reported the severity of illness and the distribution of home zip codes of children hospitalized at our pediatric healthcare facility in New York City (NYC) during the first wave of the 2009 Influenza A (H1N1). We hypothesized that during the second wave the severity of illness would increase and the distribution of home zip codes of hospitalized children would be more diverse as the pandemic spread.
OBJECTIVE: To compare severity of illness and distribution of home zip codes of hospitalized children in the first vs. second wave of the 2009 Influenza A (H1N1).
DESIGN/METHODS: We reviewed the electronic medical records of patients < 18 years old with positive laboratory test(s) for influenza A hospitalized from May 2009-April 2010. Differences in the severity of illness in the first vs. second wave were assessed by means and proportions using appropriate statistical tests. Cartographic representations and spatial cluster analyses of cases by home zip code were performed.
RESULTS: During the second vs. first wave, fewer children were hospitalized (76 vs. 115), but a comparable portion were admitted to the Pediatric ICU (20 vs. 30%), had bacterial superinfections (1.3 vs. 3.5%) and/or died (0% vs. 0.9%). In both waves, cluster analysis revealed that a similarly high number of hospitalized children lived in zip codes close to the uptown children's hospital. During the second vs. first wave, more hospitalized children were from zip codes outside of NYC (17/76, 22.4% vs. 8/115, 7.0%, $p< 0.002$). Of these 25 children, 13 (52%) had been seen previously at our facility for chronic medical conditions.
CONCLUSIONS: At our pediatric facility in NYC, fewer children were hospitalized with 2009 Influenza A(H1N1) during the second wave, but both waves had a similar illness severity, low mortality, and geographic clustering. However, more patients from distant zip codes were hospitalized during the second wave, 50% of whom had been previously treated at our facility for comorbid conditions. These findings suggest that as the pandemic spread beyond NYC, affected children with comorbid conditions continued to appropriately seek care at their 'medical home'. These findings have important implications for future pandemic planning and resource allocation in pediatrics.

37

Increased LDL-Cholesterol (LDL-C) in HIV-Infected Children on Highly Active Antiretroviral Therapy (HAART)

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BACKGROUND: HAART has converted pediatric HIV into a chronic disease. As the number of HIV + children survive into adulthood, the adverse effects of HAART has surfaced. A wide range of lipid abnormalities has been described in HIV infected adults on HAART but fewer data exist in children.
OBJECTIVE: To measure the prevalence of elevated LDL-C in HIV-infected children on HAART attending our pediatric ID clinic and identify associated risk factors.
DESIGN/METHODS: A retrospective chart review was done for all HIV-infected children on HAART(0-18 years old) attending our Pediatric ID Clinic from Jan,08- Dec,08. The data on variables including gender, age, race, BMI, HIV RNA count, CD4 count and antiretroviral medications were collected. These factors in association with elevated LDL-C were then investigated using logistic regression analysis. NCEP(National Cholesterol Education Program) guideline was used to compare the elevated LDL-C levels.

RESULTS: All 27 patients, ≤18 yrs on HAART who attend our pediatric ID clinic were included.

Demographics

No of HIV infected patient on HAART	**27**
GENDER	
a)Male	13
b)Female	14
MODE OF TRANSMISSION	
a) Vertical transmission	25
b) Horizontal transmission	2
RACE	
a) Hispanic	9
b) African -American	17
c) Asian	1
TYPE OF ANTIRETROVIRAL	
a) PI regimen	25
b) NNRTI/NRTI regimen	2

11/27(41%) were found to have a BMI of >85 percentile. 7 of these 11(64%) had BMI of >95 percentile.

15%(4/27) were found to have LDL-C > 160,11%(3/27) had LDL-C between 130-160mg/dl and 74%(20/27) had levels <130 mg/dl. No statistical association was seen between elevated LDL-C and elevated BMI (p 0.97),CD4 count (p 0.2) and type (PI/NRTI/NNRTI) of ART (p 0.7). Race,age and gender did not show a statistical correlation with elevated LDL-C. Only HIV viral load of <75/ml showed a trend towards statistical association with elevated LDL-C (p 0.07, CI 0.6-89.7).

CONCLUSIONS: The prevalence of dyslipidemia in HIV infected children on HAART as defined by elevated LDL-C in our population was 26%(95% CI,11.1% -46.3%). Only undetectable HIV-viral load indicating excellent adherence to antiretroviral medication showeda trend towards statistical association with elevated LDL-C.

Further analyses with a larger sample size will be needed to confirm our findings and evaluate factors influencing lipid changes. Further research in this area will form the basis for management guideline.

38

Racial Variation in RSV Immunoprophylaxis

Erika F. Dennis, Corrine Fager, Scott A. Lorch.

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BACKGROUND: The American Academy of Pediatrics (AAP) recommends the use of Palivizumab (Syanagis) monoclonal antibody among high risk infants. Although prior work suggests that Medicaid patients may be less likely to complete their recommended course of Synagis, it is not known if immunoprophylaxis compliance varies by race or ethnicity.

OBJECTIVE: To examine if there are racial variations in the compliance rates for Synagis prophylaxis, and explore other contributing factors to increased compliance.

DESIGN/METHODS: We performed a retrospective cohort study on discharged infants born at a gestational age between 23-36 wks who received care from one of 33 outpatient centers affiliated with The Children's Hospital of Philadelphia between 2004 and 2008. Clinical data, demographic information, and immunization records were collected from a standardized electronic health record. Racial/ethnic status was defined using maternal report. Successful completion of a recommended Synagis course was defined as receipt of the prescribed number of injections during the RSV season after initiation of the immunoprophylaxis course. We constructed multivariable logistic regression models to assess the impact of racial/ethnic status on completion of a Synagis course, after controlling for gestational age, sex, general immunization status, neighborhood income and educational levels, and insurance status.

RESULTS: There were 3,362 infants in this cohort and 42% (n=1,419) received at least one injection of Synagis. There were racial differences in rates of successful immunoprophylaxis between African Americans and Whites, with 15.7% of Whites and 29.9% of African Americans failing to complete their recommended course of Synagis once initiated (p<0.001). After controlling for other confounding factors, multivariable analysis revealed that African Americans were less likely to successfully complete the course relative to Whites (odds ratio 0.56, 95% CI, 0.34-0.93). An up-to-date general immunization status was the only other factor that was associated with completion of a Synagis course (odds ratio 5.45, 95% CI, 2.62-11.4).

CONCLUSIONS: There are racial differences in the rates of successful RSV immunoprophylaxis that are independent of markers of socioeconomic status and gestational age.

39

Role of CXCR2 and Heparan Sulphate Proteoglycan in CXCL5-Regulated Chemokine Clearance and Lung Inflammation

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BACKGROUND: Our previous work demonstrated that CXCL5/LIX elevates KC and MIP-2 levels in plasma at least in part through binding to DARC and inhibiting its chemokine scavenging in blood, thus leading to CXCR2 desensitization and unfavorable chemokine gradients from blood to the lung, impaired neutrophil migration and bacterial clearance in the lung, and increased mortality in a severe E.coli pneumonia model (Immunity, 2010 July, 33:106), indicating the critical role of CXCL5 and CXCL5-regulated chemokine scavenging in regulating pulmonary inflammatory responses and host defense to bacterial pneumonia.

OBJECTIVE: The objective is to further determine if other neutrophil chemokine-binding molecules CXCR2 and HSPGs, contribute to chemokine scavenging under both homeostatic and inflammatory state.

DESIGN/METHODS: With the Cxcr2-/-, Cxcl5-/-, Darc-/- and Cxcl5-/-Darc-/- mice, we used in vivo and in vitro chemokine scavenging assay to determine the role of CXCR2 in chemokine scavenging and the role of CXCL5 in DARC-independent chemokine scavenging under homeostatic state. With the severe E.coli pneumonia model, we also determined the role of CXCL5 in DARC-independent chemokine scavenging and inflammatory responses.

RESULTS: We found that CXCR2 dramatically contributes to chemokine scavenging in blood in vivo, but not with in vitro chemokine scavenging assay. Homeostatic CXCL5 in blood inhibits DARC-independent chemokine scavenging with both in vivo and in vitro chemokine scavenging assays. Heparin-treated blood in vivo and in vitro showed much more CXCL5. In severe E.coli pneumonia model between Darc-/- and Cxcl5-/-Darc-/- mice, CXCL5 deficiency increased neutrophil influx and accelerated bacterial clearance, and decreased plasma levels of KC and MIP-2. DARC in vitro absorbs chemokines from blood and reduces plasma chemokine levels, whereas DARC in vivo protects chemokines from being cleared in plasma and increases plasma chemokine levels.

CONCLUSIONS: Our data demonstrate that CXCR2 contribute to chemokine clearance from the plasma, and suggest that HSPGs bind homeostatic CXCL5 and play an important role in chemokine scavenging, and HSPGs contribute to CXCL5-regulated chemokine scavenging and inflammatory responses during lung inflammation. These data also provide further evidence that the controversial chemokine sink hypothesis and chemokine reservoir hypothesis for DARC are not mutually exclusive.

Neonatology
Poster Session

Friday, March 25, 2011
6:00 PM-7:30 PM

40

Less Is More: Cost Savings of Fluid Restriction in Transient Tachypnea of the Newborn

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BACKGROUND: Transient tachypnea of the newborn (TTN) is a self-limited respiratory distress syndrome of the first days of life. Respiratory distress due to TTN increases management intensity and therefore cost of hospitalization. Although TTN is a common diagnosis of term and late preterm neonates, little data underlie current management of TTN. We executed a successful prospective randomized controlled trial to demonstrate the clinical utility of mild fluid restriction for neonates with TTN. Here we evaluate the financial implications of our fluid management strategy.

OBJECTIVE: To determine whether fluid restriction in neonates with TTN leads to decreased cost of hospitalization.

DESIGN/METHODS: Term and late preterm neonates with TTN were randomized to either standard fluid management or restricted fluid management mimicking early breast feeding. The primary study outcome was total charges generated during the birth hospitalization. Secondary outcomes included component charges such as physician, nursing, hospital direct, and hospital indirect charges. Charges were defined as total billable amount before negotiated discounts, not amount actually received for services.

RESULTS: The financial records of 61 study patients were available. There were no significant demographic or clinical differences between the standard and restricted fluid groups. No adverse events due to fluid restriction occurred. Analysis by t-test demonstrated no difference in costs for the study cohort as a whole. Those patients with severe TTN who received fluid restriction had mean total hospital charges of $29,406.54 while patients with severe TTN who received standard of care fluid management had mean hospital charges of $46,706.92 (p=0.003). This significant decrease in charges for fluid restricted neonates with severe TTN was seen in physician billing, hospital direct, and hospital indirect charges (p=0.001 to p=0.012).

CONCLUSIONS: This is the first study to demonstrate a potentially cost-saving treatment for TTN. Transient tachypnea of the newborn is a common disease with an estimated 2% incidence among 4 million US births annually. Approximately 40% of cases are severe. If the $17,000 average savings we saw in our study are replicated nationally, the savings could reach a potential $544 million annually in the US alone. Mild fluid restriction may not only improve care for patients with severe TTN, but also may reduce health care costs as well.

41

Effect of Perinatal Prophylaxis for Group B Streptococcus on Severity of Transient Tachypnea of the Newborn

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BACKGROUND: Inflammatory response to group B streptococcus (GBS) cell wall phospholipids causes respiratory distress in baby lambs. Newborn humans born to appropriately managed GBS positive mothers are exposed to GBS cell wall components at the time of delivery when antibiotics lyse colonizing organisms. Up to 30% of neonates in the United States are exposed to GBS in this manner. If newborn humans respond in the same way as lambs, there should be increased incidence and severity of tachypnea in babies born to GBS positive mothers who are also exposed to antibiotics. These patients would appear to have transient tachypnea of the newborn (TTN) in the absence of GBS infection. This study compares severity of disease in newborns with TTN based on their GBS and antibiotic exposure history.

OBJECTIVE: To determine the role of exposure to GBS cell wall phospholipids in the clinical course of TTN.

DESIGN/METHODS: This is a retrospective case-control study of newborns admitted to the NICU with TTN between 2001 and 2006. Student's t-test, linear regression and analyses of variance were performed to determine the relationship between perinatal exposure to GBS, exposure to antibiotics, and severity of TTN. Severity of TTN was defined by number of hours of continuous positive airway pressure (CPAP) support, number of hours of supplemental FiO2, and duration of admission in the NICU.

RESULTS: During the study period, 875 term and late preterm neonates were identified in our local discharge diagnosis database as having TTN. Only 478 (55%) had TTN confirmed on medical record review. Perinatal GBS exposure was known for 272 patients. Antibiotic exposure was known for all. One hundred seventy-nine patients with known maternal GBS status were exposed to antibiotics in the perinatal period. Of these, 61 were GBS-exposed and 118 were not. There was no difference in severity of TTN amongst neonates with GBS and antibiotic exposure, antibiotic exposure alone, or neither GBS nor antibiotic exposure.
CONCLUSIONS: In our patients with TTN, exposure to GBS and antibiotics does not correlate with increased severe of respiratory illness. This retrospective study indicates that it is unlikely that human neonates experience clinically significant respiratory symptoms due to exposure to GBS cell wall phospholipids. Additionally, this study demonstrates the inadequacy of discharge diagnosis databases for case identification of patients with TTN.

42

The Development of a Decision-Aid To Guide Counseling of Parents Facing Imminent Extreme Premature Delivery

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BACKGROUND: Greater parental autonomy in decision-making at lower limits of neonatal viability warrants effective communication of complex information at a time of high stress. Transparent decision-aids may assist this goal.
OBJECTIVE: To develop and assess the validity of a decision-aid for parents facing extreme premature delivery.
DESIGN/METHODS: Semi-structured interviews were conducted until saturation was reached, to define the content and presentation formats of a decision aid. Interviews with health care professionals and with parents of premature infants <26 wks GA identified items and formats of information valued by parents when making resuscitation decisions. Standard methods of item development, selection and reduction distilled items into a novel decision aid. Validity was evaluated by testing the hypothesis that an effective decision-aid would improve knowledge in a group of 'experienced' parents (previous premature delivery) and a group of healthy women with no prior ('naïve') knowledge of premature infants. Sample size estimations were 10 per group (power 90%, α 0.05, with clinically relevant knowledge increment of 30%).
RESULTS: 31 health care workers (nurses, neonatologists, obstetricians) and 30 parents were interviewed to obtain saturation of themes. Both clinicians and parents identified a visual format as preferable for presenting complex information on survival, short-term morbidities, and long-term outcomes. Parents also stressed a need for numeric figures. Accordingly, a set of six 13cm x 23cm cards covered: size and appearance of an extremely premature infant; BPD, IVH, and ROP. A horizontal icon array depicted survival rates from 22+0 to 25+6 wks and risk for the individual components of neurodevelopmental impairment at 24 months. Pre- and post-test knowledge in a hypothetical counseling session showed significant improvement in a group of 13 'experienced' parents ($p=0.04$); and an even greater improvement in a group of 11 'naïve' women ($p<0.0001$). Moreover, in a 5-question survey, most participants found the cards useful and easy to understand.
CONCLUSIONS: A decision-aid used at the time of counseling prior to delivery of an extremely premature infant was constructed that conveyed both numeric and qualitative information that could be understood. Such aids may improve the transfer of complicated information from clinicians to parents.

43

Fellow in Training

Placental Transfusion Strategies in Preterms <1000 g BW: Meta-Analysis of Short and Long Term Outcomes

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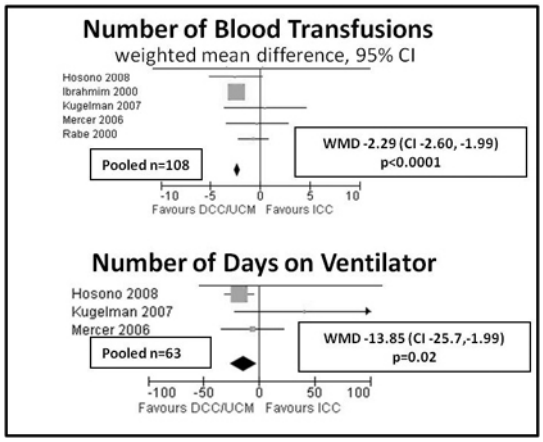
BACKGROUND: Delayed umbilical cord clamping (DCC) or umbilical cord milking (UCM) in neonates <1000 g BW carries promise to minimize transfusions. NRP now recommends DCC in term infants, but there is little information on outcomes of preterms <1000g BW with DCC/UCM.
OBJECTIVE: To perform a meta-analysis of short and long term outcomes of infants < 30 weeks GA and < 1000 g BW randomized to either DCC or UCM as opposed to immediate cord clamping (ICC).
DESIGN/METHODS: We searched for trials that randomized preterms to either experimental (DCC or UCM) or control (ICC) groups. Inclusion criteria included infants <1000 g BW. Primary outcome was 24 month Neurodevelopmental Impairment (NDI) using standardized outcomes; secondary outcomes included transfusions. Two independent investigators conducted searches with full agreement. Additional information was requested of authors. Data was summarized by RevMan5 as weighted mean difference (WMD) and 95% CI.
RESULTS: Searches yielded 15 studies, of which 6 were included, describing 108 infants. Short term benefits of DCC/UCM included: mean blood pressure on admission (WMD -4.9;CI -5.58,-4.22) and increased hemoglobin on admission (WMD 3.71;CI 3.94, 3.47). Clinically relevant, statistically significant short term benefits included reduced number of blood transfusions and shortened number of days on ventilator (see Figure). Data on NDI was limited and could not be pooled. One study (Mercer J) recorded Bayley at 7 months for 27 infants (WMD MDI -4.40; CI -18.02, +9.22; p=NS). Another study (Hosono) followed survivors to 24 months using a Japanese scale. This study found no significant differences in rates of disability (UCM 3/16 19% vs ICC 4/15 27%; p=NS).
CONCLUSIONS: Only one study reports 24 month NDI, and no pooling is possible. Short term benefits of DCC include rise in hemoglobin, decreased number of transfusions and shorter days on ventilator.



44

Fellow in Training

Age Dependent Inter-alpha Inhibitor Protein (IAIP) Concentration in Plasma and Expression in Ovine Liver, Kidney and Heart

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BACKGROUND: IAIPs are a family of protein inhibitors that reduce proinflammatory cytokines during sepsis, increase survival in newborn mice with sepsis, and reduce ischemic brain injury in rats. Low plasma IAIP levels predict necrotizing enterocolitis and sepsis in premature infants. We have shown that the 125 kDa and 250 kDa proteins are expressed in brain throughout ovine development. The 250 kDa protein is higher in adult than newborn and fetal brain and 125 kDa expression lower in newborn brain than all other ages.
OBJECTIVE: To determine IAIP levels in plasma and protein expression in liver, kidney, and heart during ovine development.
DESIGN/METHODS: We developed an ELISA for ovine plasma IAIPs and measured levels in fetuses at 70% and 90% gestation, newborn, and adult sheep. Liver, heart, and kidney samples were frozen, protein expression determined by Western immunoblot, densitometry performed, and results expressed as a ratio to an internal control.
RESULTS: Plasma IAIP concentrations were higher ($P<0.05$) in newborns (110±30 µg/ml) than fetuses at 70% (64±29) and 90% (55±29) gestation, and higher in adults (102±30) than fetuses at 90% gestation. IAIPs were detected as 250 kDa and 125 kDa proteins in liver, kidney, and heart in fetal, newborn, and adult sheep. The 250 kDa IAIP expression was higher ($P<0.05$) in liver and kidney of adults than fetuses and newborns, but did not differ among age groups in heart. The 125 kDa expression was highest in liver in fetuses at 90% gestation, higher in kidney in fetuses at 70% gestation, adults than fetuses at 90% gestation, and higher in heart in fetuses at 70% gestation than 90% gestation, newborns, and adults.
CONCLUSIONS: Plasma IAIP levels increased after birth in sheep. IAIPs were detected in liver, kidney and heart throughout ovine development as 250 kDa and 125 kDa proteins. Similar to our findings in brain, expression of the 250 kDa proteins was higher in adults than fetuses and newborns in kidney and liver, but not heart. We have shown for the first time that this immunomodulatory protein is present in ovine liver, kidney, and heart, and the proteins exhibit organ specific patterns of developmental regulation. Although the functions of IAIPs are not known, their presence in large amounts raises the possibility that they represent endogenous anti-inflammatory molecules with organ specific differential production or modulation during development.

45

Fellow in Training

Transient In Utero Knockout (TIUKO) of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Gene Results in Gut Immaturity and Inflammation in Adult Sprague-Dawley Rats

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BACKGROUND: CFTR mediates stretch-induced transmembrane flow, signalling organ differentiation in developing lung & intestine. TIUKO of CFTR during embryonic period results decreased respiratory function in adult animals. In the intestine, TIUKO of CFTR results in obesity & insulin resistance, suggesting altered gut function.
OBJECTIVE: To determine gut maturation & intestinal inflammation in adult Sprague-Dawley Rats (SDR) exposed to TIUKO.
DESIGN/METHODS: 2 litters of time-pregnant SDR underwent in-utero injection of replication-deficient adenovirus vector containing the antisense CFTR (AS CFTR) gene fragment or Enhanced Green Fluorescence Protein control on embryonic day e15. At 18 months, intestines were harvested in both the fed & 24hr fasting states. Polymorphonuclear cells (PMNs) were counted in 15 high power fields at 40x magnification from from upper, middle & lower intestine. Myeloperoxidase staining was performed. Immuno-histochemistry of CD 25,TNFα, IL1β & stains for Synaptophysin & Synaptic Vesicle Protein 2 (SV2) was performed. Digital image analysis was used for quantification. ANOVA testing with Bonferroni correction was used for analysis.

RESULTS: AS CFTR-treated intestine demonstrated increased levels of SV2, Synaptophysin & CD 25. AS CFTR upper intestinal segments in the fed state had increased levels of PMNs/hpf than fed controls p<0.001). In the middle intestinal segments, PMNs were increased in AS CFTR fed animals compared to control (p<0.01) but were not different from fasting groups. PMNs were increased in the lower intestine of the fed AS CFTR group compared to control (p<0.05), but were lower than levels from the AS CFTR fasting group. IL1B levels were increased in the AS CFTR fasting group compared to controls in the upper intestine (p<0.001). Levels in the lower intestine were highest in the AS CFTR feeding group compared to both the AS CFTR fasting & control feeding groups (p<0.001 for both). AS CFTR fasting animals had increased TNF-alpha levels in the upper intestine compared to control fasting animals (p<0.05). No differences were seen between AS CFTR & control animals in the middle & lower intestinal segments.
CONCLUSIONS: Alterations of stretch-induced differentiation via TIUKO of CFTR resulted in delayed intestinal development & intestines more prone to PMN infiltration during feeding and increased acute inflammation with prolonged fasting.

46

Fellow in Training

Real-Time Cerebral, Splanchnic, and Renal Near-Infrared Spectroscopy (NIRS) in Very Low Birthweight Neonates: An Analysis of Baseline Variability

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BACKGROUND: Suboptimal O_2 delivery at global or vascular bed-specific sites has been shown to increase morbidity and mortality in critically ill patients. Current methods for assessing adequacy of tissue oxygenation are not able to detect alterations in regional perfusion status. NIRS is emerging as a vascular bed-specific monitoring tool but neonatal normative data is sparse. Knowledge of baseline NIRS signal stability and variability is necessary before assigning clinical relevance of a given alteration in NIRS signals over time. Our study is the first to address the use of differing epoch lengths in assessing signal variability.
OBJECTIVE: To determine the baseline stability and variability of multi-site NIRS measurements.
DESIGN/METHODS: This is a prospective, observational, non-interventional study of preterm neonates with BW of 500-1250g. Continuous real-time cerebral, renal and splanchnic NIRS was recorded for 7d beginning in the first 72h after birth. Demographic, cardiopulmonary & NIRS data were collected. Variability analyses of NIRS were performed during periods of relative quiescence for four different time epochs for each site as well as between sites using ANOVA.
RESULTS: Subjects (n = 14, GA 26 ± 1 wk; BW 920 ± 170g; x ± sd) had average coefficients of variation (CoV) calculated for 4 time epochs from each NIRS site.

Average Coefficients of Variation

Site	5-min*	15-min*	30-min*	60-min*
Cerebral	0.030	0.032	0.036	0.038
Renal**	0.057	0.076	0.082	0.089
Splanchnic***	0.153	0.188	0.206	0.219

Regardless of epoch lengths, cerebral CoVs were smallest as compared to renal & splanchnic sites. All between-site comparisons for each monitoring epoch were statistically significant (*P<0.01). Shorter epochs showed significantly smaller CoVs at the renal (**P=0.0001) & splanchnic (***P=0.04) sites. The splanchnic site exhibited the highest CoV over all epochs with a SD representing 15-22% noise relative to its mean.
CONCLUSIONS: NIRS signal variability as a function of monitoring epoch length has important implications for the interpretation of regional NIRS measurements. This site-specific degree of variability should be taken into account when designing studies utilizing this technology.

47

Complications Associated with Peripherally Inserted Central and Non-Central Catheters in the Newborn Intensive Care Unit

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BACKGROUND: Peripherally inserted central catheters (PICCs) are utilized in critically ill newborns for stable intravenous access. Ideal tip position for a PICC is the superior or inferior vena cavae. In instances where central position can not be achieved, peripherally inserted non-central catheters (PINCCs) may still be utilized. Little data exists, however, as to their rate of associated complications.
OBJECTIVE: To compare complication rates in PINCCs versus PICCs in a neonatal intensive care unit (NICU) and to evaluate the risk of a complication with duration of catheter use.
DESIGN/METHODS: Using an existing database, we identified all lines placed in the Yale NICU from July 2005 through August 2010. Data included demographics and catheter position, duration of use, and associated complications including associated bloodstream infections, phlebitis, infiltration, obstruction, and effusions. Unadjusted and adjusted complication rates were compared between PINCCs and PICCs. Risk factors for complications were assessed using Generalized Linear Equations (GEE) modeling, accounting for multiple catheter insertions per infant. Risk of complication by duration of catheter was further assessed use via Kaplan-Meier survival estimates.
RESULTS: Data were available from 980 lines placed in 750 neonates. 91 were PINCCs and 889 PICCs. Neonates with a PINCC were of significantly higher gestational age (34 weeks *v.* 30 weeks; p<0.0001) and birth weight (2252 grams *v.* 1495 grams; p<0.0001). 44% of PINCCs had a major complication as compared with 25% of PICCs (p=0.0001), with the most common PINCC-related complication being infiltration. The overall, unadjusted complication rate among PINCCs was 51.7 per 1,000 line days and 15.9 for PICCs (rate ratio: 3.25; 95% CI: 2.32, 4.55). After adjusting for multiple confounders such as birth weight, the adjusted odds ratio for complications from GEE remained significantly higher for PINCCs (adj OR: 2.41; 95% CI: 1.34, 4.37). The median time to onset of a complication with the use of a PINCC was 11 days as compared with 45 days for PICCs (p<0.0001).
CONCLUSIONS: PINCCs are associated with a significantly higher rate of line-related complications as compared with PICCs. The median time to onset of a complication with the use of PINC is about 11 days. Particular care should be taken with the use of a PINCC beyond 10 days and subsequent removal or replacement should be considered.

48

House Officer

Developmental Outcome in Late Preterm Infants at 24 to 30 Months of Age

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BACKGROUND: Late preterm births (LPBs), infants born from 34-36 weeks gestation, account for more than 70% of all preterm births and the percentage of all births that are LPBs has increased from 7.3% in 1990 to 9.1% in 2005. Few studies have described the subsequent developmental profile of LPBs in early childhood: one study followed a cohort at 12-18 months of age and found no significant cognitive differences, but another observed some cognitive and behavioral problems at preschool age.
OBJECTIVE: To assess developmental outcomes of LPBs in comparison to term infants at 24-30 months of chronological age.
DESIGN/METHODS: This was a case-controlled, prospective study conducted at the Medisys Child Development and Educational Center at Flushing Hospital Medical Center(FHMC) from Sept-Oct 2010. Birth records from FHMC were reviewed to identify LPBs who would be within the age range of 24-30 months at the time of the study. After obtaining informed consent from parents who spoke English or Spanish, cases were enrolled along with equal numbers of age-matched controls (term infants born 37–42 weeks gestation). The developmental performance of both groups was scored using the Brigance Screen, a standardized tool to measure performance in 5 domains: basic assessment (measure of cognition), language, physical development, social-emotional and self-help skills. Raw scores were obtained in each domain for each infant and converted into standard and percentile scores. Means were calculated, and these were compared between groups, using t-test for statistical analysis, with a p-value <0.05 considered significant.
RESULTS: A total of 40 infants were tested (20 cases, 20 controls). Of the total group, 57% were girls and 40% were from English-speaking families. The mean standard scores and percentile scores for both cases and controls were in the normal range. However, the mean standard score in basic assessment was lower among the LPBs than controls (98.45 vs. 102.25) and this difference was statistically significant (p=0.014). Percentile scores also showed statistically significant differences between cases and controls, 49.35 vs. 56.30 (p=0.010). The results in all 4 other domains were not significantly different.
CONCLUSIONS: Developmental outcomes of LPBs at 24-30 months were in the average range. The standard and percentile scores in basic assessment were lower in LPBs than for term infants.

49

House Officer

Breastmilk Science: Critical Review of Publications over the Last 30 Years

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General Pediatrics, Goryeb Children's Hospital at Atlantic Health, Morristown, NJ; Atlantic Neonatal Research Institute, MidAtlantic Neonatology Associates and Atlantic Health, Morristown, NJ.

BACKGROUND: Breastmilk is an essential component of neonatal nutrition and maternal-infant health. Although breastmilk science has been promoted by healthcare professionals for over 30 years, there are concerns of a perceived imbalance of anecdotal versus scientific approach to breastmilk science among healthcare professionals, particularly with regards to high quality quantitative research publications.
OBJECTIVE: The objective of this study is to critically review research characteristics of published literature in breastmilk science in peer-reviewed journals over the last thirty years.
DESIGN/METHODS: Published manuscripts on breastmilk science from 1980-2009 were identified using PubMed (keywords "breastmilk" or "breast milk" and limits of the English language and human infants under 24 months). Articles related to drug pharmokinetics, HIV, and toxin exposure were excluded.
Abstracts were reviewed by five study personnel. Articles were categorized by study type (biochemical, clinical, randomized controlled trial, or review-opinion) and topic (nutrition, immunology, and neurology). Pertinent articles were further separated into preterm and full-term subgroups. Data was collected on the citation, publication year, journal type, sample size, and inclusion of statistically-significant data (p-value < 0.05).
RESULTS: A total of 530 publications met inclusion criteria. The number of publications per five-year period fluctuated (86, 36, 82, 135, 70, and 121). There was a predominance of review-opinion articles, representing 45% of all publications. Clinical studies comprised 36% of the published studies, which had a median sample size of 70. Only 4.5% of the publications were randomized-controlled trials. The majority of publications focused on nutrition (42%), followed by the immunologic (36%) and neurologic (6.8%) properties of breastmilk. Preterm infants were included in 42% of the articles. Only 7% of publications included a statistically-significant p-value in their abstract.
CONCLUSIONS: Through the decades, research related to breastmilk science has maintained a steady presence in science citation index journals. However, there is a lack of randomized-controlled trials and studies with statistically-significant results. As breastmilk science continues to be advanced, it must maintain a high standard of scientific rigor in key peer-reviewed journals.

50

Fellow in Training

Increased Odds of Mechanical Ventilation at 36 Weeks Gestation: Gestational Age Paradox

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BACKGROUND: Late preterm births comprise 8.1 % of all live births. Most of the increase in preterm birth rates in the US is attributed to late preterm births. Limited data is available regarding the relationship between advancing gestation and respiratory morbidity in late preterm infants.

OBJECTIVE: To assess respiratory support in late preterm infants stratified by gestational age.

DESIGN/METHODS: Retrospective cohort analysis of late preterm infants (34-36$^{6/7}$ wks) at a regional NICU, Christiana Hospital, from Jan' 05 to Dec' 09. ANOVA and chi-square were used to analyze continuous and dichotomous variables respectively. Linear and logistic regression analysis applied to control for confounding variables affecting respiratory outcomes.

RESULTS: The GA groups were similar in c-section rate, clinical chorioamnionitis, and Apgar scores. Infants 36 wks were less likely to receive steroids and more likely to be SGA compared to 34-35 wks (p<.01). Despite advancing gestation, 36wk infants had similar rates of mechanical ventilation as those 34 and 35 wks, and required longer mechanical ventilation. Infants born at 36 wks were less likely to receive CPAP than those born 34 and 35 wks.

Total n=1524	34 wks (n-551)	35 wks (n-436)	36 wks (n-537)	p
BW (gms)	2140 ±354	2393 ±443	2597 ±542	<.01
C-section	301 (55%)	212 (49%)	270 (50%)	0.23
SGA	84 (15%)	73 (17%)	181 (34%)	<.01
Apgar <7 at 5mins	28 (5%)	21 (5%)	38 (7%)	0.23
Chorioamnionitis	15 (3%)	6 (1%)	20 (4%)	0.08
Antenatal steroids	157 (28%)	55 (13%)	41 (8%)	<.01
CPAP	157 (28%)	123 (28%)	117 (22%)	0.02
Mech Ventilation	104 (19%)	103 (24%)	124 (23%)	0.13
Resp support (any)	187 (34%)	154 (35%)	168 (31%)	0.39
Mech. vent. days	2.6 ±2.7	2.7 ±2.7	4.1 ±6.4	0.02

After controlling for confounding variables including antenatal steroids, 36 week gestation infants had increased odds of requiring mechanical ventilation (OR 1.23, 95% CI, 1.06-1.5) and 36 week gestation was associated with increased ventilator days (p<0.05).

CONCLUSIONS: In our population of late preterm infants admitted to the NICU, infants born at 36 wk gestation had an increased odds of requiring mechanical ventilation, and required a longer course of ventilation compared to infants 34-35 weeks. Our data highlight that within the population of late preterm infants, those of relatively advanced gestation remain at increased risk of respiratory morbidity.

51

Red Blood Cell Storage Time and Morbidities of Prematurity

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BACKGROUND: Red blood cell (RBC) transfusions in the neonatal intensive care unit (NICU) are common, especially in the very low birth weight infant (VLBW, <1500 g). Studies have shown that RBC storage time is directly associated with increased morbidities and multiple system organ dysfunction in both adult and pediatric populations. Prior studies have looked at RBC transfusions and morbidities such as necrotizing enterocolitis (NEC), chronic lung disease (CLD) and retinopathy of prematurity (ROP), but few have looked at RBC storage time.

OBJECTIVE: The primary objective of this study was to examine the relationship between RBC storage time and the development of common morbidities seen in VLBW infants, namely CLD, NEC, sepsis, patent ductus arteriosis (PDA) and ROP.

DESIGN/METHODS: VLBW infants admitted to a tertiary NICU between January 2007 and December 2009 were cross-referenced with the hospital blood bank's transfusion database to acquire all VLBW infants who received a RBC transfusion. Infants were divided into 2 groups based on median age of RBC transfusions (A ≤ 14 days and B > 14 days). Demographical and admission data were collected along with various outcomes seen in premature infants.

RESULTS: A total of 188 infants received at least one RBC transfusion over the study period. Group A (n=142) and group B (n=46) were not different in gestational age, birth weight, gender, race, and Apgar or CRIB-II scores. There was a significant difference in mean age of RBCs transfused (8 vs 19 days, p<0.001) between groups A and B. There were no differences in number of exposures to RBC units, platelets or FFP, or need for surgery. Group B had a significant increase in late-onset sepsis (43% vs 24%, p<0.02) and need for PDA ligation (35% vs 9%, p<0.01) compared to group A. Group A was able to reach full feeds faster (21 days vs 27 days, p<0.01) and was discharged sooner (77 days vs 93 days, p<0.03). There was no difference in NEC or surgical ROP and only a trend for higher rates of CLD (60% vs 43%, p=0.058) and PDA (76% vs 61%, p=0.056) in group B. Similar results were found when looking at only infants under 26 weeks EGA. Multiple regression analysis is pending.

CONCLUSIONS: The length of storage time of RBC transfusions may play a role in several morbidities seen in VLBW infants including sepsis, feeding tolerance and the need for PDA ligation. Prospective studies are needed to determine if RBC storage time has a direct relationship with premature infant morbidities.

52

Fellow in Training

Late Preterm Infants' Skill at First Oral Feeding Predicts Length of Hospital Stay

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BACKGROUND: The average length of hospital stay (LOS) for a late preterm (LP) infant is four-fold greater and their hospital cost is ten-fold greater than that of a term infant. The delay in hospital discharge most often is due to suboptimal oral feeding ability, although feeding issues unique to this population are yet to be identified. No evidence-based clinical approaches are available to assess oral feeding skills in LP infants.

OBJECTIVE: To document the relationship between oral-feeding skills (OFS) at time of the first feeding and LOS in LP infants.

DESIGN/METHODS: A convenience sample of 35 healthy, appropriate-for-gestational age infants born between 34 and 35 weeks gestation (GA), were recruited if their first oral feeding of 15 mL was ordered within 24 hours of birth. The following information was collected: volume of intake in the first 5 minutes of the feeding, total volume taken, and duration of feeding. Oral feeding skill (OFS) was assessed as a function of efficiency (EFF, mL/min during the entire feeding) and proficiency (PRO, % mL transferred during the first 5 min/total mL ordered for that feeding). These variables defined 4 levels of OFS. Level I = PRO ≤ 30% and EFF ≤ 1.5 mL/min, level II = PRO ≤ 30% and EFF > 1.5 mL/min, level III = PRO > 30% and EFF ≤ 1.5 mL/min, and level IV = PRO > 30% and EFF > 1.5 mL/min (Lau, EPAS 2009:2839.370). The primary outcome was LOS. Multiple regression analyses were used to assess the relationship between LOS and OFS, with covariates of GA, comorbidities such as apnea, and mode of delivery.

RESULTS: LOS (7.1 ± 3.7 d, mean ± SD, range 3 to 16 d) correlated inversely with GA (r = -0.56, p = 0.001) and comorbidities (r = 0.60, p<0.001), but not to mode of delivery (r = 0.22, p = 0.24). LOS was inversely related to the mL consumed in the first 5 min of the feeding, independent of GA and comorbidities, p = 0.027. LOS was positively correlated with PRO, p = 0.025. There is a significant inverse relationship between LOS and OFS level, p = 0.001.

CONCLUSIONS: These preliminary data indicate that by using this simple clinical tool to assess OFS at the time of first oral feeding in otherwise healthy LP infants, we may be able to identify those infants who will be at risk for feeding problems that prolong hospital stay. By recognizing these infants early, clinicians may be able to develop a plan for oral feeding intervention(s) that is initiated soon after birth and thus, potentially shorten the LOS.

53

House Officer

Enhancement of Accuracy of the Umbilical Vein Catheter Tip Localization: Using Echocardiography and X-Rays

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BACKGROUND: Several complications like myocardial perforation and cardiac tamponade have been reported with the use of Umbilical venous catheter (UVC) use even with optimal catheter position as revealed by anterio-posterior (AP) chest x-ray. Echocardiography (ECHO) provides direct visualization of the catheter tip in relation to heart.However, for feasibility of routine performance in the NICU, this procedure needs to be performed by the care providers like neonatal attending or the resident physicians.

OBJECTIVE: To compare the location of the UVC tip position, using echocardiography vs. radiography.

To assess the feasibility and accuracy of UVC tip localization by echocardiography when performed by a Novice (Neonatologist or pediatric resident) and to determine the level of training needed in order to interpret the study accurately.

DESIGN/METHODS: All the infants who required placement of UVC were enrolled in the study. An AP view of X-ray chest and abdomen was performed to localize the UVC tip. The x-ray was initially interpreted by neonatologist and subsequently by a radiologist. 2D echo were performed by the pediatric cardiologist or a novice trained for this purpose. The novice underwent a two-step training protocol prior to performing ECHO in this study. It involved an observation session with the pediatric cardiologist followed by a satisfactory performance of at least 5 ECHOs by the novice under the direct observation of the pediatric cardiologist.

Both novices and cardiologist were blinded to each other's interpretation of the echocardiogram as well to X-ray results. The novices' report was compared to that of the cardiologist.

RESULTS: A total of 18 infants were enrolled in the study. Gestational age ranged from 24 to 40 weeks. Birth weight ranged from 270 to 4490 g. Comparing optimal UVC position as revealed by the chest X-ray to subsequent ECHO by the cardiologist, in 4 out of 18 (22%) patients it was sub-optimal. In comparison to the cardiologist, the novices had accurately reported 12 out of 18 (67%) ECHO studies.

CONCLUSIONS: In conclusion use of radiographs to localize UVC tip position is suboptimal. Use of Echocardiograph is feasible and it will identify malpositioned catheters that are missed on the x_rays and reduce the need for repeat radiographs. Comparing the accuracy of echo when performed by a novice with cardiologist is also reliable and can be improved with further training.

54

Fellow in Training

Thyroid Function in Late Preterm Infants in Relation to Respiratory Morbidity and Mode of Delivery

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BACKGROUND: Transient hypothyroxinemia has been associated with illness severity and adverse neurodevelopment in extremely preterm infants. Late preterm infants have increased morbidity and mortality compared to term infants, and are frequently delivered by cesarean section which potentially influences thyroid hormone production and increases risk for respiratory distress. The relationship between thyroid function, respiratory morbidity, and mode of delivery in late preterm infants has not been well studied.

OBJECTIVE: We hypothesized that late preterm infants who require respiratory support after delivery and those born by cesarean delivery will have lower total thyroxine (T4) levels in the first week of life.

DESIGN/METHODS: We enrolled babies with gestational ages 34 0/7-36 6/7 weeks admitted to the NICU and well newborn nursery. Bloodwork for total T4 and TSH was obtained in the first 24 hours of life and again with the routine newborn screening between day of life 2 and 5. Any respiratory support was defined as need for mechanical ventilation, nasal CPAP, or nasal cannula. Groups were analyzed using repeated measures ANOVA and Pearson correlation.

RESULTS: 103 patients were included in the study. Mean gestational age was 35.6±1.0 weeks and birth weight was 2559±459 grams. The first specimens were obtained at 9.1±7.1 hours and the

second specimens were obtained at 63.7±20.7 hours of life. Neither initial total T4 nor TSH were correlated with gestational age or birth weight. Infants who required respiratory support had lower total T4 levels compared to infants who did not require respiratory support (Resp. support (n=36): Initial T4 8.4 ± 3.2 µg/dl, 2nd T4 9.6 ± 3.8 µg/dl; No Resp. Support, Initial T4 10.1 ± 4.3 µg/dl, 2nd T4 12.7 ± 3.9 µg/dl, p=0.03). TSH levels did not differ between these two groups (p=0.35). There was no correlation between total T4 levels and days on oxygen (p=0.1). There were no associations between total T4 levels and mode of delivery (p=0.66) or induction of labor (0.91).

CONCLUSIONS: In our study sample of late preterm infants, infants who required respiratory support had lower total T4 levels than infants who did not require respiratory support. There was no association between total T4 or TSH levels and mode of delivery. From our data, we cannot determine if hypothyroxinemia is causal for, or associated with, the common respiratory morbidities observed in late preterm infants.

55

Fellow in Training

Premature Infants Conceived Via Artificial Reproductive Technology (ART) Are More Immature Than Naturally Conceived (NC) Infants of Similar Gestational Age (GA)

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BACKGROUND: Increasing numbers of infants are conceived via ART. Many of these infants are born preterm. Anecdotal observations suggest that these infants are physiologically more immature than those conceived naturally even when born at the same gestational age.

OBJECTIVE: To evaluate the NICU needs of ART infants compared to naturally conceived infants of similar gestational age.

DESIGN/METHODS: We reviewed the medical records of inborn infants conceived via ART born at 30-36wk GA admitted to Georgetown University Hospital from 2006 to 2010. Maternal and infant demographics, perinatal events, level of respiratory support, time to full oral feedings (PO), length of hospital stay (LOS) and discharge with home monitor were recorded. Data from naturally conceived infants matched for GA, sex and year of birth served as controls. Infants with severe congenital abnormalities were excluded. Continuous variables were analyzed using unpaired t-test and Wilcoxon rank sum test while categorical data were analyzed using Fisher's exact test.

RESULTS: Data were analyzed for 186 ART and 186 control infants. ART mothers were older but there were otherwise no differences in antenatal steroid use, chorioamnionitis, or other perinatal events between groups. ART infants required more respiratory support & oxygen, took longer to reach full feeds and full PO, had longer LOS and were discharged more often on home monitoring than controls.

	ART n=186	Control n=186	p value
Maternal age (years) *	38±4.5	32±5.5	<0.0001
Mat steroids (any)	66 %	57%	NS
GA (weeks) *	33.4±1.6	33.4±1.6	NS
Male n (%)	100 (54)	93 (50)	NS
Birth Weight *	2009±402	2134±476	0.007
Ventilator (d)*	0.24±0.8	0.34±1.2	NS
CPAP (d)*	1.7±2.3	1.2±1.8	0.009
Nasal Canula (d)*	3.3±6.7	2.1±4.4	0.04
Days to Full Feed*	7.7±5.1	6.3±4.6	0.006
Days to PO	17.2±18.3	12.1±12.6	0.015
LOS (days)*	23.3±15.2	19.6±12.7	0.012
Home monitor	43%	28%	<0.001

* mean ± SD

CONCLUSIONS: ART infants are physiologically more immature, have more intensive care needs and stay longer in the hospital than naturally conceived infants of the same GA. This potentially adds to the cost of care for these infants. The impact of this immaturity needs to be taken into account when decisions are made to deliver these infants early.

56

Fellow in Training

Role of 4G/5G Single Nucleotide Polymorphism in the Spontaneous Closure of Patent Ducutus Arteriosus?

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BACKGROUND: We, and others have demonstrated an imbalance of fibrinolysis in those preterm infants with more severe RDS, as well as those who progress to BPD. In neonatal RDS, impaired fibrinolysis contributes to intra-alveolar accumulation of fibrinogen, fibrin and their degradation products impairing surfactant function, provoking an inflammatory response and remodeling the terminal airways.Fibrin deposition promotes inflammation by activating endothelial cells to produce proinflammatory mediators and an increase in vascular permeability.

The significance of PAI-1 in hyperoxia-induced fibrin deposition has been demonstrated in PAI-1 deficient mice, which failed to develop intra-alveolar fibrin deposits, showed a less severe phenotype, and were more resistant towards hyperoxia-induced mortality. 4G/5G, rs2227631 and rs2227672 single nucleotide polymorphisms (SNPs), which have been associated with PAI-1 expression were studied.

OBJECTIVE: We tested the hypothesis that these specific SNPs of PAI-1 are associated with the development of BPD and spontaneous closure of the Ductus in preterm infants.

DESIGN/METHODS: DNA was isolated from buccal mucosal swabs from neonates with birth weight < 1 kg, following informed parental consent. Allelic discrimination was performed using specific probe for PAI-1(rs 2227631,4G/5G,rs2227672) with RT PCR. Chi square with Yates' correction was used to calculate p value, with significance when $p < 0.05$.

RESULTS: The patients were grouped into 2 categories based on oxygen requirement at 36 weeks corrected gestational age. No significance was found between any of the PAI-1 or PLAUR SNPs or BPD. However, the rs2227631 SNP and 4G/5G were found to be significantly associated with the need for medical or surgical treatment of Patent Ductus Arteriosus (PDA).

4G/5G

4G/5G	Spontaneous Closure	PDA requiring Treatment
4G/4G AND 4G/5G	4	44
5G/5G	12	19

p=0.002

CONCLUSIONS: In the initial phase of this study we did not find any significance between the PAI-1 SNPs in the development of BPD. We did however find a significant association between the 4G/5G and rs2227631 promoter SNP and the need for treatment of the PDA. We speculate that altered PAI-1 expression from these SNPs may disrupt the fibrinolytic balance, favoring patency of the DA through an augmented proinflammatory response.

57

Association of Placental Inflammatory Changes with Maternal Fever and Elevated Neonatal CRP: A Guide To Initiate Antimicrobial Therapy

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BACKGROUND: Chorioamnionitis(CA)complicates 1 to 10% of all pregnancies, and presents an infection risk to the neonate. Early diagnosis of infection continues to be diagnostic dilemma, as standard hematological tests(HT) like band count, immature to mature neutrophil ratio(I/T)and C reactive protein(CRP), have limited predictive values. Maternal fever(MF) is often used as a clinical predictor of infection, but may be affected by other factors such as epidural(EPI)or spinal anesthesia(SE). Histologic CA, the inflammation(IF)of the chorion laeve and amnion, the most common pathologic finding during placental examination, can occur in absence of risk factors or clinical symptoms. Invasion of fetal umbilical vessels by inflammatory cells (funisitis), has been reported to have a definitive association with positive signs and symptoms, cultures and other markers of IF.

OBJECTIVE: To determine whether antepartum MF correlates with histologic evidence of IF on maternal and/or fetal placental surfaces. To determine whether histologic umbilical vasculitis correlates with CRP and I/T in neonates. To determine whether SE/EPI can produce placental changes similar to CA.

DESIGN/METHODS: Study subjects (ST) were full term(FT) neonates(N=62) born to febrile mothers(>/= 38F). Control subjects(N=62) were FT neonates born to afebrile mothers, matched with gestational age and mode of delivery. HT including CBC with differential, I/T, CRP and cultures were performed on all ST. Placenta were examined for acute inflammatory changes along maternal and fetal membranes in both groups. Maternal records were reviewed for type of anesthesia received(EPI/SE).

RESULTS: There was significant association of cases vs controls with maternal IF (28/62 vs 5/62), chorionic plate IF (34/62 vs 7/62)and umbilical cord IF (fetal)(19/62 vs 3/62)(each P=<.0001). There was no correlation between EPI/SE and placental IF. The presence of fetal IF was associated with significant rise in neonatal CRP (3.9 +/- 2.5 vs 0.59 +/- 0.25, P=.001). I/T >0.2 was uncorrelated with placental IF.

CONCLUSIONS: Acute inflammatory changes in the placenta strongly correlate with MF and rise in CRP in neonates. Maternal anesthesia(EPI/SE)do not correlate with MF and placental IF. Findings of histologic funisitis is a reliable marker of congenital infection, when found in conjunction with an elevated CRP, can be used as guide to initiate antimicrobial therapy in neonates born to febrile mothers.

58

Fellow in Training

Urinary Biomarkers of Acute Kidnew Injury (AKI) in Critically Ill Neonates

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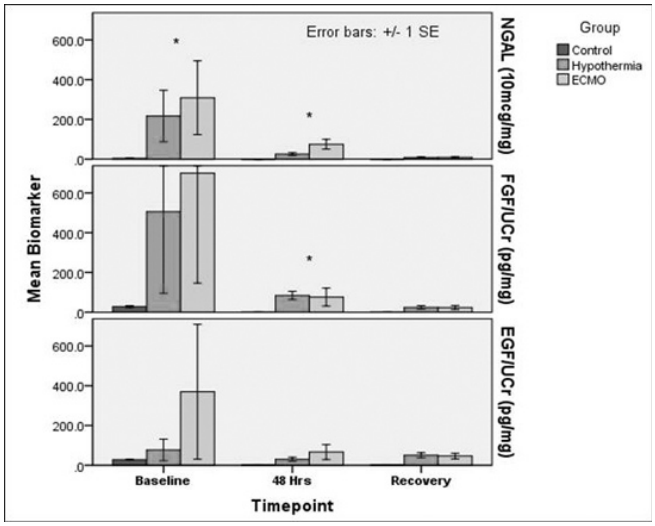
BACKGROUND: In the critically ill neonate, AKI is a significant morbidity and can be difficult to diagnose as serum creatinine is unreliable in the first days of life. Urinary biomarkers of renal injury such as urine neutrophil gelatinase-associated lipocalin(NGAL), fibroblast growth factor-2(FGF), and epidermal growth factor(EGF) have been previously proposed as a method of early detection of AKI.

OBJECTIVE: To determine if urinary biomarker values are different between neonates at risk for AKI compared to healthy newborn controls.

DESIGN/METHODS: A prospective cohort study of NICU patients at-risk for AKI (Group1: encephalopathic newborns treated with therapeutic hypothermia, Group2: neonates with hypoxemic respiratory failure treated with extracorporeal membrane oxygenation (ECMO)) was conducted. Urine was collected at 24 and 48hrs of illness, and >24hrs post recovery (e.g. post decanulation for Group 1 and post rewarming for Group 2). Demographic and clinical data, including serum creatinine and estimated creatinine clearance(eCCl) for each time point were collected. Urine was analyzed for NGAL, FGF, and EGF and compared to control samples collected from healthy newborns. Differences between cases and controls were evaluated using independent samples T-test analysis.

RESULTS: 18 patients (12 Hypothermia and 6 ECMO) and 15 controls were enrolled in this study. As compared to controls, at-risk newborns had higher NGAL at baseline and 48 hrs and FGF at 48hrs ($p<0.05$).



Only 44% of at-risk patients had significant improvement (>50% over baseline) in eCCL by time of recovery. EGF at recovery was lower in patients who failed to improve eCCL (38,434 pg/mg vs. 82,181 pg/mg; p=0.019). NGAL and FGF were not associated with improvement in eCCL.

CONCLUSIONS: Newborns at-risk for AKI have higher NGAL and FGF levels in the acute phase of illness. Persistence of low EGF at recovery may be associated with impaired renal function. The use of urinary biomarkers in the in the NICU population may be useful in stratifying patients at risk for AKI.

Neonatology - Pulmonary I
Platform Session

Saturday, March 26, 2011
8:15 AM-10:30 AM

59

8:15 AM

Fellow in Training

Generation of Mice with Lung-Specific Expression of Nuclear Heme Oxygenase-1

Fumihiko Namba, Ping La, Amal P. Fernando, Guang Yang, Phyllis A. Dennery.
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BACKGROUND: Although the stress protein heme oxygenase (HO)-1 is integral to the smooth endoplasmic reticulum, it can translocate to the nucleus under oxidative stress in several models. This nuclear form of HO-1 lacks the C-terminus and has no enzymatic activity. Nevertheless, HO-1 knockout MEF cells transfected with nuclear HO-1 demonstrated increased viability, decreased apoptosis, and decreased production of reactive oxygen species in hyperoxia compared with cells transfected with cytoplasmic HO-1.

OBJECTIVE: To understand the role of nuclear HO-1 in the neonatal lung *in vivo*.

DESIGN/METHODS: Newborn C57BL/6 mice less than 12 hours old were injected into the left lung with 20 µl adenovirus encoding mouse C-terminally truncated HO-1 cDNA (TR) tagged with c-myc and FLAG and containing 3 copies of a nuclear localization sequence (NLS). Controls were injected with empty vector (VEC) or with a full-length HO-1 cDNA (FL). In another model, constructs carrying FL or TR HO-1 tagged with hemagglutinin at the N-terminus and containing 3 NLS driven by the human surfactant protein C promoter were microinjected into fertilized mouse eggs. Transgenic mice were identified by PCR. The expression and the localization of HO-1 were confirmed by Western blot and immunohistochemistry. Poly-ADP rivose polymerase (PARP)-1 and 8-oxoguanine DNA glycosylase (Ogg1) levels were evaluated as indices of apoptosis and oxidative DNA repair using Western blot.

RESULTS: The delivery of exogenous HO-1 into the lung resulted in over-expression of the protein for 48 h as well as induction of endogenous HO-1. In the transgenic model, the nuclear and cytoplasmic localization of HO-1 were consistent with the transgenic overexpression of TR and FL respectively. Protein levels PARP-1 and Ogg-1 were lower in the animals injected with the nuclear HO-1 construct compared to VEC- and FL-injected mice. Similarly TR HO-1 transgenic mice had decreased PARP-1 levels compared to FL HO-1 mice.

CONCLUSIONS: Nuclear HO-1 may protect against cellular damage *in vivo* as previously observed in cultured cells *in vitro*. These models will allow us to determine the physiologic significance of nuclear HO-1 in the neonatal mouse lung exposed to oxidative stress.

60

8:30 AM

VEGF Heparin-Binding Isoform Attenuates Hyperoxia Via Neuropilin-1 in Explanted Embryonic Lung

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Pediatric Respiratory Medicine, Yale University, New Haven, CT; Pediatric Respiratory Medicine, Yale University, New Haven, CT; Internal Medicine-Nephrology, Yale University, New Haven, CT.

BACKGROUND: VEGF is regulated by oxygen and plays an important role in vascular development and epithelial cell morphogenesis. During hyperoxia, VEGF expression is reduced and can impair airway development. VEGF-165 and VEGF-121 bind fetal liver kinase receptor (Flk1) but VEGF-165 unlike VEGF-121 binds heparin sulfate proteoglycans and signals through neuropilin-1 (Nrp-1). Our preliminary work determined that VEGF-165 was able to attenuate effects of hyperoxia in the embryonic lung.

OBJECTIVE: To determine whether VEGF-121 a non heparin-binding isoform was able to attenuate lung injury during hyperoxia and to investigate whether Flk1/neuropilin-dependent signaling may be critical for the attenuation effects of hyperoxia in the embryonic lung.

DESIGN/METHODS: First, we harvested lung explants from embryonic day 12 (E12) mouse embryos and cultured in a) 3% oxygen alone, b) 50% oxygen alone, c) 50% oxygen+ human recombinant VEGF-165 (100 ng/ml) daily, d) 50% oxygen+ human recombinant VEGF-121 (50 ng/ml) daily at 37ºC in a sealed chamber for 2 days.

Second, E12 mouse lung explants were cultured in a)50% oxygen, b)50% oxygen+VEGF-165, c)50% oxygen+Isotype control and then VEGF-165 and d)50% oxygen+anti-Nrp-1 antibody (10 micrograms/ml) for 30 minutes and then VEGF-165 daily at 37ºC in a sealed chamber for 2 days.

RESULTS: First, quantitation of the total number of lung bud branches and total branch length were significantly reduced in explants cultured in 50% oxygen + VEGF-121 (3% oxygen: 22.5±4.5 and 6.6±0.4 mm; 50% oxygen: 11.6±1.4 and 4.2±0.4 mm $p< 0.05$ vs 3% oxygen alone; 50% oxygen+VEGF-165: 16.1±2.1 and 5.1±0.5 mm $p< 0.05$ vs 50% oxygen alone; 50% oxygen+VEGF-121: 9.6±2.5 and 3.6±0.5 mm $p< 0.05$ vs 50% oxygen+VEGF-165, n=6).

Second, we found that the total number of branches and total branch length were significantly reduced after 2 days in 50% oxygen alone and 50% oxygen+anti-Nrp-1 antibody + VEGF-165 as compared to 50% oxygen+VEGF-165 (16.2±4.7, 14.7±3.2 vs 27.5±9.8 and 2.5±0.8 mm, 2.5±0.8 mm vs 3.6±1.4 mm respectively, $p<0.05$; n=4).

CONCLUSIONS: VEGF-165 attenuates hyperoxic lung growth retardation in the absence but not in the presence of anti-Nrp-1. This finding suggests that manipulation of Flk1/neuropilin-dependent pathway might provide a therapeutic approach to attenuate effects of hyperoxic injury in the embryonic lung.

61

8:45 AM

Fellow in Training

S-Nitrosylation of Surfactant Protein-D Upregulates C-C Chemokine Ligand 2 (CCL-2) Expression in Macrophages

Rania El-Khawam, Changjiang Guo, Andrew Gow.
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BACKGROUND: Surfactant protein-D, a pulmonary collectin, has both pro- and anti-inflammatory function in the lung. Previously, we have identified that the pro- and anti-inflammatory role of SP-D is regulated by NO through S-nitrosylation of the protein. S-nitrosylation of SP-D resulted in disruption of the protein multimeric structure and induced macrophage migration. However, the mechanism of SNO-SP-D mediated cell migration remains elusive.

OBJECTIVE: We hypothesized that SNO-SP-D might induce chemokine expression.

DESIGN/METHODS: Raw264.7 macrophages were incubated with SP-D over-expressing broncheal lavage (OE-BAL) or S-nitrosylated OE-BAL (SNO-OE-BAL) in the presence or absence of LPS (1ng/mL). Gene expression of beta-chemokine CC ligand-2 was analyzed by real-time qPCR assay.

RESULTS: SNO-OE-BAL indeed induced CCL-2 expression. OE-BAL inhibited LPS induced CCL-2 expression. This inhibitory effect was diminished when the BAL was S-nitrosylated. The SNO-OE-BAL mediated induction of CCL-2 expression was SP-D dependent since removal of SP-D from the BAL by maltose beads dramatically decreased the CCL-2 expression. Investigation of the mechanism of SNO-SP-D induced CCL-2 expression revealed that SNO-SP-D stimulated NF-kappa B activity. Pre-incubation with caffeic acid phenethyl ester (CAPE), a specific and potent NF-kappa B inhibitor, completely abrogated SNO-SP-D mediated CCL-2 expression.

CONCLUSIONS: These data provide new evidence that dichotomous nature of SP-D in the lung is regulated by S-nitrosylation. Understanding the mechanism of NO modified molecules in the lung will lead to new strategies of designing the therapeutic approach for pulmonary inflammatory disorders.

62

9:00 AM

Neonatal Hyperoxia Restricts Somatic Growth, Induces Chronic Lung Disease (CLD) & Pulmonary Hypertension (PH) in Adult Mice

Vasanth H. Kumar, Huamei Wang, Daniel D. Swartz.
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BACKGROUND: Prolonged exposure of newborn mice to O_2 leads to lung changes similar to CLD in infants. We have previously shown that neonatal hyperoxia alters airway responsiveness & alveolization in adult mice at 3 months. The lasting effects of neonatal O_2 exposure in adult mice are not known.

OBJECTIVE: To assess the effects of neonatal hyperoxia on indicies of structure & function of internal organs in adult mice.

DESIGN/METHODS: Newborn litters were randomized at 3d to 85% O_2 or room air (RA) for 12d. On d15, all mice were recovered in RA until sacrifice at 9 months of age & weighed. Lungs, heart, kidneys, spleen, liver were weighed & sectioned for histology. Lung sections were assessed for radial alveolar count (RAC).

RESULTS: Adult mice exposed to neonatal hyperoxia were significantly smaller (Table 1) & had a higher splenic to body weight (BW) ratio suggestive of splenic hypertrophy compared to RA mice. Mice in the hyperoxia group had a higher RV/BW and RV/LV+S ratio, indicies of RV hypertrophy resulting from PH. Lung sections showed alveolar simplification, lower RAC (15.1 ± 0.6 in RA Grp *versus* 7.9 ± 0.9 in Hyperoxia Grp) & features of PH (smooth muscle hypertrophy). Kidney had changes consistent with arteriosclerosis. Liver histology was consistent with cardiac failure.

Table 1: Effects of Neonatal Hyperoxia on Various Indicies in Adult Mice at 9 Months of Age

Variable	RA Grp	Hyperoxia Grp	P value
BW at 9M (gm)	34.9 ± 6.7	22.8 ± 1.3	0.0001
Spleen Wt (mg)	104 ± 22	102 ± 28	NS
Spleen / BW (mg/g)	3.0 ± 1	4.5 ± 1.2	0.02
Rt Kidney (mg)	249 ± 44	146 ± 37	0.0002
Rt Kidney / BW (mg/g)	7.2 ± 1.2	6.5 ± 1.5	NS
Heart (mg)	141 ± 16	99 ± 16	0.001
RV (mg)	33.6 ± 5.2	31.8 ± 3.1	NS
LV + S (mg)	107 ± 14	70 ± 3.5	0.0001
RV / BW (mg/g)	0.98 ± 0.1	1.4 ± 0.1	0.0004
LV / BW (mg/g)	3.1 ± 0.4	3.0 ± 0.2	NS
RV / LV + S	0.32 ± 0.05	0.46 ± 0.05	0.0004

Values are means ± SDM; BW - body weight; RV - right ventricle; LV - left ventricle; S - septum

CONCLUSIONS: Prolonged neonatal O_2 exposure is toxic to adult mice. Oxygen not only restricts somatic growth but also permanently alters the structure & function of many organs in adult mice. The fundamental mechanisms on how O_2 alters postnatal lung development & somatic growth needs to be explored further.

63

9:15 AM

NFκB Is Essential in Regulating Rev-erbα Promoter Activity in Hyperoxia

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BACKGROUND: Neonatal mice lacking the transcription factor NFκB subunit p50 (KO) have increased hyperoxia-induced lung injury compared to wild-type (WT) controls. We have previously shown that lung mRNA of Rev-erbα, a nuclear receptor that coordinates circadian rhythm and metabolism, decreases 10 fold in KO neonates compared to WT littermates. The Rev-erbα promoter region has several putative NFκB binding sites, which could regulate its transcription under hyperoxia.

OBJECTIVE: To evaluate whether the Rev-erbα promoter can be regulated in hyperoxia via NFκB.

DESIGN/METHODS: A 0.9 kb genomic DNA fragment upstream of the transcriptional initiation site of Rev-erbα was amplified from mouse tail DNA using PCR. The product was sub-cloned into a luciferase reporter vector to obtain pGL4Nd0.9luc (0.9kb). Two putative NFκB binding sites, named N1 and N2, were identified and deleted to obtain pGL4Nd0.9lucΔN1 (ΔN1) and pGL4Nd0.9lucΔN2 (ΔN2). Also, two linear deletions were generated to obtain pGL4Nd0.6luc (0.6kb, excluding N2) and pGL4Nd0.2luc (0.2kb, excluding both N1 and N2). The constructs were transfected to mouse primary fibroblasts and subjected to hyperoxia (95% O2 and 5% CO2) or normoxia (95% air and 5% CO2) for 0 to 48 hours. Luciferase activity was measured using an in vivo imaging system or a luminometer and normalized to cell number or protein content. Co-transfection with a renilla luciferase vector was performed to verify transfection efficiency between constructs.

RESULTS: Hyperoxia significantly increased 0.9kb luc activity by 2, 4 and 9 fold compared to nomoxia after 4, 24 and 48 h of exposure. At 4 h, the ΔN1 and ΔN2 luc activity was decreased to 7% and 17% of the 0.9kb level in normoxia, and had no further increase in hyperoxia. However both luc activities of the 0.6kb and 0.2kb were maintained at the level of 0.9kb in normoxia and only marginally reduced to the hyperoxia-induced level of 0.9kb.

CONCLUSIONS: We conclude that the 0.9kb Rev-erbα promoter activity is upregulated in hyperoxia. Both N1 and N2 binding sites are essential to maintain the basal and hyperoxia-induced activities of the 0.9kb. We speculate that Rev-erbα may be regulated in hyperoxia via NFκB in neonatal mouse lung.

64

9:30 AM

Angiogenesis in Neonatal Hyperoxic Lung Injury

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BACKGROUND: Bronchopulmonary dysplasia (BPD) is a major long-term morbidity of prematurity. The lung pathology in BPD is primarily impaired development of the alveolar unit, composed of the alveolar epithelium and the underlying microvascular bed. Microvascular remodeling is an important component of alveologenesis and is disrupted in BPD. We have shown that Pigment Epithelium Derived Factor (PEDF), an important angiostatin, is upregulated in developing lung during hyperoxic exposure associated with impaired capillary and alveolar development.

OBJECTIVE: Test the hypothesis that PEDF has a mechanistic role in O_2-injured alveolar unit development.

DESIGN/METHODS: Mouse pups of postnatal d5 (P5) were exposed to 90% O_2 or room air (RA) through P13. PEDF and Vascular Endothelial Growth Factor (VEGF) proteins were measured by Western blot. Cell-specific PEDF mRNA expression was determined in lungs from these pups by in situ hybridization. A fetal mouse lung endothelial cell line (MFLM-91U cells) was used for *in vitro* studies. Angiogenesis was assayed to examine the anti-angiogenic property of PEDF in room air and hyperoxia (40% and 90% oxygen). Cultures were treated with VEGF and/or PEDF. The effect of PEDF on endothelial cell apoptosis was tested by examining activated caspase 3. Knockdown of PEDF by siRNA was performed in P5 mouse lung organ cultures cultured for 48 hrs in room air or 90% O_2. The development of alveolar crests was examined.

RESULTS: PEDF protein increased 6-fold and VEGF protein fell by 50% in lungs exposed to hyperoxia compared to RA. PEDF mRNA was markedly increased in hyperoxia-exposed lungs in the tips of alveolar crests, in alveolar type II cells and in the endothelium. *In vitro* angiogenesis was significantly reduced in both 40% and 90% O_2. PEDF blocked baseline and VEGF-stimulated *in vitro* angiogenesis. PEDF did not cause apoptosis of endothelial cells, even in hyperoxia. Organ cultures of P5 lungs showed reduced alveolar crests in 90% O_2. The development of alveolar crests was restored by knockdown of PEDF with siRNA.

CONCLUSIONS: The angiostatic cytokine PEDF is upregulated in neonatal mouse lung with hyperoxic exposure. The sites of upregulation are consistent with abnormal development of the alveolar unit in neonatal lung hyperoxia. In vitro studies show PEDF impairs capillary and alveolar development. Early postnatal intervention with angiostatin inhibitors may be an effective strategy in the treatment and prophylaxis of BPD. Support: NIH HL37930.

65

9:45 AM

Ph.D. Student

miR-221 and miR-130 Regulate Hox Genes Controling Vascular and Epithelial Morphogenesis in Developing Lung

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BACKGROUND: MicroRNAs regulate Hox transcription factors. Hoxa5 and Hoxb5 have distinct important functions in lung airway and alveolar formation. In other cell types, Hoxa5 and Hoxb5 have opposing roles in vasculogenesis and are regulated by miR-130a and miR-221, respectively. Hoxb5 and Hoxa5 regulation by these miRNAs in developing lung is unknown.

OBJECTIVE: We hypothesized that miR-130a and miR-221 help control lung development and lung vasculogenesis through Hoxb5 and Hoxa5 regulation.

DESIGN/METHODS: MiR-130a and miR-221 temporal and cellular expression were determined by qRT-PCR and in situ hybridization in E15-18 fetal mouse lungs. Lung-specific effects of miR-130a and miR-221 were studied in mouse E14 whole lungs cultured 48hr with anti-miRs or mimics to miR-130a and miR-221. After culture, immunohistochemistry for Hoxb5, Hoxa5, VEGFR2 and Nkx2.1 was done. Morphometry determined changes in lung structure.

RESULTS: Changes in each miRNAs were consistent with specific regulation of Hoxb5 and Hoxa5. Compared to constant levels of miR-130a and miR-221 from E15-E17, at E 18 miR-130a decreased by 50%, while miR-221 increased significantly by ≥10 fold. With advancing development, miR-130a increased in bronchiolar epithelium but was absent in saccular epithelium. MiR-221 increased in mesenchyme but remained present in saccular epithelium. Anti-miR-130a treatment led to smaller lungs with reduced airway branching with increased Hoxa5 and decreased VEGFR2 in mesenchyme. Mimic 130a treated lungs had numerous finely arborized branches extending into central lung regions with decreased Hoxa5 and increased VEGFR2 in mesenchyme. The distal airways of these lungs were lined with cuboidal cells with intense Nkx2.1 expression. Conversely, anti-miR-221 treated lungs had more distal branch generations with increased Hoxb5 and VEGFR2 around Nkx2.1 positive airways. Mimic 221 treated lungs had reduced airway branching, dilated airway tips and decreased Hoxb5 and VEGFR2 in mesenchyme. Morphometry and Nkx2.1 staining confirmed visual changes observed in airway branching.

CONCLUSIONS: MiR-130a and miR-221 temporal, spatial and cell-specific expression and their opposing effects on airway branching support lung-specific regulation of Hoxa5 and Hoxb5 expression by miR-130a and miR-221, respectively. We speculate that miRNA-Hox regulatory interactions in developing lung contribute to vascular and epithelial differentiation. Support: HD04478, HL37930, Peabody Foundation.

66

10:00 AM

Neonatal Hyperoxia Leads to Arrested Lung Development with Absent Compensatory Lung Growth in Adult Mice as Measured by Radial Alveolar Count (RAC)

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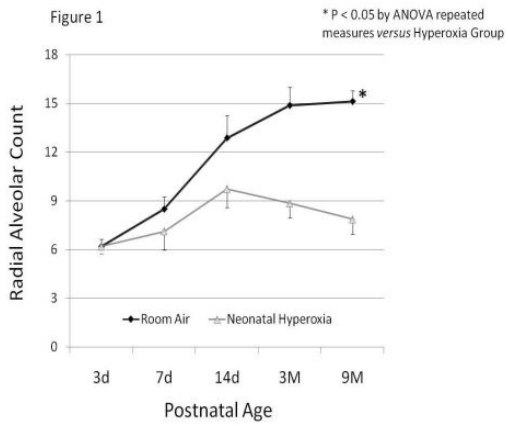
BACKGROUND: Prolonged exposure of newborn mice to O_2 leads to structural changes in the lung similar to infants with bronchopulmonary dysplasia (BPD). Longitudinal assessment of lung growth in normal & abnormal lung has not been well quantified.

OBJECTIVE: To perform a quantitative assessment of lung growth in mice by RAC measurement at various times from Day 3 to 9 months (M) following neonatal hyperoxia.

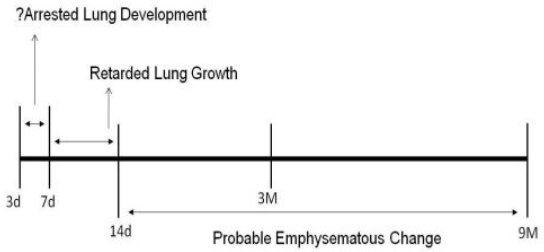
DESIGN/METHODS: Newborn litters were randomized at 3d to 85% O_2 or room air (RA) for 12 days. On d15, half were sacrificed & half were recovered in RA until sacrifice at 3M or 9M of age. Some mice were also sacrificed following 72h of hyperoxia on d7 in both groups. Sections were cut from lungs obtained at 3d (prior to hyperoxia), 7d, 15d, 3M & 9M in both groups; stained with H&E for histopathology. Lung growth was assessed by measuring RAC.

RESULTS: RAC increased significantly in the RA group into adulthood (Fig 1). There was a significant decrease in RAC at all time points following hyperoxia suggestive of retarded lung growth. RAC curves diverge gradually after 14 days upto 9M, suggesting absence of compensatory lung growth & alveolar simplification. Pulmonary arteries showed smooth muscle hypertrophy suggesting pulmonary hypertension.



CONCLUSIONS: High concentrations of O_2 during the early phase of lung development leads to alveolar arrest & retard lung growth. These findings suggest that neonatal hyperoxia may lead to functional & structural changes in the lung that are more likely to be permanent & persist throughout adulthood (fig 2).

Figure 2: Possible Pathologies of Neonatal Hyperoxia Induced Lung Injury in Adult Mice from the Longitudinal Assessment of RAC



67

10:15 AM

Hox Control of Vasculogenesis in Developing Mouse Lung

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BACKGROUND: The Hox proteins Hoxb5 and Hoxa5 uniquely control lung morphogenesis. In other tissues, Hoxb5 promotes and Hoxa5 inhibits vasculogenesis, but their role in lung vasculogenesis is unknown. We previously reported that modest O_2 exposure (0.4 FiO_2) to ex vivo developing mouse lungs alters the balance of Hoxb5 and Hoxa5 expression while inhibiting airway branch development and peri-airway vasculogenesis.

OBJECTIVE: Determine the direct contribution of Hoxb5 and Hoxa5 to lung vasculogenesis. We hypothesized that the individual effects of Hoxb5 and Hoxa5 on lung morphogenesis are mediated in part by control of lung vascular development.

DESIGN/METHODS: Human fetal lung fibroblasts (HLF cells) and E14 fetal mouse whole lungs were cultured in the presence of DNA expression plasmids to specifically over express Hoxb5 or Hoxa5 in lung mesenchyme or siRNAs to specifically inhibit Hoxb5 or Hoxa5. Controls included no treatment, vehicle control, scramble and GAPDH siRNA in siRNA-treated cultures and plasmid lacking the Hoxb5 or Hoxa5 constructs for over expression cultures. Cultures were visualized daily to monitor fetal lung growth, airway development and HLF cell confluency. At 48 hours, cultures were prepared for Western blots and immunohistochemistry (IHC) of Hox proteins and VEGFR2 and morphologic analysis via microscopy.

RESULTS: SiRNA targeting Hoxb5 in HLF cells decreased Hoxb5 protein levels by 44% and VEGFR2 by 22% compared to controls. Conversely, over expression of Hoxb5 in E14 fetal mouse lungs showed strongly increased mesenchymal Hoxb5 expression. VEGFR2 expression increased by 23%. IHC showed profoundly increased intensity of VEGFR2 in peri-airway regions. Airway development was more complex with increased 3-D structure and multi-podal branch generations. Hoxa5 over expression had strong Hoxa5 expression in lung mesenchyme of E14 fetal mouse lungs. However, VEGFR2 expression was decreased and the lungs had a more finely arborized airway branching patttern that was more organized than that seen with Hoxb5 over expression.

CONCLUSIONS: Hoxb5 and Hoxa5 play important regulatory roles in balancing lung vascular development. We speculate that specific modulation of these Hox proteins contributes to dys-coordinated lung vasculogenesis in lung injury after preterm birth. Mesenchymal-epithelial cell communication regulating airway development may be influenced by the coordination of lung vasculogenesis by these Hox proteins. Support: HD04478, HL037930, Peabody Foundation.

68

8:15 AM

Lipases as Virulence Factors in Candida Albicans and Parapsilosis Infection in a Neonatal Rat Model of Invasive Candidiasis

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Medicine, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY; Microbiology and Immunology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY; Pediatrics, Children's Hospital at Montefiore, Bronx, NY; Microbiology, University of Szeged, Szeged, Hungary.

BACKGROUND: Candidal infections are a leading cause of neonatal sepsis, particularly in those receiving parenteral lipids. *Candida spp* secrete extracellular lipases that aid in lipid digestion, adhesion to host cells, and defense against competing microflora. Nonetheless, the role of lipases in the pathogenesis of neonatal candidiasis has not been defined.

OBJECTIVE: To determine the contribution of secreted lipases to the pathogenesis of *C. parapsilosis* and *C. albicans* neonatal disease using a rat pup model.

DESIGN/METHODS: Using site-specific recombination, a *C. parapsilosis* mutant deficient in both lipases, *LIP1* and *LIP2* was generated (CpKO). A *C. albicans* mutant deficient in *LIP8* was similarly generated (CaKO). 2-3 day old Sprague Dawley pups were used (approximately 6-8 pups/condition). The 3 models of infection were: intravenous (IV), intragastric (IG) and intraperitoneal (IP). Primary outcomes were organ fungal burden (FB) in pups infected with Wild type (WT) compared with lipase deficient Candida strains at day 3 of infection. Histologic evaluation of tissues was performed.

RESULTS: Pups infected IV with CpKO exhibited significantly less FB (ranging from 65-84% lower) in the blood, kidney, spleen and liver compared with pups infected with CpWT. Likewise, pups infected IV with CaKO showed less FB in all organs, though reaching statistical significance only for the liver. Pups infected IG with CpKO exhibited significantly less kidney, stomach and liver FB (28.1%, 30.0%, and 39.4%, respectively) compared with pups infected with CpWT. FB in the kidneys and livers of pups infected IG with CaKO were also significantly less (20.7% and 38.9%, respectively) compared with those infected with CaWT. Following IP infection, there was significantly less FB in the kidneys, spleens and livers of pups infected with CpKO compared with CpWT. No differences in FB were detected for pups infected IP with Ca variants. Histologic examination IV infected pups revealed more fungal disease and inflammation for CaWT strain compared with CaKO strain, including hyphae in the renal cortex and medulla, hepatocellular necrosis and granulomatous inflammation in the spleen.

CONCLUSIONS: These studies highlight the importance of lipases in the pathogenesis of neonatal invasive candidiasis. Additional studies are needed to characterize the role of specific lipases secreted at various stages of infection.

69

8:30 AM

Fellow in Training

Prolonged Antibiotics in the First Week of Life Increase the Odds of Chronic Lung Disease (CLD) in Very Low Birth Weight Infants

Alexandra Novitsky, Deborah Tuttle, Robert G. Locke, Lisa Saiman, Amy Mackley, David A. Paul.
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BACKGROUND: Very low birth weight (VLBW) infants are at increased risk for bacterial infection. Infants often receive extended antibiotic courses for culture negative sepsis following birth which may have risks including later changes in respiratory tract colonization.

OBJECTIVE: To determine if prolonged antibiotic coverage in the 1st week of life alters tracheal colonization and increases the odds of chronic lung disease (CLD) in VLBW infants.

DESIGN/METHODS: Retrospective cohort study of VLBW infants from a single Level 3 NICU, between 7/04 to 6/09. A short course of antibiotics was defined as a ≤ 48 hours duration, and long course of antibiotics a continuous course > 48 hours duration following birth. CLD was defined as a need for supplemental O_2 at 36 weeks post-menstrual age. Weekly ETT cultures were obtained to monitor colonization. Statistical analysis included ANOVA, x^2, Mann-Whitney U Test and logistic regression. Data are expressed as mean SD.

RESULTS: Study sample included 906 infants,747 (82%) received a short course, and 159 (18%) received a long course of antibiotics following birth. Infants receiving a long course were of lower gestation (27±5.3 vs 28.3±2.9 wks, p<.01) and birthweight (944±274 vs 1053±296 g, p<.01) and more likely to require mechanical ventilation (93% vs 72%, p< .01) compared to infants receiving a short course. There was no difference in culture proven early onset sepsis between groups. Infants who received a long course were more likely to develop ETT colonization (39% vs 17%, p<.01), and more likely to be colonized with resistant gram negative organisms (6% vs 2%, p=.017) compared to the short course group. Infants who received a long course had an increased occurrence of CLD compared to those receiving as short course (17% vs 38%, p<.01). After controlling for confounding variables including gestation, birthweight and mechanical ventilation, infants receiving a long course had an increased odds of CLD: adjusted odds ratio 2.3 (95% CI: 1.5-3.6).

CONCLUSIONS: In our population of VLBW infants, a long course of antibiotics following delivery was associated with an increase in tracheal colonization with gram negative resistant organisms, and an increased odds of CLD. We speculate that antibiotics given for greater than 48 hours after delivery may alter respiratory colonization and enhance risk for CLD.

70

8:45 AM

Fellow in Training

The Role of Nitrated Fatty Acids in Modulating Inflammation in Neonates

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BACKGROUND: Neonates are susceptible to inflammatory disorders due to intrinsic defects in clearing activated immune cells, so it is important to identify signals that trigger the resolution of inflammation. Nitroalkene derivatives of fatty acids (FA), such as linoleic acid (LA, LNO_2) and oleic acid (OA, OA-NO_2), are formed via nitric oxide-dependent oxidative reactions. These compounds are increased in the presence of leukocyte-derived NO, and very high levels are seen in inflammatory diseases. While ω-6 FA generally exert inflammatory effects, nitrated FA bind PPAR-γ, a nuclear transcription factor that down regulates inflammation. Consistent with this, recent studies suggest that LNO_2 and OA-NO_2 inhibit the production of adhesion molecules, cytokines, and cytokine receptors.

OBJECTIVE: We hypothesize that nitrated FA suppress respiratory burst activity and production of inflammatory cytokines in response to LPS and mono-(2-ethylhexyl) phthalate (MEHP), a potent PPAR-γ antagonist.

DESIGN/METHODS: Neutrophils from cord and adult peripheral blood were isolated by density centrifugation and treated with LA, OA, LNO_2, OA-NO_2 (1-2 μM) or medium control, in the presence or absence of inflammatory stimuli (MEHP 500 μM, LPS 100 ng/ml). H_2O_2 production was measured by Amplex Red fluorescence. Inflammatory cytokines were measured by cytometric bead array analysis.

RESULTS: LNO_2 and OA-NO_2 inhibited both basal and MEHP-stimulated IL-1β production and LPS-induced IL-8 and IL-6 production in adult and neonatal neutrophils. They decreased MEHP-induced production of IL-8 and LPS-induced production of IL-1β and MIP-1β in adult, but not neonatal cells. Nitrated FA also inhibited MEHP-induced H_2O_2 production in neonatal cells.

CONCLUSIONS: LNO_2 and OA-NO_2 down regulate generation of inflammatory cytokines and inhibit respiratory burst activity, with distinct patterns of response in adults and neonates. Neonatal neutrophils may be less responsive to the transcriptional effects of nitrated FA because of decreased expression or activity of PPAR-γ. Endogenous NO and FA are present in excess in tissues during inflammation, suggesting that nitrated FA may be key regulators of inflammation with physiologic and therapeutic relevance in ameliorating inflammatory diseases in newborns. Nitrated lipids may also constitute a cGMP-independent mechanism for the protective effects of inhaled NO in BPD.

Supported by NIH HD058019, ES005022

71

9:00 AM

Fellow in Training

Usefulness of Urinary Immune Biomarkers in Evaluation of Neonatal Sepsis: A Pilot Project

Sukumar Suguna Narasimhulu, Karen D. Hendricks-Munoz, William Borkowsky, Pradeep V. Mally.

Division of Neonatology, New York University School of Medicine, New York, NY.

BACKGROUND: Early diagnosis of neonatal sepsis is a major diagnostic challenge in neonatology. Currently no non-invasive methods are available for diagnosis and there is no data assessing the value of urinary pro and anti-inflammatory cytokines in predicting early onset neonatal sepsis.

OBJECTIVE: To conduct a pilot prospective hospital based longitudinal observational study to test urine of term neonates with a 13 biomarker panel of pro and anti-inflammatory cytokines including IL6, IL8, IL-10, IP 10, MCP 1.

DESIGN/METHODS: Bagged urine samples were collected from 30 term neonates, born at Tisch and Bellevue Hospitals, NY. Infants were enrolled within 2 days of birth after parental consent. The specimens were processed within 4-6 hrs and stored -80°C. Biomarkers were determined using Luminex human cytokine bead-based ELISA, Millipore. Infants were divided into control, N=15 and NICU admissions for presumed sepsis (test), N = 15. Statistical analysis was performed with MSFT EXCEL & SPSS 18. t-test: significance level p≤ 0.05.

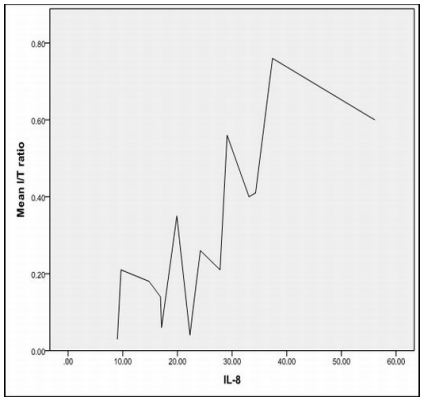
RESULTS: Urinary IL8, IP-10 and MCP -1 were significantly increased in the test group compared to control group, as seen in Table 1

Table 1

	Control (Mean ± SD)	Test (Mean ± SD)	P value
IL 8	13.2 ± 11	24.9 ± 12.1	0.004*
IP -10	16.7 ± 29.7	134.2 ± 161	0.007*
MCP – 1	632.6 ± 495	1662.6 ± 1823.8	0.02*

* p<0.05 significant,

IP-10, MCP-1 and IL-8 levels correlated with increasing I/T ratio. This trend is demonstrated for IL-8 below.



CONCLUSIONS: ·This study demonstrates that urinary biomarkers IL 8, IP-10 and MCP -1 are pro-inflammatory cytokines that are increased in the neonate during an infectious inflammatory response. These biomarker may be useful predictors and an adjunct to the current evaluation protocol to recognize neonatal sepsis.

Future Implications: Further research is needed to identify a panel of inflammatory and anti-inflammatory biomarkers that may be useful to prognosticate, monitor and direct therapy in neonatal sepsis.

72

9:15 AM

House Officer

Enhanced Neonatal Cord Blood (CB) Natural Killer (NK) Cell Activation Following Stimulation with Genetically Engineered K562 Cells: Potential for CBNK Amplification for Neonatal Adoptive Cellular Immunotherapy (ACI)

Michele A. Levin, Janet Ayello, Jessica Hochberg, Carmella Vandeven, Frances Zhao, Mitchell S. Cairo.

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BACKGROUND: Neonates are at great risk for serious infection and develop malignancies like neuroblastoma and acute leukemia in part due to deficiencies in adaptive cellular immunity (Satwani/Cairo et al. *Biol Neonate* 2005). CBNK immaturity is characterized by reduced expression/ production of NK regulatory cytokines IL-15, IL-12 and IL-18 (Qian/Cairo et al. *Blood* 1997; Lee/Cairo et al. *Blood* 1996; Satwani/Cairo et al *Br J Haem* 2005).

OBJECTIVE: To determine invitro and invivo antitumor effects, mechanism and activity following stimulation with genetically reengineered K562 expressing IL-15 and 4-1BBL (K562mbIL15-41BBL; MODK562).

DESIGN/METHODS: MODK562 (generously supplied by D.Campana MD, PhD) were cultured with CBMNC for 7d. NK CD107A, perforin and granzyme B were determined by FACS and cytotoxicity by europium release assay at 20:1 E:T ratio with Ramos (BL) and K562 (NK sensitive) tumor targets (TT) .The mammalian expression construct ffLUCZeo-pcDNA (supplied by L.Cooper, MD, PhD) was transfected into BL cells. 6wk old NODSCID mice received $5x10^6$ BLcells IP. Xenografted mice were grouped: PBS, BL only, $5x10^6$ CBMNC wildtype (WT) K562 expanded (E), MODK562E ($5x10^6$) and MODK562E ($5x10^7$). ECBMNC were injected weekly for 5wks and tumor growth monitored by volume, BLI and survival for 10 wks (estimated using the Fisher exact test).

RESULTS: After 7d, MODK562 ECBMNC showed significantly increased perforin and granzyme B expression vs WTK562 (42±1.5 vs 15±0.5%, p<0.001; 22±0.5 vs 11±0.3%, p<0.001, respectively) and CD107a expression (p<0.05). MODK562 ECBMNC cytotoxicity against K562 and BL was increased vs WTK562 (80±10 vs 34±4%, p<0.001; 42±3 vs 18±2%, p<0.01, respectively). At 5wks, tumor vol in mice receiving either dose of MODK562 ECBMNC was significantly decreased vs WTK562 (1.92±0.6 and 0.37±0.05/mm^3, p=0.0086 and p=0.0001, respectively). At 10wks, survival of BL xenografted NODSCID mice treated with $5x10^7$ MODK562 ECBMNC vs WTK562 was increased (p<0.001).

CONCLUSIONS: CBMNCs stimulated with MODK562 exhibit increased NK activation marker (CD107a), perforin and granzyme B granule exocytosis and enhanced invitro and invivo (survival) cytolytic activity. Future translational applications using this expansion approach could involve neonatal ACI.

73

9:30 AM

Inflammation in Neonatal Bacterial Meningitis: The Role of Novel Biomarkers

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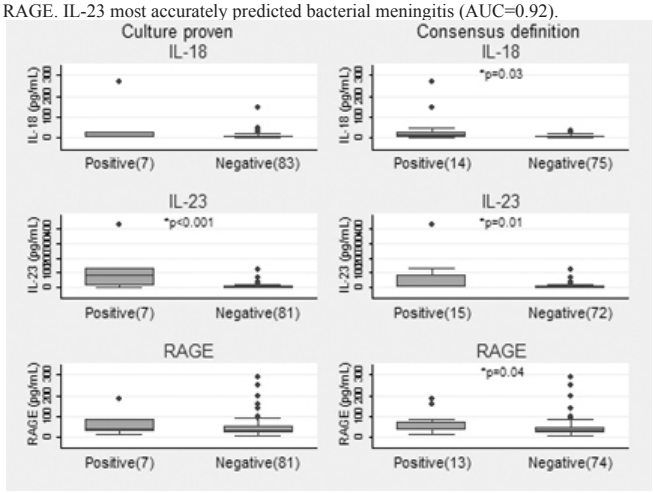
BACKGROUND: Bacterial meningitis is associated with significant morbidity and mortality. Lumbar puncture (LP) is often deferred in critically ill infants, and antibiotics administered presumptively, thereby reducing the yield of cultures. One of the hallmarks of bacterial meningitis is the influx of immune cells into cerebrospinal fluid (CSF). Interleukin 18(IL-18), (IL-23) and RAGE(receptor for advanced glycation end-products) are mediators of neutrophil influx in severe inflammation. However, the pattern of mediator release in meningitis is not well defined.

OBJECTIVE: To examine the predictive ability of IL-18, IL-23 and RAGE in the diagnosis of bacterial meningitis.
DESIGN/METHODS: This prospective multicenter study included infants <6 mos undergoing LPs. IL-18, IL-23 and RAGE were measured by ELISA. Levels were compared between infants with and without meningitis diagnosed by cultures or consensus definition (combination of CSF gram stain, WBC, glucose and protein) (Mann Whitney test).
RESULTS: 88 subjects had a median GA of 34 wks [interquartile range (IQR) 28-38wks] and a median PNA of 25 d [IQR 8–51d]. 7 infants had meningitis by positive cultures;15 by consensus definition. Bacteria isolated from CSF included GBS(2), S. aureus(2), Coagulase negative staph.(2) and Enterococcus(1). 82% received antibiotics prior to LP.
IL-23 was significantly elevated in culture proven bacterial meningitis (p< 0.001) while IL-18 and RAGE did not differ versus controls (p=NS). By consensus definition, all 3 markers were significantly elevated (p<0.05). CSF WBC correlated with IL-23 and IL-18 (p<0.001), but not with RAGE. IL-23 most accurately predicted bacterial meningitis (AUC=0.92).



CONCLUSIONS: IL-18, IL-23 and RAGE are useful in diagnosis of bacterial meningitis in antibiotic pre-treated infants, but only IL-23 identifies culture positive subjects with high accuracy. The correlation of IL-23 and IL-18 with elevated CSF WBCs may reflect the role of these cytokines in immune cell infiltration into the CSF.

74

9:45 AM

Fellow in Training

Docosahexaenoic Acid (DHA) Upregulates the Innate Immune Response in Neonatal Cord Blood

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BACKGROUND: Recent attention has focused on the potential role in neonates of DHA, an *n*-3 polyunsaturated fatty acid, as a modulator of immunity and inflammation. Neonates, whose host defenses are immature, are a population especially vulnerable to infection. We hypothesized that DHA has an upregulatory effect on the neonatal immune response as measured by cytokine response to lipopolysaccharide (LPS).
OBJECTIVE: To determine whether pretreatment of neonatal cord blood with DHA potentiates the immune cytokine response to LPS.
DESIGN/METHODS: Neonatal cord blood samples were freshly obtained from healthy full term infants (n=9) and incubated with/without DHA at concentrations of 25 or 100 μM for 24h, then stimulated with LPS for 18h. Supernatants were collected and assayed by multiplex analysis (MSD 7-plex Human Pro-inflammatory Cytokine Assay) for cytokines IL-1β, IL-6, IL-8, IL-10, IL-12p70, TNF-α, and IFN-γ (pg/mL).
RESULTS: The effect of pretreatment with DHA on response to LPS varied among cytokines. Compared to untreated cord blood, pretreatment with 100 μM DHA resulted in significant enhancement of IFN-γ (Fig. 1) response to LPS (p<0.05). IL-12p70 and IL-6 responses were also enhanced (p<0.05). No effects were observed for IL-1β, IL-8, IL-10, or TNF-α. Pretreatment with 25 μM DHA had neither a significant inhibitory nor potentiating effect on response to LPS for all cytokines tested.

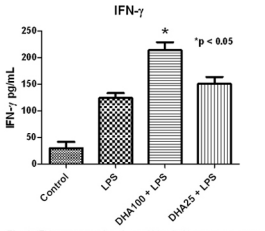


Fig. 1. IFN-γ concentrations in cord blood without pretreatment or LPS stimulation (Control), with LPS stimulation without pretreatment (LPS), or with LPS stimulation following pretreatment with either 100 or 25 μM DHA.

CONCLUSIONS: Treatment with DHA potentiates IFN-γ, IL-12p70, and IL-6 response to LPS in neonatal cord blood, but has no potentiating or inhibitory effect on IL-1β, IL-8, IL-10, or TNF-α. This effect is dose dependent and not apparent at low dose (25 μM). Enhancement of IFN-γ and IL-12 responses suggests DHA may potentiate neonatal immunity by mediating Natural Killer (NK) cell and T lymphocyte activation, without potentiating a pro-inflammatory response (TNF-α, IL-1β, IL-8). Further investigation is needed to elucidate this effect and its potential clinical significance as a means of enhancing the neonate's defense against infection.

75

10:00 AM

Reference Ranges for Cerebrospinal Fluid (CSF) Parameters in Non-Infected Preterm and Term Infants in the NICU – A Multicenter Prospective Study

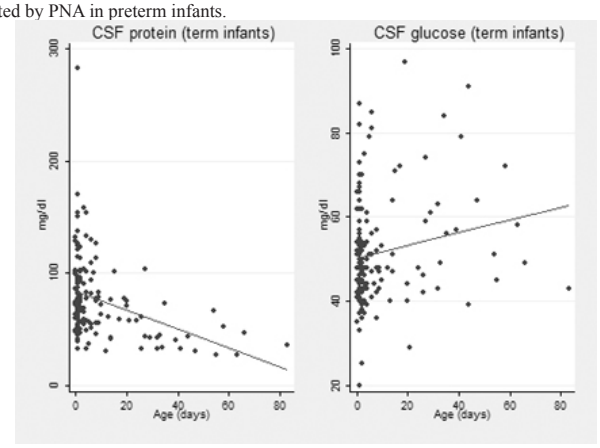
Lakshmi Srinivasan, Samir S. Shah, Michael A. Padula, Soraya Abbasi, Karin L. McGowan, Mary C. Harris.
The Children's Hospital of Philadelphia, Philadelphia, PA; Pennsylvania Hospital, Philadelphia, PA; University of Pennsylvania School of Medicine, Philadelphia, PA.

BACKGROUND: Neonatal meningitis is a significant cause of morbidity and mortality in infants. Studies examining normal ranges of CSF parameters are often retrospective, and provide limited information in preterm infants.
OBJECTIVE: To determine reference ranges of CSF parameters in term and preterm infants hospitalized in NICUs.
DESIGN/METHODS: Data were collected prospectively as part of a multi-site study of infants < 6 mos in 3 NICUs receiving a lumbar puncture (LP) for diagnosis of suspected meningitis. Infants with proven bacterial or viral meningitis and traumatic taps were excluded. The relationships of CSF white cell count (WBC), protein and glucose with postnatal age (PNA) were examined in the entire cohort and in gestational age (GA) subsets.
RESULTS: 333 infants had a median GA of 36wks (range 23-42wks) and median PNA of 6d (range 0-158d). 74% received antibiotics prior to LP.

CSF parameters	Infants<37 wks	Infants≥37 wks	All infants
Median (95%)	*(Median GA 31 wks)*	*(Median GA 39 wks)*	*(Median GA 36 wks)*
WBC(/mm^3)	3 (29)	3 (23)	3 (29)
Glucose(mg/dl)	49 (81)	49 (81)	49 (81)
Protein(mg/dl)	103 (208)*	68.5 (133)*	86 (173)

*p<0.001

There was an age related decline in CSF protein levels in term infants by 5 mg/dl/wk (p<0.001). In contrast, CSF glucose levels increased by 1.5 mg/dl/wk in term infants (p=0.003). There was no correlation between CSF WBCs and PNA in either GA category. Glucose and protein values were unaffected by PNA in preterm infants.



CONCLUSIONS: Contrary to popular teaching, CSF WBCs are not significantly different between non-infected preterm and term infants. While the use of antibiotics may affect CSF parameters, our data reflect common NICU practices with regard to performance of LPs in hospitalized infants. We also quantify age related changes in CSF protein and glucose levels. These values can be used to accurately interpret the results of CSF studies in young infants.

76

10:15 AM

Fellow in Training

Efficacy of Als3p-Specific Monoclonal Antibody in a Mouse Model of Neonatal Candidiasis

Nancy Y. Tsai, Sonia S. Laforce-Nesbitt, Lois L. Hoyer, Joseph M. Bliss.
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BACKGROUND: *Candida albicans* is the leading fungal pathogen causing invasive disease in premature infants. Despite treatment with antifungal agents, these infections lead to high mortality and neurodevelopmental impairment among survivors. Novel therapeutic strategies are needed to treat these infections.
OBJECTIVE: To evaluate the therapeutic potential of a monoclonal antibody (MAb) against the *C. albicans* adhesin, Als3p, in a neonatal mouse model for disseminated candidiasis.
DESIGN/METHODS: Two-day-old BALB/c mouse pups were given a lethal dose of *C. albicans* by intraperitoneal injection, and randomized to receive anti-Als3p antibody or sterile saline. Control animals received anti-Als3p antibody only. Pups were examined every 3-8 hours for death and were euthanized if moribund. Surviving pups were euthanized at 72 hours after injection and organs were harvested. Kidney, lung and brain were homogenized at time of death and plated to assess fungal burden.
RESULTS: Infection with *C. albicans* in animals receiving saline (n=8) led to a median survival of 34 hours. A single dose of anti-Als3 MAb given 1.5 hrs after infection (n=12) led to increased survival to a median of 55 hours (p = 0.07). Median colony counts (in colony forming units (CFU)/organ) in the kidney were 1110 [600-4100]* in the treatment group vs. 5250 [3325-36,000]* for *C. albicans* alone. Colony counts for lung tissue were comparable in both groups, 1340 [535-3055]* in the treatment group vs. 1450 [300- 3075]* in *C. albicans* only group. Uninfected pups injected with anti-Als3 MAb alone remained healthy until study endpoint. Death due to candidiasis in

infected animals was confirmed by colony counts of homogenized kidney, lung, and brain tissue. *inter-quartile range

CONCLUSIONS: Although limited by small sample size, a single dose of anti-Als3 MAb given to neonatal mice infected with *C. albicans* shows a trend toward reduced mortality. Targeted immunotherapy may be a useful approach for translation to human neonates.

GI / Hematology - Oncology / Nephrology / Nutrition Platform Session

Saturday, March 26, 2011
8:15 AM-10:30 AM

77

8:15 AM

House Officer

Changes in Vitamin D Status in Incident Pediatric Crohn Disease

Aaron R. Prosnitz, Mary B. Leonard, Justine Shults, Babette S. Zemel, Bruce W. Hollis, Robert N. Baldassano, Meena Thayu.

Yale-New Haven Children's Hospital, New Haven, CT; Children's Hospital of Philadelphia, Philadelphia, PA; Department of Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, PA; Department of Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, SC.

BACKGROUND: Vitamin D is essential for musculoskeletal health and immune function. Prior studies have reported a high prevalence of vitamin D deficiency in pediatric Crohn disease (CD); however, no studies have examined changes in vitamin D status in an incident cohort or included healthy controls.

OBJECTIVE: This prospective cohort study characterized 25(OH)D, $1,25(OH)_2D$, and parathyroid hormone (PTH) levels in pediatric CD at diagnosis, compared with controls, and identified correlates of changes in these parameters following diagnosis.

DESIGN/METHODS: Serum vitamin D and PTH levels were measured at diagnosis, 6, 12, and a median of 43 months later in 78 CD participants, and once in 221 controls. Multivariate linear and logistic regression models identified correlates of baseline levels, and quasi-least squares regression models identified factors associated with changes over time.

RESULTS: At diagnosis, 25% of CD participants were vitamin D deficient [25(OH)D < 15 ng/mL], and the odds ratio for deficiency was 4.9 (95% CI 2.0, 11.8; $p<0.001$), compared with controls, adjusted for age, race, and season. Serum $1,25(OH)_2D$ levels were lower compared with controls, independent of 25(OH)D levels ($p<0.001$), and were lower relative to PTH in CD (interaction $p=0.02$). Among CD subjects and controls with 25(OH)D < 30 ng/mL, CD was associated with lower PTH levels ($p<0.05$). Both 25(OH)D and $1,25(OH)_2D$ (both, $p<0.0001$) levels improved over time. At follow-up, 4% were vitamin D deficient, and PTH was no longer low relative to 25(OH)D levels in CD, compared with controls. Greater increases in 25(OH)D were correlated with lower baseline 25(OH)D, a summer study visit, lower baseline CD activity, and vitamin D supplementation (all, $p<0.05$). Greater increases in $1,25(OH)_2D$ were correlated with greater increases in PTH ($p<0.02$).

CONCLUSIONS: This study demonstrates significant 25(OH)D deficiency in incident pediatric CD, which resolves following diagnosis. Further, $1,25(OH)_2D$ improved following diagnosis, and the relative hypoparathyroidism at baseline resolved at follow-up. Inflammatory cytokine suppression of PTH and downregulation of renal 1-α-hyroxylase may contribute to an altered vitamin D-PTH axis. Future studies should address the impact of vitamin D supplementation on clinical outcomes in pediatric CD.

78

8:30 AM

Medical Student

Preliminary Results of Phase I/II Study of Clofarabine (CLO) in Combination with Cytarabine (ARA-C) and Total Body Irradiation (TBI) Followed by Allogeneic Stem Cell Transplantation (AlloSCT) in Children, Adolescents and Young Adults (CAYA) with Poor-Risk Acute Leukemia

Angela Ricci, Mark Geyer, Lauren Harrison, Dierdre Duffy, Monica Bhatia, James Garvin, Diane George, Prakash Satwani, Alexa Cheerva, Julie Talano, M. Fevzi Ozkaynak, Theodore Moore, Joseph Schwartz, LeeAnn Baxter-Lowe, Mitchell S. Cairo.

Pediatrics, Columbia University, New York, NY; Pediatrics, University of Louisville, Louisville, KY; Pediatrics, Medical College of Wisconsin, Milwaukee, WI; Pediatrics, New York Medical College, Valhalla, NY; Pediatrics, Univeristy of California Los Angeles, Los Angeles, CA; Pathology and Cell Biology, Columbia University, New York, NY; Surgery, University of California San Francisco, San Francisco, CA; Medicine, Columbia University, New York, NY.

BACKGROUND: CAYA with ALL/AML in 3rd complete remission (CR3), refractory relapse (RR) or induction failure (IF) continue to have very poor prognosis, <20% EFS (Gaynon, BJH, 2005, Wells et al, JCO, 2003). CLO, an inhibitor of DNA polymerase and ribonucleotide reductase, has activity in CAYA with relapsed ALL/AML (Jeha et al., JCO, 2006, 2009). CLO with CYT demonstrates synergy and greater rates of CR than CLO alone (Faderl et al, Blood, 2005, 2008).

OBJECTIVE: We sought to determine maximum tolerated dose of CLO and assess safety, progression-free survival (PFS) and overall survival (OS) of CLO, ARA-C and TBI followed by AlloSCT in CAYA with poor-risk ALL/AML.

DESIGN/METHODS: This is a multi-center phase I/II trial of a novel conditioning regimen of CLO (dose escalation: 40mg/m2 [n=3], 46mg/m2 [n=3], 52mg/m2 [n=9]) x5d with ARA-C 1000mg/m2 4 hrs later x6d and TBI (1200cGy) followed by AlloSCT from matched related or unrelated donors in CAYA with ALL/AML in CR3, RR or IF. Pts with unrelated grafts received R-ATG. GVHD prophylaxis consisted of tacrolimus and MMF (Bhatia/Cairo et al., BBMT, 2009).

RESULTS: 15 pts: median age 10.6 yrs; M:F 11:4, ALL/AML 12:3 (9 CR3, 3 RR, 3 IF), 6 related donors, 9 unrelated donors (5 BM/PBSC, 4 UCB). Median TNC/CD34 dose was 5.0x108/kg/ 5.0x106/kg for BM/PBSC and 3.8x107/kg/4.0x105/kg for UCB. Probabilities of neutrophil and platelet engraftment and grade II-IV aGVHD were 100%, 90.9% and 48.1%. All achieved 100% whole blood donor chimerism by day 30. Day 100 TRM is 0%. CLO dose tolerated at 52mg/m2/ d, which is being used in phase II. No SAEs related to CLO were observed. 2 pts had disease progression at days 90 and 126. 11 pts are alive in continuous CR at median 182 days (42-876). Probabilities of 1-yr PFS and OS are 64.7% and 60.2%.

CONCLUSIONS: Preliminary results suggest this regimen followed by AlloSCT is safe and well tolerated in CAYA with poor-risk ALL/AML with CLO dose of 52mg/m2. Early results are encouraging with respect to low risk of early leukemic relapse with this conditioning regimen.

79

8:45 AM

House Officer

Are Children with Elevated Body Mass Index at Increased Risk for Gastroesophageal Reflux? A Community-Based Study

Sowmya Angusamy, Babu Bangaru, Louis Primavera, Rapaport Susana, Fernanda Kupferman.

Pediatrics, Flushing Hospital Medical Center, Flushing, NY; School of Health Sciences, Touro College, New York, NY.

BACKGROUND: Childhood obesity has reached epidemic proportions worldwide and is a leading public health concern in the US. Emerging data suggest that elevated body mass index (BMI) in children is associated with many adverse health consequences. Elevated BMI has been associated with gastroesophageal reflux (GER) in adults, but the presence of this association in children remains uncertain.

OBJECTIVE: To identify whether elevated BMI is associated with GER in children.

DESIGN/METHODS: We conducted a cross-sectional study at Flushing Hospital Medical Center from May to October 2010. Children 2-19 years of age who attended the outpatient department were recruited. Consent was obtained from their parents and assent for children over 7. Children with illness in the past 2 weeks were excluded. Height and weight of enrolled subjects was recorded, and they or their parents were asked to complete a validated questionnaire used to diagnose GER in children. The questionnaire obtained demographic data on the patients and their exposure to smoking, caffeine, antireflux medications and any illness in the past 2 weeks. In addition, there were questions related to GER symptoms experienced over the previous week including vomiting, nausea, heartburn, epigastric pain, abdominal pain, regurgitation and difficulty swallowing. Each symptom was given a weighted score. A total score of ≥ 3 was considered positive for GER. BMI was defined according to published standards, calculated for each patient, and subdivided into percentile groups of underweight ($<5^{th}$), normal (5^{th}-84^{th}), overweight (85^{th}-95^{th}) and obese ($> 95^{th}$). Descriptive data were reported using frequencies, means and standard deviations (SD). Associations between BMI and GER were analyzed using Chi-squares. A p-value of <0.05 was considered significant.

RESULTS: A total of 390 subjects were recruited; 48 were excluded due to recent illness. The 342 subjects studied had a mean age of 7.2 ± 4.3 years, were 47% male and 70% Hispanic. The subjects' BMIs classified them as underweight 2%, normal 46%, overweight 22% and obese 31%. Nine subjects (2.6%) had GER; of these, 5 had normal BMI, 1 overweight and 3 obese. Chi-square analysis showed that being overweight or obese had no association with the presence of GER compared to children with normal BMI.

CONCLUSIONS: Elevated BMI was not significantly associated with GER symptoms in children in our community-based study.

80

9:00 AM

House Officer

Thyroid Dysfunction in Children with Immune Thrombocytopenia (ITP)

Jennifer Hughes, Zoltan Antal, James Hurley, Mary J. James, James Bussel.

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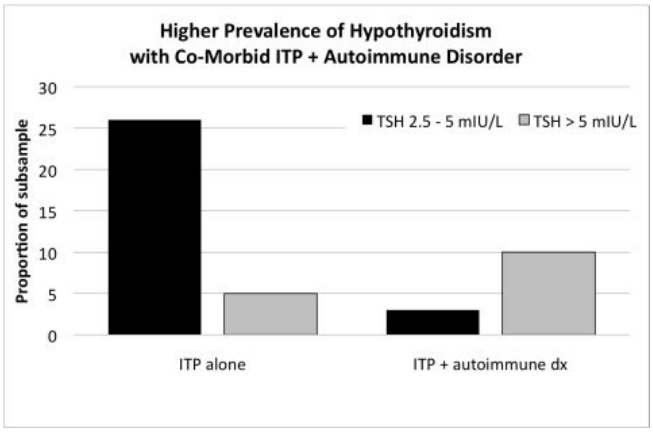
BACKGROUND: ITP is associated with thyroid disorders in adults; the prevalence of both thyroid autoantibodies and thyroid autoimmune disease is higher in adults with ITP than age matched normal controls. For children, such data are very limited.

OBJECTIVE: Define prevalence of thyroid dysfunction in children with ITP and explore correlates of hypothyroidism in pediatric ITP.

DESIGN/METHODS: A retrospective review of medical records from the Platelet Disorders Center at the Weill Medical College of Cornell University from 1/1980 to 12/2008. Inclusion criteria: diagnosis of ITP, age 1 to 21 years, and testing of thyroid function.

RESULTS: The review yielded 265 subjects. Average age was 10.1 years (s.d.=5.9 years). Prevalence of presumed subclinical hypothyroidism (TSH 2.5-5.0 mIU/L) was 24%; 3.4% of subjects had hypothyroidism with TSH levels (>5.0 mIU/L). Subjects with secondary ITP with co-morbid autoimmune and immunodeficiency disorders were less likely to have subclinical hypothyroidism (5% vs. 26%), ($p<0.05$) but more likely to have hypothyroidism (10% vs. 3%) than subjects with primary ITP alone ($p<0.05$). No significant correlation of TSH levels was found with age, sex, serum ANA, lupus anticoagulant, AST, ALT, IgA, IgM, or IgG.



CONCLUSIONS: Prevalence of thyroid dysfunction appears to be higher among children with ITP (3.4% overt and 24% subclinical) than in the general pediatric population (0.04-1.2%). In addition, overt hypothyroidism appears to be particularly elevated among children with ITP plus co-morbid autoimmune disease. Children with concurrence of thyroid dysfunction and ITP may have a stronger autoimmune etiology and may later develop multi-endocrine deficiency. Future studies can further define these associations using longitudinal analyses and serum studies of thyroid autoantibodies, anti-gliadin, anti-endomisium, and other markers of autoimmune disorders.

81

9:15 AM

Bone Mineral Metabolism in Pediatric Kidney Transplant Recipients

PJ Galutira, S. Beste, N. Samtani-Gaffney, M. DelRio, B. Goilav.

Division of Pediatric Nephrology, University of Santo Tomas Hospital, Manila, Philippines; Nephrology, Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: The kidneys play a major role in bone and mineral homeostasis by regulating calcium (Ca), phosphorus (P), parathyroid hormone (PTH), and vitamin D metabolism. Disordered regulation of mineral metabolism occurs early in the course of chronic kidney disease (CKD) and results in alterations in bone modeling, remodeling, and growth also known as CKD Mineral and Bone Disorder (CKD-MBD). Currently, there is a paucity of information regarding timing of normalization of CKD-MBD parameters in pediatric kidney transplant (KT) recipients.

OBJECTIVE: To investigate the timeline until normalization of biochemical parameters of bone metabolism after kidney transplantation in children.

DESIGN/METHODS: Retrospective chart analysis of 45 patients transplanted from 2000 to 2010 was performed. Information such as anthropometrics and underlying diagnosis, as well as serum levels of P, Ca, magnesium (Mg), iPTH, vitamin D, alkaline phosphatase (AP) and serum creatinine were obtained at weekly intervals in the immediate post-transplant period, tri-monthly in the first year, and every 6 mo thereafter.

RESULTS: Of 45 KT recipients, 27 were M, 18 were F. Mean age at transplant was 11.5 years. 7 KT recipients had >1 KT (2-3). Mean follow up (f/u) was 50 mo. Table 1 depicts the percent of abnormal bone mineral parameters as a function of time post KT.

Longitudinal F/U of Bone Mineral Parameters

% Parameter/Time post KT	2wk	1mo	6mo	12mo	24mo	36mo
Abnl GFR	51	30	14	18	21	35
Hypo-P	62	53	7	13	15	28
Hypo-Mg	60	40	37	24	31	43
Hypo-Ca	11	4	2	3	0	0
Abnl iPTH	2	4	2	3	0	0
Abnl AP	16	24	22	11	0	7

The majority of patients required prolonged supplementation with Ca, Mg, P, and ergocalciferol to maintain normal levels. Despite lower target levels of calcineurin inhibitors (CNIs), the requirement for Mg was lifelong for most KT recipients with most levels being borderline low.

CONCLUSIONS: "Hungry bone" is a commonly known entity in the KT population resulting in the requirement of supplementation with P and Ca for the most part. This study revealed that iPTH levels normalize rapidly post KT and do not correlate with such requirements. AP levels are a slightly better parameter. Most KT recipients experience profound hypomagnesemia and require supplementation throughout the life of the graft and the requirements do not subside, despite lower target levels for CNIs.

Special attention to Mg levels should be paid in pediatric KT recipients.

82

9:30 AM

Coordinated Synthesis of Heme and Iron-Sulfur Clusters in Mammalian Cells: Implications for Cell Function

Ping La, Phyllis A. Dennery.

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BACKGROUND: Iron, an essential element for nearly for all forms of lives, is incorporated into heme or iron-sulfur clusters (Fe-S). These are critical for many biological functions, such as mitochondrial electron transport. Although Fe-S assembly is independent of heme metabolism in yeast, this is not known in mammals. We speculate that heme metabolism regulates Fe-S assembly in mammals.

OBJECTIVE: To determine the effects of heme metabolism on Fe-S assembly in mammalian cell lines.

DESIGN/METHODS: The expression of heme oxygenase (HO)-1, the rate-limiting enzyme in heme degradation and delta-aminolevulinate synthase 1 (ALAS1), the first enzyme in heme synthesis, were inhibited using lentivirus shRNA in mice embryonic fibroblasts NIH3T3 cells. Human liver carcinoma cells HepG2 or cervical cancer cells Hela were also incubated with 2.5μM succinylacetone (SA), an inhibitor of delta-aminolevulinate dehydrogenase (ALAD), the second enzyme in heme synthesis, for 16 hours. Aconitase activity was also measured as an index of Fe-S assembly. Mitotracker green labeling was determined as a measure of mitochondrial biogenesis.

RESULTS: shRNA infection decreased ALAS1 and HO-1 expression to at least 20%. The inhibition of ALAS1 reduced heme cellular amount and cytosol Fe-S assembly without affecting HO-1 protein level. However, when HO-1 was inhibited, cytosol Fe-S synthesis was decreased despite increased heme levels, suggesting that heme is not the only factor affecting Fe-S assembly. Nevertheless, ALAS1 protein levels were decreased in cells where HO-1 was inhibited. Moreover, incubation with SA decreased heme levels in Hela and HepG2 cells but enhanced ALAS1 expression. Furthermore, the imbalance of heme metabolism, due to disrupted HO-1 or ALAS1 expression, significantly inhibited cell proliferation while accelerating cellular iron accumulation and mitochondrial biogenesis.

CONCLUSIONS: These data suggest that heme metabolism modulates Fe-S synthesis in mammalian cells, likely through ALAS1. We speculate that this regulatory pathway modulates iron homeostasis, cell proliferation and mitochondria biogenesis.

83

9:45 AM

Medical Student

Pediatric Pharmacokinetics (PK) of IV Busulfan (Bu) in Allogeneic Stem Cell Transplantation (AlloSCT) Recipients: Dosing q12 Hours Schedules Are Safe and Comparable to q6 Hours Schedules

John LeGall, Michael Milone, Ian Waxman, Les Shaw, Lauren Harrison, Deirdre Duffy, Olga Militano, Monica Bhatia, Prakash Satwani, Diane George, James H. Garvin, M. Brigid Bradley, Carmella van de Ven, Mitchell S. Cairo.

Pediatrics, Columbia University, New York, NY; University of Pennsylvania, Philadelphia, PA; Medicine, Columbia University, New York, NY; Pathology and Cell Biology, Columbia University, New York, NY.

BACKGROUND: IV Bu divided q6h in pediatric AlloSCT conditioning has been demonstrated to be safe and effective at doses of 4 mg/kg/day in pts <4 years and 3.2 mg/kg/day in pts >4 years (Wall et al, PBC, 2010). Less frequent dosing of IV Bu would be attractive for ease of administration and increased efficiency.

OBJECTIVE: To compare the PK of IV Bu q12h to those of IV Bu q6h.

DESIGN/METHODS: For comparison of PK data two cohorts of pediatric AlloSCT pts receiving IV Bu during conditioning were established. Cohort A received IV Bu q6h x 16 doses and cohort B received IV Bu q12h x 8 doses (age ≤4yrs 4 mg/kg/day; age >4yrs 3.2 mg/kg/day). Heparinized plasma was obtained at 1,2,3,5,6, and 8 hrs after the first dose of IV Bu to determine drug levels as measured by gas chromatography–mass spectroscopy (GC-MS). Bu levels were used to determine volume of distribution (Vd), half-life (t1/2), and clearance (Cl) of Bu. Area under the curve (AUC) was calculated using a 1-compartment first order kinetic model. An estimated AUC/day was calculated by AUC/dose*doses/day.

RESULTS: In comparing PK of cohort A (n=89; mean age 7.9 yrs) vs cohort B (n=38; mean age 8.2 yrs) there was no statistically significant difference in the Vd, t1/2, or Cl.

Table 1

	Cohort A Q6 IV Bu	Cohort B Q12 IV Bu	P values
N	89	38	N/A
Age(yrs)	7.9±6.9	8.2±6.3	0.586
Vd(L)	20.6±16.6	19.4±13.7	0.676
Half-life(min)	132.0±31.1	129.10±38.15	0.678
Cl(ml/min/kg)	3.6±0.9	4.0±1.5	0.215
AUC(mmol *min/L)	1077±352	1886±420	<0.0001
AUC/day	4310 ± 1406	3773 ± 841	0.030

As expected there was a significant increase in the AUC in cohort B vs cohort A (1886 vs 1077 mmol*min/L; p <0.0001). The AUC/day of cohort B was less than that of cohort A (3773 ± 841 vs 4310 ± 1406 mmol*min/L/day; p <0.031).

CONCLUSIONS: In summary, besides an expected increase in AUC, IV Bu q12h administration in conditioning of pediatric AlloSCT pts results in a PK profile (Vd, t1/2, Cl, AUC/day) clinically comparable to IV Bu q6h. Improved efficiency of administration may make the IV Bu q12h dosing an attractive alternative to the conventional q6h dosing.

84

10:00 AM

Medical Student

GA101, a Type II Glycoengineered Antibody Against CD20 Induces Significant InVitro Cell Death of PreB-ALL (PBALL) and PreB Lymphoblastic Lymphoma (PBLL)

Christina Cho, Janet Ayello, Andrew Stier, William Quish, Mitchell S. Cairo.

Pediatrics, Medicine, Pathology and Cell Biology, Columbia University, New York, NY.

BACKGROUND: CD20 is an excellent tumor target and rituximab, a chimeric type I antibody (ab) directed at CD20, has shown enhanced activity in adult and pediatric B-cell nonlymphoblastic NHL but eventually relapse and refractoriness occur (Coiffier et al *NEJM* 2002; Cairo et al *ASCO* 2010). GA101 is type-II glycoengineered and humanized anti-CD20 ab exhibiting superior activity of direct and cellular immune mediated cytotoxicity against $CD20^+$ nonlymphoblastic NHL invitro and in human NHL xenograft models (Mössner et al. *Blood* 2010). CD20 is also expressed in childhood PBALL and PBLL (Jeha et al. *Blood* 2006).

OBJECTIVE: To determine optimal GA101 dose and incubation time for invitro cell death induction in PBLL and PBALL.

DESIGN/METHODS: PBALL (Tanoue) and PBLL (U698M; DSMZ) tumor targets (TT) were cultured in RPMI+10% FBS. The T-ALL cell line Loucy, $CD20^-$, (ATCC), served as a negative control; Tcell leukemia line Jurkat (ATCC) with camptothecin, acted as positive cell death control. TT stained with fluorescein-conjugated anti-CD20 mAb to assess CD20 expression by flow cytometry. TT ($3x10^5$/well) were incubated with 1.0, 10 and 100ug/ml of GA101 (generously supplied by Roche) or IgG isotype control at 37^o ,5% CO_2 for 24,36,48,or 72h. Cells stained with

annexin V/propidium iodide and cell death assessed within 1h by flow (Ayello/Cairo et al *Exp Heme* 2009).
RESULTS: CD20 expression on PBALL and PBLL cell line was 8.2±2 and 53±2.5%, respectively. At 36h the PBALL line demonstrated no significant change in cell death; while cell death in PBLL was significantly increased at 100μg/ml GA101 compared to 10 and 1.0 (16±.3 vs 7.3±.04vs 5±.42%, respectively, p<.001) and compared to isotype and Loucy (16±.3 vs 1.1±.26 vs 0.8±.2%, respectively, p<.001). Despite low CD20 expression in PBALL increased cell death induction was demonstrated when PBALL was cultured for 72h at 100 ug/ml vs 36 hrs (p<0.001). Following 72h incubation, GA101 induced a significant increase in cell death in BLL (53% $CD20^+$) vs PBALL (8% $CD20^+$) vs isotype vs neg control (Loucy $CD20^-$) [59±0.3 vs 39±2.3 vs 0.02vs 2.86±0.13%, p<0.001).
CONCLUSIONS: GA101 induced significant cell death in PBALL and PBLL and appears to be dependent in part on degree of $CD20^+$ expression and is active in $CD20^+$ lymphoblastic disease. Future xenograft studies are underway as well as comparative studies with rituximab.

85

10:15 AM

House Officer

Vitamin D Levels and Bone Density of Children with IBD: Experience of a Pediatric Digestive Disease Center in Northern Virginia

Vahe Badalyan, Stacie Townsend, Samantha Fish, Ian Leibowitz.
Pediatrics, Inova Fairfax Hospital for Children, Falls Church, VA.
BACKGROUND: Children with inflammatory bowel disease (IBD) have lower levels of Vitamin D than their healthy peers. Because Vitamin D is essential for bone mineralization, its deficiency may result in lower bone density. IBD children may need regular measurements of their Vitamin D levels and bone densities so that their intake of Vitamin D and bone health can be optimized. However, currently no guidelines exist on frequency of such monitoring or optimal doses of Vitamin D supplementation.
OBJECTIVE: This is a cross-sectional study of Vitamin D levels and bone density of children with IBD seen at a pediatric digestive disease center in Northern Virginia.
DESIGN/METHODS: Charts and electronic medical records of 254 children seen at our center between 2006 and 2010 were reviewed.
RESULTS: Data on Vitamin D levels were available on 215 children. Vitamin D levels were categorized into three groups: serum levels <20 ng/ml = deficiency, 20 – 30 ng/ml = insufficiency, and >30 ng/ml = normal levels. The average serum Vitamin D level was 26 ng/ml, with standard deviation of 10.7 ng/ml. 56 children were Vitamin D deficient (mean Vit D level = 14.17, CI 12.92-15.43), 97 had Vitamin D insufficiency (mean Vit D level = 24.66, CI 24.02-25.31), and 62 had normal Vitamin D levels (mean Vit D level = 39.32, CI 37.41-41.24).
Data on bone density using dual X-ray absorptiometry (DXA) technique was available on 126 children. DXA results were categorized into the following groups: lowest z- or t- score <-2.5 = osteoporosis, score from -2.5 to <-1 = osteopenia, score from -1 to 1 = normal bone density, score >1 = high bone density. The average DXA z or t-score was -1.2 standard deviations below the mean for age. Using the above-defined criteria, a total of 14 children had osteoporosis, 52 had osteopenia, 57 had normal bone density and 3 had high bone density.
There appeared to be significant correclation between Vitamin D levels and DXA results (Pearson correlation -0.23, p = 0.014).
CONCLUSIONS: Significant proportion of children with IBD had low Vitamin D levels and bone densities. Periodic monitoring of levels and supplementation of calcium and vitamin D is needed to ensure good bone health.

General Pediatrics I
Platform Session

Saturday, March 26, 2011
8:15 AM-10:30 AM

86

8:15 AM

House Officer

Effectiveness of a Brief Health Education Intervention To Address Chronic Malnutrition in Quito, Ecuador

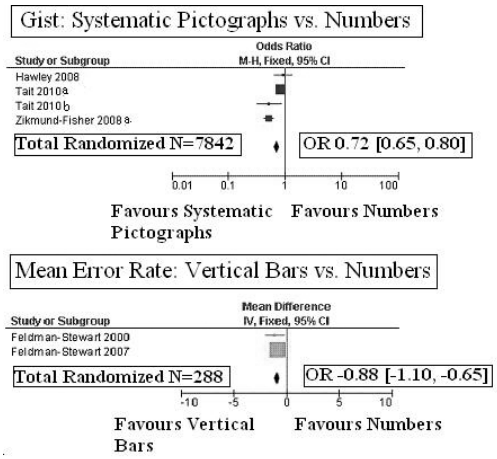
Preetha J. Iyengar, Kathryn Scharbach, Sandra F. Braganza.
Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY.
BACKGROUND: Chronic malnutrition is associated with childhood mortality and affects up to a quarter of children in Ecuador. In southern Quito, lack of knowledge and poor diet diversification are contributing factors. Local collaborators have identified health education as an area in need of improvement.
OBJECTIVE: To assess the effectiveness of a health education intervention given at a government-run clinic in Quito, Ecuador.
DESIGN/METHODS: Public health researchers and local collaborators created a 20-minute workshop and pictogram handouts. The workshop was offered daily over a 4-week period and described the effects of protein malnutrition, identified local protein sources, and utilized interactive questions to reinforce the message. After the workshops, a handout highlighting the main points and showing local, affordable protein sources in pictures was provided to a subset of participants in a quasi-randomized manner. Oral questionnaires were developed to assess protein nutrition knowledge and confidence and protein intake pre and post-workshop. A home visit conducted 3 weeks later reassessed knowledge, confidence and protein intake. Knowledge scores were based on number correct of 13 questions. Confidence was rated using a 4-point scale. Protein intake was monitored using a validated food frequency survey.
RESULTS: A total of 98 participants completed pre- and post-workshop questionnaires and 57 completed home visit questionnaires. Participants were 88% women with a median age of 31 years and a median of 2 children. Knowledge scores increased from 73% to 87% (p<0.0001) pre- to post-workshop. Confidence improved with 42% reporting an increase and 57% staying the same (p<0.0001). Knowledge and confidence scores did not change significantly from post-workshop to home visit. The median number of times that participants recalled eating a surveyed source of protein increased by 4.5 times per week among those who received a handout, compared to 1.25 times per week among those who did not receive a handout (p=0.02).
CONCLUSIONS: Knowledge and confidence increased after protein education workshops with excellent retention at home visits. The utilization of pictogram handouts in educational sessions improved protein intake. These findings support working with the Ecuadorian government to further develop one-time, concise educational interventions to improve dietary behavior.

87

8:30 AM

Which Visual Formats of Complex Data Best Help Patients Make Informed Health Decisions?

Sanghee Suh, Ursula Guillen, Haresh Kirpalani.
Division of Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Department of Clinical Epidemiology and Biostatistics, McMaster University, Ontario, Canada.
BACKGROUND: Shared patient decision-making requires that patients, or surrogate decision-makers in pediatrics, accurately understand risks and benefits. Different formats of presentation may enhance or worsen comprehension.
OBJECTIVE: To systematically review randomized trials assessing the comprehension of different formats of health-related risk statistics.
DESIGN/METHODS: PubMed, MEDLINE, CINAHL, PsychInfo and Google Scholar databases were searched up to September 2010. Articles were included if randomized studies compared which formats of health risk statistics improved the outcome of knowledge and interpretation of data.
RESULTS: Of 1682 publications, 16 were eligible and 9 were included in the final analysis. Three types of knowledge outcomes were identified: (1) verbatim (the ability to interpret numerical values) (2) gist (the ability to choose the lowest-risk treatment option) and (3) mean error rate (identifying the larger or smaller quantity between two health risks). These papers tested 7 formats: simple numbers, pie graph, line graph, horizontal bar graph, vertical bar graph, random pictograph (displaying risk statistics in randomly shaded icons) and systematic pictograph (displaying risk statistics in groups of shaded icons). Systematic pictographs resulted in better comprehension/interpretation than simple numbers judged by either verbatim (OR 0.52; 95% CI 0.46 to 0.58, p<0.01) or gist knowledge (Fig. 1). For mean error rates, vertical bar graphs and systematic pictographs (OR -0.70; 95% CI -0.95 to -0.46, p<0.01) resulted in better comprehension/interpretation (Fig 1). Pie graphs resulted in more errors when compared to the use of simple numbers (OR 1.22; 95% CI 0.76 to 1.69, p<0.01); random pictographs also lead to more errors compared to simple numbers (OR 0.51; 95% CI 0.13 to 0.89, p<0.01).



CONCLUSIONS: Vertical bar graphs and systematic pictographs are more effective formats for presenting health risk information to adults. Pie graphs and random pictographs appear to be ineffective in communicating risk information.

88

8:45 AM

Does Umbilical Cord Length — An Indirect Measure of Fetal Activity — Predict Hyperactivity in Grade School Children?

Andrew Adesman, Jennifer K. Leung, Ruth Milanaik, Sarah A. Kiem.
North Shore-LIJ Health System, New Hyde Park, NY; Nationwide Children's Hospital, Columbus, OH.
BACKGROUND: Although fetal *hypo*activity has been associated with short umbilical cord length (UCL) and neurodevelopmental disorders, the clinical implications of fetal *hyper*activity (HA) are less clear. While two small prospective studies found no association between fetal movements and activity at 18 months or 6 years, a retrospective study reported a positive association between fetal and childhood HA. To date, there has been no large-scale, prospective analysis of fetal HA or UCL and later HA.
OBJECTIVE: Using data from the National Collaborative Perinatal Project (NCPP), a large-scale prospective cohort study of pregnancy and child health to age 8 years, our goal was to examine the relationship between UCL as an indirect measure of fetal activity and later childhood inattention (IA), impulsivity (IMP), and HA. We hypothesized that children with a longer UCL are more active *in utero* and more likely to later exhibit signs of IA, IMP, and/or HA.
DESIGN/METHODS: The NCPP followed 59,407 pregnancies; we limited analyses to 25,485

off-spring for whom UCL and follow-up data at least to age 7 was available. Exclusion criteria were prematurity, SGA, LGA, oligo- or polyhydramnios, or multiple gestation. Children were also excluded if neurological risk factors were present (e.g., blind, deaf, MR, CP). The primary outcome variables were ratings of IA, IMP and HA during testing by a psychologist at ages 4 and 7, and a speech-language pathologist at age 8. Multivariate logistic regression was performed; Odds Ratios (OR) were adjusted for sex, SES, race, and maternal age, smoking, & parity.
RESULTS: Increasing UCL (5-cm increments) was associated with IA at age 7 (adjusted OR 0.979; 95% CI [0.961, 0.997]) and at age 8 (adjusted OR 0.942 with 95% CI [0.891, 0.996]). Although increased UCL was associated with IA+IMP+HA (combined) at age 4, (unadjusted OR 1.029 with 95% CI [1.000, 1.058]), this was not significant when adjusted. There was no relationship between UCL and IMP or HA at ages 4, 7, or 8 years.
CONCLUSIONS: Contrary to our hypothesis, a longer UCL was not associated with IMP or HA when assessed during testing at ages 4, 7 and 8 years. Unexpectedly, a shorter UCL was associated with IA when independently assessed at ages 7 and 8. If UCL is a reliable indirect biometric marker of fetal activity, then mothers who report fetal HA may be reassured knowing there is no increased association with observed IMP or HA at ages 7 and 8 years.

89

9:00 AM

Fellow in Training

Pretesting Health Reform: Impact of State Laws Extending Parents' Health Insurance Coverage to Young Adults

Alexander B. Blum, Joseph S. Ross, Lawrence C. Kleinman.
Health and Evidence Policy, Mount Sinai School of Medicine, New York, NY; General Internal Medicine, Yale University School of Medicine, New Haven, CT.

BACKGROUND: As part of recently enacted national health care legislation, insurance companies must allow young adults to remain eligible for their parents' health plan until age 26. Nearly half of all states had previously enacted similar laws.
OBJECTIVE: To examine the impact of state laws extending coverage to young adults and their access to care.
DESIGN/METHODS: We examined changes in access to care in 5 states enacting laws extending coverage to young adults in 2005 or 2006 and compared to 26 states without any such law. We used data from the CDC's Behavioral Risk Factor Surveillance System, a representative survey of community-dwelling adults, selecting 19-23 year olds from each state in years before (2002-2004) and after (2008-2009) state law enactments. We studied 4 measures of access to care: health insurance coverage, identification of a personal physician (PMD), physical exam from a physician within the past 2 years, and report of having foregone care in the past year due to cost.
RESULTS: All measures of access to care improved significantly ($p<0.001$; Table) in states that enacted laws compared to states that had not. As documented in the right hand column of the table, we found differential improvement in health insurance coverage rates (3.8%), identification of a personal physician (1.6%), physical exam rates (3.0%), and decreased need to forego care due to cost (3.9%).

Results Summary

States	N	% Before	% After	Δ	Difference (95% CI)
Health Insurance					
With laws	7,561	71.3	75.2	3.9	3.8% (3.6, 3.8)
Without laws	13,252	68.3	68.4	.1	
Personal doctor (PMD)					
With laws	6,115	64.5	68.6	4.1	1.6% (1.5,1.7)
Without laws	29,757	60.4	62.9	2.5	
Physical exam within 2 years					
With laws	3,286	81.3	83.4	2.1	3.0% (3.0, 3.1)
Without laws	16,552	78.0	77.0	-0.9	
Forgone care due to cost					
With laws	4,874	18.5	16.1	-2.4	-3.9% (-4.0, -3.8)
Without laws	21,865	18.7	20.2	1.5	

CONCLUSIONS: Compared to states which did not enact such legislation, states which required insurance plans to extend parent health insurance benefits beyond age 19 showed increases in the percent who were insured, identified a personal physician, received a physical exam, and a decrease in those who went without needed care due to cost. These findings suggest that this requirement within national health care reform is likely to improve access to care for young adults.

90

9:15 AM

Do Questions about Parent Concerns Provide Adequate Surveillance?

Emily N. Neger, Shela Merchant, Brandi S. Henson, R. Christopher Sheldrick, Ellen C. Perrin.
Pediatrics, Floating Hospital, Tufts Medical Center, Boston, MA.

BACKGROUND: The American Academy of Pediatrics recommends surveillance of children's behavior and development by asking parents "Do you have concerns about your child's behavior? Development? Learning?", but no published data confirm the usefulness of these questions.
OBJECTIVE: As part of a larger questionnaire, parents were asked these 3 questions. Data were analyzed to determine how well parents' concerns reflected problems identified by validated screening measures.
DESIGN/METHODS: 432 parents of children ages 2 months to 5.5 years were recruited from primary care pediatric waiting rooms. In addition to specific questions about development, behaviors, and concerns, parents completed the Ages and Stages Questionnaire-Social/Emotional (ASQ-SE), a behavioral screener, and the Ages and Stages Questionnaire (ASQ-3), a developmental screener. Using clinical scores on the ASQ-3 and ASQ-SE as criteria, children were classified as having a) coexisting developmental and behavioral problems, b) developmental problems alone, c) behavioral problems alone, or d) no identified problems.
RESULTS: 106 parents (23%) reported having a concern about their child on one or more questions. Multinomial logistic regressions showed that concerns about behavior and development were each independently associated with coexisting positive screens in both domains. Only concerns about behavior predicted at risk scores on the ASQ-SE alone and no type of concerns predicted at risk scores on the ASQ-3 alone. Concerns about learning were not predictive of any category.

Table. Frequency, sensitivity & specificity of parent concerns

	ASQ only	ASQ-SE only	both positive	neither (no risk)
Concerns about development	2%	2%	3%	8%
No concerns	13%	4%	3%	66%
sensitivity	.1	.38	.48	
specificity				.89
Concerns about behavior	2%	4%	2%	7%
No concerns	13%	2%	3%	66%
sensitivity	.15	.66	.44	
specificity				.90
Concerns about learning	1%	1%	2%	6%
No concerns	13%	5%	3%	68%
sensitivity	.09	.21	.4	
specificity				.92

CONCLUSIONS: While only a small number of children recognized to be at risk by formal screening were identified by their parent's stated concerns (modest sensitivities), very few of the children in the normal range on screening tests aroused a concern in their parents (high specificities).

91

9:30 AM

House Officer

Comparison of Anthropometric Measures in the Longitudinal Assessment of Fat Mass

Thao-Ly T. Phan, Michelle M. Maresca, Hossain Jobayer, George A. Datto.
Nemours, A.I. duPont Hospital for Children, Wilmington, DE.

BACKGROUND: Many studies have examined the relationship between anthropometric measures and body fat mass (FM) at a single time point with variable results. However, no study to date has examined the longitudinal relationship between FM and anthropometric measures. Understanding which anthropometric measures are most clinically useful over time would help inform providers who manage obese patients over time.
OBJECTIVE: To determine which anthropometric measure best correlates with change in FM over time.
DESIGN/METHODS: We performed a retrospective cohort study of 76 obese patients (mean BMI of 38.04, S.D. 8.15) between 9 and 18 years of age who presented to a single provider at a weight management clinic between 2005 and 2010. For each patient, during both an initial and subsequent visit to the clinic, FM was measured by bioelectrical impedance analysis using the RLJ Quantum X. During each visit, the following measures were also obtained: BMI, waist circumference (WC), hip circumference (HC), waist to height ratio (WHtR), waist to hip ratio (WHR), and neck circumference (NC). We calculated partial correlation coefficients (adjusting for age, gender, and race) to test the relationship between the percent change in each anthropometric measure per month and the percent change in FM per month.
RESULTS: Change in BMI over time correlated better with change in FM over time than any other anthropometric measure (see table below). This was statistically significant ($p < 0.01$) and held true even when racial and gender groups were assessed separately ($p < 0.01$).

Correlation with % Change FM per Month

	% Change BMI per Month	% Change WC per Month	% Change WHtR per Month	% Change NC per Month	% Change HC per Month	% Change WHR per Month
Total (n=76)	0.93	0.70	0.69	0.49	0.49	0.37
Male (n=38)	0.96	0.81	0.81	0.45	0.56	0.50
Female (n=38)	0.92	0.76	0.73	0.57	0.51	0.39
White (n=46)	0.93	0.74	0.73	0.34	0.48	0.39
Non-White (n=30)	0.94	0.68	0.67	0.74	0.49	0.36

All correlations with $p < 0.05$

CONCLUSIONS: In this study, change in BMI was strongly correlated with change in FM over time. Other anthropometric measures do not appear to add to the assessment of change in FM for any subgroup. We suggest that in the clinical management of obese children, BMI is an adequate measure of change in FM.

92

9:45 AM

Improving Response Rate for Mailed Pediatric Questionnaires: Effect of Cover Letter Tone and Literacy Level

Andrew Adesman, Alison Cohn, Nina Kohn, Helen Papaioannou, Ruth Milanaik.
North Shore-LIJ Health System, New Hyde Park, NY; Washington University, St. Louis, MO.

BACKGROUND: Questionnaires are an important research tool to assess pediatrician practices and knowledge; however, response rate (RR) by physicians is notoriously low, which can skew or bias results.
OBJECTIVE: The aim was to determine if RR by pediatricians for a mailed questionnaire could be increased by adding humor or a personal plea in the cover letter (CL). A secondary aim was to assess the impact of the cover letter's readability.
DESIGN/METHODS: A 6-minute questionnaire on parenting myths was mailed to 5,000 primary care pediatricians in the U.S. Four different CLs were created to go to 4 randomly selected groups of 1250 pediatricians. One CL had a humorous tone, and one had an imploring/desperate tone (written by a 3rd year fellow required to complete the research project for her training). The 2 control CLs were were written in a dry tone: one at a 5th grade reading level (RL) and one at a college RL.

Cover Letter Characteristics

Tone of Letter	Total # Words	Total # Sentences	Words per Sentence	Flesch Reading Ease*	Flesch-Kincaid Grade Level	
Dry - 5th Grade	271	21	11.3	73.8	5.7	
Dry - College	295	12	20.3	28.6	13.9	
Humorous	412	25	15.6	52.3	9.8	
Desperate	380	21	16.8	42.9	11.4	

* Flesch Reading Ease: lower score = easier to read

The mailings were otherwise identical; all included a postage-paid return envelope. RR was the outcome variable. Chi-square analysis examined whether RR varied by CL; logistic regression examined an association between RR, CL, and gender.

RESULTS:

Response Rate by Cover Letter

	Male	Female	Total
Total # mailed†	2034	2960	4994
Total # responded	413	578	991
Response Rate: Total	20.30%	19.53%	19.84%
-- Dry, 5th Gr version	16.70%	17.82%	17.37%
-- Dry, College version	18.27%	17.15%	17.61%
-- Humorous version	19.84%	17.73%	18.57%
-- Desperate version	26.25%	25.51%	25.82%

† 5,000 mailed; gender data missing on 6 cases

There was a significant association between RR and CL version ($p<0.0001$). Although humor did not appear to improve RR, the letter with the desperate plea had the highest RR. No gender difference was noted in RR overall or RR for any specific CL version. RR did not differ with the CL ease of reading (5th Grade vs. College level).

CONCLUSIONS: RR was not influenced by a humorous tone nor by the ease of reading. Male and female pediatricians were more likely to answer a questionnaire when the cover letter had an emotional tone with a desperate appeal.

93

10:00 AM

Development and Initial Validation of the Preschool Pediatric Symptom Checklist (PPSC)

Shela Merchant, Brandi S. Henson, R. Christopher Sheldrick, Ellen C. Perrin, J. Michael Murphy.

Pediatrics, Floating Hospital, Tufts Medical Center, Boston, MA; Child Psychiatry, Massachusetts General Hospital, Boston, MA.

BACKGROUND: The American Academy of Pediatrics' Task Force on Mental Health recommends behavioral health screening with a validated instrument for all children. The Pediatric Symptom Checklist (PSC) is a validated and frequently-used measure for children over 4 years of age.

OBJECTIVE: In the course of creating a comprehensive instrument to screen for developmental-behavioral problems in young children, we created a downward extension of the PSC for children 1.5 - 5 years of age, and carried out an initial validation.

DESIGN/METHODS: After review of available instruments that solicit parent reports about young children's behavior, we wrote and pilot-tested 73 questions relevant to preschool-aged children. We enrolled 648 parents from pediatric waiting rooms and specialty clinics to complete the PPSC questions, the Child Behavior Checklist (CBCL), the Ages & Stages Questionnaire-Social/Emotional (ASQ-SE), and demographic data. We chose final PPSC items using Principal Components Analysis (PCA) and Item-Response Theory (IRT), and calculated the sensitivity and specificity of the PPSC in detecting performance on the CBCL and ASQ-SE.

RESULTS: PCA identified four factors: Internalizing, Externalizing, Attention Problems, and Child Care Issues. IRT was used to determine the discrimination and difficulty of each item. We chose 24 items based on these analyses. Cronbach's alphas for scales ranged from .77 to .81. Sensitivity and specificity are presented in Table 1.

Table 1. Sensitivity & Specificity of the Preschool Pediatric Symptom Checklist (PPSC) (24 items)

	CBCL	ASQ-SE
In primary care pediatrics:		
Sensitivity =	.70	.65
Specificity =	.85	.88
In specialty clinics:		
Sensitivity =	.97	.75
Specificity =	.71	.82

CONCLUSIONS: The PPSC assesses four domains that are highly relevant to mental health for young children and can be reliably reported by parents using a brief instrument. The PPSC shows promise as a brief screening instrument for use in pediatrics. Further research using independent samples is needed and in process.

94

10:15 AM

House Officer

Doing the FDA's Bidding: Off-Label Pediatric Drug Studies in the Medical Literature

Douglas Nassif, Luis Gamboa, Priya Bhasker, Susannah Olnes, Karen Carpenter.

Department of Pediatrics, Inova Fairfax Hospital for Children, Falls Church, VA.

BACKGROUND: Since the establishment of the US Food and Drug Administration (FDA) in 1906, the FDA has scrutinized new drugs to determine their safety and efficacy. Once a drug is approved by the FDA, physicians are free to use it in other populations, for different indications and at varying dosages from those for which it was approved. This "off-label" use is protected because the FDA does not have regulatory power over the actual practice of medicine by physicians. Off-label prescribing has many benefits: it can lead to the discovery of new indications, allow testing in children that had not taken place while in Investigational New Drug (IND) status, and can avoid the long and costly process of modifying FDA labeling.

OBJECTIVE: To examine the impact of off-label drug studies published in high impact journals.

DESIGN/METHODS: Five high impact medical journals were examined for the publication of both FDA-approved and off-label drug studies. Those articles reviewing a specific medication prescribed to a child less than 18 years of age in the *Journal of the American Medical Association*, *The New England Journal of Medicine, Pediatrics*, *Journal of Pediatrics*, and *Archives of Pediatrics and Adolescent Medicine* from November 2009 to October 2010 were evaluated.

RESULTS: A total of 889 articles were reviewed; 98 (11%) articles discussed a total of 146 medications. When examined by country of the lead author, almost one half, 46% (45/98), of the articles originated outside of the USA, with Canada, 9%, and Australia, 9%, the most frequent non-US contributors. Comparing US authors to non-US authors, non-US authors were more likely than US authors to submit and have published an off-label drug study, 63% vs 37% ($p = 0.026$). When funding by pharmaceutical companies was explored, US authors and non-US authors, 22% vs 18%, were equally likely to accept drug company dollars ($p = 0.80$).

CONCLUSIONS: Pediatric research involving off-label drugs is responsible for one half of the drug study articles currently published in high impact journals in the US. One-half of all drug studies published in US journals are performed outside the US. Most (80%) of all pediatric drug studies are not funded by industry.

General Pediatrics - Vulnerabilities Platform Session

Saturday, March 26, 2011
8:15 AM-10:30 AM

95

8:15 AM

House Officer

Urine STD Screening of Pediatric Patients Presenting to the Emergency Department with Behavioral/Psychiatric Complaints. Are They at High Risk of Infection?

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BACKGROUND: A 2008 CDC report on sexually transmitted disease (STD) activity found a continued unacceptably high level of disease and recommended screening specific populations to reduce the rate of STD. Studies have established the connection between patients with known psychiatric disorders and high incidence of risk taking behaviors. High risk taking behavior in teens can increase exposure to STD's.

OBJECTIVE: To determine if adolescent patients seen in the the Pediatric ED for psychiatric evaluation represent a high risk group that should be specifically targeted for routine urine STD screening.

DESIGN/METHODS: Subjects were recruited from patients who presented to the St. Barnabas Hospital Pediatric Emergency Department (PED) a mid sized urban community hospital with an annual census of 25,000 patients < 18 years of age. The study group included patients 12-17 years of age presenting for psychiatric or behavioral evaluations to the PED. Patients were excluded if they had autism, significant mental retardation or were unable to give their verbal understanding and consent due to sedation. A matched cohort of patients presenting with non-psychiatric complaints were recruited as a control group. Urine was collected in GEN-PROBE® specimen collection tubes for laboratory analysis.

RESULTS: 160 behavioral health patients were invited to participate, 36 refused, 6 were excluded and 4 patient specimens were lost or insufficient, leaving 114 subjects. 93 control samples were collected (5 refused). The groups were similar in gender, but the control group was older (15.1 ± 1.5 vs 14.5 ± years $p=.001$). A total of 8 patients had positive tests for any STD (7 chlamydia and 1 gonorrhea), 3 in the behavioral health group (2.7%) and 5 in the control group (5.4%), p=NS. 6.7% of females tested positive and 1% of males ($p=.03$). When controlling for age by logistic regression, there was still no difference in STD rate between the study and the control groups.

CONCLUSIONS: The data suggests that patients presenting to a PED with behavioral/ psychiatric complaints are not at higher risk of STD compared with patients with a non behavioral/ psychiatric complaint. Most patients with STD identified through screening were female. Females adolescents should be targeted for screening, but patients with behavioral/ psych complaints are not at increased risk of STD.

96

8:30 AM

Impact of Shared Decision Making on Behavioral Impairment among US Children with Special Health Care Needs

Alexander Fiks, Russell Localio, Stephanie Mayne, Evaline Alessandrini, James Guevara.

The Children's Hospital of Philadelphia, Philadelphia, PA; University of Pennsylvania, Philadelphia, PA; Cincinnati Children's, Cincinnati.

BACKGROUND: The Institute of Medicine has prioritized shared decision making (SDM), yet little is known regarding the impact of SDM on behavioral outcomes for children.

OBJECTIVE: To assess the impact of SDM on behavioral impairment for US children with special health care needs (CSHCN).

DESIGN/METHODS: CSHCN 5 -17 years in the 2002-2006 Medical Expenditure Panel Survey (MEPS) were followed longitudinally for 2 years. Our primary outcome was behavioral impairment, assessed through the validated 13 item Columbia Impairment Scale (CIS, Score≥15 indicates impairment). SDM (high, medium, low) was defined by a latent class analysis based on 7 items in MEPS addressing clinicians' involving families in decisions, explaining all options, communicating clearly, respecting families' preferences and concerns, listening carefully, and taking enough time. We used generalized linear models to assess the impact of change in SDM from year 1 to 2 (increase, decease, same) on the CIS score, multinomial regression to assess the impact of SDM on change in impairment (becoming unimpaired, impaired, or no change), and logistic regression to assess the impact of SDM in year one on impairment in year 2, controlling for baseline impairment. We considered children with asthma and ADHD in secondary analyses.

RESULTS: Table 1 details outcomes in each SDM group. Among 2282 subjects representing 9.6 million CSHCN, increasing versus unchanged and decreasing SDM was associated with a 1.2 (P=.02) and 1.7 (P=.01) point decrease on the CIS score, respectively. Impaired CSHCN were less likely to remain impaired if SDM increased versus remained unchanged (p=.04). Higher levels of year 1 SDM predicted less impairment in year 2 in the overall population (OR=0.27, p<.001), among those with asthma (OR=0.23, p<.001) and ADHD (OR=0.14, p=0.055).

Change in Outcomes by SDM Pattern

	SDM Increase, n=391	SDM Same, n=1543	SDM Decrease, n=348
CIS Score Year 1	11.7	10.1	11.7
Year 2	11.2	10.8	12.9
Change (95% CI)	-0.5 (-1.5, 0.5)	0.7 (0.3, 1.1)	1.2 (0.2, 2.3)
% CSHCN Impaired Year 1	40.8	34.6	38.5
Year 2	37.6	35.9	44.1
Change	-3.2 (-10.6,4.3)	1.3 (-1.9, 4.4)	5.6 (-1.3,12)

CONCLUSIONS: Increasing SDM is associated with decreased behavioral impairment and higher baseline SDM predicted a greater decline in impairment in year 2. Results support research to develop and evaluate interventions to foster SDM for CSHCN.

97

8:45 AM

Utilization of Onsite Domestic Violence Services at a Pediatric Hospital: A 4-Year Review

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BACKGROUND: Exposure to Domestic Violence (DV) has profound adverse effects on children. As a result, the AAP has recommended routine screening and intervention on behalf of affected families. In response, St. Christopher's Hospital for Children (SCHC) has instituted hospital wide DV training for residents and staff as well as routine screening of all female caregivers. To support these efforts SCHC has had a fulltime, onsite DV counselor since 2005.

OBJECTIVE: To describe the utilization of onsite DV services by the medical and social work staff in both the inpatient and outpatient settings at SCHC.

DESIGN/METHODS: Retrospective review of case records from DV victims referred to the onsite DV counselor between September 2005 and February 2010. Descriptive statistics were used to examine the number of referrals per unit, referral source (type of health care provider or staff member), time spent by DV counselor for initial consultation, services provided to DV victim and DV victim demographics.

RESULTS: Over the 46 month study period the DV counselor responded to 453 identified cases of DV. 72% of victims were identified by routine screening, 26% by risk-based screening. 36% of DV victims were identified in the primary care clinics, the remainder came from other hospital departments (26% inpatient units, 11% Emergency Department, 13% outpatient subspecialty clinics, 7% child protection clinic, 4% self referred/employees, 4% other). The most common referral source was social workers (55%), followed by attending physicians (17%), residents (13%), nurses (7%), and self-referrals (4%). Referral patterns varied over time with approximately 6 to 22 new referrals each month. The average initial DV consultation required 42 minutes with 33% requiring one or more hours of intervention. The longest cases required up to 300 minutes of intervention. The median age of DV victims was 25. 44% were Latina, 40% African American. Supportive counseling, housing support, safety planning, and legal advice were the services most often provided to DV victims.

CONCLUSIONS: DV services are frequently used across the inpatient and outpatient settings at SCHC. Most referrals come from hospital-based departments. Routine DV screening yielded more positive screens than did risk factor-based screening. Given the frequency of DV service utilization and the significant impact of DV exposure on child health, pediatric hospitals and practices should strongly consider onsite DV services.

98

9:00 AM

Association of Shared Decision Making with Health Care Expenditures and Utilization among US Children with Special Health Care Needs

Alexander G. Fiks, Stephanie Mayne, James P. Guevara, Evaline Alessandrini, Russell Localio.

The Children's Hospital of Philadelphia, Philadelphia, PA; University of Pennsylvania, Philadelphia, PA; Cincinnati Children's, Cincinnati.

BACKGROUND: The Institute of Medicine has prioritized shared decision making (SDM), yet little is known regarding the impact of SDM on child health care expenses and utilization.

OBJECTIVE: To understand the association between SDM and health care expenses, emergency department (ED) visits, and inpatient (IP) stays among US children with special health care needs (CSHCN).

DESIGN/METHODS: CSHCN in the 2002-2006 Medical Expenditure Panel Survey (MEPS) were followed longitudinally for 2 years. Primary outcomes were health care expenses, ED visits, and IP stays. The primary exposure was change in SDM from year 1 to 2 (increase, decrease, same), defined by a latent class analysis of 7 items in MEPS addressing clinicians' involving families in decisions, explaining all options, communicating clearly, respecting families' preferences and concerns, listening carefully, and taking enough time. We used generalized linear models with variances adjusted for the survey design to assess the association of change in SDM from year 1 to 2 on change in health care expenses, ED visits, and IP stays. To avoid bias from outliers, the top and bottom 2.5% of values for expenses were truncated to the 2.5 and 97.5 percentile.

RESULTS: Table 1 details the change in outcomes in each SDM group. In our sample of 2858 subjects representing 12 million CSHCN, increasing SDM was associated with a $164 (p=.2) and $563 (p=.02) relative drop in health care expenses compared to SDM unchanged and decreased. As SDM increased, IP stays decreased by 4.6 (p=.03) and ED visits decreased by 8.5 (p=.04) per hundred patient years relative to those with SDM unchanged.

Change in Outcomes by SDM Pattern

	SDM Increase, n=483	SDM Same, n=1927	SDM Decrease, n=448
Mean Truncated Expenses Year 1 ($)	1747	1770	1721
Year 2	1488	1675	2025
Change (95% CI)	-259 (-497,22)	-95(-224,34)	304(-78, 686)
Mean # IP Stays Year 1 (per 100 CSHCN)	7.5	5.4	10.2
Year 2	3.5	6.0	7.4
Change	-4.0 (-7.9, -.04)	0.6 (-1.4,2.7)	-2.8(-9.0,3.4)
Mean # ED Visits Year 1 (per 100 CSHCN)	26.1	26.5	30.3
Year 2	14.7	23.6	25.5
Change	-11.4 (-18.2,-4.6)	-2.9 (-7.0, 1.2)	-4.8 (-14.8, 5.2)

CONCLUSIONS: We found that increasing SDM is associated with decreased health care expenses and utilization for CSHCN. Results suggest that interventions to foster SDM for CSHCN may impact these outcomes.

99

9:15 AM

Cervical Dysplasia in Immunocompromised vs. Immunocompetent Adolescents

Amanda M. Jacobs, Melissa J. Fazzari, Susan M. Coupey.

Pediatrics, Childrens Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY; Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Pap smear screening is recommended to begin at age 21. Adolescents with immune compromise may be at increased risk of cervical dysplasia [low grade (LGSIL) or high grade (HGSIL) squamous intraepithelial lesion]. There are no guidelines for Pap smear screening of immunocompromised women under age 21 and little data on prevalence of dysplasia in this group.

OBJECTIVE: To compare the prevalence of LGSIL & HGSIL in women <21 yrs with and without an immunocompromising diagnosis.

DESIGN/METHODS: Clinical Looking Glass (CLG), a searchable database for a large health care system, was used to query for females aged 12–20 years from 1997-2010 who had both a Pap smear & one of the following diagnoses as defined by ICD-9 codes: HIV; transplant; inflammatory bowel (IBD); Hodgkin's; lupus (SLE); and other immune deficiency (e.g. common variable, Wiskott-Aldrich). We randomly selected age & time matched controls from CLG who had Pap smears & none of the diagnoses listed above as well as no neoplastic, rheumatologic, renal, or autoimmune condition.

RESULTS: We identified 1,095 immunocompromised (IC) adolescents with 2,532 Pap smears and 1,202 controls with 2,499 Pap smears (2.3 & 2.1 Pap smears/patient; mean age at first Pap smear 18.6 & 18.2 years; race/ethnicity 54% & 44% Latino, 34% & 39% black, respectively). For the total IC group, 342/1095 (31%) had dysplasia (LGSIL or HGSIL) on at least one Pap smear as compared to 245/1202 (20%) of controls (p<0.001). Adolescents with HIV [97/158 (61%)], transplants [7/13 (54%)] & other immune deficiencies [20/65 (31%)] were more likely to have dysplasia than those with IBD [112/799 (14%)], Hodgkin's [4/29 (14%)], or SLE [2/31 (6%)]. When compared to the total IC group, HIV+ adolescents were significantly more likely to have dysplasia (61% vs 31% respectively, p<0.0001). None of the Pap smears indicated cervical cancer. Among the 2,532 Pap smears from the IC group, those done within one year of diagnosis were less likely to indicate dysplasia than Pap smears done more than one year after diagnosis [188/1598 (12%) vs 154/934 (17%) p<0.05].

CONCLUSIONS: Immunocompromised adolescents have a higher prevalence of cervical dysplasia than immunocompetent adolescents. Adolescents with HIV & transplants have the highest prevalence of cervical dysplasia.

100

9:30 AM

Suicidal Ideation and Intent in a Community Sample of Preadolescent Youth: A Case-Control Study

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BACKGROUND: Suicide is the third leading cause of death in adolescents in the US. While research has focused on better understanding of risk factors in older youth, less is known regarding preadolescents who endorse suicidal ideation and intent.

OBJECTIVE: To examine characteristics associated with endorsement of suicidal ideation and intent in youth ages 10-13 y.

DESIGN/METHODS: A community sample of 387 youth of mixed SES, enrolled in a prospective study assessing precursors of risk behaviors, was administered two questions related to suicide as part of Achenbach's Youth Self-Report (YSR): "I think about killing myself" and "I deliberately try to hurt or kill myself". 23 youth endorsed (Suicidal Ideation Endorser [SIE]) as follows: 21 (91%)"think about killing themselves", 11 (48%)"deliberately try to hurt or kill themselves", and 9 (39%) endorsed both. To assess factors associated with endorsement, each SIE was matched with a control (non-SIE) of the same age, gender, race, and, when possible, zip code, school, or grade. The 23 pairs were: 16 males, White (17)/African American (6), with mean age 11.6 ± 0.5. Groups were compared on: Impulsivity (IMP)(Eysenck I7 Junior Impulsivity Subscale); Sensation Seeking (SS)(Reduced Brief Sensation Seeking Scale); YSR Syndrome Scales (YSRSS); Executive Function (EF) 8 tasks; Youth medications and behavioral/emotional issues by Parent Report (PR); Parental Monitoring (PM); and self-report of Risk-Taking (RT)(CDC Youth Risk Behavior Survey, Monitoring the Future).

RESULTS: SIE had higher levels of IMP and SS (both p≤.001), were more likely in the borderline/clinical range for 5 of 8 YSRSS: Anxious/Depressed (p=.017); Withdrawn/Depressed (p=.047); Somatic Complaints (p=.029); Social Problems (p=.022); Aggressive Behavior (p<.001), and reported more RT (p=.004). SIE and non-SIE were similar in EF. More non-SIE (n=5) were on stimulants than SIE (n=1), but groups were similar in PM (p=.41) and PR of behavioral/emotional

issues (p=1.0). SIE and non-SIE families were similar in SES and marital status.
CONCLUSIONS: In this study, preadolescent SIE report significantly more problem behaviors than non-SIE. However, parental monitoring and parent report of problems do not differ between groups. Given these findings, we suggest that at-risk youth may be under-recognized at young ages, a time at which initiation of interventions may reduce adolescent risk behaviors and suicidal ideation.

101

9:45 AM

Fellow in Training

Maternal Factors Associated with Medicaid/SCHIP Renewal for Low-Income, Minority Children

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BACKGROUND: One-third of children living in the US are publicly insured, and many lose coverage despite remaining eligible. Gaps in coverage decrease access to a medical home, reduce preventive care visits and increase unmet medical needs. Lack of caregiver's knowledge about the renewal process has been a major barrier to retention of children in public insurance programs, especially among minorities. However, little is known about which caregivers may be at highest risk for suboptimal knowledge of renewal procedures.
OBJECTIVE: To examine the role of caregiver demographic factors on knowledge of Medicaid/SCHIP renewal for children from a low-income, minority population.
DESIGN/METHODS: A survey was developed to assess families' experience with discontinuous coverage and renewal procedures, including knowledge, attitudes and behaviors. A convenience sample of 64 mothers, of children aged 2-18 years attending a community health center, were interviewed. Associations between renewal process knowledge, attitudes and behaviors and sociodemographics were assessed using bivariable analyses and multivariable logistic regression.
RESULTS: Overall, 85% of children were Latino,13% Black, 94% enrolled in a Medicaid health plan, 2% in SCHIP and 4% in Medicaid. Most (75%) mothers were foreign born. 23% of children experienced loss of coverage since birth and 14% in the past year. Only 6% of mothers with less than a high school education knew when their child was due for renewal, compared to those who completed high school (33%) or were college educated (48%; p=0.02). The renewal process was reported as more difficult among mothers who lived in the US for <10 years compared to those with longer residence (46% vs. 12%; p=0.018). Younger mothers had less knowledge of mandatory renewal than older mothers (42% vs. 5%; p<0.0001). After controlling for education level, length of time in US and prior experience with coverage loss, younger mothers were far less likely to know about mandatory renewal than older mothers (AOR 0.07, 95%CI: 0.02- 0.34).
CONCLUSIONS: In this study sample, children with mothers who are younger, recently immigrated or have lower education level may be at heightened risk of losing coverage due to mothers' decreased awareness of the renewal process, lack of knowledge about timing of renewal and reported difficulties with renewal. These findings identify potential target groups for focused interventions to improve public insurance retention for minority children.

102

10:00 AM

House Officer

Improving Teacher Knowledge of Safety in Preschoolers

Michael A. Ferguson, Nancy Miller, Jennifer Friderici, Margaux Frank.
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BACKGROUND: Accidental injuries are the most common causes of morbidity and mortality in young children. A previous survey found that parents ranked daycare teachers as the second most trusted source for safety information after pediatricians.
OBJECTIVE: To assess daycare teachers' knowledge of critical safety issues involving young children before and after an educational presentation by a resident pediatrician.
DESIGN/METHODS: Prior to a 20 minute education session, 64 teachers at 4 sites of a non-profit daycare in Springfield, MA completed 22-item questionnaires evaluating knowledge of critical safety issues for young children and described their confidence in advising parents about safety issues. After the education session the teachers completed the same 22-item questionnaire. Knowledge scores were compared pre- and post-presentation.
RESULTS: A total of 44 teachers completed questionnaires (mean/SD age 36.0/11.9 years; mean/SD years of experience 13.4/9.2). Sixty-three percent (23/36) felt they were *somewhat comfortable* and twenty-seven percent (4/15) felt *very comfortable* in their safety knowledge. Pre-presentation, the average participant correctly answered 15.1 items; this knowledge score increased to 19.2 post-presentation (P<0.0001). Safety items showing greatest improvement were knowledge of safe water temperature settings (25.7% correct pre-education vs. 97.6% post, P<0.0001), age to advance to forward facing car seats (34.3% vs. 90.5%, P<0.0001), danger of infant walkers (65.7% vs. 100.0%, P<0.0001), and safe water depth to prevent infant drowning (65.7% vs. 92.9%, P<0.01). Forty-two percent (15/36) of teachers reported parents asking them for safety information. Most teachers (80.6%) indicated that they would appreciate more regular safety advice especially if offered by a pediatrician.
CONCLUSIONS: Parents rank daycare teachers just behind pediatricians as most trusted sources for safety information, yet daycare teachers exhibit considerable knowledge gaps of child safety. Pediatricians providing regular safety education to daycare teachers may lead to an increase in teacher knowledge, appropriate confidence in daycare teachers providing accurate safety information to parents and ultimately fewer accidental injuries.

103

10:15 AM

Swaddling and Safe Sleeping Practices in an Inner City Population

Barbara A. Kelly, Monique Mondesir, Natalia A. Isaza, Matilde M. Irigoyen.
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BACKGROUND: SIDS is the leading cause of death in infants and its prevalence is higher in African American populations. Sleeping prone and co-sleeping are major risk factors for SIDS. In 2009 a survey of mothers of infants <3 months of age seen at our inner city pediatric clinic found only 61% of infants were placed to sleep on their back and 51% were co-sleeping with parents. Swaddling, an ancient practice, has been shown to enhance infant comfort and decrease the likelihood of SIDS but has not been evaluated as a strategy to promote safe sleeping practices.
OBJECTIVE: to conduct a feasibility study to assess the acceptability of swaddling and its potential association with safe sleeping practices in an inner city patient population.
DESIGN/METHODS: A systematic sample of postpartum mothers whose infants were admitted to the term nursery and who planned to follow up in our pediatric clinic were offered a swaddling blanket, taught how to use it, and followed for up to 6 months to explore their use and satisfaction with swaddling and their implementation of safe sleeping practices.
RESULTS: 80 mothers were invited to participate: 70 were enrolled: mean age 24 yrs (17-42 yrs); 84% were African American, 10% Latinas; 21% had less than high school; 90% had Medicaid. 59% were primipara; 70% of fathers helped with the care of their infants; 60% of infants were initially breastfed; 78% were followed for up to 6 months. The majority of mothers (85%) swaddled their babies and 74% swaddled for at least 6 weeks. Most mothers felt their babies liked being swaddled (baby sleeps well, goes to sleep faster, comforts baby, it prevents scratching face) and very few (5%) expressed concerns (baby cannot move, too hot, too tight). When babies were swaddled, 95% were placed on their backs to sleep and 90% slept in a crib or bassinette. There was a positive correlation between swaddling and back sleeping (Spearman corr 0.287, p 0.03) at the one week visit but not at later visits.
CONCLUSIONS: In an inner city population, swaddling was well accepted and the vast majority of mothers used safe sleeping practices when swaddling their infants. Swaddling appears to be a promising public health strategy to promote safe sleeping practices in infants and should be explored further.

Pulmonary & Asthma Platform Session

Saturday, March 26, 2011
8:15 AM-10:30 AM

104

8:15 AM

Fellow in Training

An Intronic ABCA3 Mutation Responsible for Respiratory Disease

Amit Agrawal, Aaron Hamvas, F. Sessions Cole, Daniel Wegner, Carl Coghill, Keith Harrison, Lawrence Nogee.
Pediatrics, Johns Hopkins Hospital, Baltimore, MD; Pediatrics, Washington University, St. Louis, MO; Pediatrics, University of Alabama, Birmingham, AL.

BACKGROUND: Member A3 of the ATP-Binding Cassette family of transporters (ABCA3) is essential for surfactant metabolism. Mutations in coding regions of the ABCA3 gene cause neonatal respiratory failure (NRF) and interstitial lung disease inherited in an autosomal recessive fashion. Patients with a phenotype consistent with ABCA3 deficiency but without identified mutations have been reported.
OBJECTIVE: We tested the hypothesis that mutations in the non-coding regions of the ABCA3 gene may cause lung disease.
DESIGN/METHODS: Frozen lung tissue was obtained from a child who died from NRF and had a known disease-causing ABCA3 mutation (p.E690K) on one allele, but no second mutation identified. Total RNA was isolated and overlapping amplicons that spanned the full length of ABCA3 cDNA generated by RT-PCR. Genomic DNA was prepared from peripheral blood from the proband and his parents.
RESULTS: The proband's ABCA3 cDNA contained inserted sequence derived from intron 25. A genomic heterozygous C>T transition at the -98 position of intron 25 was identified, creating a new donor splice site which when coupled with an upstream potential splice acceptor site accounted for the inserted sequence. The inserted intronic sequence was derived from the allele in trans to that of the known mutation and segregation analysis confirmed the genomic IVS25-98T and p.E690K mutations were on opposite alleles. 7 additional infants with the phenotype of ABCA3 deficiency but whose genetic findings were uncertain also had the IVS25-98T mutation, 3 who were compound heterozygotes for IVS25-98T and a known mutation, and 4 homozygous IVS25-98TT. In contrast, IVS25-98T was not found on any of 326 chromosomes from control infants without lung disease.
CONCLUSIONS: The ABCA3 variant IVS25-98C>T resulted in aberrant splicing which is predicted to result in the insertion of 50 amino acids in the carboxy-terminal portion of ABCA3 and likely to alter the routing, stability, and/or function of the ABCA3 protein. The finding of this mutation in multiple unrelated patients with an ABCA3 deficient phenotype and unresolved genotype, but not in controls, supports it is a disease-causing mutation, and may account for additional cases of ABCA3 deficiency with negative genetic studies. These findings also highlight the importance of obtaining tissue suitable for RNA studies from biopsies or autopsies of children dying from unexplained respiratory failure.

105

8:30 AM

Cryptococcus Neoformans-Specific IgA in Bronchoalveolar Lavage Fluid from Children with Poorly-Controlled Asthma

Alfin G. Vicencio, Kalliope Tsirilakis, Xiaoxiao Lee, Arturo Casadevall, David L. Goldman.

Pediatrics, Cohen Children's Medical Center of New York, New Hyde Park, NY; Pediatrics, Albert Einstein College of Medicine, Bronx, NY; Microbiology, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Increasing evidence highlights the potential role of unrecognized fungal infection in asthma, including recent reports that anti-fungal therapy can improve symptoms in a select cohort of patients with fungal sensitization. Previously, we demonstrated in a rat model that a single intra-tracheal inoculation of *C. neoformans* results in chronic infection, sustained allergic inflammation in the lung, and airway hyper-reactivity. In addition, we demonstrated that infection with *C. neoformans* is exceedingly common in residents of the Bronx, an urban area known for its high prevalence of severe asthma, compared to rural areas where asthma is much less prevalent. Collectively, these findings suggest that *C. neoformans* may directly contribute to poorly-controlled asthma in Bronx residents. However, our previous diagnostic studies in children were based on IgG serology, which may simply reflect prior exposure. Thus, we utilized an IgA-based assay to analyze bronchoalveolar lavage fluid (BALF), a more direct reflection of pulmonary exposure.

OBJECTIVE: We sought to determine whether *C. neoformans*-specific IgA in BALF is more common from patients with poorly-controlled asthma compared to controls.

DESIGN/METHODS: Bronchoalveolar lavage fluid was collected from children undergoing clinically-indicated flexible bronchoscopy with lavage and analyzed for the presence of fungal-specific IgG and IgA.

RESULTS: Among 38 patients analyzed, 29 were asthmatic and 9 were non-asthmatic. The median serum IgE level for asthmatics and controls was 748 IU/ml (range 219-1765 IU/ml) and 8 IU/ml (range 1- 293 IU/ml), respectively. While BALF from asthmatics appeared to contain more IgG to fungi than non-asthmatic BALF, these differences were not statistically significant. Interestingly, IgA reactivity to *C. neoformans* was found in 16 of 18 (88%) asthmatics compared to 2 of 9 (22%) controls (Fisher's exact test, $p = 0.038$).

CONCLUSIONS: Increased IgA reactivity to *C. neoformans* is present in the BALF of Bronx asthmatics compared to controls and may reflect a local response to pulmonary cryptococcosis. Our previous and current findings support a potential connection between pulmonary fungal infection and the development of asthma among Bronx children. Additional studies are needed to understand this potential relationship and may lead to the development of new therapies for a subset of asthmatics with severe disease.

106

8:45 AM

Undergraduate Student

Corticosteroid Timing and Length of Stay for Children with Asthma in the ED

Stephanie Davis, Georgia Burke, Emily Hogan, Sharon R. Smith.

University of Connecticut, Storrs, CT; Department of Pediatrics, Connecticut Children's Medical Center, Hartford, CT; Department of Pediatrics, University of, Pittsburg, PA.

BACKGROUND: The current standard of care for children presenting to the ED with an acute asthma exacerbation is treatment with oral corticosteroids in conjunction with inhaled bronchodilators. With overcrowding and a trend of rising lengths of stay a problem for many EDs, early treatment with corticosteroids may offer an avenue to decrease the length of stay of pediatric asthma patients.

OBJECTIVE: To determine if administering corticosteroids to children with acute asthma exacerbations within one hour of arrival to the ED will decrease the mean length of stay when compared to those children receiving steroids an hour or later.

DESIGN/METHODS: A retrospective chart review of ED patients was conducted. All children between the ages of 2 and 18 years who presented to the ED with acute asthma exacerbations were included. Children receiving corticosteroids within 60 minutes of triage were assigned to Group 1 and children receiving corticosteroids 61 minutes or later were assigned to Group 2. Children were excluded if they had significant medical co-morbidites, were already on corticosteroids, or had been in the ED in the past 7 days. The primary outcome was mean length of stay in minutes.

RESULTS: Children in both groups had similar age, gender, and ethnicity. Table 1 shows the demographic breakdown of the study participants. Group 1 had a mean length of stay of 158 minutes (SD 78.6) while Group 2 had a mean length of stay of 185 minutes (SD 71.6), $p<0.0001$. Shorter stays in Group 1 were not affected by gender, ethnicity, or disposition.

	Receiving corticosteroid less than or equal to 60min from triage (Group 1)	Receiving corticosteroid greater than 60min from triage (Group 2)
	N=492	N=426
Age (SD)	6.66 (4.2)	6.64 (4.4)
Gender (female)	37%	39%
Caucasian	16%	22%
African-American	30%	22%
Hispanic	46%	48%
Discharged	83%	82%
Admitted	14%	17%
PICU	3%	1%
Length of stay minutes (SD)	158 (78.6)	185 (71.6)

CONCLUSIONS: Administering corticosteroids to pediatric asthma patients in the ED within an hour of triage is associated with a greater than or equal to 27 minutes average decrease in length of stay. For any one child, a decrease in length of stay by 27 minutes may not seem important; however, with large numbers of asthma visits this can have a significant impact on the ED.

107

9:00 AM

House Officer

Composite Clinical Respiratory Disease Scoring Tool: Does It Predict the Need for Hospitalization in Children with RSV Bronchiolitis?

Gaston I Zylberg, Ramkumar Natarajan, Fernanda Kupferman, Susana Rapaport, Lily Q. Lew, Rusly Harsono.

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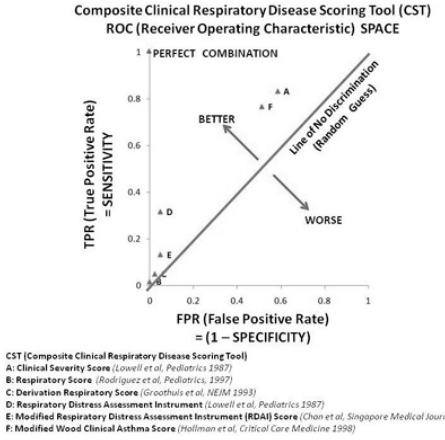
BACKGROUND: Respiratory syncytial virus (RSV) bronchiolitis is the most common diagnosis among hospitalized infants in the US. Composite clinical respiratory disease scoring tools (CST) for bronchiolitis have been developed to determine severity, but none are used to assist decision for hospitalization.

OBJECTIVE: To compare 6 different CST as predictors of morbidity in children with RSV bronchiolitis infection.

DESIGN/METHODS: We retrospectively studied previously healthy children ≤ 2 years with RSV bronchiolitis that were admitted to our urban community hospital for 2 consecutive RSV seasons (Oct'08 to Apr'10). The need for hospitalization (HOSP) was defined as: oxygen therapy (OXY), positive pressure ventilation (PV), apnea (AP), feeding problem (FEED) and frequent bronchodilator nebulization (NEB). We studied 6 different CST (A, B, C, D, E and F). Each child was assigned a total CST score at presentation and daily throughout hospitalization. A positive test was defined as any score above the highest for mild disease for any of the 6 CST. We computed sensitivity and specificity of each CST. Comparison was done with Fisher test and ANOVA (significant: $p < 0.05$).

RESULTS: Of the 101 children (mode gestational age 39 weeks, median corrected age 23.3 weeks) there were 52.5% OXY, 3% PV, 3% AP, 39.6 FEED and 59.4% NEB for need of HOSP. CST score children with more than mild disease was 73.3% in A, 1% B, 4% C, 20.8% D, 10% E and 66.3% F. All CST showed comparable trend in predicting disease severity and above the ROC random guess line. CST A (83%) and F (77%) had better sensitivity in identifying HOSP ($p = 0.40$).



CONCLUSIONS: Although clinical judgment remains the gold standard for admission of children with RSV bronchiolitis, we identified 2 CST that strongly predicted the need for hospitalization. When in doubt negative CST might reassures an outpatient care.

108

9:15 AM

Inhaled Corticosteroids Improve Short-Term Symptoms after a Pediatric Emergency Visit for Asthma: A Randomized Clinical Trial

Esther M. Sampayo, Joey Mechak, Amber Chew, Richard Scarfone, Joseph Zorc.

Division of Emergency Medicine, Children's Hospital of Philadelphia, Philadelphia, PA; University of Pennsylvania School of Medicine, Philadelphia, PA.

BACKGROUND: Few studies have evaluated the effects of initiating inhaled corticosteroids (ICS) on short-term clinical outcomes after a pediatric emergency department (ED) visit for acute asthma. National asthma guidelines recommend ED physicians consider initiating ICS but note the lack of evidence evaluating this recommendation.

OBJECTIVE: To determine whether a prescription for an ICS added to standard discharge therapy for children with persistent asthma leads to improved symptoms, asthma-related quality of life (ARQOL), rescue medication use, and functional disability during the 2 weeks after an ED asthma visit.

DESIGN/METHODS: This randomized clinical trial enrolled children age 1-18 years who met symptom criteria for persistent asthma but had not been prescribed controller medications prior to an acute asthma visit to an urban children's hospital ED. Intervention subjects received a one-month prescription for an ICS in addition to standard asthma therapy including a 5-day course of oral corticosteroids, education, and discharge instructions. Follow-up phone interviews were conducted at 2 weeks after the ED visit. Asthma symptoms, severity and ARQOL were assessed using validated measures.

RESULTS: 151 subjects were enrolled and baseline demographic, asthma history, ARQOL and severity measures were similar between study groups. Compared to parental report for controls, ICS subjects had reduced number of nights of cough while asleep, days of shortness of breath (SOB) while awake, and decreased rescue albuterol use at 2 weeks after the ED visit ($p=.04$) [See Table 1]. Functional limitations (i.e. missed school/work), ARQOL, and ED/PCP relapse did not differ between study groups.

Asthma Symptoms during the 2 weeks after ED visit

Symptoms while Awake				**Symptoms while Asleep**		
Median Days				Median Days		
	Control	ICS	P value	Control	ICS	P value
Cough	4	3	0.68	3	2	0.03
SOB	1	0	0.03	0	0	0.12
Wheeze	1	0	0.17	0	0	0.13

ICS=Inhaled Corticisteroids

CONCLUSIONS: For children with persistent asthma, initiating ICS at ED discharge reduced the number of nights with cough, days with SOB and use of rescue albuterol reported by parents during the 2 weeks after an ED visit. Potential short-term benefits may inform the decision to prescribe ICS after an ED visit.

109

9:30 AM

Relationship between Parental Health Literacy and Self-Efficacy with Managing Child Asthma

Iman Sharif, Debra Roter, Laurie Bauman, Roopa Chari, Tara Ketterer, Mary Ann Abrams, Katherine Freeman, Arthur E. Blank, Benard P. Dreyer, Ruth E.K. Stein.

Pediatrics, Nemours/A.I. duPont Hospital for Children, Wilmington, DE; Pediatrics, Albert Einstein College of Medicine/Children's Hospital at Montefiore, Bronx, NY; Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; Pediatrics, NYU School of Medicine, New York, NY; Iowa Health System, Des Moines, IA.

BACKGROUND: Few studies have tested the relationship between parental health literacy and self-efficacy with managing their child's illness. As the most common chronic condition affecting children, self-efficacy with managing asthma is of particular interest.

OBJECTIVE: To test the relationship between parental health literacy and self-efficacy with managing child asthma.

DESIGN/METHODS: We analyzed baseline data from an ongoing cohort study that enrolled parents of children with asthma at a primary care visit. Seventy-six percent of the children in this study had uncontrolled asthma, as measured by the Asthma Control Test. We used the Newest Vital Sign (NVS) a 6-item administered test to measure reading comprehension and numeracy. A trained research assistant administered a 22-item Caretaker Asthma Self-Efficacy survey (CASE) previously validated in the National Cooperative Inner-City Asthma Study. CASE scores range from 20 (best self-efficacy) to 100 (worst).

We used the NVS and CASE scores as ordinal variables, and used spearman correlation to test the relationship between them. We used education as an ordinal variable based on years of school completed. We used the Kruskal-Wallis rank sum test to compare median CASE scores across the NVS categories of "limited literacy" (0-1), "possible limited literacy" (2-3), and "adequate literacy" (4-6).

RESULTS: Complete data was available for 37 subjects; mean age(SD) was 36(10); 24% had completed less than a high school education, 33% had completed high school, and 43% had some post-high school education. 100% of subjects were Black; 100% were Medicaid recipients.

By NVS category, 26% scored limited, 40% possibly limited, and 34% adequate literacy. CASE ranged from 24(high self-efficacy) to 53, with a median value of 40.

Better self-efficacy was associated with younger age (rho=0.28, p=0.08), higher education (r=0.32, p=0.04), and higher NVS (rho=0.61, p<0.0001). The median value for CASE varied by NVS category: limited(48) vs. possibly limited(40) vs. adequate(36) literacy; p=0.0005.

CONCLUSIONS: This preliminary work suggests a relationship between parental health literacy and caretaker self-efficacy with child disease management. The NVS is a brief tool that may serve as a particularly useful measure for identifying parents with low self-efficacy for managing their child's asthma.

110

9:45 AM

House Officer

The Role of Pre-Operative Pulmonary Function Testing as a Screening Tool in Patients with Adolescent Idiopathic Scoliosis

Gina T. Coscia, Joshua P. Needleman, Lisa S. Ipp, Mary J. Ward.

Pediatrics, New York Presbyterian Hospital/Weill Cornell Medical College, New York, NY; Pediatrics, Hospital for Special Surgery, New York, NY.

BACKGROUND: Patients with Adolescent Idiopathic Scoliosis (AIS) routinely undergo Pulmonary Function Testing (PFTs) as part of their pre-operative evaluation prior to spinal fusion surgery.

OBJECTIVE: To evaluate the utility of eight years of pre-operative PFTs at a large spine service.

DESIGN/METHODS: A retrospective chart review was conducted for subjects with AIS as the primary diagnosis, ages 12-18 years, who underwent spinal fusion surgery between January, 2000 and December, 2007. The review yielded 200 subjects. Pulmonary function tests, degree of curvature, length of hospital stay, number of days on oxygen and number of days on mechanical ventilation post-operatively were recorded. Subjects with neuromuscular, congenital, or juvenile scoliosis were excluded.

RESULTS: Table 1 includes all descriptive data.

Variable	Mean	S.D.	Range	% of sample with normal PFT
FEV1% predicted	85.11	16.59	42-136	81%
FVC% predicted	93.06	16.9	48-153	92%
FEV1/FVC	81.74	9.2	59-98	84%
FEF 25-75%	76.9	22	28-135	75%
# of days in hospital post-operatively	6.5	1.4	2-16	-
# of days on oxygen post-operatively	0.5	0.8	0-8	-
Degree of curvature (primary curve)	41.87	13.5	15-80	-

Mean FEV1 %predicted, mean FVC % predicted, mean FEF25-75% predicted, and mean FEV/FVC all were within normal limits. Correlations between pulmonary function (FEV1, FVC, and FEV1/FVC) and number of hospital days and number of days on oxygen were zero-order and non-significant. PFT results showed no correlation with degree of curvature. In addition, using 60 degrees to define the index group, there was no correlation between degree of curvature and PFTs or length of stay.

CONCLUSIONS: The majority of subjects with AIS who underwent spinal fusion had normal PFTs. Abnormal PFTs were not associated with degree of curvature, length of hospital stay, or number of days on oxygen. Patients with AIS may not need to undergo pre-operative pulmonary function screening prior to surgery as most studies may be normal without other complicating factors. Defining which patients benefit from lung function testing may lead to more targeted testing, a reduction of medical costs to society, as well as fewer days of work and school missed unnecessarily for these patients and their families.

111

10:00 AM

Exercise Improves Lung Function & Habitual Activity in Children with Cystic Fibrosis

Shruti M. Paranjape, Laura A. Barnes, Kathryn A. Carson.

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BACKGROUND: Cystic fibrosis (CF) lung disease leads to progressive declines in lung function and exercise capacity. Developing routine exercise programs in CF may be beneficial since exercise is known to improve lung function and quality of life (QoL).

OBJECTIVE: Increasing activity in CF subjects with a 2-month exercise regimen leads to improved exercise capacity and other outcomes.

DESIGN/METHODS: Exercise capacity was assessed in CF subjects (6-16y) before and after a 2-month exercise regimen using the Modified Shuttle Walk Test (MSWT), a valid field test of exercise. Routine spirometric (FEV_1) and body mass index (BMI) data were obtained at two study visits along with two surveys, the Habitual Activity Estimation Scale (HAES) and the Revised CF Quality of Life Questionnaire (CFQ-R). Based on these data, a clinic physical therapist recommended a 2-month regimen of activities chosen by the subject. Change from baseline was analyzed using paired t-tests, and group comparisons were made using two-sample t-tests and Fisher's exact tests.

RESULTS: Fifty-eight subjects (37M, 21F) performed the MSWT before and after the 2-month exercise regimen. Mean±SD baseline FEV_1 (% predicted) was 98±17% and increased 1±10%. Mean baseline BMI percentile was 55±22 and increased 1±9. The mean baseline number of completed shuttles was 99±28 and increased significantly by 7±13 shuttles ($p<0.001$). Body image perception on the CFQ-R showed a statistically significant increase ($p=0.006$). At baseline, subjects with $FEV_1 \leq 80\%$ had lower BMI ($p=0.003$) and exercise capacity ($p=0.048$) compared to subjects with $FEV_1 > 80\%$. Subjects who improved their exercise capacity by ≥10 shuttles showed significant increases in FEV_1 (+5% *vs.* -2%; $p=0.02$) and self-reported HAES weekday ($p=0.04$) and weekend ($p=0.02$) activity levels.

CONCLUSIONS: After a 2-month exercise program, CF subjects showed significant improvement in exercise capacity and improvements in lung function, self-reported habitual activity, and QoL. Those who increased exercise capacity by ≥10 shuttles showed significant improvements in FEV_1 and self-reported activity. These findings demonstrate that the HAES and MSWT are useful measures of exercise capacity that are easily implemented in an outpatient setting. Further studies are needed to determine if these tools can be used to standardize exercise assessment and prescribe individualized exercise regimens that can lead to improved clinical outcomes in CF.

112

10:15 AM

Fellow in Training

Intrauterine Growth Restriction Alters Lung Morphology and Function during Postnatal Growth in Rats

Catalina Bazacliu, Melissa F. Carmen, Satyan Lakshminrusimha, Julie Basu-Ray, Rita M. Ryan, Daniel D. Swartz.

Neonatology, University at Buffalo, Buffalo, NY.

BACKGROUND: The effect of intrauterine growth restriction (IUGR) on later adult pathology is well known. IUGR alters lung morphometry in animal models (Karadag, 2009).

OBJECTIVE: To evaluate the differences in tracheal and pulmonary artery (PA) reactivity and lung morphology in an IUGR rat model.

DESIGN/METHODS: IUGR was induced by feeding the pregnant dams a low protein diet (LPD) during pregnancy. After weaning at 3wks the pups were fed standard (SRC) or high fat diet (HFD). The control group was fed standard diet throughout the study. Rat offspring were sacrificed at 3wks, 16wks and 1yr. The tracheae and the PAs were used for reactivity studies, while the lungs were used for inflated fixation and morphometric analysis.

RESULTS: The pups born to dams fed LPD during pregnacy weighed significantly less at birth and 3wks. They caught up in growth to their controls by 16wks wheather fed SRC or HFD post-weaning. The weights of the IUGR and control groups were similar at 1yr.

IUGR lungs had increased cellularity and thickened alveolar walls. Mean linear intercept (MLI) varies with age in both IUGR and control rats but was significantly higher in IUGR rats at 3wks and 16wks and decreased to the control level by 1yr.

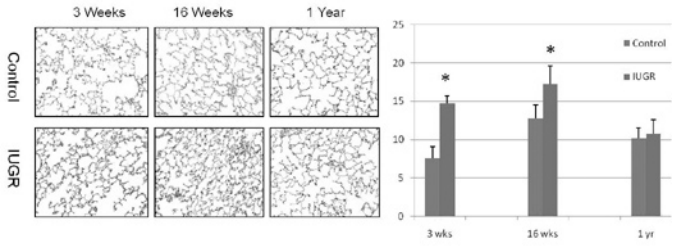
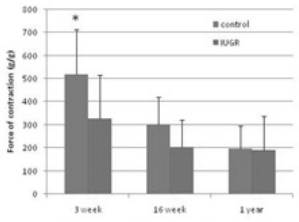
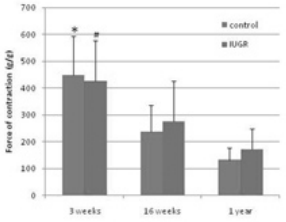


Figure 1: Lung morphology of control and IUGR rats with corresponding mean linear intercept.

Tracheal response to methacholine decreases with aging in control and IUGR rats.
PA response to norepinephrine significantly decreases with aging in controls, but not in IUGR.



PA response to 10^{-5} Mol Norepinephrine in control and IUGR rats (* P<0.05 in control group, ANOVA).



Tracheal constrictive response to 10^{-5} Mol Methacholine in control and IUGR rat (*P<0.05 in control group, # P< 0.05 in IUGR group, ANOVA).

CONCLUSIONS: The lung morphometric and functional changes induced by IUGR start in early development and become atenuated with advancing in age.

Plenary II
Young Investigator Presentations

Saturday, March 26, 2011
2:00 PM-4:00 PM

113

2:00 PM

Validation of a Pediatric Resident Disaster Triage Evaluation Tool

Mark X. Cicero, Antonio Riera, Veronika Northrup, Fangyong Li, Marc Auerbach, Carl R. Baum.

Pediatrics, Yale School of Medicine, New Haven, CT.

BACKGROUND: When disasters strike, patient triage is a crucial skill for pediatrics residents. No pediatric resident evaluation tool is widely used.
OBJECTIVE: We aimed to validate a resident triage evaluation tool created for use in a pediatric disaster medicine curriculum.
DESIGN/METHODS: We derived a checklist-based evaluation tool that includes expected knowledge and skills during disaster triage. Skill performance was rated via trichotomous scoring (yes, no, unable to determine). The tool was applied to a 10-patient school bus crash scenario, and included a global assessment of function. Actors and simulation manikins portrayed patients, and responded physiologically to airway maneuvers. Subjects were 1st – 4th year pediatrics residents at our institution. Subjects had previous training in JumpSTART triage, including airway and circulation assessment skills. Subjects triaged patients independently. Triage performance was video recorded. Videography angles were standardized, as was a script used by the facilitators. Three evaluators independently viewed the recordings and scored the performance using the tool. We constructed a database of evaluator scores. Intraclass correlation among the evaluators was calculated for each patient, for each skill, and for the global assessment.
RESULTS: There were 37 video recordings and three repeat observations of each video, for 111 total observations. Overall correlation among scores was 0.83 (95% confidence interval 0.74,0.89). Scores showed high correlation regarding triage skills, including airway management (0.96 [0.93-0.98]), triage assessment (0.98 [0.96-0.99]), and triage speed (0.87 [0.80-0.92]). An exception to this was breathing assessment (0.53 [0.35, 0.67]). Individual patient score correlation was high, including patients with head injury (0.86 [0.79, 0.91]), chest injury and tachypnea 0.86 [0.79, 0.91]), and an impaled patient with no signs of life (0.87 [0.80, 0.92]). Correlation was low for one ambulatory patient (0.29 [0.07, 0.48]). The global assessment scores had moderate correlation for overall skills and knowledge (0.63, 0.64 [(0.47, 0.75), (0.49, 0.76)]), and lower correlation for professionalism (0.49 [0.30, 0.64]).
CONCLUSIONS: We report the first validation of a pediatric disaster triage evaluation tool. Perhaps due to subjectivity, the global assessment of function scores correlated only moderately. Correlation for most patients, knowledge, and specific skills was high.

114

2:15 PM

Reiterated Roles for Jun in the Second Heart Field and Neural Crest during Heart Development

Jason Z. Stoller, Tao Zhang, Eldhose B. Thekkethottiyil, Julie De Mesmaeker, Shoumo Bhattacharya, Jue Zhang, Fen Wang.

Pediatrics/Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA; Cardiovascular Medicine, Wellcome Trust Centre for Human Genetics, Univ. of Oxford, Oxford, United Kingdom; Center for Cancer and Stem Cell Biology, Texas A&M Health Science Center, Houston, TX.

BACKGROUND: Mice missing the proto-oncogene *Jun* have a thin right ventricle, prominent endocardial cushions, and a 100% incidence of persistent truncus arteriosus (PTA). The common thread among these structures is their second heart field (SHF) origin. In concert with other cells, such as neural crest (NC), SHF derivatives play a critical in outflow tract development. Similar outflow tract defects are commonly seen in DiGeorge syndrome (DGS) and the DGS gene, *Tbx1*, is expressed in the SHF. Although Jun is critical for proliferation, cell cycle regulation, differentiation, and cell death, all biologic functions crucial for embryogenesis, there is little known about its role during cardiac development.
OBJECTIVE: To elucidate the role of Jun during heart development and in DiGeorge syndrome.
DESIGN/METHODS: Tbx1-interacting proteins were discovered in a high throughput mammalian coactivator trap. Functional interactions were confirmed in luciferase assays. Physical interactions were verified by protein complementation assays. Cre-loxP mouse models were utilized for tissue-specific knockout studies. Mouse embryos were analyzing using routine histology and/or Optical Projection Tomography.
RESULTS: The screen revealed multiple transcription factors, including the proto-oncogene Jun, which mediate a significant increase in TBX1-dependent transcriptional activity. Tbx1 and Jun physically and functionally interact and are both expressed the SHF. Tissue-specific knockout of *Jun* in either SHF or NC cells recapitulates cardiac and aortic arch artery remodeling defects reminiscent of *Jun* mutant mice, *Tbx1* mutant mice and patients with DGS. Specifically, the loss of *Jun* in the SHF results in NC-like defects including interrupted aortic arch (IAA) and pulmonary valve defects, while the loss of *Jun* in NC cells results in PTA, IAA, right aortic arch, and exencephaly.
CONCLUSIONS: Our results suggest that Jun has reiterated roles in different tissues important for heart development and tissue-specific mouse knockouts of *Jun* phenocopy important aspects of the DGS phenotype. Jun is required in the SHF and may have non-cell autonomous effects on NC cells. Independently, there is a cell autonomous role of Jun in NC cells. The role of Jun in the SHF may be due to a *Tbx1*-expressing subset of SHF progenitors. The role of JUN in human congenital heart disease remains to be determined. NHLBI K08-HL086633.

115

2:30 PM

Cell Death after Oxidant Stress Is Determined by Inhibitory Proteins of the NF-κB Activation Cascade

Clyde J. Wright, Fadeke Agboke, Manasa Muthu, Phyllis A. Dennery.

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BACKGROUND: Oxidant and inflammatory stress contribute to lung injury in preterm infants. The transcription factor NF-κB regulates the cellular response to these stresses. In contrast inflammatory stress, how oxidant stress induces NF-κB activation remains to be elucidated.
OBJECTIVE: To characterize the roles of members of the Inhibitory Kappa-B family (IκB), specifically IκBα and IκBβ, in mediating the cellular response to oxidant stress.
DESIGN/METHODS: Wild type (WT) and IκBβ knock-in mice (AKBI), in which the IκBα gene is replaced by the IκBβ cDNA, were used for this study. Adult mice were exposed to hyperoxia (>95% O2) or normoxia for 96h (n=3/point) and BAL samples obtained. Lung injury was assessed by BAL protein content and multiplex cytokine analysis was performed. Survival curves were generated through 10d (n=20). Murine embryonic fibroblasts (MEF) were genterated and exposed to glucose oxidase (GO) to generate intracellular H2O2 for 3 and 6h. Reactive oxygen species were measured by DCF assay. Levels of the NF-κB inhibitory proteins, kinases and subunits were determined by Western blot. Cell cycle analysis was performed by flow cytometry and apoptosis by caspase-3 activity assay.
RESULTS: After 5d of hyperoxia, WT mice had 100% mortality; at this time point AKBI mice had 95% survival. AKBI mice did not have 50% mortality until 8d exposure (p<.001). WT lung protein content was significantly elevated at 96h exposure (p<.001) vs. AKBI. AKBI mice had blunted expression of the NF-κB targets IL6 and G-CSF at 96h. WT and AKBI MEF cells express similar amounts of p65, p50, cRel, IKKa, and IKKb; AKBI lacked expression of IκBα and expressed greater levels of IκBβ. WT and AKBI did not differ in ROS production following exposure to GO at increasing doses or longer time points. Degradation of both IκBα and IκBβ occurred in both cell lines after exposure to GO. Following 6h exposure, >20% of WT MEF transitioned into subG1 phase, compared to <2% of AKBI cells (p<.001) and showed significantly higher levels of caspase-3 activity when compared to AKBI (p<.05).
CONCLUSIONS: These data demonstrate that individual IκB isoforms are responsible for specific responses to oxidant stress. Both cells and animals lacking IκBα and overexpressing IκBβ have improved survival following exposure to oxidant stress. This suggests that manipulation of this pathway could have therapeutic applications for neonates exposed to hyperoxia and oxidative stress.

116

3:00 PM

House Officer

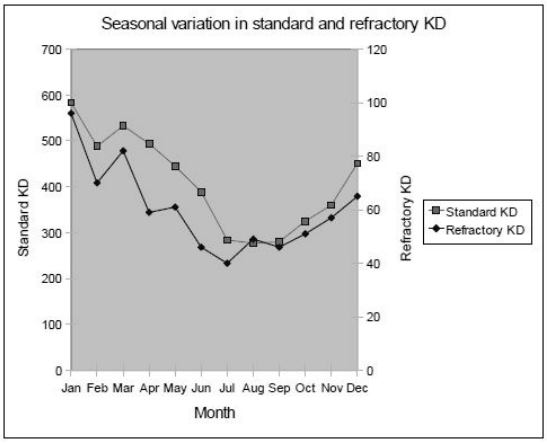
Epidemiology of Refractory Kawasaki Disease: Analysis of 42 US Pediatric Hospitals from 2005 to 2008

Sunil J. Ghelani, Kavita Parikh.

Children's National Medical Center, Washington, DC.

BACKGROUND: Rising incidence of Kawasaki Disease(KD) has been reported in many countries and it continues to be a leading cause of acquired heart disease. A variety of infectious triggers have been speculated, but the underlying etiology remains unknown. About 10-15% of KD is refractory to initial intravenous immunoglobulin (IVIG) therapy.
OBJECTIVE: To describe the epidemiology of refractory KD(RKD) to better understand the disease process.
DESIGN/METHODS: This retrospective, descriptive study utilized the Pediatric Health Information System, an administrative database that includes demographic and diagnostic information for inpatients at 42 free-standing pediatric hospitals. Patients with principle discharge diagnosis of KD from January 2005 to June 2008 were included. RKD included patients who received more than one dose of IVIG or an alternate KD medication (methylprednisolone or infliximab).
RESULTS: Of 5540 patients meeting inclusion criteria, 4818(87%) patients received one dose of

IVIG(standard KD), while 722(13%) patients had RKD. Median(interquartile range, IQR) ages of patients with RKD and standard KD were 30[14-53] and 30[15-54] months respectively (p=0.438). Male to female ratio was 1.59:1 in RKD and 1.55:1 in standard KD(p=0.71). Median(IQR)length of stay was significantly higher in the refractory group(4[2-6] days in RKD vs. 3[2-4] days in standard KD; p=<0.001). Ethnic distribution of RKD resembled standard KD: 42.1% vs 38.3% Non-Hispanic White, 21.2% vs 20.4% African American, 17% vs 19.6% Hispanic White, 7.6% vs 8.9% Asian(p=0.079). RKD followed a similar seasonal trend as standard KD with a remarkable peak in winter.



CONCLUSIONS: This is the first study describing multicenter epidemiology of RKD. RKD has similar age, sex, and ethnic distribution as standard KD, and follows the same seasonal pattern. Perhaps the etiology of standard KD and RKD are similar and it is the host inflammatory response that determines refractoriness. Further studies are necessary to understand KD triggers and host responses.

117

3:15 PM

Staphylococcus aureus Infections in Women and Neonates Following Late Pregnancy Anovaginal Colonization

Karina A. Top, Amanda Buet, Jiang Yao, Susan Whittier, Adam J. Ratner, Lisa Saiman.

Pediatrics, Columbia University Medical Center, New York, NY; Mailman School of Public Health, Columbia University, New York, NY; Biomedical Informatics, Columbia University Medical Center, New York, NY; Pathology, Columbia University Medical Center, New York, NY; Microbiology and Immunology, Columbia University Medical Center, New York, NY; Infection Prevention & Control, NewYork-Presbyterian Hospital, New York, NY.

BACKGROUND: In 2009, we studied the prevalence of *Staphylococcus aureus* anovaginal colonization among pregnant women undergoing Group B streptococcal screening at Columbia University Medical Center (CUMC) (Top et al., 2010). Among 2921 women, the prevalence of methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) anovaginal colonization was 11.8% and 0.6%, respectively. The risk of MSSA and MRSA infections in these women and their infants was not determined.

OBJECTIVE: To determine the rate of *S. aureus* infections in pregnant women from 3 months before delivery to 3 months after delivery and the rate of infections in their infants in the first 3 months of life.

DESIGN/METHODS: We conducted a retrospective cohort study of women included in the prior study who delivered at CUMC, and their infants. We reviewed the electronic medical records of mothers and infants and the clinical microbiology laboratory database for cultures positive for *S. aureus*.

RESULTS: The cohort included 2702 women who delivered at CUMC and their 2789 infants. During the study period, 13 (0.49%) of 2702 women analyzed developed *S. aureus* infections: 9 women had skin and soft tissue infections (SSTIs), 2 of which were due to MRSA, and 4 women had MSSA urinary tract infections (UTIs). Only 4 of 13 women with *S. aureus* infections had concordant anogenital colonization. Among infants born to women in the cohort, 11 (0.39%) of 2789 had *S. aureus* infections, including 1 MRSA SSTI and 10 MSSA infections. These were bacteremia (4), SSTI (5), ventriculosubgaleal shunt infection (1), and UTI (1). Six additional infants were colonized with MSSA. The average postnatal age at initial *S. aureus* culture was 30 days. Among 17 infants with positive *S. aureus* cultures, 10 (58.8%) were born preterm (<37 weeks), 11 (64.7%) were admitted to our Neonatal ICU, and 2 (11.8%) were born to mothers colonized with MSSA. MRSA or MSSA anovaginal colonization was associated with a trend toward an increased risk of infection in mothers (risk ratio (RR) 3.09, 95% confidence interval (CI) 0.96–9.97, p=0.047), but not in their infants (RR 0.92, 95% CI 0.21–4.03, p=0.919).

CONCLUSIONS: The frequency of *S. aureus* infections in pregnant and post-partum women and their infants is low. Maternal anovaginal *S. aureus* colonization may be a risk factor for *S. aureus* infections in women, but was not associated with increased *S. aureus* infections in infants.

118

3:30 PM

Medical Student

Blood Cultures in the Emergency Department Evaluation of Childhood Pneumonia

Maria H. Dugan, Joshua P. Metlay, Louis M. Bell, Robert W. Grundmeier, Todd Florin, Elizabeth Hines, Samir S. Shah.

University of Pennsylvania School of Medicine and The Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Blood cultures are frequently obtained in the emergency department evaluation of children with community-acquired pneumonia (CAP).

OBJECTIVE: To determine the prevalence of bacteremia in children presenting to the emergency department with CAP, identify subgroups at increased risk for bacteremia, and quantify the impact of positive blood cultures on management.

DESIGN/METHODS: This multisite case-control study was nested within a cohort of children followed at 35 pediatric primary care practices. Patients from this cohort who were 18 years of age or younger, evaluated in the emergency department in 2006-2007, and diagnosed with CAP were eligible. Cases were those with bacteremia. Controls included those with negative blood cultures (control group 1) and those without blood cultures performed (control group 2).

RESULTS: 877 (9.6%) of 9,099 children with CAP were evaluated in the emergency department. The mean age was 3.6 years; 53% were male. Blood cultures were obtained in 291 children (33.2%). Overall, the prevalence of bacteremia was 2.1%. Bacteremia occurred in 2.6% (95% confidence interval [CI]: 1.0%-5.6%) of those with an infiltrate on chest radiograph and in 13.0% (95% CI: 2.8%-33.6%) of children with contiguous infection such as empyema.

Prevalance of Bacteremia in Children with Pneumonia

	Bacteremia	95% CI	P
All patients with blood culture obtained (n=291)	2.1%	0.8-4.4	
Disposition after evaluation in ED			
Inpatient (n=227)	2.6%	1.0-5.7	0.189
Outpatient (n=64)	0%	0-5.6	
Pneumonia-associated complications			
Any complication (n=51)	7.8%	2.2-18.9	0.001
No complication (n=240)	0.8%	0.1-3.0	

Abbreviations: CI, confidence interval; ED, emergency department

Streptococcus pneumoniae was most common, accounting for 4 of the 6 cases of bacteremia. Blood culture results altered management in 5 of the 6 bacteremic patients of whom 1 had an appropriate broadening of coverage and 4 had an appropriate narrowing of coverage. The contamination rate was 1.0% (95% CI: 0.2%-3.0%).

CONCLUSIONS: Children from an ambulatory cohort presenting to the emergency department with CAP are at low risk for bacteremia. Although blood cultures positive for pathogenic bacteria frequently resulted in appropriate changes to antibiotic therapy, the impact on clinical management among all patients was small given the low prevalence of bacteremia.

119

3:45 PM

Fellow in Training

Superoxide Anions Mediate Increased Pulmonary Arterial Contractility in 100% O_2 Resuscitated Asphyxiated Lambs

Jayasree Nair, Stephen Wedgwood, Bobby Mathew, Robin Steinhorn, Satyan Lakshminrusimha.

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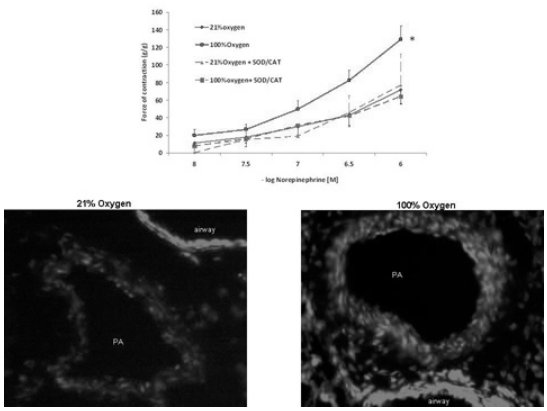
BACKGROUND: The optimal oxygen concentration for resuscitation of asphyxiated infants is controversial. While the NRP guidelines do not mandate use of 100% O_2, it is still an option for asphyxiated term neonates with low heart rate. We previously showed that brief exposure to 100% O_2 in normal term lambs increased pulmonary arterial (PA) contractility (Lakshminrusimha et al Ped Res 2006).The mechanism of increased PA contractility following 100% O_2 exposure remains unclear. Also, there is no information on PA contractility following resuscitation with 21% and 100%O_2 in asphyxiated animal models.

OBJECTIVE: We hypothesized that ventilation with 100%O_2 during resuscitation in asphyxiated lambs increased contractility in isolated PA compared to 21%O_2 and this effect was mediated by superoxide anions.

DESIGN/METHODS: 141d gestation lambs (term~145d) were asphyxiated by umbilical cord occlusion for 10min or until heart rate decreased <60 /min.They were randomized to resuscitation with 21% or 100%O_2 for 30min and sacrificed as previously described (Savorgnan et al PAS2010). Fifth generation PA rings were isolated and their contractile response to norepinephrine (NE) studied.Some were pretreated with SOD (75u/cc) and catalase (1200u/cc) for 20min prior to NE.Superoxide anion levels in PA were assessed by dihydroethidium (DHE) fluorescence.

RESULTS: PA contractility to NE was significantly increased by resuscitation with 100%O_2. Pretreatment with SOD and catalase significantly reversed this increased contractility in the 100%O_2 group but did not alter contractility in the 21%O_2 group.Superoxide anion levels in 100%O_2 PAs were 2.24±0.46 times higher compared to 21%O_2 resuscitation.



CONCLUSIONS: We conclude that in asphyxiated newborn lambs even brief exposure to 100% O_2 during resuscitation increases contractility and superoxide anion levels in PAs. Scavenging superoxide anions and H_2O_2 with SOD/catalase confirms that oxidant injury mediates this increased contractility.

Cardiovascular & Critical Care Platform Session

Saturday, March 26, 2011
4:15 PM-5:45 PM

120

4:15 PM

Fellow in Training

Outcomes of Tight Glycemic Control in Critically Ill Children

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BACKGROUND: Hyperglycemia is common in critically ill patients and is associated with increased mortality and duration of stay in the intensive care unit (ICU). Randomized controlled trials (RCT) on tight glycemic control (TGC) in critically ill adults, where blood glucose (BG) is controlled at 80-110 mg/dl with intravenous insulin, report conflicting effects on mortality and ICU stay. A single center RCT in critically ill children suggested that TGC is beneficial.
OBJECTIVE: Determine the outcomes of critically ill children treated with TGC.
DESIGN/METHODS: We performed a retrospective cohort study comparing outcomes in critically ill children where BG was controlled to 80-120 mg/dl (TGC group) using intravenous insulin with a similar historical cohort of children where no BG control (non-TGC group) was done. Non-diabetic children in the ICU with persistent BG ≥150 mg/dl and on mechanical ventilator or vasopressors were included. Primary outcome measure was ICU length of stay with organ dysfunction including mortality as secondary outcomes. Mann-Whitney and chi-square tests were used as appropriate.
RESULTS: The TGC and non-TGC groups had 63 and 69 patients, respectively. Patient characteristics including age and severity of illness were similar between the two groups. BG in the TGC group was 142 ±25 mg/dl compared to 159 ±35 mg/dl in the non-TGC group (P<0.01). Glucose variability in the TGC group was 16.6 ±12.8 vs. 11.3 ±16.4 mg/dl/hr in the non-TGC group (P<0.01). Hypoglycemia rate was higher in the TGC group (16% vs. 3%, P=0.01). Patients in the TGC group received an average of 0.05 ±0.04 units of insulin/kg/hr. The TGC group stayed in the ICU longer at 16.4 ±18.6 vs. 8.9 ±9.4 days for the non-TGC group (P<0.01). Duration of mechanical ventilation was higher in the TGC group (12.4 ±17.3 vs. 6.1 ±7.6 days, P<0.01). Duration of vasopressor use (6.0 ±9.9 days) and mortality (16%) in the TGC group were similar to the non-TGC group (4.8 ±10.1 days, P=0.60; and 16%, P=0.99 respectively). Infection rates were also higher in the TGC group (60%) compared to the non-TGC group (33%; P<0.01).
CONCLUSIONS: TGC appears to be associated with worse outcomes in critically ill children. The conflicting results of TGC in critically ill adults and our contrasting data in children strongly advocate the conduct of multicenter randomized trials on TGC in critically ill children.

121

4:30 PM

Fellow in Training

Spontaneous and Pharmacological Closure of PDAs in ELBW Infants Is Influenced by Thrombocytopenia

Kiran Dwarakanath, Narendra R. Dereddy, Divya Chabra, Christine Schabacker, Johanna Calo, Lance A. Parton.
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Neonatology, Maria Fareri Children's Hospital, Westchester Medical Center at New York Medical College, Valhalla, Select.

BACKGROUND: PDA is present in 49-70 % of ELBW infants and is associated with significant mortality and morbidity if left untreated. Animal studies have shown that platelets contribute to the closure of PDA. Also, the relative risk for PDA has been noted to be significantly higher in infants with thrombocytopenia (<150K).
OBJECTIVE: 1.To determine the effect of platelet counts during the first 3 days of life on spontaneous closure of DAs in ELBW infants.
2.To determine the effect of platelet counts on the closure of PDA in ELBW infants treated with indomethacin or ibuprofen.
DESIGN/METHODS: Database of 148 ELBW infants born between June 2006 –March 2010 was reviewed. Platelet counts were noted for all the infants in the first 3 days of life. For those infants who needed indomethacin or ibuprofen for PDA closure, the platelet counts during that time period were tabulated.
RESULTS:

Spontaneous Closure is Decreased with Thrombocytopenia

	Thrombocytopenic (n=61)	Non-thrombocytopenic (n=87)
GA weeks median (IQR)	26 (25-27)	26 (24-27)
B wt grams median (IQR)	680 (580-870)	770 (652-870)
SGA (%)*	33	9
pre-eclampsia (%)¶	40	12
Male (%)	55	46
Steroids (%)	80	58
Platelet count 1000/μL median (IQR)†	112 (94-128)	199 (167-265)
Spontaneous closure of DA (%)§	16	42

*p=0.006 ¶p=0.004 †p<0.001 §p=0.012

The incidence of PDA,SGA and maternal pre-eclampsia were more in the thrombocytopenic group.

Comparison of infants treated with ibuprofen or indomethacin.

	Ibuprofen (n=49)	Indomethacin (n=19)
Bt wt grams mean ±SD	752 ± 145	711 ± 164
GA weeks median (IQR)	25 (24-26)	26 (24-27)
Male (%)	47	52
SGA (%)	16	26
Pre eclampsia (%)	24	47
Maternal Steroids (%)	83	89
Chorioamnionitis (%)	20	36
IVH (%)	20	26
Platelets median (IQR) 1000/μL	171 (116-230)	140 (109-165)
Failure of PDA to close in thrombocytopenic patients (%)	29	67
Failure of PDA to close in non-thrombocytopenic patients (%) *	52	0

* P=0.039

Ibuprofen induced closure of PDAs 17/24 times when infants were thrombocytopenic and 31/63 times when infants were not thrombocytopenic (P=0.31). However for indomethacin, it was 4/12 and 12/12 respectively (P=0.001).
CONCLUSIONS: Spontaneous and indomethacin-treated ductal closure were significantly impaired in thrombocytopenic ELBW infants. Closure following ibuprofen treatment was not affected by thrombocytopenia.

122

4:45 PM

Fellow in Training

Developmental Expression of Pepsinogen C in a Gene Trap Mouse Model

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BACKGROUND: Pepsinogen C (PGC), an alveolar type II cell specific aspartic protease and a gastric prozymogen, mediates the developmental and cell-type specificity of SP-B production in human lung and participates in protein hydrolysis in the stomach.
OBJECTIVE: To evaluate the developmental expression of PGC using a PGC gene trap animal model.
DESIGN/METHODS: Mice with a gene trap vector inserted LacZ in an intron sequence between exon 7 and 8 of the endogenous PGC gene were bred with C57Bl/6J (WT) mice for six generations to obtain an homogeneous genetic background. b-galactosidase activity and localization were evaluated by ß-Gal Assay and X-Gal staining in lungs and stomachs of postnatal mice. PGC and SP-B mRNA levels were determined by RT-PCR, and protein expression was evaluated by immunoblotting and immunohistochemistry (IHC). Results were expressed as mean ± SE and analyzed by ANOVA where applicable.
RESULTS: PCR genotyping demonstrated that the gene trap exhibited Mendelian inheritance (n=78, 22% wild type, 51% heterozygous, 27% homozygous). No perinatal lethality was observed. In WT littermates, PGC expression in stomach was low until 3 wks of age, but was not detectable in KO animals (RNA relative quantity WT 0.61 ± 0.2 vs KO 0.0007 ± 0.0003, n=3-5, p<.01). Reflecting the developmental expression pattern of PGC, KO animals demonstrated increased ß-gal activity at 3-4 wks of age (19.4 ± 2.08 ß-gal units at 0-2 wks vs 211.1 ± 36.77 ß-gal units at 3-4 wks, n=13-16, p<.001). X-gal staining of KO stomachs showed LacZ expression in gastric chief cells, at the basal portion of the fundic glands. Expression of PGC and the LacZ reporter in lung was markedly different than in stomach. At 4 wks of age PGC expression was lower in lung than in stomach (Ct 15.48 ± 0.54 WT stomach vs 22 ± 2.49 WT lung by RT-PCR), yet was still detectable in KO lungs compared with KO stomach (Ct of 25.53 ± 2.91 KO lung vs 31.45 ± 5.35 KO stomach). ß-gal activity was not detectable in KO lungs, and PGC protein was detected in KO lungs by WB and IHC. SP-B levels in KO lungs were not different from WT.
CONCLUSIONS: The PGC gene trap is functionally a knock-in/knock-out in the dominant site of PGC expression, the gastric mucosa, and displays developmental regulation with onset of expression at the time of weaning. By contrast, the gene trap did not express in mouse lung.
HL059959.

123

5:00 PM

Undergraduate Student

Mutation of Ryanodine Receptor Type 1 Causes Fetal Heart Failure and Demise

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Cardiovascular Research Institute, University of Rochester Medical Center, Rochester, NY.

BACKGROUND: The Ca2+-induced Ca2+-release mechanism initiates striated muscle contraction through ryanodine receptors in the sarcoplasmic reticulum. The type 2 receptor (RyR2) exists primarily in cardiac muscle and type 1 (RyR1) in skeletal muscle. Our lab has produced evidence that the RyR1 is also present in the inner mitochondrial membrane of cardiac muscle cells and plays an important role in the excitation-contraction-metabolism (ECM) coupling within the mitochondria, providing sufficient stimulation by Ca2+ for oxidative metabolism. It has been found that the YS mutation of the RyR1 gene (a human mutation that causes malignant hyperthermia) may alter cardiac function in heterozygous adult mice while the homozygous mutation (YS/YS) is lethal in-utero.

OBJECTIVE: We hypothesized that these YS/YS mice die during embryonic development of heart failure and not from skeletal defects. This is based on the observation that fetuses that die in-utero typically die of heart or blood complications, not skeletal or muscular malfunction.

DESIGN/METHODS: We paired YS/+ mice, harvested embryos at various gestational ages, and correlated their gross and histological morphology to their genotype. We also cultured ventricular myocytes from these hearts to determine changes in mitochondrial structure and function.

RESULTS: At embryonic day 13.0 (E13.0), the YS/YS mice appear to be morphologically identical to wildtype and heterozygous mice, but may have mild cardiac hypertrophy. By E16.5 the YS/YS fetuses develop skeletal and intestinal defects and appear to die of heart failure with edema and abnormal ventricular muscle while the +/+ and YS/+ fetuses appear normal.

CONCLUSIONS: These preliminary studies suggest that YS/YS fetuses die of heart failure and support our hypothesis that RyR1 is important in heart development.

124

5:15 PM

Fellow in Training

The Embryonic Mitochondrial Permeability Transition Pore Controls Cardiac Myocyte Mitochondrial Maturation and Differentiation

Jennifer R. Hom, Rodrigo A. Quantanilla, David L. Hoffman, Karen L. de Mesy Bentley, Jeffery D. Molkentin, Shey-Shing Sheu, George A. Porter.

University of Rochester, Rochester, NY; Cincinnati Children's Hospital Medical Center and Howard Hughes Medical Institute, Cincinnati, OH.

BACKGROUND: The heart is the first functional organ to form in the embryo, beginning at about embryonic day (E)8 in the mouse, becoming a looped tube at E9.5, and resulting in a fully septated heart at around E13.5. Embryos can survive with abnormally formed hearts, but cannot survive if the heart does not function well enough to provide effective circulation. Despite the recent advances, in many cases the exact causes of embryonic cardiac failure are not understood. A few studies demonstrated that dysfunction of the mitochondrial electron transport chain (ETC) can cause heart malformation and embryonic death, suggesting that mitochondrial function is essential to cardiac function and survival of the embryo.

OBJECTIVE: To investigate the role of the mitochondrial permeability transition pore (mPTP) in mitochondrial structure and function, and myocyte differentiation in the embryonic murine heart.

DESIGN/METHODS: Primary cultures of cardiac myocytes from E9.5 to 13.5 were stained using vital dyes and by immunocytochemistry using epifluorescence microscopy. Whole hearts from embryonic day E9.5 to 13.5 were examined using electron microscopy.

RESULTS: Mitochondria of E9.5 ventricular myocytes displayed less dense cristae and were shorter in length and less branched. By E13.5, mitochondria had abundant cristae, were longer, branched and networked, and were more closely associated with the contractile apparatus. Functional measurements demonstrated dramatic increases in mitochondrial membrane potential, an increased reliance on complex I, and a decrease in oxidative stress as the heart developed. These structural and functional data suggested an increase in inner mitochondrial membrane permeability, and closure of the mPTP using cyclosporin A or cyclophilin-D null embryos caused premature maturation of mitochondrial structure, mitochondrial function, and myocyte differentiation. Furthermore, long term opening of the mPTP using carboxyatractyloside after E9.5 inhibited mitochondrial maturation and myocyte differentiation.

CONCLUSIONS: These data suggest a critical role of the embryonic mPTP as a mediator of mitochondrial maturation and cardiac differentiation, and suggest that the mPTP may be a novel target to modulate cardiac development and function in the embryo and fetus and to enhance cardiac myocyte differentiation for cardiac regeneration.

125

5:30 PM

Medical Student

Prostaglandin E2 Receptor Gene Polymorphisms Are Associated with Reduced Spontaneous Closure of Ductus Arteriosus in ELBW Infants

Kristen Aland, Kiran Dwarakanath, Johanna M. Calo, Lance A. Parton.

Pediatrics, Division of Newborn Medicine, Maria Fareri Children's Hospital, Westchester Medical Center; New York Medical College, Valhalla, NY; Neonatology, Maria Fareri Children's Hospital, Westchester Medical Center at New York Medical College, Valhalla, NY; Neonatology, Maria Fareri Children's Hospital, Westchester Medical Center at New York Medical College, Valhalla, NY.

BACKGROUND: ELBW infants have an increased sensitivity to prostaglandins (PG), suggesting that at least partial sensitivity of the PDA to closure may reside in the receptor for PG. Single nucleotide polymorphisms (SNPs) in the untranslated region of the gene for the prostaglandin E2 receptor (PTGER2) have been associated with sensitivity of the inflammatory response to NSAIDs in aspirin-intolerant asthma, exemplifying the heterogeneity of the PG receptor.

OBJECTIVE: We tested the hypothesis that spontaneous PDA closure in ELBW infants is associated with SNPs of the PTGER2 gene.

DESIGN/METHODS: Preterm infants weighing <1 kg at birth (ELBW), without congenital or chromosomal abnormalities were enrolled following parental consent. PDA was determined by echocardiogram on day 2-3 of life. PDAs were treated with ibuprofen, up to 3 courses. Those unresponsive to ibuprofen were surgically ligated. Patient DNA was isolated from buccal mucosal swabs and allelic discrimination was performed using specific Taqman probes for PTGER2 SNPs with real-time PCR. Chi square and ANOVA analyses of data were performed with $P<0.05$ denoting statistical significance.

RESULTS: Lower gestational age and birth weight were associated with an increased risk for PDA. The majority (8/9) of ELBW infants whose PDAs closed spontaneously had the AA genotype for the PTGER2 SNP rs708494. More infants requiring medical or surgical interventions had the G allele of this SNP.

rs708494	Spontaneous closure	Medical Rx	Surgical Ligation
GG	0	4	4
GA	1	8	7
AA	8	5	5
p=0.04			
Any G	1	12	11
AA	8	5	5
p=0.007			

CONCLUSIONS: We conclude that an A/G substitution for the SNP rs708494 of the PTGER2 gene is associated with the need for medical or surgical intervention for closure of PDAs in ELBW infants, while the presence of the wild-type AA genotype is associated with spontaneous closure of the ductus. We speculate that the presence of the G allele of this SNP increases the sensitivity of the prostaglandin receptor to circulating prostaglandins in ductal tissue, making this tissue more responsive to the vasodilatory effects of circulating prostaglandins, and less prone to spontaneous closure.

General Pediatrics - Medical Education & Quality Improvement
Platform Session

Saturday, March 26, 2011
4:15 PM-5:45 PM

126

4:15 PM

Framework for Quantifying & Matching Workload & Workforce in Healthcare Settings

E. Fieldston, L. Zaoutis, P. Hicks, D. Geiger, E. Sladek, P. Agosto, L. Bell.

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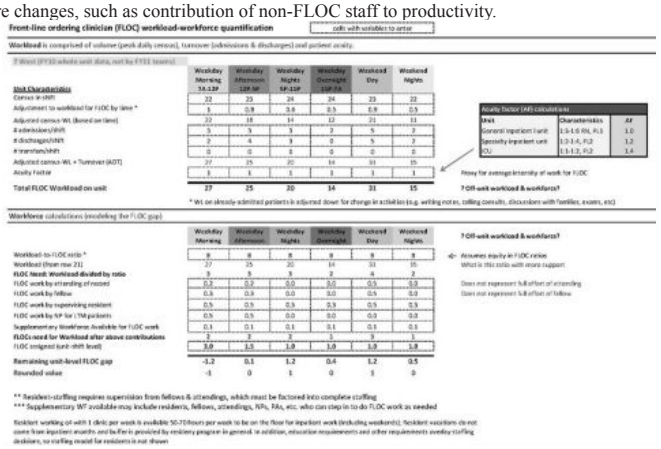
BACKGROUND: Healthcare workload (WL) and workforce (WL) are complex and dynamic. A significant challenge is measuring and defining the match of WL & WF to optimize processes of care.

OBJECTIVE: Develop and obtain face validity for an objective yet flexible tool to match front-line ordering clinician (FLOC) workforce to workload in a variety of inpatient settings.

DESIGN/METHODS: Iterative multi-disciplinary development of a matrix to represent WL & WF based on literature review, clinical leadership, and repeat validation sessions.

RESULTS: A tool to represent WL & WF was produced (Fig 1), allowing entry of volume, turnover (admissions & discharges), acuity, and variations in WL for discrete periods of time. Predicted WF needs are contrasted with actual WF assignments and contributions from other clinicians to FLOC work in medical, surgical, and intensive care units. The tool gained widespread acceptance among physician, nursing, and administrative leadership. Across >25 meetings with 14 divisions, comments included: "makes sense to us and will help us plan" (specialty attending). The hospital will use this decision matrix to identify gaps and guide staffing in FY12. The tool can capture future changes, such as contribution of non-FLOC staff to productivity.



CONCLUSIONS: Despite complexity, by considering multi-dimensional aspects of WL, it is possible to construct a flexible yet objective tool to quantify WL & WF with widespread agreement on face validity to assist with future staffing, particularly for consistency across divisions & units. The progressive, cell-based approach allows for adjustment in the same framework. Future work can assess how well WL-WF matching predicted by the tool corresponds to actual experiences and quality of care, changes in coverage, and increased handovers. The tool also allows for incorporation of how other staff affect productivity of FLOC in caring for patients and ultimately be designed to match various WF contributors to the needs of patients to optimize their care.

127

4:30 PM

Qualitative Analysis of Student Attitudes towards Teaching and Counseling: Three Student Profiles Emerge

Judith A. Turow, Amy Rothkopf, Stacy Henderson, Lindsey Lane.
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BACKGROUND: Physicians often avoid teaching and counseling on awkward topics.

OBJECTIVE: To analyze variation in medical student responses to performing a challenging patient-counseling task.

DESIGN/METHODS: Twenty-one medical students on the pediatric clerkship taught first-time mothers with public insurance, one-on-one on the postpartum floor about shaken baby syndrome. Using grounded theory, we interviewed each student, recorded, transcribed, coded, and thematically categorized their responses. After qualitative analysis and identification of major themes and subthemes, the students were categorized according to the thematic content of their responses.

RESULTS: Five major themes emerged that characterized students' responses to performing the counseling task: orientation to task, beneficiary of task, value of teaching/counseling, engagement with task, student role in the medical team. These themes were used to develop a profile of each student on a continuum from self/doctor-centered, through learning-centered, to patient-centered.

Summary of Student Profile by Theme

	Student Profiles		
Theme in Student Responses	**Self/Doctor-Centered**	**Learning-Centered**	**Patient-Centered**
Orientation to Task	Disease Oriented	Learning Oriented	Psychosocially Oriented
Beneficiary of Task	Self	Student/Self as Learner	Patient
Value of Teaching/ Counseling	Not Valued	Valued as Learning Opportunity but Unprepared/Hesitant to Teach	Valued
Engagement with Task	Minimal	Moderate	Maximal
Role and Status as Part of the Team	Negative/Low	Mixed	High

These student profiles were consistently associated with the thematic content of their responses. An additional sub theme of awkwardness was not considered a defining factor as it was seen in all three profiles.

Role of Awkwardness in the Student Response to a Challenging Counseling Task

	Student Profile		
	Self/Doctor Centered	**Learning-Centered**	**Patient-Centered**
Percentage of Students who Specified Awkwardness	100	67	56

CONCLUSIONS: Based on their response to performing the challenging counseling task, students' responses were categorized into characteristic profiles that fit the previously recognized model of a doctor-centered to patient-centered continuum. Given that some students need help to develop a more patient-centered style of care, this challenging counseling task may have use as a diagnostic method to identify students who could benefit from interventions to increase their sensitivity to patient needs.

128

4:45 PM

New Pediatric Interns' Infant Lumbar Puncture Skills

David O. Kessler, Todd P. Chang, Joshua M. Sherman, Nikhil B. Shah, Geetanjali B. Srivastav, Christopher G. Strother, Kajal Khanna, Michael Holder, Stephen J. Cico, Renuka S. Mehta, Matei Petrescu, Jennifer Reid, Kiran B. Hebbar, Noel S. Zuckerbraun, Martin B. Pusic , Marc Auerbach.
Pediatrics, Columbia University Medical Center/New York Presbyterian Morgan Stanley Children's Hospital of New York, New York City, NY; Children's National Medical Center, Washington, DC; Cohen Childrens Medical Center, New Hyde Park, NY; Weill Cornell Medical College, New York, NY; University of Texas Southwestern Medical Center, Texas; Mount Sinai School of Medicine, NY; Children's Hospital of Los Angeles, Los Angeles; Emory University, Atlanta; Medical College of Georgia, Georgia; University of Washington and Seattle Children's, Seattle; Children's Hospital of Pittsburgh, Pittsburgh; Tulane University, New Orleans; Yale University School of Medicine, New Haven; Akron University, Akron.

BACKGROUND: Pediatric and emergency medicine interns are routinely expected to perform infant lumbar punctures (LP); however, limited data exists regarding their competency at the start of residency training.

OBJECTIVE: We hypothesize that new pediatric and emergency medicine interns are not sufficiently skilled to perform infant lumbar puncture (LP) procedures independently.

DESIGN/METHODS: Interns from 24 academic pediatric training programs were enrolled in the first two months of the academic year. All subjects viewed an infant LP training video to review the procedure. Skills were assessed on an infant LP task trainer capable of producing fluid. Evaluators read a script directing the interns to perform "to the best of their ability as if it were a real baby." Performance was rated using a 15-item checklist of procedural steps and a global skills rating scale. Both measures were developed via modified Delphi method and adapted from previous studies. Evaluators were experts in the infant LP procedure and completed a uniform train-the-trainer module.

RESULTS: 501 interns participated in the mastery training session. Using a global skills rating: 66% of interns were assessed as beginners, 25% as competent, 7% as proficient and 2% as experts. On average interns needed help with at least 25% of the steps in the procedure (SD 19%). Performance on the checklist is reported in table 1.

Table 1. Intern performance on skills checklist of critical steps

STEP	Needed help, done incorrectly or not done.
Plans insertion site	26%
Prepares for procedure	29%
Cleanses	18%
Maintains sterility	37%
Instructs holder	29%
Inserts needle in proper interspace	15%
Inserts needle midline of back	15%
Needle inserted perpendicular to skin	28%
Advances needle towards umbilicus	30%
Advances smoothly/ avoids coarse motion	32%
Advances slowly, checking for fluid	38%
Takes proper corrective action if no fluid	36%
Acquires fluid	22%
Removes needle after replacing stylet	24%
Discards sharps properly	20%

CONCLUSIONS: Despite viewing a procedural training video, interns are unable to perform the infant LP procedure independently on a LP task trainer without considerable prompting from an instructor. These descriptive data are part of an ongoing multi-center trial evaluating mastery training and just in time refreshers to improve LP skills and success rates. Our sample includes 1/5 of all pediatric interns from accredited programs.

129

5:00 PM

House Officer

Resident Medication Reporting Errors during Pre-Rounding

Misha Bhat, Kathleen M. Donnelly, Swati Agarwal.
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BACKGROUND: Changes in resident work hour regulations have increased the number of patient handoffs. One study estimated medication errors during handoffs to be 27%. Time available to pre-round is also limited and residents might eliminate checking the active medication list as a part of their pre-rounding effort. An erroneous active medication list may then be reported during attending rounds leading to clinical misjudgment and improper documentation in the daily progress note. There is currently no data regarding the frequency of medication errors following pre-rounding.

OBJECTIVE: Our primary objective is to establish the frequency of resident medication reporting errors following pre-rounding. Secondary objectives include investigating resident medication reporting errors to resident workload and patient complexity.

DESIGN/METHODS: During a 4 week period, resident pre-rounding notes on the inpatient pediatric wards at one childrens' hospital were compared to the active medication list. Scheduled and PRN medications were evaluated for accuracy. TPN and fluid rates were not included in the study. Resident workload was assessed noting the number of patients per resident and patient complexity was assessed by noting total medications per patient. Medications were labeled as completely correct, partially correct (with wrong or omitted route, dose or interval) or missed medications. For continuous medication infusions, the notes were compared to the bedside chart for accuracy regarding infusion dose. Residents were not informed of the purpose of the study and no data was recorded linking errors to a particular resident.

RESULTS: A total of 212 pre-rounding notes with 961 scheduled medications and 491 PRN medications were analyzed. Overall medication error reporting frequency was 32% with 22% of scheduled medications having missing or erroneous information. This is significantly different from PRN medications ($p < 0.0001$). Error rates were significantly lower with increased resident workload (>6 patients, $p=0.04$) and complexity (>10 medications, $p=0.04$).

	Correct	**Partially Correct**	**Missed**
Scheduled Medications (n=961)	78%	13%	9%
PRN Medications (n=491)	48%	25%	27%

Table 1. Accuracy of medication reporting.

CONCLUSIONS: Frequency of medication reporting errors following pre-rounding is 32%. Surprisingly error rates were lower with increased resident workload and patient complexity. In the future, direct communication between the sign out software and active medication lists should greatly reduce these errors.

130

5:15 PM

Reliability of Parental Self-Report of Inhaled Corticosteroid Adherence in Inner-City Children with Persistent Asthma

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BACKGROUND: Physicians often rely on parental self-report of inhaled corticosteroid (ICS) medication adherence to guide asthma management in children with persistent asthma. The reliability of parental self-report of ICS adherence has not been well established in inner-city minority population.

OBJECTIVE: To examine reliability of parental self-report in assessing ICS adherence in inner-city children with persistent asthma.

DESIGN/METHODS: Prospective observational study of parents of young children with persistent asthma. All children have been prescribed ICS with a dose counter by their physician prior to enrollment. At enrollment, children received a new, marked ICS at the prescribed dose. Parents were instructed to administer ICS as per physicians' orders (2 puffs 2 times/day). If used as directed, 120 actuations in the new inhaler suffice for 30 days of treatment. Thirty days post-enrollment, we measured ICS adherence by parental self-report and objectively, using the number of puffs left as displayed on a dose counter. Parental self-reported ICS adherence was defined as follows: when parents administered ICS "every day" - 100%; "almost every day" - 75%; "several times a week" - 50%; "once a week"- 25%; and "less than once a week" - 0%. Adherence was

calculated as the number of puffs used relative to the number of puffs expected to have been used at 30-day follow-up. Wilcoxon signed-rank test compared the two adherence methods.
RESULTS: Overall, 40 parents participated (mean age=32.7 (SD 6.6), 66% Hispanic, 29% completed less than high school). Parental self-report overestimated ICS adherence (40% of parents reported being 100% adherent as compared to 5% being 100% adherent as per dose counter). Parents under-reported nonadherence (3% of parents reported 0% adherence as compared to 10% having 0% adherence as per dose counter). Wilcoxon signed-rank test revealed a statistically significant overall difference between parental self-report and objectively measured adherence (p<.0001).
CONCLUSIONS: Parental self-report proved to be a non-reliable method for assessing ICS adherence. A dose counter that most ICS inhalers are equipped with may be a more reliable alternative measure of ICS adherence. These results may have implications for physicians using parental self-report in managing persistent asthma.

131

5:30 PM

Medical Student

Do Caregivers of Children with Persistent Asthma Know How To Use Metered Dose Inhaler Plus Spacer Device?

Yu Cao, Jacquelyn Dorsky, Marina Reznik.
Pediatrics, Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Metered dose inhaler (MDI) with spacer is the most recommended delivery system used for administering medications to children with asthma. Improper MDI-spacer technique can result in decreased drug delivery and poor asthma outcomes. Limited data exists on the caregiver ability to correctly use MDI-spacer technique when administering medication to inner-city minority US children with persistent asthma.
OBJECTIVE: To determine whether caregivers of young children with persistent asthma can correctly demonstrate MDI-spacer technique.
DESIGN/METHODS: A pilot study of caregivers of children (ages 2-9 years) with persistent asthma receiving care at an inner-city comprehensive health care center. First, we asked caregivers if their child has a spacer and frequency of its use. Then, subjects were asked to demonstrate how they would administer two puffs of Albuterol with an MDI-spacer device. We decided to use the two-way valve AeroChamber Plus with mask (Monaghan Medical, Plattsburgh, NY), the most commonly used spacer device in pediatric asthma management. We coded the subject's performance as correct or incorrect using the manufacturers' instructions as the criterion standard. Descriptive statistics were performed.
RESULTS: 66 caregivers participated (mean age 32.3 yrs (SD 8.3); 59% Hispanic; 96% mothers; 27% attained less than a high school diploma). Overall, 92% of caregivers reported that their child has a spacer and 78% stated that their child is using the spacer every time they use MDI. While 97% of caregivers reported that "a doctor explained how to use pump-spacer device", only 49% stated that a doctor had asked them to demonstrate how they would use the MDI-spacer system. When asked to demonstrate how they would use the MDI-spacer device, only 2% of subjects correctly demonstrated all the steps (see Table).

Proportion of caregivers who correctly demonstrated the steps of MDI-spacer use

Steps	% demonstrated correctly
Shakes MDI for 5 sec	67%
Forms tight seal	97%
Instructs to exhale	24%
Presses down once	83%
Correct no. breaths	39%
Waits correct interval for next puff	27%

CONCLUSIONS: Although physicians instructed caregivers on MDI-spacer use, the caregivers did not know how to use the device. Further improvement efforts should include formal assessment of physician ability to teach the technique as well as repeated caregiver instruction to ensure proper use of the device.

Infectious Diseases & Immunology Platform Session

Saturday, March 26, 2011
4:15 PM-5:45 PM

132

4:15 PM

House Officer

The Etiology of Respiratory Infection and Severity of Illness

Therese Canares, Paul Chambers, Kathryn Scharbach.
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BACKGROUND: Respiratory tract infections are a leading cause of hospital admission in children. Respiratory viral testing may predict severity of illness and limit costs associated with treating these illnesses.
OBJECTIVE: To determine whether certain respiratory infections are associated with increased severity of illness.
DESIGN/METHODS: This is a retrospective chart review at an urban, tertiary care children's hospital evaluating respiratory viral testing from Oct 2009-Sept 2010. ED protocol dictated respiratory viral panel (RVP)(xTAG, Luminex Corp) testing on patients with influenza (flu)-like illness (fever plus cough, rhinorrhea, or sore throat), who were either admitted or had a risk factor for serious illness (<2 years old, pregnancy, chronic medical condition). RVP reports 12 viral subtypes. Fisher's exact and chi-square tests were used to perform bivariate analysis of categorical variables, and Kruskal-Wallis tests to compare medians. Logistic regression was used for multivariate analysis.
RESULTS: 1,382 patients had RVP results: negative in 474(34%), RSV (A,B) only in 172(12%), flu A (human H1,human H3,swine H1N1) in 67(5%), flu B in 0, parainfluenza (1,2,3)) in 84(6%), hMPV in 128(9%), rhinovirus in 369(26%), adenovirus in 15 (1%), and co-infections with >1 virus in 73 (5%). A negative RVP was associated with higher ICU admission rates (9.8% vs 5.8%, p=0.007) and longer length of stay (LOS)(median 3 vs 2 days, p<0.0001) when compared to any positive result. Differences amongst viral subtypes did not reach statistical significance for ICU stay(p=0.9). Differences in median LOS were seen in RSV and hMPV (3days); flu, parainfluenza, and rhinovirus (2days); and adenovirus (2.5days), p<0.0001. Adjusting for race, gender, ethnicity, language, insurance and age, RVP positive patients had 37% lower odds of ICU admission (p=0.04), and 25% greater odds of LOS <3 days (p=0.03), as compared to RVP negative.
CONCLUSIONS: The presence of viral infection by RVP correlated with a lower ICU admission rate and shorter LOS, suggesting identification of a respiratory virus may predict less severe disease. This supports previous reports that viral respiratory infections found on rapid antigen tests are associated with lower disease severity. Prospective evaluation of differences in severity of illness by viral etiology is ongoing.

133

4:30 PM

Medical Student

Time to and Predictors of CD4+ T-Lymphocytes Recovery in HIV-Infected Children Initiating Antiretroviral Therapy in Ghana

Meghan Prin, Lorna Renner, Fang-Yong Li, Bamenla Goka, Veronika Northrup, Elijah Paintsil.
Department of Pediatrics, Yale University School of Medicine, New Haven, CT; Department of Pediatrics, University of Ghana Medical School, Accra, Ghana.

BACKGROUND: The therapeutic goal of highly active antiretroviral therapy (HAART) is to suppress HIV viral replication and restore immune function (i.e., CD4+ T-lymphocyte recovery). However, basic testing to monitor the efficacy of HAART, like CD4+ T-lymphocyte measurements, is not routinely available in most resource-limited settings.
OBJECTIVE: We sought to investigate predictors of the time to CD4+ T-lymphocyte recovery in HIV-infected children on HAART. This information could guide HAART in places where routine monitoring is not otherwise available.
DESIGN/METHODS: This is a retrospective study of a cohort of HIV-infected children who received HAART between April 2004 and December 2009 at Pediatric HIV Clinic of Korle-Bu Teaching Hospital in Accra, Ghana. The main study outcome was time to CD4+ T-lymphocyte recovery, defined as achieving and maintaining percent CD4+ T-lymphocytes of 25 during the study follow up period. The predictor variables were gender, age, HAART regimen, WHO clinical staging and WHO immune classification at baseline, mode of transmission, HIV and living status of parents, TB co-infection, and adherence to treatment regimen. We used Cox proportional hazard models for identifying significant predictor variables.
RESULTS: During the study period, 351 children were initiated on HAART. 305 of these children had medical charts available, of which 233 had complete records on CD4+ T-lymphocyte counts and were included in our analysis. The mean age at HAART initiation was 5.5 (SD= 3.1) years. The mean duration of follow-up was 110 (SD= 67.7) weeks. Seventy-four percent of study participants achieved immunological recovery. The median recovery time for all ages was 60 weeks (95% CL: 55-65). Children aged between one and five years recovered faster than the other age categories (55 weeks [95% CL: 38 -60]). Evidence at baseline of severe suppression in CD4+ T-lymphocyte count adjusted for age, child's age at HAART initiation, gender, and having parents alive were statistically significant in predicting time to CD4+ T-lymphocyte recovery. Of note, children with no or moderate suppression in the age-adjusted CD4+ T-lymphocytes recovered faster.
CONCLUSIONS: Our findings suggest that in resource-limited settings, a targeted approach based on predictors of CD4+ T-lymphocyte recovery could be a cost-effective way of monitoring HAART in HIV-infected children.

134

4:45 PM

Simulation of Nosocomial and Occupational Risks of Hepatitis C Virus Transmission

Elijah Paintsil, Brett D. Lindenbach, Robert Heimer.
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BACKGROUND: Nosocomial and occupational transmissions of hepatitis C virus (HCV) infection occur approximately ten times more frequently than that of human immunodeficiency virus (HIV). We hypothesized that the prolonged viability of HCV in fomites on work surfaces may contribute significantly to higher incidence. Healthcare workers may come into contact with HCV dried upon surfaces during preparation of plasma, handling of hemodialysis equipment, following placement or removal of venous lines.
OBJECTIVE: We sought to perform a set of experiments to replicate these conditions.
DESIGN/METHODS: We determined the volume of misplaced drops during transfer of serum or plasma from vacutainer tube to other vials for storage or analysis. Thereafter, aliquots equivalent median drop volume of plasma spiked with a genotype 2a HCV reporter virus were loaded into 24-well plates. Plates were stored uncovered at three temperatures: 4°, 20°, and 37°C, representing drops left in a refrigerator, on a bench top, or in an incubator, respectively, for up to 14 days before viral infectivity was determined in a microculture assay. The assay uses relative luciferase activity from the reporter gene as a function of HCV infectivity.
RESULTS: The median volume of an accidental drop was 27 µl (min - max of 18 - 33 µl). At day 7 of storage, the percentage of wells that was positive was 95 ± 7.1, 70, and 63± 10.6 at 4º, room temperature, and 37º, respectively. After 14 days of storage, the percentage of wells that were positive was 95 ± 7.1, 15± 7.1, and 0 at 4º, room temperature, and 37º, respectively. Based on relative luciferase activity, viral infectivity was reduced by 50% from that time zero before 3 hr at room temperature and 37° and after 6 hr at 4º.
CONCLUSIONS: The infectivity of the recovered virus was inversely related to duration and temperature of storage. The hypothesis of potential transmission from fomites was supported by the experimental results.

135

5:00 PM

House Officer

The Utility of Rapid RSV and Influenza Testing Versus a Multiplex PCR Viral Assay in Cohorting Hospitalized Patients

Therese Canares, Kathryn Scharbach.
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BACKGROUND: Rapid RSV and influenza (flu) testing significantly reduce length of ED stay, hospitalization rates, diagnostic testing, and antibiotic prescription. These tests are frequently used in the hospital to cohort patients. Most sensitivity and specificity reports for rapid RSV and influenza tests are published by test manufacturers.

OBJECTIVE: To determine the sensitivity and specificity of rapid RSV and influenza detection as compared to respiratory viral panel (RVP), a multiplex PCR assay, as the gold standard.

DESIGN/METHODS: The 3M Rapid Detection RSV and Influenza A&B assays, as well as RVP (xTAG, Luminex Corp), were performed as per hospital protocol on children in the ED with influenza-like illness (fever plus cough, rhinorrhea, or sore throat), who either required admission or had a risk factor for severe illness (<2 years old, pregnancy, or chronic medical condition). Patients seen in the pediatric ED of an academic, urban, tertiary care children's hospital from Oct 2009-Sept 2010 with the above testing were included in this retrospective chart review.

RESULTS: A total of 1,401 patients had results available for rapid and RVP testing. A subset of 630, 690, and 673 results for rapid RSV, flu A and flu B, respectively, were analyzed. Sensitivity for rapid RSV was 51% and specificity was 95%. Sensitivity for rapid flu A was 27% and specificity 97%. No subjects were positive for flu B on RVP, and rapid flu B specificity was 95%. False positives for rapid RSV, flu A and flu B were 5%, 2% and 100%, with 62% of false positives for rapid flu B positive for another virus on RVP. The sensitivities of rapid RSV (38%) and flu A (8%) were lower among the patients > 2 years old.

CONCLUSIONS: The sensitivity of 3M Rapid Detection RSV and Influenza A&B found here is lower than reported by the manufacturer (88%, 80% and 58.3%, respectively). Specificity in this study is comparable to manufacturer reports. The use of rapid RSV and influenza tests as a screening tool for cohorting in-patients may be limited in utility. The decreased sensitivity in patients >2 years old demonstrates a further limitation of rapid tests. The benefits of cohorting to prevent nosocomial infection by using a more sensitive multiplex PCR test must be weighed against the costs of such tests.

136

5:15 PM

Distribution of Respiratory Syncytial Virus (RSV) Subtypes A and B among Infants Presenting to the Emergency Department (ED) with Lower Respiratory Tract Infection (LRI) or Apnea

Hasan S. Jafri, Kelly J. Henrickson, Xionghua Wu, Doris Makari, Hanaa Elhefni.
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BACKGROUND: RSV is a leading viral respiratory pathogen worldwide. RSV has two major subtypes, A and B. Data on the distribution of RSV A and B across the U.S. and parameters of disease severity associated with these subtypes are limited.

OBJECTIVE: To describe the distribution and parameters of disease severity associated with RSV A and B in infants with LRI or apnea in the ED.

DESIGN/METHODS: A U.S. multi-center active surveillance study was conducted over 2 RSV seasons (Season 1: 23 states, 31 sites; Season 2: 20 states, 27 sites). Infants <1 yr of age with symptoms of LRI or apnea were enrolled during Sep 1, 2006 - May 31, 2007 (Season 1), and Sep 1, 2007 - May 31, 2008 (Season 2). RSV subtypes were detected in nasal or nasopharyngeal swabs by PCR assays for RSV A and B.

RESULTS: 4172 patients were enrolled: 2023 in season 1 and 2149 in season 2. 656/2023 (32.4%) were positive for RSV A or B in season 1, while 643/2149 (29.9%) were positive in season 2. In season 1, 492/2023 (24.3%) were positive for RSV A, while 169/2023 (8.4%) were positive for RSV B. In season 2, 361/2149 (16.8%) had RSV A, and 284/2149 (13.2%) had RSV B. The distribution of RSV A and B was also analyzed by CDC-defined geographic regions dividing the U.S. into 10 regions and Florida. Both subtypes were detected in each region except for region 1 as no sites participated in the study from region 1. No demographic parameters were consistently associated with RSV subtype infection, except in season 1 where RSV A infection was significantly higher than B among Whites (RSV A, 64.8%; RSV B, 48.5%; *P*=0.0008). In season 1 alone, a higher proportion of hospitalizations were observed in RSV A–positive cases compared with those with RSV B (RSV A, 54.9%; RSV B, 39.1%; *P*=0.005). In seasons 1 and 2, a higher proportion of RSV B cases had antibiotic use (RSV A, 32.4%; RSV B, 47.8%; *P*=0.0004).

CONCLUSIONS: RSV subtypes A and B were documented across all U.S. regions studied in this protocol in seasons 1 and 2. The only demographic or disease severity parameter consistently associated with either subtype was higher use of antibiotics in RSV B cases. To date, this is the largest epidemiologic study reporting the trends in RSV subtypes. More studies across additional geographic regions within and outside the U.S. may be needed to expand on the findings of this study.

137

5:30 PM

Genetic Variation in Antimicrobial Peptide, Human-β-Defensin-1 (DEFB1) Is Associated with Recurrent Staphylococcus aureus Skin Infection in Children

Hitesh S. Deshmukh, Howard R. Faden, Lucy C. Holmes, Steven R. Gill.
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BACKGROUND: Skin infections due *Staphylococcus aureus* (*S. aureus*) remain a serious, common, and costly medical concern in children. Antimicrobial peptides (AMP) expressed by keratinocytes are the key mediators of skin innate immunity. Clinical significance of variation in innate immunity genes response in initiation, severity and recurrence of skin infections caused by *S. aureus* is incompletely understood.

OBJECTIVE: The determine if genetic variations in AMP expressed by keratinocytes, human β-defensin (DEFB) 1, DEFB2, cathelicidin antimicrobial peptide (CAMP), secretory leukocyte protease inhibitor (SLPI) and lipocalin 2 (LCN2) are associated with serious *S. aureus* skin infection.

DESIGN/METHODS: We used a family based cohort study to investigate the genetic association of innate immunity genes with serious *S. aureus* skin infections requiring surgical drainage. 10 haplotype tagging single nucleotide polymorphisms (ht-SNPs) in DEFB1, DEFB2, CAMP, SLPI and LCN2 were chosen from the CEU (European) population of the International HapMap project. DNA from the first 44 nuclear families (affected child with *S. aureus* skin infection, mother and father) out of 102 nuclear families recruited for this study was genotyped for these htSNP. The presence of Hardy-Weinberg equilibrium was examined using the chi-squared test for goodness of fit. Single-point and haplotype association was assessed using the Transmission Disequilibrium Test (TDT) in Haploview.

RESULTS: Of 44 families, 25 (56%) were Black, 10 (23%) were White and 6 (14%) were Hispanic. Of 44 children (mean age 7.5 1.3 yr), 33 (75 %) were female, 11 (25 %) were male and 14 (33 %) had prior *S. aurues* skin infection. After adjusting for co-variates; age, gender, ethnicity and history of prior infection, the single-point analysis revealed that the risk allele (A) of htSNP rs2741127, was over transmitted to affected children with severe *S. aureus* skin infections (2=3.84, *P*=0.0476, df = 1). Genotyping and testing for association of ht-SNPs in DEFB2, hCAP-18, SLPI and NGAL is underway.

CONCLUSIONS: These data suggest that some children presenting with serious *S. aurues* skin infection, in the present outbreak of community acquired *S. aureus* skin infections have increased susceptibility due to genetic variation in DEFB1. Anti-microbial peptides play a crucial role in *S. aureus* infection and are thus clinically relevant.

Neonatology - Clinical Studies I
Platform Session

Saturday, March 26, 2011
4:15 PM-5:45 PM

138

4:15 PM

Low Vagal Tone Is Associated with Impending Necrotizing Enterocolitis in the Preterm Infant

Kim Kopenhaver Haidet, Charles Palmer.
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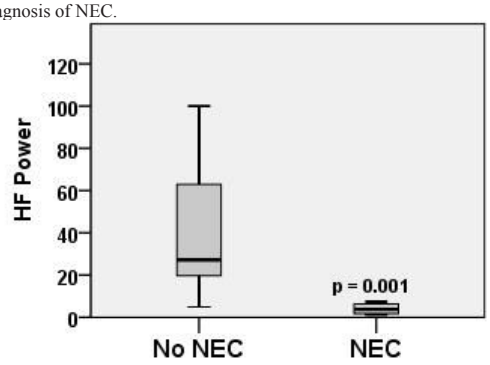
BACKGROUND: Necrotizing Enterocolitis(NEC)is a common and often devastating GI disorder that primarily afflicts preterm infants with an incidence of approximately 6-10%. Success of treatment depends on early diagnosis. Heart rate variability(HRV)provides information on the balance of sympathetic and parasympathetic(vagal)systems. Autonomic dysregulation is an early marker of impending illness. We hypothesized that diminished GI motility and low vagal tone measured by HRV would predict susceptibility to NEC.

OBJECTIVE: To determine if low vagal tone measured by HRV during the first week of life would be associated with the development of NEC in preterm infants.

DESIGN/METHODS: 30 infants(29-36wks)were enrolled in this prospective, observational study. Infants were excluded for congenital anomalies, CNS lesions, or if they required ventilation. On day 5-7 of life, resting HRV was measured postprandially and analyzed using frequency domain analysis. The high frequency(HF)power spectrum band(.2-2Hz)was selected specifically to reflect parasympathetic(vagal)activity. Infant health outcomes were obtained by chart audit by coders blinded to HRV analysis.

RESULTS: Subjects were 32.6±1.5wks GA (mean±SD) and weighed 1878±409 gms. Four (13%) of the 30 study infants developed NEC confirmed by radiologic (pneumatosis intestinalis) and clinical findings. Of the 26 infants that did not develop NEC, we excluded 7 who were treated for sepsis within the first 10 days of life. 19 infants who remained healthy for the first month of life were compared to those infants with confirmed NEC. NEC infants had significantly lower power in the HF band, 2.8±1.4msec2 (mean±SE) compared to healthy infants, 45±10msec2, p=0.001. Interestingly, the detection of low HF power was obtained from 12 hrs to 9 days prior to the confirmatory diagnosis of NEC.



CONCLUSIONS: Our pilot study findings were that markedly lower HF power(ie. lower vagal tone)was associated with the onset of NEC in preterm infants. Low vagal tone identifies a subgroup of infants most susceptible to developing NEC.

4:30 PM

Fellow in Training

Intrauterine Growth Restriction Alters Vascular Reactivity in Adult Female Rats

Melissa F. Carmen, Catalina Bazacliu, Bobby Mathew, Sylvia Gugino, Satyan Lakshminrusimha, Daniel D. Swartz.

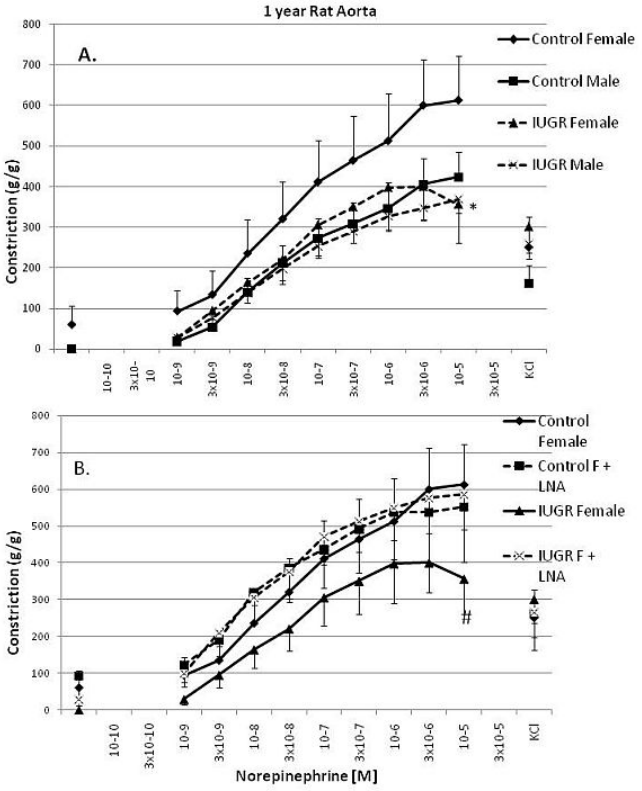
Pediatrics, State University of New York at Buffalo, Buffalo, NY.

BACKGROUND: Intrauterine growth restriction (IUGR) affects 10% of all newborns. There is a link between low birth weight and the subsequent development of disorders that contribute to cardiovascular disease in adulthood. Gender affects the onset and severity of certain adult diseases. Further research into the roles of IUGR and gender in the onset of adult disease is warranted.

OBJECTIVE: To evaluate gender differences in aortic reactivity of IUGR and control rats at 1 year of age.

DESIGN/METHODS: Control rats were fed a standard diet throughout the study. Pregnant dams were fed a low protein diet (LPD) to induce IUGR in the pups. After birth, the mothers continued on a LPD while nursing the pups. Once the pups were weaned, they were placed on a high fat diet in an effort to obtain "catch-up" growth. At 1 year of age, aortic rings were tested for constriction response to norepinephrine (NE) and relaxation to SNAP (nitric oxide donor). Some vessels were pretreated with L-arginine (LNA) to evaluate to effects of IUGR on the eNOS system.

RESULTS: Maternal protein restriction did not affect NE-induced contractility in male rat vessels but significantly impaired contractility in the vessels of female IUGR rats at 1 year of age(FigA). There is a significant increase in aortic contractility to NE in female IUGR rats following pretreatment with LNA(FigB). There is no significant difference in vascular reactivity in male rats, both control and IUGR, when the vessels were pretreated with LNA. Relaxation response to SNAP was similar in control and IUGR rats, regardless of gender.



* p < 0.05 IUGR Female vs. Control; # p < 0.05 IUGR Female vs IUGR Female + LNA.

CONCLUSIONS: Maternal protein restriction during pregnancy induces long term alteration of vascular reactivity in female offspring. Increased constriction of the aorta in female IUGR rats following LNA treatment suggests an increased endogenous production of NO in these tissues. We speculate that IUGR due to maternal undernutrition increases endogenous NO release, thereby reducing aortic contractility in adult females.

140

4:45 PM

Location of Spontaneous Intestinal Perforation (SIP) – Role of Initial Peristalisis

Bobby Mathew, Jayasree Nair, Melissa F. Carmen, Daniel D. Swartz, Sylvia F. Gugino, Satyan Lakshminrusimha.

University at Buffalo, Buffalo, NY.

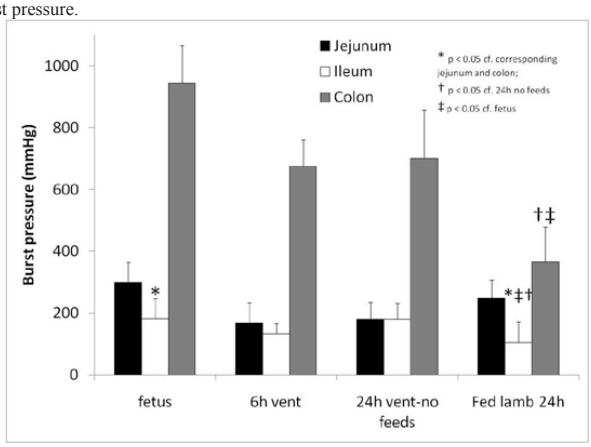
BACKGROUND: SIP occurs in premature neonates at approximately 8d of age. Similar to necrotizing enterocolitis, SIP is more common in the ileum. Unlike NEC, ischemia does not play a role in the etiology of SIP. The reason for localization of SIP to the ileum is not known.

Gordon et al have suggested the role of early intestinal peristalsis in the etiology of SIP. As intestinal peristalsis reaches the ileum that is predisposed to perforation, the ileum perforates to the increased intraluminal pressure. Early peristalsis may be induced by feeding the premature gut or by increased air swallowing that occurs with mechanical ventilation.

OBJECTIVE: The objective of the study was to evaluate the intestinal burst pressures in the jejunum, terminal ileum and ascending colon in a preterm lamb. We also evaluated the effect of early peristalisis induced by ventilation and feeds on intestinal burst pressures.

DESIGN/METHODS: Lambs were delivered at 134 d gestation by cesarean section. The animals were studied in four groups: (1) fetal lambs sacrificed at delivery (n=5), (2) lambs ventilated for 6 h (n=7), (3) lambs ventilated for 24 hours without feeds (n=11) and (4) lambs fed for 24 hours (n=4). Animals were sacrificed and intestinal burst pressures were evaluated by injecting saline into a 5 cm portion of the intestine connected to a pressure transducer.

RESULTS: Terminal ileal burst pressures were significantly lower compared to jejunum and ascending colon. Terminal ileal burst pressures were significantly lower following 6 hours of ventilation as compared to the fetus. Animals that were fed for a period of 24 hours had the lowest ileal burst pressure.



Prolonged feeding increased ileal burst pressure to fetal values (data not shown).

CONCLUSIONS: Terminal ileum is the part of the intestine that is most prone to rupture by distending pressure. Factors such as feeding, ventilation (swallowed air) that initiate peristalsis may transiently predispose to the perforation of the premature ileum.

141

5:00 PM

Randomized Controlled Trial of Early Total Parenteral Nutrition (TPN) Cycling To Prevent Cholestasis in VLBW Infants (VLBWI)

Agnes Salvador, Michael Janeczko, Rachel Porat, Romal Sekhon, Anja Mowes, David Schutzman.

Pediatrics, Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: Cholestatic jaundice as a complication of prolonged TPN (TPNAC) is the most common cause of direct hyperbilirubinemia in premature infants. Since no effective therapy is currently available, focus should be on prevention. Cycling of TPN infusion has been used in children with short bowel syndrome to prevent cholestasis. To date, there is limited data on the efficacy of cycled TPN in VLBWI.

OBJECTIVE: (1) Compare the incidence of cholestasis in VLBWI receiving cycled vs. continuous TPN.(2) Determine factors that predispose to TPNAC.

DESIGN/METHODS: We conducted a randomized controlled trial of cycled TPN (CyTPN) vs. continuous TPN (ConTPN) initiated within the first 5 days of birth in VLBWI ≤ 1250-gram birth weight (BW). ConTPN received amino acid (AA) infusion for 24 hours/d. CyTPN received AA for 20 hours/d with a 4-hour break, when dextrose water was infused. Demographics, morbidities, feeding profile and hepatic lab. data were collected. Cholestasis was defined as direct bilirubin >2 mg/dL.

RESULTS: 70 infants completed the study; CyTPN = 34, ConTPN = 36. CyTPN and ConTPN groups were similar in gestational age (GA) (25.9 wks vs. 26.1 wks) and BW (0.81 kg vs. 0.83 kg). Morbidities (early-onset sepsis, RDS, BPD, PDA, and NEC ≥ Stage 2) were similar in both groups. Groups were similar in duration of TPN, total NPO days, number of infants NPO >2 wks, postnatal age (PNA) trophic feeds were started, and PNA full feeds were reached. Incidence of TPNAC was similar in both groups (32 % vs. 31%). Mean peak direct bilirubin in CyTPN and ConTPN (2.9 mg/dL ± 2.2 vs. 1.5 mg/dL ± 1.9) occurred at week 10 in both groups. More babies in CyTPN vs. ConTPN had presumed and culture proven late onset-sepsis (P=.045). Multiple logistic regression of risk factors for cholestasis showed that GA (OR= .36, 95% CI=.16-.82, P=.014) and BPD (OR=10.6, 95% CI=1.9-57.9, P=.007) were significant risk factors for TPNAC. For each one-week decrease in GA, the odds of cholestasis increased 2.8 times.

CONCLUSIONS: Early cycling did not reduce the incidence of TPNAC. The association between TPN cycling and presumed or late-onset sepsis is uncertain, but may be related to the number of times the central line was accessed. Of the risk factors for TPNAC, GA and BPD emerged as the strongest predictors. Further understanding of the pathogenesis of TPNAC may lead to different interventions and preventive strategies.

142

5:15 PM

Fellow in Training

Enteral Feeding and Antenatal Betamethasone Alter Mesenteric Vascular Reactivity in Late Preterm Lambs

Jayasree Nair, Bobby Mathew, Melissa Carmen, James Russell, Satyan Lakshminrusimha.

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Physiology, State University of New York, Buffalo, NY.

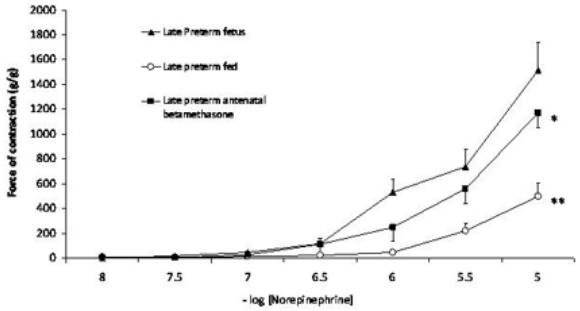
BACKGROUND: Intestinal ischemia is an important predisposing factor for necrotizing

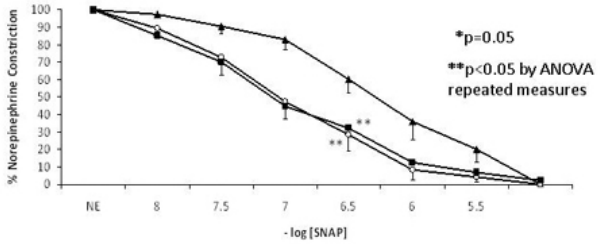
enterocolitis (NEC). We previously showed that norepinephrine(NE) mediated mesenteric artery(MA) constriction peaks at late preterm gestation in fetal lambs(Nair et al PAS 2010) corresponding to the period of peak incidence of NEC(31-33 wk postconceptional age). Increased response to contractile agents like NE and decreased relaxation to nitric oxide(NO) donor increases the risk of intestinal ischemia and NEC. Antenatal steroids reduce the incidence of NEC.The effect of early enteral feeds and antenatal steroids at this gestation on mesenteric vasoreactivity is not known.

OBJECTIVE: To study changes in contractile response of ovine MA at late preterm gestation (134d, term~145d) to NE and relaxation to NO donor S-nitroso-N-acetylpenicillamine(SNAP).We also evaluated the effect of antenatal betamethasone(beta) and early enteral feeds on mesenteric vasoreactivity.

DESIGN/METHODS: Time dated pregnant ewes received antenatal beta(n=6) at 132 and 133d gestation. Lambs were delivered by C-section at 134d gestation and sacrificed at birth. 8 lambs, not exposed to beta were delivered at the same gestation.Of these,5 were sacrificed at birth and 3 were fed expressed maternal milk for 24h and then sacrificed.MA of lambs were dissected, pretreated with propanolol and constricted with increasing doses of NE(10^{-8}-10^{-5}M) and relaxed with SNAP(10^{-8}-10^{-5}M).

RESULTS: NE constricted 134d gestation fetal lamb MA in a dose dependent manner. Exposure to antenatal beta significantly reduced contractile response to NE as did postnatal enteral feeds. Relaxation to SNAP improved with antenatal beta and postnatal feeds.





CONCLUSIONS: In the late preterm lamb,decreased constriction to NE and enhanced relaxation to SNAP may be indicative of NO mediated mesenteric vasodilation in response to antenatal beta and enteral feeds. Antenatal betamethasone and early enteral feeds may reduce NEC by facilitating ovine mesenteric vasorelaxation.

143

5:30 PM

Fellow in Training

The Proinflammatory Role of Serotonin in a Murine Model of Necrotizing Enterocolitis

Maria M. Talavera, Kara Gross, Sam Li, Korey Stevanovic.
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BACKGROUND: Necrotizing enterocolitis (NEC) is a devastating gastrointestinal disease of prematurely born infants, characterized by extensive hemorrhagic inflammation of the distal ileum and proximal colon. Pathogenesis is unknown but known risk factors include prematurity, formula feeding and bacterial translocation.

While serotonin (5-HT) is a neurotransmitter that has classically been recognized for its functions in the brain, 95% of 5-HT is stored in the gut where it plays a large role in motility, secretion and intestinal inflammation. Mucosal 5-HT can only cross lipid bilayers of the plasma membrane with the assistance of serotonin transporter (SERT). Thus, inhibition of mucosal SERT leads to high extracellular levels of 5-HT. The role of 5-HT and SERT in an animal model for NEC have never been evaluated.

OBJECTIVE: Because 5-HT and SERT have been shown to potentiate the inflammation seen in animal models of chemically induced colitis, we hypothesized that 5-HT is an important proinflammatory mediator in NEC as well.

DESIGN/METHODS: Used a previously established animal model for NEC to study the role of serotonin as a proinflammatory mediator. The two experimental groups were SERT KO mice (C57 Bl6 background) and WT mice at day 10 of life. The NEC protocol includes every 3hr formula feedings and twice daily hypoxic exposure. The control groups included SERTKO and WT groups that were not exposed the the NEC protocol. Weight loss and mortality rates were followed in the experimental groups. At the conclusion of the 5 days, tissue was harvested for histological evaluation and RT-PCR.

RESULTS: Out of the two groups exposed to the NEC protocol, the SERT KO mice exhibited a significantly faster and higher rate of weight loss than the WT group (P value < 0.0001). Preliminary histological analysis of the tissue sections showed a trend toward worsened histological scores in the SERTKO group. RT-PCR of the intestinal tissue taken from both groups demonstrated significantly higher upregulation of the proinflammatory cytokines IL-18 (P<0.025) and iNOS (P-value 0.033) in SERTKO vs WT group.

CONCLUSIONS: Our findings suggest that SERT and mucosal serotonin do indeed play a proinflammatory role in necrotizing enterocolitis. Future studies evaluating the protective effect of serotonin antagonism may further confirm the role that 5-HT plays in NEC and may ultimately lead to the design of novel therapies for its treatment.

Neonatology - Epidemiology & Follow Up Platform Session

Saturday, March 26, 2011
4:15 PM-5:45 PM

144

4:15 PM

Fellow in Training

Variation in NICU Late Preterm Admisison Rates without Identifiable Cause

Kathryn Ziegler, David A. Paul, Matthew Hoffman, Jonathan Cohn, Robert Locke.
Neonatology, Christiana Hospital, Newark, DE; Pediatrics, Thomas Jefferson University Hospital, Philadelphia, PA; Obstetrics and Gynecology, Christiana Care Health Services, Newark, DE.

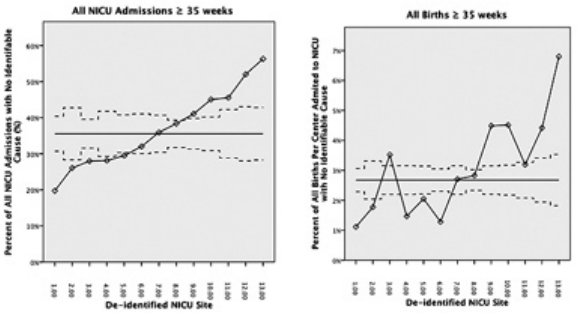
BACKGROUND: NICU admission rate is an important indicator of birth outcome. In addition to infant physiologic compromise, admission to the NICU can be influenced by hospital care protocols, especially in the case of late preterm and older gestation infants. Providing appropriate level of monitoring in an NICU setting must be balanced with minimizing costs, and other potential adverse consequences, of NICU admission.

OBJECTIVE: To determine the variation in NICU admissions rates among term and late preterm infants.

DESIGN/METHODS: Consortium on Safe Labor Database was used to determine NICU admission rates and infant health data from 156,983 infants ≥ 35 wks and ≥2500 grams birthweight within 13 centers in the US from 2002-2008. NICU admission rates were controlled for infant health compromise: any oxygen use (including all modes of ventilation), sepsis, pneumonia, intracranial hemorrhage, asphyxia, HIE, seizures, NEC, TTN, blood product transfusion, and maternal chorioamnionitis. Process control charts were utilized to evaluate the variation among different hospitals in their NICU Admission rates.

RESULTS: The percent of all births per center that did not have a clearly identifiable cause for a NICU admission ranged from 1.1 - 6.8%.

Within all NICU admissions per center, the percentage of infants ≥35wks and ≥2500gms without an identifiable cause for intensive care services ranged from 19.7 - 56.3%.



CONCLUSIONS: There is significant variation in NICU admission rates that can not be fully explained by infant health compromise, birthweight, or gestational age. Further analysis is needed to determine cause of individual site variation and potential opportunities to refine hospital care protocols and optimal use of NICU services.

145

4:30 PM

Fellow in Training

Very Early Language Skills of Late Preterm Compared to Term Infants at Birth and 44 Weeks Corrected Age

Katharine Johnson, Bonnie Stephens, Richard Tucker, Betty Vohr.
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BACKGROUND: Late preterm infants are the largest group of preterm infants, yet limited data exist about their neurodevelopmental outcomes. The effect of prematurity and missed exposure to maternal speech in late fetal life on language outcomes is unknown.

OBJECTIVE: To evaluate 1) early language skills of late preterm and term infants by measuring infant vocalizations and conversational turns (reciprocal vocalizations within 5 sec) 2) exposure to adult speech by measuring adult word counts.

DESIGN/METHODS: This prospective cohort study of medically stable infants without identified hearing impairment, congenital anomalies, or significant comorbidities includes late preterm infants from the NICU (LPNICU n=19, mean GA=34.5wk) and newborn nursery (LPNBN n=13, mean GA=35.8wk) compared to healthy term infants (n=15, mean GA=39.3wk). Langauge assessment during their birth hospitalization and at home at 44 weeks corrected age (44wkCA) included a 16h recording using the LENA™ system to measure adult word count, infant vocalizations, and conversational turns. Statistical analysis included ANOVA and regression models controlling for gestational age to determine independent effects of adult words on child vocalizations.

RESULTS: (To date) The groups differed only by gestational age (p<.0001). During the newborn period, LPNICU infants had less exposure to adult language, fewer infant vocalizations, and fewer conversational turns compared to infants primarily rooming-in with their mothers (LPNBN and term). At 44wkCA, these differences did not persist.

	LPNICU	LPNBN	Term
Newborn recording			
n	19	13	15
chronologic age (days)	6*†	2	2
adult word count/hr	680*†	2598	1824
infant vocalizations/hr	15*†	30	44
conversational turns/hr	5*†	13	12
44wkCA recording			
n	10	7	9
chronologic age (days)	68*	64*	32
adult word count/hr	1514	1151	1514
infant vocalizations/hr	74	86	62
conversational turns/hr	24	22	19

*p<.01 vs term †p<.01 vs LPNBN

After adjusting for gestational age, adult word count independently predicts child vocalizations during the newborn period. For each 100 adult words/hr, child vocalization rates increase by 2% (p=.05).

CONCLUSIONS: Late preterm infants in the NICU had less exposure to adult speech and fewer infant vocalizations in the newborn period, but displayed equal skills to other infants by 44wkCA. The analysis uncovered independent effects of adult speech on infant vocalizations for the cohort in the first days of life.

146

4:45 PM

Fellow in Training

Adult-Infant Conversations in the NICU Are Associated with Higher Cognitive and Language Scores at 7 Months in Very Preterm Infants

Melinda A. Caskey, Bonnie Stephens, Richard Tucker, Betty Vohr.

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BACKGROUND: Language delays are common among preterm infants. Our previous studies have shown that preterm infants begin to make vocalizations in response to caregivers prior to their expected due date and increase vocalizations and conversational turns with caregivers significantly over time. Studies in older children have shown an association between adult-child conversation and improved measures of language ability.

OBJECTIVE: To test the effects of mean adult daily word counts, conversational turns and child vocalizations at 32w & 36w post-menstrual age (PMA) in the NICU with Bayley-III Cognitive and Language scores at 7m corrected age (CA).

DESIGN/METHODS: Prospective cohort study. 36 medically stable and non-intubated infants ≤ 1250 grams b wt. (mean= 896 ± 195g) and gestational age at birth of 27 ± 2 wks were enrolled. 16h recordings were made using a digital language processor inserted into a vest worn by the infant at 32w and 36w PMA. Bayley-III was completed at 7m corrected age (CA). Regression analyses were performed to determine the impact of adult word count, conversational turns and child vocalizations in the NICU on 7m Bayley scores and adjusted for gestational age at birth.

RESULTS: More conversational turns/hr at 32 weeks correlated with higher 7 m Bayley III cognitive composite (r= 0.36; p=0.04), language composite (r= 0.38; p=0.048) and receptive language scores (r= 0.36; p=0.045) in unadjusted regressions. After adjustment of gestational age at birth, higher 36w adult word count/hr (r= 0.42; p=0.03), conversational turns/hr (r= 0.45; p=0.02) and child vocalizations/hr (r= 0.37; p=0.05) were associated with higher 7 m Bayley-III cognitive composite scores . For every turn count per hour, the 7 m cognitive score increased on average by 1.7 points (p = 0.005). In regression analysis to predict 7 m cognitive scores, 36 week turn count/hr accounted for 26% of the variance (p = 0.02).

CONCLUSIONS: Increased number and quality of parent and caregiver early conversations with preterm infants in the NICU are associated with higher 7 m CA Bayley language and cognitive scores. These findings open the door for language intervention in the NICU.

147

5:00 PM

Fellow in Training

Can Prenatal Steroids Be a Risk Factor for Preterm Delivery?

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BACKGROUND: Infection-mediated preterm labor results from in utero immune alterations caused by decreased activity of placental interleukin-10 (IL-10), an essential anti-inflammatory cytokine and/or up-regulation of pro-inflammatory cytokines including IL-1β. In response to threatened preterm labor, it is recommended to give pregnant women prenatal glucocorticoids to enhance fetal lung maturity. However the effects of prenatal glucocorticoids on placental cytokine production in the setting of placental infection is not well studied.

OBJECTIVE: To determine if the commonly used prenatal glucocorticoids, Dexamethasone (Dexa) and Betamethasone (Beta), will alters expression of placental pro- and anti-inflammatory cytokines in response to placental infection.

DESIGN/METHODS: Second trimester placental explants (n= 5) were cultured for 18 hrs with increasing doses of Dexa (12-100ng/ml) and Beta (35-300ng/ml) in the presence or absence of infection (10^6 heat-inactivated E. coli). The doses used in our experiments reflected glucocorticoids levels observed in maternal serum after prenatal glucocorticoids administration. Supernatants were collected and cytokine profiles were assayed using the Bio-Plex array.

RESULTS: The observed effects on unstimulated second trimester placental cytokine levels were similar for both Dexa and Beta. There was decrease in all basal cytokine levels measured (30-70% range reduction for IL-1β, TNF-α and IL-10) after both Dexa and Beta treatments. IL1-β/IL-10 ratio was decreased from 1.7 to 1.3 only after high dose Dexa and Beta treatments, indicating that prenatal glucocorticoids skewed the basal placental cytokines production toward anti-inflammatory environment. However after E.coli stimulation, both Dexa and Beta significantly exaggerated the pro-inflammatory environment induced by E.coli. IL1-β/IL-10 ratio was increased from 1.8 to 3.3 after high dose Dexa and Beta treatments. Surprisingly, this pro-inflammatory environment was more pronounced in low dose Dexa and Beta treatments, compared to high dose (IL1-β/IL-10 ratio = 5.8).

CONCLUSIONS: Dexamethasone and Betamethasone treatments modulate second trimester placental cytokine production. In the absence of infection, glucocorticoids exert a potent anti-inflammatory environment. However in the presence of infection, glucocorticoids alter placental immunologic equilibrium toward exaggerated pro-inflammatory milieu that can augment the tendency toward a preterm delivery.

148

5:15 PM

House Officer

Longitudinal Neurodevelopmental (ND) Outcome in Congenital Diaphragmatic Hernia (CDH) Survivors during the First 3 Years of Life

Enrico Danzer, Marsha Gerdes, Jo Ann D'Agostino, Casey Hoffman, Judy Bernbaum, Michael W. Bebbington, Jennifer Siegle, Natalie E. Rintoul, Holly L. Hedrick.

The Center for Fetal Diagnosis and Treatment, The Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: There is increasing recognition of adverse ND sequelae during the first year of life in CDH survivors, but less is known about ND impairment later in early childhood.

OBJECTIVE: To longitudinally evaluate the ND outcome in CDH survivors during the first 3 years of life.

DESIGN/METHODS: 47 CDH survivors enrolled in our prospective follow-up program between 06/2004 and 09/2010 underwent serial ND evaluations during the first 3years of life. ND outcomes were evaluated using the Bayley Scales of Infant Development (BSID)-II or BSID-III. Persistent impairment was defined as a score that remained ≤79 for the cognitive/language, and motor domains at the most recent follow-up visit compared to the first assessment. Perinatal predictors were evaluated by Chi-square, Fishers exact, or t-test.

RESULTS: Gestational age at birth was 37.8±2.6 weeks, 79% had left-sided CDH, 49% had intrathoracic liver position, 26% required ECMO, 55% required patch repair, age at extubation was 21.2±17.2 days, 34% required supplemental O2 at day of life (DOL) 30, and age at discharge was 60.4±70.9 days. Age at first and last assessment was 9.1±3.1and 28.6±4.7 months, respectively. At initial evaluation more children had motor impairments compared to language/cognitive skills (P<0.001). No difference between these domains was found at the last assessment (P=0.41). During the follow-up cognitive/language scores improved to average (17%), remained average (60%), remained delayed (10%), and deteriorated from average to delayed (13%). Motor scores improved to average (36%), remained average (36%), remained delayed (26%), and deteriorated (2%). Intrathoracic liver-position (P<0.01), supplemental O2 requirement at DOL 30 (P<0.01), age at discharge (P=0.03), GERD (P=0.05), periventricular leukomalacia (P<0.01), and hypotonicity (P<0.01) were associated with persistent motor delays. No relationship was found between patient characteristics and persistent cognitive/language delays.

CONCLUSIONS: Almost a quarter of CDH survivors continue to have ND deficits in early childhood. Motor impairments are more like to improve during early childhood compared to cognitive/language skills. CDH severity is predictive of persistent motor delays. Early ND assessment identifies children who may benefit from early intervention and rehabilitative services.

149

5:30 PM

House Officer

The Increase in Neonatal Morbidity Associated with Cesarean Birth Varies with Gestational Age among Full Term Neonates

Shaon Sengupta, Vivien Carrion, Rita Ryan, James Shelton, Ralph Wynn, Satyan Lakshminrusimha.

State University of New York at Buffalo, Buffalo, NY.

BACKGROUND: Delivery by cesarean section is associated with increased neonatal morbidity, predominantly secondary to respiratory distress. In the present study, we attempt to elucidate the association between gestational age, mode of delivery and incidence of respiratory morbidity in full term neonates born in Erie County, NY.

OBJECTIVE: We propose to study the effect of gestational age and mode of delivery upon respiratory morbidity and need for NICU admission amongst full term neonates.

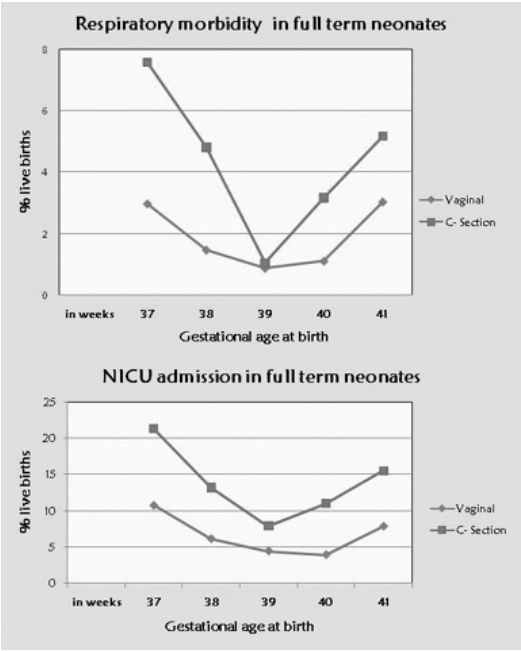
DESIGN/METHODS: This study was a retrospective cohort study of all full term live births in Erie County, NY which included both low risk and high risk pregnancies.

Baseline characteristics of the pregnancies

	Vaginal birth	Cesarean birth	p value
Maternal age (yrs)	27.5 (± 6.1)	30.1(± 5.7)	< 0.01
Received prenatal care (%)	99.5	99.8	0.10
Length of hospital stay of newborn (days)	3.3 (±0.8)	2.1 (±1.2)	<0.01

The data was obtained from the Birth registry database for Erie County. The medical records of the neonates requiring NICU admission and/or respiratory morbidity were reviewed.

RESULTS: There is a difference among the risk associated with each gestational age within each mode of delivery (test of homogeneity p <0.01). Both NICU admissions and respiratory morbidity among all full term neonates born via cesarean section showed a significant trend towards adverse outcome at 37-39 weeks.



The increase in the respiratory morbidity within vaginal births with lower gestational age was not significant. The average length of NICU stay of the newborn born via C-section was 5 days compared to 4 days for vaginal births.

CONCLUSIONS: Delivery by cesarean section markedly increases respiratory morbidity at 37 and 38 weeks gestational age. Attempts to postpone cesarean section to 39 weeks or later as recommended by American Congress of Obstetricians & Gynecologists in elective situations may reduce respiratory morbidity and admission to the NICU.

Neurobiology I
Platform Session

Saturday, March 26, 2011
4:15 PM-5:45 PM

150

4:15 PM

Fellow in Training

Notch Receptors and Their Ligands in Intraventricular Hemorrhage

Sabrina Malik, G. Vinokunda, F. Hu, P. Ballabh.
Neonatal Medicine, Maria Fareri Childrens Hospital, Valhalla, NY; Cell Biology and Anatomy, New York Medical College, Valhalla, NY.

BACKGROUND: Intraventricular hemorrhage (IVH) is a major neurological disorder of premature infants that results in white matter injury. Our previous study has shown that IVH leads to arrested maturation of oligodendrocyte (OL) lineage in pre-OL stage rendering hypomyelination in the white matter of premature rabbit pups. Notch signaling inhibits the differentiation of OL, while enhances astrocytosis. Therefore, we hypothesized that Notch1 receptors or their ligands would be elevated in rabbit pups with IVH compared with controls without IVH.

OBJECTIVE: To evaluate temporal and spatial expression of Notch1 receptor and its ligands, Jagged-1 and Delta-4, in rabbit pups with IVH compared to controls without IVH.

DESIGN/METHODS: We used our model of glycerol-induced IVH, in which rabbit pups (E29) with IVH exhibit hypomyelination and gliosis at 2 weeks of postnatal age. We assessed protein expression of Notch1, Jagged-1 and Delta-4 in premature rabbit pups with and without IVH at postnatal day 3 and 7 using immunohistochemistry and Western blot analyses. For immunolabeling, we used astrocyte(GFAP), neuron (NeuN and Tuj1),oligodendrocyte(O4) antibodies in combination with Notch, Jagged-1 and Delta-4.Western blot analysis was performed on homogenates from a coronal slice taken at the level of mid-septal nucleus.

RESULTS: Notch1 was expressed in radial glia and neuronal progenitors (Tuj1+) of the germinal matrix, OL progenitors (Olig2) in the white matter and neurons (NeuN+) in the cerebral cortex. Immunoreactivity to Jagged-1 was intense in the ependyma and subjacent radial glia, weak on neuronal precursor cells of the germinal matrix, and absent on neurons of the cerebral cortex. Delta-4 antibody labeled ependyma and neuronal precursors cells of the germinal matrix, as well as mature neurons in the cerebral cortex and white matter. Notch-1 expression was more abundant in the brain region around the ventricle of pups with than without IVH. Western blot analyses confirmed that notch protein levels were higher at postnatal day 3 (P=0.029,n=6e) in the forebrain of pups with IVH compared to controls without IVH, but not at day 7. Delta-4 and Jagged-1 levels were comparable in pups with and without IVH at both day 3 and 7.

CONCLUSIONS: IVH induced upregulation of Notch1 protein levels in the forebrain of rabbit pups. We speculate that notch inhibition might reduce gliosis and enhance maturation of OL, thereby promoting myelination in premature infants with IVH.

Supported by: RO1 NS071263 NIH grant (PB).

151

4:30 PM

The Effect of Src Kinase Inhibition and EGFR Inhibition on Caspase 9 Activity Following Post-Hypoxic Recovery

Kirstie Marcello, Jarle Stone, Anli Zhu, Om P. Mishra, Maria Delivoria-Papadopoulos.
Dept. of Pediatrics, Drexel University and St. Christopher's Hospital for Children, Phila, PA.

BACKGROUND: We have demonstrated that hypoxia results in increased activity of caspase-9 in the cytosol of the cerebral cortex of newborn piglets. We have also shown hypoxia results in activation of Src kinase and EGFR kinase. It is known inhibition of these kinases prevents caspase-9 activity immediately post hypoxia.

OBJECTIVE: The present study tests the hypothesis that hypoxia results in Src kinase and EGFR kinase mediated increased activation of caspase-9, that it is sustained during post-hypoxia recovery.

DESIGN/METHODS: Newborn piglets were divided into: normoxia, hypoxia, hypoxia pretreated with a selective inhibitor of EGFR ((PD168393), 1 mg/kg i.v., 30 min prior to hypoxia) and hypoxia pretreated with selective inhibitor of Src (PP2,1mg/kg i.v., 30 min prior to hypoxia) . Hypoxic piglets were exposed to an FiO_2 of 0.07 for 1 hour. Normoxic piglets were exposed to an FiO_2 of 0.21. The piglets were allowed to recover at 1 day (Nx1d, Hx1d, Hx+PP2-1d, Hx+EGFRi-1d) and 14 days (Nx14d, Hx14d, Hx+PP2-14d, Hx+EGFRi-14d). ATP and phosphocreatine (PCr) were determined biochemically to document energy status. The cytosolic fraction from the cortical tissue was isolated and the activity of caspase-9 was determined spectroflourometrically using a specific flourogenic substrate for caspase-9, at 37° C for 500 sec and expressed as nmoles/mg protein/hr.

RESULTS: Caspase-9 actvity was 3.13±0.23 in Nx1d, 4.11±0.29 in Hx1d ($p<0.05$ vs Nx1d), 3.26±0.12 Hx+PP2-1d ($p<0.05$ vs Hx1d, p=ns vs Nx1d). Two week post-hypoxia, caspase-9 activity was 4.1±0.57 in Hx14d ($p<0.05$ vs Nx1d), 3.42±0.02 in Hx+PP2-14d (p=ns vs Nx1d), and 4.18±0.43 in Hx+EGFR-14d is ($p<0.05$ vs Nx1d). ATP and PCr levels were not significant among the treatment and control groups. One day post-hypoxia, caspase 9 activity is elevated. The activity remains elevated 14 days post-hypoxia, and near normoxic levels with the administration of the PP2 inhibitor. Inhibition of EGFR decreases over the 14 day post-hypoxic period.

CONCLUSIONS: Inhibition of Src kinase prevents the apoptotic pathway two weeks post hypoxia, while the effect of EGFR inhibition decreases over the two week period. The hypoxia-induced activation of apoptotic cascade is maintained for at least 2 weeks post hypoxic insult. The Src kinase inhibition-based prevention of hypoxia-induced apoptosis is a potential strategy for translational studies in newborns.

152

4:45 PM

Fellow in Training

Overexpression of Extracellular Superoxide Dismutase (EC-SOD) Has a Protective Role Against Hyperoxia Induced Brain Injury in Neonatal Mice

Nahla Zaghloul, Mansour Nassim, Hardik Patal, Champa Codipilly, Philippe Marambaud, Stephen Dewey, Mohamed Ahmed.
Pediatrics, NS-LIJ, Manhasset, NY; Pathology, Ns-LIJ, New hyde Park, NY; Feinstein Institute for Medical Research, Manhasset, NY.

BACKGROUND: There is increasing evidence that hyperoxia particularly at the time of birth may result in neurological injury, in particular to the susceptible vasculature of these tissues.

OBJECTIVE: To determine whether over-expression of EC-SOD is protective against brain injury induced by hyperoxia.

DESIGN/METHODS: Transgenic mouse (TG, with an extra-copy of human EC-SOD knocked in) and wild neonate mice (WT) were exposed to hyeproxia (95% of FiO_2) for 7 days after birth versus control group in RA. Brain PET scan using FDG (fludeoxyglucose) isotope uptake was done after exposure. Western blot for the following inflammatory markers was done: GFAP, IBA1, MIF, pAMPK and ACC. Quantitative western blot was presented as a ratio of each marker band density to Actin density. To assess apoptosis induced by hyperoxia exposure, caspase3 assay by ELISA was done for all groups. Histopathological studies were done.

RESULTS: Brain PET scan using FDG isotope uptake showed a significant higher uptake in WT hyperoxic neonates brain group (0.14±0.03) than both TG hyperoxic neontes (0.09±0.01) and Control room air group (0.08±0.02) ($P<0.05$). Quantitative western blot for inflammatory markers and activated caspase assay are listed below.

Table 1

Markers	N/group	RA WT	RA TG	H WT	H TG
GFAP	10	2.16±0.35	2.19±0.17	3.38±0.22	2.77±0.11*
IBA1	10	0.17±0.01	0.18±0.01	0.25±0.03	0.18±0.01*
MIF	10	0.49±0.04	0.50±0.04	0.83±0.17	0.49±0.06*
pAMPK	10	0.22±0.01	0.23±0.02	0.28±0.02	0.22±0.02*
ACC	10	0.58±0.08	0.48+/-0.04	0.89±0.15	0.54±0.09*
Caspase3	10	0.44±0.07	0.042±0.08	0.81±0.11	0.58±0.14*

RA: room air WT: wild type TG: transgenic H: hyeproxia of 95% for 7 days Values are mean ± SE * H WT vs H TG ($P<0.05$)

Histopathological studies showed more apoptotic and dead neurones in cortical, cerebellar and hippocampal brain section of WT neonate mice after exposure to hyeproxia compared to TG ones.

CONCLUSIONS: Overexpression of EC-SOD in neonate brain offers a significant protection against hyeproxia induced brain damage.

153

5:00 PM

Fellow in Training

Hyperthermia Following Hypoxia-Ischemia in the Neonatal Rat Has a Biphasic Response: Increased Infarct or Selective Hippocampal Damage

Matthew A. Rainaldi, Susan J. Vannucci, Jeffrey M. Perlman.
Pediatrics, Weill Cornell Medical College, NY, NY.

BACKGROUND: Hypoxic-ischemic encephalopathy (HIE) remains one of the most common causes of mortality and neurologic morbidity in the term neonate. Evidence suggests an association between injury and temperature during and after HI. A recent clinical study demonstrated that spontaneous hyperthermia following HIE in term neonates was associated with increased risk of adverse outcome; whether this is due to hyperthermia or reflects an underlying brain injury was not determined.

OBJECTIVE: To determine the effect of hyperthermia on HI brain damage in the term-equivalent rat pup.

DESIGN/METHODS: Postnatal day (P) 10-12 Wistar rat pups underwent unilateral common carotid artery ligation plus hypoxia (8% O_2/ bal N_2) for 75-90 minutes. Following HI, rat pups were exposed to normoxic normothermia (NORMO) (36.5°C, n = 23) or hyperthermia (HYPER) (38.5°C, n = 22) for 2 hrs. After 48-72 hrs, animals were sacrificed, brains removed and frozen in isopentane (-30°C). 18 µm coronal cryosections were stained with H&E. Infarct area (%) of the ipsilateral hemisphere was calculated using Image J, NIH software. Data were analyzed using Fisher's exact test and Student's t-tests.

RESULTS: When the entire cohort was analyzed, the % infarct was not different between NORMO vs HYPER groups, i.e. 63.5 ± 11.9 vs 59.9 ± 24.11%, respectively (p = 0.53). However, HYPER produced a nearly biphasic response: 4/22 rats demonstrating only selective hippocampal damage vs 0/23 in NORMO rats (p = 0.04). Re-analysis of the remaining HYPER group (n = 18) resulted in significantly increased damage, 70 ± 10.5 vs 63.5 ± 11.9% (p = 0.03).

CONCLUSIONS: Exposure to mild hyperthermia immediately following HI in the neonatal rat produced a wider spectrum of damage than in rats recovered in a normothermic environment. In those rats with significant infarcts, HYPER recovery was associated with increased damage; selective hippocampal damage without extensive infarct was observed in ~ 18% of HYPER rats. These results support that hyperthermia alone following HIE is sufficient to produce increased damage in most animals. The selective hippocampal vulnerability with hyperthermia in a subset of HIE requires further investigation. These observations may have important implications regarding the optimum temperature to achieve during and following delivery room resuscitation of a depressed newborn.

154

5:15 PM

House Officer

DNA Methyl-Transferase Activity during Hypoxia in Neuronal Nuclei of Newborn Piglets

Amit Mukhia, David Fralinger, Anli Zhu, Om P. Mishra, Maria Delivoria-Papadopoulos.
Dept. of Pediatrics, Drexel University and St. Christopher's Hospital for Children, Philadelphia, PA.

BACKGROUND: Methylation of DNA at the cytosine phosphate guanine (CpG) islands is known to regulate the expression of a number of genes including proapoptotic proteins Bax and Bad. Demethylation allows access to the promoter triggering gene transcription. We have shown that hypoxia results in increased expression of proapoptotic proteins Bax and Bad. We have also shown that hypoxia results in increased methylation of nuclear DNA. The relative activities of DNA methyl-tranferase and DNA demethy-ltransferase regulate gene expression by regulating the level of DNA methylation.

OBJECTIVE: The present study tests the hypothesis that increased methylation of nuclear DNA during hypoxia is due to increased DNA methyl-transferase activity in the cerebral cortex of newborn piglets.

DESIGN/METHODS: Newborn piglets were divided into normoxic (Nx, n=5) and hypoxic (Hx, n=5) groups. Hypoxia was induced by decreasing inspired oxygen (FiO_2 = 0.07) for 60 min. Nuclei were isolated from the cortical tissue. Tissue hypoxia was documented biochemically by ATP and phosphocreatine (PCr). DNA methy-ltransferase activity was determined in a medium (40µl) containing nuclear protein (10µg), poly [d(I-C) d(I-C)] (DI-DC) template (20µg), and radiolabeled ^{3}H-S-adenosyl-methionine (3µg). The reaction was carried out at 37^{0}C for 2 hrs and stopped by the addition of 10µl (40%) perchloric acid. Twenty µl of the medium was spotted on GT membranes, and counted after being washed with 5% perchloric acid and 70% ethanol. DNA methyl-transferase activity was measured by ^{3}H-CH_3 incorporation into DI-DC template.

RESULTS: Brain tissue high energy phosphate ATP (µmoles/g brain) was 4.53±0.41 in Nx and 1.31±0.30 in Hx (p<0.05 vs Nx). PCr (µmoles/g brain) was 3.61±0.21 in Nx and 1.01±0.23 in Hx (p<0.05 vs Nx). The activity of DNA methyl-transferase (µmoles/mg protein/hr) was 3.40±0.24 in Nx and 7.8±3.6 in Hx (p<0.05 vs. Nx). The data show that the activity of DNA methyl-transferase increased in neuronal nuclei of the cerebral cortex of hypoxic newborn piglets.

CONCLUSIONS: Hypoxia results in activation of DNA methyl-transferase in neuronal nuclei of newborn piglets. The increased activity serves as a mechanism of increased DNA methylation resulting in modification of the neuronal nuclear DNA. Altered methylation of nuclear DNA during hypoxia lead to silencing and re-awakening of genes, promoting programmed neuronal cell death in the hypoxic newborn brain. (NIH-HD 20337)

155

5:30 PM

Behavioral and Neurodevelopmental Changes in a Neonatal Rat Model of Inflammation and Global Hypoxia – "Dual Hit Model"

Lamia M. Soghier, Solomon Moshe, Aristea Galanopoulou.
Pediatrics - Neonatology, Children's Hospital at Montefiore, Bronx, NY; Neurology and Neuroscience, Albert Einstein College of Medicine, Bronx, NY.

BACKGROUND: Postnatal hypoxia in neonates exposed to prenatal inflammatory conditions, such as maternal chorioamnionitis, carry a risk of significant neurodevelopmental delay.

OBJECTIVE: 1) To develop a neonatal rat model that combines a prenatal inflammatory insult with postnatal global hypoxia without carotid artery ligation and 2) To define the neurodevelopmental and behavioral outcomes of rat pups exposed to prenatal inflammation and/or postnatal hypoxia with respective controls.

DESIGN/METHODS: Pregnant Sprague Dawley rats were intraperitoneally injected with Lipopolysaccharide (LPS) 200 µg/kg/day or Sterile Water (SW) at gestational days E18-19 or E20-23. Offsprings of E18-19 injected dams (E18 group) were exposed to either global hypoxia (4% oxygen) or normoxia at P10. Offsprings of E20-23 injected dams (E20 group) were subjected to either global hypoxia (4% oxygen) or normoxia at P1. Four subgroups were compared in each group: HI (LPS + hypoxia), HYP (SW + hypoxia), LPS (LPS + normoxia), control (SW + normoxia). Daily weight measurements and standard developmental test for rodents were performed daily (P3-P20) to study neurodevelopmental outcomes: surface righting (SR), open field activity (OFA), negative geotaxis (NG). Furthermore, Barnes Maze testing of visuospatial learning and memory was done at P16-19. The comparison of P3, P12, and P20 ages only is presented here.

RESULTS: 30% of pregnant rats died following LPS at E18 (n=3) compared to 18% at E20 (n=11) and 0% in SW groups (n=10). Litter size was significantly smaller in LPS groups injected at E18-19 (p<0.01) and smaller in E20-23 compared to SW of the same gestational age. From the E18 group, prenatal LPS exposure caused a worsening of OFA scores at P12. No other significant differences were found in the developmental tests. From the E20 group, LPS and HI pups showed a tendency to have lower weights at P3. Furthermore, a slower learning curve was found in Barnes maze testing for the male HI group.

CONCLUSIONS: Prenatal inflammation decreases the litter size, regardless of age of exposure. However, prenatal inflammation closer to the expected day of delivery (E20) has greater impact on the neurodevelopmental outcome of the offspring. In the absence of postnatal ischemic injury, prenatal inflammation and neonatal hypoxia can cause delay in weight growth and slower learning curves in the offspring. Futher tests to determine degree of histological injury will be performed.

General Pediatrics
Poster Session

Saturday, March 26, 2011
6:00 PM-7:30 PM

156

Teaching Airport Personnel about Children with Autism

Yahaira I. Marquez, Rebecca B. Jackel, Roger Ideishi, Angela Jones, Clara E. Notredame, Matilde M. Irigoyen, Wendy J. Ross.
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BACKGROUND: Families of children with autism frequently avoid air travel because of prior negative experiences with airport personnel secondary to the child's behavior. Airports seek compliance with the American with Disabilities Act (ADA). Access for children with autism falls within this purview.

OBJECTIVE: To assess the knowledge of autism among airport personnel before and after an educational intervention.

DESIGN/METHODS: In collaboration with the ADA liaison at the Philadelphia International Airport, we designed a multi-faceted initiative to improve access for families with children with autism. At part of this initiative, a developmental pediatrician and a child psychologist conducted a 30-minute educational session on autism during an annual ADA training for airport personnel. Participants were invited to complete the Practical Knowledge about Autism Questionnaire (PKAQ) Airport Workers Edition pre- and post- session. The 10-item questionnaire assesses four basic areas of autism: general perception, language, stereotypical behaviors, and social skills.

RESULTS: The sample included 131 participants; 31% were 20-30 yrs, 13% 31-40 yrs, 24% 41-50 yrs, 32 % 50+; 43% were males; 45% were African American, 31% White, 8 % Hispanic; 44 % had worked at the airport <5 yrs, 36% 6-10 yrs, 20% >11 yrs; 34% worked security, 18% gate, 12% curbside, 10% check-in, 26% worked at multiple sites. A third of participants had learned about autism from airport training, a third from family or friend, more than half from media. The educational session resulted in a significant increase in the number of correct answers (p< 0.001). For example: "Children with autism usually make eye contact": Correct answer NO: 11% pre vs. 87% post. "Children with autism can communicate wants and needs easily": Correct answer NO: 58% pre vs. 85% post. "Children with autism should be given medication to relax them when they travel": Correct answer NO: 23% pre vs. 72% post. "Children with autism may repeat what they hear": Correct answer YES: 51% pre vs. 92% post. Older workers with more years of experience obtained a lower score on the posttest knowledge score. Overall, airport personnel showed great interest in learning more about autism.

CONCLUSIONS: This study revealed airport personnel is in need and interested in education about autism. A brief educational intervention was effective increasing autism knowledge among the airport personnel.

157

Development and Initial Validation of the Baby Pediatric Symptom Checklist (BPSC)

Shela Merchant, Brandi S. Henson, R. Christopher Sheldrick, Ellen C. Perrin, J. Michael Murphy.

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BACKGROUND: The American Academy of Pediatrics' Task Force on Mental Health recommends behavioral health screening with a validated instrument for all children. The Pediatric Symptom Checklist (PSC) is a validated and frequently-used measure for children over 5 years of age.

OBJECTIVE: As part of the process of developing a comprehensive instrument to identify young children with developmental-behavioral problems, we have created a downward extension of the PSC for children 2 to 18 months of age.

DESIGN/METHODS: After review of a range of instruments that measure behavior and temperament among very young children, we wrote and pilot-tested 25 questions relevant to infants. We enrolled 260 parents from pediatric waiting rooms to complete the BPSC questions, the Ages & Stages Questionnaire-Social/Emotional (ASQ-SE), and demographic data. We chose final BPSC items based on results of Principal Components Analysis (PCA) and Item-Response Theory (IRT), and calculated sensitivity and specificity of the BPSC in detecting ASQ-SE status.

RESULTS: PCA identified three factors: Reactivity, Dysregulation, and Child Care Issues. Within each factor, IRT analysis determined the discrimination and difficulty of each item. Based on these analyses, 18 items predicted ASQ-SE scores in the clinical range with sensitivity = .70 and specificity = .74. Cronbach's alphas for scales ranged from .74 to .79.

CONCLUSIONS: The BPSC shows promise as a brief screening instrument for use in pediatrics. The BPSC assesses three domains that are highly relevant to infant mental health and can be reported reliably by parents in the context of a pediatric waiting room. Further research using independent samples is in process.

158

Exploring the Risks, Trends, and Opportunities for Improvement Regarding Security for Hospitalized Children at Baystate Children's Hospital

Jackcy Jacob, Karine Issa-El-Khoury, Linda George, Jennifer Friderici, Nancy Miller.

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BACKGROUND: Children's Hospitals (CH) must provide a secure and safe environment. Federal standards (Conditions of Participation) mandate, "The patient has the right to receive care in a safe setting." Nationally CHs have reported significant threats to the security of hospitalized children. There is neither a national standard nor best practice for security in CHs.

OBJECTIVE: To identify the nature and extent of security risks reported via incident reports at a CH.

DESIGN/METHODS: A retrospective review and analysis of security incident reports during 2007 in all non-Nursery pediatric units of a CH in Western MA was conducted to identify patterns such as type or date/time of event and to assign a harm score (HS) to each event: 0: No actual event; 1: Event-No Harm; 2: Event-Harm. Binary scores were compared by unit, shift, and time of week. For events with potential or real harm, diagnosis of the patient was documented when available.

RESULTS: 407 security reports filed over 403,189 patient days (PD) were reviewed. Most (75%) were coded as "No actual event" (HS=0) and were primarily false baby security alarms. These occurred most frequently between the hours of 1500-1900; on Sundays (P=0.013); and during the months of June or July (34/1000 PD vs. average of 21/1000 PD).

Only 102 of 407 reports were coded as "true events" (HS=1,2); these were described most frequently as stand-by related to Child Protective Services cases (34%) or restraint (30%). True events were more likely to occur during 0600-1800, and were more likely to occur in December than any other month (25.9/1000 PD vs. an average of 9.9/1000 PD).

Only 39 events (HS=2) resulted in any harm to patient, visitor, or staff. Harm events occurred more frequently on the adolescent unit than infant/child unit (2.7 vs. 1.7 events/1000 PD, P=0.03) and were concentrated overnight between 1200-0600 than all other 6 hour shifts (23% vs. 9%, P=0.001). There was a non-significant trend towards higher rates of temporary harm vs. event-no harm in patient who held a psychiatric diagnosis.

CONCLUSIONS: Although most security incidents in a children's hospital were false alarms, a significant minority pose potential harm to patients, visitors or staff. Further study of the spatial and temporal risk factors for security threats may inform security practices at this and similar institutions.

159

Exploring Opportunities for Improving Security in Children's Hospitals: Focus Groups

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Pediatrics, Baystate Children's Hospital, Springfield, MA.

BACKGROUND: Children's Hospitals (CH) must provide a secure and safe environment. There is no national standard or best practice for security in CHs.

OBJECTIVE: To explore employees' understanding of security policies and risks for hospitalized children, visitors and staff.

DESIGN/METHODS: As part of a study of security in non-Nursery units, employees at a CH in Western MA (nursing staff [NS], physicians, child life specialists [CLS]) were invited to 90 minute focus groups. Self selected groups yielded 8 NS and 6 CLS.

RESULTS: Transcript analyses revealed the following issues.

1. Staff security training: No recall of initial training topics; yearly computer training recall only of fire alarms and oxygen shut off; no training to educate patient/family about security.
2. Patient/family education: No specific staff, time, topics or print material to orient patients/families to CH security; staff inconsistently provide security education; concern that security education may cause anxiety in patients/families.
3. Physical environments: Unlocked/unmonitored halls, stairs and doors; inconsistent nursing station presence where baby security alarms sound; "panic button" location on unit unknown by most.
4. Security policy implementation: staff differentially enforce visiting policies; posted visitor restrictions at hospital entrances unheeded by adults with children; no follow up after security reports; few security concerns relayed during shift hand off; no training to respond to agitated patients/families.
5. Staff security: Personal security of staff threatened by psychiatric patients, child placed into protective custody, verbal threats or show force/weapon by families, illegal drugs in patient room.
6. Perception of families' security concerns: Family may voice concern with patient/family in double occupancy room, unidentified person may approach their child, patient observation by NS may be inadequate when parents leave; "admission information overload" decreases family's interest in security.

Best actions to improve security ranked: 1. lock units, 2. screen all visitors at hospital entrances, 3. hallway security cameras.

CONCLUSIONS: Focus groups identified opportunities for improving CH security, and voiced confidence in reporting concerns,"We are trained to keep our patients safe". These issues informed a survey for all CH employees. CH implemented a locked infant/child unit after the focus groups convened.

160

Nonresident Fathers and Fatherhood: A Needs Assessment

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BACKGROUND: Research has shown that a father's involvement in a child's life impacts every domain in their functioning, from birth through adolescence. However, 24 million children in the United States do not live with their biological father. This trend is more pronounced for African American children, with 50% living in single mother homes (2007). Despite the magnitude of this issue little is known about the experiences of nonresident fathers and the roles they play in their children's lives.

OBJECTIVE: To obtain data on the parenting experience of nonresident fathers by exploring their perceived roles, learning processes, challenges, and supports.

DESIGN/METHODS: A qualitative study was undertaken using semi-structured interviews (n=5) with nonresident fathers recruited from a community health care center in the Bronx and a focus group recruited from a community-based organization. The data was professionally transcribed and coded for themes by two investigators, with differences resolved by a third investigator.

RESULTS: Participants ranged in age from 15 to 52 years and 28% were self-identified as Hispanic, 39% as African American, and 11% as other. 44% reported incomes of <$10,000 per year and 22% reported completing some middle school, 39% some high school, and 17% some college education. The nonresident fathers emphasized the importance of their role as fathers. In exploring how they learned to parent, observing other fathers and recall from their own childhood experiences were highlighted. Many of the subjects reported being raised with an absent father and commented on how that affected their parenting; making decisions based on what they had wanted from their own fathers but had not received. Significantly, many of the fathers had desired to be reached out to and integrated into the prenatal time period and described how removal from this heightened their sense of isolation. The unique challenges of nonresident fatherhood, such as fathering from a distance, and the emotional strains of these challenges were also illustrated. Finally, several of the subjects expressed anger about being made to feel invisible, even when present at child health care visits, and emphasized the importance of being included in the provision of their child's care.

CONCLUSIONS: In order to provide quality family centered care, physicians need to be aware of the unique challenges and perspectives of nonresident fatherhood in order to provide appropriate education, support, and anticipatory guidance.

161

House Officer

Accessing Sources and Knowledge of Reproductive Health in 14-21 Year-Old High School Students in the Bronx

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BACKGROUND: Adolescents in inner cities bear some of the highest burdens of the negative consequences of sexual behavior with high rates of teen pregnancy, STI's, and HIV. There is limited research focused on where this population receives its information regarding sexual health. Moreover, there is little data on the emergence of the internet and social networking technologies in disseminating accurate health information to adolescents.

OBJECTIVE: The objectives of this study are to obtain information about where teenagers receive their information about sexual health topics, to obtain information about the use of the internet/social networking, and to evaluate adolescent knowledge concerning reproductive health.

DESIGN/METHODS: Male and female adolescents between the ages of 14 and 21 were recruited at a community health center in the South Bronx during their clinic visits. They were asked to complete an anonymous survey which included basic demographic information, internet availability, a knowledge assessment, and questions assessing sources of information and their usefulness. Participants were also asked specifics about websites/social networking resources utilized. Responses to survey questions were tabulated in Excel and descriptive statistics were calculated.

RESULTS: Fifty adolescents were surveyed during their clinic visits. Ninety-four percent were African-American or Latino. 82% had internet access at home. The median percent correct on knowledge questions was 65%. The most common sources were medical professionals (92%), mothers (81%), friends (80%), teachers (78%), and the internet (77%). Information provided by medical professionals was seen as the most useful (89%) followed by the internet (83%). The most common websites used were Google (66%), Yahoo (32%), and Wikipedia (32%). The top four search terms were birth control (67%), sex (64%), HIV (52%), and plan b (52%).

CONCLUSIONS: As this was a sample of teenagers who sought medical care, it was not surprising that almost all received information from medical professionals and found it useful. However, the poor performance on basic knowledge questions is concerning. A novel finding was the extent to which inner city youth are using the internet to access reproductive health information. This study suggests the importance of incorporating the internet into sexual health education in clinical and nonclinical settings.

162
House Officer

Effect of Time Management Training on the Efficiency of Pediatric Residents in Training

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BACKGROUND: Residents are required to juggle competing responsibilities in their professional and private lives. Some possess innate abilities to assign priorities; others are easily overwhelmed by them. Residents frequently identify poor time management as an area requiring improvement. Faculty evaluations of residents concur.

While popular in other disciplines, little has been published on exposure to time management training among resident physicians and whether such training is effective.

OBJECTIVE: To assess the effect of sequential time management workshops on the self reported efficiency of pediatric residents in an inner-city community hospital.

DESIGN/METHODS: During 2006/2007 residents participated in a 2-part workshop (one hour each) on time management consisting of instructions in: tracking daily activities, creating goals, delegating, establishing routines, setting time limits for tasks.

Workshops involved interactive sessions with application of time management tools such as daily/monthly planners, time/motion study, and a time management matrix, intended to help them prioritize important activities and identify non-important ones.

Residents completed pre/post questionnaires at workshop completion. Questions focused on effect of workshops on their daily routines and ability to achieve desired goals. Four areas were identified: internal time management factors(ITM), time and motion awareness(TMS), application of time management matrix(TMM), setting goals and priorities(SP), and use of time management forms(TMF).

Answers were on a scale of 1-5: 1=Never/Untrue; 5=Always/Definitely true

RESULTS: There were 18 participants: 8 PGY 1, 10 PGY2.

Descriptive statistics

	Before(mean)	After(mean)	Difference	P-value
ITM	3.44	3.83	0.38	<0.05
SP	3.83	4.29	0.45	<0.05
TMF	3.76	4.12	0.35	<0.05
TMS	3.98	4.08	0.15	<0.1
TMM	3.66	3.78	0.11	NS

The difference noticed above is independent of year of training or prior time management training.

The magnitude of difference for SP, TMF, ITM, and TMS, correlated well on Pearson's 2-tail analysis.

CONCLUSIONS: Our study shows residents were able to improve their time management skills after attending two time management workshops in all domains except utilization of time management matrix.

Programs should consider time management training for all residents, especially those requiring remediation for inefficiency.

163
Medical Student

NYC Girls Are Steps Away from Growing up Healthy: Patterns of Activity Behaviors in an Inner City Minority Cohort

Caroline Gluck, Maureen Miller, Maida P. Galvez, Kathleen McGovern, Jessica Montana, Nancy Mervish, Susan L. Teitelbaum, Mary S. Wolff, Barbara Brenner.

Department of Preventive Medicine, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Childhood obesity is epidemic in the US, especially in low income, minority communities. Physical inactivity is a major contributing factor.

OBJECTIVE: The aim of this project was to characterize physical activity in NYC girls and compare reported physical activity levels to current recommendations.

DESIGN/METHODS: Physical activity data was collected by interviewer administered questionnaires from a cohort of 367 African American and Latina girls aged 6-8 in NYC. In addition, a subgroup of 300 girls wore a pedometer for seven days. Weekly physical activity, daily number of steps, and daily screen time were compared with national averages and AAP recommendations.

RESULTS: 85% of girls reported walking to school ≥3 days per week, compared to less than 16% for national children aged 5-15. Yet, pedometer data averaged 9,933 steps/day compared to AAP's 11-12,000 steps/day recommendation. Girls reported 6.2 hrs/week in non-scheduled physical activity, 4.7 hours of which were spent outdoors. However, only 34% of girls reported participating in organized sports or after school programs, compared to 56% of national 9th grade girls. This accounted for 43 min/week in organized sports. This is less than AAP's 1 hour/day recommendation. In addition, girls spent only 56 min/week in P.E. classes per week compared to 180 min/week for national 8th graders. With respect to sedentary behaviors, girls reported an average of 2.6 hours of screen time daily, compared to the AAP's < 2 hours recommendation.

CONCLUSIONS: NYC girls reported unique physical activity patterns which can inform targeted interventions. While the majority of girls walk to school this is insufficient to meet daily step requirements. Targeted interventions to decrease childhood obesity could focus on increasing participation in organized activities, enhancing opportunities for moderate to vigorous physical activity in non-scheduled activities, and enhancing the outdoor environments, both built and natural, where NYC girls report spending active time.

164
House Officer

Does Bedside Nursing Presence during Family-Centered Rounds Decrease the Number of Pages to Ward Interns?

Samantha Fish, Bridget Allard, Kathleen Donnelly.

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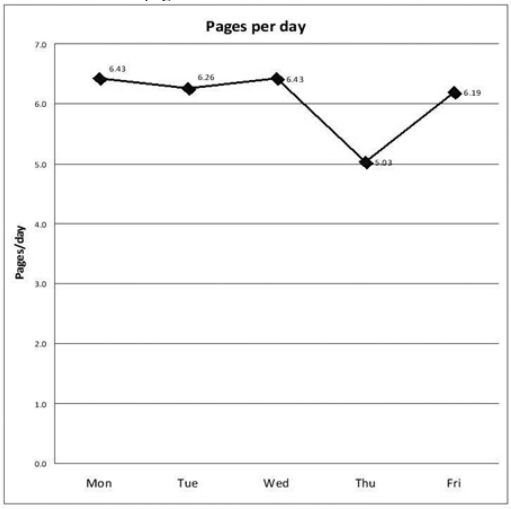
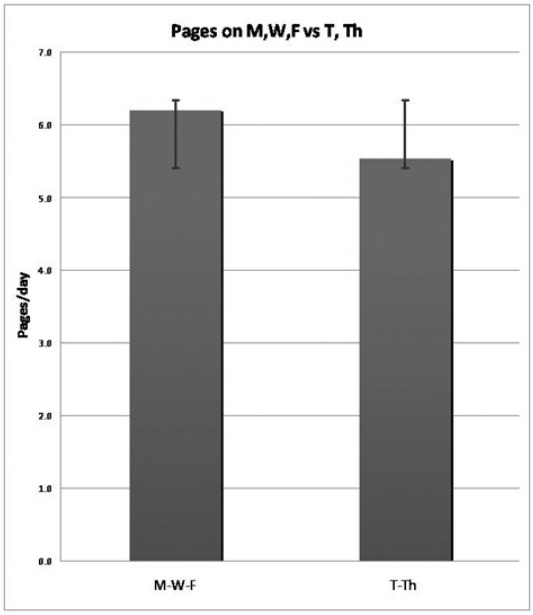
BACKGROUND: Family centered rounds (FCR) including attendings, residents, nurses and families have been promoted as a tool to increase communication and the understanding of the care plan between all team members. At IFHC, family-centered rounds were introduced in 2008. More recently in the spring of 2010, a renewed QI initiative began to bring the bedside nurse consistently into FCR. Upon implementation, it was hypothesized that the resulting improvement in communication would decrease the number of pages sent by nurses to the floor interns.

OBJECTIVE: To evaluate the effect of FCRs on communication between nurses and residents by comparing the number of nursing pages to interns on days with family centered rounds (M,W,F) to those without family centered rounds (T, Th).

DESIGN/METHODS: At the time of the addition of the bedside nurse to FCRs, the number of pages that interns on the wards received from the nurses between 6:00 AM and 7:00 PM each day was tracked. Over 1000 pages received by the ward interns were reviewed, and those sent by the floor nurses were identified. The mean number of pages on days with FCR (M,W,F) was compared to that on days without FCR (T,TH). Standard t-test was used for comparison of the two groups.

RESULTS: The mean number of pages did not decrease with the addition of nursing to FCR.





CONCLUSIONS: While FCR has created an atmosphere in which the nurses and residents subjectively report improved communication, a decrease in the number of paging contacts was not achieved.

165

Release Planning for Juveniles in Detention in New Jersey

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BACKGROUND: Adolescents who interface with the juvenile detention system are at disproportionate risk for morbidity and mortality from medical problems compared to the general adolescent population. We investigated the process of release/reentry planning for juveniles in detention, including assessment of health insurance and effect of health insurance on release planning.

OBJECTIVE: To explore qualitatively release planning for local juveniles, including potential barriers to obtaining healthcare for adolescents and health insurance assessment.

DESIGN/METHODS: This qualitative study involved semi-structured interviews of local administrators of juvenile corrections systems, probation officers, social workers, and families of adolescents in detention. Interviews focused on release planning and barriers to release planning. Qualitative data were reviewed by participants for validity, as well as an independent reviewer.

RESULTS: Eleven staff participants and 3 families of juveniles participated. Qualitative analysis of family and staff interviews revealed common themes. Assessment for health insurance only occurred if there was a new medical or mental health need during detention. Adolescents with mental health problems had the advantage of a case manager responsible for release planning with the family. Families of first-time offenders supported the idea of release planning but were not necessarily involved unless court-ordered.

CONCLUSIONS: Juveniles in the local corrections systems with mental health disorders benefited from case management responsible for release planning. Juveniles under Probation also had a consistent person involved in release planning. However, juveniles new to the system or those without new medical or mental health needs often faced a complicated, inconsistent release planning system where health insurance assessment was not a systematic priority. Future research should address latent errors in the current release planning system which place certain adolescents at risk for lack of health insurance with subsequent lack of access to recommended services and increased recidivism.

166

Pediatric Medication Dosing Errors

Kathryn M. Scharbach, Philip O. Ozuah.
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BACKGROUND: Prescribing errors are more prevalent in pediatric patients. Cephalosporins are among the most commonly prescribed medications. It is unclear whether extremes of weight at either end of the spectrum are risk factors for prescribing errors.

OBJECTIVE: To test the hypothesis that children at the extremes of weight have a higher prevalence of dosing errors of cephalosporins.

DESIGN/METHODS: A retrospective review of medication orders was performed at an academic, urban, tertiary care children's hospital using an electronic search engine. Patient records were queried for January to December of 2009 for all cephalosporin orders in which a weight was recorded within 120 days before the order entry. Each order entry was considered a unique event. An error was defined as a dose outside of published dosing standards (by 10% or more) according to Harriet Lane Handbook and Nelson's Pediatric Antimicrobial Therapy. Chi square tests were used to compare error rates for those at the lowest 5th (<2.5kg), middle 90th (2.5-83kg) and highest 5th (>83kg) percentiles for weight. Multivariate logistic regression was used to determine an adjusted odds ratio.

RESULTS: Overall, 3,899 orders were analyzed. Prevalence of dosing errors was 7.7% for all. The prevalence of a dosing error was highest among patients in the lowest 5th percentile (36%) for weight compared to those in the middle 90th (6.1%) and highest 5th percentile (4.1%) for weight, $p<0.001$. Patients up to 2.5kg had an adjusted odd ratio of a dosing error of 8.6 (95%CI: 6.2-11.9) compared to those >2.5kg (adjusted for race, ethnicity, gender, insurance and preferred language), $p<0.001$. Underdosing errors represented 92% of dosing errors in patients up to 2.5kg compared to 78% in those >2.5kg, $p=0.004$.

CONCLUSIONS: Infants weighing less than 2.5kg had the highest prevalence of dosing errors. Underdosing errors comprised the majority of dosing errors. These findings have implications for the treatment of infections in young children, especially the smallest patients.

167

House Officer

Maternal Factors Associated with Intention to Exclusively Breastfeed or Breast and Formula Feed among Urban Minority Women

Shilpa G. Hundalani, Stefan Mandakovic Falconi, Ramesh Matam, Matilde Irigoyen.
Pediatrics, Albert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: Prenatal maternal intention to breastfeed is a major predictor of successful breastfeeding practices.

OBJECTIVE: To examine the association of maternal factors on the intention to exclusively breastfeed or breast and formula feed in an urban minority population.

DESIGN/METHODS: We conducted a cross sectional survey of women whose infants were born 7/10-9/10 and discharged from the term nursery at an academic community hospital in Philadelphia, PA. Prior to delivery, women were asked how they planned to feed their infant: exclusively breastfeed, breast and formula, or formula. We used multivariate ordinal logistic regression to assess the associations of ethnicity, age, parity, pregravida BMI, and insurance type on the odds of intention to exclusively or partially breastfeed.

RESULTS: The study population included 680 mothers: 18% ≤19 ys, 25% ≥30 yrs; 60% were African American, 18% Latinas; 85% had Medicaid. 56% of mothers intended to breastfeed (44% exclusively, 12% breast and formula), 37% formula and 7% were undecided. On average, older mothers were more likely to intend to breastfeed exclusively than to use both breast and formula or to use formula alone ($p= 0.02$) controlling for all other factors. Similar results were found for women with higher BMI ($p=0.001$) and lower parity ($p=0.002$). Ethnicity and type of insurance were not independent predictors of intent to breastfeed ($p>0.26$).

CONCLUSIONS: In an urban minority population, intention to breastfeed was low overall and many women either plan to breast and formula feed or have not made deliberate decisions before birth. Strategies are needed to promote breastfeeding prenatally among urban minority women.

168

House Officer

Intent to Breastfeed and Successful Breastfeeding in an Inner City Population: Does Obesity Matter?

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Pediatrics, ALbert Einstein Medical Center, Philadelphia, PA.

BACKGROUND: Studies have shown intention to breastfeed and initiation of breastfeeding are negatively correlated with obesity.

OBJECTIVE: To examine the relationship of pregravida body mass index (BMI) to intention to breastfeed and initiation of breastfeeding in an inner city population.

DESIGN/METHODS: We conducted a retrospective study of mothers of infants born 7/10-9/10 and discharged from the term nursery at an academic community hospital in Philadelphia, PA. Mothers were classified as underweight (BMI <18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25-29.9), obese (BMI >30). Outcome measures were prenatal intention to breastfeed (exclusive or breast and formula) and breastfeeding at discharge (exclusive or breast and formula).

RESULTS: 635 mothers participated: 61% were African American, 18% Latino; 85% had Medicaid; 26% were overweight, 24% obese, 4% underweight.

Mothers with higher BMI were more likely to intend to breastfeed exclusively than to use both breast and formula or to use formula alone after controlling for ethnicity, age, parity and insurance ($p= 0.001$). Obese women were 3 times more likely than underweight women to intend to breastfeed (OR 3.08, 95% CI 1.17-8.15; $p=0.023$). However, rates of breastfeeding at discharge were not significantly different across BMI categories.

Intent to Breastfeed (BF) and BF at discharge by maternal Pregravida weight categories

	Intent to breastfeed		Breastfeeding at discharge	
N=635	exclusive BF	Breast+formula	exclusive BF	Breast+formula
Underweight	19%	19%	14%	23%
Normal Weight	42%	13%	19%	27%
Overweight	46%	13%	22%	34%
Obese	59%	5%	25%	28%

CONCLUSIONS: In this inner city population, obese women showed a higher intent to breastfeed but were less likely to progress to successful breastfeeding at hospital discharge. Increased support in the postpartum period may boost breastfeeding rates in obese women.

169

House Officer

Impact of Delivery Type and Maternity Care Practices on Initiation of Breastfeeding in an Inner City Population

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BACKGROUND: Type of delivery and maternity care practices have been shown to significantly affect whether a woman chooses to start breastfeeding and how long she continues to breastfeed.

OBJECTIVE: To examine the relative contribution of type of delivery and maternity care practices on initiation of breastfeeding in an inner city population.

DESIGN/METHODS: We conducted an observational retrospective study of mothers of infants born 7/10-9/10 and discharged from the term nursery at an academic community hospital in Philadelphia, PA. We assessed the associations of delivery type (vaginal vs C section) and maternity care practices (initial breastfeeding in delivery room and term nursery) on exclusive and breast and formula feeding at discharge.

RESULTS: The study population included 680 mothers: 18% were ≤19 ys, 25% ≥30 yrs; 60% were African American, 18% Latinas; 85% had Medicaid; 33% underwent C section. More than half (56%) intended to breastfeed; 44% exclusively, 12% both breast and formula. At discharge 21% of infants were exclusively breastfed and 29% were both breast and formula fed. Mothers who had a C section were less likely to exclusively breastfeed at discharge (16.7% C section vs 22.7% vaginal) but this was not statistically significant. Infants who initially breastfed in the delivery room or the term nursery were 6.7 and 3.6 times more likely, respectively (both $p<0.001$), to be exclusively breastfed at discharge.

CONCLUSIONS: In an inner city population with a low maternal intent to breastfeed, C section deliveries posed a challenge to inititation of succesful breastfeeding. However, maternity care practices were the most critical factors to support successful breastfeeding through discharge.

170

Fellow in Training

Teaching Pediatric Code Leadership Skills: Integrated vs. Stand Alone Curriculum

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BACKGROUND: Simulation can be used to accurately educate, measure, and discriminate residency competencies in the medical management of pediatric urgent and emergent events.

OBJECTIVE: Previous studies have demonstrated that education of procedural skills and medical decision making is enhanced through a simulation program. This study was conducted to answer the question of whether a dedicated curriculum of leadership training, simulation sessions and teaching targeted at these topics; is superior to our traditional integrated approach, trying to teach these skills at the same time as medical care.

DESIGN/METHODS: First year residents were educated using the integrated simulation curriculum and evaluated during their regularly scheduled simulation center times using the Ottawa Crisis Management Global Rating Scale (OCMGRS). A subset of these residents was then given an experimental educational session: a simulation session and debriefing with a focus on communication, leadership, and problem solving around a medical problem that was not within

their scope of practice. At a subsequent scheduled simulation session they were again evaluated using the OCMGRS.
RESULTS: Of the 29 first year residents in the three training programs, 18 were evaluated in 2 or more traditional simulation sessions. Within this group the first score was compared to the last score using a Wilcoxon signed-rank test for paired data. For the first score the median is 23 with an interquartile range (IQR) of 21 to 26. For the last score the median is 23 with an IQR of 20 to 26. p=0.13. A nonparametric test for trend across ordered groups where the groups are the time points revealed a p value of 0.81. 6 residents received the experimental educational session. For this group the pre intervention data and the post intervention data were compared using a Wilcoxon signed-rank test for paired data. The median score before intervention was 19.5 with an IQR of 16 to 26. The median score after intervention was 33 with IQR of 32 to 33 with a p=0.03.
CONCLUSIONS: The traditional curriculum of an integrated education of leadership skills within a simulation program was not effective in teaching code leadership skills to first year residents. An experimental simulation curriculum that focuses on communication, leadership, and problem solving markedly improved the OCMGRS for those residents who participated.

171

The Influence of Military Bases and Public University Campuses on Chlamydia Rates in Florida Counties: A Spatial Analysis Using a Geographic Information System (GIS)

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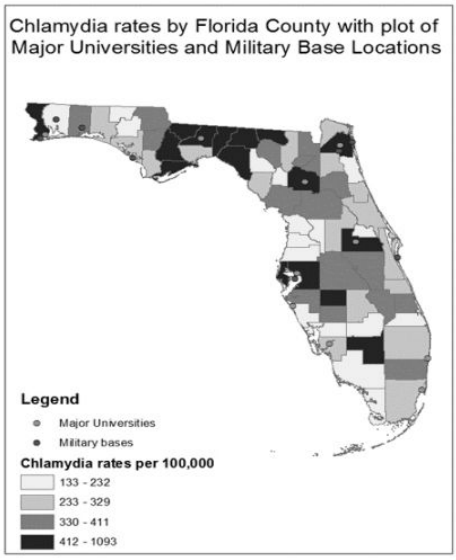
BACKGROUND: Chlamydia is the most frequently reported sexually transmitted infectious disease in the United States with over 1 million cases reported annually. Recent studies have found high rates of Chlamydia in both military populations and college students. Complications of Chlamydia for women include chronic pelvic pain, ectopic pregnancy, pelvic inflammatory disease, infertility; and for men, epididymitis and infertility.
OBJECTIVE: The purpose of this study was to determine if Florida counties with major military bases or public university campuses have higher rates of Chlamydia when compared to counties without.
DESIGN/METHODS: Using a Geographic Information System, (ArcMap®), a digital color density map of 2008 Florida Chlamydia rates by county was created. Next, the locations of public universities and major military installations were plotted. Using the 2-proportion test statistic in MINITAB®, rates of Chlamydia for counties with a military base (vs. no military base), major university (vs. no university) and both (vs. not having both military base and university) were compared.
RESULTS: Statistically significant increased rates of Chlamydia were seen in those counties which had a military base vs. no base (488 vs. 341 per 100,000; Z=36.56; p <001) or a public university campus vs. no campus (428 vs. 316 per 100,000; Z=39.49; p <0.001). Greater differences were seen in counties which had both a military base and university campus vs. not having both (576 vs. 338 per 100,000; Z=47.07; p <0.001). This corresponds to what was visually seen on inspection of the digitally created map



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CONCLUSIONS: Counties that have military or public university communities have higher rates of Chlamydia when compared to counties that do not. Focused Chlamydia screening, patient education, and preventive programs at military bases and public university campuses may be an efficient approach to reduce disease burden in the neighboring communities.[figure1]

172

House Officer

Identifying Patient Characteristics That Influence a Mandated Reporter's Decision To Report Child Abuse

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BACKGROUND: Child abuse (CA) is prevalent and underreported in our society. Health care professionals are mandated to report suspected cases of CA in all states. Less than 10% of all maltreatment reports to Child Protective Service's (CPS) come from medical personnel. Studies have demonstrated that barriers exist for health care professionals to recognize and report child abuse. The factors that affect a clinician's decision to report child abuse are still being elucidated.
OBJECTIVE: We surveyed health care professionals in an urban, multicultural area to better understand how characteristics such as age, race, type and timing of injury can influence reporting of CA.
DESIGN/METHODS: A survey was developed with suspected CA case studies and distributed to health care providers in an urban hospital. Eighteen cases were given to each participant with 2 questions per case. The questions included variations of ethnicity, age, type and timing of injury. The first question asked about a clinician's level of suspicion of CA ranging from no suspicion to certainty, recorded on a 10 cm visual analog scale (VAS). The second question asked whether the clinician would report the case to CPS. A 1-way ANOVA test was used to test for significance.
RESULTS: Results of the 86 survey's completed, showed clinicians suspected and reported CA in an infant who presented with unknown timing of injury compared with immediate or delayed presentation of injury. Age of child was also statistically significant with a higher clinical suspicion and reporting of CA in a 1 month old infant compared to a 6 month and 18 month old child. Ethnicity and type of injury were not factors contributing to suspicion or reporting of CA.

Mean VAS scores for suspected CA cases in children ages 1,6 and 18mos.

Age Groups	Mean VAS
1 month	70.2
6 month	64.0
18 month	55.3

p< .0001

Mean VAS scores for Suspected CA Cases with No History or Varying History.

History Groups	Mean VAS
No History	76.9
Immediate Presentation	51.0
Delayed Presentation	65.1

P < 0.0001

CONCLUSIONS: This study suggests that health care professionals are more likely to suspect and report CA in younger infants and that history on presentation is important. It failed to demonstrate the increased likelihood of suspicion and reporting of CA among ethnic groups or based on type of injury. This could be survey inadequacy or because ethnicity and type of injury are not primary factors in suspecting or reporting CA.

Emergency Medicine
Poster Session

Saturday, March 26, 2011
6:00 PM-7:30 PM

173

Fellow in Training

Pediatric Residents' Procedural Experience: How Much Is Enough?

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BACKGROUND: Procedural skills competencies are mandated for completion of pediatric residency training. Residents need adequate numbers of opportunities to practice these procedures in order to achieve competency. The purpose of our study was to quantify clinical experience, simulation experience, and self-perceived competence of recent pediatric residency graduates in eight of the required procedural skills.
OBJECTIVE: We hypothesized that recent graduates would report few experiences and low levels of competency with required procedures. Our secondary aim was to evaluate the effect of simulation-based training on perceived competency.
DESIGN/METHODS: A survey tool was distributed to 168 graduating residents from seven US tertiary care institutions (n=55, response rate = 33%). Data was collected on the number of real patient and simulated procedures performed and the number of each procedure they deemed necessary to achieve competence. Procedures assessed included endotracheal intubation, intraosseus line placement, intravenous line insertion, arterial puncture, central venous line, lumbar puncture, suturing, and thoracentesis. Subjects were asked to rate the comparative effectiveness of real patient and simulated experience.
RESULTS: The majority of respondents had insufficient experience to achieve competency in 5 of the 8 procedures. 47% sought elective rotations to obtain additional procedural experience.
81% of respondents reported having had some form of simulation training, most commonly in endotracheal intubation. Simulation experience correlated with increased self-reported competence.
Among respondents who received both simulation and real patient procedural training, simulation experience was deemed to be 64% as effective as real patient experience.

Procedure	Percent Competence	Simulation Effectiveness	Proficiency, Real Patient Only	Proficiency, Real and Simulated
Endotracheal Intubation	28	63	42	21
Intraosseous Line	31	72	75	87
Peripheral IV	54	54	39	68
Arterial Puncture/ Line	49	51	46	73
Central Venous Line	9	75	13	25
Lumbar Puncture	89	60	86	89
Suturing	70	67	61	77
Chest Tube/ Thoracentesis	16	71	43	100

CONCLUSIONS: Pediatric residency graduates report insufficient experience to achieve competency in required procedures. Reductions in residents' work hours will likely further reduce the number of experiences. Thus, a combination of simulation and real patient experiences is necessary to provide adequate procedural experiences during residency.

Saturday, March 26, 2011
6:00 PM-7:30 PM

174

Impact of BASE Camp: Simulation-Based Multidisciplinary Team Training for Pediatric Emergency Medicine Fellows

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BACKGROUND: Pediatric emergency medicine (PEM) fellows must acquire necessary knowledge and skills to lead a multidisciplinary team under crisis conditions. Without consistent training in teamwork however, many PEM fellows rely on mock codes or rare resuscitation events for experiential learning. In order to introduce, review, and practice teamwork behaviors and skills, we organized a 2-day multi-institutional, multidisciplinary program, *BASE Camp 2010: Basic Training for Pediatric Emergency Medicine*.

OBJECTIVE: To determine the skills PEM fellows identified as essential for effective teamwork, and to characterize potential barriers to integrating these principles in practice.

DESIGN/METHODS: Using qualitative methods, we conducted 2 focus group interviews (n=16). Fellows described their teamwork experiences at BASE Camp, how they would integrate team principles into future practice, and prior resuscitation experiences. Responses to open-ended questions were recorded, transcribed, and analyzed by a constant comparative method in Atlas.ti (qualitative data analysis program). Data was cross-coded to ensure agreement. Themes were identified by content analysis. The study was IRB approved and all subjects consented.

RESULTS: 17 PEM fellows (12 first and 5 second years) from 10 fellowships in NY, CT, and RI participated in BASE Camp (Oct 23-24, 2010). 29% were male.

Five themes reflecting 5 core teamwork principles were identified; in order of response frequency: *role clarity* (37%), *communication* (26%), *leadership* (17%), *situational monitoring* (13%), and *mutual support* (7%).

A sixth theme emerged from an inductive interpretation of coded data segments. *Barriers* to integrating the 5 core principles are categorized by: **Hierarchy** (n=16): discomfort asserting teamwork principles with more experienced multidisciplinary practitioners. **Inexperience** (n=15): challenges to integrating teamwork principles when resuscitation events are rare. **Communication** (n=8): difficulty implementing communication strategies with colleagues untrained in teamwork principles.

CONCLUSIONS: Fellows acquired basic teamwork principles during BASE Camp training and are eager to incorporate these behaviors and skills into future practice despite the barriers identified. BASE Camp may be useful to overcome these challenges, and our results will help inform future iterations of our educational intervention.

175

House Officer

Communication Malfunction: Utilizing Electronic Order Systems To Improve Communication and Reduce Radiation Exposure for Children with Ventricular Shunts

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BACKGROUND: Patients with shunted hydrocephalus receive multiple head CTs in their lifetime for shunt evaluation. These scans expose them to excessive amounts of radiation. Multiple studies show that low dose radiation protocols evaluate shunt function with the same quality and less radiation than standard scans. We hypothesized that low dose protocol CT was underutilized due in part to poor communication between providers and radiology technicians.

OBJECTIVE: To investigate if a change in an electronic ordering system can improve communication between physicians and radiology technicians and reduce radiation exposure in patients with shunted hydrocephalus.

DESIGN/METHODS: We reviewed electronic records to abstract data regarding physician ordering instructions and Head CT parameters for all patients who presented to the Johns Hopkins Pediatric Emergency Department with a suspected shunt malfunction over a three-month period. The electronic ordering system submenu for Head CT was then altered to add the indication "Pediatric Shunt Malfunction." The same data was then abstracted for patients with suspected shunt malfunction presenting to the Pediatric Emergency Department for the three-month period immediately after the change.

RESULTS: 133 patient visits met inclusion criteria, 70 with CT done in the control period and 63 after the intervention. Prior to the intervention, 33/70 (47%) of scans included communication of shunt malfunction in the electronic order. After the change, 53/63 (84%) included this information (P<0.001). However, this did not translate into a change in the scan performed by the CT technician: prior to the change 39/70 (56%) of scans were low-dose vs. 31/63 (48%) afterwards (P=0.49). As a result, mean effective radiation dose was 2.13 mSv before the intervention and 2.60 mSv after the intervention (P=0.1). When utilized, the low dose protocol mean effective radiation dose was 1.24 mSv vs. 3.60 mSv for standard head CT protocol (P<0.001).

CONCLUSIONS: The effective radiation dose was approximately 66% lower for patients when the technician used a low dose protocol scan. Rapid adoption of the new ordering indication led to a significant increase in orders that should have triggered the low dose protocol. However, this increase in communication was paradoxically associated with decreased utilization of the low-dose scan in this tertiary care pediatric emergency department.

176

Fellow in Training

"Missing" Mutations: Post-Zygotic Mosacism in Congenital Hyperinsulinism

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BACKGROUND: Genetic analysis of peripheral blood fails to identify mutations in approximately 50% of infants with congenital hyperinsulinism (HI).

OBJECTIVE: We hypothesized that some children with "missing" mutations have post-zygotic mutations of genes associated with dominant forms of HI in the pancreas.

DESIGN/METHODS: Direct sequencing of dominant HI genes was performed on pancreatic DNA from 3 of 4 children with HI whose blood was negative for mutations in SUR1, Kir6.2, glutamate dehydrogenase (GDH), and glucokinase (GK).

RESULTS: Patient 1 had diazoxide-responsive HI, protein-induced hypoglycemia, and elevated blood ammonias. She was diagnosed with hyperinsulinism/ hyperammonemia syndrome (HI/HA) and had a 95% pancreatectomy due to family concerns about diazoxide side effects. Pancreatic DNA identified a known HI/HA missense mutation (p.S445L) in GDH. Patient 2 had diazoxide-unresponsive HI that clinically was not consistent with a mutation in SUR1 or Kir6.2. GK-HI was suspected and she underwent a 92% pancreatectomy. Pancreatic DNA identified a low-level mosaic mutation (p.454dupAla) in GK. Patient 3, born at 27 weeks, had presumed perinatal-stress induced HI that failed to resolve. GK-HI was suspected based on failure to respond to diazoxide and having a low glucose requirement. At surgery, a focal lesion was not identified and she had a 10% pancreatectomy for histologic and genetic diagnosis. Analysis of the pancreas failed to identify a mutation in GK. Patient 4 was diagnosed with HI/HA after presenting with hypoglycemia and elevated ammonias. She demonstrated protein-induced hypoglycemia. She was well controlled on diazoxide and did not require surgical intervention.

CONCLUSIONS: These four patients with negative mutation analysis from peripheral blood had clinical phenotypes suggestive of autosomal dominant forms of HI. In 2 of the 4, suspected mutations in GK and GDH were confirmed in pancreatic DNA. The third patient may have a mosaic GK mutation below the limit of detection by conventional sequencing. The possibility of post-zygotic mutation should be considered in children with the appropriate phenotype who are negative for mutations in peripheral blood.

177

Fellow in Training

Markers of Body Composition as Predictors of Total and Undercarboxylated Osteocalcin in Healthy Children

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BACKGROUND: Recent studies suggest a novel relationship between bone and energy metabolism. One postulated link is osteocalcin (OCN), a known marker of bone formation whose undercarboxylated form has been associated with insulin sensitization and secretion in animal models. A few studies have found a negative association between total OCN (tOCN) and obesity, however the relationship between body composition and either tOCN or undercarboxylated OCN (ucOCN) in healthy children has not been explored.

OBJECTIVE: To determine if serum tOCN and ucOCN levels are associated with markers of body composition indicative of obesity in a cohort of healthy children.

DESIGN/METHODS: tOCN (175M/174F) and ucOCN (93M/84F) levels were obtained in a cross-sectional sample of healthy children recruited as part of the Reference Data Project on Skeletal Development at Children's Hospital of Philadelphia. tOCN was expressed as a Z score relative to BSAP and sex to account for the expected changes in tOCN associated with rapid bone formation across this age range. Height, weight, BMI, and pubertal stage were assessed. Bone mineral content (BMC), fat mass (FM) and lean body mass (LBM) were measured by dual-energy x-ray absorptiometry (DXA) and converted to age, sex, and race-specific Z-scores. Multivariable regression models were constructed using a multi-stage approach to determine the association of BMC-Z, FM-Z, and LBM-Z to tOCN after adjustment for age, sex, pubertal stage (TS), and bone specific alkaline phosphatase (BSAP). Similar analyses were used to study ucOCN.

RESULTS: 13.1% (46/351) and 12.4% (22/177) of subjects with tOCN and ucOCN were obese (BMI>95%). tOCN-Z was negatively associated with LBM-Z (p<0.001) and females TS4 (p<0.001), TS5 (p=0.002), and BSAP (p=0.004); and positively associated with age (p=0.002), and female gender (p=0.014); R^2=0.14. ucOCN was positively associated with LBM-Z (p=0.032), female gender (p=0.009), and tOCN (p<0.001); and negatively associated with TS3 (p=0.033) and BSAP (p.0<001); R^2=0.75. There was no association with FM-Z or BMC-Z for either tOCN-Z or ucOCN.

CONCLUSIONS: In a cohort of healthy and largely healthy weight children, tOCN and ucOCN are associated with LBM, and not FM or BMC. tOCN and ucOCN may not be sensitive markers of bone energy metabolism in children at a time of active bone remodeling.

178

Fellow in Training

Nature and Nurture: Multifactoral Rickets in Two Pre-School Aged Children

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BACKGROUND: Rickets is characterized by defective skeletal mineralization and disordered growth plate biology. Rickets most commonly results from vitamin D deficiency, but can also arise from defects in phosphorus metabolism in children with normal vitamin D status. Although the clinical features of rickets in children with vitamin D deficiency or genetic disorders of phosphorus metabolism are similar, the conventional biochemical profiles and clinical response to therapy are distinct.

OBJECTIVE: We describe two unusual cases of preschool aged children who presented with apparent vitamin D deficiency rickets not improving with conventional vitamin D treatment.

DESIGN/METHODS: Patient 1, a son of consanguineous Orthodox Jews, presented at 20 months of age. Patient 2, a daughter of consanguineous Muslims, presented at 22 months of age. Both patients had been breastfed without vitamin D supplementation, and presented with abnormal gait, short stature, bowed legs and radiological evidence of metaphyseal defects. Initial biochemical data are shown in the table.

Biochemical Data at Presentation

	$sCalcium_{corr}$, mg/dL*	sPhos, mg/dL	Alk phos, U/L	25(OH)D	intact PTH	TP/GFR mg/dL
Normal	9.4 - 10.8	3.8 - 6.5	145 - 320	> 30 ng/mL	10-65 pg/mL	2.9 - 6.1 mg/dL
Patient 1	8.3	2.2	318	19.3	95	2.8
Patient 2	8.8	2.8	844	15.8	128	2.2

*Calcium corrected for albumin

RESULTS: Both patients were treated with vitamin D and calcium with normalization of serum levels of 25(OH)D and PTH, but continued to have elevated alkaline phosphatase and low serum phosphorus concentrations and TP/GFR. Based on these results, we suspected a primary defect in phosphorus metabolism and initiated treatment with calcitriol and phosphorus. The patients subsequently improved with this therapy, and were found to have likely disease causing mutations in the *PHEX* gene consistent with X-linked hypophosphatemic rickets.

CONCLUSIONS: The resurgence of vitamin D deficiency, particularly among breastfed patients and those wearing religious dress, has heightened awareness of vitamin D rickets. The present cases emphasize that vitamin D deficiency can mask other causes for rickets, and thus nutritional vitamin D deficiency and genetic hypophosphatemic rickets may coexist in many children. It is important to carefully monitor alkaline phosphatase and phosphorus metabolism after conventional vitamin D treatment to confirm that vitamin D deficiency is the only cause for rickets.

179

Association of Serum Sphingolipids and Serum Adipocytokines with Insulin Resistance in Adolescents at Risk for Metabolic Syndrome

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BACKGROUND: Obesity is associated with low grade chronic inflammation mediated partially by tumor necrosis factor-alpha (TNF-α), free fatty acids (FFAs), and interleukin-6 (IL-6), and low serum adiponectin (AN). TNF-α increases sphingomyelinase activity *in vitro*. Serum ceramide (Cer), sphingosine (Sph) and sphingosine 1-phosphate (S1P), byproducts of sphingomyelin metabolism, are elevated in genetically obese (*ob/ob*) mice.

OBJECTIVE: 1) Compare serum levels of S1P, Sph, and ceramide in overweight vs. lean adolescents. 2) Correlate serum sphingolipid levels with anthropometric parameters (body mass index (BMI) and waist circumference (WC)), measures of insulin resistance (calculated homeostasis model of insulin resistance (HOMA-IR)), lipid profiles, and serum adipocytokines.

DESIGN/METHODS: Healthy overweight adolescents (age 13-18) with BMI ≥ 85% and lean (BMI 10-85%) controls were recruited. Anthropometric measurements and fasting blood samples were collected. Serum glucose, insulin, and fasting lipid profiles were measured. Serum adipocytokine levels were measured by ELISA or colorimetric assay. Serum sphingolipids were measured by HPLC mass spectroscopy.

RESULTS: The study enrolled 30 overweight and 15 lean adolescents. The subjects were similar in age and sex distribution. Significant differences in HOMA-IR (4.5±3.2 vs. 1.2±0.7*), FFAs (0.8±0.3 m.mol/l vs. 0.4± 0.3 m.mol/l*), and AN (6.4 ± 3.8 µg/ml vs. 12.6± 9.9 µg/ml *) were seen between groups (overweight vs. lean). There were no differences in TNF-α, IL6, or sphingolipid levels between groups. There were significant correlations between Sph and triglycerides ($r=0.362^{\wedge}$), Cer to S1P ratio and LDL cholesterol ($r=0.453^{-}$), Cer and TNF-α ($r=0.429^{-}$); Cer and HOMA-IR ($r=0.307^{\wedge}$), which persisted after adjustment for BMI-Z, sex, and Tanner stage. Upper 20th vs. lower 80th percentile Cer levels were associated with HOMA-IR > 3.29 (OR** = 5 (CI^{Ψ} = 1.04-24.9)). *Mean±SD; **OR= Odds ratio; $^{\Psi}$ CI= Confidence Intervals; $^{\wedge}P<0.05$; $^{-}P<0.005$.

CONCLUSIONS: This population of obese adolescents has significant insulin resistance and altered adipocytokine levels compared to lean controls. Elevated sphingolipid levels correlate with HOMA-IR, TNF-α and altered lipid profile. Ceramide is a potential biomarker for development of insulin resistance in obese adolescents. Future longitudinal studies will address the correlation between serum sphingolipids and risk factors for the development of T2DM in adolescents.

180

House Officer

Vitamin D Supplementation Improves Metabolic Parameters in Obese African American Adolescents

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BACKGROUND: Vitamin D deficiency is highly prevalent in African American adolescents. Vitamin D supplementation has been recently shown to improve arterial stiffness (Dong Y et al J Clin Endocrinol Metab. 2010 Oct; 95(10): 4584-91).

OBJECTIVE: To determine if in obese African American adolescents, Vitamin D supplementation, as compared to control and Metformin treatment, would improve the blood pressure and lipid profile.

DESIGN/METHODS: 43 obese African American boys (n=15) and girls (n=28) were evaluated in either the Vitamin D treated (2000 IU/d, n=10), metformin treated (n=15) or a control group (n=18). All participants underwent an extensive weight loss program. Anthropometric data, fasting glucose, insulin, lipid profile and Vitamin D levels were collected. BP percentiles, QUICKI and TG/HDL ratios were calculated. These parameters were evaluated at baseline and after 9 to 12 months.

RESULTS: All groups were similar at baseline except for higher BP in the Vitamin D group and higher TG/HDL ratio in the Metformin Group (Table 1). After the weight loss program the control group remained unchanged except the increase in TG/HDL ratio. In the vitamin D group, the SBP%,DBP% and vitamin D levels improved.

	Age (years)	BMI (%)	SBP (%)	DBP (%)	TG/HDL	QUICKI	Vitamin D 25
Baseline							
Control	12.7	98.4	67.6	59.6	2.08	0.30	12
Vitamin D treated	12.1	98.0	92.1*	62.4	2.01	0.32	14.3
Metformin treated	13.6	98.3	78.4	54.6	3.55*	0.30	14
End of study period							
Control	13.5	98.5	69.2	54.9	2.52	0.30	16.8
Vitamin D treated	12.7	97.8	68.2	52.3	1.69	0.33	27.7
Metformin treated	14.6	95.9	61.1	51.1	1.59#	0.30	16.5
Change							
Control	0.9	0.1	1.6	-4.7	0.2	0.0	4.8
Vitamin D treated	0.6	-0.2	-23.9	-10.1	-0.3	0.0	13.4
Metformin treated	1.0	-2.4	-17.9	-3.5	-2.0	0.0	2.5

* Denotes P<0.01 at baseline and # denotes P<0.01 after 1 year

In the metformin group the TG/HDL ratio significantly decreased. The insulin sensitivity as measured by QUICKI did not change in any group.

CONCLUSIONS: Daily vitamin D supplementation had the greatest effect on decreasing BP, and Metformin treated group had the greatest decrease in TG/HDL ratios. Vitamin D supplementation may play an important role in the vascular complications of metabolic syndrome.

181

Fellow in Training

Pituitary Volume by MRI Is Associated with IGF-1 in Children with Growth Failure

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BACKGROUND: Magnetic resonance imaging (MRI) of the pituitary gland is often performed as part of the evaluation for growth failure in children. Previous studies have shown that pituitary volume (PV) correlates with age, height and nocturnal plasma growth hormone levels. Reports of the relationship of PV to indices of the pituitary-growth hormone axis are lacking.

OBJECTIVE: We hypothesized that MRI PV correlates, not only with height, but also with insulin-like growth factor (IGF-1) and insulin-like growth factor binding protein (IGFBP-3).

DESIGN/METHODS: We performed a retrospective chart review of patients followed for growth failure who had a pituitary MRI reviewed by the same neuroradiologist (BD), bone age x-ray, as well as IGF-1 and IGFBP3 measured by the same laboratory (Esoterix Inc., Calabasas Hills, CA). MRI PV was calculated using the accepted formula for an ellipsoid, (pi/6)xLxWxH. Pearson correlation tests were used to evaluate for associations of PV with age, bone age, height standard deviation (SD), BMI SD, IGF-1, IGF-1 SD, IGFBP-3 and IGFBP-3 SD. Student t-tests were used for group comparisons (prepubertal vs. pubertal) with PV, IGF-1 and IGFBP-3.

RESULTS: Data on 69 patients were analyzed. There were 53 males and 16 females, with an average age of 11.2 ± 2.7 years; 38 patients were pubertal. There were no significant differences for age, bone age, height SD or BMI SD between males and females. PV positively correlated with age, bone age, height SD, IGF-1, IGF-1 SD, BMI SD and IGFBP-3.

Correlations of PV with Growth and Laboratory Parameters

Parameter	r Coefficient	p Value
Age	0.60	<0.0001
Bone Age	0.66	<0.0001
Height SD	0.42	0.0003
BMI SD	0.25	0.0353
IGF-1	0.55	<0.0001
IGF-1 SD	0.40	0.0007
IGFBP-3	0.26	0.0304
IGFBP-3 SD	-0.04	0.6859

Pubertal children had a higher PV and IGF-1 but not IGFBP-3 than the prepubertal children.
CONCLUSIONS: The strong correlation between PV and IGF-1 suggests that pituitary size may be an important component of the evaluation of children with growth failure.

182
House Officer

Knowledge, Attitudes and Clinical Practices of Pediatric Residents in a Community Hospital Regarding Vitamin D: Pre- and Post-Intervention Analysis

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BACKGROUND: The American Academy of Pediatrics (AAP) has published new guidelines on Vitamin D (ViD) intake. However, ViD deficiency is still widespread in all age groups. Physicians may not address this issue adequately during routine health care visits due to lack of knowledge and training.
OBJECTIVE: To assess knowledge, attitudes and practices (KAP) of pediatric residents (PRs) regarding ViD and to assess if enhancing their knowledge improved clinical practice.
DESIGN/METHODS: This was a prospective, interventional study conducted at Flushing Hospital Medical Center. PRs at all years of training (YoT) who consented to participate completed a 28-item survey including demographics to assess their knowledge about ViD. The possible knowledge score (KS) on the survey ranged from 0-26. Based on the chart review of 4 patients (2 infants aged < 1 year and 2 children aged 6-12 years) per resident regarding their assessment of the patients' ViD intake and supplementation, each resident was graded with a practice score (PS). Afterward, an educational intervention (EI) based on an Academic Pediatric Association designed module on ViD was provided to the PRs by either lecture or email. Post-EI, PRs were retested using the same survey and chart review repeated for their respective patients to determine change in PS. Frequencies, mean and standard deviation (SD) were used to analyze descriptive data and comparative analyses were done using Chi-square test, t-test, ANOVA and Wilcoxon signed rank tests.
RESULTS: Of the 28 total PRs who participated in the study, 9 were in their 1st YoT, 10 in the 2nd and 9 in the 3rd; 19 received EI via lecture and 9 by email. The pre-EI mean KS was 18.3 (SD± 3.60) which was not significantly affected by YoT, ethnicity, prior course in nutrition, being a parent or having completed an endocrinology rotation. The post-EI mean KS improved to 22.1 (SD± 2.51, p <.001) and was slightly higher in the lecture group (22.7) than PRs that received email (21). PRs level of comfort in providing anticipatory guidance to parents about ViD also improved (p 0.034). The PS for infants <1 year was better than for children aged 6-12 years, both before (p0.012) and after EI (p 0.001).
CONCLUSIONS: KAP about ViD is insufficient in PRs and improved significantly after EI. Further strategies are needed to improve clinical practice for older children.

183
Fellow in Training

Novel Presentations of Congenital Hyperinsulinism Due to Mutations in Hepatocyte Nuclear Factor 1 and 4 Alpha

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BACKGROUND: Hepatocyte nuclear factors 1 and 4 alpha are transcription factors implicated in the intricate transcriptional regulatory loops of the hepatocyte and pancreatic beta cell. Mutations of both factors cause familial monogenic diabetes (MODY3 & MODY1). Recently, HNF4 alpha MODY1 mutations were identified in infants with congenital hyperinsulinism (HI), resolving in early childhood and later progressing to insulinopenia.
OBJECTIVE: The purpose of this report is to describe 2 unusual cases of hyperinsulinism associated with mutations of these genes.
DESIGN/METHODS: Retrospective chart review and gene sequencing were used to characterize the 2 cases.
RESULTS: Case #1 presented at age 20 months with HI, was initially treated with diazoxide and was later found to have a paternally inherited, known MODY3 mutation in HNF1 alpha (p.Glu32X). Multiple paternal relatives had diabetes, typical of MODY3. Case #2 presented as a newborn with diazoxide-responsive HI, but developed renal Fanconi syndrome, hypophosphatemic rickets and hepatomegaly with histologic evidence of increased hepatic glycogen stores. Although clinically suggestive of Fanconi-Bickel syndrome, genetic tests of the GLUT2 gene and her clinical improvement did not support this diagnosis. She was found to have a known, de novo MODY1 mutation in HNF4 alpha (p.Arg76Trp). In both cases, the HI improved with age, with no evidence of hypoglycemia after 6 years of age.
CONCLUSIONS: These results show that mutations of HNF1 alpha may cause congenital HI, adding to previous evidence implicating only HNF4 alpha. Moreover, as shown in Case #2, HNF4 alpha mutations may affect liver and kidney producing a non-progressive disease phenotype similar to GLUT2 deficiency. This also expands the list of genetic causes of Fanconi syndrome. We speculate that these 2 factors are not directly responsible for all the clinical findings, but rather their mutations perturb their regulatory loops and function of other proteins – such as GLUT2, in the case of HNF4 alpha – leading to a variable phenotype.

184
House Officer

Adherence to 2008 Vitamin D Suplementation Recommendations in Infants

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BACKGROUND: In 2008 the AAP (American Academy of Pediatrics) recommended that infants who were fed breast milk and/or less than 1 liter of formula per day receive 400 IU/day of Vitamin D supplement, beginning on the first few days of life. Recent studies have shown <40% adherence to this recommendation among U.S. infants.
OBJECTIVE: Review adherence to the AAP recommendations for Vitamin D supplementation in a pediatric, urban clinic.
DESIGN/METHODS: We conducted a cross sectional survey of 244 consecutively-seen infants <6 months of age, with at least 1 visit in the first 60 days of life, and another visit in the first 130 days of life at a pediatric clinic serving an inner city population (75% African American, 12% Latino, 85% Medicaid). We extracted documentation from chart review regarding age of patient at each visit, type and amount of feedings, and Vitamin D supplementation prescription and compliance.
RESULTS: A total of 244 infant charts were surveyed: Mean age was 14.3 days at the first visit (SD 8.5 days), and 55.8 days (SD 18 days) at the second visit. 39% of the exclusively breast fed babies were prescribed Vitamin D supplementation at the first visit; 45% at the second visit. Among the formula fed infants only 4% were prescribed at the first visit and 1% at the second. Compliance with Vitamin D supplementation among breast fed infants was 50% and 64% at first and second visit. Among formula fed, compliance was 5% and 4% respectively.
CONCLUSIONS: Adherence to the AAP 2008 guidelines for Vitamin D supplementation was higher than the national average in most of the groups, but was still inadequate. Strategies are needed to improve provider compliance with Vitamin D supplementation in the primary care setting. Suggested intervention include preprinted prescriptions, placing a check box for Vitamin D prescription on the office visit encounter form and/or discharge papers, and educational activities for medical staff and parents. Another approach would be for formulas to have an increased content of Vitamin D.

185
Fellow in Training

FKBP4 Causing Glucocorticoid Resistance (GR) Is a Novel Reason for Premature Adrenarche

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BACKGROUND: Premature adrenarche(PA) occurs before age 8 yr in girls and 9 yr in boys. PA can be a normal variant of maturation, precursor of metabolic syndrome, NC-CAH, tumor, Cushing's disease and previously was considered to be a rare sign of GR. There has been only been two reports of GR presenting as PA. We present 4 children with premature adrenarche, who had in addition to elevated androgens, fluctuating elevations of ACTH and/or cortisol levels.
OBJECTIVE: To study glucocorticoid sensitivity in children with premature adrenarche.
DESIGN/METHODS: F-Dex binding assays were used to evaluate differential binding to the glucocorticoid receptor versus control. DNA was extracted and the glucocorticoid receptor gene(NR3C1) and FKBP4(molecule in glucocorticoid receptor complex) were amplified using PCR and sequence analysis was performed.
RESULTS: Patient 1: 7y female with adult body odor and elevated ACTH: 88 pg/mL and cortisol: 20.9 ug/dL, DHEA: 321 ng/dL. Genetic Analysis of NR3C1: polymorphism in E9: N766N and FKBP4: homozygous novel intronic mutation C6130G. F-Dex binding assays showed 30% less binding to the glucocorticoid receptor than control.
Patient 2: 7y female with adult body odor and elevated ACTH: 235 pg/mL and cortisol: 27 ug/dL and DHEAS: 63 mcg/dL.Genetic Analysis of NR3C1(-); analysis of FKBP4: novel intronic mutation C6130G. F-Dex binding assays showed 30% less binding to the glucocorticoid receptor than control.
Patient 3: 6y male that presented with pubic hair and axillary hair growth. The patient had elevated cortisol level: 27.2 ug/dL with elevated DHEA:1027ng/dL. F-Dex binding assays showed 20% less binding to the glucocorticoid receptor than control. Mutational analysis of NR3C1 and FKBP4: pending.
Genetic analysis in cases 1-3 of 21-hydroxylase gene was normal. Diurnal variation, Dexamethasone suppression and ACTH stimulation test was normal.
Patient 4: 5y female who presented for premature adrenarche. ACTH level: 180 pg/mL and cortisol: 10 ug/dL at 12pm. F-Dex binding assays showed 20% less binding to the glucocorticoid receptor than control. Mutational analysis of NR3C1and FKBP4: pending.
CONCLUSIONS: GR has not been shown to be a frequent cause of premature adrenarche. However, screening of our patients with premature adrenarche with fluctuating elevated ACTH and/or cortisol showed 4 children with novel mutations in FKBP4, showing that GR should be considered in patients presenting with premature adrenarche.

186
Fellow in Training

Weight Loss and Metabolic Benefit with the Addition of Glucagon-Like Peptide Agonists and Pioglitazone to Type 2 Diabetes Mellitus Adolescent Treatment

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BACKGROUND: Glucagon-Like Peptide agonists has been shown to stimulate insulin secretion from the β cell and inhibit β cell apoptosis. Pioglitazone is known to improve insulin sensitivity as well as inhibit β cell apoptosis. We used Glucagon-Like Peptide agonists with Pioglitazone in newly diagnosed adolescents with Type 2 diabetes mellitus (DMT2) to induce remission.

Hypothesis

Evaluate whether Glucagon-Like Peptide agonists use with Pioglitazone in newly diagnosed adolescents with DMT2 will induce remission.

OBJECTIVE: To analyze the safety and effectiveness of GLP-1 agonists and Pioglitazone in newly diagnosed adolescent with DMT2.

DESIGN/METHODS: 9 Overweight adolescent's with DMT2 and BMI >24 kg/m2 were studied. GLP-1 agonists 5mcg subcutaneous was prescribed once daily once patients were clinically diagnosed with DMT2 then the dose was increased to 10 mcg bid after 1 month. Lantus average 30 units daily with Actoplus Met 15mg/850mg once daily was used.

Anthropometric parameters, metabolic parameters, Gastrointestinal and neurological complications assessment were obtained at the baseline and 6 months after treatment.

RESULTS: Anthropometric and Biochemical Characteristics of 9 adolescents with DMT2.

Base Line and post 6 months treatment:

N=9	Baseline	6 months later
BMI (Kg/m2)	33.7 +/- 15.9	31.4 +/- 9
SBP (mmHg)	127.6 +/-36	120.8+/- 22
DBP(mmHg)	72.7 +/- 18.5	70 +/- 5
HBA1C %	9 +/- 1.7	6.1+/-1.2
Cholesterol	182.3+/- 29	153+/- 40
TG	94+/- 60	61+/-22
HDL	34.6+/-18.6	40.6+/-6
LDL	125.6+/-34.4	100+/-35
AST	27+/-29	26.5+/-5.6
ALT	47.5+/-9.1	39.5+/-8

#Values are means +/- SD

CONCLUSIONS: After 6 months on therapy 75% of patients showed a remission of DMT2 based on improved HbA1C .Lantus therapy was discontinued after one month of use only. Short acting insulin use was not necessary .BMI % was decreased in all patients.

All patients showed improvement in there lipid panel and in there liver enzymes. No documented Gastrointestinal or neurological complications were notified.

Gastroenterology / Nutrition / Hematology & Oncology Poster Session

Saturday, March 26, 2011
6:00 PM-7:30 PM

187

Novel Coagulopathy and Severe Hemorrhage with Epstein-Barr Virus-Associated Disease

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BACKGROUND: The coagulopathy accompanying acute Epstein-Barr virus (EBV)-associated lymphoproliferative disorder (LPD) has not been well-described. We reviewed the clinical course of recent pediatric patients with this disorder.

OBJECTIVE: To demonstrate the association of severe coagulopathy with EBV-LPD.

DESIGN/METHODS: Retrospective case series over 3 years at our medical center including all pediatric patients with acute (symptom onset<1 month) EBV infection and EBV associated LPD involving CD8+ cytotoxic T-cells.

RESULTS: Five patients (median age: 17, range: 2-20 years) presented with fever and sore throat, hepatosplenomegaly, and pancytopenia with elevated serum ferritin; all met criteria for hemophagocytic lymphohistiocytosis. Plasma D-dimer values on admission and during hospitalization (until death or a fall in EBV PCR or hematopoietic cell transplant) were elevated while plasma fibrinogen values on admission were depressed. One non-survivor was treated with heparin (5 to 7 units/kg/hour) for 36 hours without improvement in fibrinogen or D-dimer levels. During the 3 months following admission, all patients developed multiorgan system failure and 4 patients died with severe hemorrhage. EBV PCR titers in 3 non-survivors did not decline and D-dimer levels did not improve. EBV PCR titers declined in 2 patients treated with chemotherapy concurrent with improvement in plasma fibrinogen and D-dimer levels; 1 of these patients was the only survivor.

Coagulation profile

	Prothrombin time (seconds)	Activated partial thromboplastin time (seconds)	Fibrinogen (mg/dL)	D-dimer (μg/mL)
Median value (range) on admission	15 (13-20)	37 (25-69)	126 (90-460)	>20 (16->20)
Median values (range) during illness	14 (13-15.7)	34 (27-54.3)	255 (213-396)	>20 (5->20)

CONCLUSIONS: A novel coagulopathy with severe hemorrhage characterized by thrombin activation and vigourous fibrinolysis without intrinsic or extrinsic system abnormalities was noted in patients with acute EBV-associated LPD; most of these patients did not survive. We speculate that this coagulopathy is a marker of EBV-associated LPD.

188

House Officer

Etiology of Kidney Disease and Kidney Transplant Outcome in Pediatric Minorities

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BACKGROUND: Most information currently available on etiologies of pediatric chronic kidney disease (CKD) is drawn from studies of predominantly white populations. At our institution, an urban university-based hospital, the majority of patients are Hispanic or Black, and nearly 1/3 of the population lives below the poverty level. We examined the etiology of CKD, as well as management and outcomes after kidney transplantation (KT) to supplement the otherwise scarce data on minority populations.

OBJECTIVE: To explore how race impacts the underlying diagnosis of CKD and whether race affects management and outcome of children requiring KT.

DESIGN/METHODS: Retrospective chart analysis of 49 patients transplanted between 2000 and 2010 was performed. Information such as anthropometrics, demographics, race, underlying diagnosis, type of KT, and timing thereof were obtained. The rate of rejection episodes stratified by race was assessed as well.

RESULTS: Of 49 patients transplanted at our institution over the last decade, 45 KT recipients had complete records. Of them, 27 were M, 18 were F. Mean age at transplant was 11.5 years. 7 KT recipients had >1 KT (2-3). Mean follow up (f/u) was 50 mo. 18% of KT were pre-emptive, while 30% of KT were from living donors (10% unrelated). A total of 10 rejections occurred during f/u, of which 8 occurred within 12 mo post KT. Table 1 provides the breakdown of our study population by race for etiology of CKD, preemptive KT, live donation, and episodes of rejection.

Characteristics of Study Population

	Hispanic	Black	White	Other
% Population	38	27	24	10
% Focal segmental glomerulosclerosis	33	23	33	11
% Dysplasia	83	0	0	17
% Reflux/Obstr. Uropathy	29	43	17	8
% Glomerulonephritis	29	43	14	14
% Cystic disease	20	40	40	0
% Other	33	0	50	17
% Preemptive KT	37	13	25	25
% Living Donor	25	31	44	0
% of all Rejections	40	30	30	0

CONCLUSIONS: Our study is the first of its kind to assess etiology of pediatric CKD and KT outcomes in a population primarily comprised of minorities. National registries are vastly comprised of White children and offer a skewed statistical view of minority populations. Our study provides insight into the etiology of CKD and outcome of KT recipients and demonstrates that the data are not significantly different in minorties and children of low socioeconomic status, compared to white middle-class cohorts, when adequate care is provided.

189

House Officer

Use of Screening Urine Dipsticks in Well-Child Care To Detect Asymptomatic Proteinuria without Proper Interpretation Leads to Unnecessary Referral of Pediatric Patients

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BACKGROUND: Pediatricians continue to use screening urine dipsticks in well-child care despite the American Academy of Pediatrics recommendation in 2007 to discontinue this screening . A previous review of our experience before that recommendation was made demonstrated that 9 of 9 patients(pt) would not have been referred if the primary care physician had used the algorithm published for the evaluation of asymptomatic proteinuria in 2000.

OBJECTIVE: To review our more recent experience to determine the nature of the referrals and compare them with our previous data to see if unecessary referrals continue.

DESIGN/METHODS: A retrospective study of pts referred for asymptomatic proteinuria to the pediatric nephrologist at Nassau University Medical Center, a public health sector facility, from July 2008 to December 2009. Data was collected for age, sex, prior lab data, random urinalysis(UA), 1st morning UA, urine protein/creatinine ratio, diagnosis and follow-up. The data was compared with our experience from February 2005-February 2007.

RESULTS: 9 pts were referred before the AAP recommendation & 13 pts afterwards for a total of 22 pts. Male:Female ratio was 1:1, age ranged from 5-17 years. 6/22 pts had no prior labs available at the time of referral. In 19/22 pts the proteinuria was transient or resolved & 3/22 pts had orthostatic proteinuria. In all of the pts the algorithm was either not applied or not applied properly.

CONCLUSIONS: 1. None of the pts referred for evaluation of asymptomatic proteinuria had significant renal disease. 2. The need for referral could have been determined if the algorithm had been used. 3. Use of the algorithm would have led to savings in terms of cost and anxiety. 4. The algorithm should be used by primary care physicians to evaluate children and adolescents with asymptomatic proteinuria. 5. Without proper interpretation, the use of screening urine dipsticks used in well-child care still leads to unnecessary referral of pediatric patients to a nephrologist. 6. A study involving multiple centers would be of value in determining whether our experience is unique to our community or not and if it represents a dysparity in health care.

Saturday, March 26, 2011
6:00 PM-7:30 PM

190

Fellow in Training

Early Fortification of Expressed Breast Milk (EBM) Improves Calcium (Ca) and Phosphorus (P) Intake and Reduces Peak Alkaline Phosphatase (AlkP) Level in Premature Neonates

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BACKGROUND: Premature infants are at significant risk for extrauterine growth failure and metabolic bone disease(MBD) because of poor Ca, P and protein intake.Unfortified EBM is also low in Ca and P.The optimal time for fortification of feeds is not known.

OBJECTIVE: We hypothesized that early fortification of feeds to 24Cal/oz would improve growth and reduce incidence of MBD without increasing feed intolerance.

DESIGN/METHODS: This was a randomized study of infants<32 wk gestation.The standard protocol in our NICU is to fortify EBM/formula to 22Cal/oz at a feed volume of 50ml/kg/d and to 24Cal/oz at 100ml/kg/d. The early fortification group received feeds fortified to 24Cal/oz at a feed volume of 50ml/kg/day.The clinical team was blinded to the feed between enteral volumes of 50 and 100ml/kg/d("study period").We evaluated growth velocity,time to reach full feeds(120Cal/kg/day),serum Ca,P and AlkP and the incidence of feed intolerance.

RESULTS: Early fortification resulted in higher caloric,Ca and P intake during the study period. Peak AlkP was lower in the early group compared to standard, reaching significance in infants on EBM.Serum Ca levels were higher in the early fortification group at 1 mon of age.There was no difference in time to full feeds or average growth velocity during their NICU stay.

Results(mean+/-SD)

	Early fortification(n=23)	Standard fortification(n=19)
Gestational age(wk)	29±1.9	28.6±2.4
Birth weight(g)	1221±318	1229±353
Day of life at first feed	3.3±3.7	2.9±2.5
Infants on EBM	10(43%)	10(53%)
"Study period"(d)	4.3±3.2	3.8±1
Total calories/d during study	110±35	99±12
Enteral Calories/day during study	63±20*	52±10
Ca intake/kg/d(mg) during study	134±34*	88±24
P intake/kg/d during study(mg)	82±27*	60±7
Average wt gain(g/d)	22.2±10.4	24.7±5
Time to full feeds	19.3±16	22.9 ± 20.5
Peak AlkP(all)	372±179	453±143
Peak AlkP(EBM)	383±142*	537±116
Serum Ca(at 1 mon of age,mg/dL)	10±0.3*	9.7±0.4
Feeding intolerance(during study feeds)	2/23	1/19
NEC(stageII/higher)	1/23	3/19

*p<0.05 compared to standard fortification

CONCLUSIONS: Early fortification of EBM to 24Cal/oz at 50ml/kg/d feed volume significantly increased Ca and P intake and reduced peak AlkP.We speculate that in preterm infants on EBM,early fortification may improve bone mineralization and prevent MBD.

191

Fellow in Training

Tidal Volume Needed for Normocapnia in Infants with Meconium Aspiration Syndrome

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BACKGROUND: Meconium Aspiration Syndrome (MAS) is a complex disease ranging from mild respiratory distress to severe respiratory failure. Optimal ventilatory strategy would avoid/treat pulmonary hypertension and avoid overventilation of lungs at risk for overdistention and air leak. Such strategy for MAS has not been defined. To minimize volutrauma, Volume Guarantee ventilation is the primary mode of support in our institution. The appropriate tidal volume (VT) for patients with MAS has not been studied. Because MAS leads to increased physiologic dead space and functional residual capacity, we hypothesized that MAS patients may require higher VT than infants with homogeneous lung disease to achieve adequate ventilation.

OBJECTIVE: To provide normative data for VT required to achieve adequate $PaCO_2$ in neonates with MAS.

DESIGN/METHODS: We reviewed medical records of infants with MAS admitted to Georgetown University Hospital from 2000 to 2010 managed with conventional ventilation. Demographics, ventilator settings, observed VT, respiratory rate (RR) and corresponding blood gas values were recorded. Minute ventilation (MV) was calculated as a product of RR & VT. Only VT values with corresponding $PaCO_2$ in an acceptable range of 35 to 60 mmHg were included. Mean VT/kg and MV/kg were calculated for each patient and these mean values were subjected to descriptive statistical analysis. We also collected data from 40 term infants with severe uniform lung disease without pulmonary hypoplasia to serve as controls.

RESULTS: Twenty eight patients were ventilated conventionally during this period. Mean gestational age (GA) and birth weight (BW) were 39.7 ± 0.84 wk and 3330 ± 500g. Mean GA and BW for the controls was 37.4 ± 1.5 wk and 3300 ± 640 g. Two patients in each group required ECMO for severe persistent pulmonary hypertension. Infants with MAS required significantly higher VT and MV than controls to maintain equal $PaCO_2$.

	MAS (n=28)	Control (n=40)	p value
VT (ml/kg)	6.11 ± 1.05	4.86 ± 0.77	<0.0001
MV (ml/kg/min)	371 ± 110	262 ± 53	<0.0001
PaCO2	41.0 ± 3.9	41.5 ± 3.12	0.55
PIP (cmH_2O)	18.5 ± 5.9	20 ±4.9	0.25

Mean±SD

CONCLUSIONS: These findings are consistent with the known pathophysiologic derangements in MAS mainly air trapping with heterogeneous aeration and increased physiologic dead space. These are the first normative data to guide selection of VT in infants with MAS.

192

Mechanical Ventilation at Postnatal Day 7 and Bronchopulmonary Dysplasia among Extremely Preterm Infants

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BACKGROUND: Despite improvements in the care of preterm infants, bronchopulmonary dysplasia (BPD) remains an important morbidity that varies in prevalence among centers after adjusting for biologic risk factors. Identifying elements of current clinical practice associated with BPD may lead to interventions that reduce the prevalence or severity of the disorder.

OBJECTIVE: We sought to evaluate the importance of potential biologic and clinical risk factors for BPD, defined as oxygen requirement at 36 weeks post-menstrual age (PMA), in a contemporary cohort of extremely preterm infants. We focused on potentially modifiable elements of care, including mechanical ventilation (MV) at postnatal day 7 and late-onset infection (LOI).

DESIGN/METHODS: As part of a two-hospital cohort study of lung injury among infants born before 29 weeks gestational age (GA), we studied infants born 2004 to 2009 who survived to 36 weeks PMA and had complete information to hospital discharge. We used univariate analyses and time-oriented logistic regression modeling to identify factors associated with BPD, focusing on variation in risk between infants receiving and not receiving MV at postnatal day 7.

RESULTS: BPD developed in 52% of the entire cohort of 633 infants, in 33% of the 357 infants not receiving MV at day 7, and in 77% of the 276 infants receiving MV at day 7. Factors associated with BPD in the final multivariate models for the entire cohort as well as for subgroups defined by MV status at day 7 are shown in the table.

Final Models - Significant Results

	All Infants		No MV Day 7		MV Day 7	
	OR	95% CI	OR	95% CI	OR	95%CI
GA 25-26 wks (vs 27-28)	2.5	1.6-3.9	3.3	1.9-5.7	1.5	0.7-3.2
GA <25 wks (vs 27-28)	3.1	1.6-5.9	20	4.2-97	1.6	0.7-3.7
FGR	2.1	1.4-3.4	2.5	1.3-4.8	2.1	1.0-4.3
Female					2.7	1.4-5.2
Hospital 1	1.9	1.3-2.8			1.8	1.0-3.5
Apgar 1 min 5-7 (vs 8-10)	2.0	1.1-3.7				
Apgar 1 min 0-4 (vs 8-10)	2.5	1.3-5.0	2.6	1.1-6.2		
pCO2 at 6-18 hrs ≤35			0.4	0.2-0.7		
PDA medically treated	1.5	1.0-2.3				
MV day 7	2.9	1.9-4.6				
LOI	1.8	1.2-2.6			2.4	1.3-4.5

CONCLUSIONS: In this cohort of infants born before 29 weeks GA, the most important determinants of BPD were MV at postnatal day 7, younger GA, FGR, and LOI. Modeling of subgroups showed GA to be associated with BPD only among infants not on MV at day 7. MV at day 7 and LOI represent potentially modifiable determinants of BPD.

193

IFN-γ and IP-10 in Tracheal Aspirates from Premature Infants: Relationship with Bronchopulmonary Dysplasia

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BACKGROUND: Interferon gamma (IFN-γ) and interferon-inducible protein of 10 kDa (IP-10) are potent inflammatory mediators and may contribute to acute lung injury in adults. The roles of IFN-γ and IP-10 in neonatal lung injury and the development of bronchopulmonary dysplasia (BPD) are unknown.

OBJECTIVE: To study the association between IFN-γ and IP-10 in tracheal aspirates (TA) and the development of BPD in premature infants.

DESIGN/METHODS: TA samples collected within 48 hours after birth from 79 mechanically ventilated premature neonates [gestational age (GA) <30 weeks (w), birth weight (BW) <1250 grams (g)] were analyzed. The level of IP-10 was determined using a commercially available ELISA kit (R & D Systems, Minneapolis, MN). IFN-γ was measured in a subgroup of 38 infants by using a biochip multi-analyte immunoassay (Randox Laboratories, Antrim, UK). Total protein in TA was measured by Bradford assay to correct for sampling related dilution. BPD was defined as the need of supplemental oxygen at 36 weeks postmenstrual age (PMA).

RESULTS: Twenty infants (GA 26.4±1.9w, BW 860±201g) survived without BPD at 36 weeks PMA and 59 infants (GA 25.5±1.5w, BW 751±163g) died before 36 weeks PMA or developed BPD. The mean IP-10 and IFN-γ levels were higher in infants who died or developed BPD compared to those who survived without BPD.

		No BPD	BPD/Died	p
IP-10	pg/ml	18.5±7.5	63.4±17.5	0.02
	pg/mg of protein	38.2±16.5	140.9±48.8	0.05
IFN-γ	pg/ml	3.1±1.1	9.7±2.8	0.03
	pg/mg of protein	4.4±1.8	13.3±3.7	0.04

mean ± SD

CONCLUSIONS: Higher IFN-γ and IP-10 levels in TA samples are associated with the development of BPD or death in premature infants. We speculate that IFN-γ and IP-10 play an important role in acute lung injury in premature infants.

194

Impact of Histological Chorioamnionitis on Tracheal Aspirate Cytokines in Premature Infants

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BACKGROUND: Elevated cytokines in tracheal aspirates (TA) of premature infants are associated with the development of bronchopulmonary dysplasia (BPD). Histological chorioamnionitis (CHORIO) may increase inflammatory mediators in the lungs of preterm infants.

OBJECTIVE: To study the impact of CHORIO on TA cytokines in ventilated infants.

DESIGN/METHODS: TA samples collected within 48 hours after birth from 40 ventilated neonates [gestational age (GA) <30 weeks (w), birth weight (BW) <1250 grams (g)] were analyzed. Levels of 12 cytokines {Interleukin-1 α (IL-1α), IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, Epidermal Growth Factor (EGF), Interferon-γ (IFN-γ), Monocyte Chemotactic Protein-1 (MCP-1), Tumor Necrosis Factor-α (TNF-α), Vascular Endothelial Growth Factor (VEGF)} were measured using a biochip multi-analyte immunoassay (Randox Laboratories, Antrim, UK). Total protein in TA was measured by Bradford assay to correct for sampling related dilution. Assessment of CHORIO was done by a blinded pathologist.

RESULTS: Twenty six infants (GA 26.6±1.4w, BW 852±162g) had no CHORIO and 14 infants (GA 25.1±1.0w, BW 776±164g) had CHORIO. The levels of IL-1α, IL-1β, IL-8 and VEGF were significantly higher in TA samples of preterm infants with CHORIO with levels remaining higher after correcting for dilution with protein. There was also a trend towards higher levels of EGF, MCP-1 and TNF-α in CHORIO infants.

Cytokines (median, 25th and 75th percentile)

Cytokines (pg/ml)	No Chorio (n=26)	Chorio (n=14)	p
IL-1α	0 (0-1.0)	*3.6 (0.8-12.7)	< 0.01
IL-1β	3.3 (0-8.1)	*18.6 (3.4-33.0)	0.2
IL-2	1.8 (0-3.9)	3.7 (0-4.4)	0.4
IL-4	1.8 (1.7-1.9)	1.8 (1.7-1.9)	0.6
IL-6	88 (52-451)	267 (48-425)	0.7
IL-8	1017 (257-2038)	*2268 (1018-2268)	0.02
IL-10	0 (0-0)	0 (0-1.4)	0.16
VEGF	12.5 (0-34.9)	*59.4 (13.5-138.6)	0.03
IFN-γ	2.4 (0-8.2)	7.1 (0-13.1)	0.4
TNF-α	0.6 (0-2.3)	3.3 (0-19.4)	0.1
MCP-1	356 (156-1003)	985 (216-1186)	0.1
EGF	5.0 (2.1-17.9)	8.3 (2.3-27.6)	0.1

CONCLUSIONS: CHORIO is associated with the increased pro-inflammatory mediators in TA samples of preterm infants, which may contribute to the development of bronchopulmonary dysplasia.

195

Fellow in Training

Screening for Autism in Former Preterm Infants

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BACKGROUND: Autism spectrum disorder (ASD) is a complex, behaviorally defined disorder of the brain. The Modified Checklist for Autism in Toddlers (MCHAT) has been validated to be a sensitive screening tool for ASD. When followed by a structured follow up interview (SFI) its positive predictive value increases from 57% to 76%. Few studies have looked at screening for ASD in preterm infants (PT). Those that have, showed a positive screening rate of 21% to 25% utilizing the MCHAT among extremely low birth weight infants. However these were without the use of SFI.

OBJECTIVE: This study sought to estimate the prevalence of a positive screen for ASD utilizing the MCHAT and SFI among all PT infants in a regional follow- up program and to identify risk factors associated with a positive screen.

DESIGN/METHODS: This is a prospective, on going collection of data which started January 2009. A sample size of 250 will be sought. This is based upon a 10% overall positive screening rate when SFI had been used in previous studies. Infants with cerebral dysgenesis or chromosomal disorders were excluded. The incidence of a positive screening for ASD utilizing the MCHAT were determined for all PT infants pre and post SFI at 24±6 months adjusted age (AA). Correlations between a positive ASD screen and demographic, socioeconomic, antenatal/ delivery and NICU conditions were determined. Secondary analysis stratified results by gestational age (GA): very preterm (VP:<28 wks), moderately preterm (MP:28-33wks), late preterm (LP:34-36wk). Data was collected utilizing SPSS 18.0. t-test compared continuous variables and X^2 for categorical data. P<0.05 was considered significant.

RESULTS: Interim analysis is based upon 165 former PT children. Subjects were evaluated at an AA of 25±3 months. The pre SFI positive screening rate for all PT children was 14%. Whereas post SFI positive screening rate was 6%. 10% of VP, 18% of MP and 6.5% of LP screened positive pre SFI. 6% of VP, 10% of MP and 0% of LP had an abnormal MCHAT score post SFI. Significant correlations with positive screening were maternal age (35±3v32±6) male sex 9(90%) and PVL 7(70%).

CONCLUSIONS: Amongst PT infants, a significant number of them will screen positive for ASD. This may be due to morbidities of prematurity affecting a rapidly growing brain such as PVL. However the SFI will significantly reduce the amount of infants who will need further referral for more formal testing.

196

House Officer

Status of Neonatal Resuscitation Efforts in Resource-Poor Countries: Challenges and Opportunities

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BACKGROUND: Each year approximately 814,000 newborns die from intrapartum-related causes and there are more than 1 million intrapartum stillbirths. Effective neonatal resuscitation (NR), utilizing basic techniques, is often unavailable where most births occur. Simplified training tools (e.g., AAP's Helping Babies Breathe) and innovative, affordable equipment provide new opportunities to train and equip health workers in low-resource settings, yet constraints exist to scaling up this intervention.

OBJECTIVE: We performed a survey to assess the current status of NR in selected high burden countries.

DESIGN/METHODS: We designed, piloted and implemented a survey of key decision-makers and program experts using Saving Newborn Lives program managers as an entry point in each country. Program managers obtained information from Service Provision Assessments, national/ local data sources, and from local experts. Results were analyzed in Excel.

RESULTS: Responses were obtained from 16 countries, together accounting for around 50% of global neonatal deaths: 6 in Asia (Afghanistan, Bangladesh, Indonesia, Nepal, Pakistan, Vietnam), 9 in Africa (Ethiopia, Ghana, Malawi, Mali, Mozambique, Nigeria, South Africa, Tanzania, Uganda), and 1 in Latin America (Bolivia). In most countries, NR was not mentioned in policy documents regarding child health. All countries had current and previous NR training programs, but some were perceived to have failed for key reasons, notably a lack of systematic implementation planning, insufficient equipment, or a lack of trainers. Implementation constraints mentioned in every country included a lack of adequately trained personnel at all levels of the healthcare system (e.g., tertiary/referral, district, primary and community) and a lack of equipment at each level. Many countries indicated under-utilizing available cadres of healthcare providers (e.g., community midwives) to provide NR. Some countries have begun to pilot test whether NR training of existing extension workers is feasible, acceptable, and effective. Monitoring and evaluation of coverage, quality and logistics of NR programs were uniformly insufficient.

CONCLUSIONS: Our results identified policy opportunities, lessons learned from NR programs, and gaps in coverage of trained and equipped providers in areas of high neonatal mortality. Country-specific "entry points" were identified for NR training to be integrated into current programs.

197

Fellow in Training

Late-Onset LipopolySaccaride (LPS) Challenge Alters the Serum and Pulmonary Inflammatory Response in Three-Week Old Sprague-Dawley Rat Pups Preconditioned with Birth Hyperoxia

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BACKGROUND: Hyperoxia-induced lung injury is characterized by increased pulmonary permeability & endothelial cell injury, predisposing to systemic inflammation. Mediators of this response contribute to bronchopulmonary dysplasia. Premature infants with hyperoxia exhibit increased mortality from respiratory-acquired pathogens at older ages from systemic bacteremia. The mechanism underlying this process is not well known.

OBJECTIVE: To determine the effect of late-onset infection after birth hyperoxia on the serum inflammatory response.

DESIGN/METHODS: 4 litters of newborn Sprague-Dawley rats were exposed to either hyperoxia (100% oxygen) for 24 hours or room air. Animals were returned to normoxia for 3 weeks prior to receiving intranasal LPS (10ug) or phosphate buffered saline control. The animals were sacrificed 24hrs later. Blood was collected by cardiac puncture & analyzed for Tumor Necrosis Factor Alpha (TNF-alpha), Interleukins (IL) IL-1 alpha, IL-1B, IL-2, IL-4, IL-6, IL-10, IL-10, Interferon gamma (INF-gamma) and Granulocyte Macrophage Colony Stimulating Factor (GMCSF) by Luminex Multiplex micro-bead (Enzyme-linked immunosorbent assay) ELISA. Results were analyzed for statistical significance by ANOVA with post-hoc Bonferroni Correction. P<0.05 was used to determine significance.

RESULTS: Serum TNF-alpha & IL-1B levels were increased in LPS-treated animals preconditioned with hyperoxia compared to those with LPS alone ($p<0.001$, $p<0.05$). IL-1 alpha levels were decreased in LPS-treated animals exposed to birth hyperoxia compared to LPS-infected animals alone ($p<0.001$). GMCSF increased with administration of hyperoxia compared to the control ($p<0.05$) but were decreased in the LPS-exposed hyperoxia group compared to the hyperoxia group alone ($p<0.001$). IL-4 levels increased with hyperoxia alone, but were not altered in combination with LPS. LPS administration decreased INF-gamma levels compared to control ($p<0.01$), but were increased in animals exposed to birth hyperoxia as compared to LPS alone ($p<0.001$). No differences in IL-2, IL-6, IL-10 and IL-12 levels were noted.

CONCLUSIONS: LPS increases the early inflammatory response in animals who received birth hyperoxia. Late-phase and anti-inflammatory mediators are not changed, resulting in an increased early-phase systemic inflammation. We speculate birth hyperoxia increases susceptibility to systemic inflammation.

198

Fellow in Training

Localization of Sirtuin 1 in Fetal Membranes: Possible Role in Perinatal Inflammation

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BACKGROUND: Infection induced up-regulation of inflammatory cytokines has been proposed to be the causative link between chorioamnionitis and adverse neonatal outcomes. Sirtuins (SIRTs) are class III histone deacetylators and play a role in regulating key inflammatory mediators. In animal models and adults, SIRTs are protective against inflammation. The role of SIRTs in the pathogenesis of chorioamnionitis is unknown.

OBJECTIVE: To study the effect of chorioamnionitis on expression of SIRT1 in fetal membranes from preterm placentas.

DESIGN/METHODS: In an IRB approved protocol, stored blocks of fetal membranes from 41 preterm (GA < 32 W) placentas were analyzed. Sixteen preterm placentas had histological evidence of chorioamnionits (CHO group) on H & E stain and 25 did not (NO-CHO group). The immunoreactive SIRT1 was localized by immunohistochemistry using rabbit polyclonal antibodies. SIRT1 staining was quantified in the cytoplasm and the nucleus by 3 independent observers on a score of 0-4 as described by Yan et al (Placenta 2002 (23): 288-293).

RESULTS: There was no significant difference in GA (25.7±2.3 vs. 26.7±3.5 W) and BW (949±328 vs. 851±341 G) between the CHO and NO-CHO groups. SIRT1 was localized in the cytoplasm (C) and the nuclei (N) of all tissue studied. There was no significant difference in SIRT1 localization in the cytoplasm of amnion epithelium (AE), mesenchyme (M) and chorion (Ch) between the two groups. The localization of SIRT1 was significantly decreased in the nuclei of AE in the CHO group.

	No-CHORIO	CHORIO
AE-C	3 (2-3)	3 (2-3)
M-C	2 (2-3)	2 (2-3)
Ch-C	2 (2-3)	2 (1.5-3)
AE-N	4 (3-4)	*2 (1-2.5)
M-N	2 (2-3)	2 (2-3)
Ch-N	2 (1-2)	2 (1-2)

Median (25^{th} percentile-75^{th} percentile); *P < 0.001

CONCLUSIONS: SIRT1 is expressed in the fetal membranes from preterm placenta and its localization is decreased in the nuclei of AE cells with chorioamnionitis. We speculate that SIRT1 plays an important role in perinatal inflammation.

199

Contaminant or Pathogen: Predictors of Coagulase Negative Staphylococcal Bacteremia in the NICU

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BACKGROUND: Coagulase-negative staphylococci (CoNS) are the most frequent cause of late onset sepsis (LOS) in the neonate. Differentiating definitve disease (DD) from potentially contaminated culture (PCC) results is a challenge; one standard for diagnosing DD is the presence of ≥ 2 positive cultures. Clinicians are often hesitant to discontinue antibiotics with a single positive culture in an infant who appeared ill and/or improved on antibiotics.

OBJECTIVE: To distinguish characteristics of DD from PCC in infants treated for CoNS LOS.

DESIGN/METHODS: Retrospective chart review of all infants treated for CoNS LOS in a single NICU between 2000-2009. DD (n=54) was defined as infants with ≥ two positive blood cultures for CoNS. PCC (n=48) was defined as infants treated for CoNS LOS despite only a single positive blood culture (culture was negative prior to vancomycin). We compared the two groups using t-tests for continuous variables, chi-square for nominal variables, and multivariable logistic regression.

RESULTS: Infants with DD had lower platelet counts (DD 167 vs. PCC 228, p< .01) and a higher incidence of thrombocytopenia (<150) at the time of diagnosis (DD 53% vs. PC 26%, p = .004). Infants with DD had a shorter time to first positive culture (DD 17h vs. PCC 22h, p = .003). Birthweight, gestational age, presence of a central catheter, need for mechanical ventilation or parenteral nutrition at diagnosis of LOS were not significantly different between the two groups. The average total number of clinical symptoms (6 possible) present at diagnosis of LOS was similar; only the presence of feeding intolerance was significantly different (more common in the PCC). In addition, there were no significant differences regarding the total white blood cell count (WBC), left shift, or number of infants with an abnormal WBC (<5 or > 20). Logistic regression confirmed the association of thrombocytopenia (OR 3.6, 95% CI 0.69-5.4) with DD, but also found an abnormal WBC included as an effect modifier for positive first culture < 18 hours (OR 35, 95% CI 2.5 – 488) was significantly associated with DD.

CONCLUSIONS: Thrombocytopenia has been associated with persistent CoNS bacteremia but is also strongly predictive of true CoNS LOS if present at the time of diagnosis. Clinical symptoms are not reliable in predicting DD. WBC are not consistently helpful in distinguishing DD from PCC, but an abnormal WBC in the face of rapid culture positivity is associated with DD.

200

Fellow in Training

Racial Differences in the Effects of Maternal Age on NICU Admission Rates

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BACKGROUND: Admission to the NICU is an indicator of maternal-fetal well-being with implications for long-term health status. The integrity of the fetal-placental unit may reflect the cumulative health history, including social determinants of health, of the mother.

OBJECTIVE: To determine the relative and interactive influences of maternal age and race on NICU admission risk.

DESIGN/METHODS: Consortium on Safe Labor Database (n=233844 births;19 US hospitals 2002-2008) was used to determine maternal age, teenage (13-18 yrs) and advanced maternal age (AMA=35-48 yrs), and NICU admission rate. Analysis was performed between three maternal race descriptions (White, Black, and Hispanic) and controlled for gestational age, percentage of births by maternal age, and weighted to reflect national US nativity.

RESULTS: Teenage and AMA accounted for 5.8% and 16.3% of NICU admissions. The proportion of NICU admissions corrected for birthrate was not different (p=0.36) with a NICU admit OR=1.14 for both age groups compared to 19-34 yr old mothers. There was a marked racial influence with maternal age on NICU admission rates [Table 1]. Black mothers with advancing age had higher risk of a NICU admission. In contrast to the increased risk in Blacks, White and Hispanic AMA mothers had lower risk of a NICU admission than teenagers in their same racial group.

NICU Admission Risk: Maternal Race x Age

Race	Maternal Age	OR (95% CI)
Black	≤ 18	Reference
Black	19 - 34	1.086 (1.075-1.097)
Black	≥ 35	1.342 (1.327-1.356)
Hispanic	≤ 18	Reference
Hispanic	19 - 34	0.794 (0.787-0.802)
Hispanic	≥ 35	.0828 (0.820-0.836)
White	≤ 18	Reference
White	19 - 34	0.926 (0.919-0.933))
White	≥ 35	0.930 (0.924-0.937)
Gestational Age (week)		0.610 (0.610-0.611)

CONCLUSIONS: The effect of maternal age on infant health outcomes, as measured by NICU admission rates, varies among racial groups.

These data are consistent with the "weathering" hypothesis in which individual and community experiences are differentially experienced.

201

Short-Term Hyperoxia Alters Lung Levels of T-Lymphocytes in Newborn Gram-Negative-Infected Sprague-Dawley Rat Pups

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BACKGROUND: Hyperoxia causes oxidant stress & inflammation, leading to simplified alveolarization & disrupted vascularization, resulting in progression toward chronic lung disease. Gram-negative infection similarly increases inflammation, leading to fibrosis and remodeling. Recognition of gram-negative infection in the lung is mediated by the CD14-Toll-Like Receptor 4 (TLR4) complex, which not only causes CD4 lymphocyte activation via secondary messengers MyD88 and Interleukin-1 Receptor Associated Kinase (IRAK) but is hyperoxia sensitive.

OBJECTIVE: To determine the effect of hyperoxia on the short-term levels of TLR4, MyD88, Interleukin-1 Receptor Associated Kinase (IRAK) and lymphocyte subsets CD3, CD4, CD8, CD14 & CD45 in the lungs after gram-negative infection.

DESIGN/METHODS: 4 litters of time-pregnant Sprague-Dawley rats pups were exposed 10 ug of intranasal lipo-polysaccaride (LPS) or saline control after birth. 24hrs later, a litter was exposed to 6 hours of 100% hyperoxia or control. Immediately after hyperoxia, lungs were harvested and immuno-histochemistry was performed on frozen sections to assay for levels of TLR4, MyD88, IRAK, CD3, CD4, CD8, CD14 & CD45.Pixel count was used for quantification and 20 microscopic images per antibody were obtained & normalized to DAPI nuclei stain. One way ANOVA testing with Bonferroni Correction using GraphPad software was used for analysis.

RESULTS: TLR4 levels decreased with LPS administration but increased with hyperoxia & in combination resulted in no difference compared to control levels.MyD88 levels were reduced with LPS alone, hyperoxia alone and in combination, compared to control. IRAK levels were increased with LPS exposure, but were unaffected by hyperoxia and in combination, did not differ from control levels.CD4 & CD14 levels were reduced in all study groups. CD45 levels were increased with LPS exposure, but unaffected by hyperoxia and in combination, did not differ from control. LPS reduced levels of CD3 in the lung, and remained low despite hyperoxia.

CONCLUSIONS: Hyperoxia & gram-negative infection are not synergistic in altering lung T-cell populations. Hyperoxia & LPS are associated with immediate alterations in T-cell subsets and may be associated with changes in the TLR4-CD14 signaling pathway. Hyperoxia-induced CD14 reductions are associated with reductions in MyD88 levels, but not with IRAK, suggesting this pathway is not exclusive in regulating CD4 T-cell activation in the lung.

202

Short-Term Hyperoxia Alters Lung Levels of Pro-Inflammatory Cytokines Tumor-Necrosis Factor Alpha (TNF-a) and Interleukins 2 and 8 (IL-2, IL-8) in Newborn Gram-Negative-Infected Sprague-Dawley Rat Pups

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BACKGROUND: Hyperoxia causes oxidant stress with fibrosis culminating in chronic lung disease. In the short term, hyperoxia releases pro-inflammatory cytokines interleukins 1-Beta (IL-1B), Interleukin 6 (IL-6) IL-8 & TNF-a within the lung. IL-8 levels inversely correlate with duration of birth hyperoxia in month-old Sprague-Dawley Rats. Lung levels of TNF-a in month-old animals directly relate to birth hyperoxia. Gram-negative infection also increases inflammation, leading to tissue remodeling & release of TNF-alpha, Interleukin 1 Beta (IL-1B).

OBJECTIVE: To determine the effect of hyperoxia on the short-term levels of inflammatory mediators TNF-a, IL-1B, IL-2, IL-6, IL-8 & IL-10 in the lungs of Sprague Dawley rats after initial gram-negative infection.

DESIGN/METHODS: 4 litters of rat pups were exposed to 10 ug (2mcg/ml) of intranasal lipo-polysaccaride (LPS) or saline at 2 days of post-natal life. 24hrs later, a litter from each group was exposed to 6 hrs of 100% hyperoxia or control. Immediately after hyperoxia, lungs were harvested & immuno-histochemistry was performed on frozen sections to assay for levels of TNF-a, IL-1B, IL-2, IL-6, IL-8 & IL-10. Pixel count was used for quantification & 20 microscopic images per antibody were obtained & normalized to DAPI nuclei stain. One way ANOVA testing with

Bonferroni Correction using GraphPad software was used for analysis.
RESULTS: TNF-a levels were increased with both Hyperoxia & LPS exposure compared to the Room Air, Room Air plus Saline & Hyperoxia plus Saline groups ($p<0.001$). IL-8 levels were increased in the Hyperoxia plus LPS group compared to other study groups ($p<0.001$). Levels of IL-1B & IL-10 were increased in the Hyperoxia plus LPS group compared to the Room Air plus Saline group ($p<0.05$, $p<0.01$). IL-6 levels increased in the Hyperoxia plus Saline group vs. the Room Air plus Saline group ($p<0.05$) & the Hyperoxia plus LPS group vs. the Room Air plus LPS group ($p<0.001$). Levels of IL-2 were increased in the Room Air plus LPS & Hyperoxia plus LPS group compared to their respective controls ($p<0.01$ & $p<0.001$).
CONCLUSIONS: In the LPS-primed newborn rat, birth hyperoxia results in synergistic increases in TNF-a, IL-1B & IL-8 levels. IL-6 increases in the preterm lung are more sensitive to hyperoxia than LPS exposure, while IL-2 & IL-10 levels respond greater to gram-negative infection than hyperoxia.

203

Clinical Characteristics, Demographics and Outcomes of Neonates with Fetomaternal Hemorrhage, 1993-2008

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BACKGROUND: Fetomaternal hemorrhage (FMH) occurs when the placenta fails and fetal blood flows into the maternal circulation. Life-long disability is common in fetuses who survive the severe anemia that can result. Despite the potential severity of this disease, no comprehensive epidemiologic studies of the condition exist.
OBJECTIVE: To determine 1) clinical characteristics, 2) socioeconomic demographics, and 3) common clinical outcomes of neonates with FMH over the past 15 years.
DESIGN/METHODS: We analyzed a multiyear dataset concatenated from the 1993-2008 Nationwide Inpatient Sample, a statistically representative sample of hospital care in the United States. Among peripartum mother and baby hospitalizations, patients diagnosed with FMH were identified via the ICD-9 codes 762.3 (placental transfusion syndromes) and 772.0 (fetal hemorrhage into mother). Twin pregnancies were removed from the analysis to avoid confusion with twin-twin transfusion syndrome. Frequencies, univariate, and multivariable regression analyses were used to identify clinical characteristics and sociodemographics of the patient population with FMH and associated clinical outcome diagnoses of interest. Trends in diagnosis incidence were calculated based on weighted frequencies.
RESULTS: Fetomaternal hemorrhage was identified in 0.02% of non-twin births. Patients with FMH required high intensity of care with 26.3% receiving mechanical ventilation, 22.4% receiving blood product transfusion, and 27.8% undergoing central line placement. On multivariable analysis, preterm delivery (OR 11.97, $p<0.0001$) was the most significant clinical characteristic of neonates with FMH. Important racial and socioeconomic differences were identified. Increasing patient income was associated with increased likelihood of FMH diagnosis (OR 1.19-1.21, p=0.01-0.05), and whites were more likely to be diagnosed than blacks (OR 1.60, $p<0.0001$), Hispanics (OR 1.90, $p<0.0001$), or Asians (OR 1.56, $p=0.004$). The diagnosis was more commonly made at teaching than community hospitals (OR 1.27, $p=0.006$).
CONCLUSIONS: Fetomaternal hemorrhage, as identified in this large, nationally representative dataset, causes significant morbidity and mortality. Further study is needed to distinguish between diagnostic coding bias and true epidemiology of the disease. This is the first report of socioeconomic and racial/ethnic disparities in FMH, which may represent disparities in detection of disease that require national attention.

204

Protein Binding at 5'UTR mRNA in Surfactant Protein A Splice Variants

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BACKGROUND: Surfactant protein A (SP-A) is one of the immune regulatory proteins for the lung. SP-A dysfunction may be related to quantitative or qualitative defects. SP-A 5'UTR mRNA is composed of splice variants of four different exons (A, B, C, and D). Prior studies identified Exon B as an important contributor to SP-A translation and as such Exon B may reflect a site for binding of trans-acting factors that regulate expression.
OBJECTIVE: To identify *trans*-acting factors that bind to Exon B and 5'UTR mRNA of common SP-A splice variants that may impact gene expression.
DESIGN/METHODS: **Constructs of splice variants:** 5'UTR splice variants (ABD, AD', as well as Exon B) were generated by PCR. The constructs were amplified, isolated and purified. **Cell protein preparation:** NCI-H441 cells were grown in culture. Whole cell lysates were extracted using both a hypertonic as well as hypotonic buffer systems. Cytosolic and nuclear fractions were isolated using a commercial kit. The lysates were purified and quantified using the Micro BCA Protein Assay. Purity of cell fractions was determined by Western blot using cytosol specific (mek 1/2)) and nuclear specific (c-Jun) antibodies. **mRNA synthesis:** Capped mRNA was transcribed from DNA templates, purified via phenol:chloroform extraction and quantified using nanodrop. The transcripts were then end labeled using γ-^{32}P. **Protein-RNA binding via electron mobility shift assay (EMSA):** mRNA-protein binding was determined by EMSA run on 6% acrylamide gels. The gels were exposed to x-ray films.
RESULTS: Purity of cell lysates fractions was shown by western blot for cell fraction specific markers. Band shifts were identified for all constructs (ABD, AD', and Exon B). These band shifts were seen in the nuclear fraction of the cell lysates and from lysates derived via hypertonic buffer extraction as opposed to hypotonic lysate buffers.
CONCLUSIONS: Formation of protein-RNA complexes is not specific for Exon B. This may indicate either multiple proteins and/or targets. The protein-RNA complexes are visualized in the nuclear fraction of the cell in this model. Therefore, we hypothesize that protein binding may be involved in functions specific to the nucleus such as stabilization of secondary structure, localization or transport of mRNA from the nucleus to the cytoplasm. Further studies will be conducted to localize and characterize these proteins. Supported by NIH HL-34788.

205

Fellow in Training

Risk Factors for Surgical Necrotizing Enterocolitis in VLBW Infants Admitted to a Tertiary Care Neonatal Unit

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Division of Newborn Medicine, Penn State Children's Hospital, Hershey, PA; Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA.

BACKGROUND: Necrotizing enterocolitis (NEC) is a serious illness in premature babies. Causal factors have been linked including infectious agents, inherent weakness in the neonatal immune system, alterations in mesenteric blood flow and milk feeding. Surgical intervention is required in 27% to 63% of confirmed cases. The risk factors predisposing to surgical intervention have not been well defined.
OBJECTIVE: To determine which risk factors predict the greatest risk of need for surgical intervention in NEC.
DESIGN/METHODS: The primary outcome was need for surgical intervention. All babies with a birth weight of less than 1500 grams admitted to the Penn State Hershey Children's Hospital NICU who developed necrotizing enterocolitis (N=57) between 2005-2009 were included. Risk factors analyzed were birth weight, sex, gestational age, breast milk or formula feeds prior to development of NEC, ventilation and oxygen requirements, presence of a patent ductus arteriosus (PDA), treatment of PDA with indomethacin or surgical ligation, and the use of caffeine and steroids. Demographic variables were analyzed by frequency distributions and chi-square testing. Logistic regression was used to evaluate risk factors. A p-value <0.05 was considered significant.
RESULTS: A total of 457 eligible babies were admitted to the NICU during the study time period. Incidence of NEC was significantly different within inborns (10.6%) vs. outborns (18%) p-value<0.001. Similarly among patients with NEC, need for surgical intervention was also significantly different (inborns 5.4% vs. outborns 18.6%, p-value<0.001). Baseline characteristics of the outcome groups were similar. Presence of a PDA was associated with an increased risk of surgery [OR 10.119 (CI 2.892-35.406, p-value 0.0004)]. Similarly treatment of PDA with indomethacin was associated with an increased risk for surgery [OR 3.9 (CI 1.182-13.113, p-value 0.0256)]. Treatment of PDA with surgical ligation was also associated with an increased risk [OR 6.052 (CI 1.180-31.048, p-value 0.0309, adj. p-value 0.0325)]. When analyzed for early vs. late ligation of PDA, there was no statistical difference seen.
CONCLUSIONS: Risk for surgical treatment in NEC is increased with the co-morbidity of a PDA. This risk remains regardless of medical or surgical intervention. This needs to be evaluated with a larger prospective study to establish a potential causal relationship.

206

Fellow in Training

Overexpression of Extracellular Superoxide Dismutase (EC-SOD) Preserves Macrophage Function in Neonatal Mice Exposed to Hyperoxia

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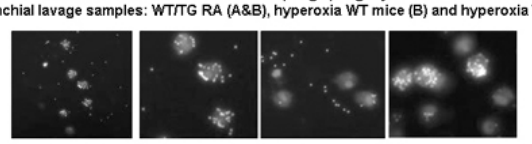
BACKGROUND: Oxidant injury and infection with released cytokines, are major contributors to chronic lung disease in premature infants. Deficient antioxidant systems, especially (EC-SOD), are implicated in this injury. Exposure to reactive oxygen species may result in macrophage damage that reduces their phagocytosis function.
OBJECTIVE: 1. *T*o demonstrate that hyperoxia impairs phagocytosis in alveolar macrophages.
2. To demonstrate that TG mice (with an extra copy of hEC-SOD gene) have preserved macrophage phagocytosis when exposed to hyperoxia as compared to WT mice.
DESIGN/METHODS: TG and WT mice were exposed to hyperoxia (95% oxygen x 7 d) or room air (RA). Macrophages were harvested from bronchoalveolar lavage samples on day 8 and cultured. To assess phagocytosis function macrophages were incubated with labeled latex minibeads and evaluated using an immunofluorescent microscope. To assess killing capacity, macrophages were incubated with *Pseudomonas aeruginosa* and assessed by counting colony forming unit/ml (CFU/ml).
RESULTS: There was marked inhibition of phagocytosis (by immunofluorescence) during hyperoxia in WT mouse cells but not in TG or room air exposed mice.

Figure: Immunofluorescence studies of macrophage phagocytosis function from neonatal mouse bronchial lavage samples: WT/TG RA (A&B), hyperoxia WT mice (B) and hyperoxia TG (C)



(A) RA WT group (B) RA TG group (C) WT hyperoxia group (D) TG hyperoxia group

There was significantly greater PA killing by phagocytes from TG-hyperoxia vs WT-hyperoxia groups, $14.4 \pm 3.3 \times 10^4$ vs $5.1 \pm 1.1 \times 10^4$ CFU/ml, ($P<0.05$).
CONCLUSIONS: Overexpression of EC-SOD preserves phagocytosis function of alveolar macrophages in neonatal mice after exposure to hyperoxia.

207

House Officer

Morbidity and NICU Admissions among Early Term (37-38 wk) and Term (39-41 wk) Neonates in Erie County (NY)

Shaon Sengupta, Alyssa Herrmann, Priya Singhal, James Shelton, Vivien Carrion, Ralph Wynn, Rita M. Ryan, Kamal Singhal, Satyan Lakshminrusimha.

University at Buffalo, Buffalo, NY; Sisters of Charity Hospital, Buffalo, NY; Department of Gynecology-Obstetrics, State University at Buffalo, Buffalo, NY.

BACKGROUND: Full term neonates are perceived as a homogenous, low risk population. The difference in morbidity by gestational age (GA) among term neonates is not known.

OBJECTIVE: We hypothesize that amongst full term neonates, early term neonates (37-38 6/7wk GA) would have significantly increased rates of NICU admission and morbidity compared to term neonates (39-41 6/7wk).

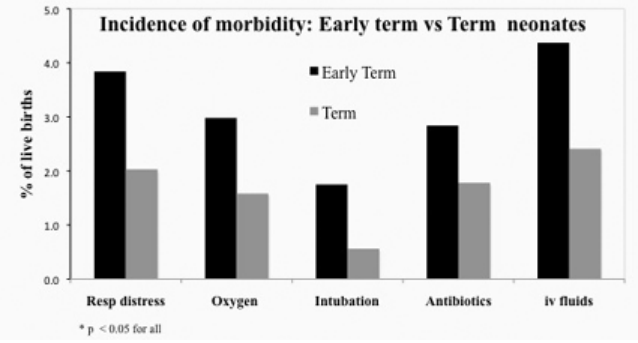
DESIGN/METHODS: We obtained data from the birth registry regarding all live births and NICU admissions among fullterm neonates born in Erie County (NY) between Jan 1, 2006 & Dec 31, 2008. The medical records of all early term and term neonates admitted to NICUs within the county in 2007 were reviewed to determine the incidence of respiratory morbidity, antibiotic use, and need for IV fluids.

RESULTS: Of the 33,488 live births in Erie County over the 3 year period, 27 % were early term births.

NICU Admission in Erie County (2006-2008)

	EarlyTerm (37-38 6/7 wks)		Term (39-41 6/7 wks)		
Year	Total births	NICU admissions *	Total births	NICU admissions *	OR (CI)
2006	3035	302 (9.95%)	6971	368 (5.28%)	1.98 (2.14-1.82)
2007	3072	314 (10.22%)	7019	413 (5.88%)	1.30 (1.14-1.47)
2008	2829	281 (9.93%)	6710	436 (6.49%)	1.51 (1.35-1.67)
Total	8936	897 (10%)	20700	1217 (5.9%)	1.75 (1.66-1.84)

More than 10% of early term neonates were admitted to the NICU. In 2007, the incidence of NICU admission, respiratory morbidity, need for respiratory support and/or intubation, IV fluids as well as requirement for antibiotics was significantly higher in the early term babies compared with term births.



CONCLUSIONS: We conclude that the early term neonates are at significantly increased risk for morbidity in the immediate neonatal period. Even a modest increase in the morbidity in the early term group adds a significant health burden because of the large number of births at this GA.

208

Increased Methemoglobin (MHb) Levels Predict Response to Inhaled Nitric Oxide (iNO) in Persistent Pulmonary Hypertension of the Newborn (PPHN)

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Pediatrics, University of Rochester Medical Center, Rochester, NY; Pediatrics, Women & Children's Hospital at Buffalo, Buffalo, NY.

BACKGROUND: About 1/3 of infants with PPHN do not respond to inhaled iNO. Response to iNO depends on successful delivery to pulmonary vessels. Since methemoglobin (MHb) is formed when iNO reacts with hemoglobin in red blood cells of pulmonary vessels, increases in MHb may indicate iNO delivery and predict response. A retrospective analysis showed a higher MHb/NO exposure ratio among infants who respond to iNO compared to non-responders.

OBJECTIVE: To determine whether infants with PPHN who respond to iNO (increase in PaO_2/F_{iO2} ratio ≥20 mmHg) have a greater increase in MHb after starting iNO, as compared with non-responders (<20 mmHg increase).

DESIGN/METHODS: In this two-center, prospective study, data (including ventilator support and arterial blood gases in the first 8h after starting iNO) were collected on 18 infants with PPHN requiring iNO at ≤1 wk of age. PaO_2/F_{iO2} and oxygenation indices (OI) were calculated. MHb levels were analyzed before and after starting iNO. Data were analyzed by Fisher's exact or t test.

RESULTS: Of 18 infants, 12 were responders and 6 were non-responders to iNO (Table). In contrast to non-responders, responders showed significant improvements in their mean PaO_2/F_{iO2} and OI. Improved oxygenation was associated with a significant increase in the mean MHb level.

Characteristics of Infants (mean ± SD)

	Responders (n=12)	Non-responders (n=6)
GA (wk)	37.3±4.6	39.0±1.5
BW (g)	2809±1383	2804±437
Diagnosis	Pneumonia (4), Respiratory distress syndrome (2), Asphyxia (2), CDH (1), MAS (1), Trisomy 21 (1), Metabolic disorder (1)	MAS (2), CDH (3), Cardiomyopathy (1)
iNO initiation (hrs of age)	58±56	56±58
Respiratory status before iNO		
PaO_2/F_{iO2} (mmHg)	76±41	125±98
OI	24±17	19±13
Respiratory status & outcome after iNO		
Change in PaO_2/F_{iO2} (mmHg)	+71±65	-20±25*
Change in OI	-9±11	+4±7†
Change in MHb	+0.19±0.19	-0.03±0.12†
ECMO (# infants)	1	0
Death (# infants)	0	2

*p<0.01 vs responders, †p=0.02 vs responders, CDH=congenital diaphragmatic hernia, MAS=meconium aspiration syndrome

CONCLUSIONS: Improved oxygenation with iNO is associated with increased MHb levels. Successful iNO delivery to pulmonary vessels may be an important determinant of response. We speculate that optimal alveolar recruitment before starting iNO may be critical in PPHN associated with lung disease.

209

Medical Student

The Role of Manganese Superoxide Dismutase in the Pathogenesis of Neonatal Lung Disease and Other Newborn Ailments

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Pediatrics, New York Medical College, Valhalla, NY; Division of Newborn Medicine, Maria Fareri Children's Hospital at Westchester Med Center, Valhalla, NY.

BACKGROUND: The development of neonatal lung disease is a multi-factorial clinical condition that involves inflammation, mechanical trauma, genetic factors and oxidative stress. We examined how a specific antioxidant enzyme, MnSOD, affects both the development and severity of BPD. MnSOD is encoded by genomic DNA but functions in the mitochondria, where it converts superoxide anion to hydrogen peroxide. We investigated 2 SNPs in the MnSOD gene. The first SNP is rs4880, which is believed to affect how the enzyme is transported into the mitochondria. The second, rs2758330, is an intronic SNP, whose function is unknown.

OBJECTIVE: We hypothesize that certain genotypes for MnSOD SNPs affect the development and severity of BPD in neonates.

DESIGN/METHODS: DNA was isolated from buccal mucosal swabs (N=193). Infants were enrolled who weighed <1 kg at birth and had no congenital or chromosomal abnormalities. Real-time PCR discriminated alleles for the rs4880 SNP. BPD severity was classified by the the criteria of Jobe and Bancalari.

RESULTS: The rs4880 SNP shows association with both the presence and severity of BPD, especially in Caucasian subjects. Caucasian subjects with at least one C-allele were more likely to have BPD (P=0.018), and if they do have BPD then it was more severe (P=0.001). Caucasian subjects with the CC genotype were also more likely to have chorioamnionitis (P=0.006). There were no similar correlations for nonwhite subjects. The presence and severity of BPD of SNP rs4880 approached significance (P=0.055), when comparing the presence of any C allele to TT . Subjects with the CC/CT genotype tended to have more severe BPD (P=0.066). Subjects with the CC genotype required surfactant treatment more (P=0.05), while those with CC/CT genotypes received significantly more surfactant doses (P=0.038).

CONCLUSIONS: The rs4880 SNP for MnSOD is associated with the presence and severity of BPD in ELBW white infants. Our data is significant for the wild-type allele, not the mutant allele. The latter allele (T) has been found to decrease the transport of MnSOD into mitochondria. We are not the first group to find such contradictory findings. We speculate that the wild-type allele (C) results in increased oxidative stress via a yet unknown mechanism. We argue that the racial difference in sensitivity to rs4880 is likely due to other SNPs, that are either punitive or protective.

210

Fellow in Training

Omegaven™ (O) a Novel Omega-3 Fatty Acid Emulsion Reverses Parenteral Nutrition Associated Cholestasis (PNAC) in Infants Requiring Prolonged PN without Side Effects

Michael M. Espiritu, Jeffrey M. Perlman.

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BACKGROUND: PNAC (Direct Bilirubin (DB) > 2mg/dl) is an important clinical problem with a reported incidence of between 40 – 60%. Risk factors include ¯ GA and BW, delay in feedings and duration of PN. Persistent PNAC is associated with bile duct proliferation and liver fibrosis at autopsy. Components of currently formulated soy based IL are considered important in the genesis of PNAC. The use of an alternative fish oil based lipid emulsion consisting of primarily omega-3 fatty acids O™, has been shown experimentally not to induce hepatic injury and avoid essential fatty acid deficiency.

OBJECTIVE: We evaluated O™ (Frasenius Kabi) in a Phase 1 study (IND # 102802) in infants with PNAC who had failed strategies to limit liver dysfunction including trophic feedings (TF), cycling PN, and limiting lipids based on triglyceride levels to determine whether PNAC can be reversed (DB <2mg/dl) as well as improvement in liver synthetic and secretory function and without side effects i.e. bleeding.

DESIGN/METHODS: From 10/2007 to 8/2010, 5 neonates with PNAC secondary to prolonged PN and inability to establish feedings were enrolled and administered O™ at 1mg/kg/day. DB, liver enzymes and coagulation levels were obtained frequently.
RESULTS: The diagnoses were NEC (n=4), gastroschisis (n=1). O™ was started on DOL 72±32 (range 40-126d) and has been continued for > yr (n=2), 6m (n=1), 48 d (n=1),36 d (n=1). The PNAC resolved slowly >6 week after initiation with normalization of DB and liver enzymes in all cases despite the continued requirement for PN (see table). No side effects attributed to Omegaven were identified.

Patient	Gestational Age (w)	Birthweight (g)	Time on Lipid Emulsion Prior to Omegaven (d)	Peak Direct Bilirubin (mg/dL)	Direct Bilirubin at Start of Omegaven (mg/dL)	Time to Direct Bilirubin <2.0mg/dL (d)
1	32	1160	125	9.8	6.9	90
2	35	2860	52	5.6	5.6	43
3	28	635	64	11.7	7.0	119
4	28	560	71	3.9	3.8	19
5	29	988	24	6.7	5.5	60

CONCLUSIONS: In this single center Phase I clinical trial, O™ was successful in slowly reversing PNAC as reflected by normalization of DB levels and hepatic enzymes in all 5 patients treated. Given the anti-inflammatory properties of O™ these preliminary findings suggest the value of a randomized study comparing it to soy based IL.

211

Medical Student

Lipopolysaccaride and Hyperoxia Effects on Alveolar Development and Surfactant Protein B in Newborn Rats

Fiona Yuen, Liji B. Chacko, Shetal Shah, Avinash Chander.
Neonatology, Stony Brook University School of Medicine, Stony Brook, NY.

BACKGROUND: Hyperoxia and bacterial infection are serious concerns in the NICU, as associated lung injury can have persistent long-term effects on lung development. Newborns with bacterial sepsis and respiratory distress would require oxygen therapy, but can suffer from resulting oxidant injury and infection related lung inflammation and elevated cytokines. Although effects of hyperoxia or bacterial infection have been extensively reported, limited studies have reported their combined effects in the newborn lung.
OBJECTIVE: Since lungs continue to develop and differentiate in the early post-natal life, we aimed to determine if supplemental oxygen in the newborns with bacterial infection would exacerbate the lung injury and be reflected in alveolar differentiation.
DESIGN/METHODS: Newborn rats at 2 days of post-natal life (PN2) received intra-nasal saline or 10mg/5ml lipopolysaccharide (LPS), the principal virulence factor in gram negative bacteria. Twenty four hours later, some animals were treated for 6hours with100% O_2, while others remained in room air. At the end of the exposure, all rats were sacrificed and the lungs harvested. Immuno-staining for ABCA3 (exclusive to type II cells) and eNaC (predominantly in type I cells) were performed to evaluate alveolar development. A total of 11-20 fields were evaluated for eNaC and ABCA3. Westerns blots were performed for lung surfactant protein B (SP-B) and for myeloperoxidase (MPO), a marker for neutrophils.
RESULTS: LPS with or without hyperoxia caused modest increase in MPO levels in the lung. Objects staining for ABCA3 were normalized to the number of nuclei. The ABCA3 positive objects were 38% in the Controls (saline with room air), 43% in the LPS with room air, 30% in the hyperoxia group and 42% in the LPS plus hyperoxia group. In comparison to controls, hyerpoxia increased the levels of mature SP-B, but not of proSP-B. Hypeoxia exposure in LPS-treated animals, however, caused an increase in proSP-B, but not in the mature SP-B. Thus, the LPS effect on type II cell number did not alter with superimposition of hyperoxia. Similarly, hyperoxia did not affect the LPS-mediated decrease in type I cells as determined by eNaC staining.
CONCLUSIONS: Both hyperoxia and LPS, alone or together, do not acutely affect the cellular composition of alveolar epithelium. However, these insults, alone or in combination, cause acute changes in post-translational processing of surfactant proteins.

212

House Officer

Selective Fluconazole Prophylaxis for Very Low Birth Weight (VLBW) Infants Colonized with Candida

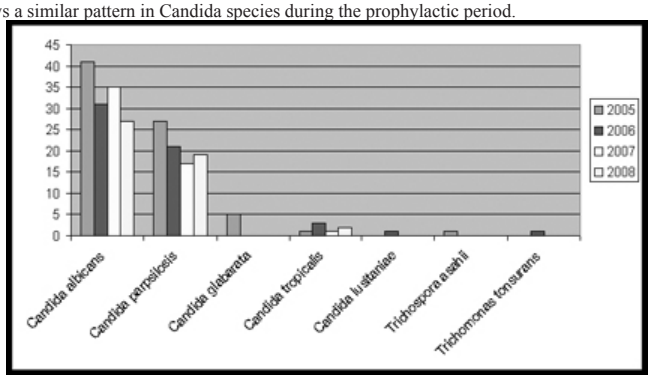
M. Roger Kim, Praveen Chandrasekharan, Munmun Rawat, Dominique Jean-Baptiste, Myron Sokal.
Pediarics, Brookdale University Hospital and Medical Center, Brooklyn, NY.

BACKGROUND: The effectiveness of Fluconazole prophylaxis in very low birth weight (VLBW) infants has studied including our study in 2004-2006. We report the updated analysis of the study.
OBJECTIVE: To reduce the morbidity and mortality of VLBW infants by Fluconazole prophylaxis.
DESIGN/METHODS: During 07/2004 to 12/2008 surveillance/cultures were performed for fungal colonization in all infants weighing less than 1500g at birth and weekly thereafter. Prophylactic fluconazole was instituted at a dose of 3mg/kg every 48 hrs in colonized infants for 6 weeks or when weight reached 1500g. Fungal blood cultures were taken if the infant showed signs of sepsis. Deaths in L&D or less than 4 days of life were excluded. We compared a pre-fluconazole period (1/02-5/04) with the intervention period (07/04-12/08)of fluconazole prophylaxis given to the VLBW infants colonized with Candida.
RESULTS: During the intervention period the incidence of invasive Candidiasis significantly decreased from 12.9% to 5.8% (p=0.035).

Outcome	Pre-Fluconazole(%)	Fluconazole(%)	p value
No	132	241	
Candida sepsis	17(12.9)	14(5.8)	0.035*
C. albicans	10(7.5)	8(3.3)	0.13
C. parapsilosis	4(3)	6(2.4)	0.73
Other species	3(2.2)	0(0.0)	0.045*
NEC	3(2.2)	3(1.2)	0.67
CLD	32(24.2)	48(19.9)	1.00
LOS	61.3±33.6	65.3±63.4	1.00
Mortality	14(10.6)	42(17.4)	0.134

* significant p value

No adverse effects of Fluconazole therapy were noted. Surveillance data for Candida colonization shows a similar pattern in Candida species during the prophylactic period.



CONCLUSIONS: An intense fungal surveillance with Fluconazole prophylaxis has reduced the risk of candida sepsis in VLBW infants. Multicenter randomized trial for further defining criteria for prophylaxis is needed.

213

House Officer

SNIPPV vs. NIPPV: Does Synchronization Matter?

Vikramaditya Dumpa, Karol Katz, Veronika Northrup, Vineet Bhandari.
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BACKGROUND: Use of nasal intermittent positive pressure ventilation (NIPPV) in the neonatal intensive care unit (NICU) has shown promise with better clinical outcomes in premature neonates. It is not known if synchronization makes a significant clinical impact when using this technique.
OBJECTIVE: To compare outcomes of premature infants on synchronized NIPPV (SNIPPV) vs. NIPPV in the NICU.
DESIGN/METHODS: Retrospective data were obtained (1/04 to 12/09) of infants who received NIPPV anytime in the NICU. SNIPPV (Infant Star with StarSync) was utilized from 2004-06, while NIPPV (Bear Cub) was used from 2007-09. BPD was defined using the NIH consensus definition. Unadjusted associations between potential risk factors and BPD/death were assessed using the chi-square or Wilcoxon Sum Rank test. Adjusted analyses were performed using generalized linear mixed models, taking into account correlation among infants of multiple gestation.
RESULTS: There was no significant difference in the mean gestational age and birth weight in the 2 groups: SNIPPV (n=172; 27.0w; 1016g), NIPPV (n=238; 27.7w; 1117g). There were no significant differences in maternal demographics, histologic chorioamnionitis, use of antenatal steroids, gender, multiple births, SGA, or Apgar scores in the 2 groups.
More infants in the NIPPV group required resuscitation in the delivery room (SNIPPV vs. NIPPV: 44.2% vs. 63%, p<0.001). Surfactant use (84.4% vs. 70.2%; p<0.001) was significantly higher in the SNIPPV group. There were no differences in the rate of PDA, IVH, PVL, ROP, and NEC in the 2 groups. However, BPD/death, based on the unadjusted analyses, was significantly increased in the SNIPPV group (63.4% vs. 51.6%, p<0.02). After adjusting for the significant variables, use of SNIPPV vs. NIPPV (OR 0.71; 95%CI: 0.40, 1.24) was not associated with BPD/death.
CONCLUSIONS: These data suggest that use of SNIPPV vs. NIPPV does not significantly impact on clinical outcomes.

General Pediatrics II
Platform Session

Sunday, March 27, 2011
9:45 AM-12:00 PM

214

9:45 AM

Medical Student

Construction of a Flavonol and Lignan Database for Assessing Phytoestrogen Intake in an Inner City Minority Cohort of Girls

Eliza W. Gardiner, Nancy Mervish, Susan L. Teitelbaum, Maida P. Galvez, Kathleen McGovern, Mary S. Wolff.
Department of Preventive Medicine, Mount Sinai School of Medicine, New York, NY; Department of Pediatrics, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Phytoestrogens are dietary micronutrients with known hormonal properties and research suggests that they may be associated with later onset of puberty. Dietary data and phytoestrogen content are needed in order to investigate this relationship. However, a database that contained quercetin, total flavonol, and lignan content of all foods in the NDSR (Nutrition Data

System for Research) 24-hour dietary recall did not exist.
OBJECTIVE: To construct a micronutrient database of quercetin, total flavonol, and lignan content in foods reported in 24-hour dietary recalls, and to use the database to evaluate phytoestrogen intake in a study assessing pubertal timing in African American and Latina girls recruited in East Harlem, New York.
DESIGN/METHODS: For each food (N=2319) quercetin, flavonol, and lignan values were obtained using the 2007 USDA Database for the Flavonoid Content of Selected Foods as well as literature reported lignan values. Trained dietitians conducted 24-hour dietary recalls by telephone to obtain type and quantity of all foods consumed by each girl. Multiple dietary recalls (n=2-4) were conducted to account for daily and seasonal variation in food consumed. Phytoestrogen intake for each dietary recall was calculated for each reported food by multiplying quantity consumed (grams) and phytoestrogen content (mg/gram). Each participant's daily phytoestrogen intake was calculated by summing all foods within a single dietary recall. All recalls were averaged for a girl's average daily phytoestrogen intake.
RESULTS: Participants (n=367, average age 7.34±0.88, average energy intake 1469±412 kcal/day, 40% with BMI>85th%ile, 23% breast stage 2+) had average quercetin, total flavonol, and lignan values of 4.03±2.31 mg/day, 5.01±3.17 mg/day, and 0.107±0.064 respectively. Phytoestrogen intake did not differ by race, BMI, caregiver education, or breast stage.
CONCLUSIONS: To our knowledge, this is among the first reports using 24-hour dietary recalls to describe intake of phytoestrogens, specifically, quercetin, flavonol, and lignans, in girls ages 6-8 years. This database establishes an important consolidation of phytoestrogen levels and diet data which will allow for future analysis of phytoestrogen consumption and pubertal development in this at risk population.

215

10:00 AM

Fellow in Training

Efficacy of Primary Care Clinics Offering Increased Influenza Vaccine Delivery

Daniel M. Fein, Andrew D. Racine.
Pediatric Emergency Medicine, Children's Hospital at Montefiore, Bronx, NY; General Pediatrics, Children's Hospital at Montefiore, Bronx, NY.

BACKGROUND: Despite recommendations from the CDC and the AAP in 2008 that all pediatric patients older than 6 months of age receive the annual influenza vaccine (IV), average IV coverage among children in 2009-2010 was just over 26%. Testing innovative methods of IV delivery therefore merits the attention of the research community.
OBJECTIVE: To test whether a public health model of IV delivery including after hour and weekend vaccine panels would increase the number of patients vaccinated by busy urban pediatric practices during the influenza season and affect the morbidity of the practices' patients as measured by emergency department (ED) visits and hospitalizations for respiratory illness.
DESIGN/METHODS: We performed a before and after difference-in-difference cross sectional comparison of four outpatient pediatric practices affiliated with a single large urban academic quaternary care center over two influenza seasons: 2008-2009 and 2009-2010. All four sites delivered IV in a routine fashion for the 2008-2009 season. Two sites employed the public health model in the 2009-10 season while no change was made to IV administration practices at the other two sites. Data were obtained by querying a replicate data warehouse that captures information throughout the medical center where the 4 sites are located. ANOVA was used to compare means and logistical regression was used to estimate the independent impact of the public health approach.
RESULTS: From 2008-2009 to 2009-2010 the mean number of patients immunized with IV at intervention sites increased by 31% (4158 to 5431, $p<0.001$) and by 1% at non-intervention sites (1961 to 1983, $p=0.9$). This difference between intervention and control sites was statistically significant ($p=0.002$). Small increases in the number of ED visits that did not reach statistical significance were found for both groups year over year. The number of admissions increased 40% for the intervention group ($p=0.04$) and 38% for the non-intervention group ($p<0.001$), a between group difference that was not significant.
CONCLUSIONS: Conversion to a public health model of IV delivery can successfully increase the number of people vaccinated against influenza by busy pediatric practices. Larger studies are needed to evaluate the downstream clinical effects of the public health model including influenza-specific outcomes, days missed from school/work, duration of respiratory illness, and length of hospital admissions.

216

10:15 AM

Family Centered Rounds in Theory and Practice: An Ethnographic Case Study

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BACKGROUND: Family centered rounds (FCRs) are a means to incorporate family centered care in inpatient settings. Guidelines have been established to guide FCR practice; these include advocating for rounds at the bedside, avoiding jargon, recognizing the bedside as the patients/family's personal space, introducing team members, and engaging patients/families by inviting them to participate in the discussion.
OBJECTIVE: To assess how FCRs in practice embody the theory of family centered care.
DESIGN/METHODS: We conducted an ethnographic study on a general pediatric teaching ward that has routinely conducted FCRs for the last three years. Over nine months, we observed the medical team interact with family members/patients, recorded field notes, and collected patient demographics. Data in the form of field notes were coded iteratively. Codes were revised with incorporation of new data and reconciled with two investigators (PH, DB) through consensus.
RESULTS: Structure: Of the 185 total rounding events, 145(78%) took place in the patient room, with 127(88%) including a family member. Of the total rounding events, 40(22%) took place in the hallway, with 5(3%) including a family member and 35(19%) without a family member. Use of medical jargon with limited translation into lay language and awkward team positioning around family given space limitations were commonly observed. Engagement: Verbal solicitation for patient/family participation was routinely made. Introductions were mostly unidirectional; i.e. teams introduced themselves by name while family members were called "mom" or "dad". Some families actively engaged in rounds; they incorporated rounds in their daily schedule, prepared notes on relevant issues, and participated in making key decisions. These families tended to have children with chronic disease or previous admissions. Conversely, families who were new to the inpatient setting seemed ill-prepared and often asked questions that were tangential to what the medical team discussed.
CONCLUSIONS: Even in a relatively mature FCR program, we surmise that following FCR guidelines may be insufficient to fulfill the theoretical goals of family centered care. Minimizing barriers to structure and preparing families to engage in FCRs may serve to align family centered rounds theory and practice. Further in-depth perspectives from families who participate in FCRs will inform what next steps should be taken to prevent this misalignment.

217

10:30 AM

Limited Impact of Reducing Length of Stay on Daily Peak Census at a Children's Hospital

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BACKGROUND: To address high occupancy and patient flow challenges hospitals often focus on earlier discharge--reduction in length of stay (LOS)--to increase functional capacity. For children's hospitals, where typical LOS is short, this strategy may be of limited value.
OBJECTIVE: Describe how reducing LOS would impact hospital daily peak census for one large, urban, tertiary-care children's hospital.
DESIGN/METHODS: Retrospective administrative-data study with admission-discharge-transfer (ADT) data for inpatient admissions for July 1, 2007 to June 30, 2008. Data included date/time of all arrivals and departures from inpatient units, as entered by unit clerks into electronic ADT system. Peak daily census was extracted for each day using a SAS macro. Using timestamps, LOS was calculated; theoretical LOS values were created by reducing it by absolute hours and relative % amounts. For hypothetical reductions, limits were placed, so that patients could not be discharged after 11 PM or before 7 AM. The macro was run again using hypothetical discharge times to generate daily peak census figures.
RESULTS: 22,310 patients were admitted with median LOS of 2.3 days. Mean daily peak census was 375 and reductions of 8 hours in LOS resulted in a mean decrease of census by 4 patients (1.1%) and maximum reduction of 10 patients (2.2%) (Table 1).

		Reducing LOS by hours*			Reducing LOS by %**		
	Base	1 hr	2 hr	8 hr	5%	10%	15%
Mean daily peak census	375	373	371	371	364	352	337
Median daily peak census	378	377	375	376	368	354	339
Min daily peak census	279	279	279	278	270	260	253
80%ile daily peak	409	406	406	406	399	385	370
Max daily peak census	452	447	445	442	435	422	406
% mean reduction daily peak	-	0.7%	1.2%	1.1%	2.9%	6.2%	10.2%
% median reduction daily peak	-	0.4%	0.9%	0.7%	2.8%	6.3%	10.3%
% min reduction daily peak	-	0.0%	0.0%	0.4%	3.2%	6.8%	9.3%
% max reduction daily peak	-	1.1%	1.5%	2.2%	3.8%	6.6%	10.2%
Difference in mean daily peak census	-	3	4	4	11	23	38
Diff in median census	-	2	4	3	11	24	39
Diff in min census	-	0	0	1	9	19	26
Diff in 80%ile census	-	3	3	3	10	24	39
Diff in max census	-	5	7	10	17	30	46

* Hypothetical discharge time could not be before 7AM or after 11PM for both hour and % reductions. Thus, an 8-hour reduction from an 11 AM discharge was set at 7AM, not the mathematical result of 3AM.
** % reduction in LOS apply to all patients, so that a 10% reduction on a 48-hour stay is 4.8 hours and on a 10-day stay, is 24 hours.

CONCLUSIONS: Realistic earlier discharge times have a minimal impact on census, particularly at time of day when beds would be most in need: daily peak. While % reductions in LOS have a larger impact, those findings must be interpreted with caution, as reductions of that size may not be realistic. While optimizing discharge is an important part of patient flow, its limitations should be recognized and it may raise risk for other negative outcomes. Steps to improve LOS, such as 7-day service availability, evening and early morning (or pre-round) discharges when appropriate, may improve patient flow and provide some additional bed capacity, but other strategies may be required to substantially increase functional capacity.

218

10:45 AM

Implementation and Outcome Analysis of an Institutional Pediatric Acute Hematogenous Osteomyelitis (AHO) Diagnosis and Management Pathway

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BACKGROUND: In the pediatric population, osteomyelitis frequently occurs by hematogenous spread of bacteria. Prior to 2008, at Children's National Medical Center (CNMC), there was not a uniform approach to the diagnosis and treatment of patients with suspected acute hematogenous osteomyelitis (AHO). On April 1, 2008, a multi-disciplinary clinical pathway was implemented to create a consistent approach for managing AHO.
OBJECTIVE: 1. To evaluate AHO pathway implementation by comparing pre and post-implementation cohorts, specifically blood culture and MRI utilization, and time to obtain MRI. 2. To compare clinical outcomes, specifically length of hospital stay (LOS) and rate of pathogen identification, between the pre and post-implementation cohorts.
DESIGN/METHODS: Retrospective cohort study reviewing patient charts with principal discharge diagnosis of osteomyelitis from pre-pathway (January 1, 2005 to March 31, 2008) and post-pathway implementation (April 1, 2008 to October 31, 2010) periods. Original medical records were reviewed. Patients were excluded if there was underlying immunodeficiency, fracture, implanted hardware, or chronic ulcer at the site of osteomyelitis.

RESULTS: 46 charts were reviewed, 22 patients in the pre- implementation cohort and 24 patients in post-implementation cohort. Demographic factors between the two cohorts were similar, including age (7 yrs vs 7.25 yrs) and sex (64% male vs 58% male) as well as disease severity level (2.1 vs 2.1). In the post-implementation cohort, 96% of patients had blood cultures and 96% had a MRI study for diagnosis, compared to 77% and 73%, respectively, in the pre-implementation cohort. A clinically significant decrease in time to obtain MRI was noted from 48 hrs in the pre-implementation cohort to 20 hrs in the post-implementation cohort. However, mean length of stay was 6.5 days in both cohorts. Pathogen identification was not improved in the post-implementation cohort (58% post-implementation versus 73% pre-implementation).
CONCLUSIONS: Implementation of a AHO pathway at our institution has been successful, with an increased rate of blood cultures and MRI for diagnosis, and a decreased time to obtaining MRI. However, improved clinical outcomes such as shortened LOS and increased pathogen identification were not demonstrable in this small study. A larger study is needed to fully evaluate the impact of pathway implementation.

219

11:00 AM

Communication between Families and Physicians: A Comparison Study of Family Centered Rounds

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BACKGROUND: Family centered rounds (FCRs) are increasingly becoming the predominant way rounds are conducted in pediatric hospitals. Although most studies show family satisfaction, there are no outcome measures showing effectiveness.
OBJECTIVE: To compare family knowledge of discharge plans between teams that conduct FCR and teams that do not conduct FCR.
DESIGN/METHODS: Families of patients on pediatric medicine services, including FCR patients whose attendings conduct FCR and non-FCR patients whose attendings do not conduct FCR, at an urban academic medical center were approached to complete a survey assessing knowledge of discharge plans. A research assistant blinded to patient type approached families identified as being within 24 hours of discharge to complete a self-administered written survey in English/Spanish. Family knowledge of discharge date, discharge medications and discharge criteria were compared to the medical chart. Demographic differences between groups were compared using chi-square and t-test; multivariable regression was used to assess for differences in survey responses between groups.
RESULTS: Of the families approached, 75% (n=167) completed the survey, with 118 FCR patients and 49 non-FCR patients. There were no significant differences between FCR and non-FCR families in language, respondent (mother/other), gender and insurance. Patients in the FCR group had a shorter length of stay, were younger aged and were more likely to be White-Hispanic and Black compared to the non-FCR group. Controlling for patient age, length of stay and race/ethnicity, significantly more FCR families reported being knowledgeable about discharge criteria compared to non-FCR families (AOR 2.14; 95% CI 1.11,4.14). There was no significant difference between FCR families' and non-FCR families' answers to when they were being discharged. Controlling for patient age, length of stay, race and number of discharge medications, there was no difference between FCR and non-FCR groups on whether families knew which medications they were being discharged on.
CONCLUSIONS: Patients' families on pediatric teams that routinely conduct FCRs are more likely to know what discharge criteria are for their children compared to those on teams that do not routinely conduct FCRs. FCRs may improve communication between the medical team and families and hasten timely discharge.

220

11:15 AM

Fellow in Training

Practice Differences of Hospitalists vs Non-Hospitalists in Bronchiolitis: A Multi-Center Study

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BACKGROUND: Hospitalists are a new subgroup of pediatric providers. However, data comparing quality of care from hospitalists and non-hospitalists are limited to surveys and self-reports. Bronchiolitis, the most common cause of hospital admission in children, is a logical condition for evaluating quality of inpatient care.
OBJECTIVE: To assess differences in clinical outcomes and management of children with bronchiolitis admitted to hospitalist and non-hospitalist pediatricians based on the 2006 AAP guidelines for diagnosis and management.
DESIGN/METHODS: Chart review of children admitted to two academic centers in 2007-2008. Reviewers selected charts by primary or secondary discharge diagnosis of bronchiolitis and gathered data on evaluation, treatment, length of stay (LOS), readmission, and adverse outcomes. LOS was analyzed by Wilcoxon rank sum and categorical variables by chi-square analysis.
RESULTS: 708 charts met inclusion criteria. Factors differing between study sites included LOS (2.48 days Site 1 vs 3.83 days Site 2, p=0.0002), and readmission rates (7.3% vs 3.4%, p=0.031). Demographic data were similar. Hospitalists used significantly less corticosteroid therapy and antibiotic therapy when no indication existed compared to non-hospitalists (Table 1). For children without history of reactive airway disease or asthma and who did not respond to therapy, hospitalists and non-hospitalists discontinued albuterol and racemic epinephrine similarly.

Management, outcome measures of hospitalist, non-hospitalist care

	Hospitalist	Non-Hospitalist	p-value
LOS (days, n=708)	2.71	2.75	0.78
Readmission w/in 4 weeks (n=708)	4.7%	6.9%	0.2
Corticosteroid cont (n=102)	25.6%	57.6%	0.001
Antibiotics cont, no bacterial infection (n=139)	29.4%	50.7%	0.011
Albuterol cont in non-responders (n=157)	16.1%	19.7%	0.55
Epinephrine cont in non-responders (n=49)	7.1%	6.3%	0.91

CONCLUSIONS: Hospitalist management of bronchiolitis does not affect length of stay or readmission rates. Physicians routinely discontinue unneeded racemic epinephrine but insufficiently stop albuterol when proven ineffective. Hospitalists stop systemic corticosteroid therapy and antibiotic therapy when no indication exists more frequently than non-hospitalists. These data suggest hospitalists better adhere to bronchiolitis guidelines and so provide higher quality of care.

221

11:30 AM

Repeat Lab Testing from the Emergency Department: How Often and How Important?

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BACKGROUND: At a population level, repeat lab testing is known to be frequent and expensive, but little is published on repeat lab testing for children admitted to children's hospitals from the emergency department (ED). There are perceptions among different clinical staff that repeat testing for certain studies happens at a high rate, that repeat studies are necessary to rule-out unexpected abnormalities, and that repeating studies delays the flow of patients out of the ED.
OBJECTIVE: Describe the pattern of repeat laboratory testing from the ED at one large, urban tertiary care hospital for commonly-ordered laboratory tests.
DESIGN/METHODS: Data were drawn from the hospital laboratory information system (Meditech) over date ranges 2002-10. The system was queried for complete blood counts (CBCs) (7 years of data), basic metabolic panels (BMPs) (2.5 years of data), and coagulation studies (coags) (7 years of data) ordered in the ED and then ordered again in the ED within 8 hours. Duration from first to second study and the results of each were generated.
RESULTS: Over 7 years, 37,035 CBCs were ordered in the ED and 674 (1.8%) were repeated in the ED. Over 7 years, 3,903 coags were ordered and 92 (2.36%) were repeated in the ED. Over 2.5 years, 11,414 BMPs were ordered and 432 (3.8%) were repeated in the ED. Mean time to repeat testing was 1.8 hours across all tests (90% in 3.5 hours). Only 12% of samples with platelets <100 had a result <100 on repeat. For coags, 23% of repeats were for missing values and 32% for high PT values; of these, 11.5% continued to be high on repeat. For CBCs, 26% of repeats were for a missing value on the initial draw and 38% for a platelet count <100, 11% for hemoglobin <9, and 15% for WBC <4.5 or >20. On repeat, 9% of platelet counts were still <100, 72% of Hb <9, and 25% of WBC counts were outside the 4.5-20 range.
CONCLUSIONS: Despite the perception of clinical staff on the frequency and utility of repeat lab testing, this happens relatively infrequently. Most tests, when repeated with 4 hours, due to an apparently unexpected initial result were normal on repeat. Further analysis of findings such as these may reduce the need for waiting for repeat test results that delay transfer of patients from the ED to inpatient settings when the initial result appears to be unexpected for clinical condition. Further patient-level analysis is warranted.

222

11:45 AM

Urogenital Symptom-Reporting after Sexual Abuse vs. Genital Irritant Contact in Pre-Menarchal Girls

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BACKGROUND: The diagnosis of sexual abuse may include a girl's history of urogenital symptoms temporally related to inappropriate genital contact. Girls may also experience a variety of urogenital symptoms when chemical/physical irritants contact their genitalia. Little is known about girls' physical/emotional responses to these contacts (sexual abuse vs. irritants).
OBJECTIVE: To examine the frequency/quality of urogenital symptom-reporting by girls after genital contact with irritants compared to sexual abuse.
DESIGN/METHODS: We enrolled 2 groups: 5-12 y/o pre-menarchal girls arriving for well-child visits at an urban, hospital-based pediatric office or a suburban pediatric office that had recent exposures to genital irritants (control group) and girls arriving for sexual abuse exams at a regional abuse referral center that disclosed inappropriate genital contact (abuse group). Parents/girls were separately asked about girls' prior urogenital symptoms. Parents were asked about girls' exposure to genital irritants (tight-fitting clothes, nylon underwear/tights, bike or horseback riding, bubble baths, soap, shampoo, genital hygiene and trauma). Control group parents named the most recent contact type. Girls were asked scripted, open-ended questions to elicit symptoms temporally related to the most recent genital irritant contact or inappropriate touching; their responses were compared. Medical records were reviewed for Tanner stage, BMI, and medical conditions.
RESULTS: We enrolled 187 control-group girls and 64 abuse-group girls. Both groups had similar ages (mean 8.0 yrs, SD 2 yrs), Tanner stages, and prevalence of eczema, recent antibiotic use, overweight or obesity. A greater proportion of abuse-group parents reported their girls had genital soreness and dysuria; no difference was seen with genital pruritus. When girls were asked how their genitalia felt after inappropriate touching vs. genital irritant contact, 89% of the abuse group vs. 28% of controls said it hurt, felt bad, uncomfortable, funny, etc. ($p<0.01$) and 69% of the abuse group girls said this contact bothered her body and her feelings vs. 6% of controls ($p<0.01$).
CONCLUSIONS: While both groups of girls described urogenital symptoms temporally related to the genital contact (sexual abuse or irritant), more girls from the abuse group reported having symptoms and more described their symptoms with an emotional component. This information may help clinicians evaluating girls for sexual abuse.

Emergency Medicine
Platform Session

Sunday, March 27, 2011
9:45 AM-12:00 PM

223

9:45 AM

House Officer

Fever: What Is an Effective Way of Educating Parents?

David M. Pinter, Carolina M. Cuba, Fernanda E. Kupferman, Lily Lew, David DiJohn, Rusly Harsono, Louis Primavera, Susana Rapaport, Gagan J. Gulati.
Pediatrics, Flushing Hospital Medical Center, Flushing, NY; Graduate School of Psychology and Health Science, Touro College, NYC, NY.

BACKGROUND: Fever in children is common and lack of parental knowledge about it can be problematic, resulting in often unnecessary visits to the emergency department (ED). Educating parents regarding fever is an effective way to increase their knowledge and decrease their frequency of seeking medical advice.

OBJECTIVE: To compare the effectiveness of verbal versus written information about fever and its management as a means of educating parents.

DESIGN/METHODS: This was a prospective study. A sample of convenience comprising parents of children over 3 months old seen in the ED at Flushing Hospital Medical Center (FHMC) without a life threatening illness from August to November 2010 was considered for the study. Inclusion criteria were the ability to understand both written and oral instructions in English or Spanish. Signed consent was obtained, and demographic data about the age of the child and the level of education and native language of the parent were recorded. A 14 item questionnaire was administered to the parent to assess their knowledge (K) and practices (P) about fever. Parents were then divided into two groups: group 1 (G1) parents were given a brochure regarding fever, and group 2 (G2) parents were told the content of said brochure without being given one. Parents were then called 1-2 weeks later and re-asked the same questions. Pre-test and post-test scores were compared for G1 and G2. Data on the frequency of correct answers were collected, and means and standard deviations (SD) were calculated. Comparisons between the two groups were done by t test, with confidence interval of 95% and p values of <0.05 considered significant.

RESULTS: Of 100 subjects enrolled, 98 completed the study, 48 in G1 and 50 in G2. The demographics of these groups were similar, and their pre-test scores were not significantly different (p value >0.05). No significant post-test improvement was found for G1 (p value >0.05), but there was significant improvement for G2 (mean = 7.74 ± SD 2.16 pre-test vs mean = 8.6 ± SD 2.29 post-test, p = 0.008). Neither level of education nor language spoken had contributed (p value >0.05).

CONCLUSIONS: Giving verbal information about fever and its management was found to be a more effective method than providing written information for educating parents. Further study is needed to determine whether such educational efforts would change the frequency of seeking medical advice.

224

10:00 AM

Undergraduate Student

Multiple Critically Ill Children in the Pediatric Emergency Department Impacts Quality of Care as Indicated by Prolonged Length of Stay

Alexandra E. Remus, Sharon Smith, Christopher Carroll, Adam M. Silverman.
University of Connecticut, Storrs, CT; Emergency Medicine, Connecticut Children's Medical Center, Hartford, CT; Critical Care, Connecticut Children's Medical Center, Hartford, CT.

BACKGROUND: Critically ill children in the PED (Pediatric Emergency Department) require significant resources. We theorize that when more than one critically ill child presents to the PED, quality of care represented by length of stay (LOS) is prolonged for the non-critically ill children exposed to this potentially resource-depleting situation.

OBJECTIVE: To determine if multiple critically ill children in the PED prolongs LOS for non-critically ill children.

DESIGN/METHODS: During calendar year 2009, we identified all times in which there was overlap in the care of critically ill children in the PED. Critical illness was defined as admission to a pediatric intensive care unit. We defined the study group as those children exposed to >1 critically ill child and matched these children to controls seen in the PED without a critically ill child. Demographics, confounding variables, and outcomes were compared between study patients and controls.

RESULTS: There were 36 periods in which multiple critically ill children were seen in the PED. During these periods, there were 1573 non-critically ill children also seen. These were compared to 1694 controls. Children in both the control and study population were similarly classified as having a low-risk diagnosis 66% of the time. Children in lower risk diagnostic categories had significantly longer LOS when cared for during periods of multiple critically ill children in the PED, compared to children with no exposure (Fever/viral 169.6 ± 87.7 min vs. 144.0 ± 88.2, p<0.01 and Upper airway 133.3 ± 79.4 vs. 118.0 ± 65.5, p<0.01). By regression analysis when children with high-risk diagnoses are excluded, exposure to critically-ill children had a significant effect on LOS (p=0.01). In addition, children with low-risk diagnoses exposed to multiple critically ill children, patient disposition (p<0.01), triage acuity (p<0.01) and age (p<0.01) all independently influenced PED LOS.

CONCLUSIONS: During time periods when multiple critically ill children are present in the PED, LOS was increased for children with low risk diagnoses and low acuity triage levels. During such times of high resource utilization, quality of care, represented by PED LOS may be significantly affected. Having a specific team or area of the PED set aside for these low acuity patients could help maintain flow through the PED, improving quality of care.

225

10:15 AM

House Officer

Draining Ears and Tympanostomy Tubes: A Survey of Pediatric Otolaryngologists and Pediatric Emergency Medicine Physicians

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BACKGROUND: Post-tympanostomy tube otorrhea (AOMT) occurs in 30% of children with tympanostomy tubes. Although the management of acute otorrhea through tympanostomy tubes has become fairly standardized among pediatric otolaryngologists (PENTs), physicians specializing in pediatric emergency medicine (PEMs) have few guidelines to use for management of this condition. Use of evidenced-based guidelines can maximize the use of topical antibiotics to the middle ear mucosa and reduce unnecessary use of oral antibiotics.

OBJECTIVE: The purpose of this survey is to compare management of AOMT by PENTs, who have recommendations published by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS), with PEMs, who do not have such guidelines.

DESIGN/METHODS: A 27-question online survey was formulated for the purpose of obtaining information on the care of children who present with AOMT. An initial e-mail was sent out to consecutive PENT and PEM physicians nationwide who were listed in membership directories of their respective subspecialty organizations. During the following 2 months, three reminder e-mails were sent to those who did not respond. A print copy of the survey, along with a self-addressed/stamped envelope, was mailed to all non-responders. Our goal was to receive 150 evaluable surveys from each group.

RESULTS: One hundred eighty-three and 174 responses were received from PEM and PENT physicians, respectively (66% of each group). Twenty-eight percent of the PEM, versus 80% of PENT, respondents routinely cleaned the ear canal prior to starting ototopical antibiotic drops (p < 0.001), and 7% and 79%, respectively, used suction for aural cleaning (p < 0.001). Oral antibiotics were prescribed by 54% of PEMs versus 9% of PENTs (p< 0.001). Eighty-six percent of PEM and 99% of PENT respondents prescribed ototopical antibiotics, preferably fluoroquinolone/steroid ear drops (p< 0.001).

CONCLUSIONS: This study on AOMT management highlights an opportunity for PEMs to reduce the use of oral (systemic) antibiotics and, thereby, decrease the threat of antibacterial resistance. Ototopical fluoroquinolone/steroid drops should be first-line treatment; they are non-ototoxic compared to aminoglycosides and have a high cure rate without significant systemic absorption. To improve the efficacy of ototopical therapy, cleaning the ear canal with aural suction and not dry mopping of the ear should be practiced by PEMs.

226

10:30 AM

Fellow in Training

Does the IVC Diameter Correlate with Central Venous Pressure (CVP) in the Assessment of Intravascular Volume in Children?

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BACKGROUND: Clinical parameters of hydration status are not always reliable, and while invasive hemodynamic monitoring of central venous pressure (CVP) is a reliable, objective guide in directing early resuscitative efforts in acutely ill children, it has practical limitations in the pediatric emergency department (PED) setting. Bedside emergency ultrasound (BEU) may provide a rapid, painless, non-invasive and objective modality to determine a patient's volume status. Collapsibility index (CI) of the inferior vena cava (IVC) of >50% and an IVC/Aorta ratio of <0.8 by BEU have been suggested to predict intravascular volume based on studies using clinical parameters as determinants of hydration status.

OBJECTIVE: To determine if BEU measurements of the CI of the IVC of >50% and an IVC/Aorta ratio of <0.8 correlate with CVP measurements as an indicator of hydration status in acutely ill children.

DESIGN/METHODS: Children < 18 years old who were admitted to the Pediatric ICU and required CVP monitoring had IVC and Aortic measurements using BEU at the same time as CVP measurement. Patients were placed in the supine position and the IVC was measured in two views: (1) subxiphoid sagittal view and (2) transverse view at the level of the renal vein. The CI and IVC/Aorta ratio were calculated from these measurements. Dehydration was considered as a CVP <8 mm Hg.

RESULTS: 27 patients were studied; the mean age was 39 months (range 2 days- 14 yrs). Of these 27 participants, 15 (56%) had a CVP <8. 6 of 26 (22%) children had a CI >50% and 9 of 22 (33%) had an IVC/Aorta ratio of <0.8. The correlation between CI and CVP was 0.10 (p=NS) and between IVC/Ao and CVP was -0.13 (p=NS). There were no significant differences in the ability of either the CI or the IVC/Aorta to predict the presence of dehydration as determined by the CVP.

CONCLUSIONS: IVC and Aortic measurements by BEU, at this time, are not reliable indicators of hydration status (as determined by CVP) in acutely ill children.

227

10:45 AM

Fellow in Training

Little Fingers, Big Trouble: Child Self-Unbuckling

Lilia B. Reyes.

Pediatrics, Section of Pediatric Emergency Medicine, Yale School of Medicine, New Haven, CT.

BACKGROUND: According to the National Highway Traffic Safety Administration, motor vehicle collisions are the leading cause of death among 4-8 year olds. Inappropriate vehicle restraint places children at 3.5 fold increased risk for serious injuries. Previous studies have demonstrated many potential child and parental barriers towards appropriate restraints. Young children may acquire the motor skills to unbuckle from restraints before developing the cognitive ability to understand the necessity of automotive restraints. To date there has been no study assessing the age and frequency of child self-unbuckling from vehicle restraint, a potential safety hazard.

OBJECTIVE: To identify the age at which a child begins to self-unbuckle and to determine the frequency of children self-unbuckling while the car is in motion versus at a full stop.

DESIGN/METHODS: A self-administered survey was given to a convenience sample of parents with children less than 6 years of age. Surveys were distributed in five urban & suburban general pediatric offices. One hundred surveys were distributed to each practice. Information regarding the age and gender of children in the household and current safety seat use was collected. Parents were asked at what age their children first self-unbuckled from their respective restraint. The parents were questioned regarding their children's self-unbuckling while the car is in motion versus at a full stop. The parents were allowed to give free text regarding their response to this behavior.

RESULTS: 378 surveys (76%) were completed. Seventy five percent of children who self-unbuckle were 3 years of age or under, with a range of 12-78 months (mean 40 months). Unbuckling was reported as early as 12 months. There were a larger proportion of males (59%) than females (42%) self-unbuckling. Of the children self-unbuckling, 43% were found to do so with the car in motion. The most common parental response to self-unbuckling while car was in motion was "pull over, reprimand, and re-buckle child".

CONCLUSIONS: In this pilot study, the majority of children who first unbuckle were 3 years of age or under. Many children unbuckle while the vehicle is in motion. Further research, should include a larger prospective study to assess which restraint device would be safer. Development of passive safety locks on the seatbelt can be studied as a potential intervention option.

228

11:00 AM

Training Experiences of Pediatric Emergency Medicine Fellows before Fellowship

Kevin Ching, Marc Auerbach, Frank Overly, Linda Brown, Chaoyan Dong, Colleen Gillespie, Michael Falk, Nikhil Shah, Eric Weinberg, David Kessler.

Emergency Medicine and Pediatrics, New York University School of Medicine, New York, NY; Pediatrics, Columbia University Medical Center/New York Presbyterian Morgan Stanley Children's Hospital of New York, New York, NY; Pediatrics, Yale University School of Medicine, New Haven, CT; Emergency Medicine and Pediatrics, Warren Alpert Medical School of Brown University, Providence, RI; Emergency Medicine, SUNY Downstate College of Medicine, Brooklyn, NY; Emergency Medicine and Pediatrics, Weill-Cornell Medical College, New York, NY.

BACKGROUND: Pediatric emergency medicine (PEM) fellows are expected to possess an aptitude for crisis resource management and to graduate with an ability to perform multiple life-saving surgical procedures and advanced airway maneuvers. We organized a 2-day multi-institutional, multidisciplinary program, *BASE Camp 2010: Basic Training for Pediatric Emergency Medicine* to introduce, review, and provide practice opportunities in teamwork skills, surgical procedures, and advanced airway skills. Little is known about the training and skills fellows possess at the start of their fellowship.

OBJECTIVE: To determine what experiences and training PEM fellows possess in critical teamwork and procedural skills before beginning fellowship.

DESIGN/METHODS: BASE Camp participants were asked to complete an anonymous online survey (multiple choice and open-ended) about their training and experiences before fellowship in crisis resource management, surgical trauma procedures, and advanced airway techniques. This study was IRB approved and all subjects granted consent.

RESULTS: 17 PEM fellows from 10 fellowships in NY, CT, and RI participated in BASE Camp (Oct 23-24, 2010). 29% were male. 15 fellows responded (11 first and 4 second years). 53% had prior experiences as an attending before or during their fellowship.

67% reported prior teamwork training (only 1 with formal training). 50% had limited training in surgical trauma procedures, 5% had advanced airway training, and 50% had central line training. The average experiences are listed in Table 1.

Table 1. Average team management and procedural experience at the start of fellowship

Skill	Mean Number of Experiences
Team Leader for code	2.5
Team Leader for trauma	0.5
Intubations	8.5
Advanced Airway Technique	0
Surgical Airway	0
Chest Tube	0.5
Thoracotomy	0
Pericardiocentesis	0
Central Venous Line	1.5

CONCLUSIONS: PEM fellows do not have sufficient teamwork and procedural experiences or training prior to fellowship. There is a need for formal instruction in these skills as well as clinical or simulated experiences for fellows in training. BASE Camp is one educational strategy that employs both formal instruction and experiential simulation to teach these behaviors and skills. Further research is needed to determine the full impact of such training on fellow clinical performance.

229

11:15 AM

Fellow in Training

Analgesia Use for Infant Lumbar Puncture by Interns after an Educational Intervention

Daniel M. Fein, Jeffrey R. Avner, Marc O. Auerbach, Eileen J. Klein, Geetanjali Srivastava, Elizabeth B. Seelbach, Joshua A. Rocker, Christopher Strother, David O. Kessler.

Pediatric Emergency Medicine, Children's Hospital at Montefiore, Bronx, NY; Pediatric Emergency Medicine, Yale-New Haven Children's Hospital, New Haven, CT; Pediatric Emergency Medicine, New York Presbyterian Morgan Stanley Children's Hospital of New York, New York, NY; Pediatric Emergency Medicine, Cohen Children's Medical Center of New York, New Hyde Park, NY; Hospital Medicine, Children's National Medical Center, Washington, DC; Pediatric Emergency Medicine, Seattle Children's Hospital, Seattle, WA; Pediatrics, UT Southwestern Medical Center, Dallas, TX; Mount Sinai Medical Center, New York, NY.

BACKGROUND: Despite increasing evidence that appropriate pain management for infant lumbar puncture (ILP) improves success rates, ILP is often performed without the use of any analgesia. Rates of analgesia use by interns for ILP and associated factors have not been clearly established.

OBJECTIVE: To describe rates and associated factors of analgesia use for ILP by interns after an educational intervention.

DESIGN/METHODS: Interns from 24 pediatric or emergency medicine training programs in the POISE network were enrolled in a study to assess the utility of Just-in-time-training (JITT) sessions on ILP success. JITT is an educational strategy where brief training sessions are conducted in close temporal proximity to a clinical encounter. Included in this procedural training was instruction on analgesia use. Interns watched an online procedure video and participated in an individualized hands-on LP mastery training session (MTS) during orientation. Throughout the year, interns completed a JITT session with their supervisor prior to performing a LP on an infant < 1 year of age. Information about the clinical LP (including analgesia use) was collected by the instructor.

RESULTS: 501 interns were enrolled in the study. 165 ILPs were performed; the median age of the patients was 27 days (IQR = 11 to 47 days). Some form of analgesia was used in 117 ILPs (74%). Methods of analgesia included one or more of the following: topical analgesics (60%), oral sucrose (37%), injectable lidocaine (17%), sedation (8%) and other (1%). A family member was present during the LP in 64 (39%) cases. If a family member was present, ILP was more likely to be performed with analgesia (84% vs 66%; 95%CI for difference = 5% to 31%). Analgesia use was more common in the ED (79 of 101, 78%) when compared to the NICU (12 of 22, 55%); 95%CI for difference = 1% to 45%.

CONCLUSIONS: Analgesia use for ILP by interns who had a MTS and JITT is in the higher range of what is reported in the literature. Presence of a family member during the procedure and performance in the ED are associated with increased use of analgesia. Further research should identify and address barriers of analgesia use for ILP.

230

11:30 AM

Medical Student

Electrocardiograms in Children with Lyme Meningitis: Should We Screen for Lyme Carditis?

Elizabeth J. Welsh, Keri A. Cohn, Lise E. Nigrovic, Amy D. Thompson, Elizabeth M. Hines, Samir S. Shah.

The Children's Hospital of Philadelphia, Philadelphia, PA; Children's Hospital Boston, Boston, MA; A.I. DuPont Hospital for Children, Wilmington, DE.

BACKGROUND: Both meningitis and carditis are serious complications of early disseminated Lyme disease. The prevalence of cardiac manifestations of Lyme disease in children with Lyme meningitis is unknown.

OBJECTIVE: To determine the prevalence of and identify risk factors for electrocardiographic (EKG) changes in children with Lyme meningitis.

DESIGN/METHODS: We performed a multi-center case-control study nested within a cohort of children 90 days to 19 years of age seen at one of three pediatric emergency departments and diagnosed with Lyme meningitis. Patients who underwent EKG testing were included. The primary outcome measure was the presence of one of the following EKG abnormalities associated with early disseminated Lyme infection: atrioventricular block, ST-T wave changes and prolongation of the corrected QT interval. Cases had EKG abnormalities while controls did not. We performed multivariate logistic regression to identify factors independently associated with carditis in patients with Lyme meningitis.

RESULTS: 69 (59%) of the 117 children with Lyme meningitis underwent EKG testing. The median age of children who underwent EKG testing was --9.8 years (interquartile range, 7.4 – 12.9 years); 70% were male. Of those patients that underwent EKG testing, 23 (33%) had the following EKG abnormalities consistent with Lyme carditis: atrioventricular block (n=14; 20%), ST-T wave changes (n=10; 15%), and prolongation of the corrected QT interval (n=6; 9%). Fever was present in 61% of patients with carditis and 36% of those without carditis. After adjustment for cranial nerve palsy and erythema migrans rash on presentation, history of fever (adjusted odds ratio, 3.20; 95% CI: 1.09-9.35) and older age (adjusted odds ratio, 1.22 for each 1 year increase in age; 95% CI: 1.06-1.41) were each independently associated with carditis.

CONCLUSIONS: Lyme carditis occurs commonly in children with Lyme meningitis. Screening EKGs should be performed routinely on children presenting with Lyme meningitis.

231

11:45 AM

Fellow in Training

Just in Time Simulation-Based LP Training: A Qualitative Evaluation

Gunjan Kamdar, Lindsey Tilt, David Kessler, Kajal Khanna, Geetanjali Srivastava, Todd Chang, Amanda Krantz, Stephen Cico, Mike Holder, Jennifer Reid, Martin Pusic, Kevin Ching, Marc Auerbach.

Yale University School of Medicine, New Haven, CT; Columbia University Medical Center/New York Presbyterian Morgan Stanley Children's Hospital of New York, New York, NY; Children's Hospital of Los Angeles, Los Angeles, CA; University of Texas Southwestern Medical Center, Dallas; Children's National Medical Center, Washington, DC; Tulane University, New Orleans; Seattle Children's Hospital, Seattle; Children's Hospital Medical Center of Akron, Akron; New York University School of Medicine, New York.

BACKGROUND: Just in time training (JITT) is an educational strategy where simulation-based training sessions are conducted in close temporal proximity to a clinical encounter. An ongoing multi-center study is prospectively evaluating the impact of just in time simulation-based lumbar puncture (LP) training on intern clinical infant LP success rates.

OBJECTIVE: To qualitatively describe intern perceptions of the benefits and barriers of JITT.

DESIGN/METHODS: Ten pediatric interns from one institution participated in a face to face semi-structured interview. Questions explored the benefits and barriers of the LP JITT. Questions were iteratively revised during the interview process to obtain a comprehensive response to our study questions. The interviews were transcribed by a professional transcription service. After reviewing the transcripts, 2 investigators independently assigned codes to the responses and then met together to determine themes.

RESULTS: Themes fell into 3 categories: barriers to JITT performance, positive effects, and negative effects of JITT. Interns described feeling nervous prior to their initial infant LP and many had performed LPs only on adults prior to residency. Reported positive effects of JITT included: review of anatomical landmarks and procedure rehearsal prior to the performance of the clinical LP; an opportunity to ask questions in the absence of parents; and improved comfort and confidence with the procedure.

Some interns reported that JITT was not performed prior to each of their clinical LP attempts. Common barriers to the performance of JITT included lack of time in a busy clinical setting and lack of interest by instructors.

A reported negative effect was that the mannequin, as well as the training, did not provide an accurate representation of the clinical infant LP. Interns mentioned that the variability with the skill of the holder and movement of the baby, as well as parental anxiety, were not simulated in the JITT.

CONCLUSIONS: JITT was perceived to improve procedural comfort and confidence with an infant LP, but identified barriers to JITT performance included time constraints and lack of instructor interest. Optimal JITT may include considerations beyond the mannequin. This qualitative data will aid in the iterative development of future simulation based training.

Neonatology - Clinical Studies II
Platform Session

Sunday, March 27, 2011
9:45 AM-12:00 PM

232

9:45 AM

Prospective Randomized Controlled Trial of Restrictive Fluid Management in Transient Tachypnea of the Newborn

Annemarie Stroustrup, Ian R. Holzman.

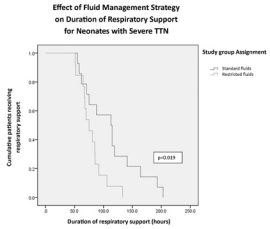
Division of Newborn Medicine, Kravis Children's Hospital, Mount Sinai Medical Center, New York, NY; Department of Pediatrics, Kravis Children's Hospital, Mount Sinai Medical Center, New York, NY; Department of Preventive Medicine, Mount Sinai Medical Center, New York, NY; Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Transient tachypnea of the newborn (TTN) is a self-limited respiratory distress syndrome of the first days of life caused by delayed pulmonary salt channel switching and fluid clearance. Respiratory distress due to TTN requires ICU admission and inhibits early parent-child bonding. Although TTN is a common diagnosis of term and late preterm neonates, little data underlie current fluid management for the disease.

OBJECTIVE: To determine whether fluid restriction speeds resolution of respiratory distress in neonates with TTN.

DESIGN/METHODS: In this prospective randomized controlled trial, term and late preterm neonates diagnosed with TTN were randomized to either standard fluid management or restricted fluid management. Neonates in the restricted fluid group received 20 mL/kg/day total fluids less than neonates in the standard fluid group for the first 3 days of life. The primary study outcome was duration of respiratory support. Secondary outcomes were length of time to first enteral feed and time to discharge from the ICU.

RESULTS: Sixty-four patients completed the study protocol. No adverse events (weight loss > 10% of birth weight, increased hyperbilirubinemia, hypoglycemia, or hypernatremia) due to fluid restriction occurred. Survival analysis demonstrated no difference in duration of respiratory support between the two groups as a whole (p=0.215). In the significant subpopulation of patients requiring respiratory support ≥ 48 hours there was a significant reduction in duration of respiratory support among fluid restricted patients (p=0.019).



CONCLUSIONS: This is the first study to demonstrate benefit of a treatment for TTN beyond supportive care. Mild fluid restriction mimicking physiologic breast milk production is safe in otherwise healthy term and late preterm neonates with TTN. Fluid restriction reduces duration of respiratory distress in neonates with TTN who require respiratory support beyond 48 hours of life. Mild fluid restriction is recommended for all patients with TTN who require respiratory support.

233

10:00 AM

Quality of Reporting in Neonatal Clinical Trials

Sara B. DeMauro, Annie Giaccone, Haresh Kirpalani, Barbara Schmidt.

Department of Pediatrics, Division of Neonatology, The Children's Hospital of Philadelphia and The University of Pennsylvania, Philadelphia, PA.

BACKGROUND: Variation in the reporting of randomized clinical trials (RCTs) makes it difficult for readers to assess the quality of the design, conduct, and analysis of a trial and, therefore, the validity of the results. The Consolidated Standards of Reporting Trials (CONSORT) statement is a checklist of items essential to high quality design, conduct, and reporting of RCTs. Adoption and enforcement of CONSORT improves the quality of RCT reports.

OBJECTIVE: 1) To perform a systematic review of the quality of reporting in neonatal RCTs. 2) To identify RCT characteristics associated with quality of reporting.

DESIGN/METHODS: RCTs enrolling infants <12 months and published during 2005-2009 in 6 pediatric and general medical journals (Pediatrics, J Pediatr, Arch Dis Child Fetal Neonatal Ed, N Engl J Med, JAMA, Lancet) were reviewed. Eligible RCTs were evaluated for the presence of 11 quality criteria, adapted from the CONSORT statement. The relationships between quality of reporting and key study characteristics were tested with appropriate non-parametric statistics.

RESULTS: Two reviewers had very good agreement about inclusion of studies (kappa=0.85) and presence of quality criteria (kappa=0.80). In 179 eligible RCTs, reporting of individual quality criteria varied.

Table: Quality Criteria Reported

Report contains	Number (%)
Inclusion/exclusion criteria	150/179 (84)
Primary outcome	142/179 (79)
Sample size estimate	138/179 (77)
Randomization method	106/179 (59)
Allocation concealment method	123/179 (69)
Blinding method	96/115 (83)
No. centers if multicenter	75/80 (94)
Study diagram	89/179 (50)
No. study participants	177/179 (99)
No. subjects analyzed	168/179 (94)
Result of primary outcome	137/142 (96)

RCTs did not always report if sample size and primary outcome were determined a priori or post hoc. 37 RCTs (21%) did not identify a primary outcome. Higher quality of reporting was associated with greater number of study participants, publication in a general medical journal, and greater number of centers (p<0.0001 for each comparison). Geographic region and positive study outcome were not associated with quality of reporting.

CONCLUSIONS: The quality of reporting of neonatal RCTs is inconsistent. Therefore, the reader cannot accurately assess the validity of many RCT results. Enforcement of the CONSORT guidelines, particularly in pediatric journals, would lead to increased quality of reporting of neonatal randomized trials.

234

10:15 AM

Fellow in Training

Reciprocal Vocalizations between Female Caregivers and Their Infants Surpass Those of Male Caregivers in the First Months of Life

Katharine Johnson, Bonnie Stephens, Richard Tucker, Betty Vohr.

Pediatrics, Warren Alpert Medical School of Brown University, Providence, RI.

BACKGROUND: Hearing, language acquisition, and auditory memory are processes that begin in utero. Infants have shown a natural preference for their own mother's voice, but the father-infant language relationship has not been well established.

OBJECTIVE: To evaluate 1) differences between the verbal interactions of male and female caregivers with their baby including adult word count and response to infant vocalizations 2) an infant's vocal response to adult male vs female speech. We hypothesize that females caregivers will have more infant-directed speech; and, in response, infants will vocalize more with female than male caregivers.

DESIGN/METHODS: This prospective cohort includes medically stable late preterm (n=34, mean GA=35.6 weeks) and term (n=16, mean GA=39.8 weeks) infants without identified hearing impairment, congenital anomalies, or significant comorbidities. Assessment during their birth hospitalization and at 44 weeks corrected age (44wkCA) included a 16 hour recording using the LENA™ language environment analysis system. Adult male and female word count, infant vocalizations, and conversational turns (reciprocal vocalizations within 5 seconds) were measured. Regression models were used to compare differences between adult male and female language interactions with their infant.

RESULTS: 47 recordings in the newborn period (3 excluded for irregularities) and 26 recordings at 44wkCA (to date) were analyzed. Adult word count per hour was higher for female than male

caregivers during the newborn period (1130 vs 446, p<.0001) and 44wkCA (963 vs 453, p<.0001). Females respond to a baby's verbal cues with reciprocal vocalizations more than males respond. Of all infant vocalizations initiating an adult response; 73% of responses were adult female only, 5% adult male only, and 22% both male and female during the newborn period (p<.0001) and 72% vs 8% vs 20% at 44wkCA (p<.0001). Infants also vocalize in response to female speech more often than to male speech during the newborn period (11% vs 8%, p<.0001) and 44wkCA (19% vs 12%, p<.0001).
CONCLUSIONS: Infants are exposed to more adult female than male speech in the first months of life. Language interactions including reciprocal vocalizations between female caregivers (primarily mothers) and their infant surpass those of male caregivers (primarily fathers) in the newborn period and 44 weeks corrected age.

235

10:30 AM

Fellow in Training

A Novel Murine Model of Preterm Birth Based on the Genetic Ablation of Decorin and Biglycan

Megan Calmus, Elyse E. Macksoud, Renato V. Iozzo, Richard Tucker, Beatrice E. Lechner.

Department of Pediatrics, Women and Infants' Hospital of Rhode Island/Brown University, Providence, RI; Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA.

BACKGROUND: Preterm premature rupture of fetal membranes causes one third of preterm births. Ehlers-Danlos Syndrome (EDS) is associated with preterm premature rupture of fetal membranes in humans; an EDS variant is caused by a mutation resulting in abnormal biglycan and decorin secretion. Decorin and biglycan are highly homologous proteoglycans expressed in reproductive tissues. Decorin/biglycan double knockout mice are a model of Ehlers-Danlos Syndrome.
OBJECTIVE: We utilized this model to test the hypothesis that biglycan and decorin play a role in the attainment of successful term gestation.
DESIGN/METHODS: Wild type, single and double knockout pregnancies were assessed for length of gestation, pup and placenta weight and litter size. Quantitative real-time PCR was performed to measure biglycan and decorin transcript and immunohistochemistry was performed to assess protein expression in placenta and fetal membranes at embryonic day E12, E15 and E18.
RESULTS: Decorin/biglycan double knockout dams and dams with only one biglycan or decorin allele display preterm birth. The possession of at least two biglycan or decorin alleles is protective of preterm birth. In mixed litters, homozygous double knockout pups are decreased at postnatal day P1 but not at embryonic day E18. Biglycan and decorin are upregulated in the placenta in each other's absence and are developmentally regulated in placenta and fetal membranes.
CONCLUSIONS: The decorin/biglycan double knockout mouse is a model of genetically induced preterm birth and perinatal loss. Biglycan and decorin display compensatory mechanisms and contribute to gestational success in a dose dependent manner. This model presents novel targets for preventive or therapeutic manipulation of preterm birth.

236

10:45 AM

Fellow in Training

Effects of Bilirubin on Neutrophil Inflammatory Responses in Newborn Infants

Suganya Kathiravan, Faith E. Archer, Anna M. Vetrano, Daniel S. Hirsch, Barry I. Weinberger, Thomas Hegyi.

Pediatrics, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

BACKGROUND: Newborns are susceptible to inflammatory diseases due to intrinsic defects in clearing activated immune cells from affected tissues. Therefore, it is likely that mechanisms have evolved to protect neonates from leukocyte-mediated cytotoxicity. While moderate levels of bilirubin in jaundiced infants have antioxidant effects comparable to α-tocopherol, bilirubin may also exert effects directly on cellular immune responses, such as cytokine production and generation of antioxidant enzymes. Bilirubin has also been shown to decrease expression of the heme-dependent enzymes NOX-1 and COX-2, which mediate inflammatory responses in neutrophils.
OBJECTIVE: We hypothesize that bilirubin increases expression of antioxidant genes, and decreases production of inflammatory cytokines and expression of inducible heme-dependent enzymes in neonatal neutrophils.
DESIGN/METHODS: Cord blood neutrophils were isolated by density centrifugation and treated with bilirubin or medium control, in the presence or absence of bacterial lipopolysaccharide (LPS). Bilirubin concentration of 100 μM was used to model concentrations of free (unbound) bilirubin present in neonatal serum under normal physiologic conditions. Bilirubin was dissolved in 0.1 M NaOH and neutralized using an equal volume of 0.1 M HCl. Production of inflammatory cytokines was quantified by cytometric bead array analysis. RNA expression of antioxidant genes (SOD, HO-1) and heme-dependent enzymes (NOX-1, COX-2) was measured by real time PCR.
RESULTS: Bilirubin increased basal production of cytokines, but down regulated LPS-induced generation of IL-1ß, IL-6, IL-8, MCP-1,and MIP-1ß. It increased SOD and HO-1 expression in both resting and LPS-activated cells. In addition, we observed an unexpected bilirubin-induced increase in gene expression of NOX-1 and COX-2 in both resting and activated cells.
CONCLUSIONS: Bilirubin suppresses inflammatory activity and increases antioxidant enzyme generation in activated neonatal neutrophils. The unexpected increases in NOX-1 and COX-2 expression may represent an early response to LPS stimulation, with physiologic effects that are abrogated by increased production of antioxidants. Elevated levels of unconjugated bilirubin may represent a protective mechanism against inflammatory diseases in infants. Further studies will be required to define levels that optimize these effects while minimizing potential neurotoxicity.

237

11:00 AM

Fellow in Training

Elevated Blanket Temperatures during Whole Body Cooling with Servo-Controlled Blanketrol III

Mario Zichella, Dorothy McElwee, Susan Adeniyi-Jones.

Pediatrics, Thomas Jefferson University Hosp/DuPont Children's Hosp, Philadelphia, PA.

BACKGROUND: Therapeutic hypothermia (TH) is neuroprotective in newborns with hypoxic ischemic encephalopathy (HIE). Conversely, hyperthermia worsens prognosis following HIE. During whole body cooling (WBC) infants are placed on a cooling blanket for 72 hours. Using the servo-controlled Blanketrol III (Cincinnati Sub-Zero) in Gradient 10°C/Smart mode we noted elevated blanket temperatures (BT) >40°C during WBC while the infant's occiput was in direct contact with the blanket. There are no data available describing the extent of this phenomenon.
OBJECTIVE: To determine the frequency of BT elevations above 35°C, 37°C, and 40°C during the 72 hours of WBC.
DESIGN/METHODS: 24 infants with GA 37.9 ±2.0 weeks and BW 3.038 ±0.6 kg who underwent WBC at Thomas Jefferson University Hospital from 2/17/08 to 10/1/10 were studied. During WBC hourly rectal temperatures (RT) and BT are routinely recorded. The number of times the BT exceeded 35°C, 37°C, and 40°C were documented for each patient. The entire infant was placed on the cooling blanket in 21/24 of subjects. Following a practice change 3/24 infants were placed on the blanket from shoulders to feet (excluding the head). The mean ± SD and median (range) number of time points at ≥35°C, ≥37°C, and ≥40°C were calculated for all subjects.
RESULTS: Wide fluctuations in BT from 10°C to ≥ 40°C were observed in 22/24 infants. During WBC, BTs were recorded an average of 71.5/72 times per patient. The mean number of BTs recorded per patient at ≥35°C was 31.4 ±14.2 (44%, median 33, range 7-51). BT ≥37°C was present 27 ± 14.1 (38%, median 27, range 5-49) times and BT ≥40°C was noted on 17.9 ±11.55 (25%, median 18.5, range 1-47) occasions. In some instances, up to 8 consecutive BT elevations (≥35°C) were observed. The RTs for all infants cooled with blankets under their entire body remained tightly controlled at 33.28 ±0.13. Following a practice change to avoid direct contact between the heated blanket and the occiput by placing the cooling blanket at the level of the shoulders, optimal RTs were still achieved during WBC [RT= 33.16 ±.01 (n=3)].
CONCLUSIONS: When the entire infant is placed on the Blanketrol III during WBC inadvertent application of heat directly to the occiput occurs for > 25% of the cooling time. This may have implications for neurologic outcomes. WBC may be safely achieved with the blanket placed at the level of the shoulders. Additional patients are needed to fully evaluate the reliability of this method of WBC.

238

11:15 AM

House Officer

Yield of Surveillance Cultures for Infants Transferred to the NICU

Theodore Macnow, Dana O'Toole, Lisa Saiman, Jennifer Duchon.

Pediatrics, Columbia University Medical Center, New York, NY; Villanova University, Villanova, PA; Infection Prevention& Control, New York Presbyterian Hospital, New York Presbyterian Hospital, NY.

BACKGROUND: Infections caused by antibiotic resistant organisms (AROs) have increased in the neonatal intensive care unit (NICU) during the past decade. Efforts to reduce ARO infections include identification of infants colonized with these potential pathogens. We routinely perform surveillance cultures for methicillin-resistant *Staphylococcus aureus* [MRSA], vancomycin-resistant enterococci [VRE] and extended spectrum ß-lactamase [ESBL]-producing organisms in infants transferred to our NICU, but the yield of this strategy has not been systematically evaluated.
OBJECTIVE: To examine the yield of our targeted surveillance strategies, trends in colonization and infection with AROs in infants transferred to our NICU, and risk factors for ARO colonization.
DESIGN/METHODS: We performed a retrospective chart review of patients transferred to our NICU from 2004-2009 to determine compliance with surveillance cultures, yield of such cultures, and risk factors for ARO colonization. The nares and skin were cultured for MRSA and the rectal verge was cultured for VRE and ESBL-producing organisms.
RESULTS: Of 1555 tranferred infants, 67%, 64%, and 50% had cultures performed for MRSA, VRE, and ESBL-producing strains, respectively, although compliance significantly improved during the study period. The overall yield was 3.7%, 2.0%, and 1.0% for MRSA, VRE and ESBL-producing strains, respectively. In all, 67 infants had ≥ one positive surveillance culture of whom only 2 developed an ARO infection. In a multivariable model, patients colonized with ≥ one ARO were significantly older upon transfer (p=0.001) and more likely to be transferred from certain NICUs (p<0.001).

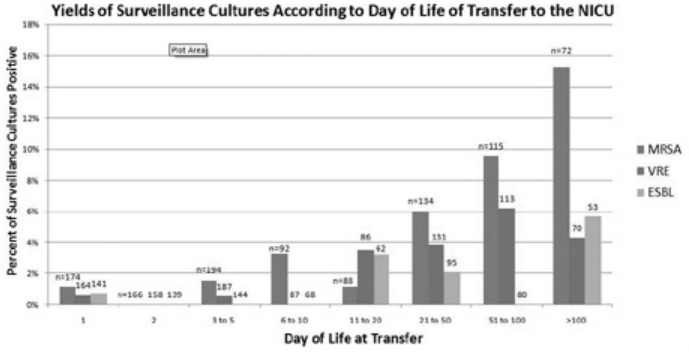


Figure 1 demonstrates the relationship between positive surveillance cultures and increasing age at transfer.
CONCLUSIONS: The overall yield of AROs from surveillance cultures was low and MRSA was most common. Our findings suggest further targeting surveillance cultures to older infants transferred to our NICU. Future direction includes a cost-efficiency analysis of our current policy.

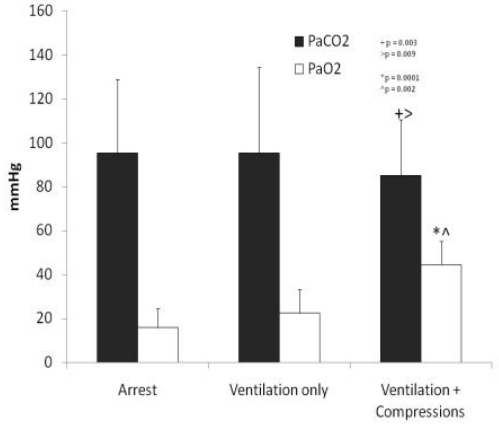
239

11:30 AM

Gas Exchange in the First Minute of CPR Following Asphyxial Cardiac Arrest in Newborn Piglets

Bobby Mathew, Daniel D. Swartz, Melissa Carmen, Sylvia F. Gugino, Jayasree Nair, Rita M. Ryan, Satyan Lakshminrusimha.
Pediatrics (Neonatology}, Universtiy at Buffalo, Buffalo, NY; Physiology, University at Buffalo, Buffalo, NY.

BACKGROUND: Asphyxia is a leading cause of death and neurodevelopmental disability in the term newborn. Current NRP guidelines recommend 30 sec of positive pressure ventilation (PPV) prior to initiating chest compressions (CC). We have previously shown that in newborn lambs asphyxiated by umbilical cord occlusion resulting in bradycardia (heart rate 46±7/min), PPV for 30 sec with 100%O_2 decreased $paCO_2$ from 113±14 to 75±15 mmHg and increased paO_2 from 5±1 to 132±39 mmHg. The effectiveness of ventilation alone in improving gas exchange in a neonatal model of asphyxial cardiac arrest is not known.
OBJECTIVE: To study the effectiveness of PPV alone and CC+PPV for 30 sec each on gas exchange in a newborn asphyxial model of cardiac arrest.
DESIGN/METHODS: Seven newborn piglets (1-3d) were anesthetized and venous and arterial access was established. Asphyxial cardiac arrest was induced by clamping the ETT until asystole. Animals were resuscitated with PPV for 30sec followed by PPV and CC. Blood gases were obtained at the point of cardiac arrest, following 30sec of ventilation alone, and at 1min following ventilations and chest compressions for 30sec.
RESULTS: There were no differences between the ABGs obtained at cardiac arrest and following 30sec of PPV. ABGs were significantly better for PaCO, and PaO, following 30sec of PPV+CC.



CONCLUSIONS: In this neonatal model of cardiac arrest, ventilation alone provides no effective gas exchange. Cardiac compression pumps blood into the pulmonary circulation and is critical for gas exchange and successful resuscitation. We speculate that during resuscitation of an asphyxiated neonate in asystole, CC initiated simultaneously with PPV will provide better gas exchange than PPV alone and shorten the duration of cerebral hypoxemia.
The results from this study should be interpreted with caution as cardiac arrest in a postnatal piglet may not be representative of birth asphyxia.
Funded by the NRP Young investigator award grant (BM).

240

11:45 AM

Fellow in Training

Maternal Microchimerism in the Fetus

Arlene E. Balubayan, Rakhi Mehrotra, Heber C. Nielsen, Christiane E.L. Dammann.
Newborn Medicine, Floating Hospital for Children at Tufts Medical Center, Boston, MA.

BACKGROUND: Maternal cell microchimerism (MCM) is defined as the presence of maternally derived cells in fetuses. Maternal cells, which travel to the fetus through the placenta, are present in the human fetal blood beginning at 13 weeks gestation and persist into adulthood. Studies show that these maternally derived cells are associated with autoimmune disorders. It is unclear whether they cause disease or participate in the repair of injury. MCM has been studied in post-natal mice, in which organ-specific MCM was present in brain, heart, lung, kidney, liver, spleen, and small bowel. Heart and lung had the highest numbers of maternal cells. The development of organ-specific MCM in the fetus in utero has not been studied.
OBJECTIVE: To establish the frequency and quantity of organ-specific MCM in fetal tissues.
DESIGN/METHODS: MCM was studied using a green fluorescent protein (gfp) mouse model. Hemizygous gfp positive C57Bl/6 females were bred with wild-type males. Timed-pregnant females were sacrificed at E18. Fluorescent maternal cells in brain and lungs of wild-type pups were quantified using FACS (fluorescence-activated cell sorting) analysis.
RESULTS: The distribution of MCM showed that fetal brain contains 4 times as many maternally-derived gfp positive cells than fetal lungs at E18 of gestation.
CONCLUSIONS: In contrast to the post natal distribution of MCM, MCM is skewed to the brain in late gestation fetuses. This raises important questions of the fate of maternal cells in late gestation and after delivery. Further, the function, and fate of maternally derived cells in the fetal and neonatal brain, specifically in the setting of injury, requires study. (Support: NIH HD 049341, and Ikaria's Advancing Newborn Medicine Grant Program for Fellows in Neonatology).

Neonatology - Pulmonary II
Platform Session

Sunday, March 27, 2011
9:45 AM-12:00 PM

241

9:45 AM

Effect of FiO_2 and NO on Oxygenation and Pulmonary Vascular Resistance at Birth

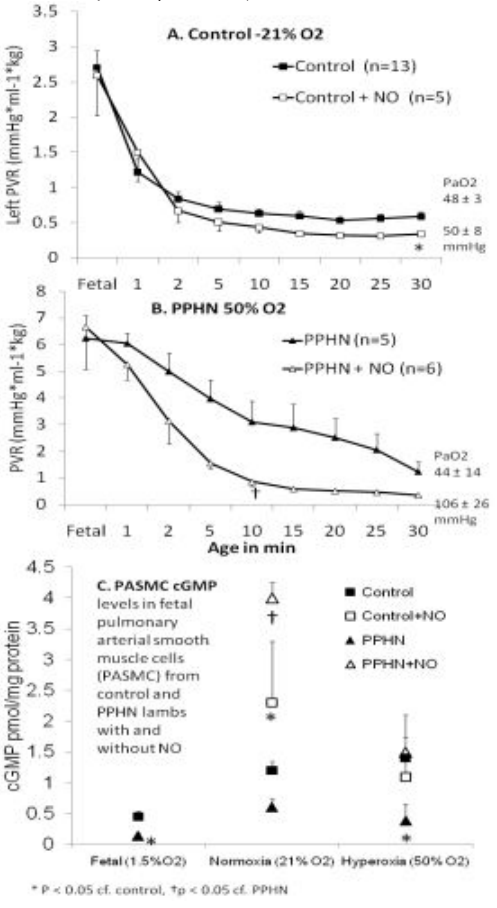
Satyan Lakshminrusimha, Daniel D. Swartz, Bobby Mathew, Sylvia F. Gugino, Stephen Wedgwood, Robin H. Steinhorn.
University at Buffalo, Buffalo, NY; Northwestern University, Chicago, IL.

BACKGROUND: Ventilation at birth reduces PVR, an event that is mediated by NO and cGMP. The effect of varying FiO_2 and NO on the pulmonary vascular transition in normal vs PPHN neonates is unknown.
OBJECTIVE: To study the effect of varying FiO_2 and NO on PaO_2, PVR and cGMP in control and PPHN lambs.
DESIGN/METHODS: PPHN was induced by antenatal ductal ligation. Control and PPHN lambs were ventilated with 21%, 50% and 100%O_2 ± NO at 20ppm. 18 control and 11 PPHN lambs were instrumented and ventilated at birth to achieve a PaO_2 of 45-50mmHg (control 21%, PPHN 50%O_2) ± NO. PASMC from control and PPHN lambs were incubated in 1.5%, 21% and 50%O_2 ± NO donor, and cGMP levels were measured.
RESULTS: NO had minimal effect in control lambs, but markedly improved PaO_2 and decreased PVR in PPHN lambs. Increasing PO_2 increased cGMP levels in control but not PPHN PASMC (fig.C). NO increased cGMP levels to a greater degree in PPHN cells, but the effect was blunted at high pO_2.

PaO2 in the first 30min of life

Group O2%	n	Fetal	5min	15min	30min
Control 21%	42	20±1	38±3	45±3	48±3
Control 21%+NO	9	23±2	49±9	52±7	50±8
PPHN 21%	6	20±1	22±4	26±9	35±9
PPHN 21%+NO	1	18	25	42	50
Control 50%	12	18±2	112±16	149±21	142±16
Control 50%+NO	5	22±5	117±20	162±8	147±23
PPHN 50%	11	19±2	18±4	37±13	45±14
PPHN 50%+NO	5	16±3	40±9	75±28*	106±26*
Control 100%	36	17±1	337±25	374±21	338±22
Control 100%+NO	7	16±2	333±78	345±53	365±37
PPHN 100%	54	20±1	25±3	61±10	102±20
PPHN 100%+NO	9	17±3	26±16	95±13*	206±50*

CONCLUSIONS: This is the first study to compare the effects of NO at birth on oxygenation in normal and PPHN lambs. In normal lambs, 21%O_2 is sufficient to increase vascular cGMP and decrease PVR from fetal levels, and iNO has little effect. In PPHN lambs, increased PO_2 does not increase PASMC cGMP. Addition of NO in PPHN markedly increases cGMP, significantly reduces PVR, and improves PaO_2.



242

10:00 AM

Medical Student

Age-Dependent *In Vitro* Mouse Lung Type II Cell Behavior

Rony O. Dey Hazra, Cristina Scapin, Oya Guengoeze, Katja Zscheppang, Heber C. Nielsen, Christiane E.L. Dammann.

Newborn Medicine, Floating Hospital for Children, Boston, MA; Pediatric Pulmonology and Neonatology, Hannover Medical School, Hannover, Germany.

BACKGROUND: Responses to injury are known to be developmental-age and context-specific for multiple tissues. Chronic lung disease (CLD) develops in immature lungs after shorter injury exposure than in adult lungs. Both are associated with fibrosis. Fetal tissue is capable of injury repair without scarring and fibrosis. Fetal and adult type II (TII) cells are known to require different culture conditions to maintain their differentiated epithelial cell phenotype in vitro. An understanding of mechanisms causing differences in developmental-age related cell behavior might help discover treatment strategies for CLD. We showed that MLE12 cells, similar to primary adult TII cells, loose epithelial cell markers after Transforming Growth Factor beta (TGFβ)1 treatment. In contrast, TGFβ1 did not induce this response in fetal TII cells. ErbB receptors are important in lung development, injury, and cancer development and their expression pattern in TII cells is age-dependent.

OBJECTIVE: We hypothesize that TII cells behave in vitro in a developmental age-related fashion.

DESIGN/METHODS: MLE 12 cells and primary fetal and adult TII cells (>95% pure) were pretreated with cis-OH-proline to eliminate remaining fibroblasts. Epithelial and mesenchymal cell markers and ErbB receptor expression were studied in different culture conditions and following a 5-day treatment with 2.5 ng/ml TGFβ1.

RESULTS: TTF-1 expression peaked shortly before birth, and adult type II cells kept their epithelial cell phenotype in HITES medium, while DMEM containing FCS, the ideal culture condition for fetal TII cells, induced mesenchymal marker expression. The response to TGFβ1 was age-related. TGFβ1 treatment induced epithelial markers and ErbB4 expression in fetal TII cells. ErbB4 overexpression decreased TGFβ1-induced upregulation of mesenchymal marker expression in adult TII cells.

CONCLUSIONS: These data suggest that there are developmental-age related differences in cell behavior in TII cells. ErbB4 regulates this age-related behavior. Further analyses are required to fully understand the regulation of TII cell behavior and the role of ErbB receptors in this process.

Funding: NIH HL085648, Tufts Institutional Grant, Deutsche Forschungsgemeinschaft Da 375/3-2.

243

10:15 AM

How Accurate Are Measures of Tidal Volume, Compliance and Resistance on Neonatal Ventilator Displays?

Soraya Abbasi, Emidio Sivieri, Robin Roberts, Haresh Kirpalani.

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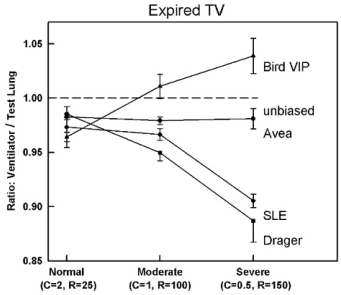
BACKGROUND: Microprocessor neonatal ventilators compute and display expired tidal volume (VTE), flow and pressure signals. The accuracy is unknown.

OBJECTIVE: To determine the accuracy of tidal volume and calculated compliance (Cdyn) and resistance (R) measures by four neonatal ventilators, as compared to a passive physical lung model of known fixed compliance and resistance.

DESIGN/METHODS: Three test lungs simulated 3 severities of neonatal lung disease, (Cdyn: 2.0, 1.0, 0.5 and R: 25, 100, 150). Each ventilator was calibrated using manufacturer's specifications prior to measurements. Default time cycled pressure limited ventilator modes were used. Each ventilator was tested using 27 combinations of PIP (15, 20, 25 cmH2O), PEEP (5, 6, 7 cmH2O), and rate settings (20, 40, 60 bpm). Comparisons of ventilators by simulated lung severity, used the ratio of ventilator read-out to test lung value.

RESULTS: The figure shows VTE, where the line of perfect agreement would be a horizontal line of unbiased value. Each ventilator read-out is shown by each lung severity. SLE and Dräger consistently underestimated VTE, more so at increasing lung severity. In contrast, the VIP Bird underestimated VTE for normal and overestimated for sick lungs. Avea had the least bias and tighter confidence limits across all 3 lung severities. In similar analyses for Cdyn and R, three of the four ventilators consistently underestimated Cdyn for all 3 lung severities. Dräger, overestimated Cdyn in normal lungs, was accurate in moderate disease, but underestimated in severe lung condition. All except Dräger showed much larger inaccuracies for R measurements. The Dräger R calculation improved with increased severity of lung condition. Avea, by manufacturer design, did not display resistances >100cmH2O/L/sec.



CONCLUSIONS: Biases were observed in all ventilators. This was not a uniform uni-directional bias according to lung severity. To use ventilator dynamic respiratory mechanics, clinicians need to understand machine differences.

244

10:30 AM

Intravenous Sildenafil Improves Oxygenation and Suppresses PDE5 Activity in Lambs with PPHN

Satyan Lakshminrusimha, Stephen Wedgwood, Kathryn N. Farrow, Sylvia F. Gugino, James A. Russell, Robin H. Steinhorn.

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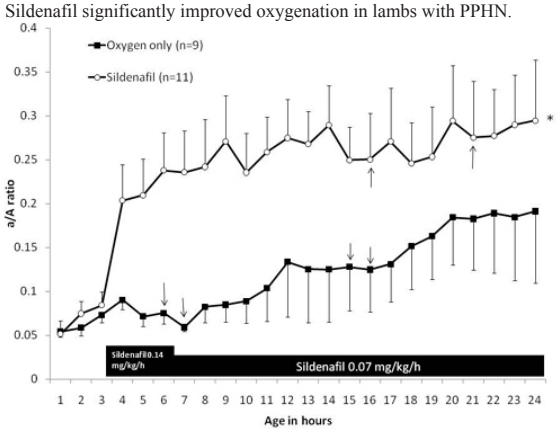
BACKGROUND: Persistent pulmonary hypertension of the newborn (PPHN) is a serious disorder associated with high morbidity and mortality. Inhaled NO does not always result in sustained improvement, and when used with 100%O_2can promote formation of oxidants such as peroxynitrite. IV sildenafil is a phosphodiesterase 5 (PDE5) inhibitor that may offer an alternative to NO in the management of PPHN.

OBJECTIVE: To measure the effects of IV sildenafil on hemodynamics and oxygenation in lambs with PPHN, and to determine the effects of sildenafil on enzymes in the NO pathway and markers of vascular oxidative stress.

DESIGN/METHODS: PPHN was induced by ligation of the ductus arteriosus 8d prior to delivery. Twenty PPHN lambs were ventilated with 100% O_2 for 24h. In 11 lambs, at 2h of age, IV sildenafil was infused at 0.14mg/kg/h (load) for 3h followed by 0.067mg/kg/h maintenance, a dose based on published pharmacokinetic studies in neonates with PPHN. After sacrifice, lung sections were stained for superoxide anions and 3-NT, and 5th generation PA were analyzed for eNOS and PDE5 protein and activity.

RESULTS: Sildenafil significantly improved oxygenation in lambs with PPHN.



Four lambs in the O_2-only group and 2 lambs in the sildenafil group died before 24h (shown by arrows in the figure). Hypotension requiring dopamine was observed in 2 lambs in the O_2 group and 3 lambs in the sildenafil group. Sildenafil reduced vascular PDE5 activity by 66%, and also decreased PDE5 protein (0.7±0.1 vs. 1.7±0.3 fold fetal control) and increased PA eNOS levels (14±4 vs. 2±0.3 fold of fetal control in sildenafil and O_2 groups respectively). Sildenafil significantly reduced 3-NT in PA and tended to reduce superoxide levels.

CONCLUSIONS: IV sildenafil improves oxygenation, and reduces formation of oxidants such as peroxynitrite in lambs with PPHN. Sildenafil also increases eNOS and reduces PDE5 expression in PA. Clinical trials are needed to evaluate this promising therapy in neonates with PPHN.

245

10:45 AM

Fellow in Training

Effect of Inspired Oxygen and Inhaled Nitric Oxide (iNO) on Oxygen Uptake from the Lung and Arterial Oxygen Content in Newborn Lambs and Lambs with Persistent Pulmonary Hypertension of the Newborn (PPHN)

Melissa F. Carmen, Bobby Mathew, Sylvia Gugino, Jayasree Nair, Daniel D. Swartz, Satyan Lakshminrusimha.

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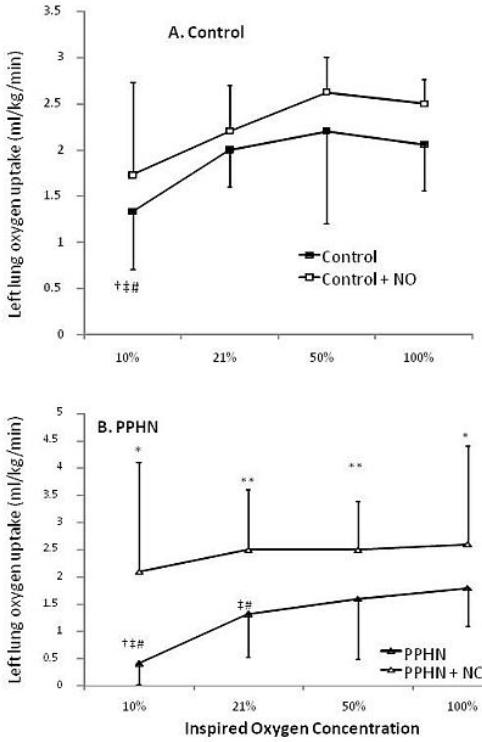
BACKGROUND: Clinicians often increase the FiO_2 with the assumption that this will increase arterial O_2 content and O_2 uptake from the lungs during management of PPHN. The effect of FiO_2 and iNO on O_2 uptake in the lungs in PPHN is not known.

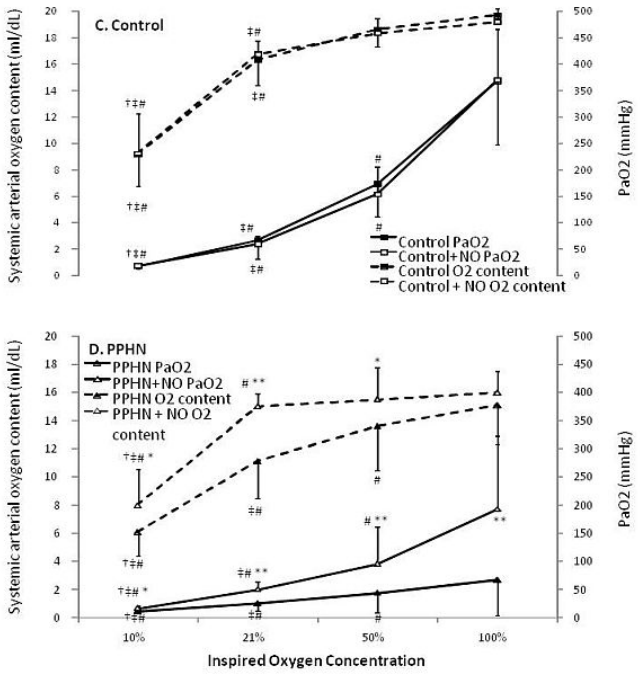
OBJECTIVE: To determine the relationship between FiO_2, arterial oxygen content and O_2 uptake from the lung during ventilation with and without iNO in newborn lambs with PPHN.

DESIGN/METHODS: Fetal lambs underwent in utero ductal ligation to induce PPHN and were compared to control lambs (n=12 each). Six lambs from each group were ventilated with iNO at 20 ppm. Two hours after birth, lambs were randomly and sequentially ventilated with 10%, 21%, 50% and 100% O_2. Blood gases from aorta and pulmonary artery and pulmonary blood flow were measured. Oxygen uptake from the lungs was calculated by multiplying pulmonary blood flow with the difference between systemic arterial and pulmonary arterial oxygen content.

RESULTS: Despite a marked increase in PaO_2 with increasing O_2 from 21 to 100% in control lambs, there was no significant increase in the uptake of O_2 from the left lung. Inhaled NO did not significantly increase O_2 uptake from the left lung or systemic arterial oxygen content in control lambs(Fig A&C). In lambs with PPHN, increasing from 21%O_2 to 50%O_2 increased O_2 uptake from the lungs. Increasing inspired O_2 from 50 to 100% did not further increase uptake from the lungs (FigB). Increasing FiO_2 resulted in a progressive increase in PaO_2 and systemic O_2 content at every step in PPHN lambs (Fig D) and iNO further increased O_2 uptake from the lungs.



* p < 0.05 and * * p < 0.01 compared to corresponding value without iNO by ANOVA; # p <0.05 compared to corresponding 100% oxygen, ‡ p < 0.05 compared to 50% oxygen and † p < 0.05 compared to 21% oxygen. Data shown as mean ± standard deviation.



* p < 0.05 and * * p < 0.01 compared to corresponding value without iNO by ANOVA; # p <0.05 compared to corresponding 100% oxygen, ‡ p < 0.05 compared to 50% oxygen and † p < 0.05 compared to 21% oxygen. Data shown as mean ± standard deviation.

CONCLUSIONS: Inhaled NO is effective in improving systemic oxygenation and O_2 uptake from the lungs in PPHN lambs, but not in controls. Hyperoxic ventilation increases PaO_2 and increases risk for oxygen toxicity but does not increase O_2 uptake from the lung.

11:00 AM

Vascular Endothelial Growth Factor in Tracheal Aspirates from Preterm Infants: Effect of Surfactant Therapy

Avinash Purohit, Rajeev Mehta, Anna Petrova.
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BACKGROUND: Vascular endothelial growth factor (VEGF) regulates vascular endothelial cell differentiation and angiogenesis, and maturation of epithelial cells of the developing lungs. Different reports have described the role of VEGF in lung cells proliferation, differentiation, growth, and permeability. It has been shown that reduced VEGF levels increase the risk for development of respiratory distress syndrome (RDS) in preterm infants, and recovery from RDS is associated with increased expression of VEGF in alveolar epithelial cells. Exogenously administrated surfactant that affects lung cells biochemical and biophysical properties may also perhaps impact VEGF production by the lung cells.

OBJECTIVE: To investigate the effects of exogenous surfactant administration on the level of vascular endothelial growth factor (VEGF) in tracheal aspiration fluid (TAF) of very preterm born infants.

DESIGN/METHODS: Pre term infants with clinically diagnosed RDS who were intubated on day 1 of life and received surfactant therapy were studied.We studied the change in TAF VEGF levels within 20-24 hours after administration of the first dose of exogenous surfactant. Multiple regression analysis was used to identify the independent effect of pulmonary VEGF concentration on the number of surfactant treatments, duration of ventilation, and development of bronchopulmonary dysplasia (BPD).To determine the levels of VEGF in the tracheal aspirate, samples were assayed in duplicate using a Human VEGF Flex Set and BD FACSArray Bioanalyzer. VEGF concentrations in the sample were determined from a standard curve ranging from 10 to 2500 pg/mL.

RESULTS: VEGF levels prior to and after the surfactant administration were studied in 31 preterm infants with gestational age 23-35 week (29.5+/-3.3 weeks). TAF VEGF levels increased within 20-24 hours after surfactant administration as compared to the baseline in all infants (40.0+/-42.5 pg/ml vs. 55.0+/-43.8 pg/ml, P<0.001). TAF VEGF levels were indirectly associated with the gestational age (P<0.01), but did not independently impact the number of surfactant treatments, duration of ventilation, and development of BPD.

CONCLUSIONS: VEGF in tracheal aspirate increases in association with exogenous surfactant therapy.The mechanism of the identified association requires further explanation because to our knowledge no experimental model was designed to identify the role of exogenous surfactant in VEGF production.

11:15 AM

Fellow in Training

Hyperoxia Modulates Bacterial Lipopolysaccharide-Induced Inflammation and Nitric Oxide Synthase

Mohammed Rashed Shareef, Tudevdagva Gerelsaikhan, Pavan Vasa, Joseph DeCristofaro, Avinash Chander.
Department of Pediatrics, Division of Neonatology, Brady Russell Laboratory, Stonybrook University Medical Center, Stony Brook, NY.

BACKGROUND: Bacterial sepsis, a serious concern in very low birth weight infants, accounts for ~5% of NICU admissions. Those with respiratory distress may require supplemental oxygen. Lipopolysaccharide (LPS) in gram negative bacteria can cause respiratory distress as it induces nitric oxide synthase (iNOS) and release of pro-inflammatory cytokines in the lung. Hyperoxia produces reactive oxygen species that can cause inflammation. Thus, the two insults together can cause serious lung injury. Only a few reports have studied the combined effects of these two agents.

OBJECTIVE: We hypothesized that LPS and hyperoxia would have additive effects on iNOS induction and release of proinflammatory cytokines.

DESIGN/METHODS: Macrophages cells (Raw 264.7) were incubated for 3, 6, 12 and 24h, respectively, in room air with 5% CO_2 (Control), hyperoxia (95% O_2, 5% CO_2), LPS (1µg/ml), and hyperoxia plus LPS. The culture medium was assayed for nitrite levels by Griess reaction to assess iNOS induction and for various cytokines by Luminex multiplex ELISA. At least three separate experiments were conducted for each group. Results were analyzed for statistical significance ($P < 0.05$) by ANOVA followed by post-hoc Tukey's test.

RESULTS: LPS increased the nitrite levels at 6h, which steadily increased for up to 24h. Hyperoxia itself had no effect, but potentiated the LPS-induced nitrite increase (LPS and O_2, 307 ± 55; LPS, 127 ± 28 nmoles). L-NAME (iNOS inhibitor) completely blocked the nitrite increase in LPS ± hyperoxia-treated cells. LPS also increased the pro- (IL-1β, TNF-α and IL-6) and anti-inflammatory cytokines (IL-10) in a time-dependent manner. Hyperoxia alone was without effect, but increased LPS effects on TNF-α and IL-6 at 12 and 24h and IL-10 levels at 6h. Thus, hyperoxia increased the pro- and anti-inflammatory cytokines in LPS-treated cells in a time-dependent manner. All cytokines declined after reaching a maximum at 6 or 12h, possibly because of biological degradation. However, the initial decline was cytokine-dependent and was different in the LPS ± hyperoxia groups, suggesting hyperoxia effects on stability of cytokines.

CONCLUSIONS: Prolonged hyperoxia exacerbates the injurious effects of LPS, suggesting minimally necessary oxygen therapy in gram negative sepsis with respiratory distress. However, short-term hyperoxia may be beneficial as it increases IL-10 without affecting TNF-α in LPS-treated cells.

248

11:30 AM

Fellow in Training

Antenatal Betamethasone Improves Pulmonary Transition in Late Preterm Lambs Delivered by Elective Cesarean Section

Pritha Nayak, Daniel D. Swartz, Bobby Mathew, Sylvia F. Gugino, Karen A. Wynn, Stephen Wedgwood, Robin H. Steinhorn, Satyan Lakshminrusimha.

Pediatrics, University at Buffalo, Buffalo, NY; Pediatrics, Women and Infants Hospital, Providence, RI; Pediatrics, Northwestern University, Chicago, IL.

BACKGROUND: Antenatal steroid therapy for women in preterm labor <34wk gestational age (GA) is standard of care. However, the effect of antenatal steroids on pulmonary transition in late preterm (34-36wk) infants is not known. Abnormalities of transition such as pulmonary hypertension (PPHN), transient tachypnea of newborn (TTN) and respiratory distress syndrome (RDS) are common in late preterm infants delivered by C-section.

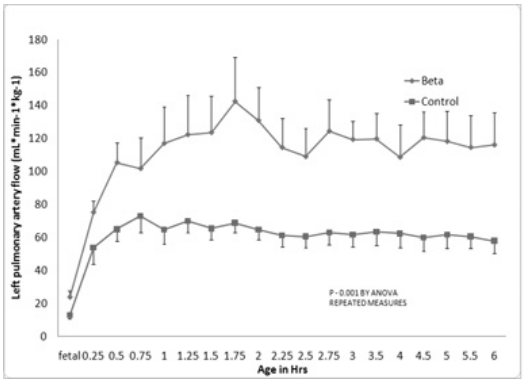
OBJECTIVE: To evaluate the effect of 2 doses of betamethasone given 24 and 48h prior to delivery by elective C-section on pulmonary transition in late preterm lambs.

DESIGN/METHODS: Betamethasone injections were administered to time dated pregnant ewes on 132 and 133d GA (term~145d) at the end of saccular stage of lung development, similar to late preterm infants. Lambs were delivered at 134d by C-section and ventilated for 6h.

RESULTS: Antenatal betamethasone reduced fetal lung liquid volume and pulmonary vascular resistance and increased pulmonary blood flow and lung compliance. There was no significant difference in oxygenation.

Results comparing control versus betamethasone

	Control (n=6)	Betamethasone (n=6)	p value
Birth weight (kg)	3.22 ± 0.13	3.38 ± 0.20	0.5
Fetal lung liquid (mL/kg)	15 ± 1	4.4 ± 1.3	< 0.0001
Fetal left pulmonary vascular resistance (mm*mL^{-1}*min*kg)	2.2 ± 0.2	7.5 ± 2.3	0.14
PVR at 6h of age	0.8 ± 0.1	0.3 ± 0.06	0.004
Compliance at 6h	0.4 ±0.08	0.58± 0.03	0.05
OI at 6h	18.5 ± 13	4.4 ± 1.1	0.3
PaO2/FiO2 ratio at 6h	264.8 ± 46	217.8 ± 38.8	0.4



CONCLUSIONS: Antenatal betamethasone decreases PVR, increases compliance and reduces lung liquid in late preterm lambs delivered by elective C-section. This therapy may reduce the incidence of PPHN, RDS and TTN in late preterm neonates, and is being currently evaluated in clinical trials.

249

11:45 AM

Fellow in Training

Inhibition of Pro-Inflammatory Cytokine Release from Macrophages of the Newborn: Insensitivity to Glucocorticoids Compared to Interleukin-10

Olena Predtechenska, Hardik Patel, Ivana Vancurova, Dennis Davidson, Kavita Kasat.

Division of Neonatal-Perinatal Medicine, Cohen Children's Medical Center of New York, New Hyde Park, NY; Feinstein Institute for Medical Research, Manhasset, NY; Department of Biology, St. John's University, New York, NY.

BACKGROUND: For newborns likely to develop bronchopulmonary dysplasia (BPD), macrophages become the predominant cells in the airway responsible for the regulation of both pro-inflammatory (PI) and anti-inflammatory (AI) cytokine release. Levels of endogenous interleukin (IL)-10, a potent AI cytokine, are undetectable or extremely low in the tracheal aspirates of babies who develop BPD. The use of anti-inflammatory steroids has decreased due to concerns about short and long term adverse effects.

OBJECTIVE: To determine the inhibitory effect of exogenous IL-10 versus dexamethasone (DEX) or betamethasone (BETA), as well as the effect of endogenous IL-10 on PI cytokine release by macrophages of the newborn.

DESIGN/METHODS: Monocytes were isolated from cord blood of healthy term infants. Histology and flow cytometry surface markers confirmed differentiation into macrophages after 7 days of cell culture. Plasma therapeutic levels of DEX for BPD are in the range of 10^{-8}M. Macrophages were preincubated with serial, increasing equimolar concentrations of DEX, BETA or IL-10, and then stimulated with lipopolysaccharide (LPS) for 4 hours or 18 hours. PI cytokine (TNFα, IL-6, IL-8) release was measured by ELISA. Anti-IL-10 antibody or an IgG control was incubated with macrophages prior to LPS stimulation to determine the effect of endogenous IL-10 on PI cytokine release.

RESULTS:

Percent change in PI cytokine levels from LPS-stimulated macrophages after exposure to IL-10, DEX or BETA compared to LPS alone.

	Time (hours)	IL-10 (10^{-8}M)+LPS	DEX(10^{-8}M)+LPS	BETA(10^{-8}M)+LPS
TNFα	4	-60(±5)*	-7(±7)	-25(±7)
	18	-87(±8)*	-5(±42)	-23(±12)
IL-6	4	-85(±3)*	-1(±2)	2(±7)
	18	-82(±4)*	-10(±8)	5(±8)
IL-8	4	-75(±2)*	-2(±5)	-3(±5)
	18	-73(±3)*	-5(±3)	-31(±8)

Values=Mean±SE (n=7). *different from LPS alone ($p<0.01$).

DEX and BETA did not demonstrate inhibition of PI cytokine release until exposure to supratherapeutic concentrations only (10^{-5}M and 10^{-7}M respectively). When endogenous IL-10 was blocked with a monoclonal antibody, the levels of all PI cytokines increased by at least 4 fold.

CONCLUSIONS: Endogenous IL-10 controls excessive PI cytokine release in macrophages of the newborn. Exogenous IL-10 may be an effective treatment for BPD as shown by the marked reduction of PI cytokine release compared to equimolar, clinically therapeutic concentrations of DEX and BETA.

Endocrinology / Obesity Platform Session

Sunday, March 27, 2011
9:45 AM-12:00 PM

250

9:45 AM

Fellow in Training

Is There a Different Relationship between Vitamin D 25-OH and Parathyroid Hormone in Children with Type 1 Diabetes (T1D)?

Emily Frydman, Crystal Wittcopp, Holley F. Allen, Paul Visintainer, Edward O. Reiter, Nancy S. Dunbar.

Pediatric Endocrinology, Baystate Children's Hospital, Tufts Univeristy School of Medicine, Springfield, MA.

BACKGROUND: Previous studies have shown that vitamin D deficiency is common in the adolescent population. T1D and Vitamin D deficiency have negative effects on bone mineral health. In adult populations, several studies have reported that PTH levels are inversely associated with 25-OHD and begin to plateau in adults who have blood levels of 25-OHD between 30 –40 ng/ml. We are unaware of any studies that have looked at this relationship in pediatric population with T1D.

OBJECTIVE: Evaluate the relationship between 25-OHD and PTH in children and adolescents with TID.

DESIGN/METHODS: This is a cross-sectional study with data obtained from patients aged 2 through 21 years with T1D seen in our Pediatric Endocrinology program. Laboratory measurements included 25-OHD, PTH, spot urinary calcium/creatinine ratio (ur ca/cr ratio), and HbA1C. Data collected included gender, ethnicity, weight, height, and BMI (z-score). Patients with a known malabsorptive disorder or parathyroid disease were excluded. Our primary analysis was the relationship between 25-OHD levels and PTH.

RESULTS: Of 135 T1D patients, 122 had PTH and 25-OHD levels. Of these 54.5% were female and 45.5% male . The mean age was 14.8 yrs ± 3.6 (SD) yrs. The mean 25-OHD level was 27.0 ± 10.3ng/ml; 24% had 25-OHD <20 ng/ml, 42% between 20 to 30 ng/ml and 33% > 30 ng/ml. The mean PTH was 34.5 ±14.4pg/ml. Overall, PTH and 25-OHD were inversely associated, adjusting for age, season of sampling, and BMI z-score. PTH declined 0.45 pg/ml with each 1 ng/ml increase in 25-OHD ($p = 0.001$). However, a threshold effect of 25-OHD at 21 ng/ml was observed. Below 21 ng/ml, PTH increased 1.67 pg/ml with each 1 ng/ml decline in 25-OHD ($p = 0.009$), while above 21 ng/ml the association was negligible (-0.18 ng/ml per 1 ng/ml increase in 25-OHD, $p = 0.30$).

CONCLUSIONS: The correlation between PTH and 25-OHD previously seen in adolescent populations was also demonstrated in our pediatric T1D cohort. Our data suggest that children and adolescents withT1D experience a normalization of PTH at a lower level of 25-OHD than adults. Perhaps, the current clinical practice for treatment of children with 25-OHD levels in the "insufficiency range (20-30ng/ml)" may not be warranted in this population.

251

10:00 AM

Fellow in Training

Effects of the GLP-1 Receptor Antagonist Exendin-(9-39) on Postprandial Hypoglycemia after Fundoplasty

Andrew Calabria, Stephanie Givler, Paul Gallagher, Diva De Leon.

Endocrinology, The Children's Hospital of Philadelphia, Philadelphia, PA; Biostatistics Core, The Children's Hospital of Philadelphia, Philadelphia, PA; Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA.

BACKGROUND: Postprandial hypoglycemia (PPH) is a common complication of fundoplasty in children. The mechanism of PPH involves an exaggerated insulin response to a meal, triggered at least in part by early hyperglycemia resulting from rapid gastric emptying. Children with PPH after fundoplasty have higher levels of glucagon-like peptide-1 (GLP-1) after a glucose load compared to controls. We hypothesize that GLP-1 is at least in part responsible for the dramatic postprandial increase in insulin secretion and subsequent hypoglycemia.

OBJECTIVE: To evaluate the effects of the GLP-1 receptor antagonist exendin-(9-39) (ex-9) on blood glucose levels, plasma insulin and glucagon levels, and gastric emptying after a meal challenge in children with PPH after fundoplasty.

DESIGN/METHODS: After an overnight fast, subjects with PPH after fundoplasty underwent a mixed meal tolerance test (10 mL/kg Pediasure®) on 2 consecutive days. Using an open label randomized crossover design, subjects received either an IV infusion of vehicle (0.9%NS) or ex-9 (300 pmol/kg/min) for 4 hours (1 hour before and 3 hours during the meal) on the first day and the alternate treatment on the next day. After the first 3 subjects safely tolerated ex-9, the dose was increased to 500 pmol/kg/min. Samples were taken for glucose, insulin, glucagon, and GLP-1 levels. Acetaminophen (30 mg/kg) was mixed into the formula, and gastric emptying was estimated using the acetaminophen absorption method.
RESULTS: Five subjects with PPH after fundoplasty (7-18 yrs) have been studied to date. Mean glucose area under the curve (AUC) was greater for ex-9 (29106 mg•min/dL) than vehicle (26875 mg•min/dL) with a dose-dependent effect identified for ex-9 (31678 and 27393 mg•min/dL for 500- and 300 pmol/kg/min, respectively). Mean glucagon AUC was greater for ex-9 than vehicle (12876 vs. 11394 pg•min/mL). Mean acetaminophen AUC was greater for ex-9 than vehicle (3245 vs. 2948 mcg•min/mL). Determinations of plasma insulin and GLP-1 levels are pending.
CONCLUSIONS: Antagonism of the GLP-1 receptor by ex-9 raises blood glucose levels in children with PPH after fundoplasty. Our work to date provides further insights into the pathophysiology of GLP-1 in PPH after fundoplasty and shows promise for GLP-1 receptor antagonists as a possible therapy. Ongoing enrollment will further elucidate the metabolic response to antagonism of the the GLP-1 receptor in PPH.

252

10:15 AM

House Officer

Screening Patients with Type 1 Diabetes for Celiac Disease and Hypothyroidism

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BACKGROUND: The American Diabetes Association's (ADA) recommendations for screening type 1 diabetic patients for celiac disease (CD) and hypothyroidism (HT) have changed over the past 5 years. The current recommendation (*Diabetes Care* January 2010) states that children with type 1 diabetes should be screened for CD and HT soon after the diagnosis of diabetes (universal screening) with consideration for periodic rescreening of asymptomatic individuals. With the new recommendation, a pediatric endocrinology practice ceased only symptomatic screening and began screening all diabetics at diagnosis and annually thereafter. This presented a unique opportunity to investigate the prevalence of CD and HT detected by universal screening vs. symptomatic screening.
OBJECTIVE: To determine the prevalence of CD and HT in type 1 diabetic patients, comparing universal to symptomatic screening.
DESIGN/METHODS: Records of a cohort of type 1 diabetic patients less than 21 years of age in a pediatric endocrinology clinic from 2005-2010 were reviewed. Patients were divided into two groups: universal screen and symptomatic screen. The results of screening tests for CD and HT were recorded, as well as the presence or absence of symptoms.
RESULTS: In the universal screen group, 89 patients had 101 thyroid panels and 86 celiac panels; 2.0% (2/101) of thyroid panels were positive for HT and no (0/86) celiac panels were positive for biopsy-proven CD. In the symptomatic screen group, 29 patients had 23 celiac panels and 25 thyroid panels; 4.0% (1/25) of thyroid panels were positive for HT and 8.7% (2/23) of celiac panels were positive for biopsy-proven CD. Symptomatic screening is more efficient at picking up patients with biopsy-proven celiac ($p = 0.043$), but not HT ($p = 0.48$). Symptomatic screening for CD is less costly than universal screening ($2,047 vs. $15,308) per patient identified. Moreover, the $15,308 is an underestimation because universal screening failed to find one biopsy-proven case of CD in this study. Symptomatic screening for HT is less costly per patient identified than universal screening ($6,170 vs. $12,463).
CONCLUSIONS: This preliminary study raises the question whether all newly diagnosed type 1 diabetic patients need to be universally screened for CD and HT at diagnosis and routinely thereafter. There is significant cost associated with universal screening and the cost per diagnosis of disease should be further studied with a larger sample size.

253

10:30 AM

Fellow in Training

Sex Steroids: Better Indices of Pubertal Suppression Than Gonadotropins in Histrelin Treated Patients?

Michelle Klein, Molly Regelmann, Elizabeth Chacko, Sharon Hyman, Dennis Chia, Elizabeth Wallach, Robert Rapaport.
Pediatric Endocrinology, Mount Sinai School of Medicine, New York, NY.

BACKGROUND: Treatment with Histrelin (HT), a depot GnRH analogue implant, was recently approved for pts with central precocious puberty (CPP). Despite clinical evidence of pubertal suppression, we observed a discordance between levels of gonadotropins and sex steroids during HT. Studies of the suppressive effect of HT on non-stimulated LH compared to estradiol(E) and testosterone(T) are lacking, especially in males(M).
OBJECTIVE: Compare the effect of HT on non-stimulated LH to ES and TS.
DESIGN/METHODS: Retrospective chart review of pts with HT for CPP and early and/or rapidly advancing puberty naïve to treatment. LH, FSH, E, and T before(pre) HT and ≥90 days after(post) were assayed(ultrasensitive, Esoterix, CA). Biochemical suppression was defined as prepubertal: LH<0.3 mIU/mL, E<2.0 ng/dL and T<20 ng/dL. Clinical suppression was defined as lack of progression or reversal of breast development in females(F) and testicular volume in M. Bone ages (BA) prior to and after HT[0.5-1 years(yr)] were available in 24 pts.
RESULTS: The age range (mean±SD) yr of 31 pts(15F) was 5.0-13.5(10.4±2.4) in F and 9.7-16.0(12.4±1.9) in M. LH before HT was 0.53-13 mIU/mL in F and 0.87-3.3 mIU/mL in M. All had clinical evidence of pubertal suppression 90 days after HT.

Laboratory Data

Mean±SD	F(15) Pre	Post	M(16) Pre	Post
LH mIU/mL	3.01±3.5	0.33±0.18[a]	1.8±0.65	0.53±0.35[d]
FSH mIU/mL	8.7±12.65	1.31±0.64[b]	2.68±1.84	0.28±0.17[e]
ES/TS ng/dL	3.15±2.92	0.11±0.04[c]	117.8±99.7	8.5±4.8[e]

p value: a=0.003,b=0.02,c=0.0002,d=0.00001,e=0.0001

While significantly lower than baseline, LH was >0.3 mIU/mL in 46% of F and 63% of M during HT even though E and T levels were prepubertal.

Post LH>0.3mIU/mL

Mean±SD	F(7) Pre	Post	M(10) Pre	Post
LH mIU/mL	2.4±1.82	0.48±0.15[f]	1.81±0.65	0.68±0.32[h]
E/T ng/dL	3.27±1.41	0.13±0.03[g]	127.4±110.6	9.4±5.09[i]

p value:f=0.02,g=0.0005,h=0.0008,i=0.002

The mean±SD BA/CA ratio before HT was 1.17±0.26 in F(n=12) and 1.04±0.13 in M(n=12) and after HT 1.15±0.26 in F and 1.02±0.11 in M.
CONCLUSIONS: HT is effective in suppressing puberty in M and F. While the effect on LH was variable, sex steroids were suppressed to prepubertal levels in all suggesting that E and T reflect clinical pubertal suppression better than LH. Our data may also have implications on the mechanism of action of HT.

254

10:45 AM

Fellow in Training

Vitamin D Deficiency Is Associated with Cardiovascular Disease Risk Factors but Not Obesity in Pediatric Type 1 Diabetes

Chelsea Gordner, Chrystal Wittcopp, Nancy Dunbar, Elsina E. Hagan, Holley Allen, Paul Visintainer, Edward O. Reiter.
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BACKGROUND: Previous studies have shown that vitamin D deficiency is common in the population and even more so in those with obesity and diabetes. Data in adults support a link between hypovitaminosis D and obesity, HTN, diabetes, albuminuria and cardiovascular (CV) disease. There is relatively little data on 25-OHD and CV risk factors in children and adolescents with type 1 diabetes (T1D).
OBJECTIVE: To relate 25-OHD and CV risk factors in a cohort of pts with T1D.
DESIGN/METHODS: This was a retrospective chart review of 136 children and adolescents with T1D followed in our Pediatric Endocrinology Clinic. Children ages 2 through 21 with a diagnosis of T1DM and a 25-OHD level measured during the study period were included. Pts with malabsorption, parathyroid disease or non-essential HTN were excluded. Our primary analysis was the relationship between 25-OHD and CV risk factors: HbA1C, BMI, hyperlipidemia, and urine microalbumin.
RESULTS: Mean age was 14.8±3.5 (SD) yrs (47.8% female, 52.2% male). Median BMI% was 78.5% (25^{th}-75^{th}%, 48.8-90.5%) and 35% of pts were > 85^{th} for BMI%. Three pts were on vitamin D supplementation. Ethnicity profile was 72% Caucasian, 16% Hispanic, 7% African American and 5% other. The prevalence of vitamin D insufficiency (25-OHD<30 ng/mL) was 67%. As expected, mean 25-OHD levels were significantly higher in the summer (31.2±12.2 ng/mL) compared to winter (21.2±8.5, $p=0.001$). When adjusted for season, BMI and age, there was a significant inverse correlation between 25-OHD and HbA1C ($r=-0.28$, $p=0.001$) and mean HbA1C was significantly higher ($p<0.001$) when 25-OHD was < 20 ng/mL (9.7%; 95% C.I. (9.2-10.3%)) compared to 25-OHD levels of 20-30 (8.2% (7.8-8.6)) and >30 (8.0% (7.6-8.5)). Total cholesterol ($r=-0.29$; $p=0.002$) and LDL cholesterol ($r=-0.31$, $p=.028$) were also inversely correlated with 25-OHD. There was no association between 25-OHD and BMI z-score, age, HDL, trigs or urine microalbumin.
CONCLUSIONS: In our study of 136 children and adolescents with T1DM, there was an inverse correlation between 25-OHD and HbA1C, total cholesterol and LDL cholesterol which was not impacted by seasonality. In contrast to non-diabetic adolescents, there was no association between 25-OHD and obesity. It is unclear whether normalization of the 25-OHD levels could result in improved glycemic control, a more favorable lipid profile and reduced CV risk.

255

11:00 AM

Fellow in Training

Counter-Regulatory Hormonal Responses to Single vs Recurrent Hypoglycemia and Its Effect on Catecholamine Synthesis

Necla Kirtok, Bistra Nankova, Owen Chan, Edmund F. La Gamma.
The Regional NICU, Maria Fareri Children's Hospital at Westchester Medical Center - NYMC, Valhalla, NY; Internal Medicine, Endocrinology, Yale School of Medicine, New Haven, CT.

BACKGROUND: Hypoglycemia is a common and serious problem in insulin dependent diabetes (IDDM). In acute hypoglycemia, glucagon and epinephrine (Epi) constitute the immediate counter regulatory (CR) responses, whereas cortisol and growth hormone impact within hours-to-days. Insulin blunts the glucagon response and recurrent hypoglycemia attenuates the Epi-release which eventually fails entirely resulting in a condition referred to as hypoglycemia associated autonomic failure (HAAF). Throughout these events, adrenal nerve impulse activity continues to fire suggesting the failure to release originates within the adrenal medulla.
OBJECTIVE: We aim to determine whether the Epi responses to acute and recurrent insulin-induced hypoglycemia correlate with altered adrenal Epi production.
DESIGN/METHODS: 7 days after vascular cannulation of adult male Sprague-Dawley rats (carotid artery for blood sampling & jugular vein for insulin & glucose infusion). The animals were divided into 4 groups: S1 (once daily saline), S2 (twice daily saline), RH1 (once daily hypoglycemia), RH2 (twice daily hypoglycemia).After 3d of treatment, on day 4, all animals underwent a hyperinsulinemic, hypoglycemic glucose clamp for 90 min. Blood glucose was monitored every 5 min (target glucose 40-50 mg/dl), also blood was collected for CR hormones at 0, 30, 60, 90 mins during hypoglycemic glucose clamp. The adrenal medullas were removed for

tyrosine hydroxylase (TH) mRNA analysis (marker for cell capacity to synthesize Epi). Epi levels measured by ELISA and TH mRNA by Northern Blot.
RESULTS: Insulin-induced hypoglycemia increased Epi levels in S1, S2 & RH1 rats, & was also associated with corresponding increase in TH mRNA levels. In contrast, RH2 rats displayed a significant attenuation in Epi response when compared to the other groups. Corresponding TH mRNA levels in the RH2 group were also lower when compared to RH1 group.
CONCLUSIONS: Once daily hypoglycemia does not impair Epi release or the increased TH mRNA response to subsequent hypoglycemia or handling stress. Twice daily hypoglycemia attenuates both Epi release and the TH mRNA levels. This novel finding may represent the molecular explanation of the attenuated Epi response in HAAF. Our observation may enable future pharmacological modification of adrenal medullary responses as adjunctive therapy in diabetic patients to modify the maladaptive response in HAAF.

256

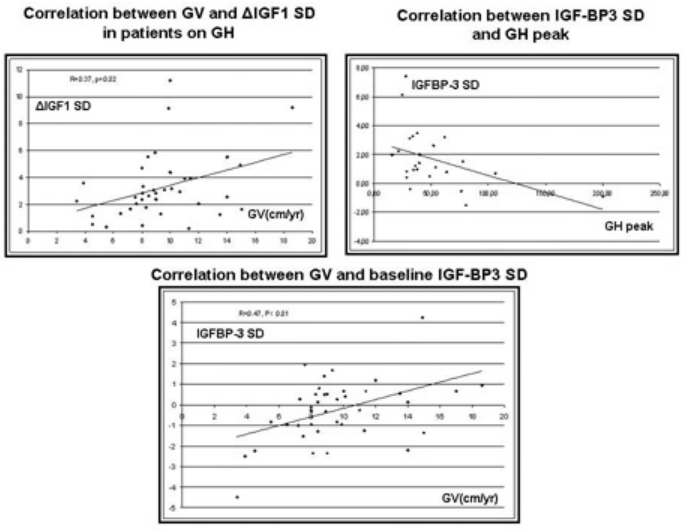
11:15 AM

Fellow in Training

IGF-BP3 Is a Good Predictor of Response to GH and Increlex in Non-GHD Patients with Low IGF1

O. Lazareva, I. Predescu, S. Malik, A. Bhangoo, S. Ten.
Pediatric Endocrinology, State University of New York Downstate Medical Center, Brooklyn, NY; Pediatric Endocrinology, Maimonides Medical Center, Brooklyn, NY.

BACKGROUND: Currently there is no reliable prediction model of response to therapy in patients with growth hormone insensitivity (GHIS). The new data showed that IGFR1 receptor signaling is potentiated by IGFBP-3. In PREDICT study in GHD patients polymorphism of IGFBP3 gene was associated with good response to GH therapy. Combination of low IGF1 and IGF-BP3 was recently recognized as a marker of more severe phenotype of GHIS.
OBJECTIVE: To study relationship of baseline IGF-BP3 and IGF1 and response to GH and IGF1 therapy in patients with normal GH secretion and low IGF1 level.
DESIGN/METHODS: 43 children (age 9.07±2.75 y., Ht -2.72±0.7 SD, baseline IGF1 -2.76±0.58 SD), who passed GHRH stimulation test (>15ng/ml) were included in the study. IGF1 and IGF-BP3 levels were done at baseline and 6 months after GH initiation (0.46±0.1 mg/kg/wk). Patients with poor response to GH (growth velocity (GV) <-1 SD for 6 months, or <7 cm/year), were switched to IGF1 therapy 0.24 mg/kg/d. According to GV patients were divided in 3 groups: **Mild GHI**- responders to GH (n=23, 14 boys), **Moderate GHI**- non-responders to GH, responders to IGF1 (n=14,10 boys), **Severe GHI**- non-responders to either GH/IGF1 (n=6, 5 boys).
RESULTS: There were no differences in age, BW, Ht SDS, IGF1 SD at baseline, IGFBP-3 on GH treatment and GH peaks after GHRH between groups. **Mild GHI** group had higher IGBP3, ΔIGF1, IGF1 after GH treatment, ΔHt SD comparing to others.There was no difference between moderate and severe GHI in IGF1 SD on GH and ΔIGF1 after 6 months of GH therapy, while IGFBP3 and ΔHt SD were higher in moderate than severe. IGFBP-3 correlated with GV(r=0.47, p< 0.01), and inversely correlated with GH peak(r=-0.45, p=0.02).GV correlated with ΔIGF1 SD (r=0.37, p=0.02).



CONCLUSIONS: This pilot data in GHI patients with IGF1<–2 SD revealed that IGF-BP3 is a good predictor of response to GH and Increlex therapy.ΔIGF1 after GH can identify who can benefit from GH or Increlex therapy. In case of low IGFBP-3 and low ΔIGF1 response to either therapy was poor.

257

11:30 AM

BP/Height Ratios: Simple and Accurate Method of Detecting Elevated Blood Pressure in Children

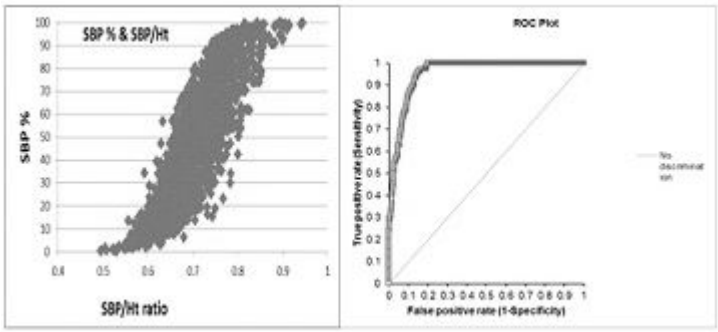
Minu M. George, Sudhakar Basetty, Iuliana Predescu, Anil Mongia, Svetlana Ten, Amrit Bhangoo.
Department of Pediatrics; Division of Pediatric Endocrinology, SUNY Downstate Medical Center, Brooklyn, NY; Department of Pediatrics; Division of Pediatric Endocrinology, Infant's & Children's Hospital of Brooklyn at Maimonides, Brooklyn, NY; Department of Pediatrics; Division of Pediatric Nephrology, SUNY Downstate Medical Center, Brooklyn, NY.

BACKGROUND: Blood pressure (BP) percentiles in childhood are assessed according to age, gender and height. Interpretations of BP values in a busy pediatric office can sometimes be cumbersome.
OBJECTIVE: To study the simplified ratios of BP/height for an accurate detection of elevated BP and to study the correlation of BP/height ratios with BP percentiles.
DESIGN/METHODS: We analyzed data of approx. 3775 children from the NHANES 2005-2006 (*National Health and Nutrition Examination Survey)*. Data on height, weight, waist circumference, BMI, & BP was collected. BMI and BP percentiles were calculated.
Receiver-operating characteristic (ROC) curve analyses were performed to calculate sensitivity and specificity of SBP/Ht and DBP/Ht ratios as diagnostic tests for elevated (>90%) systolic blood pressure (SBP) and diastolic blood pressure (DBP), respectively. Correlation analysis was performed between ratios and percentiles.
RESULTS: The average age was 12.54 ±2.67, range 8-16 years. SBP/Ht and DBP/Ht ratios strongly correlated with SBP percentiles and DBP percentiles in both boys and girls ($p<0.01, R^2=0.80$). The cutoffs of SBP/Ht and DBP/Ht ratios in boys were ≥0.75 and ≥0.46; and in girls the ratios were ≥0.75 and ≥0.48.

Table 1: Shows the ROC analysis of SBP and DBP in boys and girls

	AUC	p value	CI	Cutoff	N	Sensitivity	Specificity
Boys							
SBP	0.95	<0.0001	0.94-0.96	≥0.75	1979	95	83
DBP	0.95	<0.0001	0.87-1	≥0.46	1972	92	91.5
Girls							
SBP	0.96	<0.0001	0.94-0.97	≥0.75	1765	97.2	83.3
DBP	0.99	<0.0001	0.98-0.99	≥0.48	1762	100	95.5

AUC – Area under Curve, CI Confidence Interval, Cutoff- Cutoff value for the ratios, N-Number of children.



CONCLUSIONS: BP/Ht ratios are simple with high sensitivity and specificity to detect elevated BP. These ratios are age independent and can be easily used in everyday care of children.

258

11:45 AM

Fellow in Training

HNF1A Is a Frequent Reason of Insulin Dependant Diabetes in Children with and without Islet Cell Antibodies with Good Response to Sulfonylurea Therapy

Steven Ghanny, Lina Nie, Dujuan Tan, Sheila Perez, Sonal Bhandari, Felicitas Lacbawan, Amrit Bhangoo, Svetlana Ten.
Pediatric Endocrine, Infants and Children's Hospital of Brooklyn at Maimonides and SUNY Downstate, Brooklyn, NY; Molecular Pathology, SUNY Downstate, Brooklyn, NY.

BACKGROUND: Mutations in the HNF1A gene has been seen to cause 58% of monogenic diabetes. This is characterized by an autosomal-dominant inheritance and absence of islet cell antibody. Patients with mutations of HNF1A respond well to sulfonylurea therapy.
OBJECTIVE: To study mutations or deletions in the *HNF1A gene* in insulin dependent diabetes mellitus patients with 3 generations of DM.
DESIGN/METHODS: We evaluated 9 patients with insulin dependant diabetes and autosomal dominant inheritance in 3 generations. We evaluated 2 Hispanics, 1 Ashkenazi Jew and 5 Caribbean Americans. DNA was extracted and protein coding regions of HNF1A were amplified using PCR and sequence analysis was performed.
RESULTS: 7 patients had mutations in HNF1A. 4 of them also had (+) islet cell antibodies.

Table 1

Pt/Ethnicity	FH of DM	Insulin Therapy	Sulfonylurea Therapy	HbA1C at Dx	Current HgbA1C	HNF1A Mutation	
1-Hispanic	FDR (+),SDR (+)	None	None	6	6	E1:c.74C>G,102A>C; E4:c.887G>C	
2-Ashkenazi Jew	FDR (+),SDR (+)	None	Glyburide	8	8.5	E1:c.74C>G, c.316C>T	
3-Caribbean American	FDR (+),SDR (+)	None	Glyburide(15mg)	13.6	5.9	E10: c.1830T>A	
4-African American	FDR (+),SDR (+)	10y	Glyburide(2.5mg)	14	5.9	Intron:(5+65bp) A-T	
5-Caribbean American	FDR (+),SDR (+)	1y	Glyburide(30mg)	16.8	7	E1:c.74C>G	
6-Caribbean American	FDR (+),SDR (+)	5y	Glyburide(40mg)	14.1	6.7	E1: c.166A>T, E7: c.1398C>T, c.1483G>A	
7-Mixed Hispanic	FDR (+),SDR (+)	4y	None	5.7	14	E7: c.1398C>T, c.1483G>A, E10: c.1830T>A	

FDR-first degree relative, SDR-Second Degree Relative

On 2 patients HNF1A was negative. Other mutational analysis is pending. Out of these 7 patients, 5 patients were switched to sulfonylurea therapy(Glyburide). On this therapy, HgbA1C improved in these patients from an average of 12 to 6.7. 3 patients had normalized HgbA1C level. Glyburide was successful in spite of previous insulin therapy from 1-10y.
CONCLUSIONS: Patients with IDM with history of 3 generations of DM with or without pancreatic antibodies should be tested for monogenic diabetes due to high prevalence of mutations in HNF1A in this population and sulfonylurea treatment should be considered in these patients.
Ref: Reference: Hattersley AT, Pearson ER 2006 The Interaction of Therapeutic Response, B-Cell Physiology, and Genetics in Diabetes. Endocrinology 147:2657-2663.

Neurobiology II
Platform Session

Sunday, March 27, 2011
9:45 AM-12:00 PM

259

9:45 AM

Fellow in Training

Mechanism of Ca^{2+}-ATPase Activation during Hyperoxia in Neuronal Nuclei of the Cerebral Cortex of Newborn Piglets

Nicholas Obiri, Kirstie Marcello-Donnelly, Meredith Monaco, Om P. Mishra, Maria Delivoria-Papadopoulos.
Dept. of Pediatrics, Drexel University and St. Christopher's Hospital for Children, Phila, PA.

BACKGROUND: We have shown that hyperoxia results in increased high-affinity Ca^{2+}-ATPase activity in cortical neuronal nuclei of newborn piglets. Clonidine, an inhibitor of Ca^{2+}-ATPase, has been used to target high-affinity Ca^{2+}-ATPase directly, preventing the increased intranuclear Ca^{2+}-influx during hypoxia. We also have shown that induction of Ca^{2+}-ATPase activity during hypoxia is nitric oxide (NO)-mediated. Intranuclear Ca^{2+} drives the transcription of proteins involved in apoptosis.
OBJECTIVE: The present study tests the hypothesis that increased activation of high-affinity Ca^{2+}-ATPase and subsequent increased nuclear Ca^{2+} influx during hyperoxia in cortical neuronal nuclei of newborn piglets is mediated by NO derived from neuronal nitric oxide synthase (nNOS).
DESIGN/METHODS: Nine newborn piglets were divided into three groups of normoxia (Nx, n=3), hyperoxia (Hyx, FiO_2 of 1.0, PaO2 >400mmHg for 1 hr, n=3) and hyperoxia-pretreated with neuronal NOS inhibitor 7-Nitroindazole monosodium salt (Hyx+7-NINA, 1 mg/kg, 30 min prior to hyperoxia, n=3). Cortical neuronal nuclei were isolated and purified, and high-affinity Ca^{2+}-ATPase activity and nuclear Ca^{2+} influx were determined. ATP and phosphocreatine (PCr) content were determined biochemically to document cerebral tissue energy status.
RESULTS: Levels of ATP (µmoles/g brain) were identical at 4.9±1.1 in Nx, 5.1±0.5 in Hyx, and 4.8±0.7 in Hyx+7-NINA (p=NS). PCr (moles/g brain) was 3.3±0.6 in Nx, 3.2±0.5 in Hyx and 3.1±0.4 in Hyx+7-NINA (P=NS). Levels of high-affinity Ca^{2+}-ATPase (nmoles Pi/mg protein/hr) were 500±32 in Nx, 775±37 in Hyx ($p<0.05$, vs. Nx), and 450±34 in Hpx+7-NINA ($p<0.05$ vs. Hyx; p=NS vs. Nx). Nuclear Ca^{2+} concentrations (pmoles/mg protein/min) were 4.77±0.12 in Nx, 9.08±0.14 in Hyx ($p<0.05$ vs. Nx), and 5.79±0.21 in Hyx+7-NINA ($p<0.05$ vs. Hyx; p=NS vs. Nx).
CONCLUSIONS: The increased Ca^{2+}-ATPase activity during hyperoxia is mediated by NO derived from nNOS. We further showed that blocking nNOS results in inhibition of intranuclear Ca^{2+} influx. We speculate that neuronal NO generated during hyperoxia results in modification of the neuronal nuclear membrane with resultant increase in high-affinity Ca^{2+}-ATPase activity. The increase in high-affinity Ca^{2+}-ATPase activity is an important mechanism for increased nuclear Ca^{2+} influx leading to CREB-mediated expression of apoptotic proteins during hyperoxia. (NIH-HD 20337)

260

10:00 AM

Fellow in Training

The Effect of a Common Hemochromatosis Gene Mutation in the Survival of Mice Exposed to Hypoxia

Asha Ittoop, Elizabeth Neely, Wint Nander, Charles Palmer, James Connor.
Pediatrics/Division of Neonatology, Penn State Milton S Hershey Medical Center, Hershey, PA; Neurosurgery, Penn State Milton S Hershey Medical Center, Hershey, PA.

BACKGROUND: H63D mutation involves the Human Hemochromatosis (HFE) gene situated in the short arm of chromosome six. It regulates the iron absorption from GI tract. The H63D variant alters the cellular iron homeostasis and increases the oxidant stress. The increased oxidant stress has been hypothesized as the causative mechanism for the association between this mutation and incidence of neurodegenerative diseases like Alzheimer's & Parkinson's disease. The effect of this mutation in fetus and newborn has not been well studied. We wanted to examine the effect of this mutation in newborns in the presence of a stress, namely hypoxia. We chose hypoxia as our stressor since hypoxic injury is a relatively common stress among newborns.
OBJECTIVE: H63D mutation will adversely affect survival in the setting of hypoxia.
DESIGN/METHODS: We used C57Bl/6 mice for the experiment. Litter size was culled to seven for both wild type and H63D homozygous litters. Average weights of the litters were similar. The mice were exposed to hypoxia by placing them in sealed glass jars connected to an external gaseous supply which provides 8% oxygen balance nitrogen mixture.The jars were then immersed in a water bath set a fixed temperature of 36 degrees. During exposure to hypoxia the mice were observed for mortality at intervals of 10 min for a total duration of 120 min. Total of 6 litters were studied, 3 Wild type litters and 3 H63D homozygous litters forming a total of 42 animals.
RESULTS: Mortality of the mice pups was higher in wild type mice compared to those homozygous for H63D HFE mutation in this model of hypoxia.
We analysed the survival data using Kaplan Meier test and the P value was <0.0001.

Time intervals(min)	H63D/Wild(no: of animals surviving)	Time intervals	H63D/Wild
10	21/21	70	9/2
20	21/21	80	7/2
30	21/21	90	4/1
40	20/18	100	2/0
50	19/8	110	2/0
60	16/3	120	1/0

CONCLUSIONS: Hypoxia induced mortality was higher in wild type mice compared to those homozygous for the H63D HFE mutation.
H63D mutation offers a survival advantage in this mouse model. The data may be consistent with cell culture models that indicate there is mild stress in the cells as a result of the H63D mutation which activate the protective pathways. Long term activation of the stress response may be problematic but at birth based on our studies there appears to be a survival benefit.

261

10:15 AM

Fellow in Training

Effect of Nitric Oxide Synthase Inhibition on Activation of Caspase-9 during Hyperoxia in Newborn Piglets

Meredith L. Monaco, Altina T. Phaire, R. Kirkland Sallas, Om P. Mishra, Maria Delivoria-Papadopoulos.
Dept. of Pediatrics, Drexel University and St. Christopher's Hospital for Children, Phila, PA.

BACKGROUND: Previously we have shown that hyperoxia results in increased activity of caspase-9, the initiator caspase, in the cytosol of the cerebral cortex of newborn piglets. We have also shown that hyperoxia results in production of nitric oxide (NO) free radicals and subsequent nitric oxide mediated modifications of neuronal proteins. NO-mediated modification of apoptosis activating factor-1 (Apaf-1) and procaspase-9 results in increased activation of caspase-9.
OBJECTIVE: The present study tests the hypothesis that caspase-9 activation during hyperoxia is mediated by NO derived from neuronal nitric oxide synthase (nNOS) in the cortex of newborn piglets.
DESIGN/METHODS: Sixteen newborn piglets were assigned to: normoxia (Nx, n=5), hyperoxia (Hyx, n=6), and hyperoxia pretreated with a selective inhibitor of nNOS, 7-nitro indazole-monosodium salt (Hyx+7-NINA, 1 mg/kg i.v., 30 min prior to hyperoxia, n=5). Piglets were exposed to an FiO_2 of 1.0 for two hours while maintaining PaO_2 > 400 mmHg. Normoxic piglets were exposed to an FiO_2 of 0.21 maintaining PaO_2 80-100 mmHg. ATP and phosphocreatine(PCr) were measured biochemically to document cerebral tissue energy status. The cytosolic fraction from the cerebral cortical tissue was isolated and the activity of caspase-9 was determined spectrofluorometrically using a specific fluorogenic substrate for caspase-9 [AC-LEHD-AMC] expressed as nmoles/mg protein/hr.
RESULTS: Levels of ATP (µmoles/g brain) were 4.9±1.1 in Nx, 5.1±0.5 in Hyx, and 4.8±0.7 in Hyx+7-NINA (p=NS). PCr (µmoles/g brain) was 3.3±0.6 in Nx, 3.2±0.5 in Hyx and 3.1±0.4 in Hyx+7-NINA (p=NS). Caspase-9 activity (nmoles/mg protein/hr) was 2.80±0.27 in Nx, 3.51±0.27 in Hyx ($p<0.05$ vs Nx), and 2.70±0.61 in Hyx+7-NINA ($p<0.05$ vs Hyx) group. The data show that administration of nNOS inhibitor prevented the hyperoxia-induced increase in caspase-9 activity.
CONCLUSIONS: The mechanism of caspase-9 activation during hyperoxia is mediated by NO derived from nNOS. NO-mediated modification of the cysteine residue at the active sites of protein tyrosine phosphatases PTP-SH1 and PTP-SH2 results in their inactivation. Tyrosine phosphorylation (negatively charged) of procaspase-9 is thus increased, leading to increased binding with the arginine residue (positively charged) of the caspase recruitment domain of Apaf-1 and subsequent increased activation of caspase-9. (NIH-HD 20337)

262

10:30 AM

Medical Student

Tract Based Spatial Statistics Diffusion Tensor Imaging Shows Anatomic Differences in White Matter Tracts in Subjects with Ornithine Transcarbamylase Deficiency (OTCD)

Nathaniel Robbins, Kyle Shattuck, John vanMeter, Andrea L. Gropman.
Medical Education, Syracuse University School of Medicine, Syrucase, NY; Center for Functional and Molecular Imaging, Georgetown University, Washington, DC; Neurology, Children's National Medical Center and the George Washington University of the Health Sciences, Washington, DC.

BACKGROUND: Ornithine transcarbamylase deficiency (OTCD) is an X-linked urea cycle disorder in which hyperammonemia results in white matter injury and impairments in working memory and executive cognition.
OBJECTIVE: To test for differences in white matter microstructure between patients and healthy controls. Diffusion tensor imaging (DTI) was used to access functional and anatomic connectivity. The fractional anisotropy (FA) is the most common quantitative measure to report white matter microstructural alterations.
DESIGN/METHODS: Subjects included 19 with OTCD and 21 age matched controls. Imaging was performed on a 3.0T Siemens Tim system. Voxelwise statistical analysis of the FA data was carried out using TBSS (Tract-Based Spatial Statistics, part of FSL). First, FA images were created by fitting a tensor model to the raw diffusion data using FDT, and then brain-extracted using BET. All subjects' FA data were then aligned into a common space using the nonlinear registration tool FNIRT, which uses a b-spline representation of the registration warp field. The mean FA image was created and thinned to create a mean FA skeleton which represents the centers of all tracts common to the group. Each subject's aligned FA data was then projected onto this skeleton and the resulting data fed into voxelwise cross-subject statistics.
RESULTS: Several regions demonstrated differences in FA, between subjects with OTCD and controls including areas of the cortical spinal tract, cingulum, callosal body and uncinate fasciculus.

CONCLUSIONS: The results suggest that there are anatomic alterations of white matter in brain regions subserving cognitive functions known to be impaired in OTCD. Thus, DTI is an appropriate measure by which to assess early brain injury, follow disease course and monitor therapies.

263

10:45 AM

Necrostatin-1 Modulates BDNF Levels in Forebrain Following Neonatal Hypoxia-Ischemia

Raul Chavez-Valdez, Lee J. Martin, Devin Mack, Sheila Razdan, Debbie L. Flock, Estelle B. Gauda, Frances J. Northington.

Pediatrics, Johns Hopkins Univ., Baltimore, MD; Pediatrics, Texas Tech Univ.-HSC, Odessa, TX; Pathology and Neuroscience, Johns Hopkins Univ., Baltimore, MD.

BACKGROUND: Necrostatin-1 (Nec-1) blocks progression of delayed neuronal death in the forebrain and thalamus in a mouse model of neonatal hypoxia-Ischemia (HI) (Northington, Chavez-Valdez et al; JCBFM 2010). Although early decrease in protein oxidation and inflammation may account for attenuated neurodegeneration, a necrostatin modulation of neurotophins could support regeneration post HI. In adult rodent models, BDNF levels increase following HI (Orlandini Pereira, Machado Nabinger et al; Brain Res 2009). However, BDNF has a dual effect, with early increase post-HI linked to necrosis (Kim, Hwang et al; Neurobiol Dis 2003) and late increase linked to improved outcomes.

OBJECTIVE: To determine if Nec-1 modulates BDNF levels at early of late stages post- neonatal HI in a mouse model.

DESIGN/METHODS: We used the Vannucci model to induce cerebral HI in C57B6 mice at p7 with unilateral carotid ligation and 45min of hypoxia (FiO_2=0.08). 0.1µl of 80µM Nec-1 or vehicle was injected intracerebroventricularly 15 min after hypoxia. Forebrain tissue was obtained at 3h, 24h and p11 following HI to determine changes in BDNF and neurotrophin receptor (p75 and TrkB) mRNAs (real time RT-PCR) and protein (ELISA and western blot) levels.

RESULTS: BDNF protein levels in forebrain were elevated by 3h post-HI (by >5-fold vs. naive control, p≤0.005) with no difference between vehicle- and Nec-1-treated animals. A ~50% decrease in BDNF levels was observed in both treatment groups by 24h post-HI (vs. 3h). While BDNF levels further decreased in forebrain from vehicle-treated animals by p11 to levels similar to naive controls, BDNF in Nec-1-treated mice were unchanged (p11 vs. 24h) with levels 2.5-fold higher than those of the vehicle group (p=0.05). TrkB and p75 mRNA and protein levels were unchanged at 3h, 24h and p11 post-HI (vs. control) in both treatment groups.

CONCLUSIONS: Nec-1 preserves elevated levels of BDNF in the forebrain during delayed recovery from brain injury post HI while TrkB and p75 expression remain unchanged. The findings are consistent with thalamic protection afforded by Nec-1 following HI (Northington, Chavez-Valdez et al; JCBFM 2010) suggesting preservation of thalamocortical neural networks. We speculate that this preservation of trophic support by Nec-1 could improve regeneration post-HI.

264

11:00 AM

House Officer

Effect of Hyperoxia on Increased Expression of Bax Protein in the Cerebral Cortex of Newborn Piglets

Erica W. Mandell, Qazi Ashraf, Simran Ahluwalia, Om P. Mishra, Maria Delivoria-Papadopoulos.

Dept. of Pediatrics, Drexel University and St. Christopher's Hospital for Children, Philadelphia, PA.

BACKGROUND: Previously we have shown hyperoxia results in increased generation of oxygen free radicals and increased expression of pro-apoptotic protein Bax in the cerebral cortex of newborn piglets. N-acetylcysteine (NAC), an antioxidant and oxygen free radical scavenger, increases intracellular glutathione (GSH) that ameliorates the free radical mediated damage.

OBJECTIVE: The present study tests the hypothesis that hyperoxia-induced increase in Bax protein expression in the cerebral cortex of newborn piglets is oxygen free radical mediated.

DESIGN/METHODS: Newborn piglets were assigned to normoxia (Nx,n=3), hyperoxia (Hyx, n=3), and hyperoxia pretreated with N-acetylcystine (Hyx +NAC, 100mg/kg i.v. 30 min prior to hyperoxia, n=3). ATP and phosphocreatine (PCr) were measured biochemically to determine cerebral tissue energy state. Neuronal nuclei were isolated and nuclear proteins were separated by 10% SDS-PAGE, and determined by Western blot analysis by probing with anti-Bax and anti-Bcl-2 antibody. Complexes were detected by enhanced chemiluminescence, analyzed by imaging densitometry and expressed as absorbance (ODxmm2).

RESULTS: ATP (µmoles/g brain) was 4.7±0.3 in Nx 4.9±0.4 in the Hyx group (p=NS) and 4.28±0.3 in the Hyx+NAC group. PCr (µmoles/g brain) was 4.1±0.3 in Nx and 4.0±0.4 in the Hyx group (p=NS) and 4.2±0.4 in Hyx+NAC group. Density of Bax protein (ODxmm2) was 446.12±67.29 in Nx, 609.16±33.66 in Hyx (p<0.05 vs Nx), and 444.28±6.14 in Hyx+NAC (p<0.05 vs. Hyx). However, there was no significant difference in the density of Bcl-2 protein between the three groups. The data show that N-acetylcysteine administration prior to hyperoxia prevents the hyperoxia-induced increase in the proapoptotic Bax protein.

CONCLUSIONS: Since N-acetylcysteine inhibits hyperoxia-induced increase in Bax protein expression, we conclude that the mechanism of hyperoxia-induced increased in Bax protein is oxygen free radical mediated. Free radicals generated during hyperoxia modify nuclear membrane high affinity Ca^{++}-ATPase leading to increase nuclear Ca^{++}-influx and subsquent activation of CaM kinase IV, resulting in increased CREB phosphorylation and transcription of the pro-apoptotic protein Bax. (NIH-HD 20337)

265

11:15 AM

Fellow in Training

Head Growth and Neurodevelopmental Outcome (ND) in Infants Treated with Head Cooling (SHC)

Raquel Gomez, Marcy Gringlas, Susan Adeniyi-Jones.

Pediatrics, Thomas Jefferson Univ Hosp/AIdHC, Philadelphia, PA.

BACKGROUND: SHC improves ND in infants after hypoxic-ischemic encephalopathy (HIE). Microcephaly (MC) has been associated with poor ND after HIE (Mercuri Peds 2000). Little is known about head growth after SHC and ND.

OBJECTIVE: The objective is to evaluate postnatal head growth in infants after SHC and compare to ND at ≥ 1 yr of age.

DESIGN/METHODS: A retrospective analysis of 87 surviving infants with HIE who were treated with SHC at TJUH from 1/2005 to 12/2009 and were followed to ≥1 yr of age. Included infants were > 36 wks, >1800 g with head circumference (HC) >10th %ile at birth. 9 infants were excluded: no recorded HC (n=6), GA< 36 wks, (n=2), and BW<1800 gm (n=1). HC was measured at birth, at discharge, and serially at 4-6, 9-12, and 24 mo and plotted on the CDC growth chart (2000). MC was defined as HC <10 %ile for age. Bayley Scales of Infant Development III (BSID III) were performed at 12 to 24 mo. Demographic and clinical data were obtained. ND includes the BSID III, diagnosis of cerebral palsy (CP), seizures (Sz), feeding disorder (need for gastrostomy tube), cortical visual impairment (CVI) and sensorineural hearing loss (SNHL).

Statistical analysis included Fisher's exact test.

RESULTS: 78 babies comprised the cohort with a GA of 39 ± 1.6 wks, BW of 3244 ± 521g, male sex 40 (51%) median Apgar score at 5 min = 3, 10 min = 4 (range 0-9), pH 6.97 ± 0.2 and base deficit -19 ± 6.5. Data are mean ± SD. The HC at birth was 34.1 ± 1.8 cm, at discharge (median age 17.5, 6-175 days): 35.2 ± 1.7 cm, at 4-6 mo of life: 41 ± 2.4 cm and at 9-12 mo of life: 44.5 ± 2.2 cm. 32/78 (41%) infants were found to have a HC <10%. MC was present by 6 mo of age in 20/32 (62.5%). Comparison of ND in infants with normal HC and MC is shown in the table.

HC and ND

	Normal HC (n=46), %	MC (n=32), %	p
BSID III <70			
Cognitive	6.5	46.9	<0.0001
Language	6.5	50	<0.0001
Motor	8.7	59	<0.0001
CP	15	59	<0.0001
Sz	8.7	28	0.032
SNHL	2	22	0.0071
CVI	6.5	25	0.0431
Feeding	10.9	37.5	0.0105
≥3 areas of impairment	10.9	50	0.0002

Global developmental delay was present in 50% of infants with MC with PPV 72%, NPV 76%, sensitivity 89% and specificity of 48%.

CONCLUSIONS: In our cohort of 78 infants, poor head growth and MC after SHC were associated with poor ND. Close monitoring of HC may allow for early detection of at risk infants.

266

11:30 AM

Fellow in Training

Interleukin-6 Reduces the Expression of the Tight Junction Protein Occludin in Isolated Cerebral Microvessels from Young and Adult Sheep

Susan S. Cohen, May Min, Erin E. Cummings, Xiaodi Chen, Grazyna Sadowska, Surendra Sharma, Barbara S. Stonestreet.

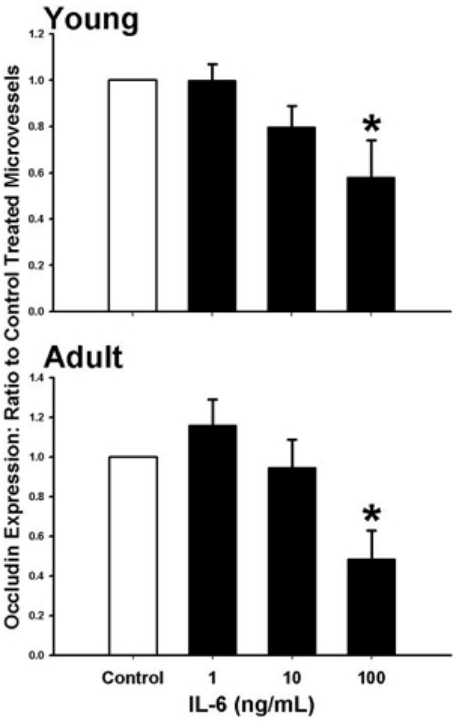
Department of Pediatrics, Women & Infants Hospital, Providence, RI.

BACKGROUND: The blood-brain barrier (BBB) is a selective diffusion barrier that maintains central nervous system homeostasis and is composed of endothelial cells connected by intercellular tight junctions (TJ) that limit the entry of substances that could alter neuronal function. TJs are composed of transmembrane and associated cytoplasmic proteins. Occludin is one of the major transmembrane protein constituents of the TJs. Pro-inflammatory cytokines have been implicated in the genesis of neonatal brain injury and may alter the protein constituents of TJ.

OBJECTIVE: To examine the effect of the pro-inflammatory cytokine interleukin-6 (IL-6) on TJ protein expression using an *in vitro* ovine model of the BBB. We hypothesize that IL-6 down-regulates key protein constituents of the endothelial TJ.

DESIGN/METHODS: Microvessels (MV) from young (n = 5) and adult (n = 5) ovine cerebral cortex were isolated after dissection, homogenization, and filtration. MV were placed into culture, incubated with IL-6 at doses of 0 (control, phosphate buffered saline), 1 (low), 10 (middle) and 100 (high) ng/mL for 24 hours, harvested and preserved for protein analysis by Western immunoblot for occludin. Densitometry was performed and results are expressed as a ratio to control values.

RESULTS: IL-6 treatment reduced occludin expression in cerebral MV from both young (ANOVA: IL-6 dose, $F = 4.09$, $P < 0.05$) and adult sheep ($F = 5.33$, $P < 0.01$). (Fig. Data presented as ratio to control PBS treated. Open bar is control; Closed bars are IL-6 treated. * P<0.05 vs control).



CONCLUSIONS: We conclude that IL-6 decreases occludin expression in cerebral cortical MV from young and adult sheep. We speculate that pro-inflammatory cytokines predispose to brain damage in part by down regulating the TJ proteins of the BBB, impairing BBB integrity and, thereby rendering the BBB more permeable to circulating substances that damage the brain.

267

11:45 AM

House Officer

Effect of Epidermal Growth Factor Receptor (EGFR) Kinase Inhibition during Hypoxia on Phosphorylation of Ca^{++}/ Calmodulin-Dependent Protein Kinase IV (CaM Kinase IV) in Neuronal Nuclei of Newborn Piglets

Mark Michael, R. Kirkland Sallas, David Fralinger, Om P. Mishra, Maria Delivoria-Papadopoulos.

Dept. of Pediatrics, Drexel University and St. Christopher's Hospital for Children, Philadelphia, PA.

BACKGROUND: We have shown that cerebral hypoxia results in increased neuronal nuclear high affinity Ca^{++}-ATPase activity and increased Ca^{++}-influx in neuronal nuclei of the cortex of newborn piglets. We have also shown that hypoxia results in increased activity of CaM kinase IV. CaM kinase IV is a Ca^{++}/calmodulin-dependent enzyme, localized to the nucleus, that phosphorylates cyclic-AMP response element binding (CREB) protein and regulates the transcription of a number of genes leading to either cell survival or cell death.

OBJECTIVE: The present study tests the hypothesis that the hypoxia-induced phosphorylation of CaM kinase IV is mediated by epidermal growth factor receptor (EGFR) kinase-dependent phosphorylation.

DESIGN/METHODS: Fourteen newborn piglets were divided into three groups: normoxic (Nx, n=5), hypoxic (Hx, n =5) and hypoxic pretreated with a selective EGFR kinase inhibitor (PD 168393, 1 mg/kg i.v., 30 min prior to hypoxia, Hx+EGFRKi, n=4). Tissue levels of ATP and phosphocreatine (PCr) were determined biochemically to document cerebral tissue hypoxia. Neuronal nuclei were isolated from the cerebral cortical tissue and nuclear proteins were separated. These were probed with anti-tyrosine phosphorylated CaM kinase IV antibody using Western blot analysis. The bands were detected by chemiluminiscence, analyzed by imaging densitometry and expressed as absorbance.

RESULTS: Brain tissue ATP (μmoles/g brain) was 4.40±0.4 in Nx, 1.51±0.3 in Hx and 1.68±0.4 in Hx+EGFRKi. PCr (μmoles/g brain) was 3.5±0.2 in Nx, 1.3±0.3 in Hx and 1.24±0.3 in Hx+EGFRKi. Density of phosphorylated CaM kinase IV protein (ODxmm^2) was 72.17±3.6 in Nx, 134.17±6.0 in Hx ($p<0.05$ vs Nx), and 80.04±2.7 in Hx+EGFRKi ($p<0.05$ vs Hx). The data show that administration of a selective inhibitor of EGFR kinase prevents the hypoxia-induced increased tyrosine phosphorylation of CaM kinase IV.

CONCLUSIONS: Hypoxia results in increased phosphorylation of CaM kinase IV and the activation of CaM kinase IV is EGFR kinase-dependent. The tyrosine phosphorylation of CaM kinase IV during hypoxia will lead to increased interaction between phosphorylated CaM kinase IV and Arg and Lysine residues of its substrate, CREB protein. Phosphorylated CREB protein will subsequently lead to transcription of pro-apoptotic proteins. (NIH-HD 20337)

Abstract Author Index

Index numerals refer to the Abstract number, not the page number.
Only Presenting Abstract Authors are included in the Index.

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Name	Affiliation(s)/Financial Interest(s) and Organization(s)
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Andersson, Hans	Consultant: Genzyme Corporation, Biomarin & Shire Therapeutics
Cairo, Mitchell	Grants: Genzyme (institution/research team salary) & Celgene (Institution/ research team salary); Consultant: LifeBank USA & LifeLine Cyrogenics; Speakers Bureau: Genzyme, Sigma Tau & Astellas
Carmen, Melissa	Grant, Consultant & Speakers Bureau: Ikaria LLC
De Leon-Crutchlow, Diva	Stock: Merck
Gelb, Bruce	Patents: Patent 1 - PTPN11 Mutations for genetic testing of Noonan syndrome; Patent 2 - SOS1 and RAF1 mutations for genetic testing of Noonan syndrome; Patent 3 - SHOC2 mutations for genetic testing of Noonan-like with loose anagen hair syndrome; Royalties: GeneDx, royalties for gene testing as described in the patent section; Prevention Genetics, royalties for gene testing as described in the patent section; Baylor College of Medicine, royalties for gene testing as described in the patent section; Harvard/Partners, royalties for gene testing as described in the patent section; Correlegan, royalties for gene testing as described in the patent section
Jafri, Hasan	Employee: MedImmune
(Tulane Chair, CME Advisory Committee)	
Kleinpeter, Myra	Speakers Bureau: Pfizer, Boehringer-Ingelheim and GlaxoSmithKline
Lakshminrusimha, Satyan	Grant, Consultant & Speakers Bureau: Ikaria LLC
Lee, Ben	Grants: Celgene (Lab/salary); Consultant: NeoMed, Inc.
Ricci, Angela	Grant & Scientific Advisory Board: Genzyme
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The following presenters have disclosed that their presentations will involve comments or discussion concerning unapproved or off-label uses of a medical device or pharmaceuticals.

Dietz, Hal - Angiotension receptor blockers
Lakshminrusimha, Satyan - Inhaled nitric oxide for use at birth in controls

Notes

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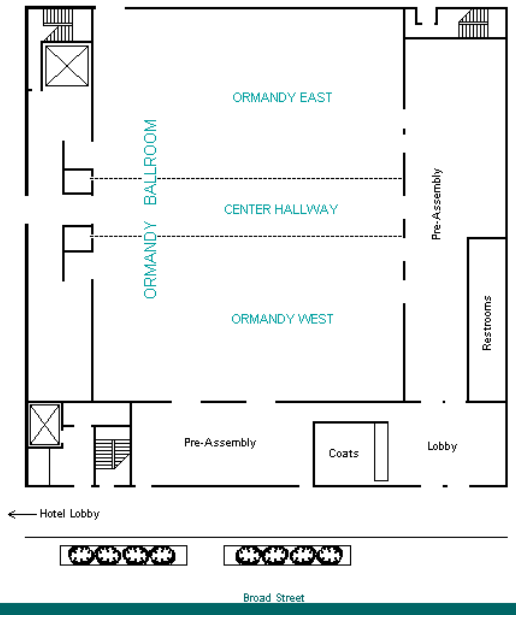

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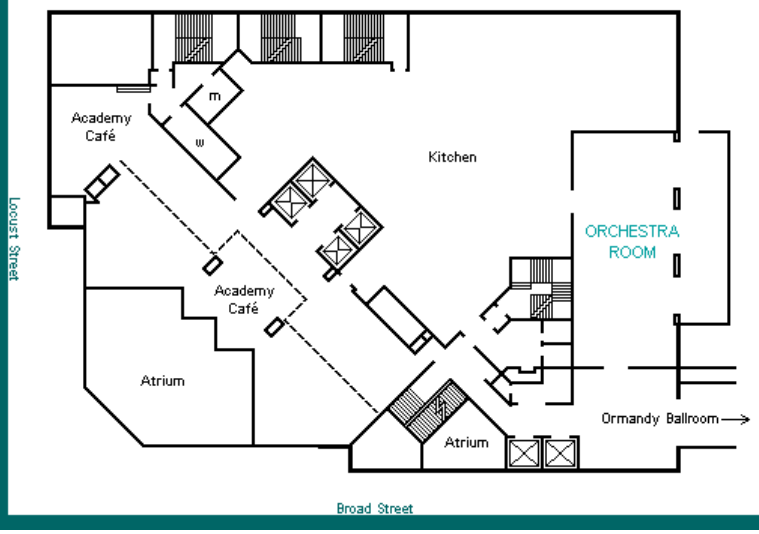

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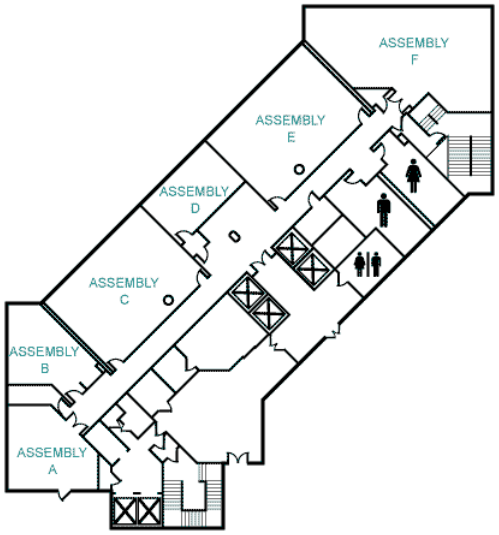

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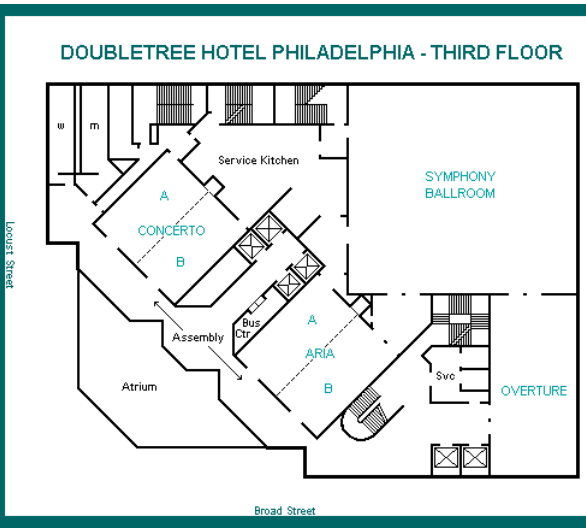

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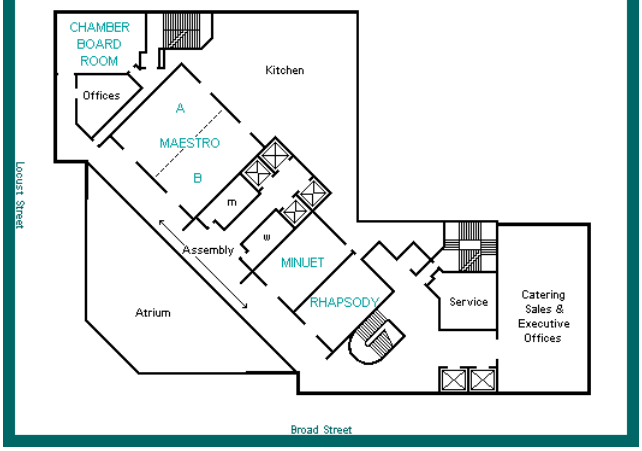

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