

NEONATOLOGY TODAY

News and information for BC/BE Neonatologists and Perinatologists

Volume 1 / Issue 2
June 2006

INSIDE THIS ISSUE

**Fetal Magnetocardiography-
An Exciting New Technique
for the Diagnosis and
Management of Fetal
Arrhythmias**

by Joel D. Temple, MD
~Page 1

**Highlights from the 28th
Annual Tiny Baby
Conference—February 2-4,
2006**

by Alan R. Spitzer, MD
~Page 7

DEPARTMENTS

**Medical Meetings, Symposiums
and Conferences**
~Page 4

**Clinical Trials—Neonatal and
Perinatal Medicine**
~Page 5

**Medical News, Products and
Information**
~Page 10

NEONATOLOGY TODAY

9008 Copenhaver Drive, Ste. M
Potomac, MD 20854 USA
tel:+1.301.279.2005
fax: +1.240.465.0692
www.NeonatologyToday.net

Neonatology Today (NT) is a monthly newsletter for BC/BE neonatologists and perinatologists that provides timely news and information regarding the care of newborns and the diagnosis and treatment of premature and/or sick infants.

© 2006 by Neonatology Today

Published monthly. All rights reserved. Statements or opinions expressed in Neonatology Today reflect the views of the authors and sponsors, and are not necessarily the views of Neonatology Today.

Neonatology Today would like to share your interesting stories or research in neonatology and perinatology.

Submit a brief summary of your proposed article to:

Article@Neonate.biz

FETAL MAGNETOCARDIOGRAPHY - AN EXCITING NEW TECHNIQUE FOR THE DIAGNOSIS AND MANAGEMENT OF FETAL ARRHYTHMIAS

By Joel D. Temple, MD

Fetal arrhythmias are estimated to occur in 1-2% of gestations. The majority of these are PVCs and PACs which are generally considered benign. More serious arrhythmias can occur including SVT, atrial flutter, and VT. Management of fetal arrhythmias has been limited by our inability to effectively monitor and diagnose them. The gold standard has been Doppler M mode echocardiography which can demonstrate the timing of atrial and ventricular contractions. Echo, however, does not give information about the electrical activity of the heart and is labor intensive. The fetal ECG can be obtained from the maternal abdomen, but there are significant artifacts in the form of both myopotentials and the maternal ECG. Of particular interest, the maternal ECG (based on voltage potential) does not attenuate and is 10-100 times as strong as the fetal signal. In addition, useful signals are difficult to obtain after 27 weeks, probably due to the insulating properties of the vernix caseosa. Fetal magnetocardiography (fMCG) is a new technique that is particularly useful for evaluating fetal arrhythmias.

When an electric or ionic current flows through a conductor, a magnetic field is generated perpendicular to the current.

As cardiac tissue depolarizes, small currents are generated across the advancing wave front and consequently, an electromagnetic field is generated perpendicular to the current. This field can be detected and is the basis of fMCG. The field generated by the fetal heart is on the order of 0.5-10 pT, or approximately one millionth the strength of the earth's magnetic field. By comparison,



Figure 1. SARA, consisting of 151 gradiometers arranged to comfortably fit the gravid abdomen.

More medicine,
less volume.



For more information,
please call 1-800-755-5560
or visit www.dey.com

Curosurf is a registered trademark of Chiesi Farmaceutici.

 © 2006 DEY®
B9-766-00 06/06
Printed in USA

 **chiesi**
Manufactured by and licensed from:
Chiesi Farmaceutici, S.p.A., Parma, Italy 43100



Figure 2. (A) Raw tracing demonstrating both fetal and maternal tracings. Maternal signals are marked with blue arrows. Fetal signals are marked with red arrows. (B) Fetal signal after attenuation of maternal signal using orthogonal projection.

“One clear advantage of fMCG is that the signal strength is inversely proportional to the square of the distance from the source.”

the maternal signal is approximately 50 pT. The device used to measure these biomagnetic fields is called a Superconducting Quantum Interference Device or SQUID magnetometer. SQUIDs must be super-cooled and shielded from all electromagnetic interference.

One clear advantage of fMCG is that the signal strength is inversely proportional to the square of the distance from the source. Consequently, if the receiver is placed close to the fetus, the maternal signal will be considerably smaller. The University of Arkansas for Medical Sciences has developed a specialized array called SQUID Array for Reproductive Analysis or SARA. SARA consists of 151 magnetometers arranged to fit the gravid abdomen. The patient leans forward onto the array while seated (Figure 1). There is no trauma to the fetus and minimal discomfort to the mother and extended recording periods are possible.

Background noise is filtered using a first order gradiometer (magnetometer). The maternal signals are identified and averaged using template matching and the maternal signal is attenuated using a technique called orthogonal projection. The result is a signal that is analogous to a surface ECG (Figure 2). If further resolution is needed, signal averaging can be performed.

Fetal magnetocardiography offers some exciting possibilities including the more accurate diagnosis of fetal



**Introducing the iE33 intelligent echo system ...
for better visualization of congenital heart defects**

Learn more at:
www.medical.philips.com/iE33
or call 800-229-6417

PHILIPS

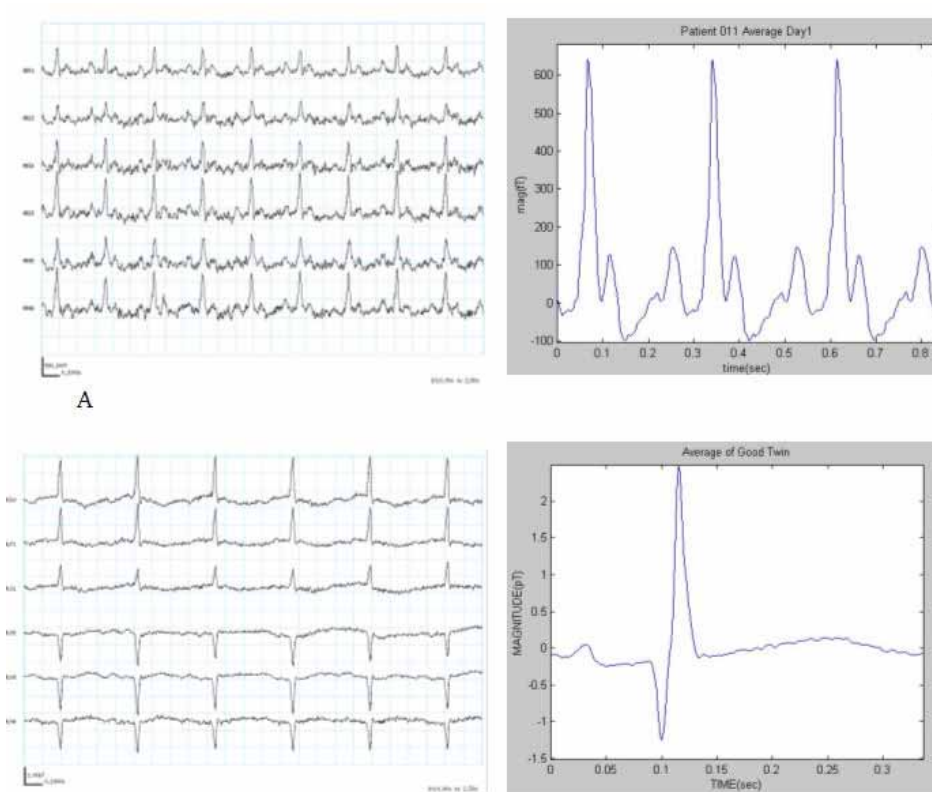


Figure 3. (A) FMCG of a twin "A" in atrial flutter with signal averaged ECG. (B) FMCG of twin "B" in sinus. Recordings were obtained simultaneously.

arrhythmias, monitoring for fetal toxicity with drugs such as Flecainide, Sotalol, and Amiodorone leading to safer use of antepartum antiarrhythmics, and prenatal diagnosis of channelopathies such as the Long QT syndrome without the need for amniocentesis.

This technology is currently expensive and cumbersome due to the need for super cooling and electromagnetic shielding. However, work is currently under way towards the development of a "high" temperature SQUID that does not require super cooling.

Fetal magnetocardiography is a safe non-invasive technique allowing monitoring of fetal heart rhythm and providing information and a degree of resolution not previously obtainable (Figure 3). The particular design of SARA allows extended monitoring without apparent harm or discomfort to the mother or fetus. As fmCG becomes more widely available, I believe it will have a significant impact on the way we diagnose and manage fetal arrhythmias.

Editor's Note: "Fetal Magnetocardiography—An Exciting New Technique for the Diagnosis and Management of Fetal Arrhythmias" by Joel D. Temple, MD was first published in the Pediatric Cardiology Today, a sister publication to Neonatology Today.

■ NT



Joel D. Temple, MD, FACC, FAAP
 Assistant Professor of Pediatrics
 Director Pediatric Electrophysiology
 University of Virginia
 Charlottesville, VA USA
 Phone: +1 (434) 924-9119
 Fax: +1 (434) 924-5656
 JDT4M@hscmail.mcc.virginia.edu

MEDICAL MEETINGS, SYMPOSIUMS AND CONFERENCES

Obstetric Challenges for Contemporary Practice 2006
 September 29, 2006; Denver (Bloomfield) CO USA
www.pediatrix.com

2006 AAP National Conference & Exhibition
 October 7-10, 2006; Atlanta, GA USA
<http://s12.a2zinc.net/clients/aap2005/aap2005/public/enter.aspx>

Europaediatrics
 October 7-10, 2006; Barcelona, Spain
www.kenes.com/europaediatrics/

NANN 22nd Annual Educational Conference—Neonatal Nursing Excellence: Growing and Knowing
 November 8-11, 2006; Nashville, TN USA
www.nann.org/i4a/pages/index.cfm?pageid=803

30th Annual Neonatal International Symposium – Neonatology 2006
 November 8-11, 2006; Miami Beach, FL USA
neonatology.med.miami.edu/conference/default.htm

Hot Topics in Neonatology 2006
 December 2-5, 2006; Washington, DC USA
www.hottopics.org

NEO-The Conference for Neonatology
 February 7-10, 2007; Orlando, FL USA
www.neoconference2007.com/

Get your event listed for free. Send an email to Meeting@Neonate.biz. Be sure to include the event name, location, dates and website.

CLINICAL TRIALS—PERINATAL AND NEONATAL MEDICINE

Use of Sucrose to Relieve Pain During Eye Exams in Infants**More Information**

Study ID Numbers: 0412007634
 Last Updated: September 11, 2005
 Record first received: September 8, 2005
 ClinicalTrials.gov Identifier: NCT00161694
 Health Authority: United States: Institutional Review Board
 ClinicalTrials.gov processed this record on 2005-11-16

This study is currently recruiting patients

Sponsors and Collaborators: Weill Medical College of Cornell University

Purpose: The purpose of this study is to see if an oral sucrose solution can comfort premature infants during their necessary eye exams. We believe that the use of this solution prior to the eye exams will lead to a decrease in pain as measured by rise in heart rate and fall in oxygen saturation. In addition this will lead to a decrease in events in the 12 hours following examination. Events include episodes when an infant temporarily stops breathing, has a drop in heart rate, or has a drop in oxygen levels.

Condition: Apnea of Prematurity; Retinopathy of Prematurity; Pain Control

Treatment or Intervention: Drug- sucrose solution

Study Type: Interventional

Study Design: Prevention, Randomized, Double-Blind, Placebo Control, Crossover Assignment, Efficacy Study

Eligibility: Ages 5 Weeks and above; both male and female

Criteria:

Inclusion Criteria: All premature infants admitted to the Neonatal Intensive Care Unit requiring serial dilated examinations to assess for retinopathy of prematurity will be candidates for this study. This includes all infants with a birth weight of less than 1500g and infants between 1500g and 2000g who require supplemental oxygen.

Exclusion Criteria: Any infant who is unable to safely suckle 0.5cc of fluid will be excluded from the study. This includes infants that are being maintained on ventilators and those with serious gastrointestinal complications that may be exacerbated by an oral fluid bolus. Any infant being maintained on narcotics for any reason will not be eligible for the study. All infants with major congenital anomalies will be excluded.

Location and Contact Information: Please refer to this study by ClinicalTrials.gov identifier NCT00161694

Tamara L Rousseau, MD; 212-746-3530;
tlrousseau2001@yahoo.com; NYPH- Weill Cornell Medical Center, New York, New York, 10021, United States

Study chairs or principal investigators: Tamara L Rousseau, MD, Principal Investigator, Neonatology Fellow at NYPH-Weill Cornell Medical Center

Study to Test the Pain-Relieving Effect of Laughing Gas in Infants**More Information**

Study ID Numbers: 05-04-029-01
 Last Updated: November 7, 2005
 Record first received: November 7, 2005
 ClinicalTrials.gov Identifier: NCT00250692
 Health Authority: United States: Institutional Review Board
 ClinicalTrials.gov processed this record on 2005-11-16

This study is currently recruiting patients

Sponsors and Collaborators: University of California, Los Angeles; UCLA Department of Neonatology

Purpose: to study infants in the Neonatal Intensive Care Unit (NICU) who are undergoing a heel stick for blood sampling, a standard procedure in patient care. Currently, these infants do not get any pain relief for this procedure. Several recent clinical studies have shown the usefulness of nitrous oxide (laughing gas) for treating pain for minor procedures in children 0 to 18 years, but these effects have not been exclusively studied in the newborn and infant populations. Animal studies have questioned the anti-nociceptive (pain-blocking) effect of nitrous oxide in very young animals. It is unclear if this also applies to humans. The reason for this difference may be due to an immaturity of the neural pathways that modulate pain in the very young. The purpose of this study is to investigate whether or not nitrous oxide has an analgesic (pain-relieving) effect in infants undergoing minor procedures in the neonatal period (less than 3 months).

Condition: Analgesic Affect

Treatment or Intervention: Drug: Nitrous Oxide

Phase III

Study Type: Interventional

Study Design: Randomized, Single Blind, Active Control, Single Group Assignment

Eligibility: Ages up to 3 Months, Both Genders

Criteria:

Inclusion Criteria: Full-term babies up to three months old scheduled for heel stick blood draw.

Exclusion Criteria: preterm, difficult airway (micrognathia, craniofacial malformation, choanal atresia, Pierre Robin syndrome, or Treacher Collins syndrome), sedated, intubated (including tracheostomy), have an oxygen requirement (FiO₂>40%), anemia, bone marrow suppression, or cardiac defect

Location and Contact Information: UCLA Medical Center, Los Angeles, California, 90095, United States; Recruiting; Samuel Wald, MD, Principal Investigator 310-206-0085; swald@mednet.ucla.edu

Study chairs or principal investigators: Samuel Wald, MD, Principal Investigator, UCLA Department of Anesthesiology

Study of MEDI-524 (Numax), for the Prophylaxis of Serious Respiratory Syncytial Virus (RSV) Disease in High-Risk Children

More Information

Study ID Numbers: MI-CP110
 Last Updated: November 4, 2005
 Record first received: August 29, 2005
 ClinicalTrials.gov Identifier: NCT00129766
 Health Authority: United States: Food and Drug Administration
 ClinicalTrials.gov processed this record on 2005-11-16

This study is currently recruiting patients

Purpose: The primary objective of this study is to compare the safety and efficacy of MEDI-524 to palivizumab when administered monthly by intramuscular (IM) injection for the reduction of the incidence of RSV hospitalization among children at high risk for serious RSV disease.

Condition: Respiratory Syncytial Virus Infections

Intervention: Drug: MEDI-524

Phase III

Study Type: Interventional

Study Design: Prevention, Randomized, Double-Blind, Active Control, Parallel Assignment, Safety/Efficacy Study

Further Study Details: Primary Outcomes: The primary objective of this study is to compare the safety and efficacy of MEDI-524. Secondary Outcomes: To compare the incidence of medically-attended lower respiratory illnesses (LRIs) between treatment groups; To compare the incidence of RSV-specific medically-attended LRI in a subset of patients; To compare the frequency and incidence of medically-attended otitis media (OM) infections between treatment groups; To compare the frequency of prescribed antibiotics for medically-attended LRI and medically-attended OM infections; To describe the trough serum concentrations of MEDI-524; To describe the immunogenicity of MEDI-524

Eligibility: Ages 6 Months - 24 Months, both Genders

Criteria:

Inclusion Criteria:

- 24 months of age or younger at randomization (child must be randomized on or before his/her 24-month birthday) with a diagnosis of chronic lung disease (CLD) of prematurity requiring medical intervention/management (i.e., supplemental oxygen, bronchodilators, or diuretics) within 6 months before randomization—or
- 35 weeks gestational age or less at birth and 6 months of age or younger at randomization (child must be randomized on or before his/her 6-month birthday)

Exclusion Criteria:

- Hospitalization at the time of randomization (unless discharge is anticipated within 10 days)
- Mechanical ventilation or other mechanical support (including continuous positive airways pressure [CPAP])
- Life expectancy < 6 months
- Active RSV infection (a child with signs/symptoms of respiratory infection must have negative RSV testing)
- Known renal impairment or hepatic dysfunction
- Chronic seizure or evolving or unstable neurologic disorder
- Congenital heart disease [CHD] (children with uncomplicated CHD [e.g., patent ductus arteriosus (PDA), small septal defect] and children with complicated CHD that are currently anatomically and hemodynamically normal can be enrolled)
- Known immunodeficiency
- Mother with HIV infection (unless the child has been proven to be not infected)
- Known allergy to Ig products
- Receipt of palivizumab, RSV-IGIV, or other RSV-specific monoclonal antibody, or any other polyclonal antibody (for example, hepatitis B IG, IVIG, VZIG) within 3 months prior to randomization
- Anticipated use of palivizumab or IVIG during the study (blood transfusions permitted)
- Previous receipt of RSV vaccines
- Participation in other investigational drug product studies

Location and Contact Information: This study is recruiting throughout the world

Guisela Torres; 301-398-4222; torresg@medimmune.com

Study chairs or principal investigators: Genevieve Lonsosky, MD, Study Director, MedImmune, Inc.

■ NT

ClinicalTrials.gov (www.clinicaltrials.gov)

*A service of the National Institutes of Health;
 Developed by the National Library of Medicine*

The information provided herein is from the ClinicalTrials.gov. ClinicalTrials.gov provides regularly updated information about federally and privately supported clinical research in human volunteers. Please see ClinicalTrials.gov for the additional detail and the most updated information.

HIGHLIGHTS FROM THE 28TH ANNUAL TINY BABY CONFERENCE - FEBRUARY 2-4, 2006

By Alan R. Spitzer, MD

The 28th annual Tiny Baby Conference was held this year at Disney World in Orlando, Florida, at the Boardwalk Resort. This meeting, started in 1978 by Drs. Willa Drummond and Gregor Alexander, is one of the longest running meetings of its type in the United States and has been jointly sponsored by The University of Florida and Arnold Palmer Children's Hospital. This year, however, marks the final edition of the Tiny Baby Conference in its current form. In February 2007, Pediatrix Medical Group will join the meeting sponsors as one of the primary organizers and the conference will morph into the newly titled, "NEO-the Conference for Neonatology," and be extended by a day. The meeting will be a great focal point for discussion of the major issues in Neonatal-Perinatal Medicine and have a series of world-class speakers for both physicians and nurses. In addition, the great resources of Walt Disney World will be utilized for a series of evening events that promise to provide a great experience for all participants.

At this year's Tiny Baby, the quality of the meeting once again reached its usual high standards, with a series of interesting and controversial presentations that attempted to address some of the critical issues in newborn care. On the first day of the conference, Joseph Neu, MD, Professor of Pediatrics at the University of Florida, discussed our current understanding of the primary factors involved in neonatal necrotizing enterocolitis (NEC). In a brilliant in-depth review of the topic, Dr.

Neu reviewed the variability and complexity of this disease, identifying those factors most likely to result in NEC. Immune factors, inflammatory mediators, the possible role of antireflux therapy, especially H2 blockers, circulatory issues, the possible role of indomethacin, the bacteriology of NEC, as well as numerous other factors, were all carefully evaluated and presented, as well as new avenues of therapy including probiotics. Probiotics refer to non-pathogenic bacteria specifically introduced into the newborn intestine during

"This year...marks the final edition of the Tiny Baby Conference in its current form. In February 2007, Pediatrix Medical Group will join the meeting sponsors as one of the primary organizers and the conference will morph into the newly titled, 'NEO - the Conference for Neonatology....'"

feeding that may reduce the likelihood of NEC. Following this review, Elizabeth Beierle, MD, Assistant Professor of Surgery from the University of Florida, examined NEC from the surgeon's perspective, providing a fascinating view of how this entity appears to the surgeon, what factors seem to precipitate NEC, and what surgical interventions are

appropriate under a variety of clinical circumstances.

The remainder of the morning then shifted to the neurological assessment and treatment of the NICU patient. Seetha Shankaran, MD, Professor of Pediatrics at Wayne State School of Medicine and Chief of Neonatology at the Children's Hospital of Michigan, reviewed the pathophysiology of neuro-



Dr. Seetha Shankaran, MD, Professor of Pediatrics, Wayne State University.

logical injury in both the term and pre-term infant. Dr. Shankaran presented the superb data collected over many years by the NIH Neonatal Network, of which her institution is a member, examining the factors that appear to provoke intracranial hemorrhage (ICH) in the very low birth weight infant, as well as the complications of this event. She also examined the antenatal factors involved

Do You Want to Recruit a Neonatologist or a Perinatologist?

Advertise in Neonatology Today.

For more information, call 301.279.2005 or send an email to:

Recruitment@neonate.biz

www.NeonatologyToday.net



Dr. Gregor Alexander, MD, Chief of Pediatrics, Arnold Palmer Hospital and Dr. Alan Spitzer, MD, Pediatrix Medical Group.

in this entity, pointing out that our understanding of the etiology of ICH has changed significantly during the past several years, with antepartum factors increasingly being identified as provocative for both ICH and periventricular leukomalacia (PVL) in the neonate. In particular, antepartum infection appears to be a critically important component of the development of ICH and PVL in the premature infant. Dr. Shankaran also examined the role of selective head and body cooling in the treatment of perinatal hypoxic-ischemic injury in the neonate. She cited the exciting work being done in this area and the ongoing studies which will, hopefully, reveal the precise role of this therapy in the armamentarium of the neonatologist.

The presentations of the first day were completed by Alan Spitzer, MD, Director of Research and Education for Pediatrix Medical Group, who discussed the emerging technique of Cerebral Function Monitoring in the care of the neonatal patient. Dr. Spitzer identified the

value of this technique in monitoring normal brain development in the premature infant, as well as the effects of injury, both to the term and pre-term neonate. By following the amplified, integrated EEG recording (aEEG), an improved assessment of the status of brain function can be monitored and a more selective course of therapy can emerge.

The second day of the meeting began with a presentation by Reese Clark, MD, Director of Neonatal Research at Pediatrix Medical Group, on normal blood pressure in neonates. Dr. Clark examined the results of data obtained from the extraordinary Pediatrix Medical Group database, which has information on more than 530,000 neonates. He also demonstrated the effects of pressor medication on the recorded blood pressure in the neonate. This presentation was followed by an outstanding talk by Mark Polak, MD, Associate Professor Pediatrics at West Virginia University, on the role of volume therapy, dopamine, and other pressors in trying to establish an appropriate blood pressure for the neonate. Dr. Polak pointed out that the




Dr. Reese Clark, MD, Director of Research Pediatrix Medical Group.



Dr. Joseph Neu, MD, Professor of Pediatrics, University of Florida.

neonatologist is often overly aggressive in trying to achieve levels of blood pressure and that it is inappropriate to simply chase numbers while ignoring the clinical circumstances and examination of the neonate. He suggested a more moderate approach that appeared to have great merit behind it.

The second day's sessions were concluded by a series of superlative discussions by Ronald Clyman, MD, Professor of Pediatrics at the University of California at San Francisco, and Carl Bose, Chief of the Division of Neonatal-Perinatal Medicine at the University of North Carolina, that assessed the role of the patent ductus arteriosus (PDA) in neonatal care. Drs. Clyman and Bose examined the PDA from somewhat different perspectives, and came to different conclusions about the urgency of ductal closure in the very premature infant. An excellent question and answer session followed, which revealed the complexity of



**Children's
Cardiomyopathy
Foundation**

In support of infants, children and teens with pediatric cardiomyopathy

CHILDREN'S CARDIOMYOPATHY FOUNDATION

P.O. Box 547, Tenafly NJ 07670

Tel: 201-227-8852 info@childrenscardiomyopathy.org www.childrenscardiomyopathy.org

"A Cause For Today.... A Cure For Tomorrow"



Dr. David Auerbach, MD, Director of Neonatology, Arnold Palmer Hospital.

the issue of ductal closure and the uncertainty that surrounds the optimal management approach to the problem.

Day Three of the Tiny Baby Conference began with discussions of safety and risk management issues in the neonatal intensive care unit (NICU) from Julie Williams, Risk Manager for Women and Newborn Services at Arnold Palmer Hospital for Children and Women, and Robert Ursprung, MD, a neonatologist in the Pediatrix Medical Group practice at Cook Children's Medical Center in Fort Worth. Dr. Ursprung is also Co-Director of Quality Improvement for Pediatrix Medical Group. Ms. Williams reviewed the potential sources of problems in the NICU and the need for unbiased and blame-free approaches to patient safety issues. Dr. Ursprung reviewed additional sources of error and how systems may fail in the course

of neonatal care. Dr. Ursprung presented his work on random audits, an outstanding technique for the identification, review, and prevention of error in the NICU.

These discussions were followed by a return of Dr. Carl Bose, who examined the processes and roles of perinatal inflammation in the etiology of neonatal diseases such as periventricular leukomalacia (PVL), bronchopulmonary dysplasia (BPD), and cerebral palsy. The importance of antenatal inflammation has become increasingly important in the modern era and there are now strong data to implicate inflammation in both preterm delivery, as well as neurological and pulmonary injury in the neonate. Dr. Bose's presentation was further supported by Dr. Alan Spitzer, who addressed the additional issues that appear to provoke neonatal injury beyond peri-



Dr. Ronald Clyman, MD, Professor of Pediatrics, University of California, San Francisco.



Dr. Frederick Miller, MD, Regional President Pediatrix Medical Group

natal inflammation such as hypo- and hypercarbia.

The conference was closed by Dr. Robert Christensen, Director of Neonatology Research for Intermountain Health Care and Medical Director of Neonatology at McKay-Dee hospital in Ogden, Utah. Dr. Christensen spoke about the great value of multi-center research programs and presented some of the highly significant work ongoing at Intermountain Health-care in such areas as bilirubin assessment, retinopathy of prematurity, and maternal drug use during gestation. This talk rounded out another outstanding Tiny Baby Meeting, which will become an even more exciting meeting next year as it expands to NEO-the Conference for Neonatology.

■ NT

Alan R. Spitzer, MD
Senior Vice President and Director
The Center for Research and
Education
Pediatrix Medical Group
1301 Concord Terrace
Sunrise, FL 33323 USA
Phone: 954-384-0175, Ext. 5660
Fax: 954-851-1957
Pediatrix University:
www.pediatrixu.com

AlanS@Neonate.biz



Barth Syndrome
Foundation

The Barth Syndrome Foundation

P.O. Box 974, Perry, FL 32348

Tel: 850.223.1128 info@barthsyndrome.org www.barthsyndrome.org

Symptoms: Cardiomyopathy, Neutropenia, Muscle Weakness, Exercise Intolerance, Growth Retardation

MEDICAL NEWS, PRODUCTS AND INFORMATION

Newborns are Unable to Mount an Effective Immune Response to Most Vaccines

Newswise — Newborn babies have immature immune systems, making them highly vulnerable to severe infections and unable to mount an effective immune response to most vaccines, thereby frustrating efforts to protect them. Researchers at Children's Hospital Boston now believe they have found a way to enhance the immune system at birth and boost newborns' vaccine responses.

In a study published in the April 25, 2006 online edition of the *Journal of Blood*, Ofer Levy, MD, PhD and colleagues in Children's Division of Infectious Diseases show that the newborn immune system functions differently than that of adults, but that one portion of the immune response is fully functional and can be harnessed to boost immunity in these tiny infants, possibly making infections like respiratory syncytial virus, pneumococcus, pertussis, HIV and rotavirus much less of a threat.

For about a decade it's been known that the first line of defense against infection is a group of receptors known as Toll-like receptors (TLRs) on the surface of certain white blood cells. Functioning like an early radar system, TLRs detect the presence of invading bacteria and viruses and trigger production of "danger signals" — proteins known as cytokines that trigger other immune cells to mount a defense against the infection. People have 10 different kinds of TLRs, and Levy's team decided to examine how well they function in newborns by studying white blood cells from their cord blood.

"We found that when most Toll-like receptors are stimulated, newborns' immune responses are very impaired," Levy says. "But there was one important exception."

Levy's team, including Harvard graduate Eugenie Suter and senior author Michael

Wessels, MD, showed that one TLR, known as TLR8, triggered a robust immune response in a group of white blood cells (called antigen-presenting cells) that is crucial for vaccine responses. When TLR8 was stimulated by various agents that mimic viral antigens, the cells produced normal, adult levels of two key cytokines — TNF-alpha and IL-12 — and another immune-system stimulant, CD40.

"These findings suggest that agents that stimulate TLR8 could be used to enhance immune responses in newborns, perhaps as adjuvants given along with vaccines," Levy says. "We plan to test this approach in animals, and eventually in human babies."

Levy notes that the ability to vaccinate newborns — rather than wait until they reach 2 months of age — would provide important global health benefits. "Birth is a point of contact with healthcare systems," he says. "Families may not see a health care provider after that. From a global health perspective, if you can give a vaccine at birth, a much higher percentage of the population can be covered."

Conceivably, TLR8 stimulators could also be given alone in special circumstances — to help a baby fight off an infection in progress, or as a preventive measure in the event of a disease outbreak or bioterrorist threat, Levy adds.

Levy's team is uncovering other differences between the newborn and adult immune systems that could lead to additional targets for drugs or vaccines. A related paper, to be published soon in the journal *Pediatric Research*, finds that when newborns' TLRs are stimulated during the first week of life, their white cells' production of the cytokine IL-6, which inhibits parts of the immune response, is greater than that in adults.

A third study, to be published in the *Journal of Immunology*, finds that newborns' cord blood also has high levels of adenosine, providing an explanation for newborns' altered immune response: adeno-

sine alters the physiology of white cells to suppress production of TNF-alpha (but not of IL-6) when TLRs are stimulated. When Levy's team used antagonists to inhibit adenosine's activity, newborns' white blood cells produced normal, adult levels of TNF-alpha in response to bacterial and viral triggers. "In the future, we could try to block adenosine in newborn animals to see if this helps protect against infection," Levy says.

Levy believes the differences his team has uncovered in newborns' immune response patterns may serve an evolutionary purpose. Nature may suppress babies' production of inflammatory cytokines like TNF-alpha and IL-12 before birth because they can trigger preterm labor, while increasing production of adenosine and IL-6, which may have a protective effect on the pregnancy.

The current study was funded by the National Institutes of Health and the Patterson Trust. For more information visit: www.childrenshospital.org.

Pediatric End-of-Life Care Lacking—Parents Recommend Six Areas of Importance

It's a scenario that most people can't even bring themselves to think about: the death of a child.

That may explain, in part, why pediatric end-of-life care hasn't received much attention, and why palliative care for children isn't widely available.

But a new study in the March issue of *Pediatrics* brings the issue to the forefront by reporting what parents who have lost their children said was needed most during the dying process.

"We can't always prevent someone from dying, but we can create a better situation," said Dr. Linda Siegel, a pediatric critical care and palliative care expert at Kravis Children's Hospital at Mount Sinai Medical Center, in New York City. For

example, she said, a child can die with monitors screeching and a code team present, shocking their heart, trying to revive them, or a child can die with a parent holding them, the room lights low and soft music playing in the background.

"Health-care providers need to be aware of the impact they have on the family at the end of life. Those memories, they carry with them for the rest of their lives," she said.

Dr. David Steinhorn, medical director of palliative care at Children's Memorial Hospital in Chicago, echoed Siegel's sentiments, "This is such an important area. You only have one chance to do end-of-life care right. We can't make it 100% pain-free or free of pain and anxiety, but we can minimize those aspects," he said.

The Boston researchers sent questionnaires to the families of 96 children who had died in one of three Boston-area hospitals. Fifty-six parents returned the questionnaires.

Of those who responded, 64% were mothers, 75% were married, and 91% were white. The average age was 42. Half of the respondents were Catholic, 34% were Protestant, 5% were Jewish, 2% were Muslim and 9% identified no religious affiliation.

Parents identified six areas of critical importance that could improve pediatric end-of-life care:

1. Honest and complete information. Families wanted health-care providers to be forthcoming with information and not try to withhold information to protect them.
2. Ready access to staff. In a rushed hospital setting, it's easy for a parent to miss the doctor on rounds. Parents suggested setting up a regular time for bedside consultations.
3. Communication and care coordination. Often, an ill child will have many different specialists caring for him or her. Some parents found talking to so many doctors confusing, particularly if doctors expressed differing opinions.
4. Emotional expression and support by staff. Parents wanted to know that staff members cared and were "real people."

5. Preservation of the integrity of the parent-child relationship. Parents wanted health-care providers to acknowledge their vital role in their child's life. They wanted to be respected and included in the decision-making process.

6. Faith. Faith was a double-edged sword for this group of parents. Some found comfort in their faith and sought counsel from religious personnel. Others felt betrayed by their beliefs at this difficult time.

Parents felt it was important for doctors to give them the big picture and to be honest with them about their child's situation, no matter how grim the prognosis. "What we cannot handle is not knowing what is going on," wrote one parent.

But it isn't always easy for doctors to deliver a poor prognosis, admitted Dr. Eugene Perlov, a physician with the hospice division of the Visiting Nurse Service of New York.

"[Health-care providers] have a hard time talking about bad news. We're so invested in good outcomes, which is natural because our mission is to heal," he said.

And, that's exactly where palliative care can come in, said Steinhorn.

"Palliative care brings in a whole set of additional support when no more curative measures are available," he said, though he added that pediatric palliative care isn't available at most hospitals, even children's hospitals, yet.

Both Steinhorn and Perlov pointed out another important obstacle to increasing the availability of palliative care -- it's currently hard to get insurance reimbursement for such care.

Siegel said palliative care can be helpful from the time of diagnosis through to the end of the child's life, however. "We need to support parents emotionally. We need to help them maintain hope, but prepare them for what's going to happen," she said, adding that there can be reluctance to calling on palliative care specialists. "It's so unnatural for children to die before their parents, it's hard for everyone to shift to palliative care."

■ NT

NEONATOLOGY TODAY

© 2006 by Neonatology Today
Published monthly. All rights reserved

Publishing Management

Tony Carlson, Founder & VP/Sales
TCarlsonmd@gmail.com

Richard Koulbanis, Publisher & Editor-in-Chief
RichardK@Neonate.biz

John W. Moore, MD, MPH, Medical Editor/
Editorial Board
JWMoore@Neonate.biz

Editorial Board

Dilip R. Bhatt, MD
Anthony C. Chang, MD
K. K. Diwakar, MD
Alan R. Spitzer, MD
Gautham Suresh, MD
Leonard Weisman, MD

FREE Subscription - Qualified Professionals

Neonatology Today is available free to qualified medical professionals worldwide in neonatology and perinatology. International editions available in electronic PDF file only; North American edition available in print. Send an email to: SUBS@Neonate.biz. Be sure to include your name, title(s), organization, address, phone, fax and email.

Contacts and Other Information

For detailed information on author submission, sponsorships, editorial, production and sales contact, send an email to INFO@Neonate.biz

For information on sponsorships or recruitment advertising call Tony Carlson at 301.279.2005 or send an email to RECRUIT@Neonate.biz. To contact an Editorial Board member, send an email to: BOARD@Neonate.biz putting the Board member's name on the subject line and the message in the body of the email. We will forward your email to the appropriate person.

Meetings, Conferences and Symposiums

If you have a symposium, meeting or conference and would like to have it listed in Neonatology Today, send an email to: MEETING@Neonate.biz. Be sure to include the meeting name, dates, location, URL and contact name.

NEONATOLOGY TODAY

9008 Copenhaver Drive, Ste. M
Potomac, MD 20854 USA
tel: +1.301.279.2005
fax: +1.240.465.0692
www.NeonatologyToday.net

Editorial Offices:

Neonatology Today
16 Cove Road, Ste C
Westerly, RI 02891 USA
EDITORIAL@Neonate.biz

When caring is critical...



INOmax[®]
(nitric oxide) **FOR INHALATION**



Infasurf[®]
(calfactant)
Intratracheal Suspension

INO Therapeutics

www.inotherapeutics.com

INO Therapeutics LLC
Clinton, NJ 08809

INOmax[®] is a registered trademark of INO Therapeutics LLC

Infasurf[®] is a registered trademark of Forest Pharmaceuticals, Inc.

© 2006 INO Therapeutics LLC
All rights reserved.

Printed in U.S.A.

IMK111-00249

2/05