



2005 PAS Annual Meeting

Late-Breaker Abstract Presentations

As you plan your meeting itinerary, be sure to include these late-breaking abstract presentations, selected for their high-quality and news-breaking research.

Saturday, May 14

3:15pm–5:15pm

4855 Late Breakers I:

Late Breaking Research in Pediatrics

PAS Platform Session ~ WCC, Room 204 AB

Moderator: Paul Young

3:15* **A Simple Method To Identify GNAS1 Gene Mutation from Peripheral Lymphocytes.** A Tip for Genetic Diagnosis of GNAS1 Related Multiple Endocrinopathies Among Masked Somatic Mosaicism. Katsuki Motomura.
..... (Late-Breaker Abstract 1)

3:30* **Procalcitonin as a Predictor of Vesicoureteral Reflux After a 1st Urinary Tract Infection in Children: European Validation Study.** S. Leroy, C. Romanello, A. Galetto-Lacour, V. Smolkin, B. Korczowski, C. Rodrigo, D. Tuerlinckx, V. Gajdos, M. Contardo, A. Gervaix, R. Halevy, B. Duhl, C. Prat, T. Vander Borght, L. Foix L'Hélias, D. Gendrel, G. Bréart, M. Chalumeau.
..... (Late-Breaker Abstract 2)

3:45 **Live Attenuated Influenza Vaccine (LAIV) Administration in Schoolchildren Coincident with the 2003–2004 Outbreak Provided Herd Immunity Against a Drifted Influenza Variant A/Fujian/411/2002 (H3N2).** Manjusha J. Gaglani, Pedro A. Piedra, Gayla Herschler, Charles Fewlass, W.P. Glezen.
..... (Late-Breaker Abstract 3)

4:00 **Reducing Early Childhood Overweight: Pediatric Practice Results from a Rural Community Intervention.** Barbara A. Dennison, Kathleen F. Sellers, Claire T. Sellers, Ida R. Baker, Patrick A. Burdick.
..... (Late-Breaker Abstract 4)

4:15 **Novel Strategy for Delivering Influenza Vaccine to Household Contacts of Infants Less Than 6 Months Old.** Donna H. Jordan, Ruth A. Merryman, Jane D. Siegel.
..... (Late-Breaker Abstract 5)

4:30 **Medication Errors in Ambulatory Pediatric Patients.** Rainu Kaushal, Donald A. Goldmann, Carol A. Keohane, Melissa Honour, David W. Bates.
..... (Late-Breaker Abstract 6)

4:45 **The Effectiveness of a Pentavalent (Human-Bovine) Reassortant Rotavirus Vaccine (PRV) To Reduce Hospitalizations and Emergency Department (ED) Visits for Rotavirus Gastroenteritis.** R. Itzler, D. Matson, T. Vesikari, M. Coia, J. Cook, G. Davies, P. Heaton, J. Heyse, G. Koch for REST Study Team.
..... (Late-Breaker Abstract 7)

5:00 **Human Coronavirus (HCoV) NL-63 in the Respiratory Tract Is Not Associated with Acute Kawasaki Syndrome (KS).** Jane C. Burns, Hiroko Shike, Chisato Shimizu, Sharon L. Reed, John V. Williams, Susan C. Baker, Vivek R. Nerurkar, Saguna Verma, Richard Yanagihara, Marian E. Melish, Stanford T. Shulman, Anne H. Rowley.
..... (Late-Breaker Abstract 8)

Monday, May 16

3:00pm–5:00pm

6750 Late Breakers II:

Clinical Trials in Neonatology

PAS Platform Session ~ WCC, Room 147

Moderators: Neil Finer and Richard Martin

3:00 **Efficacy and Safety of Methylxanthines in Very-Low-Birth Weight (VLBW) Infants: Preliminary Results from the International Caffeine for Apnea of Prematurity (CAP) Trial.** Barbara Schmidt, Robin Roberts, Peter Davis, Lex Doyle, Keith Barrington, Arne Ohlsson, Alfonso Solimano, Win Tin, The CAP Investigators.
..... (Late-Breaker Abstract 9)

3:15 **Population-Based Study of Neonatal Outcomes Following Prenatal SSRI Exposure Using the BC Health Linked Data.** Tim F. Oberlander, William Warburton, Jaafar Aghajanian, Clyde Hertzman.
..... (Late-Breaker Abstract 10)

3:30 **Multicenter Randomized Double-Blind Placebo Controlled Trial of Ibuprofen L-Lysine Intravenous Solution (IV Ibuprofen) in Premature Infants for the Early Treatment of Patent Ductus Arteriosus (PDA).** J.V. Aranda for the I.V. Ibuprofen-PDA Study Team and for the Pediatric Pharmacology Research Unit Network (NICH-PPRU).
..... (Late-Breaker Abstract 11)

3:45 **Cluster Randomized Trial of Benchmarking To Improve Survival Free of Bronchopulmonary Dysplasia (BPD).** M. Walsh, A. Laptook, S. Buchter, W.A. Engle, M. Rasmussen, S.N. Kazzi, Q. Yao, G. Heldt, W. Rhine, R. Higgins for the NICH- Neonatal Research Network.
..... (Late-Breaker Abstract 12)

4:00 **A Community-Based, Randomized Trial of Newborn Skin Cleansing with Chlorhexidine on Neonatal Mortality in Southern Nepal.** James M. Tielsch, Gary Darmstadt, Luke C. Mullany, Subarna K. Khatri, Joanne Katz, Steven C. LeClerq, Shardaram Shrestha, Ramesh Adhikari.
..... (Late-Breaker Abstract 13)

4:15* **Does the Introduction of Nasal CPAP Improve Respiratory Outcomes in Premature Infants?** Gustavo Pelligrà, Mohamed A Abdellatif, Shoo K. Lee.
..... (Late-Breaker Abstract 14)

4:30 **Randomized Controlled Trial for the Prevention of Intraventricular Hemorrhage by Indomethacin in Japanese Extremely Low Birthweight Infants.** Masanori Fujimura, Shinya Hirano, Satoshi Kusuda, Hirofumi Aotani, Noriyuki Nakanishi.
..... (Late-Breaker Abstract 15)

4:45 **Long-Term Outcomes of the Novel Peptide-Containing Synthetic Surfactant, Lucinactant (Surfaxin[reg]) vs. Animal-Derived and Synthetic, Non-Protein-Containing Synthetic Surfactants in Very Preterm Infants.** Fernando Moya, Sunil Sinha, Janusz Gadzinowski, Robert Segal, Jan Mazela, Carlos Guardia, Genzhou Liu.
..... (Late-Breaker Abstract 16)

* Indicates First Author is a Trainee (Student, Fellow, House Officer)

Late Breakers I: Late Breaking Research in Pediatrics Platform Session

Saturday, May 14

3:15pm-5:15pm

Room 204 AB

1 Presentation Time: 3:15pm Fellow

A Simple Method To Identify GNAS1 Gene Mutation from Peripheral Lymphocytes. A Tip for Genetic Diagnosis of GNAS1 Related Multiple Endocrinopathies Among Masked Somatic Mosaicism

Katsuki Motomura, Department of Developmental and Reconstructive Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki-City, Japan.

BACKGROUND: 'Mosaics' are creatures that have more than one genetically distinct population of cells derived from single zygote, as distinct from chimeras that are formed from more than one zygote. The proportion of cytogenetically abnormal cells in a mosaic is critical for manifestation of various diseases. Recent publications have been reported that the involvement of GNAS1 activating mutations on the pathogenesis of various endocrinopathies including precocious puberty, hyperthyroidism, hyperfunctioning benign tumors in pituitary or adrenal tissues. However it is obvious that mutation detection could be a help for diagnosis, till date, invasive tissue sampling procedures had been an enormous obstacle in the way of genetic diagnosis of mosaicism.

OBJECTIVE: It has been reported that mutated allele exists also in peripheral lymphocytes in very limited amount. To solve the issue of painful procedure, enrichment of the mutated allele derived PCR products by combination of designated PCR primer, restriction enzyme and qualified PCR fragments purification technique was examined.

DESIGN/METHODS: Peripheral blood sampling was executed from 10 patients (7 with typical MAS, 2 with fibrous dysplasia, 1 with PPNAD) with carefully explained informed consent. Genomic DNA was extracted from blood (approx. 200[μl]) with standard procedure. A part of GNAS1 gene Exon8 was cloned by PCR, utilizing restriction enzyme recognition site inserted primer. PCR products were digested by EagI, separated and purified by acrylamide gel electrophoresis. These processes were repeated several times for enrichment of mutated allele derived PCR products, and direct sequencing was performed. No signs of inappropriate backgrounds or contaminations were observed in control study. **RESULTS:** Out of 10 cases, 8 samples have indicated heterozygous mutation (R201C: 6cases, R201H: 2cases).

CONCLUSIONS: However further studies are required, novel method for GNAS1 mutation detection from peripheral lymphocytes have significantly succeeded to identify the mutation from a drop of patient's blood samples. This method could be a help for obtaining a genetic diagnosis of patients, who is suffering from various endocrinopathies, with less invasive technique than conventional method.

2 Presentation Time: 3:30pm Fellow

Procalcitonin as a Predictor of Vesicoureteral Reflux After a 1st Urinary Tract Infection in Children: European Validation Study

S. Leroy, C. Romanello, A. Galetto-Lacour, V. Smolkin, B. Korczowski, C. Rodrigo, D. Tuerlinckx, V. Gajdos, M. Contardo, A. Gervaix, R. Halevy, B. Duhl, C. Prat, T. Vander Borgh, L. Foix L'Hélias, D. Gendrel, G. Bréart, M. Chalumeau, Clinical Epidemiological Unit-Department of Pediatrics, Saint-Vincent-de-Paul Hospital, AP-HP, Faculté Paris V; INSERM U149, Paris, France; Departments of Pediatrics, University of Udine, Udine, Italy; University Hospital of Geneva, Geneva, Switzerland; Ha'Emek Medical Center, Afula, Israël; Regional Hospital n 2, University of Rzeszow, Poland; Germans Trias i Pujol Hospital, Badalona, Spain; UCL Mont-Godinne, Yvoir, Belgium; Antoine Bécélère Hospital, Clamart, France.

BACKGROUND: Febrile urinary tract infection (FUTI) reveals vesicoureteral reflux (VUR) in 20-40% of children. Voiding cystourethrogram (VCUG) is then recommended systematically, but is painful, expensive, exposes to radiation and is a posteriori normal in 60-80% of cases. Then, selective approaches for VCUG are needed. Procalcitonin (PCT), a new inflammatory marker, was shown to be a strong and sensitive predictor of VUR after a 1st FUTI.

OBJECTIVE: To validate a high PCT as a predictor of VUR

DESIGN/METHODS: A retrospective multicentre hospital-based cohort study included all children aged 1 month to 4 years old with a 1st FUTI. Univariate and multivariate analyses were performed.

RESULTS: 398 patients (154 boys) were included in 8 centres in 7 countries, 25% had a VUR. The median value of PCT was significantly higher in children with vs without VUR: 1.6 vs 0.7 ng/mL (p=10-4). After dichotomisation around the previously defined 0.5 ng/mL threshold, there was a significant association between VUR and high PCT [OR=2.3, 95% CI 1.3-3.9, p=10-3]. The relationship was stronger (p=10-4) for grade ≥3 VUR [OR=6.1, 95% CI 2.2-18.3, p<10-4] than for grade 1-2 VUR [OR=1.2, 95% CI 0.6-2.4, p=0.5]. After adjustment with logistic regression for all potential confounders (young age, male gender, positive family history for uropathy, urinary tract dilatation on renal ultrasonography), the association with all-grade VUR remained [ORa=2.4, 95% CI 1.4-4.1, p=10-3]. High PCT sensitivities were 75%, 89% and 100% for all-grade, grade ≥3 and grade ≥4 VUR respectively, with 43% specificities.

CONCLUSIONS: PCT is a strong, independent and now validated predictor for VUR. It could be used to identify patients with low risk for VUR to avoid unnecessary VCUG.

3 Presentation Time: 3:45pm

Live Attenuated Influenza Vaccine (LAIV) Administration in Schoolchildren Coincident with the 2003-2004 Outbreak Provided Herd Immunity Against a Drifted Influenza Variant A/Fujian/411/2002 (H3N2)

Manjusha J. Gaglani, Pedro A. Piedra, Gayla Herschler, Charles Fewlass, W.P. Glezen, Pediatric Infectious Diseases, Scott & White (S&W) Clinic, Temple, TX; Molecular Virology & Microbiology, and Pediatrics, Baylor College of Medicine, Houston, TX.

BACKGROUND: A community-based open-label field trial in Temple, TX has shown that annual LAIV immunization of 20-25% of healthy children aged 1.5 - 18 years significantly reduced medically attended acute respiratory illness (MAARI) in adults aged [gte] 35 years by 8-18%, during three influenza outbreaks (1998-2001).

OBJECTIVE: To determine the indirect effectiveness of community-based LAIV immunization of healthy school-age children (5 - 18 years old) in all persons from all age groups when vaccination occurred coincident with an outbreak.

DESIGN/METHODS: Healthy school-age children from the intervention community were immunized from October to December 2003 with LAIV and those with high-risk conditions received a trivalent inactivated vaccine (TIV). Both vaccines contained influenza A/Panama (H3N2). Age-specific MAARI rates during the influenza outbreak were compared for S&W Health Plan members in the intervention community with those in the comparison communities, where LAIV was not offered. LAIV Indirect Effectiveness was determined as (1- Relative Risk of MAARI) %.

RESULTS: A drifted variant influenza A/Fujian (H3N2) caused an early outbreak in TX (October 12 - December 20, 2003). Of 6569 children who received LAIV, 66% were 5 - 11 years old. 1376 children received TIV. LAIV Indirect Effectiveness was significant for all children < 5 and 5-11 years old, in all adults > 35 years old, and among all ages.

Age Category	<5 years	5-11 years	≥35years	Total
LAIV Effectiveness (95% CI)	5% (1%-8%)	13% (6%-19%)	10% (5%-14%)	10% (7%-12%)

Comparison of weekly MAARI rates for intervention and comparison communities showed marked reduction in rates for all children aged <12 years from the intervention community during the first half of the outbreak.

CONCLUSIONS: LAIV administered to school-age children during an influenza outbreak provided herd immunity against a drifted variant influenza by reducing its spread, possibly from early nonspecific and late specific immunity.

4 Presentation Time: 4:00pm

Reducing Early Childhood Overweight: Pediatric Practice Results from a Rural Community Intervention

Barbara A. Dennison, Kathleen F. Sellers, Claire T. Sellers, Ida R. Baker, Patrick A. Burdick, Research Institute, Bassett Healthcare, Cooperstown, NY; Columbia University, New York, NY.

BACKGROUND: The epidemic of childhood overweight is well recognized.

OBJECTIVE: As part of a multi-dimensional (healthcare, childcare and broader community), socio-ecological intervention to reduce early childhood overweight, the pediatric practice component targeted increased identification of children at-risk (85th<BMI<95th) or overweight (BMI>95th percentile) and improved counseling.

DESIGN/METHODS: The pediatric practice team of 7 providers and 14 nurses in the intervention (INT) community participated in the CDC's training module for BMI screening and three interactive educational sessions addressing barriers related to childhood overweight prevention counseling. At baseline (03/2002 to 03/2003) and F/U (06/2004 to 11/2004), at INT and control (CON; 11 providers and 12 nurses), a random sample of 15-20 charts per provider of children, aged 2-5 years, presenting for preventive care, were reviewed for height, weight, plotted BMI and counseling. Differences in changes over time between INT vs. CON groups were compared using a Z-test for rate differences.

RESULTS: At baseline, 12% (N=149) of INT vs. 0% (N=213) of CON and at F/U, 77% (N=112) of INT vs. 51% (N=150) of CON children, respectively had their BMI-for-age plotted. Between baseline and F/U, the percent of children with plotted BMI increased in both groups, with a 14% (CI: 10.3% to 18.8%) greater increase in INT vs. CON. At-risk and overweight prevalence decreased in INT, from baseline (27% and 29%) to F/U (19% and 14%), vs. no change in CON, from baseline (18% and 11%) to F/U (17% and 15%). There was a greater reduction in prevalence of at risk and overweight children in INT vs. CON of -7% (CI: -8.1% to -5.9%) and -18% (CI: -20.2% to -17.6%). Counseling to improve nutrition and reduce TV viewing was similar in INT and CON. Over time, however, more INT vs. CON providers counseled to increase physical activity (7%; CI: 4.3 to 9.4%), especially among children who were at-risk (32%; CI: 31.1 to 33.2%) or overweight (13%; CI: 16.5 to 18.1%).

CONCLUSIONS: A practice-based intervention to increase awareness, sensitivity and BMI screening was associated with greater recognition of early childhood overweight and increased counseling. This, combined with other community-based activities may have contributed to reductions in prevalence of childhood overweight observed.

Supported by NIH, DK-63460-02.

Late Breakers I: Late Breaking Research in Pediatrics Platform Session

5 Presentation Time: 4:15pm

Novel Strategy for Delivering Influenza Vaccine to Household Contacts of Infants Less Than 6 Months Old

Donna H. Jordan, Ruth A. Merryman, Jane D. Siegel. Children's Medical Center of Dallas, Dallas, TX; University of Texas Southwestern Medical Center, Dallas, TX.

BACKGROUND: Providing Influenza vaccine (IV) to household contacts (HC) of infants < 6 months of age is the primary preventive measure for this high risk group. Children's Medical Center of Dallas (CMCD), a 325 bed, free-standing, teaching, children's hospital, had a surplus of IV in 11/04 since vaccine was given only to the high risk patients according to CDC recommendations issued 10/04.

OBJECTIVE: To provide IV to HC of infants < 6 months of age at the time of their inpatient and outpatient encounters at CMCD.

DESIGN/METHODS: Administrative approval was granted and a rapid non-patient hospital registration process developed to provide vaccine to HC of infants < 6 month old at no cost. Medical, nursing, and clerical staffs were trained and staff instructions were distributed. Consent forms in English and Spanish were designed to facilitate collection of demographic information for the vaccine recipients. Data sheets were collected and data entered into a computerized database by pharmacy personnel. HC of other high risk patients were included after 1/3/05 as recommended by CDC.

RESULTS: 758 doses of IV were given to HC of high risk patients 11/17/04-2/20/05. The largest number of doses was distributed as follows: hospitalists' inpatient service 292 (38.5%); general pediatrics inpatient services 111 (14.6%); primary care clinic staffed by faculty, residents, and nurse practitioner: 96 (12.6%); HIV/low birth weight clinic: 78 (10.2%). Cardiology and Hematology inpatient and outpatient areas combined for 115 (15.2%) of delivery. Of HC vaccinated 494 (65%) were 19-50 years of age (range 6 months to >65 years). 412 (54%) had never received IV. Median number of HC vaccinated per week was 50 (range 4-104) with the peak number in week 6.

CONCLUSIONS: Children's hospitals and pediatrics offices can enhance protection of their patients by providing IV to HC accompanying the pediatric patients, rather than referring them to their own providers. This may be especially important for HC of children < 6 months of age or who are immunosuppressed. Once a system is developed, this strategy is feasible and well accepted.

6 Presentation Time: 4:30pm

Medication Errors in Ambulatory Pediatric Patients

Rainu Kaushal, Donald A. Goldmann, Carol A. Keohane, Melissa Honour, David W. Bates. Medicine, Brigham and Women's Hospital, Boston, MA; Medicine, Children's Hospital, Boston, MA.

BACKGROUND: A previous study found that medication errors were common in pediatric inpatients, but that the rate of serious medication errors was three-fold higher than in adults. Relatively few data are available regarding medication safety in pediatric outpatients. **OBJECTIVE:** To determine the rates, types and consequences of medication errors in the pediatric ambulatory setting.

DESIGN/METHODS: Prospective cohort study of patients under age 21 seen during 2-month study periods at 6 office practices. Data were collected through duplicate prescription review, telephone surveys 10 days and 2 months post visit, and chart review. Medication errors were defined as any error in medication ordering, transcribing, dispensing, administering or monitoring. Serious medication errors, defined as those that posed significant potential for harm (near misses) or actually resulting in harm (preventable adverse drug events) were reviewed, classified and characterized by two independent physician reviewers.

RESULTS: During the study period, 21,209 visits were made by 13,919 patients, of whom 3,589 (26%) received a prescription and were eligible for the survey. Of these, 1,788 (50%) completed the initial survey and 1,239 (69%) completed the second survey. In the cohort of 1788 patients, 2,186 prescriptions were written and 1,794 medication errors were detected. On review of these medication errors, the physician reviewers determined that 464 (26%) posed significant potential for harm to the patient and 57 (3%) actually resulted in harm. Another 1,177 (53%) of the 2,186 prescriptions were judged partially illegible. Overall, 91% of the errors occurred at the prescribing stage, and 8% occurred at the medication administration stage. However, 24% of the potentially harmful and 69% of the harmful errors occurred at the medication administration stage.

CONCLUSIONS: Medication errors are very common in pediatric outpatients. Those that actually result in harm to patients occurred more commonly in the drug administration than the drug prescribing stage, although both prescribing and administration were important.

7 Presentation Time: 4:45pm

The Effectiveness of a Pentavalent (Human-Bovine) Reassortant Rotavirus Vaccine (PRV) To Reduce Hospitalizations and Emergency Department (ED) Visits for Rotavirus Gastroenteritis

R. Itzler, D. Matson, T. Vesikari, M. Coia, J. Cook, G. Davies, P. Heaton, J. Heyse, G. Koch for REST Study Team. Merck & Co, Eastern Virginia Medical School, University of Tampere, University of North Carolina.

Rotavirus (RV) acute gastroenteritis (AGE) is responsible for approximately 2 million hospitalizations worldwide and 223,000 hospitalizations in industrialized countries annually. A live, attenuated orally administered human-bovine reassortant rotavirus vaccine containing 5 reassortants corresponding to human serotypes G1, G2, G3, G4, and P1 was evaluated for its effect on health care contacts (HCCs) due to RV AGE in a double blind, placebo-controlled (1V:1P) study. The efficacy of PRV against RV AGE of any severity caused by all vaccine serotypes (G1, G2, G3, and G4) through the first full rotavirus season was 74.0% [95% CI:66.8,79.9]. Efficacy against severe RV AGE was 98.0% [95% CI:88.3,100.0] (Abstract, ESPID 2005, Vesikari).

During 2001-2004, 70,301 healthy infants 6 to 12 weeks old were enrolled in 11 countries to receive 3 doses of oral PRV or placebo at 4 to 10 week intervals. The case definition of RV AGE was an episode of forceful vomiting and/or >3 watery or looser-than-normal stools within a 24-hour period and rotavirus antigen detection by EIA with confirmation by PCR. Active surveillance for hospitalizations and ED visits for RV AGE was conducted via telephone contact on Days 7, 14, and 42 after each dose and every 6 weeks thereafter for a maximum of two years. The HCC analyses were based on the per-protocol population and only included cases (n=57,134) occurring at least 14 days after Dose 3 and the evaluation of the treatment effect was based on Poisson regression.

The rates of hospitalizations and ED visits for RV AGE among vaccine recipients were reduced by 95.8% and 93.4% compared with placebo recipients.

Comparison of Hospital Admissions and ED Visits
By Treatment Group

Type of HCC	PRV (N=28646)	Placebo (N=28488)	Rate Reduction (95% CI)
Combined Endpoint	20 (1.1)†	357 (19.9)	94.40% (90.9,96.5)
Hospitalizations	6 (0.3)	144 (8.0)	95.80% (90.5,98.2)
ED Visits	14 (0.8)	213 (11.9)	93.40% (88.1,96.3)

†Rate per 1000 child years

N=subjects contributing to analysis of hospital admissions and ED visits

PRV was highly effective in reducing the rate of hospitalizations and emergency visits for RV AGE. These rates are consistent with the clinical efficacy against PBRV for severe disease.

8 Presentation Time: 5:00pm

Human Coronavirus (HCoV) NL-63 in the Respiratory Tract Is Not Associated with Acute Kawasaki Syndrome (KS)

Jane C. Burns, Hiroko Shike, Chisato Shimizu, Sharon L. Reed, John V. Williams, Susan C. Baker, Vivek R. Nerurkar, Saguna Verma, Richard Yanagihara, Marian E Melish, Stanford T. Shulman, Anne H. Rowley. Pediatrics and Medicine, UCSD School of Medicine, La Jolla, CA; Vanderbilt Univ. School of Medicine, Nashville, TN; Microbiology/Immunology, Loyola Univ Stritch School of Medicine, Maywood, IL; Retrovirology Res Lab and Pediatrics, Univ of Hawaii and Kapiolani Med Ctr, Honolulu, HI; Pediatrics, Northwestern Univ. Feinberg School of Medicine, Chicago, IL.

KS is a systemic vasculitis of children for which an infectious trigger is suspected. Recently, an association was reported between KS and HCoV-NH (highly similar to HCoV-NL63; Esper et.al. JID 2005;191).

To investigate the possible association between HCoV-NL63 in the respiratory tract and KS by RT-PCR and viral culture in a geographically and ethnically diverse population. Four U.S. centers collected respiratory samples from December 2000 to February 2005 (68% of samples collected from December-March). A total of 49 samples (34 throat swabs, 8 nasopharyngeal (NP) swabs, and 7 NP scrapings; collected on Illness Day 3-9 pre-IVIG treatment) from 39 pts (age range 4m-10y) were tested among five laboratories by RT-PCR using primer pairs located in the HCoV-NL63 N gene, ORF1b, NH-ORF1a (<http://www.pediatrics.ucsd.edu/kawasaki>). Virus isolation was attempted using CCL-MK2 and Vero E6 cell lines with 0.2% trypsin.

Only 1/39 pts (2.6%) was positive for HCoV-NL63 from an NP swab with all primer pairs tested. Viral isolation from 8 pts including the one PCR + pt was unsuccessful.

Using highly sensitive methods with appropriate positive and negative controls, HCoV-NL63-like sequence was found in the upper respiratory tract of only 1/39 acute KS pts.

Late Breakers II: Clinical Trials in Neonatology Platform Session

Saturday, May 16

3:00pm–5:00pm

Room 147

9 Presentation Time: 3:00pm

Efficacy and Safety of Methylxanthines in Very-Low-Birth Weight (VLBW) Infants: Preliminary Results from the International Caffeine for Apnea of Prematurity (CAP) Trial

Barbara Schmidt, Robin Roberts, Peter Davis, Lex Doyle, Keith Barrington, Arne Ohlsson, Alfonso Solimano, Win Tin, The CAP Investigators, McMaster University, Hamilton, Canada; University of Melbourne, Australia; McGill University, Montreal, Canada; University of Toronto, Canada; University of British Columbia, Vancouver, Canada; James Cook University, Middlesbrough, United Kingdom.

BACKGROUND: Methylxanthines reduce apnea and the need for mechanical ventilation. However, the effects of methylxanthines on common neonatal morbidities, growth and long-term development remain uncertain.

OBJECTIVE: To determine the short-term and long-term benefits and risks of caffeine in VLBW infants.

DESIGN/METHODS: Randomized placebo-controlled trial of caffeine. Infants considered candidates for methylxanthine therapy with BW 500–1250 g were enrolled from 35 centers during the first 10 days of life. The target sample size of 2000 babies was reached in 10/04. Follow up assessments at 18 months (primary outcome) and at 5 years continue. This preliminary analysis of outcomes to first discharge home includes 1982 patients.

RESULTS: Mean (SD) BW was 962 (184) g; mean (SD) GA was 27.4 (1.8) wks; 88% received antenatal steroids. Fewer than 10% of study infants were exposed to “open-label” methylxanthines. BPD rates (O2 at 36 wks) were 35% with caffeine and 44% with placebo; OR 0.7, 95% CI 0.6 to 0.8, $p < 0.0001$. Mean (SE) weight gain was 22 grams (4.8) less during the first 14 days after allocation to caffeine; 95% CI -32 to -13 g, $p < 0.0001$. The rates of death, ultrasonographic signs of brain injury and NEC were similar in both groups. PDA and PDA ligation were added to this analysis by request of the external Data Safety Monitoring Board. Post-randomization PDA rates were 30% with caffeine and 40% with placebo; OR 0.7, 95% CI 0.5 to 0.8; $p < 0.0001$. Rates of PDA ligation were 4% after caffeine and 12% after placebo; OR 0.3, 95% CI 0.2 to 0.5; $p < 0.0001$.

CONCLUSIONS: Caffeine reduces BPD but also weight gain for at least 2 weeks after the start of therapy. Caffeine also has a strong and unexpected beneficial effect on PDA and on the perceived need for PDA ligation.

10 Presentation Time: 3:15pm

Population-Based Study of Neonatal Outcomes Following Prenatal SSRI Exposure Using the BC Health Linked Data

Tim F. Oberlander, William Warburton, Jaafar Aghajanian, Clyde Hertzman, Dept. of Pediatrics, University of British Columbia; Human Early Learning Partnership, University of British Columbia, Vancouver, BC, Canada.

BACKGROUND: Prenatal exposure to selective serotonin reuptake inhibitors (SSRI) antidepressants has been associated with altered birth outcomes and behaviors suggesting a “withdrawal” syndrome. A population-based incidence of prenatal exposure and neonatal outcomes remains unknown.

OBJECTIVE: To determine a population-based incidence of prenatal SSRI exposure, to describe birth outcomes following gestational exposure and to compare outcomes with non-SSRI exposed infants using linked health data.

DESIGN/METHODS: Maternal health and birth outcomes were linked to records of all prenatal maternal prescriptions for psychotropic drugs, including SSRIs, to generate a perinatal-exposure data set covering all live births in British Columbia (BC) (1998–2001). Outcomes from infants of depressed SSRI treated mothers (SE) were compared to outcomes from infants of depressed, not medication-treated mothers (DE) and healthy controls (C). We also used propensity score matching and instrumental variables to control for potential confounders.

RESULTS: Of a total of 120,672 live births, the incidence of prenatal SSRIs exposure during any trimester increased from 2.3% to 4.1% (1998–2001). Birth weight and gestational age for SE infants were less (44 grams and 0.39 weeks; $p < 0.01$, respectively), and an increased proportion had neonatal respiratory distress compared with C infants (12.9% vs. 8.7%; $p < 0.01$). Birth weight and gestational age among DE infants were also reduced when compared with C infants ($p < 0.01$). Differences in gestational age and the incidence of respiratory distress remained when SE and DE group outcomes were compared ($p < 0.01$, respectively). After controlling for measured differences between SE and C infants using instrumental variables and propensity score matching, differences between SSRI exposure and birth weight were no longer significant; however, the effect on gestational age and increased respiratory distress remained.

CONCLUSIONS: Using population-based linked health data, the incidence of prenatal SSRI use increased 78% over a 4 year period in BC. Prenatal SSRI exposure reduced gestational age and increased the incidence of neonatal respiratory distress, even after controlling for potential confounders and the effects of exposure to maternal depression alone. Further work is needed to examine the clinical implications, pharmacological, medical and social variables associated with these findings.

11 Presentation Time: 3:30pm

Multicenter Randomized Double-Blind Placebo Controlled Trial of Ibuprofen L-Lysine Intravenous Solution (IV Ibuprofen) in Premature Infants for the Early Treatment of Patent Ductus Arteriosus (PDA)

J.V. Aranda for the I.V. Ibuprofen–PDA Study Team and for the Pediatric Pharmacology Research Unit Network (NICHHD-PPRU), Children’s Hospital of Michigan, Detroit, MI. BACKGROUND: The ductus arteriosus remains patent in about 40% to 80% of very low birth weight infants. Early treatment with IV ibuprofen has been suggested to be safe and efficacious in closing the PDA.

OBJECTIVE: To compare the efficacy and safety of IV ibuprofen with placebo for the early treatment of PDA in preterm infants with evidence of ductal shunting by an echocardiogram (ECHO).

DESIGN/METHODS: In a multicenter randomized double-blind controlled trial involving 15 sites, 136 infants (GA < 30 weeks; BW 500 – 1000 g) were allocated to receive a 3-day treatment course of 10 mg/kg, 5 mg/kg, and 5 mg/kg of IV ibuprofen (n= 68) or placebo (saline) (n= 68) within 72 hours after birth. Cerebral ultrasound was performed on the day closest to study day 4 and 14. ECHO was performed on study day 1 (baseline) and on study day 14. PDA ligation, potential side effects (renal, cerebral, respiratory gastrointestinal) and perinatal characteristics were recorded. Infants were followed to 36 weeks adjusted GA. The primary outcome was the proportion of infants that required rescue treatment for PDA (indomethacin or surgery) on or prior to study day 14.

RESULTS: 136 preterm infants (BW 500 to 1000 g) were enrolled. Demographic data (mean \pm SD) are: Birth Weight 798 \pm 130.3 g; Gestational Age 26.2 \pm 1.4 weeks; and Age at 1st Dose of Study Drug 1.4 \pm 0.7 days. There were 51% Males and 49% Females. The study has not yet been un-blinded, however the results of efficacy and safety including the percentages of death, PDA ligation, intraventricular hemorrhage, necrotizing enterocolitis, daily fluid intake/output, liver function, bronchopulmonary dysplasia, and retinopathy of prematurity will be presented at the meeting. Preliminary review of data prior to unblinding shows a very significant difference ($p < 0.01$) in the primary outcome between the two groups.

CONCLUSIONS: This is the first multicenter trial of Ibuprofen L-Lysine completed in the United States for purposes of having an FDA approved therapy for early treatment of PDA. Preliminary review of data suggests significant difference in primary outcome between two groups (placebo and drug) which will be reported at the meeting.

(Supported by Farmacon-IL and Abbott Laboratories)

12 Presentation Time: 3:45pm

Cluster Randomized Trial of Benchmarking To Improve Survival Free of Bronchopulmonary Dysplasia (BPD)

M. Walsh, A. Luptook, S. Buchter, W.A. Engle, M. Rasmussen, S.N. Kazzi, Q. Yao, G. Heldt, W. Rhine, R. Higgins for the NICHHD Neonatal Research Network.

BACKGROUND: Because BPD rates differ among centers we proposed that emulating practices of best performing centers (BPC), known as benchmarking; together with multimodal quality improvement (QI) could reduce BPD.

OBJECTIVE: To determine if benchmarking and QI improve survival free of BPD compared to usual practice.

DESIGN/METHODS: In Yr 1, 17 centers collected baseline data and outcomes for inborns with bwt < 1250g. 3 centers with lowest BPD were identified as ‘best’ and others randomized to intervention (n=7) with teams (MD, RN, RT) trained in QI, or control (n=7). Teams observed each BPC and noted low ventilating pressures, lower O2 sat limits, and tolerance of brief desaturation. In Yr 2–3, intervention teams changed practices, and received data feedback and support every 4–6 wk. Primary outcome was survival w/o BPD by physiologic definition at 36 wk comparing Yr 1 to Yr 3. Mixed models adjusted for bwt, sex, race, antenatal steroid, GA < 26 wk, and center clustering.

RESULTS: Potentially better practices (5–13 /center; median 6.5) included early surfactant, primary CPAP, reduced oxygen targets, limited PIP, aggressive weaning, limited IV fluids. Bench centers successfully adopted interventions (median 75%, range 40–100%). Despite successful changes, survival free of BPD, respiratory support and IVH were similar. Results varied by center (Survival free of BPD OR 0.37 – 1.93); 4 centers improved (2 in each group). At 2 centers in < 26wk GA survival free of BPD (OR 0.15, 95%CI 0.02–1.01; OR 0.20, 95% CI 0.04, 0.96) was reduced by an interaction between interventions and GA.

	Intervention		Control		p
	Yr 1 (n=626)	Yr3 (n=594)	Yr 1 (n=777)	Yr 3 (n=854)	
Surv w/o BPD %	63.2	62.1	62.7	62.7	0.99
Vent/CPAP, d	23 \pm 23	22 \pm 23	26 \pm 24	24 \pm 23	0.64
Mortality, %	14.7	15.8	12.5	13.7	0.66
IVH 3/4, % 14.4	18.3	13.4	14.1	0.35	

CONCLUSIONS: During an era of rapid respiratory care change despite changing practice, overall benchmarking unfortunately did not improve survival free of BPD, mortality or major morbidity compared to control. Individual centers did improve. Future studies of respiratory interventions should monitor results by gest age.

Supported by the NICHHD.

13 Presentation Time: 4:00pm

A Community-Based, Randomized Trial of Newborn Skin Cleansing with Chlorhexidine on Neonatal Mortality in Southern Nepal

James M. Tielsch, Gary Darmstadt, Luke C. Mullany, Subarna K. Khatri, Joanne Katz, Steven C. LeClerq, Shardaram Shrestha, Ramesh Adhikari. Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; NNIPS, Kathmandu, Nepal; Institute of Medicine, Kathmandu, Nepal.

BACKGROUND: Sepsis remains a leading cause of neonatal deaths in developing countries especially in home delivery settings. A trial in Malawi demonstrated that vaginal cleansing and newborn washing with a dilute chlorhexidine solution could reduce early mortality by approximately 20%. We evaluated whether newborn skin cleaning alone could work in a community setting.

OBJECTIVE: To determine the efficacy of a single skin cleansing with 0.25% chlorhexidine solution in the first few hours after birth on neonatal mortality and morbidity in a high risk population in southern Nepal.

DESIGN/METHODS: The design was a cluster randomized, placebo controlled, community-based, trial conducted between September 2002 and February 2005 among newborn infants delivered to women living in the study catchment area in Sarlahi District. Infants were randomized in clusters to receive a cleansing with normal baby wipes (Wipesters®, Procter & Gamble Co.) or Wipesters® impregnated with 0.25% chlorhexidine solution within the first few hours after delivery. The primary outcome was neonatal mortality. Infants were followed on days 1,2,3,4,6,8,10,12,14,21, & 28 for vital status and morbidity. The analysis was conducted according to intent to treat using person-time and survival analytic approaches.

RESULTS: 15,855 newborns were enrolled and followed through 28 days of life. The median time to newborn wash was 5.7 hours after birth. Overall, there was a non-significant 11% reduction in neonatal mortality in the chlorhexidine group (RR=0.89, 95% CI:0.72,1.11). However, there was a 29% reduction among low birthweight infants (RR=0.71, CI:0.54,0.95) and no impact on infants 2500 g or above (RR=1.14, CI:0.75,1.73).

CONCLUSIONS: A single cleansing of newborn skin with 0.25% chlorhexidine reduced neonatal mortality among low birthweight infants by 29%. Inclusion of this intervention in safe birthing kits is feasible and appropriate to improve neonatal survival.

14 Presentation Time: 4:15pm

Follow

Does the Introduction of Nasal CPAP Improve Respiratory Outcomes in Premature Infants?

Gustavo Pelligra, Mohamed A Abdellatif, Shoo K. Lee. Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada.

BACKGROUND: Nasal CPAP (nCPAP) is widely used for a range of neonatal respiratory conditions. It is established as an effective method of preventing extubation failure and in the management of apnea of prematurity. Despite the lack of evidence, nCPAP has been introduced in neonatology practice as an alternative to intubation and mechanical ventilation in infants with respiratory distress syndrome, based on the assumption that nCPAP will produce a significant decrease in adverse respiratory outcomes.

OBJECTIVE: To determine changes in the use of mechanical ventilation and incidence of bronchopulmonary dysplasia (BPD), defined as need for supplemental oxygen at 28 days old, subsequent to the increased use of nCPAP.

DESIGN/METHODS: Data from n=2002 neonates, with gestational age <32 weeks, admitted to the NICU at BC Children's Hospital between June 1996 and August 2004 and followed prospectively until death or discharge from hospital were analyzed. Characteristics of the study population, respiratory therapies and respiratory outcomes were compared between 2 consecutive time periods (Period 1: June 1996-May 2000; and Period 2: June 2000-August 2004), before and after introduction of early nCPAP in our NICU.

RESULTS: Characteristics of the study population between the 2 periods were similar, except for proportion of outborns (18% vs 23%, p=0.005) and deliveries by caesarean section (49% vs 56%, p=0.001). A significant increase in the use of nCPAP was noted between period 1 to 2 (53% vs 63%, p<0.001), as well as a significant reduction in the use of exogenous surfactant (51% vs 42%, p<0.001) and need for mechanical ventilation (79% vs 65%, p<0.001). There was a significant reduction in the incidence of BPD (34% vs 28%, p=0.007). The difference persisted after adjustment for death (44% vs 37%, p=0.001). The number of infants who required supplemental oxygen at 36 weeks postconceptional age did not differ between groups (12% vs 14%, p=0.1).

CONCLUSIONS: A significant increase in nCPAP therapy in our unit has been associated with a decrease in the use of more invasive therapies. Incidence of BPD has also decreased, although the number of infants who remain on supplemental oxygen at 36 weeks postconceptional age did not change.

15 Presentation Time: 4:30pm

Randomized Controlled Trial for the Prevention of Intraventricular Hemorrhage by Indomethacin in Japanese Extremely Low Birthweight Infants

Masanori Fujimura, Shinya Hirano, Satoshi Kusuda, Hirofumi Aotani, Noriyuki Nakanishi. Neonatal Research Network Japan, Osaka, Japan.

BACKGROUND: Prophylactic indomethacin (IND) has been shown to reduce the severe intraventricular hemorrhage (IVH) in extremely low birthweight (ELBW) infants. A large randomized controlled trial with neurological function as a primary endpoint showed no relevant benefit. These conclusions need to be tested in Japanese population where the neonatal care and outcome may differ. This is the report on IVH as the primary endpoint and the neurological function at 18 months and 3 years remains to be continued.

OBJECTIVE: To study the efficacy and complications of low dose IND in the reduction of severe IVH and later neurological function in Japanese ELBW infants.

DESIGN/METHODS: A multicenter prospective randomized placebo controlled trial was conducted in 21 Level III neonatal intensive care units in Japan. Newborn infants with birthweights between 400-1000 g were randomized into IND or placebo groups. On case registration the robot system on the Internet stratified for unit, one-min Apgar score, gestation, gender, and in/out born. Starting within 6 hours of birth 3 doses of IND or placebo were given with 6 hour continuous infusion every 24 hours. INDs were administered at the dose of 0.1 mg/kg/dose.

OUTCOME MEASURES: The primary outcome measure was the occurrence of grade III or IV IVH.

RESULTS: Among 718 infants assessed for eligibility 117 infants meeting the exclusion criteria and 132 refused to participate were excluded. Out of 469 eligible newborn infants, 235 infants received IND and 234 were controls. Mean birth weight (sd) for IND/control groups were 775.2 g(130.6)/784.0 g(139.8)(NS). Perinatal characteristics were similar between the groups. Number of death was 18 (7.7%) for IND and 24 (10.3%) for control groups (NS). IVHs (III or IV) were significantly less in infants who received IND (n=15, 6.4%) compared with controls (n=32, 13.7%)(p=0.013). The incidence of PDA was lower in the IND group(n=75, 31.9%) compared with controls (n=125, 53.4%) (p<0.001). No significant difference was noted in adverse events between the groups.

CONCLUSIONS: Indomethacin prophylaxis significantly reduced the severe form of IVH in Japanese ELBW infants without the risk of increase in adverse events.

16 Presentation Time: 4:45pm

Long-Term Outcomes of the Novel Peptide-Containing Synthetic Surfactant, Lucinactant (Surfaxin[reg]) vs. Animal-Derived and Synthetic, Non-Protein-Containing Synthetic Surfactants in Very Preterm Infants

Fernando Moya, Sunil Sinha, Janusz Gadzinowski, Robert Segal, Jan Mazela, Carlos Guardia, Genzhou Liu. Dept. of Pediatrics, Univ. of Texas Health Science Center at Houston, Houston, TX; James Cook University Hospital, Middlesbrough, UK; Poznan Univ. of Medical Sciences, Poznan, Poland; Discovery Laboratories, Warrington, PA.

BACKGROUND: We have reported results of two randomized, controlled trials comparing lucinactant (Surfaxin®), a new generation, peptide-based synthetic surfactant, with non-protein-containing synthetic colfosceril (Exosurf®) and bovine-derived beractant (Survanta®) (SELECT trial; N=1294, Moya F, et al. Pediatrics.2005:April;115(4) in press), and with porcine-derived poractant (Curosurf®) (STAR trial; N=252, Sinha S, et al. Pediatrics.2005:April;115(4) in press) for prevention of respiratory distress syndrome (RDS). In the SELECT trial, Surfaxin significantly reduced the incidence of RDS at 24 h, RDS-related mortality at 14-d and bronchopulmonary dysplasia (BPD) at 36 wks post menstrual age (PMA) compared with Exosurf, and RDS-related mortality vs. Survanta. The STAR trial demonstrated similar results for 28-day and 36-wks survival without BPD for Surfaxin and Curosurf.

OBJECTIVE: To compare long-term outcomes including mortality and morbidity at 1-year corrected age for Surfaxin vs. animal-derived and non-protein-containing synthetic surfactants across the STAR and SELECT trials.

DESIGN/METHODS: Infants with gestational age of 24-32 wks and birth weight (BW) of 600-1250 g were randomized to treatment with Surfaxin (175 mg/kg), Exosurf (67.5 mg/kg), Survanta (100 mg/kg), or Curosurf (175 mg/kg). An analysis of outcomes through 1-year corrected age across the two studies was performed for all randomized patients. Treatment differences were compared using the Wilcoxon test, stratified by BW strata, country, gender, and race.

RESULTS: At 1-year corrected age, survival still favored Surfaxin (73.4%) vs. the animal-derived surfactants (71.2%; p=0.05) and Exosurf (69.0%), observations consistent with the difference in all-cause mortality at 36 wks PMA for Surfaxin-treated patients (20.3%) vs. the animal-derived products (24.1%; p=0.01), and Exosurf (23.8%). Overall health and gross neurological outcomes (cerebral palsy, gross tone or reflex abnormality, deafness, blindness, seizures, and gross motor delay) trended in favor of Surfaxin over the comparator surfactants.

CONCLUSIONS: The early survival advantage observed through 36-wks PMA in premature infants treated with Surfaxin compared with animal-derived surfactants as well as a synthetic, non-protein-containing surfactant was maintained through 1-year corrected age.