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NEONATOLOGY TODAY

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IN UTERO CATHETER INTERVENTION FOR CONGENITAL HEART DISEASE

By Audrey C. Marshall, MD and Wayne A. Tworetzky, MD

Advances in diagnostic imaging and surgical technique have allowed most congenital heart disease to be anatomically repaired, even in infancy. However, until recently, the possibility of prevention of congenital heart disease seemed remote. Widespread use of sonographic obstetrical screening, in combination with improved acquisition and interpretation of fetal echocardiograms, now allows us to diagnose many cardiac anomalies by midgestation, and also to observe their prenatal progression. Not unexpectedly, the capacity for early diagnosis has generated considerable interest in prenatal therapeutic intervention.

Several fundamental principles underlie the field of fetal intervention. The fetal diagnosis must be certain, and there must be an understanding of how the disease will evolve through the remainder of gestation. The resultant condition at birth must be associated with significant mortality or morbidity. Finally, a procedure must be available that can correct the initial lesion and thereby improve the outcome at birth; this procedure must offer sufficient benefit to the child to justify the risk to both mother and fetus.

Hypoplastic left heart syndrome (HLHS), though rare, remains the congenital cardiac defect associated with the most deaths in the first year of life. Characterized by a left ventricle (LV) inadequate to support the systemic circulation, the syndrome may result from one of a number of primary left heart lesions. Included among this list of causative primary lesions is valvar aortic stenosis (AS). In fact, fetal echocardiographic observation has demonstrated that AS associated with LV dysfunction, when diagnosed in the second trimester, progresses to HLHS¹. Thus, critical AS diagnosed in the mid-trimester fetus presents an ideal target lesion for prenatal intervention.


The mechanisms through which AS begets HLHS are poorly understood. It is hypothesized that increased LV afterload and decreased coronary perfusion lead to LV myocardial damage. Initially, this LV injury is manifest as LV dilation and systolic dysfunction. With impaired LV filling, pulmonary venous return is diverted at the atrial level. The resultant decrease in left heart flow leads to growth arrest, and ultimately, hypoplasia. Consistent with this hypothesis, the echocardiographic hallmarks of critical AS of the fetus include:

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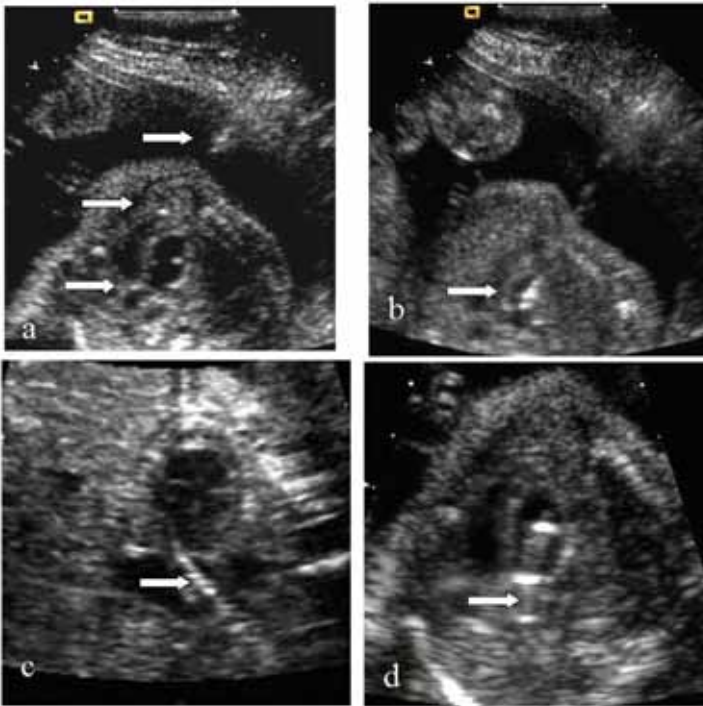


Figure 1. Transabdominal ultrasound imaging of fetal aortic valve dilation. A) The introducer cannula is seen advancing through the myometrium and into the amniotic cavity (first arrow) toward the fetal chest wall (second arrow), with the aortic valve in view (third arrow). B) The needle is advanced into the LV cavity until the tip is in the subaortic region. C) The wire is advanced through the valve and into the ascending aorta. D) The balloon is advanced over the wire and inflated while straddling the valve.

1. primary AS as evidenced by thickened valve tissue and a narrowed antegrade flow jet,
2. severe LV dysfunction,
3. echogenicity of the LV myocardium,
4. left to right flow at the atrial septum, and,
5. retrograde flow in the ascending aorta (Figure 1).

Authors had described a percutaneous fetal aortic valvuloplasty procedure as early as 1991[2]. Although the work of several groups had resulted in a total of 12 procedures reported through the year 2000, the experience yielded limited technical success and a high rate of fetal mortality[3]. The procedure did, however appear to be technically feasible. With the benefits of improved

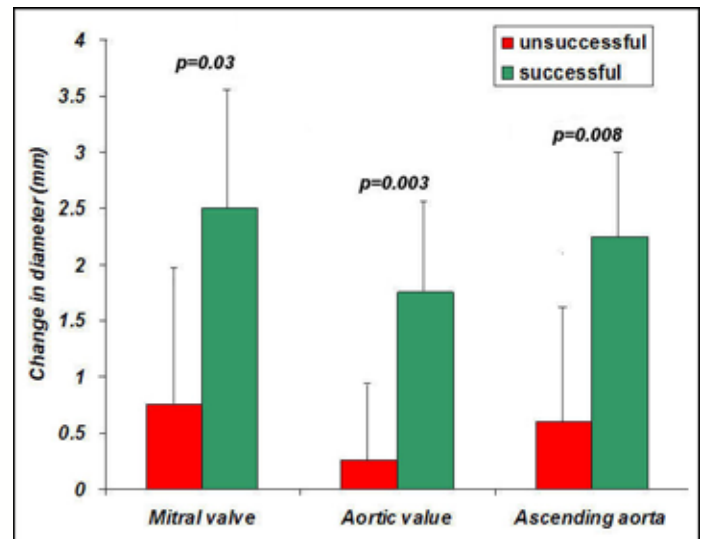


Figure 2. This graph depicts the change in dimension of left heart structures (mitral and aortic valves and ascending aorta) in fetuses that had a technically successful in-utero aortic valvuloplasty compared to those with an unsuccessful procedure and those that declined the procedure. Only fetuses with pregnancies carried to near term delivery (>33 weeks gestation) were included. The data reflects the first and last measurements made during gestation.

imaging, instruments, and intraoperative obstetrical management, we believed the procedure could be performed more safely and with better technical results.

In March 2000, we began to offer fetal aortic valvuloplasty to mothers of fetuses with critical AS at less than 26 weeks gestation, as part of an innovative therapy protocol at the Children's Hospital, Boston, and the Brigham and Women's Hospital. Candidates were required to meet all of the echocardiographic criteria described above, with at least 3 experienced fetal echocardiographers attributing a high likelihood of progression to HLHS. Furthermore, the LV had to be deemed "salvageable", that is, without significant hypoplasia (length within 2 S.D. of normal for gestational age) at the time of diagnosis.

Between March 2000 and March 2004, twenty mothers elected to undergo the procedure. All gave informed consent for the procedure after meeting with pediatric cardiologists, fetal surgeons, perinatologists, and anesthesiologists. The aortic valvuloplasty was performed successfully in 14 cases, giving a technical success rate of 70%.

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“Fetal cardiology is emerging as one of the most rapidly growing fields in our specialty. The potential for echocardiographic diagnosis in utero has already favorably impacted care of children with congenital heart disease.”

The procedure is performed with the mother under general anesthesia. In many cases, the procedure can be performed percutaneously. When transabdominal fetal positioning fails, a limited laparotomy is performed. Not only does the laparotomy afford greater access for fetal manipulation, but it also allows higher resolution imaging directly on the uterine surface.

Once ideal fetal position is established, the fetus is given intramuscular anesthetic and muscle relaxant. A 19 G needle introduced into the maternal abdomen is guided under ultrasound through the fetal chest wall and into the LV cavity. Once inside the LV, the needle is used as an introducer for a standard PTCA catheter over a wire. The balloon diameter is intended to be ~120% the diameter of the valve annulus. The wire is used to probe for the aortic valve orifice. Once the wire has crossed the valve, the balloon is advanced, and the balloon is inflated straddling the valve (Figure 2). All of the equipment is then withdrawn.

Using this technique, we have not observed maternal complications related either to anesthesia or to the catheterization procedure. A variety of fetal complications have occurred; the most common complications being bradycardia and small pericardial effusions. The fetal bradycardia responds to either intramuscular or intracardiac epinephrine. Effusions often resolve spontaneously, but can also be drained at the conclusion of the procedure. Although we

have not seen fetal demise intraoperatively, 3 fetuses were found to have expired within 72 hours of the procedure.

Of 14 fetuses who underwent successful aortic valve dilation between 21 and 29 weeks gestation, 3 were born with 2 ventricle circulations. The remainder of the liveborn fetuses who underwent either successful or unsuccessful aortic valvuloplasty procedures had a diagnosis of HLHS at birth. Although only 3 fetuses did not require a Stage I palliation, technically successful fetal aortic valve dilation was associated with significant growth of left heart structures including the mitral valve, aortic valve, and ascending aorta (Figure 3)[4].

The lack of maternal complications and the possible prevention of HLHS in 3 fetuses have encouraged us to cautiously pursue this intervention. We are in the process of developing a protocol to investigate more closely the impact of successful aortic valve dilation on the growth of left heart structures in utero.

While critical AS is currently the most common diagnosis referred for fetal cardiac intervention, indications will likely expand as additional procedures become available and practiced. One additional disease that has been proposed as a target for fetal therapy is pulmonary atresia with intact ventricular septum. Perforation and dilation of the pulmonary valve can be performed using a technique similar to that used for aortic valve procedures. The difficulty in offering intervention to this group of fetuses lies in the clinical spectrum of the disease, and our inability to predict the postnatal morbidity based on prenatal appearance. Although it seems likely that pulmonary atresia can be treated prenatally, we first need to be able to identify those fetuses who would have the poorest postnatal outcomes, and would therefore have the most to gain from fetal intervention.

In fact, the emergence of a second indication for fetal intervention has, in

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www.nann.org/i4a/pages/index.cfm?pageid=803

30th Annual Neonatal International Symposium – Neonatology 2006

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neonatology.med.miami.edu/conference/default.htm

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Figure 3. Transabdominal ultrasound imaging of a fetus during puncture through atrial septum. The needle traverses the maternal abdominal wall, the uterine myometrium, the fetal chest wall, and the free wall of the right atrium. Here, the tip of the needle distorts the intact atrial septum, driving it leftward, prior to needle entry into the left atrium.

our center, been driven primarily by the identification of a uniquely high risk set of neonates. Infants born with HLHS and an intact atrial septum have a failing circulation until left atrial (LA) decompression can be achieved. These infants have markedly elevated mortality rates, as compared to others with HLHS. We hypothesized that a prenatal procedure to create an atrial septal defect would aid in postnatal stabilization and thereby improve neonatal outcomes. By decompressing the LA in utero, one might attenuate secondary tissue/organ damage occurring in the lung, and might favorably impact longer term survival.

We have performed 7 of these procedures; 6 of 7 have been technically successful. As with the aortic valve procedure, we have not experienced any maternal complications. Furthermore, we have been able to access the atrial septum in all cases without the use of a laparotomy. Due to the tech-

nique and equipment used, the newly created atrial defects are small, but appear to persist through gestation⁵. Although we have not yet demonstrated clinical effect, we expect that the introduction of equipment and techniques dedicated to this procedure will improve our ability to make large defects in the atrial septum, and will ultimately lead to clinical benefit.

Fetal cardiology is emerging as one of the most rapidly growing fields in our specialty. The potential for echocardiographic diagnosis in utero has already favorably impacted care of children with congenital heart disease. A therapeutic arm has been added to the field with regard to management of fetal arrhythmias. Now we are developing the means of modifying structural disease in utero. It is our hope that with the continuing collaborative efforts of fetal imagers, obstetricians, fetal surgeons, and interventionalists, we can add prevention to the management of some forms of congenital heart disease.

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MEDICAL NEWS, PRODUCTS AND INFORMATION

**SOMANETICS Pioneers Cerebral/
Somatic Monitoring of Changes in
Regional Blood Oxygen Saturation
with its Next-Generation INVOS®
SYSTEM**

TROY, MI. - Somanetics (Nasdaq:SMTS) has commenced its launch of the INVOS® Cerebral/Somatic Oximeter, the first and only FDA-cleared noninvasive oximeter that can simultaneously monitor changes in regional oxygen saturation (rSO₂) of blood in both cerebral and skeletal muscle (somatic) tissue. The INVOS Cerebral/Somatic Oximeter is the fifth generation INVOS system, and the first specifically designed by Somanetics to apply the company's pioneering rSO₂ monitoring technology to simultaneously monitor the brain and other regions of the body.

In redesigning the INVOS System to enable simultaneous cerebral/somatic monitoring, Somanetics' engineers doubled the number of data channels from two to four. This allows critical care teams to place sensors over somatic tissue without moving those already on the forehead for cerebral monitoring. This provides oxygenation values for the regions directly beneath the sensors, and can result in an earlier warning signal than traditional, systemic (whole body) measures.

Simultaneous rSO₂ monitoring of cerebral and somatic tissue is most rapidly being adopted by pediatric and neonatal critical care clinicians during the acutely high-risk post-operative period when life-threatening or disabling complications can occur. Among other things, this hemodynamic data combination enables clinicians to continuously track the stability of cerebral and peripheral blood oxygen saturation and use associations between the two to more tightly manage care. For example, customer experience has shown that a drop in the somatic rSO₂ value may indicate that the peripheral circulation is shutting down to preserve the brain - a potential early indicator of shock.



Somanetics expects pediatric and neonatal intensive care units to be the biggest initial users of the new system. "Multi-site near-infrared monitoring opens up a 'window' through which we can see the distribution of blood flow, oxygen delivery and metabolism throughout the brain and body," explains George M. Hoffman, MD, Chief of Pediatric Anesthesiology and Associate Director of the Pediatric Intensive Care Unit at Children's Hospital of Wisconsin. "This is the first time we can obtain noninvasive, multi-site, continuous and real-time regional oxygen economy data to identify critical events, responses to acute interventions and trends over time. It has helped us identify conditions of low total cardiac output, mild shock, and hypoperfusion of the brain and somatic tissue early enough to guide effective interventions to reduce the risk of neurologic injury, renal failure or multi-system organ dysfunction."

Combination monitoring is also being used in the operating room.

"Cerebral and somatic oximetry incrementally increases the safety and confidence with which we treat our neonatal and pediatric cardiac surgery patients," explains Hani A. Hennein, MD, Chief of Pediatric Cardiothoracic Surgery at Rainbow Babies & Children's Hospital. "We use the INVOS System perioperatively on all our patients and find it very useful during induction of anesthesia, cannulation, deciding on the degree of hypothermia and hemodilution, and while weaning

from cardiopulmonary bypass; all scenarios that can contribute to ischemic problems."

Early use of cerebral/somatic monitoring is also being seen in adult vascular surgery or procedures that may place the brain and body at risk of dysoxygenation. These include use during carotid endarterectomy, brachial artery embolectomy (a procedure to remove clots in arteries of the arm), and aorto-bifemoral bypass (a procedure to replace arteries that supply blood to the legs when they are clogged with plaque).

According to Somanetics' President and Chief Executive Officer Bruce Barrett, "As a pioneer in cerebral oximetry, it is fitting that Somanetics introduce the next chapter in this modality's evolution with a system that enables simultaneous regional monitoring of blood in the brain and somatic tissue. We believe that in the past three years the volume of procedures monitored with the INVOS System has nearly doubled. We also believe that the introduction of simultaneous cerebral/somatic monitoring will increase the clinical use of this technology for critical care teams and a growing number and diversity of their patients."

With this latest evolution, the INVOS System may now be used for cerebral oximetry, somatic oximetry or both simultaneously. Additional enhancements were also made to improve ease of use and functionality. These include a larger screen display, enhanced user preferences, improved data management via USB, video output to a remote monitor and a reduction in weight and footprint.

The INVOS® System is the only FDA-cleared noninvasive oximeter to provide simultaneous and continuous cerebral/somatic monitoring of changes in regional blood oxygen saturation. It uses visible and near infrared spectroscopy to "reflect the color of life" by identifying hemoglobin and red-colored oxygenated hemoglobin molecules within red blood cells, and measuring the relative amounts of each. The resulting regional oxygen saturation

(rSO₂) is like a vital sign that helps critical care teams detect and correct blood oxygenation issues that can lead to complications and poor outcomes. The INVOS System is an adjunct trend monitor that can be used on adult, pediatric and neonatal patients in any clinical setting where patients are at risk of reduced-flow or no-flow ischemia. This includes uses in the operating room, intensive care unit and interventional cardiac catheterization lab. The INVOS System has an eight-year track record among customers and has more than 400 presentations, study abstracts and published papers citing clinical benefits.

Somanetics develops, manufactures and markets medical devices that can help medical professionals potentially improve surgical outcomes and patient recovery in critical care settings. The company currently has two product lines. The INVOS System provides noninvasive regional blood oxygenation change data that helps address clinical challenges faced by surgeons, anesthesiologists, perfusionists and critical care nurses. The CorRestore System is used in cardiac repair and reconstruction, including an operation called Surgical Ventricular Restoration (SVR), for the treatment of certain patients with severe congestive heart failure. Somanetics supports its customers through a direct U.S. sales force and clinical education team. Globally, Edwards Lifesciences represents INVOS System products in Japan, and Tyco Healthcare markets INVOS System products in Europe, Canada, the Middle East and Africa. For more information visit www.somanetics.com.

Multi-centre Clinical Trial Finds Two Vastly Different Surgical Procedures Produce Same Results in Infants with Intestinal Disorder

TORONTO – A minimally-invasive technique pioneered at The Hospital for Sick Children (SickKids) has proven to be as effective as surgery for treating premature infants with a severe intestinal disease, necrotizing enterocolitis, according to a study published in the May 25, 2006 issue of The New England Journal of Medicine.

The technique, called peritoneal drainage, involves placing a small drain under local anesthesia at the infant's bedside, providing an alternative to undergoing a large procedure in the operating room. The peritoneal drainage technique was developed at SickKids in the early 1970s and has since been the preferred method of treatment at SickKids for premature infants weighing less than two pounds who have necrotizing enterocolitis.

"Rather than going to the operating room and performing what can be a big operation in a high risk, tiny, premature baby, we are able to treat the infant at the bedside with minimal disruption," said Dr. Jacob Langer, chief of General Surgery at SickKids and professor at the University of Toronto. "Results from the clinical trial show that the technique first developed at SickKids and now used all over the world, is as effective as a large operation, with equally successful outcomes for the patient."

Necrotizing enterocolitis (NEC) is a severe inflammatory disease of the intestine afflicting one infant out of every 2000 births and 5 to 10% of premature infants weighing less than two pounds in Canada each year. In its most severe form, NEC results in perforation of part of the intestine, a condition with a high mortality rate.

For more than 25 years surgeons have used two radically different

operations for these babies. The first and more aggressive, laparotomy and bowel resection, involves a large abdominal incision with removal of all of the affected intestine and creation of a stoma. The alternative option, peritoneal drainage, involves making a quarter of an inch incision in the lower abdomen and placing a small drain allowing egress of stool and pus from the abdomen without removing any intestine.

The multi-centre clinical trial led by Yale School of Medicine included 117 premature infants at 15 paediatric academic medical centers from the United States, as well as SickKids. When a baby developed perforated NEC at a study site, parents were counseled by the operating surgeons and offered enrollment into the trial. If they agreed, the operation their child received was assigned randomly.

"The study found that patient survival and other major outcomes for the two drastically different operations were virtually identical," said lead author Dr. Larry Moss, chief of pediatric surgery in the Department of Surgery at Yale School of Medicine. "After 30 years of debate over which procedure is best, the first true scientific experiment addressing this question suggests that the method of the surgery may not be the important aspect of treatment."

The Hospital for Sick Children, affiliated with the University of Toronto, is Canada's most research-intensive hospital and the largest centre dedicated to improving children's health in the country. For more information, contact: www.sickkids.ca

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Risk, Researchers Find—Paper Receives March of Dimes Award

Researchers at the 26th Annual Society for Maternal-Fetal Medicine (SMFM) meeting today announced that profiling certain proteins in amniotic fluid is the fastest and most accurate way to detect potentially dangerous infections in pregnant women, and also can accurately predict whether premature delivery is imminent.

Diagnosing intra-amniotic inflammation or infection is crucial because these conditions can lead to the death of the fetus or other serious consequences of preterm birth, including brain damage, lung and bowel injury.

The study's authors were recognized by an award from the March of Dimes, marking the third year that the organization has honored SMFM members for cutting-edge prematurity research. The March of Dimes is conducting a multi-year, multi-million-dollar campaign aimed at reducing the growing rate of premature births through research and awareness.

"Our goal was to create a test that could more accurately predict which pregnancies with preterm labor are at risk for fetal complications from intrauterine inflammation/infection," said Catalin S. Buhimschi, M.D., of Yale University, the lead study author and SMFM member. "We found that profiling the proteins in amniotic fluid for markers of inflammation—a proteomic profile—not only yielded results twice as fast as other tests, but those results were also much more accurate. We discovered that the presence of fewer than two biomarkers for inflammation meant the median time for delivery was five to six days. If all the biomarkers for inflammation were present, delivery time was within hours."

"Research such as this is vital if we are to understand the basic mechanisms underlying preterm birth and find ways to prevent or treat it," said Nancy S. Green, M.D., medical director of the March of Dimes. "Dr. Buhimschi's work is exciting because it offers a potential new tool to identify women who are at highest risk for a preterm delivery. For these women, knowing their risk and managing it may

lead to dramatic improvements in the health of their babies."

Each of the 135 study participants had presented at a hospital with premature labor symptoms and underwent a routine amniocentesis to determine the maturity of the fetus's lungs. A small sample of the amniotic fluid was also immediately analyzed by screening and diagnostic tests—glucose, neutrophil (white blood cell) count, lactate dehydrogenase (LDH), Gram stain, culture, IL-6 and MMP-8—and a "fingerprint" of the proteins was generated using SELDI-TOF (surface-enhanced laser desorption ionization time-of flight). Peaks were sought for four proteins that served as evidence of inflammation. Results revealed that the proteomic profiling was more accurate, yielding results in 30 minutes and catching subtle inflammation missed by other tests such as the neutrophil count, Gram stain or culture.

The study, "Detection of Intra-amniotic Inflammation/Infection by Proteomic Profiling. Prospective Comparison with Rapid Diagnostic Tests (Glucose, WBC, LDH, Gram Stain,) IL-6 AND MMP-8," is the first to compare prospectively the traditional tests with the new proteomic profile using fresh amniotic fluid and is a joint effort by maternal-fetal medicine specialists from Yale University and the University of Kansas School of Medicine.

Proteomics is a novel technology that has found applications in various fields including cancer screening. Its potential for improving management of pregnancy complications also appears to be very promising.

The Society for Maternal-Fetal Medicine (est. 1977) is a non-profit membership group for obstetricians/gynecologists who have additional formal education and training in maternal-fetal medicine. The society is devoted to reducing high-risk pregnancy complications by continuously educating its 2000 members on the latest pregnancy assessment and treatment methods. It also serves as an advocate for improving public policy, and expanding research funding and opportunities for maternal-fetal medicine. For more information, visit www.smfm.org.

Founded in 1938, the March of Dimes funds programs of research, community services, education, and advocacy. For more information, visit the March of Dimes Web site at www.marchofdimes.com.

Premature Babies and SIDS: Doctors Should Make Special Effort to Talk to Parents About Risk

New Saint Louis University research finds SIDS strikes premies later because premature and small babies are at risk for SIDS later and longer than full-term infants. Pediatricians should adjust when they offer counseling to parents about preventing SIDS, according to research published by a Saint Louis University pediatrician who examined more than 8,000 SIDS deaths.

"Physicians should remain vigilant and, particularly for preterm infants, should provide SIDS prevention counseling beyond the first four months," says Donna R. Halloran, M.D., assistant professor of pediatrics at Saint Louis University School of Medicine and principal investigator.

The risk for SIDS is 50 times greater for premature infants compared to full-term infants when they are placed to sleep on their stomachs.

"Putting babies on their backs to sleep can prevent SIDS and should be discussed at the six-month visit for preterm infants. And doctors should talk to families during the traditional four-month visit, which is before the peak risk for infants of 22 to 27 weeks' gestation. It's an especially good time for SIDS preventive counseling in preterm."

The article was published in the January 2006 issue of *Annals of Epidemiology*.

Premature babies are at an increased risk for SIDS, which is the leading cause of post neonatal death in the United States, says Halloran, who also is a pediatrician at SSM Cardinal Glennon Children's Medical Center. Smaller babies - infants who weigh less than 10 percent of infants of the same gestational age - also have an increased risk of SIDS, she adds.

Typically, pediatricians concentrate their

SIDS prevention counseling during the neonatal and two-month well-child visits. The timing works well for counseling parents of full-term babies who are at the highest risk of SIDS when they are between two and four months old. The average age of death in full-term babies occurs at 14.5 weeks.

However, Halloran's research finds that SIDS strikes very premature babies - those born at the gestational age of between 22 and 27 weeks - an estimated six weeks later than full-term infants. Preterm babies who are born at a gestational age of 28 to 32 weeks died of SIDS almost two weeks later than full-term infants, who are born at a gestational age of 40 weeks.

Premature babies usually spend the early weeks of their lives in the hospital, Halloran says.

"They are home for the same amount of time when they die of SIDS as full-term infants," she says. "This suggests SIDS has, in part, an environmental trigger."

In addition, premature infants reach the point in their physiological development when they are most susceptible to SIDS later than full-term babies, Halloran says.

Of the more than 11 million babies born in the U.S. between 1996 and 1998 in Halloran's study sample, a total of 8,199 infants died of SIDS.

SIDS rates were greatest among male children born to women who were non-Hispanic blacks or Native American; had a low level of education; were younger than 20; were unmarried; smoked; drank alcohol or had five or more previous births.

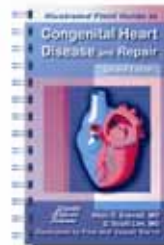
"Clinicians caring for very preterm infants need to be vigilant for longer. They must provide SIDS prevention counseling before and during peak risk, which changes with gestational length and other risk factors that may influence infant development and maturation," Halloran says.

"Mothers of preterm babies and day-care providers for these infants should stick to SIDS prevention guidelines for longer. These include placing babies on their backs to sleep, not smoking and putting babies to sleep in a safe bed of their own."

Established in 1836, Saint Louis University School of Medicine is a pioneer in geriatric medicine, organ transplantation, chronic disease prevention, cardiovascular disease, neurosciences and vaccine research, among others. The School of Medicine trains physicians and biomedical scientists, conducts medical research, and provides health services on a local, national and international level.

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 Last Updated: September 19, 2005
 Record first received: September 13, 2005
 ClinicalTrials.gov Identifier: NCT00196482
 Health Authority: Germany: Federal Institute for Drugs and Medicinal Devices
 ClinicalTrials.gov processed this record on 2005-11-16

Sponsors and Collaborators: Ernst Moritz Arndt University of Greifswald NUMICO, Dr. Heike Mueller, Friedrichsdorf, Germany

Purpose: Double-blind randomized controlled trial to investigate the impact of two human milk fortifiers on acid-base status and longitudinal growth and weight gain in preterm infants.

Two different compositions are tested, main difference is in electrolyte composition.

Condition: Premature Birth

Treatment or Intervention: Drug: changing of fortifier

Study Type: Interventional

Study Design: Treatment, Randomized, Double-Blind, Active Control, Crossover Assignment, Safety/Efficacy Study

Further Study Details:

Primary Outcomes: frequency of metabolic acidosis

Secondary Outcomes: need for oral bicarbonate administration; longitudinal growth; weight gain; amino acid levels in plasma and urine

Two groups each consisting of 15 infants with a birth weight below 2000g are studied. Randomization is stratified by three birth weight classes (<1000g, 1000-1500g, 1500 - 2000g) human milk fortifier is introduced in two steps after oral feeding is achieved. Two acid-base status and electrolyte concentrations are measured. When metabolic acidosis, defined as BE < -6 mmol/l, occurs fortifier feeding is stopped, and after a wash-out period of three days the alternative product is used. Again, occurrence of metabolic acidosis, need for oral bicarbonate and effect on longitudinal growth and weight gain are registered.

Eligibility: Ages up to 3 months; both male and female

Criteria:

Inclusion Criteria: growing premature infants with a birth weight < 2000g.

Exclusion Criteria: congenital malformation chromosomal disorders sepsis metabolic disorders need for mechanical ventilation.

Location and Contact Information:

Please refer to this study by ClinicalTrials.gov identifier NCT00196482

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Study chairs or principal investigators:

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Antepartum Betamethasone Treatment for Prevention of Respiratory Distress in Infants Born by Elective Cesarean Section*This study is currently recruiting patients***More Information**

Study ID Numbers: 894-2003
 Last Updated: August 30, 2005
 Record first received: August 29, 2005
 ClinicalTrials.gov Identifier: NCT00139256
 Health Authority: United States: Institutional Review Board
 ClinicalTrials.gov processed this record on 2005-11-16

Purpose: This is a randomized, multicenter, double blind, placebo controlled trial of betamethasone versus a placebo given prior to the mothers at term and near term gestation (>34-<40 weeks of gestation) who are scheduled to undergo a planned Cesarean section. The study design is to determine the efficacy and safety of betamethasone in the prevention of breathing problems commonly seen in this population.

In infants born by elective Cesarean section, antenatal be-

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tamethasone treatment will reduce the risk of NICU admission 11 to 8% and/or oxygen therapy +/- PPV for >30 minutes from 4.5 to 2.5%.

Condition: Elective cesarean section; Respiratory Distress Syndrome

Study Type: Interventional

Intervention Drug: Glucocorticoid (betamethasone)

Study Design: Prevention, Randomized, Double-Blind, Placebo Control, Single Group Assignment, Safety/Efficacy Study

Official Title: Randomized Controlled Trial of Antepartum Betamethasone Treatment for Prevention of Respiratory Distress in Infants Born by Elective Cesarean Section

Further Study Details:

Primary Outcomes: The primary outcome to be studied is the need for NICU admission and/or oxygen therapy or PPV for >30 minutes. The primary endpoint will be the proportion of infants who develop respiratory morbidity.

Expected Total Enrollment: 400

Study start: August 2005; Expected completion: February 2008; Last follow-up: September 2007; Data entry closure: September 2007

The purpose of this pilot study is to determine if antepartum betamethasone given to mothers undergoing elective cesarean section (ECS) delivery at term or near term gestation (>34 and < 40 weeks of gestation) is safe and feasible in reducing neonatal respiratory morbidity and the related admissions to neonatal intensive care units (NICU).

The data from this pilot study will be used to support a NIH application for a multicenter randomized trial to determine, if compared to placebo treatment, antenatal betamethasone initiated 2-7 days prior to an ECS results in decreased occurrence of respiratory morbidity and NICU admissions in the newborn.

The multicenter protocol was recently reviewed by the NICHD network for clinical trial. The reviewers were enthusiastic about the scientific merit and public health importance of the study, but asked for a pilot study to determine feasibility before launching the national trial. Given the rise in the rate of CS deliveries, we project

substantial health cost savings from this preventive strategy if it were found to be successful in reducing neonatal morbidity.

Eligibility :

Genders Eligible for Study: Female
Accepts Healthy Volunteers

Criteria:

Inclusion Criteria:

- Pregnant women \geq 34 weeks gestation scheduled to undergo operative delivery within 48-72 hours after study enrollment

Exclusion Criteria:

- Known contraindication to the use of betamethasone in the mother
- Known lethal or non-lethal congenital anomaly diagnosed antenatally
- Spontaneous labor
- Premature rupture of membranes

Location and Contact Information:

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