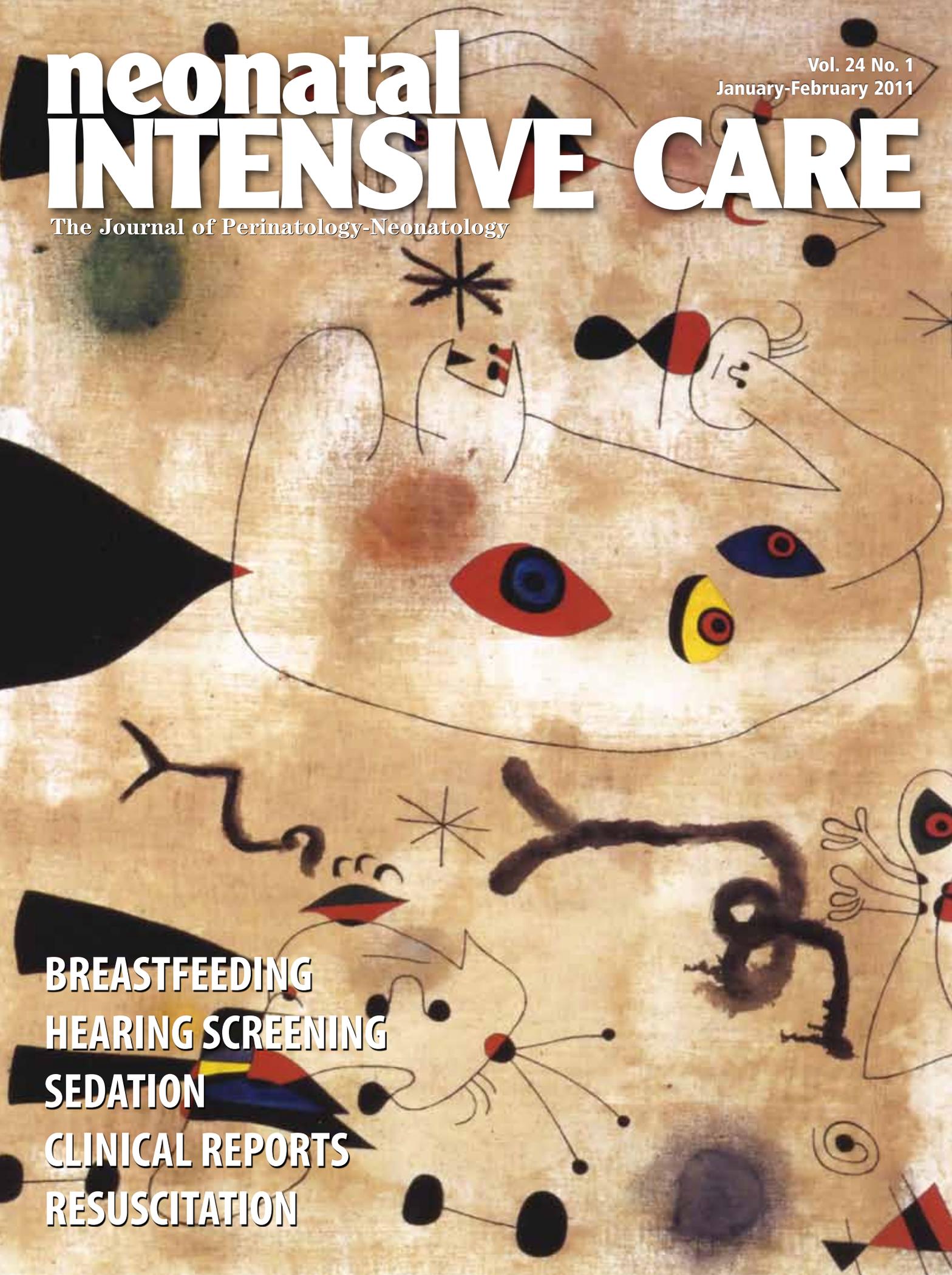


neonatal INTENSIVE CARE

Vol. 24 No. 1
January-February 2011

The Journal of Perinatology-Neonatology



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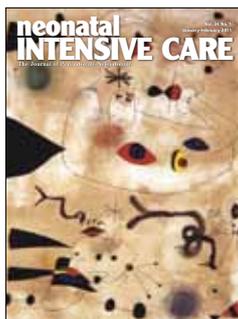
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January-February 2011

Table of Contents

DEPARTMENTS

- 4 Editorial
- 10 News
- 14 Products

ARTICLES

- 17 Monitoring Solutions
- 18 Breastfeeding for LPT Infants
- 22 Newborn Hearing Screening
- 24 Feeding Issues
- 25 Clinical Product Reports
- 27 Aluminum in Formulas
- 30 Hearing Screening and Sedation
- 34 ACFs Transmission
- 37 LMA for Resuscitation
- 42 Water Intake and Outcome
- 48 Chest Physiotherapy
- 52 Universal Newborn Hearing Screening

Editorial

A GOOD JOB, 24/7

The British Medical Journal recently published an article about the correlation of time of birth and risk of neonatal death.* The objective of the study by Pasupathy, et al, was to determine the effect of time and day of birth on the risk of neonatal death at term. The subjects were live-born singletons with cephalic presentation. The authors concluded that delivering an infant outside the normal week was associated with “an increased risk of neonatal death.”

This was the largest study of the subject, with a cohort of more than a million live births over nineteen year period. (Women who delivered out of hours were younger, more likely to be primiparous, more likely to live in an area of low socioeconomic deprivation, and more likely to deliver in either low or high throughput units. They were more likely to have had labor induced and much less likely to be delivered by planned cesarean section. Their infants were also born at later gestational ages.) The researchers noted: after exclusion of planned cesarean delivery, birth out of hours was still associated with about a 45% increased risk of death ascribed to anoxia.

The association was not explained by a confounding effect of measured maternal, infant, and obstetric characteristics. The authors said, “If we assume causality, the increased risk of delivering out of hours accounted for about a quarter of all neonatal deaths at term ascribed to intrapartum anoxia.”

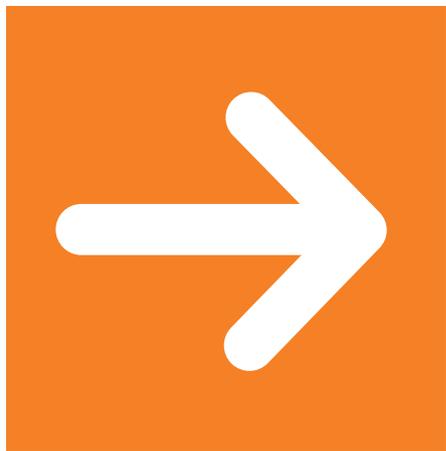
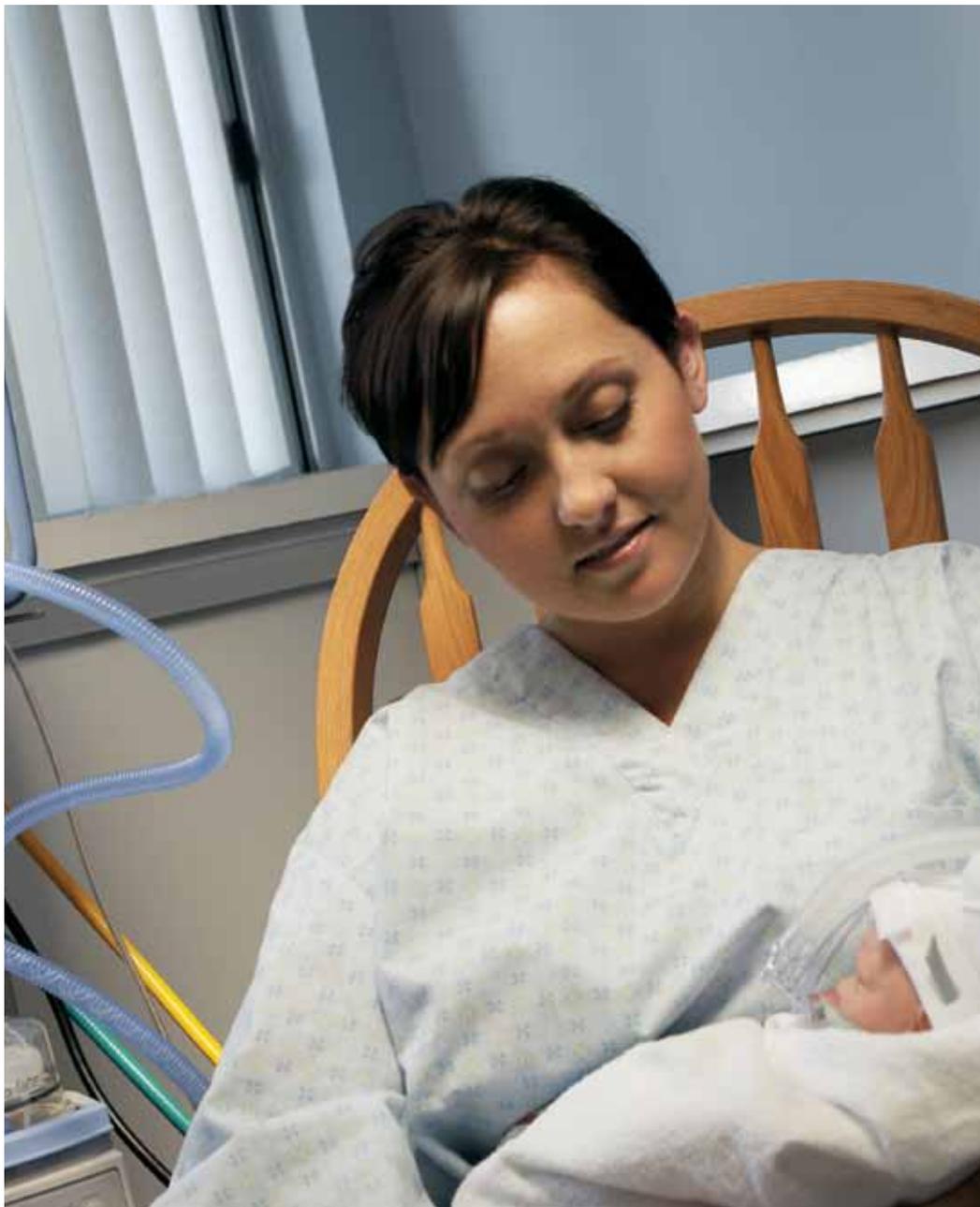
After the study’s release, Thomson Reuters reported on a new study in the journal Pediatrics, which focused specifically on VLBW infants cared for at 17 university-affiliated NICUs.** The researchers found *no* evidence of increased deaths at night or on the weekend. Interestingly, no higher risk to infants was found during the months of July or August, which is when new doctors begin their careers.

How come? Research at the University of Iowa found that NICUs have adequate around-the-clock staffing. The Iowa City study looked at 11,137 preemies born over a four year period who weighed less than 1,250 grams. (Twelve percent died in a week, 16% in the first months.) Reuters also noted that, according to the Iowa study, the timing of birth made no difference for complications, either. As an aside, studies have found that, in general, critical patients have a higher risk of dying on the weekend than the weekday. So, despite the grim healthcare landscape these days, it’s great to see some good news.

Les Plesko

* Time of birth and risk of neonatal death at term: retrospective cohort study, Pasupathy, Wood, Pell, Fleming, Smith. BMJ 2010;341:c3498, copyright British Medical Journal, an open-access article distributed under the terms of the Creative Commons Attribution Non-commercial License.

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News

□ January-February 2011

CORRECTION

The contact listed for Fisher & Paykel in the October Buyers Guide issue of NIC should be Kristin Straiter.

HAVE A HEART

Researchers from The Children's Hospital of Philadelphia reviewed cases of 240 fetuses diagnosed with HLHS from 2004 to 2009 to see the results of surgical repair. Children's Hospital has some of the world's longest and most extensive experience in performing staged surgical repair of HLHS. The researchers classified 162 of the 240 fetuses as standard-risk, and 78 of them as high-risk. In high-risk cases, in addition to the severely underdeveloped left ventricle, the fetus also had genetic and chromosomal defects, prematurity, or other heart abnormalities. Of the fetuses diagnosed with HLHS, 185 newborns underwent the first stage of surgery, the Norwood procedure, resulting in 155 survivors and 30 deaths. Ninety-three percent of standard-risk cases survived the first operation, compared to 57% of high-risk cases. As such, the researchers found a striking survival advantage for the standard-risk fetuses compared to the higher-risk cases. Two-thirds of fetuses with HLHS do not have a higher-risk form of the condition, and have a stronger chance of survival.

WHO'S YOUR DOCTOR?

The Placebo Journal reported: As per the Wall Street Journal, "health insurers are doing whatever they can to lower their costs... They are not talking about lowering premiums but instead are finding a way to keep their profits up." The Placebo Journal suggested: "check out how they are co-opting the newest and most ridiculous fads of accountable care organizations, quality performance payment plans and patient centered medical care... Aetna's chief medical officer said, 'We're insinuating ourselves more and more in the actual care of the patient.'" Placebo Journal commented: "My god, they think they are the doctors now." The Placebo Journal is a humor magazine for doctors. Contact placebojournal.com for a newsletter or magazine subscription. You won't be disappointed.

BIG BUCKS

A Creighton University School of Medicine researcher, Janeé Gelineau-van Waes, DVM, PhD, associate professor in the school's Department of Pharmacology, has been awarded a \$2.7 million grant by the NIH to investigate a possible link between the ingestion of tortillas and corn-based food products contaminated with the fungal toxin fumonisin during early pregnancy and the increased risk for neural tube defects.

NTDs affect one in 1,000 births and include anencephaly and spina bifida. Ingestion of fumonisin-contaminated corn is associated with increased risk for esophageal cancer in adults. A high incidence of NTDs, six to 10 per 1,000 births, has been reported in Guatemala, China, and South Africa, where corn is a dietary staple. Preliminary data obtained from mice will be used to validate biomarkers of exposure in blood and urine samples collected from women in Guatemala. Human samples will be analyzed and mouse models will be used to investigate underlying signaling mechanisms that result in failure of neural tube closure after fumonisin exposure. Collaborative studies with Duke University will focus on identifying genetic mutations that increase susceptibility.

A WHONN-ER

The Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) presented The Hill-Rom/Celeste Phillips Family-Centered Maternity Care Research Award to Lori Baas Rubarth, PhD, APRN, NNP, for her study entitled, Use of Online Support and NICU Education to Decrease Stress for Prenatal Patients on Bed Rest. The award is named for Celeste Phillips, a nurse and internationally recognized leader in family-centered maternity care. She worked extensively to introduce the single room maternity care concept to hospitals and physicians throughout the United States. The winner, Dr Rubarth, has been a nurse for over 30 years. Since completing her PhD in 2005, she has been teaching and coordinating the neonatal nurse practitioner program at Creighton University. She is widely published on the subject of caring for newborns. AWHONN also awarded Lynn Clark Callister, RN, PhD, FAAN, the March of Dimes Saving Babies, Together award, for her research related to postpartum depression. Callister is a Professor at the College of Nursing at Brigham Young University in Provo, Utah and an American Academy of Nursing fellow. Contact awhonn.com.

SWITCHEROO

Transplantation of the uterus looks likely to become a future treatment for women who are infertile, according to research published online in *Acta Obstetrica et Gynecologica Scandinavica*. A report by a collaborative Swedish-Spanish research group from the Universities of Gothenburg and Valencia said pregnancies were for the first time achieved in allogeneic transplanted uteri. The experiment, on rats, made use of uterus donors of one strain with the uteri then transplanted into females of another strain, a situation similar to transplantation between unrelated humans. The transplanted animals were given immunosuppressive drugs to prevent rejection and then were mated and cesarean section was performed before parturition and fetuses were found. See informahealthcare.com/aogs.

RISK IT

In a paper published in the journal *Anesthesiology*, a Cleveland Clinic-led research team announced the development of The Risk Stratification Index, developed using more than 35 million Medicare and Medicaid records, then validated on more than 100,000 patients at the Cleveland Clinic. The researchers used billing and procedure codes to develop an objective and transparent system which allows for outcomes to be compared across institutions and among individual physicians. Cleveland Clinic worked with Covidien on interpreting the data for the Risk Stratification Index. The validity of the Index was confirmed by applying it to more than 100,000 Cleveland Clinic records. The system is statistically stable to as few as 5,000 patients. The investigators have put their Risk Stratification Index in the public

domain; any entity can use it freely. Contact clevelandclinic.org or covidien.com.

GENE GENIUS

University of Missouri researchers believe they have found a critical piece of the puzzle for the treatment of Spinal Muscular Atrophy. In a new study in *Human Molecular Genetics*, researchers have found prenatal cardiac defects in mice with SMA. It's believed that this discovery has implications for eventual treatment as clinicians can no longer concentrate exclusively on the nervous system when treating SMA. The researchers examined two animal models of SMA and discovered that cardiac defects are found throughout SMA development and include neonatal fibrosis in the heart, ventricle malformation, thinning of the cardiac wall and slower heart rates. The researchers said their results were consistent with clinical reports of severe SMA cases that describe a number of cardiac defects. Spinal muscular atrophy is caused by loss of the gene SMN1. Humans have an additional gene called SMN2 which only makes a small amount of the normal SMN protein required to prevent SMA. SMN1 and SMN2 are greater than 99% identical, but a small difference between the two causes the dramatic difference in the amount of functional protein produced by SMN2. Typically, the disease moves from the outlying limbs into the trunk of the body. Most deaths are caused by respiratory failure in the lungs. Researchers have been targeting SMN2, the "partially functioning backup copy," because any increase in SMN2 means better results.

WOMB TO WHEEZE

A child's chances of developing allergies or wheezing is related to how it grew in the womb, according to scientists from the University of Southampton. Researchers revealed that fetuses which develop quickly in early pregnancy but falter later in pregnancy are likely to go on to develop allergies and asthma as children, and believe this is due to changes in the development of their immune system and lungs. Fetuses that grow too slowly are also liable to become infants who wheeze from common colds, likely as a result of narrower airways in the lungs. Researchers studied 1,500 three year-old children and discovered evidence of atopy in the 27% who had developed quickly in early pregnancy but slowly later, compared with 4% who got a slow start but picked up speed.

THE OTHER CHEEK

Pregnant women who develop slapped face syndrome have a 30% chance of passing it onto their fetus during the

first trimester, with a 5-10% chance of fetal loss, according to the NIH. The syndrome is caused by parvovirus B19, which blocks the development of red blood cells and induces inflammation presenting as a facial rash. Transmission is by sneezing and coughing, with a four to 14 day incubation period. The rash can also appear on hands, wrists, and knees, forming the characteristic facial rash. Transmission of the virus is by respiratory droplets for example sneezing and coughing. The incubation period ranges from 4-14 days after exposure but may be as long as three weeks. Most vulnerable are pregnant women with weak immune systems or hematological conditions. Fetuses with tissue inflammation and red-cell loss are also at greater risk, and fetal complications can include hepatitis, anemia, heart muscle inflammation and cardiac failure. Maternal infection in



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the first trimester is associated with a fetal death risk of 19%; 13-20 weeks with 15%, falling to 6% after 20 weeks. Diagnosis involves detecting signs of heart failure through ultrasound. There's no antiviral therapy or vaccine, so management may necessitate transfusion in the womb. The facial rash can often be misdiagnosed as measles or rubella. Information is from Medical News Today, copyright Medical News Today.

PASS THE PLIERS

The medical journal *The Obstetrician & Gynaecologist* recommended promoting instrumental delivery as a way to reduce the high rate of c-sections in the second stage of labor. The journal noted that instrumental vaginal deliveries could also reduce complications in future pregnancies. As such the paper urged hands-on training using simulators and mannequins, and noted that practical training isn't typically available, resulting in less-competent junior doctors.

SOUNDS FISHY

Fish oil has no benefits for a baby's cognitive development, and its use has no effect on postpartum depression, according to a study at the University of Adelaide, Australia. The researchers noted that past studies showing DHA's efficacy were based on small samplings. The new study involved 2,000 pregnant women who took fish oil or a vegetable oil placebo. Infants at 18 months showed no cognitive differences, and the researchers posited that while DHA is an important component of brain development, infants probably get enough in the womb. At the same time, the study found that women with a history of depression who took DHA showed a slightly lower rate of postpartum depression. Also, they pointed out that there's no risk to taking fish oil. Information is from Medical News Today, copyright 2010 National Partnership for Women & Families, all rights reserved.

SNORT AND SHOOT

Deborah Frank, MD, Director of the Grow Clinic for Children at Boston Medical Center, has received a \$3.7 million grant from the NIH to study the impact of intrauterine cocaine exposure and substance exposure. Her project will look at resilience, that is, ability to beat bad odds, among young adults exposed to illicit drugs. The study will look at 140-150 urban participants between the ages of 18-24 and their caregivers, who are being monitored from birth for exposure to violence and poverty.

SWELL HEAD

Countering folk wisdom, researchers studying patients at Yale-New Haven Hospital have found that motherhood may cause the brain to *grow*, and that moms who made the biggest deal about their babies showed the greatest growth in brain areas linked to motivation and behavior. The researchers guessed that hormonal changes, including increases in estrogen, oxytocin and prolactin may play a part. As such, the mothering instinct, they noted, may be a result of brain activity. The researchers did MRIs on the brains of 19 women and images taken at two to four weeks compared to three to four months revealed that gray matter increased in small but significant portions. In adults, gray matter doesn't typically change so quickly. The areas of growth, the hypothalamus, substantia nigra and amygdala, the parietal lobe, and prefrontal cortex, support motivation, emotion processing, sensory integration, reasoning, and judgment. Mothers who claimed that their babies were special, beautiful, ideal, perfect, etc, were more likely to get sweller heads, ie, develop bigger mid-brains than more pragmatically inclined moms. The moms

in the study were about 33 years old, with 18 years of education. Half of them already had other children; none had postpartum depression. The researchers posited that the stimulation of the mom by the baby may cause the brain growth, and wondered if postpartum depression might reveal brain shrinkage. See: "The Plasticity of Human Maternal Brain: Longitudinal Changes in Brain Anatomy During the Early Postpartum Period," Pilyoung Kim, PhD, et al, *Behavioral Neuroscience* 124, 5.

TESTING FOR PREECLAMPSIA

Researchers at Harvard Medical School and in Sweden have come with an animal model of preeclampsia and a potential lab test for human diagnosis. The researchers experimented with mice genetically engineered to lack IL-10 and hypothesized that if they isolated blood serum from human patients with preeclampsia and gave a dose of it to the mice, the rodents would develop preeclampsia symptoms, which is what happened, confirming that pregnant mice lacking IL-10 provide a unique and dependable model of the disease. After observing that preeclampsia serum caused disruption to the spiral arteries, the team reasoned that preeclampsia serum might also disrupt the formation of vasculature in the lab. They created an in vitro culture of endothelial cells and trophoblasts and exposed some to serum from women with normal pregnancies and some to preeclampsia serum. The researchers found that vasculature developed normally in the presence of serum from women with normal pregnancies but that preeclampsia serum taken from women as early as 12 to 14 weeks into their pregnancies, about 10 to 12 weeks before they were diagnosed with preeclampsia, was able to disrupt vascular formation.

OLD BEFORE ITS TIME

A 42-year old woman gave birth from an embryo frozen 20 years ago, from a couple who underwent IVF treatment. Twenty years is a world record for embryo storage that resulted in a live birth. Critics say this kind of thing will encourage cross-generation adoption and will lead to more old mothers, though they didn't say why this was a bad thing. Information is copyright Medical News Today, from an article by Catharine Paddoc, PhD.

INFECTION, SCHIZOPHRENIA, AUTISM

Columbia University researchers said a pregnant woman's immune response to viral infections may induce subtle neurological changes in the fetus that can lead to an increased risk for neurodevelopmental disorders including schizophrenia and autism. The researchers exposed pregnant mice to a synthetic molecular mimic of a replicating virus. The baby mice had impaired locomotor activity, and the exposure inhibited embryonic neuronal stem cell replication, which in turn affected brain development. The researchers also examined the role of TLR3, and found that the effects of exposure were indeed dependent on TLR3. Researchers found that pre-treatment with carprofen, the non-steroidal anti-inflammatory drug, abrogated the effects of exposure.

SWEET!

High blood sugar and insulin, and low high density lipoprotein cholesterol present before pregnancy can predict whether a woman will develop diabetes during a future pregnancy, according to a Kaiser Permanente study, which suggests metabolic screening of all pre-pregnant women, especially overweight women, as a way to find those likely to develop GDM. Women who develop GDM during pregnancy are more likely to develop Type 2 diabetes after pregnancy. GDM typically occurs

during the second or third trimester and causes complications in 7% percent of US pregnancies. It also increases the baby's risk of developing diabetes, obesity and metabolic disease. Researchers studied 1,164 women without diabetes before pregnancy who delivered 1,809 live births in a 20-year span. Impaired fasting glucose, elevated fasting insulin and low HDL-cholesterol before pregnancy were associated with higher risk of GDM. Of the 1,809 live births studied, 8.5% were GDM. Among overweight women, 26.7% with cardio-metabolic risk factors before pregnancy developed gestational diabetes versus 7.4% who didn't have the risk factors. The researchers found no association between pre-pregnancy blood pressure or hypertension and risk of GDM.

AN ILL WIND

Colorado State University Scientists report that exposure to hurricanes can cause adverse fetal distress risks and lead to longer-term health care problems for affected children. Researchers analyzed long-term health statistics for women and babies who experienced Hurricane Andrew In Florida in 1992, and compared data with non-hurricane and other hurricane locales. The researchers found that a mother's exposure to the hurricane during her second trimester increased the odds of fetal distress at birth by 20%, and by 26% for moms in the third trimester. Black moms had much higher distress rates, 45% in the third trimester. First trimester hurricane exposure showed no signs of subsequent distress. Researchers said moms who are pregnant during an approaching hurricane should think about leaving, but of course that option may not be available.

ANTIBIOTICS FOR TOXOPLASMOSIS

Prenatal treatment of congenital toxoplasmosis with antibiotics might reduce the number of babies who go on to develop brain damage, epilepsy, deafness, blindness, or who die, according to the UCL Institute of Child Health, London. About a quarter of women infected with toxoplasmosis during pregnancy transmit the parasite to their fetus. The researchers tracked 293 children in six European countries in whom congenital toxoplasmosis had been identified by prenatal or neonatal screening. Two-thirds received prenatal treatment for toxoplasmosis with the antibiotics spiramycin or pyrimethamine-sulfonamide. Twenty-three fetuses developed serious neurological sequelae or died, nine during pregnancy. The researchers estimated that prenatal treatment of congenital toxoplasmosis reduced the risk of serious neurological sequelae by three-quarters.

KNOCKOUT

Last month we reported in our sister journal *Respiratory Therapy*, on nurses moving into anesthesiology: Several recent studies highlighted by The Institute of Medicine, recommended repeal of the supervision rule. A recent study, *No Harm Found When Nurse Anesthetists Work Without Supervision* by Physicians, examined nearly 500,000 individual cases in 14 states that removed the federal physician supervision requirement for nurse anesthetists between 2001 and 2005, and revealed that patient outcomes did not differ between the states that do not require physician supervision and states that do. Further, the study confirmed that there are no differences in patient outcomes when anesthesia services are provided by CRNAs, physician anesthesiologists, or CRNAs supervised by physicians. Another study, *Cost Effectiveness Analysis of Anesthesia Providers*, considered the different anesthesia delivery models in use in the US, including CRNAs acting solo, physician anesthesiologists acting solo, and various models in which a single anesthesiologist directs or supervises one to six CRNAs.

The results show that CRNAs acting as the sole anesthesia provider cost 25% less than the second lowest cost model. Alternatively, the model in which one anesthesiologist supervises one CRNA is the least cost-efficient model. Now Douglas Farrago, MD, editor of *The Placebo Journal* (placebojournal.com), a humor magazine, has weighed in, referring to a recent California decision to opt out of the Medicare provision that requires physicians to supervise nurses administering anesthesia. Farrago wrote, "This game plan... was an effort to save money... Forget the fact that an anesthesiologist has eight years of training after college, must complete a four-year clinical residency, and must pass several written and oral exams for certification, while a nurse anesthetist has about three years of training and must pass one three-hour certification exam. A bigger issue is the tension this will cause. What was meant as a relationship built on collaboration turns into one of competition. This is happening or has happened with nurse practitioners and nurse midwives as well... This is about money not about access."

GUESS AT IVF SUCCESS

Australian scientists have developed a new measure of embryo health and the prediction of a successful pregnancy using IVF. Researchers at the University of Melbourne looked at the glucose intake of embryos from the solution in which they grow in the laboratory. By measuring the level of glucose on day four or five after fertilization, they determined how much had been consumed by a growing embryo. IVF units generate between eight and ten embryos per cycle. By measuring the glucose consumption of an embryo, the researchers said it could be determined which was the healthiest embryo for transfer back to the mom. The research involved 50 patients undergoing IVF. The 28 resultant births were from the embryos which had the highest glucose uptake. Female embryos took up more glucose than males. Information is from *Medical News Today*, copyright *Medical News Today*.

BLOG REPORTS

A look at a number of blogger comments from the internet. From the *Daily Beast*: In vitro fertilization has raised a host of issues that the US refuses to grapple with, much less resolve. Reproductive technology is regulated far more heavily in other parts of the world than it is in the US, where there is no regulation, no (or little) insurance coverage and a correspondingly greater chance for bad things to happen in what has become a multimillion-dollar industry. As reproductive technologies continue to expand, they are bringing us options that push the notion of personal choice to terrifying limits [Spar, *Blogs & Stories, Daily Beast*, 10/5]... From *Salon*: a new study in *BMJ* found no evidence that Britain's high c-section rate can be blamed on moms who are too lazy, too busy or too glamorous to pant, sweat and "hee-hee-hoo" their way to a baby. Instead, most c-sections in England have a medical basis. Most c-sections in 2008 had at least one clinical risk factor. That tells us that it isn't as simple as "too posh to push" [Clark-Flory, *Broadsheet, Salon*]... *New York Times*: A study of 11,500 British children whose mothers drank lightly showed that the kids performed better on cognitive tests at age five than children whose moms didn't drink. (Children of pregnant women who drank a lot performed worse.) Doctors have long said that a little alcohol isn't a problem, the problem is defining "little" [Belkin, *Motherlode, NY Times*]... *ACLU*: California still shackles pregnant women. Arnold Schwarzenegger vetoed a bill that would have prevented pregnant women from being shackled (by law enforcement, presumably). Current California law prohibits

the use of shackles while a woman is in labor, but only a third of county jails follow the law [Woolman, Blog of Rights, ACLU].

IT'S IN THE STARS

Indian women are scheduling c-sections to align with astrological advice, causing problems for doctors and hospitals, according to the Wall Street Journal. Some moms are even picking the time of day. The percentage of c-sections in India has gone from 5% in the 90s to 20%. The number of astrologically-influenced c-sections has gone up to 50%, and women are also choosing it when there's no medical need. Doctors said moving up a birth date can cause complications. Information copyright 2010 National Partnership for Women & Families, all rights reserved.

BELLY BAND BADNESS

Obese teen girls who have gastric bypass surgery risk having babies with mental retardation or paralysis as a result of nervous system damage, according to researchers at UC San Francisco. Recently a UC researcher discovered half a dozen cases of babies born with neural tube defects caused by nutritional deficiencies related to gastric bypass surgery and its byproduct, malabsorption and insufficient folic acid. Daily folate replacement could solve the problem, but the researchers said teens don't typically comply with medical regimens or forget to take their pills. Information is from Medical News Today, from an article by Christian Nordqvist, copyright Medical News Today.

WHAT'S GOOD FOR THE MOM...

Moms who get flu shots when pregnant minimize the chance of their baby having to go to a hospital for a respiratory infection, according to researchers at the Armed Forces Health Surveillance Center. Their study involved 1,169 women who answered questions about their vaccinations. Babies whose moms had been vaccinated against flu during pregnancy had a 41% lower chance of developing a flu virus and were 39% less likely to have to go to the hospital. Blood tests showed that these babies had higher levels of influenza antibodies. Information reported by Medical News Today, by Christian Nordqvist, copyright Medical News Today.

BAD NEWS

The rate of preterm birth climbed to one in eight babies by 2007, and stillbirths account for 58% of all perinatal deaths before 28 days of life and 48% of all deaths in the first year of life, according to a report by the Society for Maternal-Fetal Medicine. The Society's report also notes that more than 8 million US women have pregestational diabetes, which complicates pregnancies and contributes to birth defects. Diabetic ketoacidosis occurs in 5-10% of pregnant women with type one diabetes, and stillbirth can occur in up to 10% of these cases. Other medical conditions impacting pregnancy include maternal hypothyroidism, systemic lupus erythematosus, renal insufficiency, and epilepsy. The rate of cesarean delivery has increased more than 50% since 1996. The risk of an abnormally adherent placenta increases with the number of prior cesarean delivery from 3% to 11% to 40% for women with one, two and three prior cesarean deliveries. Because of the foregoing, the Society is promoting the role of the MFM specialist, noting that "MFM specialists often coordinate the care of high-risk pregnant women with the patient's obstetrician to develop a plan that's tailored to her needs as well as the needs of the unborn child. As experts understanding and balancing the risks to the mother and the fetus, MFM specialists also work directly with

other medical and surgical subspecialists, anesthesiologists, and critical care team members if the condition warrants. MFM specialists work directly with neonatologist and/or pediatric subspecialists to ensure an optimal plan for newborn care as well." Contact SMFM.org.

BMC NEWS

For those institutions that want to provide more support to their researchers, yet keep expenditures within manageable bounds, BioMed Central offers its newest type of membership: Shared Support. This membership is based on a deposit of funds that cover 50% of the article processing charges for articles submitted and accepted from researchers. The other half is covered by the authors and their grants. All institutional subscriptions to BioMed Central's products purchased by Shared Support Members qualify for a 10% discount on the list prices. This new membership feature will provide greater efficiency for both authors and repository administrators. In other BMC news, Thomson Reuters has accepted BMC Medical Education for tracking. The journal is now included in the Science Citation Index Expanded, available through the Web of Science. BMC encourages visitors to take a look at recent articles, and cite its journals, as well as to submit articles for publication. For further information contact BioMed Central.

WRAP IT UP

An extremely preterm girl survived against the odds after being kept warm in bubble wrap. When the baby was born, hospital staff put it in a small plastic bag enclosed in bubble wrap, but told the mom the kid's chances weren't good. The girl weighed 397 g and was born at 26 weeks gestation. While it's normal to wrap a tiny baby in plastic, with the head out, the bubble was the innovation.

FAMILY COUNSELOR

California Family Health Council (CFHC), a leading non-profit in the reproductive healthcare industry, is pleased to announce the appointment of health care veteran Julie Rabinovitz as the new President and CEO. She was formerly Senior Vice President of Business Operations at Planned Parenthood of Illinois, responsible for the administration of 17 health centers providing services to 65,000 women and men.

PRODUCTS

NOW HEAR THIS

Clinical data confirm the practical advantages of Aurix Newborn Hearing Screening System over popular systems on the market today. Most notably, sophisticated statistical algorithms enable superior detection of auditory brainstem response (ABR) and better handling of myogenic artifact. This advanced technology dramatically reduces the need to reschedule testing when a baby is awake, and reduces the need to rescreen due to false positive results. This translates to significant time-savings which leads to direct cost-savings. Hospitals that have replaced their current equipment with Aurix have experienced no down time as they smoothly transition technicians from their current equipment to Aurix. The Aurix system is easy to use, and its operation is very familiar to technicians trained on similar equipment. All newborn hearing screening programs that use Aurix have ready access to on-site hands-on training and 24/7 customer assistance. Vivosonic Inc manufactures the Integrity system for hearing diagnostics and the Aurix Newborn Hearing Screening System.

The company markets and sells its products through a global distributor network in over 35 countries. Aurix and Integrity are trademarks of Vivosonic. Contact donna.lakshman@vivosonic.com.

CONVERSION

Covidien announced that the Thibodaux Regional Medical Center, located in Thibodaux, LA, has converted to Nellcor OxiMax pulse oximetry technology and sensors. Nellcor OxiMax technology incorporates cardiac-based signal processing algorithms which allow clinicians to track blood oxygen levels and pulse rates during challenging situations, such as during signal interference or low perfusion. Clinicians at Thibodaux now have access to multi-parameter monitors with OxiMax technology, as well as Covidien specialty sensors. These sensors include the Max-Fast forehead sensor, which is more responsive than digit sensors for patients with poor perfusion, and the SoftCare non-adhesive sensor line for patients with sensitive skin. Thibodaux is a 185-bed facility in southeast Louisiana offering a wide range of services, including heart surgery, radiation oncology, neurology, neurosurgery, plastic and reconstructive surgery, orthopedics, obstetrics, sleep disorders, and physical rehabilitation. Contact covidien.com.

LISTEN UP

The Maico MB 11 is the only ABR hearing screening system without costly disposables. The Maico MB 11 BERAphone features an integrated, reusable earphone and electrodes, avoiding the exorbitantly high costs and medical waste associated with use of disposable electrodes and ear couplers. The cost for the supplies to perform an MB11 screening is approximately 25 cents, compared to \$9-\$12 per screening with competitive systems. MB 11 uses fast rate ABR technology with a unique, CE chirp acoustic stimulus, stimulating an ABR that is almost two times larger than the response from a traditional click stimulus. This can translate into faster test times. Contact maico.com.

NEOPUFF PIECE

Fisher & Paykel Healthcare launched its enhanced Neopuff Infant T-Piece Resuscitator and the new Ergonomic T-Piece Resuscitation Circuit. The enhanced Neopuff Infant T-Piece Resuscitator provides further functionality and usability while continuing to raise the standard of care for infant resuscitation. The experience, training, concentration and fatigue level of the operator do not affect the pressures delivered. The Neopuff can accept and deliver oxygen concentrations from 21% to 100% coming from a flow meter or a blender. The T-Piece Circuit can connect to infant resuscitation masks or endotracheal tubes. The fast-acting medical-grade manometer ensures accuracy and constant reassurance of mask seal and delivered PIP and PEEP. Consistent PEEP can be delivered to assist with breathing during transport or ventilator circuit change. The new Ergonomic T-Piece Resuscitation Circuit is the first of its kind and the third circuit in Fisher & Paykel Healthcare's range of resuscitation circuits. It includes a new PEEP valve orientation for comfortable and controlled hand positioning, especially when attached to an endotracheal tube. The circuit has an improved PEEP valve adjustment to avoid unintentional changes in PEEP and a longer circuit length for better access to your infants. Lastly, this new circuit contains a duckbill port for suctioning and surfactant delivery. The new Ergonomic T-Piece Circuit is available separately or kitted with one of five sizes of neonatal resuscitation mask, ranging from the world's smallest micro-

preemie mask through to pediatric-sized masks. All resuscitation masks are specifically designed to fit comfortably to the infant's face and provide a complete seal for optimal resuscitation. Fisher & Paykel Healthcare is also pleased to release the first humidified resuscitation system for those hospitals that need to resuscitate for an extended period of time. The Neopuff Infant T-Piece Resuscitator and Classic T-Piece Humidified Circuit deliver humidified gas to help protect the pulmonary epithelium and reduce heat and moisture loss especially during prolonged resuscitation. Contact Fisher & Paykel Healthcare at www.fphcare.com.

INTEGRATED

The Hospital for Sick Children (SickKids) in Toronto has recently purchased a Vivosonic Integrity system for the Department of Otolaryngology. The Integrity system offers advanced hearing diagnostic assessment which enables reliable auditory brainstem response (ABR) measurement without the need for sedation or anesthesia, in addition to Otoacoustic Emission (OAE) assessment, and non-invasive Electrocochleography (ECoChG). The Vivosonic Integrity provides hearing healthcare practitioners with an objective means to assess the hearing of individuals with cognitive and developmental delays who cannot be tested by typical behavioural methods. Furthermore, practitioners have found that the use of the Integrity system can mitigate "loss to follow-up" rates reported by newborn hearing screening programs, and facilitate early hearing detection and intervention by enabling immediate diagnostic testing to be performed. Integrity is a trademark of Vivosonic. Contact donna.lakshman@vivosonic.com.

KEEPING ABREAST

Lansinoh Laboratories, Inc recently launched Lansinoh Professional, a new online portal to provide International Board Certified Lactation Consultants (IBCLC), RNs, midwives, doulas, OB/GYNs and other healthcare providers with resources they need to better educate and support their patients. The portal is a means for Lansinoh to deliver its breastfeeding expertise, honed over 25 years, to professionals and their patients. The portal includes how-to videos, resource lists, info on breastmilk pumping and storage, and news. Contact (610) 228-2119 or meredith@gregoryfca.com.

OUT OF THIS WORLD

The Cosmic Nee-Noggs Facial Protection from DeRoyal have been designed and researched to be pleasing, likable and fun for children between the ages of three and eight. The staff can wear the Nee-Nogg facial products with the children to help them feel more comfortable, less frightened and a bit more playful while being treated in your facility. In addition to the added patient care aspect, the facility can use the Nee-Noggs to promote themselves as the best place to bring children for high quality yet comfortable, non-threatening care. FaceShieldZ features:

- A more convenient and cost-effective way to comply with OSHA standards;
- The ability to be used whenever eye, nose or mouth contamination can be reasonably anticipated.
- UltraClear technology;
- Anti-fog on both sides;
- An optically clear, anti-static, anti-glare surface;
- The ability to accommodate eyeglasses and face masks;
- Latex-safe. Additionally, the SPEyes Eye ShieldZ offers:
- A wrap-around disposable lens for complete protection;
- UltraClear technology that prevents glare, fog and static;
- A frame that fits completely against the forehead for splash protection from above;
- Sealed lens mounting for added fluid protection;
- A clip-on/off design for quick and

easy changing; • A colored top strip that allows fingerprint-free handling; • Latex-safe. Contact deroyal.com.

NONINVASIVE

MAQUET Critical Care recently announced the launch of NAVA for non-invasive ventilation (NIV) in neonatal patients at The Third Congress of the Paediatric Societies in Copenhagen, Denmark. Neurally Adjusted Ventilatory Assist (NAVA) has become an established method of treatment in hospitals globally and now enables both invasive and non-invasive treatment. In conventional NIV, patient-ventilator asynchrony is common. Studies suggest that leaks may play a major role in generating patient-ventilator asynchrony and discomfort. NAVA provides synchronized assist while breath triggering and cycle-off are not affected by leakage. Every patient effort is assessed and responded to equally effectively regardless of patient interface used, resulting in reduced work of breathing and increased patient comfort. In neonatal and pediatric patient populations, NAVA is associated with improved patient-ventilator synchrony and lower peak airway pressure when compared with pressure support ventilation. Benefits of NAVA include improved synchrony between patient and ventilator, and enhanced patient comfort. The Edi signal can be used as a monitoring tool to provide information about respiratory drive, volume requirements, effects of changes in ventilatory settings, and to gain indications for sedation and weaning. Contact maquet.com.

SPECIALIZED

Newborn Intensive Care Specialist (NICS) announced its partnership with Conroe Regional Medical Center to provide a Level III Newborn Intensive Care Unit (NICU) that will serve the Conroe community. The NICU will offer around-the-clock neonatal intensive care services to premature, critically ill and well babies born at the new facility. All other levels of newborn care are also offered—from moderately ill babies to healthy newborns. Newborn Intensive Care Specialist provides high quality neonatology care and services to premature, critically ill and well babies. Contact newborndoc.com.

A REAL GEM

GEM Premier 4000 from Instrumentation Laboratory is the revolutionary analyzer (BG, Electrolytes, Metabolites, Glu, Lac, Hct, tHb, O₂Hb, COHb, HHb, MetHb, sO₂, Total Bili, BUN*, Creat*, measured tCO₂*) with integrated CO-Oximetry that quickly provides consistent, accurate, lab-quality results throughout your hospital. Easy-to-use, touch-screen displays make it simple to select and customize parameters. Self-contained cartridges incorporate all components for patient testing and are maintenance-free. iQM automates quality control and continuously detects, corrects and documents to assure quality results and compliance, 24/7, regardless of operator or testing location. GEMweb Plus Custom Connectivity enables remote access to any networked analyzer for real-time status updates and supervision of remote locations. [*in development.] Contact ilww.com.

IN THE CUPS

DeRoyal offers its Umblicup umbilical cord blood collection device. The Umblicup is a cylindrical container. The upper chamber of the cylinder is funnel shaped and holds a section of umbilical cord. The bottom chamber contains a sheathed needle within a housing that accommodates a standard vacuum-type test tube into which the blood from the upper chamber drains. The Umblicup is a cord blood collection device used primarily

to extract umbilical cord blood samples used by labs to test blood type and Rh factor. The Umblicup allows for cord blood to be drawn without the utilization of an exposed sharp needle, which helps prevent needlestick injuries during the cord blood extraction process. The Umblicup is also used for the collection of large volume blood and for the entrapment of blood gases. The Umblicup is an extremely cost effective safety device. No other cord blood collection device is as efficient and economical as the Umblicup. Its Tupperware-like snap on lid ensures secure fit during transport. With its funnel-shape plastic collection design, gravity ensures blood pooling in bottom of the device. No tilting is required for collection. When placed over the needle, the cap ensures safety after the vacuum tube is filled. This new patented device promotes safety and better practice, offers ease of use, and is latex-free. Contact deroyal.com.

PATCHED IN

DeRoyal Industries Inc offers its Algidex I.V. Patch. The Algidex technology is a unique combination of Ionic Silver, Maltodextrin and Alginate. This matrix formulation creates a one of a kind antimicrobial delivery mechanism that provides an immediate and “very controlled,” sustained release of the silver ions for up to seven days. The antimicrobial activity is effective against a very broad spectrum of pathogens and because the technology originates as a gel formulation, it can be incorporated into a variety of delivery mechanisms such as foam, packing gauze, contact layers, and many others. One of the most successful and effective configurations of the Algidex Technology is the Algidex I.V. Patch. It is designed to be placed around intravenous catheters or other tubes entering the body in order to help reduce the chance of infection at the insertion site. The Algidex I.V. Patch has been studied at some prestigious NICU departments around the country and has been proven to be safe and effective even in the very low birth weight infant patient population. The Algidex I.V. Patch has been used on premature infants with birth weights as low as 600 grams. The patch can be used on a variety of lines which include peripheral arterial lines, peripheral long lines, umbilical arterial lines, umbilical venous lines and central venous lines. The goal of the Algidex I.V. Patch is to eliminate the bacterial colonization associated with catheter related infections. The product is currently in use by over 300 facilities nationwide. Contact deroyal.com.

TRAINING

KCBioMedix is a new medical device company focused on developing and commercializing products that are used by neonatal healthcare providers to assess and treat the problem of incompetent feeding in premature infants. The company's first product is the NTrainer System, which enables caregivers to better manage suck initiation by providing a standardized assessment tool to measure Nonnutritive Suck (NNS) performance. The system provides ororhythmic stimulation therapy to reinforce NNS. Ororhythmic stimulation has been demonstrated to accelerate and achieve full oral feeding 7 days sooner. Contact KCBioMedix.com.

MILKING IT

Medela hosted its second annual Human Milk (breast milk) Collection Campaign in honor of the March of Dimes National Prematurity Awareness Month. As part of the campaign, Medela donated \$30,000 in breastfeeding support products to neonatal intensive care units across the country. Throughout November, participants voted for their preferred NICU, and six NICUs
Continued on page 21...

INVOS and Nellcor Monitoring Solutions in the NICU

In the NICU, clinicians manage a range of conditions in patients from congenital heart disease (CHD) to issues related to premature birth, working to optimize perfusion and oxygen delivery to prevent further injury and development of chronic health issues.

The synergistic suite of monitoring solutions from Covidien provide clinicians with action-oriented data and timely information that helps detect the subtle but critical variations in oxygenation and end organ perfusion levels that threaten the well-being of the neonates. It's that heightened perception of patient status and timely intelligence that supports the clinician's ability to diagnose problems early and intervene immediately.

Our solutions for the NICU include:

Nellcor pulse oximetry with SatSeconds Alarm Management

To avoid damage to lung tissue and complications resulting from too much oxygen, the OxiMax N-600x pulse oximeter provides highly accurate SpO₂ monitoring, alarm management, trends data and histograms to support your NICU's oxygen management program.

- The SatSeconds alarm management feature, available with the OxiMax N-600x pulse oximeter and integrated with many multiple parameter monitors, provides a safe, practical way to reduce nuisance alarms by clearly differentiating between significant desaturations or oversaturations and minor transient events.¹
- The LoSat expanded accuracy feature can track SpO₂ in low saturation conditions – 60% to 80% SpO₂ – helping you make more informed clinical decisions for patients in low saturation ranges, such as infants with CHD. OxiMax pulse oximetry technology provides the widest accuracy range in the industry (60% to 100% SpO₂).¹

INVOS Cerebral/Somatic Oximetry

The INVOS Cerebral/Somatic Oximeter helps detect ischemic threats to the brain and vital organs by measuring blood oxygen levels in the tissue directly beneath the sensor. Monitoring site-specific perfusion often provides an earlier warning of

developing pathology and deteriorating patient condition than systemic measures or laboratory tests which can remain normal even when ischemia is occurring at the regional level.^{4,7}

OxyAlertNIRSensors

Our OxyAlert NIRSensors are expressly tailored for infants and neonates. These patient-friendly, noninvasive sensors apply to the skin's surface like an adhesive band aid. Up to four sensors may be placed (such as over the brain, abdomen and renal area), providing visibility to perfusion distribution across the brain and body. Clinicians today are using this ability to help detect and manage ischemia related to conditions such as NEC, sepsis, shock, congenital heart disease, intraventricular hemorrhage, periventricular leukomalacia and respiratory distress.

SoftCareNonadhesive SpO₂ Sensors

Research has determined the use of adhesives to be the primary cause of skin breakdown among NICU patients.² Compromising the already deficient barrier function of the premature infant's skin can cause the loss of transepidermal water. Evaporative heat loss follows, as well as higher infection risk and the need for additional calories for the skin to heal. That's why we offer SoftCare nonadhesive SpO₂ sensors with a soft, pliable, low-profile foam material. Secured with a Velcro hook and loop fastener, these sensors minimize the risk of irritating fragile skin.³

All monitors connect to patients. But monitoring solutions from Covidien connect patients to the clinician.

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Improving In-Hospital Breastfeeding Management for the Late Preterm Infant

Maria Lennon, RN, MSN, CNM, IBCLC

Introduction

The late preterm population, from 34 0/7 to 36 6/7 weeks gestation, represents 8.8% of all births. Compared to babies born at term, late preterm infants are at increased risk of postbirth morbidities and mortality. According to the March of Dimes Perinatal Center, “babies born just a few weeks too soon are six times more likely to die in their first week of life than their term counterparts and three times more likely to die before their first birthday.”¹

There is also a subcategory of term births called “early term,” from 37 0/7 to 38 6/7 weeks of gestation. Evidence indicates that these infants also have increased risks of neonatal morbidity and mortality when compared with those born later at term.²

During the last six weeks of pregnancy, fetal organ systems are continuing to mature to prepare the baby for extrauterine life. Late preterm (LPT) infants have to grow and mature outside the uterus in a less-than ideal environment. These babies are born with developmental and physiologic immaturities which predispose them to: • increased risk of feeding difficulties, • infection, • temperature instability, • hypoglycemia, • jaundice, and • respiratory distress.

Maria Lennon is a Clinical Education Specialist employed by Medela, Inc. She began her extensive nursing career in North Carolina working in hospital, public health, university education and private practice settings and has been working with mothers and babies in establishing normal lactation, problem management, and special situations for over 30 years. She is a Certified Nurse-Midwife and has been continuously Board-Certified as a Lactation Consultant since the first exam was given in 1985. Lennon established one of the first in-hospital lactation centers in North Carolina and developed a 5-day Breastfeeding Educator Program for health care professionals. She worked with the North Carolina State WIC Office developing breastfeeding programs, educational materials, and community coalitions to improve breastfeeding services all across the state. In addition, she spent several years coordinating Perinatal Outreach Education for the East Carolina University School of Medicine and has received recognition for her contribution to Nursing Leadership and Service. Previous to 2000, she was director of a faculty-based nurse-midwifery program associated with New Hanover Hospital and the University of North Carolina Department of OB-GYN. For many years she volunteered her services as a La Leche League Leader, served for two years on the editorial staff of the *Journal of Human Lactation* and is a member of the American College of Nurse-Midwives, AWHONN and Sigma Theta Tau. This article was provided by Medela.

Breastfeeding is indisputably the recommended feeding for infants. While the latest CDC data indicate that the US has met the 2010 Healthy People Goal of 75% breastfeeding initiation,³ data also show that a high percentage of mothers who initiate breastfeeding are frequently unable to continue for more than a few days or weeks. In particular, LPT infants and their mothers are vulnerable to breastfeeding problems and other morbidities related to decreased milk production and low milk intake, yet it is these same infants who need the unique protective properties of human milk and can especially benefit from the interaction of breastfeeding itself.

Healthcare providers of LPT infants must be proactive in their assessments and have specialized knowledge and skills to manage early breastfeeding and prevent lactation-associated morbidities. Strategies should be used which minimize the risk of inadequate intake by the infant and maximize the volume of the mother's milk supply.

Importance of Human Milk for the Late Preterm Infant

Human milk is not only the best nutrition for human infants, it provides well-documented protection from a wide range of infectious diseases and is optimal for brain and central nervous system development.⁴

Colostrum, the early milk present in the breasts during late pregnancy and the first few days after birth, is a vital food for the newly born human infant. Colonization of the infant's GI tract begins during the birth process and early feedings of colostrum, loaded with pre and probiotics, provide the environment in which commensal bacteria thrive.

Vulnerability of LPT Infants to Breastfeeding Difficulties

Mothers who deliver late preterm infants may be at risk for delayed onset of lactation. These mothers are likely to have underlying health problems or pregnancy complications which may cause this delay. Any one or a combination of the following conditions may result in a delay of lactogenesis II (the change from colostrum to copious milk production): • maternal stress during labor and delivery, • diabetes mellitus, • pregnancy-induced hypertension, • prolonged rupture of membranes, • Chorioamnionitis, • obesity, and • delivery by cesarean-section.^{5,6}

Late preterm infants, despite their vulnerability to complications after birth, are often initially cared for in the general maternity population using feeding guidelines for healthy, full-term infants. This can be a problem. Even though a 34-to 37-weeker may look

robust and healthy at birth, their looks can be deceiving. Many of their physiologic systems are immature and the baby may have little reserve to maintain cardio-respiratory and metabolic stability.

Late preterm infants are at risk for feeding problems, especially when breastfeeding. Studies indicate that adequate vacuum pressures are important for the baby to get enough milk.⁷ The coordination of sucking, swallowing and breathing is gestationally related and is a critical skill necessary for latching on to the breast, maintaining vacuum and transferring adequate volumes of milk.⁸

The brain weight of a 35-weeker is only 60% of that of a term infant; over the next five weeks, cortical volume increases along with maturation of the brain stem, neuronal and synaptic functions. Due to central nervous system immaturity late preterm infants:

- have immature state regulation,
- sleep more,
- have diminished muscle tone, and
- exhibit immature sucking patterns, and are therefore often unable to consume an adequate volume of milk when fed exclusively at breast.

In the first few days of lactation, milk volumes are limited⁹ and only small amounts of colostrum are available to the suckling infant. Because of their various immaturities, LPT infants may not be able to extract the milk that is in the breasts and their energy needs may far outweigh their intake.^{10,11}

After lactogenesis II, effective infant suckling and the removal of the available milk from the breasts are critical to establishing adequate milk volumes of approximately 500-700 mLs per 24 hours.¹¹ Recent research shows that milk production at six days post-birth is related to milk production at 6 weeks postpartum.¹² Thus early and frequent removal of colostrum and breastmilk in the first few days after birth is an important step in laying the foundation for a plentiful long term milk supply. Supportive clinical practices in the first few days post-partum are critical to help mothers in initiating and producing milk volumes that will be adequate for their infant's growth and development.

Strategies/Technology to Improve Breastfeeding Outcomes

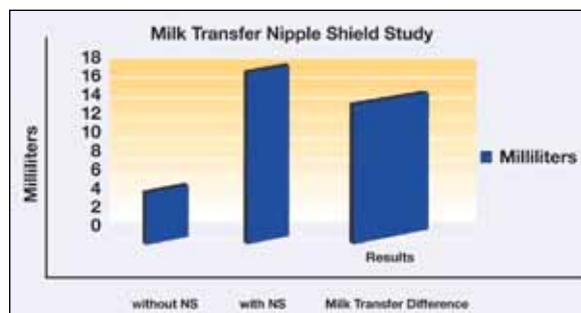
Close attention and vigilant assessment are necessary to anticipate and prevent complications. For the late preterm infant, the priorities in breastfeeding management are to ensure adequate nutritional intake and maximize maternal milk volume. A set of feeding orders or a clearly defined plan of care specifically for the LPT infants will help ensure careful monitoring.

Immediate post-birth period: Skin to Skin Contact is Essential

Continuous skin-to-skin contact is comforting, decreases stress levels for both the baby and mother and allows for early breastfeeding. Any interventions should be delayed until after the first feeding. Separating the baby from the mother causes increased crying, increased heart and respiratory rate and the release of stress hormones, all of which can deplete energy reserves and lead to hypoglycemia.

The infant should be placed prone, directly skin-to-skin on the mother's abdomen/chest and gently dried. Both baby and mother are covered with a warm blanket and a cap placed on the baby's head to conserve heat. The mother is an optimal source of heat

and, except under unusual circumstances, the infant should remain with the mother throughout the recovery period.⁴ The evidence is clear that skin to skin contact improves thermal response and increases blood glucose and cardio-respiratory stability, and a Cochrane Database Review in 2007 reported that "babies were more likely to breastfeed and to breastfeed longer, if they had early skin-to-skin contact."¹³



The First Feeding

Breastfeeding should be an essential component of delivery room care. Every opportunity should be made for the infant to breastfeed in the first hour after birth as this is an important part of the infant's transition to life outside the womb. The first breastfeeding of colostrum provides calories, begins the colonization of the infant's intestine with lactobacilli, has a laxative effect and increases meconium clearance.

Within the first hour or two after birth if the LPT infant does not latch, the mother should be shown how to express colostrum which should be stored for later feeding to the infant, if needed. If the mother and infant will be separated for any length of time (ie for NICU observation or care, etc), she should initiate breastpumping as soon as possible and within 6 hours after birth.

In-Hospital Breastfeeding Management

Family-centered couplet care provides optimal opportunities to breastfeed and allows for close assessment by the bedside nurse. A lactation consult within the first 24 hours and daily thereafter, is ideal. A feeding plan which takes into account the LPT infant's unique vulnerabilities should be developed and communicated to the family and all the staff. Breastfeeding should be observed at least every shift and an assessment made of the effectiveness of milk transfer. Mothers should be educated on the unique needs of their babies and on the use of supportive positions while breastfeeding which help the baby feed more effectively. Extended skin-to-skin contact is recommended as again, it helps to maintain temperature, cardio-respiratory and metabolic stability and allows for frequent opportunities to breastfeed. Mothers should be instructed to watch for early feeding cues and to breastfeed their LPT infants every 2-3 hours or at least 8 times in 24 hours.¹⁴ Some LPTs are able to effectively suckle at the breast for 15-20 minutes 8 to 10 times in a 24-hour period, but many are not.¹¹

Many late preterm babies tire easily and, if after several attempts (10 to 15 minutes maximum) the baby does not latch, the baby should be fed the colostrum previously expressed and stored. Mothers should be pumping their breasts after feeding attempts or approximately every 3 hours, using an evidence-based double electric breastpump, to stimulate the breasts and remove the available milk until their late preterm infants are able to feed appropriately. If the baby exhibits signs of inadequate intake,

Feeding Plan Considerations

- protect the milk supply
- pumping plan
- use of nipple shield
- in-home weight checks
- signs of feeding readiness and successful milk transfer
- determine need for supplementary feedings

ie excessive weight loss, poor feeding, significant jaundice, some supplemental feedings may be required. Hubbard, et al recommends the following (breastmilk) volumes every 2 to 3 hours: 5 to 10 mL on the first day of life, 10 to 20 mL on day 2 and 20 to 30 mL on day three.¹⁰

Lactation Technology to Improve Breastfeeding Outcomes

If the LPT infant has difficulty feeding at the breast, there are several tools designed to assist both mother and baby in obtaining an adequate milk supply.

Hospital Grade Electric Breastpump Helps Mother Maintain Her Milk Supply

Use of a double electric breastpump based on current evidence will help mothers stimulate their breasts, initiate, express and maintain an adequate milk supply to feed their baby.

Nipple Shields Help Baby Suck

A nipple shield helps the baby compensate for a weak suck and may increase intake at the breast in those babies that are having trouble feeding. A weak suck causes inadequate vacuum pressures to remove milk. Research with preterm infants has shown that some babies are able to breastfeed more effectively and efficiently with the use of an ultrathin silicone nipple shield.¹⁵

Test Weight Scale Helps Reassure that Baby is Getting Enough Milk

The use of test weights with an electronic scale that is accurate to within 1-2 grams offers a valid measurement of intake after a breastfeeding. Babies need to be weighed under the exact same conditions (same clothing, diaper, leads, etc) before and after breastfeeding. The weight increase in grams is commensurate with the baby's intake in milliliters. This information is helpful to the provider in determining adequacy of at-breast feedings and in determining the need for supplemental volumes of milk.

Supplemental Nursing System Helps Mother and Baby

A supplemental nursing system allows baby to get supplemental breastmilk via a tube while breastfeeding even if the LPT infant's suck is weak and not providing adequate vacuum. It rewards the infant for sucking efforts and helps further promote at-breast feedings and the mother/baby bond.

Discharge Planning

In planning for hospital discharge, the priorities in breastfeeding the late preterm infant at home remain the same—to ensure adequate nutrition for the baby and maximize the mother's milk supply.

Patient and family education is critical to breastfeeding success. They need to understand that their baby is immature and has special feeding needs which may take a few weeks to resolve—often until 40-42 weeks corrected gestational age.⁹

The feeding plan (see list of recommended components) should be communicated both verbally and in writing to the family. A hospital-grade electric breastpump can be rented for home use and should be used until the baby is gaining weight adequately and milk volume is well-established.

The late preterm infant will continue to need close monitoring and follow-up after hospital discharge for the development of (or worsening) jaundice, weight gain issues, and breastfeeding assessment. An initial outpatient office visit or in-home visit should occur within 24 to 48 hours and then every two to four days if needed.¹⁰

Education is Critical

In their list of Best Practices, the California Perinatal Quality Care Collaborative says, "Healthcare providers caring for late preterm infants should have the knowledge, skills and attitude to support adequate nutrition and maintain optimal communication with parents and each other. Intrapartum, postpartum and special care policies and practices should support nutrition (including breastfeeding) in a coordinated, consistent manner."¹⁶

The evidence is clear that increased duration of breastfeeding provides innumerable health benefits to both mothers and babies that can last a lifetime.^{2,4} It is essential for a mother and her family to be educated on the importance of breastmilk and how it provides not only optimal nutrition for her late preterm infant but also helps protect from disease and improved developmental outcomes. Teaching families about the possible challenges they may encounter and giving them resources on how to overcome them has been shown to help increase the success and duration of breastfeeding in the special late preterm population. For more information on how to get comprehensive education for your staff and for your patients go to www.LatePretermEducation.com.

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News – Products...continued from page 16

from various regions received \$5,000 each of Medela products or education services, including Symphony Preemie program cards, Symphony breast pumps, Waterless Milk Warmers, Creamatocrit Plus, Transport/Discharge Bags, BabyWeigh II scales and/or Medela NICU education programs. Contact medelapreemieawareness.com.

ENHANCED

Masimo announced 2011 product enhancements for its monitoring products. The **Radical-7**: Measurements – rainbow Acoustic Monitoring for accurate, easy-to-use, patient-tolerant respiration rate (RRa); rainbow Pulse CO-Oximetry for hemoglobin (SpHb), oxygen content (SpOC), carboxyhemoglobin (SpCO), methemoglobin (SpMet), and Pleth Variability Index (PVI); and “gold-standard” Masimo SET pulse oximetry for oxyhemoglobin (SpO₂), perfusion index (PI), and pulse rate. Alarms: Adaptive Threshold Alarms for audible notification only when significant changes in physiology have occurred. **Connectivity**: Integrated wireless 802.11 and Bluetooth for seamless connectivity and MyView for personalized displays through presence detection technology. Display: Flexible touch-screen display with dynamic new expanded waveforms and trend data options. **Mobility**: Compact 3-in-1 (bedside, handheld, transport) patient monitor for virtually any location and clinical setting. The new Masimo Patient Safety Net enhances and automates care on a new level. The only general floor monitoring system proven to help clinicians reduce rescue activations, ICU transfers, and ICU days, Patient SafetyNet is taking enhanced and automated care to a new level with expanded capabilities. Features: halo index for global trending and assessment of physiological parameter trends. Real-time or playback of breath sounds to assist clinicians in respiratory assessment. Plethysmographic and acoustic waveforms for real-time or playback patient assessment. MyView for personalized displays through presence detection technology. Clinician workflow analytics to help improve efficiency. Contact masimo.com.

Quality Improvement Initiative in Newborn Hearing Screening

Emily Bonilla

It began in Austin, Texas. Two company presidents met to discuss quality improvements in newborn hearing screening (NHS). Between them they sketched a proposal to bring service provider and equipment manufacturer together to collect clinical data in the well-baby nursery and neonatal intensive care unit (NICU) at several birthing hospitals in Texas.

Pain Points of a Service Provider

Ears & Hearing, PA is an independent service provider of newborn hearing screening programs for 18 hospitals in Texas. Following best practices, a team of hearing specialists apply their clinical expertise to lead and coordinate programs with a focus on quality outcomes.

In the delivery of newborn hearing screening services, Ears & Hearing noted these key pain points:

- Significant difficulty obtaining results when muscular artifact is present
- Equipment too sensitive to acoustic noise which prevents the completion of a test
- Typically difficult to obtain results in the NICU
- Testing sometimes runs more than 30 minutes before a result is generated
- Results can be inconsistent from one screen to the next
- Outpatient rescreening is costly, and leads to follow-up issues
- Equipment “cuts out” during testing which requires testing to be restarted

Vivosonic Inc, as a manufacturer of hearing screening and diagnostic equipment, believed it had designed an automated ABR hearing screening system that would overcome these issues. The company was eager to validate the system in the field, and collect data to further optimize its statistical automated ABR algorithm.

Methodology in a Nutshell

A formal plan was established to evaluate Aurix, the new hearing screening system at four hospital sites. The aim was to collect data from 100 well-babies and 100 NICU babies to assess Aurix’s performance and usability,¹ and to compare its performance to the hospital’s automated ABR screening product.

The procedures for the ABR screening followed each hospital’s hearing screening program guidelines. Babies scheduled for

newborn hearing screening with automated ABR were tested. These included those who failed automated OAE testing, and babies more than 5 days in the NICU. Each baby was screened twice, first with the hospital’s equipment, followed by Vivosonic’s Aurix.

Performance measures included screening time, variability of screening time, and refer/fail rates on initial screening only. Product usability was assessed through questionnaires, interviews, and the observations of the experienced hearing screening specialists.

Findings and Implications

Hearing screening data was collected from 179 babies at three birthing hospitals in Texas.

The experienced hearing screening technicians found Aurix easy to learn, and were immediately productive after a brief period of hands-on training. At the same time, not surprisingly, the data show that screening outcomes improved with more hands-on experience. Overall, when compared to the hospital’s equipment, Aurix demonstrated better performance on the initial screen (Table 1).

The data also suggest that several other factors affect automated ABR outcomes (Table 2): impedance, state of baby, birth age, gestational age, screening equipment, and magnetic noise.² As a consequence, the detection algorithm has been optimized to minimize the effects of the factors shown to increase referral rates and/or screening time.

Table 1. Data from Initial Screen Comparing Performance of Hospital’s Screening Equipment to Aurix²

Performance of Initial Screen	Hospital (141 ears)	Aurix (355 ears)
% of ears passed	83%	95%
Average test time (mm:ss)	5:00	1:56
Maximum test time (mm:ss)	35:00	11:38
Variability of test time (mm:ss)	12:15	3:06

Table 2. Conditions that Significantly Affected Initial Screen Performance²

Test Condition	Hospital (141 ears)		Aurix (355 ears)	
	Time (mm:ss)	% Pass	Time (mm:ss)	% Pass
Infant wakes during testing	7:32	72%	2:33	96%
High magnetic interference >=20 mG noise	-	-	1:42	95%
Premature infants	5:16	83%	1:54	95%
Infants < 24 hours old	7:15	75%	2:02	93%
Impedance difference > 5 kΩ	5:50	90%	1:50	95%

Emily Bonilla is Program Director, Ears & Hearing, Texas. This article was provided by Vivosonic. Aurix is a registered trademark of Vivosonic.

Feedback from technicians indicated that for the most part they preferred Aurix over their current equipment as it addresses key pain points. Working with the manufacturer, technicians evaluated iterative improvements to the system and clinical techniques used to prepare the babies for screening.

Findings related to the use of Aurix and the pain points described by Ears & Hearing are summarized in the following table. Implications of these findings for improved service provision are also noted.

Table 3. Findings and Implications

Findings Related to Pain Points	Implications for Service Provision
Able to test babies who woke up or moved during the test.	• Better handling of myogenic artifact reduces the need to reschedule or rescreen.
Less sensitive to intermittent noise. No need to stop testing when intermittent noise is present.	• Better handling of intermittent noise reduces or eliminates the need to restart a test.
Able to obtain screening results in the NICU environment, including babies in isolettes.	• No need to remove babies from the NICU (or isolettes) or delay screening until out of the NICU.
On average, a result is generated within 2 minutes for each ear, with a maximum time of 15 minutes for both ears.	• Fast test times reduce inconvenience to medical staff and families who require access to the baby.
Screening time is less variable.	• Less variability simplifies scheduling.
More consistent test results from one screen to the next.	• More confidence in the accuracy of the test results.
Fewer outpatient rescreens required.	• Cost savings. Avoids "lost to follow-up" issues.
Stable and reliable performance of equipment.	• Eliminates technician frustration due to unreliable equipment.

Discussion

The pain points encountered by Ears & Hearing are typical of many newborn hearing screening programs in the United States. Oftentimes, attempts to mitigate these issues are managed by establishing rigorous procedures and training based on best practices. With advancements in technology, it is now possible to further impact and improve the quality of newborn hearing screening programs and outcomes by introducing new and innovative technologies.

Advances in digital signal processing that do not rely on artifact rejection techniques are better able to handle myogenic artifact common to babies who wake during testing. The Aurix system uses a sophisticated statistical detection algorithm based on Kalman Weighted Averaging and a proprietary method of adaptively estimating noise.

Better immunity to high magnetic field noise often present in NICU environments is made possible by reducing the distance between the electrodes and the amplifier, an enhanced design of the amplifier (filter), and enabling wireless communication between the recording component and the computer.

Statistical techniques used to identify signal from noise based on waveform amplitudes provide more accurate testing of premature infants compared to template or pattern matching approaches derived from term infants. This should be considered when screening infants in the NICU.

The initiative that began in Austin, Texas, has led to significant quality improvements in the development of an advanced newborn hearing screening product, with findings that have important implications for newborn hearing screening programs



worldwide. What started as an exchange of ideas has become a rewarding partnership.

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Feeding Issues

Information for this article was provided by KCBioMedix, Inc.

The NTrainer System from KCBioMedix is an FDA cleared medical device that promotes early development of essential sucking skills in premature infants. The system includes a mobile crib-side workstation that allows real-time assessment of oromotor ability and therapeutic intervention in the premature infant.

The NTrainer System's assessment mode provides an objective, quantitative and replicable means of determining the organization of an infant's non-nutritive suck (NNS). This measurement of feeding readiness enables the NICU clinicians to more objectively determine the infant's status thus providing assessments that are more consistent from infant to infant, provider to provider. The NTrainer System represents the first objective, physiologically-based tool that gives the medical professionals almost instant feedback about the status of the infant's oromotor system through the assessments of NNS.

In the therapeutic mode, the NTrainer System utilizes a Soothie silicone pacifier with a computer-controlled air pump to transform the nipple into a dynamically patterned pulsing touch stimulus on the surface of the infant's lips and tongue. The therapy can be administered to the infant in a cradled position or inside the isolette either during gavage feeding sessions or before breast or bottle feeding sessions. The therapy is used to train the infant to develop an organized sucking pattern by reinforcing their NNS.

Studies have shown that the NNS capabilities the NTrainer System develops can lead to earlier transition to oral feeding¹ and more rapid weight gain², enabling hospitals to promote infant growth and development while reducing stress on patients and their families. Improving non-nutritive suck has also been linked to significant reductions in hospital length of stay,³ resulting in a lower cost of care. The therapy also provides the attention and care infants would normally associate with oral feeding.

The NTrainer System is designed for ease of use. It requires normal/standard medical expertise and only a few hours of training to operate, enabling NICUs the flexibility to assign operating responsibilities to several different staff members. Interpretation and reporting are simplified through easy-to-use quantitative indicators and graphical results display.

KCBioMedix is a new medical device company focused on developing and commercializing products that are used by

neonatal healthcare providers to assess and treat the problem of incompetent feeding in premature infants.

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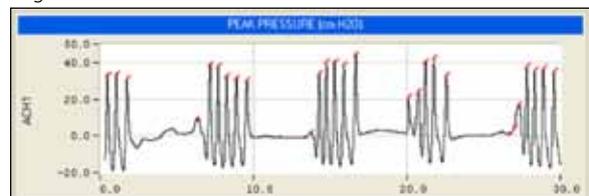
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The following charts show when an infant's NNS is non-organized, organized and the orocutaneous therapy pattern, respectively.

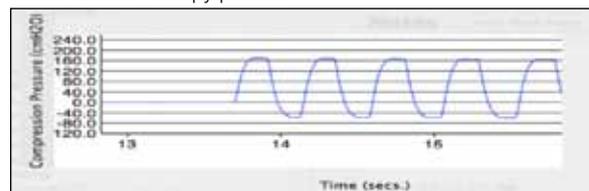
Non-organized



Organized



Orocutaneous therapy pattern



Clinical Reports

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Reducing Severe Eye Damage in Premies

A multicenter study published in *Acta Paediatrica* found that clinical practice change with Masimo SET Pulse Oximetry reduced severe eye damage by more than 50% in premature newborns. The study results showed that centers switching to Masimo SET reduced ROP rates from 12% to 5%, while another center not using Masimo SET had no change in ROP reduction rates. Researchers concluded that the “reduction in the incidence of severe ROP and need for laser therapy was associated with the use of signal extraction pulse oximetry (Masimo SET)” and the study “findings lend further support to the significance of using improved saturation monitors in managing critically-ill infants.” The aim of the study, *Prevention of Retinopathy of Prematurity in Preterm Infants through Changes in Clinical Practice and SpO₂ Technology*, by Armando Castillo, et al, was to identify if pulse oximetry technology is associated with decreased ROP and laser treatment. Infants under 1,250 gm who had eye exams were compared at two centers in 3 periods. In Period 1, SpO₂ target was >93% and pulse oximetry technology was the same in both Centers. In the second period, guidelines for SpO₂ 88-93% were implemented at both centers and Center B changed to oximeters with signal extraction technology (SET) while Center A did not, but did so in Period 3. At Center A, severe ROP and need for laser treatment remained the same in Periods 1 and 2, and decreased in Period 3 to 6% and 3% respectively. At Center B, severe ROP decreased from 12% (Period 1) to 5% (Period 2) and need for laser decreased from 5% to 3%, remaining low in Period 3. The authors concluded that in a large group of infants <1,250 gm, a change in clinical practice in combination with pulse oximetry with Masimo SET, but not without it, led to significant reduction of severe ROP and need for laser therapy. Pulse oximetry selection is important in managing critically ill infants. The authors further concluded: “there is a tendency by some clinicians to believe that non-therapeutic monitoring devices with similar functionality deliver similar performance. However, as clinicians, we all understand that the decisions we make, right or wrong, are often based on the numbers shown on patient monitors. Therefore, the accuracy and reliability of monitored physiologic information can be just as important, if not more important, than the therapeutic interventions that follow. In this study, we have shown that use of one type of pulse oximetry technology appears to strongly affect the incidence of ROP.” [The above article was provided by Masimo. At the time we went to press, it had been accepted by *Acta Paediatrica* for publication.]

Left Heart Hypoplasia

Data submitted by Mitchell R. Goldstein, MD, Citrus Valley Hospital, West Covina, CA.

A spontaneous, vaginal delivery of a 3.5 kg male occurred at term to a primigravida mother with an unremarkable prenatal history. Apgars were 9/9 and he was discharged at one day of age. Nine days later he was brought to the clinic for evaluation due to reduced intake. The child appeared pink and well perfused; mother was advised to increase his intake of clear liquids. The following morning, the infant was brought to the emergency room with the parent’s observation of labored breathing.

Salient Findings and Outcome

The dyspneic child was profoundly pale with circumoral cyanosis. CBC, electrolytes, and spinal tap were essentially normal. The ER staff was unable to obtain a blood gas or saturation reading on pulse oximetry. The in-house neonatologist was summoned. He too attempted to get several conventional pulse oximeters to read without success. He decided to try an investigational Masimo SET pulse oximeter. The Masimo SET device revealed a saturation of 30% with a pulse rate in the 40’s. The first blood gas was drawn which confirmed the Masimo SpO₂ value. The baby was intubated and moved to the NICU while hand ventilated with 100% oxygen. The Masimo SET device continued to display during the next two critical hours of resuscitation and stabilization with the readings continuing to corroborate the periodic blood gases. The base deficit values for the first two blood gases were off scale but a steady improvement occurred over the next five hours (see table below). An echocardiogram revealed a hypoplastic left heart with retrograde aortic flow. The child was placed on a ventilator and a PGE1 and Dobutamine infusion was started. The plan was to wean mechanical ventilation as tolerated and keep the SpO₂ in the 85% range to discourage excessive pulmonary blood flow. The child was further stabilized and after consultation transferred to a pediatric heart center. Eight days later he received a cardiac transplant and is healthy today.

Sequential History of the First Six Blood Gases				
Time	pHa	PaCO ₂	PaO ₂	BE
0520	6.56	88	29	off scale
0542	6.73	98	36	off scale
0730	6.88	61	23	-26.2
0830	7.07	35	65	-20.6
0930	7.24	31	54	-13.2
1030	7.42	36	43	-0.6

Discussion

Infants with a hypoplastic left heart can go undiagnosed, therefore a rapid response to their inevitable decompensation is vital. In this condition, the circulating blood volume and pulse pressure are so low as to make percutaneous vascular access impossible and a arterial cut-down is required. This makes even the assessment of pulse rate by palpation difficult. Conventional pulse oximetry does not work in such conditions. The Masimo SET oximeter acquired and displayed the SpO₂ and pulse rate

in this low perfusion state making assessment of the patient's cardiopulmonary status during resuscitation possible. Were it not for the steady rise in SpO₂ values, the resuscitative efforts for this baby would have been aborted. This newborn's life was likely saved by Masimo SET pulse oximetry.

The Impact of Masimo SET Pulse Oximetry on the Reduction of ROP

Submitted by Jorge R. Raber, RCP, RRT, Neonatal/Pediatric Respiratory Therapy Coordinator, Cedars Sinai Medical Center, Los Angeles, CA.

Retinopathy of Prematurity (ROP) is one of the most severe complications associated with the care for preterm infants. Although ROP may not yet be entirely preventable, the standard of care has proven critical in keeping the incidence and severity of this disease to a minimum. The major risk factor is the degree of the prematurity, but there are many other associations. Hypoxia, hyperoxia and fluctuations of the arterial oxygen tension, even within the normal range, have all been implicated as etiological factors. This led us to believe that if we had a tighter control on the amount of oxygen that our patients received, we could significantly reduce the fluctuations in arterial oxygen tension.

In order to accomplish tighter control of oxygen, strict guidelines in the practice of increasing and weaning of FiO₂ and the monitoring of oxygen saturation were implemented throughout the infant's hospitalization, including the delivery room, and during transport.¹ Accurate feedback relating to the patient's oxygen saturation was a critical step to ensuring the effectiveness of our program. As such, we were very interested in incorporating an accurate, reliable pulse oximetry technology that would not be affected by motion and low perfusion, and thus work effectively for this challenging patient population.

Our clinical staff compared the performance of different oximeters during challenging conditions often seen in the NICU. We selected Masimo SET (Signal Extraction Technology) because we concluded that it was more reliable during these special conditions.

After we installed Masimo Radicals, our ability to accurately monitor oxygen saturation improved dramatically. The response time of Masimo oximeters is noticeably faster, which is especially important during desaturations where every second counts. Masimo SET oximeters are also more accurate and reliable, avoiding unnecessary interventions and the nuisance of false alarms.

The table shows the incidence and trending of ROP III-IV and ROP surgery at Cedars Sinai Medical Center (CSMC) over a four-year period, as compared with the Vermont Oxford Network's (VON) data—the VON is a non-profit voluntary collaboration of over 380 NICUs of varying sizes that maintains a database including information about the care and outcomes of high-risk newborn infants.

	400 - 1500 grams ROP III - IV		500 - 1500 grams ROP Surgery	
	CSMC	VON	CSMC	VON
1997	12%	(10%)	4.5%	(3.0%)
1998	8%	(8%)	1.5%	(3.0%)
1999	4%	(8%)	1.5%	(3.4%)
2000 to present	2.6%	N/A	0%	N/A

Discussion

We believe that the use of Masimo SET technology, especially with neonates, where motion and low perfusion are common, has helped our efforts to adhere to the oxygen titration guidelines in order to reduce severe ROP in the extremely low birth weight infants in our unit. This newborn's life was likely saved by Masimo SET pulse oximetry. [Reference: 1. Chow LC, Wright KW, Forbis S, Sola A. Can Changes in Clinical Practice Decrease the Incidence of Severe Retinopathy in Extremely Low Birthweight Infants? *Pediatric Research* 2001;49(4):400A/2081.]

There is (Still) Too Much Aluminum in Infant Formulas

Shelle-Ann M. Burrell, Christopher Exley

Abstract

Background: Infant formulas are sophisticated milk-based feeds for infants which are used as a substitute for breast milk. Historically they are known to be contaminated by aluminum and in the past this has raised health concerns for exposed infants. We have measured the aluminum content of a number of widely used infant formulas to determine if their contamination by aluminum and consequent issues of child health persists.

Methods: Samples of ready-made milks and powders used to make milks were prepared by microwave digestion of acid/peroxide mixtures and their aluminum content determined by THGA.

Results: The concentration of aluminum in ready-made milks varied from ca 176 to 700 µg/L. The latter concentration was for a milk for preterm infants. The aluminum content of powders used to make milks varied from ca 2.4 to 4.3 µg/g. The latter content was for a soya-based formula and equated to a ready-to-drink milk concentration of 629 µg/L. Using the manufacturer's own guidelines of formula consumption the average daily ingestion of aluminum from infant formulas for a child of 6 months varied from ca 200 to 600 µg of aluminum. Generally ingestion was higher from powdered as compared to ready-made formulas.

Conclusions: The aluminum content of a range of well known brands of infant formulas remains high and particularly so for a product designed for preterm infants and a soya-based product designed for infants with cow's milk intolerances and allergies. Recent research demonstrating the vulnerability of infants to early exposure to aluminum serves to highlight an urgent need to reduce the aluminum content of infant formulas to as low a level as is practically possible.

Background

Infant formulas are milk-based feeds for infants which have been developed as alternatives to breast milk. Though cow's milk is the main ingredient of many infant formulas they are sophisticated products which have been designed to meet the specific nutritional needs of children from babies born pre-term

through to infants of several years of age.¹ There are also non-cow's milk-based formulas, often made from soya, for infants with intolerances or allergies to cow's milk.²

There has been a long and significant history documenting the contamination of infant formulas by aluminum^{3,9} and consequent health effects in children.¹⁰⁻¹³ Through these and other publications manufacturers of infant formulas have been made fully aware of the potentially compounded issue of both the contamination by aluminum and the heightened vulnerability, from the point of view of a newborn's developing physiology, of infants fed such formulas. There have been similar warnings over several decades in relation to aluminum toxicity and parenteral nutrition of preterm and term infants.¹⁴⁻¹⁷ To these ends the expectation would be that the aluminum content of current infant formulas would at the very least be historically low and at best would be as low as might be achieved for a processed product. We have tested this premise and we have found that the aluminum content of a range of branded infant formulas remains too high.

Methods

We have chosen 15 different branded infant formula products. These include powdered and ready-made liquid formulas based on cow's milk and a soya-based product. The categories of formulas included those for preterm babies, stage one (0-6 months) and stage two (6 months plus) infants. All products were stored according to the manufacturer's instructions. Products were sampled directly from their packaging to avoid extraneous contamination. Ready-made liquid products were shaken between each sampling.

Homogenates of each product were prepared by microwave digestion (Mars Xpress, CEM) using a 50/50 mixture of 14 M HNO₃ and 30% w/v H₂O₂. Homogenates were diluted as required in ultra pure water (conductivity <0.067 µS/cm) to give clear samples. The aluminum content of samples was measured by Transversley Heated Graphite Atomiser (THGA; Analyst 600, PE Life Sciences) using an analytical program developed in our laboratory. Five replicate samples were prepared for each of the products. Each sample was measured 3 times and its mean was accepted if the %RSD was <10%.

Results

The mean aluminum content of ready-made milk formulas ranged from ca 176 µg/L (Hipp Organic Growing-Up Milk) to ca 700 µg/L (Cow & Gate Nutriprem 1) (Table 1). Two products

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Table 1 The aluminium content of ready-made (RM) milk infant formulas

Commercial Name of Product N = 5	[Al] µg/L Mean (SD)	[Al] µg/L Range
Sma First Infant Milk	267.9 (40.9)	210.1-322.5
Sma Follow-On Milk	245.8 (59.0)	174.5-309.8
Cow & Gate First Infant Milk	338.8 (34.8)	293.0-371.0
Hipp Organic Growing-Up Milk	175.5 (34.7)	131.4-236.8
Aptamil Follow-On Milk	296.1 (13.9)	279.3-314.2
Cow & Gate Follow-On Milk	303.7 (10.8)	285.3-316.8
Cow & Gate Growing-Up Milk	430.0 (214.8)	285.3-856.5
Cow & Gate Nutriprem 1	700.4 (93.6)	602.5-863.0

(Cow & Gate Growing-Up Milk and Cow & Gate Nutriprem 1) presented a wide range of values which suggested an inhomogeneous distribution of aluminum in these products. Generally Cow & Gate products had higher contents of aluminum than the other brands tested.

The aluminum content of powders used to make milk formulas

The mean aluminum content of milk powders ranged from ca 2.4 µg Al/g powder (Sma First Infant Milk) to ca 4.3 µg/g (Sma Wysoy Soya Infant Formula) (Table 2). The range of values for the 5 replicates of each sample was high for almost all products (for example, 1.7-10.8 µg/g for Cow & gate Follow-On Milk) which suggested that aluminum was not evenly distributed within the milk powders. When the aluminum content of the powders were used to make reliable estimates of their aluminum content as ready-to-drink milks the values ranged from ca 333 to 629 µg/L (Table 2). In general, the aluminum content of formulas prepared from powdered milks were significantly higher than ready-made milks (for example, 296.1 and 592.4 µg/L for Aptamil Follow-On Milk ready-made and powdered milks respectively).

The average ingestion of aluminum in infant formulas for children aged 6 months ranged from 206 (Sma Follow-On Milk RM) to 592 (eg Sma Wysoy Soya Infant Formula P) µg Al per 24 h period (Table 3). All values were determined based upon manufacturer's guides to age-related consumption. Ingestion is predicted to be higher from formulas prepared from powders than ready-made milk formulas (for example, 296 and 532 µg Al/24 h for Aptamil Follow-On Milk ready-made and powdered milks respectively). Generally the greatest exposure to aluminum was through the Hipp Organic products and the Sma soya-based product.

Discussion

Commercially available branded infant formulas used by literally millions of parents to feed children of up to 12 months plus of age are still significantly contaminated with aluminum. The concentrations of aluminum in the milk formulas varied from ca 200-700 µg/L and would result in the ingestion of up to 600 µg of aluminum per day. The suggestion is that these products are 'contaminated' with aluminum as each of the manufacturers insist that aluminum is not knowingly added to their products. Milk formulas prepared from powders contained significantly more aluminum than their equivalent ready-made product. Aluminum products are used extensively in food processing,¹⁸ for example, as anti-caking agents, though there is no indication that they are being used in this way in powdered milk formulas.

Table 2 The aluminium content of milk powders (P) used in formulas

Commercial Name of Product N = 5	[Al] µg/g Mean (SD)	[Al] µg/g Range	[Al] µg/L*
Sma Wysoy Soya Infant Formula	4.3 (1.0)	3.7-6.0	629.0
Sma First Infant Milk	2.4 (1.4)	1.3-4.6	333.3
Hipp Organic Follow-On Milk	3.6 (1.6)	2.1-6.3	500.0
Hipp Organic Good Night Milk	2.9 (1.5)	1.7-5.5	406.0
Cow & Gate First Infant Milk	2.8 (0.6)	1.8-3.5	424.0
Hipp Organic First Infant Milk	2.7 (1.3)	0.2-4.2	394.4
Aptamil Follow-On Milk	3.1 (0.5)	2.3-3.8	592.4
Cow & Gate Follow-On Milk	2.5 (3.4)	1.7-10.8	477.8

*Based upon manufacturer's instructions for preparing the milk.

The likelihood is that many of the individual constituents of the formulas are contaminated with aluminum.^{19,20} The sources of such contamination are myriad though would probably include equipment used in both processing and storing of bulk products. In addition many of the formulas were packaged for sale using aluminum-based materials. The high content of aluminum in the soya-based formula probably reflects its prior accumulation in the soybean plant and the known aluminum tolerance of some soybean cultivars that are grown on acid soils.²¹ Previous research has also highlighted higher contents of aluminum in soya-based infant formulas.⁹

The aluminum content of infant formulas measured herein are not significantly different to historical values and this lack of improvement in lowering their content suggests either that the manufacturers are not monitoring the aluminum content of their products or that the manufacturers are not concerned at these levels of contamination. While it is the case that the present levels of aluminum in infant formulas have not been shown to cause adverse effects in healthy infants it is also the case that

Table 3 The daily ingestion of aluminium by infants at 6 months of age based upon the mean aluminium content of the product and the manufacturers recommended feeding volumes

Commercial Name of Product RM-ready made; P-powdered	Al ingested from product µg Al/24 h period.
Sma First Infant Milk RM	224
Sma First Infant Milk P	323
Sma Follow-On Milk RM	206
Sma Wysoy Soya Infant Formula P	592
Cow & Gate First Infant Milk RM	285
Cow & Gate First Infant Milk P	385
Cow & Gate Follow-On Milk RM	301
Cow & Gate Follow-On Milk P	429
Cow & Gate Growing-Up Milk RM	107 (at 12 months)
Cow & Gate Nutriprem 1 RM	112-263*
Aptamil Follow-On Milk RM	296
Aptamil Follow-On Milk P	532
Hipp Organic Growing-Up Milk RM	88 (at 12 months)
Hipp Organic First Infant Milk P	380
Hipp Organic Follow-On Milk P	592
Hipp Organic Good Night Milk P	477

*Values are for preterm infants of a very low initial body weight (< 1 kg) up to term (ca 2.5 kg)

there have not been any clinical studies which refute such as a possibility. Previous research has highlighted the potential toxicity of aluminum in infants with confounding disorders (including, prematurity, poor renal function and gastrointestinal disease) and fed infant formulas¹⁰⁻¹³ and these studies when viewed alongside aluminum's known connections with medicine and human disease²² should at least deter complacency concerning this issue. It is widely accepted that the not fully developed physiologies of infant's gastrointestinal tract, kidneys and blood-brain barrier may predispose them to aluminum toxicity^{10,11,16,23,24} and while there are no definitive links between aluminum exposure through infant formulas and immediate or delayed toxicity in healthy infants this neither should not nor does not preclude such as a possibility. The widespread use of infant formulas would necessitate that any attempt at an epidemiological study would require a Herculean effort even with well-defined levels of exposure and quantifiable end-points. However, there are clear links between toxicity in infants and parenteral exposure to aluminum. For example, parenteral exposure of preterm infants to ca 55 µg Al/kg body weight/day, which is a level of systemic exposure to aluminum which is possible from regular feeding of infant formulas over periods of weeks, resulted, at 18 months of age, in neurodevelopmental effects¹⁵ and, in the same cohort of children 15 years later, in significant affects upon bone health.¹⁷ The authors concluded, with good reason, that the potential long-term consequences of early aluminum exposure deserve renewed attention.¹⁷ The aluminum content of infant formulas is between 10 and 40 times higher than the aluminum content of breast milk, (usually ca 15-30 µg/L⁷), and will contribute significantly towards the body burden of aluminum in infants. It is clear that aluminum in infant formulas is a significant component of early life exposure to this ubiquitous contaminant and as such every effort should be made by manufacturers to reduce the aluminum content of these products to an achievable practical minimum while at the same time manufacturers should be compelled to indicate the level of contamination by aluminum on the packaged product.

Conclusions

Infant formulas are integral to the nutritional requirements of preterm and term infants. While it has been known for decades that infant formulas are contaminated with significant amounts of aluminum there is little evidence that manufacturers consider this to be a health issue. Aluminum is non-essential²⁵ and is linked to human disease.²² There is evidence of both immediate and delayed toxicity in infants, and especially preterm infants, exposed to aluminum and it is our contention that there is still too much aluminum in infant formulas.

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Infant Hearing Screening and Sedation

Laszlo Sandor

HEARING SCREENING: THE HISTORICAL BACKGROUND

A specially designed battery-powered infant hearing screener was used in the early 1960s known as the Apriton (from the auro-palpebral reflex, the involuntary body movement and eye blink resulting from sudden sound onset. The examiner presented a sudden onset narrow-band noise stimulus of 90 dB SPL followed by observation for the presence or absence of reflexive infant responses. Subsequently, motion detectors were used. In 1971, risk criteria for screening included immediate family history of malformation, a family member with hearing loss in childhood, an infant born with a structural anomaly, bilirubin levels of >20 mg 100 mg, exchange transfusions; birthweight <1500 gm, and/or abnormal otoscopic findings. Fairly current risk criteria in the first 28 days are: family history, congenital infection, craniofacial anomalies, birthweight <1,500 gm, ototoxic meds, bacterial meningitis, apgar 0-3 at 5 minutes, mechanical ventilation >10 days, and stigmata. Universal hearing screening prior to hospital discharge using OAE or ABR techniques was established at the 1993 NIH Consensus Conference. The 2000 JCIH position statement said: screen all babies prior to hospital discharge using OAE or ABER, and introduced the 1-3-6 concept: screen by one month, diagnosis by three months, early intervention prior to six months. Specifically, the criteria included an illness or condition requiring an admission of 48 hours or more to an NICU. The Joint Commission noted that VLBW infants are at risk for both sensorineural and conductive hearing loss. In 2007 CHIH changed the definition of target hearing loss, established protocols for NICU vs well babies, urged communication with parents, and returned to the criteria of one risk for late onset and progressive loss. (From History of Newborn Hearing Screening, Lylis Olsen, MS, MPH, The EAR Foundation of Arizona.)

Historical moments in newborn hearing screening, from the CDC:

1965 – Babbidge Report (Report to the Secretary of HEW): Recommended the development and nationwide implementation of “universally applied procedures for early identification and evaluation of hearing impairment.”

- 1967 – Recommendations from the National Conference on Education of the Deaf:
 - High-risk register to facilitate identification.
 - Public information campaign.
 - Testing of infants and children 5-12 months of age should be investigated.
- 1988 – The Commission on Education of the Deaf reported that the average age of identification for profoundly deaf children in the US was 2½ years.
- 1988 – An advisory group of national experts convened: Advisory group selected by the US Department of Education and Bureau of Maternal and Child Health to advise the government about the feasibility of developing early identification guidelines, and recommended that the federal government fund demonstration projects to expand and document systematically the cost efficiency of proven techniques already in existence but infrequently used.
- 1988 – Former Surgeon General C. Everett Koop issued a challenge that by the year 2000, 90% of children with significant hearing loss be identified by 12 months of age.
- 1990 – The Joint Committee on Infant Hearing (JCIH)–Position Statement recommended that high-risk infants be screened prior to their discharge from the hospital and no later than 3 months after their birth.
- 1990 – Healthy People 2000. Its goal: To reduce the average age at which children with significant hearing impairment are identified to no more than 12 months by year 2000.
- 1993 – The National Institutes of Health Consensus Development Program recommended that newborns be screened for hearing loss before leaving the hospital.
- 1994 – The JCIH Position statement recommended that “all infants with hearing loss should be identified before 3 months of age and receive intervention by 6 months of age.”
- 1999 – The American Academy of Pediatrics endorsed universal newborn hearing screening.

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- 2000 – The JCIH Year 2000 Position Statement offered principles and guidelines for early hearing detection and intervention programs.
- 2001 – Healthy People 2010. Goal: Increase the proportion of newborns who are screened for hearing loss by age 1 month, have audiologic evaluation by age 3 months, and are enrolled in appropriate intervention services by age 6 months. Also in 2000, all hospitals were mandated to provide hearing screening prior to discharge.
- 2006 – Newborn hearing screening results were included on the NDDoH's electronic birth certificate. However, preemies weren't included because the birth certificate was submitted before testing.
- 2008 – The USPSTF released an update in July 2008 concluding there is scientific evidence to recommend newborn hearing screening for all infants.

For more see cdc.gov/ncbddd/hearingloss/ehdi-history.html.

A SOURCE FOR HEARING INFO

The House Ear Institute, hei.org: The House Research Institute's Children's Auditory Research and Evaluation (CARE) Center is devoted to improving the communication ability of infants and children with auditory disorders through research, clinical services and education of professionals and families. Working with physicians of the House Clinic, CARE Center professionals provide a comprehensive interdisciplinary evaluation of a child's hearing abilities, determine appropriate treatments and make recommendations for long-term care. The Center's research laboratories continue to advance scientific knowledge of normal development of auditory and speech/language processing functions through applied and basic research. Its scientists are tracing the maturation of the auditory system from birth to 18 years of age and the impact hearing loss has on that process. The laboratory on Development of Human Auditory Function studies maturation of auditory physiology using measurement tools such as otoacoustic emissions, electrophysiology and psychophysics. It studies auditory function in human subjects across the entire age spectrum, beginning with prematurely born neonates. The lab has active collaborations with hearing scientists at Northwestern University and the University of Washington. Researchers in the Pediatric Hearing Loss and Auditory Perception Laboratory and clinicians from CARE have joined forces to create a "living laboratory" whereby children with hearing loss undergo clinical assessment and management while simultaneously participating in any number of research projects. In conducting these studies, the researchers collaborate with researchers from Johns Hopkins University, Indiana University, San Diego State University, and the University of Iowa. The research and clinical staff are experts in the areas of pediatric audiology, speech-language pathology, psychology, education, and early intervention. Its studies are supported by the National Institute on Deafness and Other Communication Disorders (NIDCD) and the NIH.

SEDATION

The Society for Pediatric Sedation, pedsedation.org, is the first and only society that specifically addresses issues involving pediatric sedation by valuing the input and collaboration of a

diverse group of individuals. SPS members represent a wide cross section of parents, child life specialists, nurses, advanced practice nurses, and physicians from across the world. Its primary interest is in improving care for children who require procedures and examine best practices through the aid of distraction and/or sedation to achieve the highest quality outcome for the patient.

SEDATION BACKGROUNDER

Joseph Cravero, MD offered a lecture on neonatal sedation at the 4th Interdisciplinary Conference on Pediatric Sedation, presented by the Society for Pediatric Sedation. The following is from his powerpoint presentation. The first question he posited was: does pain/stress control matter? Yes. Newborns learn quick responses to pain. They exhibit higher VAS during skin alcohol prep, and there's more grimacing and crying during venipuncture. He concluded that newborns anticipate pain and are more expressive when they have previous exposure. Neonatal pain has long-term effects related to the total number of invasive procedures. Stressful conditions at birth are associated, for instance, with increased salivary cortisol responses to subsequent vaccination at about six months. Pain pharmacology has issues, however, relating to development. Enzyme systems in the liver aren't fully developed until 3 to 6 months. Glomerular filtration rate is quite low at birth, and reaches adult levels by six months. Infants have diminished ventilatory responses to hypoxia and the blood brain barrier is immature.

Neonates are a high risk population for sedation. The Pediatric Sedation Research Consortium reported on pulmonary complications such as apnea and desaturation. Pulmonary complications were highest at birth. Studies in rats have shown evidence that neonatal exposure to sedatives and anesthetics can lead to neuroapoptosis.

Common sedating agents are chloral hydrate, midazolam, ketamine, dexmedetomidine, and propofol. Each has advantages and disadvantages. For instance, chloral hydrate acts quickly, but has led to decreased oral intake and increased number of bradycardia events. Midazolam has an extensive history of use, but its efficacy has lately been questioned. There is little information on dexmedetomidine and neonates, but it hasn't been implicated in neuroapoptosis. However it affects the liver; it's eliminated through the kidneys, and its half-life is two hours. Side effects can include hypertension. Propofol clearance is different in neonates than in adults: glucuronidation is limited and hydroxylation dominates. Clearance is diminished and variable, and therefore drug accumulation is more likely. Full recovery can be significantly delayed.

PAIN MANAGEMENT BACKGROUNDER

From Current Trends in Neonatal Pain Management, a powerpoint presentation.

Pain: "unpleasant sensory and emotional experience associated with actual or potential tissue damage." Preterm infants are likely to have greater sensitivity to pain than full term infants. Neonatal pain assessment tools are PIPP, NFCS, NIPS, CRIES score, N-PASS and FLACC.* Some are more reliable than others. Pain is treated with opioids, benzodiazepines, barbiturates and local anesthetics. Opioids include morphine, fentanyl, alfentanil,

and methadone. Benzodiazepines are midazolam, lorazepam, and diazepam. Barbiturates are phenobarbital, thiopental, chloral hydrate, propofol, and ketamine. Other pain relievers are non-steroidal anti-inflammatory drugs and acetaminophen. Neonatal pain guidelines are: Consensus Statement for Prevention and Management of Pain in the Newborn; American Academy of Pediatrics Prevention and Management of Pain in the Neonate 2006 Update; NANN Guidelines Pain Assessment and Management; and AWHONN Guidelines Pain Assessment and Management for Neonates.

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*Premature Infant Pain Profile; Neonatal Facial Coding Scale; Crying-Requires increased oxygen administration, Increased vital Signs, Expression, Sleeplessness; Neonatal Pain, Agitation, and Sedation Scale; Face, Legs, Activity, Cry and Consolability.

SEDATION AND ABR TECHNOLOGY

Sedation for hearing testing isn't necessarily safe, and has health risks for neonates. Auditory brainstem response testing can often eliminate the need for sedation, which reduces patient risk and the cost of administering the test.* According to Kurtz, et al, in their article, "Advancing ABR Technology,"** "ABR without sedation is a viable and practical alternative to conventional ABR practices. While ABR measurement often requires sedation and/or anesthesia to minimize the muscular activity of infants and young children, interest in a safe and effective alternative is increasing. An ABR assessment is valuable for estimating hearing thresholds of infants and young children, and for assessing suspected retrocochlear auditory dysfunction. A considerable disadvantage, however, is the use of sedation and/or anaesthesia to obtain clear ABR recordings. Sedation and anesthesia are associated with medical risks to patients, parental concern, scheduling delays, increased time and costs, and specialized resource demands."

A recent study presented at the AudiologyNOW! conference in San Diego, CA stated that ABR testing without sedation is "clinically feasible and valuable." In the study, ABR testing without sedation was performed on 103 children in a resting state using the Vivosonic Integrity system with a conventional

test protocol. The authors found that the non-sedation option enabled timely management decisions for more than 90% of the cases, reduced the need for ABR assessment with sedation or anesthesia by 66%, reduced the cost of performing an ABR by at least 85%, and significantly reduced the wait time for an ABR assessment from more than 2 months to less than 3 weeks. Another study presented in Chicago revealed that non-sedated ABR significantly reduced wait times for an ABR assessment from 5 or 6 months to 1 week. Of 124 ABR tests performed with the Vivosonic Integrity system, 110 were completed successfully without sedation. The study identified improved patient safety, parent satisfaction, and scheduling as major benefits. An added benefit was the ability to test awake newborns who had failed their screening, eliminating the need for follow-up appointments, and providing parents with same-day results.

How It Works

ABR testing without sedation using the Vivosonic Integrity system relies on new signal processing technologies, improved amplifier and design and wireless capabilities. According to Kurtz, et al, "Conventional ABR systems reject responses contaminated by artifact; the Integrity combines a proprietary method of adaptively estimating the noise in each response with the method of Leski to weight each and every response, resulting in an ABR with minimum probability of error. This technique is known as Linear Minimum Mean-Square Error Filter, or Kalman-weighted averaging." Vivosonic's patented Amplitrode design amplifies the ABR signal at the recording electrode site with no intervening wire.

In situ amplification minimizes the electromagnetic interference picked up by lead wires in conventional amplifiers, and minimizes the effects of motion artifacts that contaminate ABRs. Wireless communication between Vivosonic's VivoLink and the computer allows a baby to be held or strolled during testing. Vivosonic's Aurix Newborn Hearing Screening System, which integrates Integrity technology, is also particularly effective when screening awake babies. [* in Sokolova, et al, from Hearing Review, April 2007, Allied Media, Anthem Media Group. **Information is from "Advancing ABR Technology," by Isaac Kurtz, MHS, PE; Rose Nishiyama, BSc; Patricia Tedesco, MSc, published in BAA Magazine, British Academy of Audiology, April, 2010, and provided to Neonatal Intensive Care by Vivosonic, Inc. Aurix, Integrity, and VivoLink are trademarks of Vivosonic. Amplitrode is a registered trademark.]

ABR MEASUREMENT

The journal *Pediatrics* published a study by Mason et al, "Universal Infant Hearing Screening by Automated Auditory Brainstem Response Measurement." Its purpose was to identify infants with a bilateral, permanent, handicapping hearing loss and to provide them with amplification before age 6 months. The study population consisted of 10,372 infants born during a 5-year period. Universal hearing screening by automated auditory brainstem response was done in the nursery. Infants who failed the screening test were followed up diagnostically. Infants who were not tested in the nursery were followed up as outpatients. Hearing aids were recommended for those infants who had bilateral hearing loss. Successful screening in the nursery was achieved for 96% of infants. The failure rate was 4%. The incidence of bilateral loss requiring amplification was 1.4/1000. The false-positive rate was 3.5% after the initial screening and .2% when a two-stage screening procedure was used. The incidence

of congenital bilateral hearing loss in the well population was 1/1000, and in the neonatal intensive care unit population, 5/1000. The cost of screening was \$17 per infant, and the cost to identify each true bilateral hearing loss was \$17,750. Amplification was recommended for 15 infants; well infants who used hearing aids before age 6 months achieved age-appropriate speech and language development. The authors concluded that mild, moderate, and severe bilateral, persistent hearing loss can be identified in the nursery by automated auditory brainstem response measurement to provide amplification before age 6 months and thus optimize speech and language development. [Pediatrics Vol 101 No 2, February 1998, pp 221-228, Judith A. Mason and Kenneth R. Herrmann, from the Departments of Audiology Services and Pediatrics, Kaiser Permanente Medical Center, Honolulu, HI.]

NURSES AND HEARING TESTING

Reported in Update on Newborn Hearing Screening Programs, Pediatric Nursing, May-June, 2002, by Amy Nagorski Johnson, copyright bnet Health Publications.

Nurses in the intensive care nurseries are the front line initiators of the universal hearing program. Because the average hearing test cost, including staff, equipment, and materials, is estimated between \$30 and \$40, it is important that the infant be tested under the best circumstances. The nurse is best able to determine the optimal time for the individual infant and facilitate testing by providing good environmental testing conditions. To ensure test accuracy, the timing of the hearing test based on the individual infant's needs is essential. Infants should be tested after feeding when the infant is in a quiet alert to asleep state; the infant should remain undisturbed by nursing staff and family during the test. The environment should be free of distractions, such as noise from patient rounds, equipment alarms, music and overhead pages, and staff conversations. Nursery nurses' primary responsibilities to the universal hearing program are to ensure that all infants are screened prior to discharge and that infants with suspected hearing loss are referred for follow-up assessment. Careful documentation in the chart and on all discharge paperwork is essential for continuity of care and provision of services beyond hospitalization. In addition, infants who may have passed the initial hearing screen but are at risk for hearing impairment need referral for follow-up screening as well. These indicators include all infants admitted to a neonatal intensive care unit, those with a family history of hearing impairment, and infants with craniofacial abnormalities. Since a primary goal of the program is not to miss one child with hearing loss, it is easy to recognize the importance of the nursery nurses' role.

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Acro-Cardio-Facial Syndrome

Maria Cristina Digilio, Bruno Dallapiccola

Abstract: Acro-cardio-facial syndrome (ACFS) is a rare genetic disorder characterized by split-hand/split-foot malformation (SHFM), facial anomalies, cleft lip/palate, congenital heart defect (CHD), genital anomalies, and mental retardation. Up to now, 9 patients have been described, and most of the reported cases were not surviving the first days or months of age. The spectrum of defects occurring in ACFS is wide, and both interindividual variability and clinical differences among sibs have been reported. The diagnosis is based on clinical criteria, since the genetic mechanism underlying ACFS is still unknown. The differential diagnosis includes other disorders with ectrodactyly, and clefting conditions associated with genital anomalies and heart defects. An autosomal recessive pattern of inheritance has been suggested, based on parental consanguinity and disease's recurrence in sibs in some families. The more appropriate recurrence risk of transmitting the disease for the parents of an affected child seems to be up to one in four. Management of affected patients includes treatment of cardiac, respiratory, and feeding problems by neonatal pediatricians and other specialists. Prognosis of ACFS is poor.

Disease Name and Synonyms: Acro-cardio-facial syndrome (ACFS); Cleft palate-cardiac defect-genital anomalies-ectrodactyly (CCGE) syndrome.

Definition: Acro-cardio-facial syndrome (ACFS, OMIM 600460) is a rare genetic disorder characterized by split-hand/split-foot malformation (SHFM), facial anomalies, cleft lip/palate, congenital heart defect (CHD), genital anomalies, and mental retardation. This association was first described by Richieri-Costa and Orquiza in 1987 in a Brazilian patient born to consanguineous parents.¹ The existence of this syndrome was corroborated by the report of 8 additional patients.²⁻⁷ We are aware of an additional Turkish patient born to consanguineous parents (Kayresili, personal communication 2009), presenting with SHFM, aortic stenosis, cleft palate, hypoplastic corpus callosum, and atretic ears. The acronym CCGE (cleft palate-cardiac defect-genital anomalies-ectrodactyly) was also proposed to identify this unique constellation of anomalies.² Additional features occasionally found in these individuals include cortical atrophy of the brain,³ cerebral neuroepithelial

cyst,⁵ growth retardation,^{1-3,6} vertebral malformations,⁷ subclinical hyperthyroidism,⁷ imperforate anus.⁶ ACFS is a lethal disorder as shown by the early demise in the first months of life in most of these patients.

Epidemiology: The incidence of ACFS has not been determined, due to the paucity of the reported cases, but it is likely a very rare disease (<< 1 in 100,000 newborns). A similar occurrence among genders is expected for an autosomal disorder. The excess of male patients reported so far (7 M: 3 F) is likely biased by the low number of observations.

Clinical Description: Clinical features of ACFS are summarized in Table 1. The most important diagnostic handles are SHFM and CHD. The spectrum of defects occurring in ACFS is wide, and both interindividual variability and clinical differences among sibs have been documented. Most published cases have not survived the first days or months of life.

Limbs: Cleft hand is a constant feature, either bilateral or unilateral (figure 1C). Subluxation of metacarpophalangeal joints and finger flexion at the proximal interphalangeal joints can be also found.⁶ Cleft foot occurs in a proportion of these patients. Cutaneous finger and toe syndactyly has been reported in some cases.³⁻⁵ Radiographic findings include cleft hand/foot with agenesis of fingers¹⁻⁷ (figure 1E), abnormal structure and articulation of the first metacarpal bone,^{4,6,7} hypoplastic and short metacarpal bones,^{1,7} presence of extrabones between phalanges,^{6,7} hallux valgus,⁴ absent or abnormally modelled phalanges of toes,⁴ polydactyly of foot.⁵

Congenital Heart Defects: CHD have been detected in two third of the patients.^{1-5,7} Anatomic types are heterogeneous, including septal defects,^{1,5} left-sided obstructive lesions,^{2,3} and conotruncal defects.^{4,7} Left-sided obstructive lesions have been described, as aortic coarctation and hypoplastic left heart. Conotruncal heart defects include truncus arteriosus type 1 with dysplastic and stenotic truncal valves⁴ and tetralogy of Fallot with absent left pulmonary artery.⁷

Facial Anomalies: Facial anomalies are not distinct for the syndrome, and clinical expression appears quite variable. Reported dysmorphisms include high forehead, prominent eyes, long eyelashes, hypertelorism, flat nasal root, low-set dysmorphic ears (figure 1A,B,D). Lip and palate anomalies are often present, manifesting as bilateral cleft lip and cleft palate,^{1,7} unilateral cleft lip and palate,³ cleft palate only.^{2,5}

The authors are with the Division of Medical Genetics, Bambino Gesù Pediatric Hospital, Rome, Italy. Reprinted from BioMed Central, Orphanet Journal of Rare Diseases, © 2010 Digilio and Dallapiccola; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License.

Table 1: Major clinical features of the acro-cardio-facial syndrome

Clinical finding	References									Total	%
	1	2a	2b	3	4	5a	5b	6	7		
Sex	M	M	F	M	M	M	F	F	M	6M/3F	
Facial anomalies	+	+	+	+	+	+	+	+	+	9/9	100
High forehead	-	+	NK	-	+	+	+	NK	+	5/7	71
Prominent eyes	-	-	NK	+	+	-	-	NK	-	2/7	29
Long eyelashes	+	-	NK	+	+	-	-	NK	-	3/7	43
Hypertelorism	-	-	NK	+	+	+	+	NK	+	5/7	71
Broad/flat nasal root	+	+	NK	+	+	-	-	NK	+	5/7	71
Cleft lip	+	-	-	+	-	-	-	-	+	3/9	33
Cleft palate	+	-	+	+	-	-	NK	+	+	5/8	63
Low-set dysmorphic ears	+	+	NK	+	+	+	+	+	+	8/8	100
Limb anomalies	+	+	+	+	+	+	+	+	+	9/9	100
Cleft hand (bilateral)	+	+	+	+	-	+	+	+	-	7/9	78
Cleft hand (unilateral)	-	-	-	-	+	-	-	-	+	2/9	22
Cleft foot (bilateral)	+	-	-	-	-	-	+	-	-	2/9	22
Cleft foot (unilateral)	-	-	-	-	+	-	-	-	-	1/9	11
Congenital heart defect	+	+	-	+	+	-	-	+	+	6/9	67
Ventricular septal defect	+	+	-	-	-	-	-	+	-	3/9	33
Atrial septal defect	-	+	-	-	-	-	-	+	-	2/9	22
Aortic coarctation	-	+	-	+	-	-	-	-	-	2/9	22
Mitral atresia	-	+	-	-	-	-	-	-	-	1/9	11
Truncus arteriosus	-	-	-	-	+	-	-	-	-	1/9	11
Tetralogy of Fallot	-	-	-	-	-	-	-	-	+	1/9	11
Absent left pulmonary artery	-	-	-	-	-	-	-	-	+	1/9	11
Genital anomalies	+	+	NA	-	+	+	NA	NA	+	5/6	83
Micropenis	+	+	NA	-	-	+	NA	NA	+	4/6	67
Cryptorchidism	+	+	NA	-	+	+	NA	NA	-	4/6	67
Hypospadias	+	+	NA	-	-	+	NA	NA	-	3/6	50
Low birth weight (<3rd centile)	-	+	+	-	-	+	+	-	+	5/9	56
Growth retardation	+	+	NA	+	+	-	NA	NK	+	5/6	83
Neurological anomalies	+	+	NK	+	+	-	NK	+	+	6/7	86
Mental retardation	+	+	NK	+	+	-	NK	NK	+	5/6	83
Hypotonia/Hypertonia	+	+	NK	-	+	-	NK	NK	-	3/6	50
Cortical brain atrophy	+	-	-	+	NK	NK	NK	-	NK	2/5	40
Neuroepithelial cyst	-	-	-	-	NK	NK	NK	+	NK	1/5	20
Dead/Alive	Alive	Dead	Dead	Dead	Dead	Alive	Dead	Dead	Dead		
Age	4 y	1 m	6 h	4 m	1 m	25 y	4d	50 d	14 y		

References: 1, Richieri-Costa and Orquizas, 1987 [1]; 2, Giannotti et al., 1995 [2]; 3, Guion-Almeida et al., 2000 [3]; 4, Mingarelli et al., 2005 [4]; 5, Sivasli et al., 2007 [5]; 6, Kariminejad et al., 2008 [6]; 7, Tanpaiboon et al., 2009 [7]

Abbreviations : M, Male ; F, female ; NK, not known; NA, not applicable; y, years; m, months; h, hours; d, days

Genital Anomalies: Male patients manifest different genital anomalies, ranging from micropenis^{1,2,6,7} to cryptorchidism,^{1,2,4,6} and hypospadias.^{1,2,6}

Growth: Growth retardation is a common prenatal and postnatal finding, resulting in low birth weight,^{2,6,7} weight deficiency often in conjunction with feeding difficulties,^{1-3,7} and short stature.^{1,6,7}

Neurological Anomalies: The prevalence of mental retardation in ACFS is at present unknown, due to early demise of the majority of these patients. One of the two survivors was mentally normal by age 25 years,⁶ while the other displayed developmental delay at the age of 4 years.¹ A patient described by Tanpaiboon et al [2009],⁷ who died at age of 14 years, was mentally normal. Neurological anomalies as hypotonia, hypertonia, and seizures have been reported in the first days/months of life. Occasional

brain anomalies have been observed, including cortical atrophy^{1,3} and cerebral neuroepithelial cyst.⁵

Etiology: The genetic mechanism underlying ACFS is still unknown. Isolated or syndromic SHFM has been linked to different loci or genes. Mutations in p63 gene, responsible for Ectrodactyly-Ectodermal defects-Cleft (EEC) syndrome and related disorders with SHFM,⁸ have been excluded in a patient with ACFS.⁷ An autosomal recessive pattern of inheritance is supported both by consanguinity in a few families and recurrence in sibs born to unaffected parents.^{1,2,6} The involvement of a small chromosomal microdeletion cannot be ruled out, since CGHarray has never been performed in published patients. The possibility should also be considered that this condition could be genetically heterogeneous.



Figure 1: Facial and limb features of two patients with the acro-cardio-facial syndrome: A,B,C,E: patient reported by Mingarelli et al., 2005 [4]; D: patient reported by Giannotti et al., 1995 [2] (2a in Table 1). A: Lateral total body view; B: Facial appearance of patient 4, showing high forehead, prominent eyes, long eyelashes, hypertelorism, broad nasal root; C: Ectrodactyly of right hand; D: Facial appearance of patient 2a, showing high forehead, broad nasal root, low-set dysmorphic ears; E: X-ray of right foot, showing split foot malformation with five metatarsal (including a very hypoplastic second metatarsal) and absence of all the phalanges of second and third toes.

Diagnosis: The diagnosis of ACFS is solely based on clinical characteristics. The major diagnostic criteria include SHFM and CHD. Cleft lip/palate and genital anomalies are less common features. Although facial anomalies are not distinct, low-set dysmorphic ears appear as a constant feature. Recurrence among sibs born to unaffected parents suggests an autosomal recessive inheritance and provides a clue to differentiate ACFS from autosomal dominant disorders with similar features.

Antenatal Diagnosis: The major diagnostic features characteristic of ACFS can be detected prenatally by ultrasonography. A second trimester scan, including echocardiography and upper/lower limbs evaluation is recommended for monitoring the pregnancies of parents with an affected child.

Genetic Counselling: An autosomal recessive pattern of inheritance has been established for ACFS. Therefore, the more appropriate recurrence risk of transmitting the disease for the parents of an affected child seems to be up to one in four.

Differential Diagnosis: ACFS shares features with other ectrodactyly syndromes and clefting conditions associated with genital anomalies. However, EEC syndrome,⁹ Rapp-Hodgkin syndrome¹⁰ and ectrodactyly-cleft lip/palate-hand/foot deformities-mental retardation^{11,12} can be ruled out, based on lack of ectodermal involvement in ACFS. Malpuech syndrome can be also excluded based on distinct facial features and absent limb defects.¹³ CHD, cleft palate, and genital anomalies are features of genito-palato-cardiac syndrome, but none of the reported cases had ectrodactyly.¹⁴ DiGeorge/velo-cardio-facial

syndrome can be considered in patients with conotruncal heart defect,^{4,7} and excluded using FISH analysis of chromosome 22q11.2.⁴ CHARGE syndrome can also be included among conditions in differential diagnosis, since SHFS can be found and ears can be similar in the two conditions.³

Management: Patients with ACFS are at high risk of death in the first months of age. The co-occurrence of CHD, low birth weight and hypotonia probably play a major role onto the weakness of affected patients. Cardiac and respiratory problems should be treated by the neonatologist and other specialists, including the cardiologist and the broncopneumologist. A nutrition specialist should be consulted for feeding problems. The surviving patients will benefit from physical therapy, which should start in the first months of life in babies manifesting hypotonia/hypertonia and motor delays. In the surviving patients, neuropsychological assessment should be performed every year to check for the presence of developmental and cognitive delay. Deficits should be treated with rehabilitative programs. The correction of SHFM depends on the individual anatomic defects, and should be managed by orthopaedics and plastic surgeons. When indicated, genital anomalies should be treated by surgeons or urologists.

Prognosis: Life expectancy is very poor in ACFS individuals. Most of the known patients survived only a few hours or months. Cardiopulmonary complications were the main cause of death. Two patients were alive at time of the observation, respectively at 4 and 25 years.

Continued on page 41...

Laryngeal Mask Airway for Neonatal Resuscitation in a Developing Country

Vincenzo Zanardo, Alphonse Simbi, Massimo Micaglio, Francesco Cavallin, Leon Tshilolo, Daniele Trevisanuto

Abstract

Background: Studies carried out in developing countries have indicated that training courses in newborn resuscitation are efficacious in teaching local birth attendants how to properly utilize simple resuscitation devices. The aim of this study was to assess the knowledge and expertise gained by physicians and midwives who participated in a Neonatal Resuscitation Course and workshop organized in a Third World Country on the use of Laryngeal Mask Airway.

Methods: A 28-item questionnaire, derived from the standard test contained in the American Heart Association and the American Academy of Pediatrics Neonatal Resuscitation Manual, was administered to 21 physicians and 7 midwives before and after a course, which included a practical, hands-on workshop focusing on LMA positioning and bag-ventilation in a neonatal manikin.

Results: The knowledge gained by the physicians was superior to that demonstrated by the midwives. The physicians, in fact, demonstrated a significant improvement with respect to their pre-course knowledge. Both the physicians and the midwives showed a good level of expertise in manipulating the manikin during the practical trial session. The midwives and physicians almost unanimously manifested a high degree of approval of neonatal resuscitation by LMA, as they defined it a sustainable and cost-effective method requiring minimal expertise.

Conclusions: Further studies are warranted to test the advantages and limits of the neonatal LMA training courses in developing countries.

Background

Intrapartum hypoxia and birth asphyxia are widely regarded as major causes of morbidity and mortality in developing countries.^{1,2} All those involved in delivery room care must, consequently, possess the knowledge and expertise to perform neonatal resuscitation.³

Maintaining a patent airway and providing effective positive

All the authors are with the Department of Pediatrics, Padua University, Italy, except Micaglio, who is with the Department of Pharmacology and Anesthesiology. Reprinted from BioMed Central, BMC Health Services Research, © 2010 Zanardo et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License.

pressure ventilation, which is currently achieved in the delivery room by means of a face mask or a tracheal tube, is standard treatment and forms the cornerstone of emergency neonatal care in First World countries,² but making these interventions feasible in settings where resources are limited is particularly challenging.^{4,5} Since its introduction into clinical practice, the LMA has gained increasing popularity for resuscitation of adult as well as pediatric patients, and more recently in neonatal resuscitation. Some organizations have, in fact, made it a part of their guidelines and LMA has been included in the AAP and AHA Guidelines of Neonatal Resuscitation Program since 2000.^{3,6} It has been seen that LMA provides a low pressure airtight seal against the glottis⁷⁻¹⁰ and studies on the efficacy of ventilation by medical and paramedical personnel in neonatal training models have shown that it is characterized by ease of insertion and rapid, adequate airway patency.¹¹ Although this device cannot be considered a substitute for the TT, it could, at least theoretically, play an ancillary role in developing countries¹² where it offers practical, cost-effective, sustainable advantages over the face mask.

Some studies carried out in Third World countries have indicated that local birth attendants who have been trained in newborn resuscitation are capable of learning and properly utilizing simple resuscitation techniques (eg mouth-to-mask breathing and room air),⁴ reducing asphyxia-related deaths.¹³⁻¹⁶ It is uncertain, however, what aspects of these training programs were responsible for that outcome. The aim of this study is to assess the knowledge gained by local birth attendants (physicians and midwives) who participated in a NRP course and workshop on LMA organized in the Democratic Republic of Congo (DRC).

Methods

A 3-day NRP course was held by the Continuing Education for Africa (CEFA), in Kinshasa, the DRC, in September 2006. The course consisted of a number of didactic sessions proportionally divided into the seven steps of the NRP: (I) principles of resuscitation; (II) initial steps in resuscitation; (III) bag mask ventilation; (IV) chest compressions; (V) tracheal intubation; (VI) medications; and (VII) special considerations,³ followed by practical hands-on training session, including LMA positioning and bag-ventilation in a neonatal manikin (Neonate Airway Trainer; Laerdal, Norway).

Twenty-eight local birth attendants, (21 physicians and 7 midwives) from the Congo Brazzaville (1), Benin (1), Cameroun

Table 1 Knowledge gained by participants during a NRP training course on neonatal resuscitation focusing on LMA

Neonatal Laryngeal Mask Airway Features	Pre-test correct answers n.(%)		Post-test correct answers n.(%)	
	Physicians: n. 21	Midwives: n.7	Physicians: n.21	Midwives: n.7
Range	5	3	7	3
Size	6	1	10	3
Lubrication	3	2	11 [^]	4
Tip flattening	5	3	11 [^]	3
Advancing	5	2	10	4
Location	4	1	12 [^]	3
Cuff inflation	5	0	11 [^]	3
Connection for PPV	13	5	11	5
Correct positioning	1	0	14*	7
	47/189 (24.8)	17/63 (26.9)	97/189 (51.3)	35/63 (55.5)
Advantages over the face mask				
Less skill required	4	0	11 [^]	6
Easy placement	3	1	4	2
Better airtight seal	1	1	12*	3
Improved SO ₂	3	1	11	6
Function unaffected by anatomical factors	1	1	6	1
Less hand fatigue	7	0	10	7
	19/126 (15.0)	4/42 (9.5)	54/126 (42.8)	25/42 (9.52)
Advantages over the tracheal tube				
Easier and quicker placement by trained medical and non-medical personnel	5	2	10	4
Avoids laryngoscopy	2	5	14*	7
Avoids tracheal oedema	4	0	14*	6
Efficacy in upper airway malformations when intubation and mask ventilation fail	9	4	14	6
Avoids use of neuromuscular blocking agents	4	3	15*	7
	24/105 (22.8)	14/35 (40.0)	67/105 (63.8)	30/35 (85.7)
Disadvantages				
Gastric insufflation and aspiration	0	0	8	4
Inadequate alveolar ventilation	13	3	14	6
Impossibility of suctioning the airway	4	3	8	6
Impossibility of administering drug endotracheally	12	3	14	7
	29/84 (34.5)	9/28 (32.1)	44/84 (52.3)	17/28 (60.7)
Potential applications in neonatal resuscitation				
When face mask and tracheal tube resuscitation fail	10	6	15	7
In neonatal training models allows a patent airway in a shorter time than endotracheal tube	4	0	14*	6
Incidence of failure low with LMA	10	5	15	7
Ruinously	5	2	15*	7
	29/84 (34.5)	13/28 (46.4)	59/84 (70.2)	27/28 (96.4)

Pre- and post-test correct answers.

[^]McNemar test p value (p < 0.05), corrected by Bonferroni's adjustment (p < 0.05)*

(1), and the remaining from other areas of the DRC, participated in the course. All of the participants took—both before and after the course—a 28 question test, an adaptation of a standard one contained in the AHA/AAP Neonatal Resuscitation Manual³ and underwent a practical trial evaluating their proficiency in manipulating LMA and a neonatal manikin. The participants had 60 minutes to complete the test, which included multiple choice,

fill-in-the blank, and true/false questions. The test, which was written in French, was strictly supervised.

The questions concerned: (I) features of LMA; (II) advantages of LMA over the face mask; (III) advantages of LMA over the endotracheal tube; (IV) disadvantages of LMA; and (V) potential applications in neonatal resuscitation.

Table 2 “Improvement”, defined as the difference between the pre- and post-test scores

Neonatal LMA		Improvement n.	McNemar Test [§]	Improvement *%	Fisher test*
Features	Physicians	50	p < 0.0001	35.2	p < 0.72
	Midwives	18	p < 0.0001	40.9	
Advantages over the face mask	Physicians	35	p < 0.0001	32.7	p < 0.02
	Midwives	21	p < 0.0001	55.3	
Advantages over the tracheal tube	Physicians	43	p < 0.0001	53.1	p < 0.08
	Midwives	16	p < 0.0001	76.2	
Disadvantages	Physicians	15	p < 0.0001	27.3	p < 0.26
	Midwives	8	p = 0.08	42.1	
Potential applications	Physicians	30	p < 0.0001	54.5	p < 0.006
	Midwives	14	p = 0.001	93.3	

Facial mask, FM; tracheal tube, TT

[§] Improvement (n) = a pre-test wrong answer coupled with a post-test correct answer by McNemar's test. *Improvement (%) = improvement number over pre-test wrong answer number ratio by Fischer's test. p value (p < 0.05).

The theoretical test was followed by a practical trial during which the trainees were asked to attempt LMA insertion in a manikin (designed for skills training in neonatal resuscitation) in less than 15 seconds (successful insertion was defined as effective thorax expansion verified by the instructor). The participants were also asked to anonymously express their opinion about their degree of satisfaction (high/low) with the course and the sustainability and cost-effectiveness (yes/no) of LMA in their respective countries.

“Improvement,” defined as the difference (number or percentage) between the pre and post test scores, in the two groups (physicians and midwives) was analyzed separately by the McNemar test and Fisher's exact test, as appropriate. A post hoc multiple comparison analysis using the Bonferroni's adjustment was performed when statistically significant (p<0.05) differences were found in the groups. A p value <0.05 was considered significant.

Results

Theoretical knowledge about and practical skills in neonatal resuscitation using LMA on a neonatal manikin gained by the participants (physicians and midwives) at a neonatal resuscitation course are outlined in Tables 1 and 2.

Compared with the initial score, the overall knowledge gained by the physicians and midwives who participated in the NRP course and workshop on neonatal resuscitation by LMA was increased, but with different percentages regarding the single test questions. In particular, physicians significantly improved in 12/28 post-test items analyzed by McNemar's test and in 7/12 by Bonferroni's adjustment.

The improvement, defined by the number of correct answers in post-test coupled with a wrong answer in pre-test, was statistically significant for the physicians and midwives with reference to the questions concerning their theoretical knowledge about LMA. The improvement, defined by the percent of correct answers in post-test coupled with a wrong answer in

pre-test, with regard to the questions dealing with the advantages of LMA over the facial mask (p<0.02) and its potential applications (p<0.005) was statistically significant for the physicians alone. The degree of approval by the physicians and midwives of neonatal resuscitation by LMA and their opinions regarding its sustainability and cost-effectiveness are outlined in Table 3.

The practical part of the test showed that the physicians and midwives were skillful in their attempts at LMA insertion. One physician and one midwife failed, respectively, 3 and 2 times to insert the device correctly. All the midwives and physicians,

Table 3 Practical trial in inserting LMA in a neonatal manikin

LMA::	Physicians: n. 21	Midwives: n. 7
Successful placement:		
- number of attempts:		
1	20	6
2	0	1
3	1	0
Insertion time:		
- positioning < 15 seconds	20	6
- positioning > 15 seconds	1	1
Degree of approval:		
- high	20	7
- low	1	0
Sustainability:		
- yes	20	7
- no	1	0
Cost-effectiveness:		
- yes	20	7
- no	1	0

with the exception of one, expressed a high degree of approval with regard to neonatal resuscitation by LMA and defined it a sustainable and cost-effective procedure.

Discussion

Neonatal mortality, amounting to an estimated 4 million deaths worldwide each year takes place, in 98% of cases, in developing countries. As approximately 19% of these deaths are due to birth asphyxia,¹ identifying solutions to achieve the Millennium Development Goal of halving child mortality by 2015 by means of a wide-scale implementation of cost-effective interventions has become urgent.¹⁷

In this study, we proved the capability of learning and properly using in a manikin model LMA by physicians and midwives, trained in a developing country to a NRP course and to a workshop on LMA. The knowledge gained by the physicians related to the LMA was superior than that achieved by the midwives. Manikin-based comparative practical skills on LMA insertion showed instead, a similar high efficacy between trained physicians and midwives, in terms of number of successful attempts and of time for placement. Unanimously, midwives and physicians, except one, also manifested a high degree of approval of the neonatal resuscitation by LMA, giving a positive evaluation of his/her sustainability and cost-effectiveness in a low income country.

Some studies have demonstrated that NRP courses are effective in teaching neonatal resuscitation in developing countries¹⁸ and have indicated approaches and techniques that have proved efficacious in preliminary trials in saving newborn lives.^{14,19} Birth attendants in India²⁰ and China²¹ involved in the NRP have been able to reduce asphyxia-related deaths. There is also evidence that mouth-to-mask and bag-and-mask resuscitation are comparable techniques with regards to neonatal mortality and morbidity.^{4,22} The evidence that room air^{23,24} and mouth-to-mask could be satisfactory used for neonatal resuscitation²⁵ suggests that firstly, it is reasonable to promote the basic elements of resuscitation of newborn resuscitation, as routine part of newborn care. Meanwhile, where feasible, all birth attendants should be trained to provide positive ventilation with other conventional methods currently used in neonatal resuscitation, bag-and-mask or bag-and-LMA ventilation.

The LMA may theoretically offer many practical (ie easier transport and sterilization), cost-effectiveness, and sustainable advantages (ie low cost coupled with the fact that it can be reused) over the face mask. As mentioned above, LMA allows a low pressure airtight seal against the glottis⁷⁻⁹ and studies on the efficacy of ventilation by medical and paramedical personnel in neonatal training models have shown that the LMA combines ease of insertion and adequate, rapid airway patency.¹¹

The AHA recommends bag-and-mask ventilation, a challenging procedure for those inexperienced in neonatal resuscitation when a newborn requires PPV, while tracheal intubation may be impossible due to lack of skill or the presence of severe congenital abnormalities. Some case reports have, moreover, shown the successful use of the LMA in resuscitation of newborns with congenital airway abnormality under inadequate ventilation and difficult intubation settings.^{26,27} Tests on neonatal intubation training models have shown that midwives and interns can obtain a clear airway more rapidly with LMA than TT and with fewer failures with LMA than with TT.²⁸

While our study demonstrates that LMA can be easily taught to local healthcare workers in developing countries, it does have some limitations. The theoretical knowledge gained and the manual skills involved in manipulating LMA and a manikin concern only a scant handful of birth attendants and were never verified in real asphyxiated neonates in the delivery room or in other birth settings. The cost-effectiveness and sustainability of resuscitation by LMA in countries where resources are extremely limited require further scientific scrutiny, just as it would be useful to analyze the retention of the knowledge and skills gained by these and other birth attendants attending specialized courses.

Conclusion

In view of the minimum amount of time and resources necessary to train the participants in NRP courses and its many advantages with respect to FM and TT, LMA should be considered for further evaluation and use in developing countries.

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Acro-Cardio-Facial Syndrome...continued from page 36

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The Relationship Between Water Intake and Fetal Growth and Preterm Delivery

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Abstract

Background: Interpretation of previous associations between water intake and adverse birth outcomes is challenging given that amount and type of water consumed can be non-specific markers of exposure or underlying behavioural characteristics. We examined the relationship between water intake measures and adverse birth outcomes in participants from three study sites in the United States.

Methods: Using a prospective cohort study, we examined daily intake of bottled, cold tap, total tap, and total water in relation to birth weight and risk of small-for-gestational-age (SGA) among term births and risk of preterm delivery.

Results: Based on water consumption data collected between 20-24 weeks of gestation, the adjusted mean birth weight was 27 (95% confidence interval [CI]: -34, 87), 39 (95% CI: -22, 99), and 50 (95% CI: -11, 110) grams higher for the upper three total water intake quartiles (>51-78, >78-114, and >114 ounces/day) compared to the lowest quartile (\leq 51 ounces/day). Adjusted birth weight results were similar for bottled water, cold tap water, and total tap water intake. An exposure-response gradient was not detected for either preterm delivery or SGA with increasing total water intake and total tap water intake, but adjusted relative risks for all three upper quartiles were below 1.0 (range: 0.6-0.9) for SGA.

Conclusion: These data suggest that high water intake may be associated with higher mean birth weight following adjustment for confounding.

Background

Water consumption is critical for metabolism, temperature regulation, transporting nutrients and wastes, and tissue maintenance. Water intake is also important for pregnant

women with oligohydramnios and those at risk of developing uteroplacental insufficiency.¹ Few epidemiological studies have addressed the role of water intake on adverse reproductive outcomes with most of these focusing on the effect of specific contaminants such as disinfection by-products. Savitz et al² reported an inverse association between increased water intake and risk of preterm delivery (PTD) (ie, <37 gestational weeks) and low birth weight infants. Compared to those reporting no daily water intake, odds ratios (ORs) were 0.5 and 0.6 for >4 glasses/day for small for gestational age (SGA) and PTD, respectively. Relative to low intake (1-7 glasses/week), Aggazzotti et al³ showed little evidence of an association between high intake of tap water (>35 glasses/week) and risk of SGA or PTD (ORs=1.0 and 1.1, respectively). Other studies have shown a decreased risk of spontaneous abortion⁴ and cardiac anomalies⁵ with increased bottled water intake. Given that water intake is a non-specific marker of exposure, it is not clear if these results are due to residual confounding or actual effects of water ingestion.

Using a prospective cohort study, we examined birth weight and risk of SGA among term births and risk of PTD in relation to daily bottled, cold tap, total tap and total water intake. The primary study hypothesis examined whether water intake is associated with measures of foetal growth and protective of adverse birth outcomes.

Methods

Study design and population: The study population included 2,766 pregnant women enrolled in a prospective cohort study conducted from December 2000-May 2004 across three study sites in the United States. Participants were enrolled early in pregnancy (\leq 12 weeks' gestation) or while planning to become pregnant. Eligible subjects included those who were \geq 18 years of age, who did not have any fertility treatment for the study pregnancy, and who intended to deliver in the study area. Additional details on study design and recruitment have been published elsewhere.^{6,7} The Institutional Review Boards at the University of North Carolina, University of Tennessee and the University of Texas approved the study protocols; participants gave informed consent.

The sample size for the PTD analysis was 2039 pregnancies after the following exclusions: 259 with a missing or incomplete baseline interview, 347 with a pregnancy loss, 90 that were lost to follow-up, 16 with repeat live births, eight with multiple births, and seven with missing information on date of birth or

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Table 1 Characteristics of the study population recruited from three US cities during 2000-4

Population characteristics			PTD		SGA ^a		Birth weight (g)	
	n	%	%	%	Mean	SD		
Total population	2039	100	9	5	3382	586		
Maternal race/ethnicity								
Non-Hispanic white	1169	57	7	5	3486	596		
Non-Hispanic black	609	30	12	7	3167	545		
Hispanic	185	9	9	6	3427	632		
Other	73	4	7	–	3400	459		
Missing	3							
Maternal age (years)								
< 25	599	29	11	7	3255	558		
25-29	657	32	8	6	3393	572		
30-34	564	28	7	4	3486	587		
≥35	219	11	11	6	3425	642		
Highest maternal education level								
High school or less	573	28	13	9	3235	616		
Some college	440	22	10	5	3340	600		
College degree or higher	1025	50	7	4	3482	544		
Maternal smoking								
Yes	99	5	16	12	3073	578		
No	1940	95	9	5	3398	583		
Maternal alcohol use								
Yes	32	2	9	6	3410	702		
No	2007	98	6	6	3381	585		
Pre-pregnancy BMI (kg/m ²)								
< 19.8	232	11	8	9	3291	535		
19.8-25.9	1016	50	8	5	3410	553		
26.0-29.9	333	16	7	6	3421	535		
> 29.9	407	20	14	5	3349	713		
Missing	51	3	10	16	3255	771		
Vitamin use								
Yes	1027	50	7	5	3461	573		
No	1012	50	11	7	3302	590		
Caffeine intake (mg/day)								
None	519	25	9	4	3410	613		
1-150	468	23	8	5	3385	557		
151-300	387	19	11	6	3344	617		
> 300	665	33	9	7	3380	567		
Marital status								
Married	1390	68	7	5	3466	536		
Not married	648	32	13	8	3200	646		
Missing	1							
Parity								
Nulliparous	991	49	10	6	3323	591		
Parous	1048	51	8	4	3438	577		
Employed during past 4 months								
Yes	1430	70	9	5	3372	580		
No	608	30	9	7	3406	602		
Annual household income (\$)								
< 30,000	637	31	12	7	3245	629		
30,001-60,000	535	26	7	7	3437	545		

birth weight. 1854 live births were available for the birth weight analysis, and 1783 live term births were available for the SGA analysis due to missing information on maternal race/ethnicity, births with a reported maternal race of “Indian,” “Asian/Pacific

Table 1 Characteristics of the study population recruited from three US cities during 2000-4 (Continued)

60,001-80,000	321	16	6	5	3460	498
> 80,000	465	23	8	3	3504	571
Missing	81	4	20	10	3078	614
Recreational activity ^b						
Yes	1109	54	9	6	3423	572
No	930	46	10	5	3332	600
Vigorous recreational activity ^c						
Yes	401	20	8	7	3412	559
No	1638	80	9	5	3374	593
Swimming						
Yes	651	58	6	6	3471	549
No	1388	32	10	6	3340	599
Infant gender						
Male	1045	51	9	7	3419	585
Female	994	49	9	5	3343	586
Study site						
Site 1	929	46	6	5	3459	581
Site 2	761	37	11	6	3329	593
Site 3	349	17	13	8	3294	562

^aTerm births only

^bAny recreational physical activity or exercise, such as brisk walking, jogging, swimming, biking, tennis, soccer, or dancing

^cAny recreational physical activity or exercise, such as brisk walking, jogging, swimming, biking, tennis, soccer, or dancing that caused large increases in breathing and heart rate

SGA = small for gestational age; PTD = preterm delivery; SD = standard deviation; BMI = body mass index

Islander,” or “Other,” and births delivered at <25 or >42 weeks’ gestation.

Assessment of fetal growth and PTD: Infant date of birth, birth weight, and gender were obtained from medical records for 43% of live births, from vital records for 57%, and from participant self-report for <1%. Self-reported last menstrual period (LMP) and an early ultrasound (scheduled between gestational weeks 6-7 and no later than 14 weeks), both obtained during the first trimester, were combined with infant date of birth to estimate gestational age at birth. Gestational age derived from LMP was used for the majority of subjects (81%) unless the LMP date was incomplete (1%) or differed by more than ±7 days from the ultrasound-based estimate of gestational age (18%), in which case the ultrasound estimate was used. SGA was defined as an infant with a birth weight below the tenth percentile for gestational age at birth, gender, maternal race/ethnicity (non-Hispanic white, non-Hispanic black, or Hispanic), and parity based on United States population estimates.^{8,9}

Assessment of exposures and confounding factors: Data on exposures and potential confounding factors were collected via telephone interviews before 16 weeks of gestation (baseline interview) and between 20-24 weeks of gestation (follow-up interview). The interviews included detailed questions about the pregnancy, maternal health, demographic information, behavioural characteristics, and water use practices. Maternal health characteristics included pre-pregnancy body mass index (BMI) defined as weight/height² and categorized according to the Institute of Medicine’s¹⁰ guidelines: low (<19.8 kg/m²), normal (19.8-26.0 kg/m²), overweight (26.1-29.0 kg/m²), and obese (>29.0 kg/m²). Behavioural variables included recreational exercise, smoking, intake of caffeine, vitamins, alcohol, and illicit drugs.

Table 2 Birth weight results for daily bottled, cold tap, total tap, and total water intake

Exposure	n (%)	Follow-up data				Average of baseline and follow-up data	
		Unadjusted		Adjusted ^a		Adjusted ^a	
		β	95% CI	β	95% CI	β	95% CI
Bottled water							
None	448 (25%)	Ref		Ref		Ref	
Any	1329 (75%)	12	(-38, 63)	31	(-20, 82)	43	(-27, 113)
Cold tap water (ounces) ^b							
0-27	424 (24%)	Ref		Ref		Ref	
> 27-53	455 (25%)	12	(-50, 74)	9	(-53, 72)	25	(-38, 88)
> 53-91	444 (25%)	74	(11, 136)	52	(-11, 116)	44	(-19, 107)
> 91	453 (26%)	77	(14, 139)	49	(-14, 111)	65	(2, 128)
Per 20 ounce		12.3	(3.9, 20.7)	8.5	(0.1, 16.9)	8.5	(-1.5, 18.5)
Total tap water (ounces) ^b							
0-30	443 (25%)	Ref		Ref		Ref	
> 30-61	445 (25%)	41	(-21, 103)	44	(-18, 106)	10	(-52, 73)
> 61-96	496 (28%)	100	(40, 161)	78	(17, 139)	34	(-30, 97)
> 96	392 (22%)	85	(21, 149)	43	(-21, 107)	46	(-17, 109)
Per 20 ounce		12.0	(4.0, 20.1)	6.8	(-1.3, 15.0)	5.3	(-4.3, 15.1)
Total water (ounces) ^b							
0-51	452 (25%)	Ref		Ref		Ref	
> 51-78	439 (25%)	60	(-1, 122)	27	(-34, 87)	10	(-50, 71)
> 78-114	442 (25%)	67	(5, 128)	39	(-22, 99)	55	(-6, 116)
> 114	441 (25%)	83	(21, 145)	50	(-11, 111)	37	(-25, 98)
Per 20 ounce		9.8	(1.6, 18.1)	7.3	(-0.8, 15.5)	5.2	(-4.7, 15.2)

^aAdjusted for race, education level, annual household income, smoking, pre-pregnancy BMI, vitamin use, parity, employed during last 4 months, infant gender, and study site

^bCategorical exposure cutpoints for average data results were slightly higher than the follow-up data

BMI= body mass index.

Caffeine intake from beverages (ie, coffee, tea, and soda) was estimated and then categorized using the cut points 150 mg/day and 300 mg/day.¹¹

At each interview, study participants were asked how many bottles of water and glasses/cups of cold tap water, hot tap water and tap water-based drinks (including juice, coffee, tea, and other beverages they made from tap water) they consumed each day during a typical week. Participants were asked to define their glass or cup sizes according to three options: small (0.1-0.3 L), medium (0.4-0.6 L), or large (0.7-1.0 L) for cold tap and bottled water and small (0.1-0.3 L), medium (0.3-0.5 L), or large (0.5-0.7 L) for hot water. The midpoint for each size range was used to estimate water consumption in ounces/day. Bottled water included spring water, mineral water, distilled water, sparkling water or any water purchased in bottles or plastic jugs or obtained from a water cooler. Bottled water intake was calculated as the average amount based on reported container sizes: small (8-12 ounces), medium (14-24 ounces), and large (26-34 ounces). Among the women working outside the study area (8%), the tap water ingestion question was asked separately for consumption at home and at work. This resulted in a higher average total amount for this group. We, therefore, deflated their cold tap water consumption totals by 15.3% and hot tap water consumption by 18.2% for those reporting work and home totals separately to make their mean values equal to those women who reported the aggregated amount.

Follow-up data and an average of the baseline and follow-up data were used to examine the following exposure measures: cold tap water intake, total tap water (cold and hot) intake,

bottled water intake, and total water (tap and bottled) intake. Water use measures were divided into quartiles and analyzed using the lowest quartile as the referent. Based on self-reported data collected during the follow-up questionnaire, women were classified into the following quartiles for total water intake: 0-51 (referent), >51-78, >78-114, and >114 ounces/day. Women were classified into the following quartiles for total tap water intake: 0-30 (referent), >30-61, >61-96, and >96 ounces/day. Due to limited data on bottled water intake in the population, this variable was dichotomized to allow comparison of any versus no bottled water intake.

Statistical analysis: We calculated risk ratios (RRs) and 95% confidence intervals (CIs) for SGA and preterm delivery based on various water consumption measures using Poisson regression with robust error variance. The association with term birth weight was examined using linear regression. We considered potential confounding variables that were associated with the outcomes and were independently associated with water use exposures, but were not intermediates in the causal pathway between exposure and disease: maternal age, race/ethnicity, education level, annual household income, employment status, marital status, pre-pregnancy BMI, parity, alcohol consumption, smoking status, caffeine intake, vitamin intake, recreational activity, swimming, infant gender, season of birth, and study site. Maternal education, race/ethnicity, income, infant gender, parity, pre-pregnancy BMI, smoking, vitamin intake, employment during pregnancy, and study site were retained in multivariate models as confounders using a change-in-estimate (10% change) backwards elimination approach. We examined the extent that confounding impacted the birth

Table 3 Small-for-gestational-age results^a for daily bottled, cold tap, total tap, and total water intake

Exposure	n (%)	Follow-up data		Average of baseline and follow-up data
		Unadjusted RR (95% CI)	Adjusted RR (95% CI) ^b	Adjusted RR (95% CI) ^b
Bottled water				
None	448 (26%)	1	1	1
Any	1258 (74%)	1.1 (0.7, 1.7)	0.9 (0.5, 1.4)	1.4 (0.6, 3.0)
Cold tap water (ounces) ^c				
0-27	403 (24%)	1	1	1
> 27-53	439 (26%)	0.9 (0.5, 1.5)	1.2 (0.6, 2.3)	1.1 (0.6, 2.2)
> 53-91	429 (25%)	0.9 (0.5, 1.6)	1.3 (0.7, 2.4)	1.4 (0.7, 2.6)
> 91	439 (26%)	0.7 (0.4, 1.2)	0.9 (0.5, 1.9)	1.1 (0.5, 2.1)
Per 20 ounce		1.0 (0.9, 1.0)	1.0 (0.9, 1.1)	1.0 (0.9, 1.1)
Total tap water (ounces) ^c				
0-30	423 (25%)	1	1	1
> 30-61	426 (25%)	0.7 (0.4, 1.3)	0.9 (0.5, 1.7)	1.2 (0.6, 2.2)
> 61-96	476 (28%)	0.7 (0.4, 1.2)	0.8 (0.5, 1.6)	1.3 (0.7, 2.6)
> 96	380 (22%)	0.7 (0.4, 1.2)	0.9 (0.5, 1.9)	1.1 (0.6, 2.2)
Per 20 ounce		1.0 (0.9, 1.1)	1.0 (0.9, 1.1)	1.0 (0.9, 1.1)
Total water (ounces) ^c				
0-51	434 (25%)	1	1	1
> 51-78	418 (25%)	0.7 (0.4, 1.2)	0.8 (0.4, 1.4)	0.9 (0.5, 1.6)
> 78-114	424 (25%)	0.6 (0.3, 1.0)	0.6 (0.3, 1.0)	0.5 (0.2, 1.0)
> 114	427 (25%)	0.8 (0.5, 1.4)	0.9 (0.5, 1.6)	1.0 (0.6, 1.8)
Per 20 ounce		1.0 (0.9, 1.1)	1.0 (0.9, 1.1)	1.0 (0.9, 1.1)

^aTerm SGA models restricted to infants born to non-Hispanic White, non-Hispanic Black, or Hispanic women

^bAdjusted for race, education level, annual household income, smoking, pre-pregnancy BMI, vitamin use, parity, employed during last 4 months, infant gender, and study site

^cCategorical exposure cutpoints for average data results were slightly higher than the follow-up data

BMI= body mass index; RR= risk ratio

weight results among those variables retained in the backwards elimination model. Relative to the unadjusted models for total water intake from the follow-up data, we examined percent change-in-estimate for the linear regression models for the confounders that were retained in multivariate models.

Results

The mean birth weight in the total population (n=2039) was 3,382 grams, with 9% (n=192) born preterm (Table 1). Among the 1,854 term births, 5% (n=85) were classified as SGA. Lower mean birth weights were found among infants born to mothers who were non-Hispanic black, of younger age, were not married, had lower BMI, were less educated, and had an annual household income <\$30,000. Large differences in mean birth weight were also detected between Site 1 versus Site 3 (165 grams), non-smokers versus smokers (325 grams), and vitamin users versus non-users (159 grams). Several factors were associated with both higher mean birth weight and higher water intake. For example, mothers of non-Hispanic white ethnicity, higher BMI, and those who consumed vitamins tended to have larger infants and drink larger amounts of total water, so that adjustment for these factors attenuated the association between water intake and birth weight. Using a change-in estimate analysis, we examined the individual contribution of various confounders in the birth weight model for total water intake based on the follow-up data. Compared to the univariate results, the largest average change-in estimates across the highest three exposure quartiles were swimming (39%), maternal race/ethnicity (31%), annual household income (21%), education (20%), marital status (20%), and vitamin intake (17%).

Birth weight: Compared to the lowest quartile, the unadjusted mean birth weight in grams was higher for the upper three quartiles of total water intake, 60 (95% CI: -1, 122), 67 (95% CI: 5, 128), and 83 (95% CI: 21, 145) grams, respectively (Table 2). Following adjustment for confounding (by study site, household income, maternal education, maternal race/ethnicity, infant gender, parity, pre-pregnancy BMI, smoking, vitamin use, and employment during pregnancy), the respective adjusted differences in mean birth weight in grams were reduced to 27 (95% CI: -34, 87), 39 (95% CI: -22, 99), and 50 (95% CI: -11, 111) grams compared to the lowest quartile. When total water intake was examined as a continuous measure (per 20 ounce/day increased intake), the adjusted increase in mean birth weight was 7.3 (95% CI: -0.8, 15.5) grams. Adjusted results were similar in magnitude for the upper quartiles of cold tap water intake, total tap water intake, and total water intake for both the follow-up data and an average of the follow-up and baseline data. Compared to no bottled water intake, the adjusted mean birth weight for bottled water consumers was 31 grams (95% CI: -20, 82) based on follow-up data and 43 grams (95% CI: -27, 113) based on an average of the follow-up and baseline data.

SGA: RRs and 95% CIs comparing women who reported drinking >51-78, >78-114, and >114 versus 0-51 ounces of total water per day at follow-up were 0.7 (0.4, 1.2), 0.6 (0.3, 1.0), and 0.8 (0.5, 1.4), indicative of a decreased risk of SGA with increased water consumption above the first quartile but no gradient thereafter (Table 3). Results were similar following adjustment for confounding: 0.8 (0.4, 1.4), 0.6 (0.3, 1.0), and 0.9 (0.5, 1.6), respectively. Relative to the lowest quartile, adjusted RRs were slightly higher for cold tap and total tap water intake especially

Table 4 Preterm delivery results for daily bottled, cold tap, total tap, and total water intake

Exposure	n (%)	Follow-up data		Average of baseline and follow-up data
		Unadjusted RR (95% CI)	Adjusted RR (95% CI) ^a	Adjusted RR (95% CI) ^a
Bottled water				
None	483 (25%)	1	1	1
Any	1458 (75%)	1.2 (0.9, 1.8)	1.2 (0.8, 1.8)	0.8 (0.5, 1.4)
Cold tap water (ounces) ^b				
0-27	472 (24%)	1	1	1
> 27-53	494 (25%)	0.8 (0.5, 1.2)	0.8 (0.5, 1.3)	0.9 (0.6, 1.4)
> 53-91	485 (25%)	0.9 (0.6, 1.3)	0.9 (0.6, 1.4)	0.9 (0.6, 1.4)
> 91	490 (25%)	0.8 (0.5, 1.1)	0.8 (0.5, 1.3)	1.0 (0.6, 1.5)
Per 20 ounce		1.0 (0.9, 1.0)	0.9 (0.7, 1.3)	0.9 (0.6, 1.3)
Total tap water (ounces) ^b				
0-30	493 (25%)	1	1	1
> 30-61	483 (25%)	0.8 (0.5, 1.2)	0.8 (0.5, 1.2)	1.0 (0.6, 1.5)
> 61-96	535 (28%)	0.7 (0.5, 1.1)	0.8 (0.5, 1.2)	1.2 (0.8, 1.9)
> 96	429 (22%)	0.9 (0.6, 1.3)	1.0 (0.6, 1.5)	0.9 (0.6, 1.4)
Per 20 ounce		1.0 (0.9, 1.0)	0.9 (0.7, 1.2)	0.9 (0.6, 1.3)
Total water (ounces) ^b				
0-51	491 (25%)	1.0	1.0	1.0
> 51-78	478 (25%)	1.0 (0.7, 1.6)	1.2 (0.7, 1.9)	1.1 (0.7, 1.7)
> 78-114	481 (25%)	1.0 (0.7, 1.6)	1.1 (0.7, 1.8)	1.0 (0.6, 1.5)
> 114	478 (25%)	1.2 (0.8, 1.8)	1.4 (0.9, 2.2)	1.2 (0.8, 1.9)
Per 20 ounce		1.0 (1.0, 1.1)	1.1 (0.9, 1.4)	1.1 (0.8, 1.5)

^aAdjusted for race, education level, annual household income, smoking, pre-pregnancy BMI, vitamin use, parity, employed during last 4 months, infant gender, and study site

^bCategorical exposure cutpoints for average data results were slightly higher than the follow-up data
BMI= body mass index; RR= risk ratio

for the average follow-up and baseline data. Relative to women not drinking bottled water, the adjusted RR for SGA was 0.9 (95% CI: 0.5, 1.4) based on the follow-up data and 1.4 (0.6, 3.0) based on the average follow-up and baseline data.

PTD: As shown in Table 4, RRs and 95% CIs for PTD comparing women who reported drinking >51-78, >78-114, and >114 versus 0-51 ounces of total water per day based on the follow-up data were 1.0 (0.7, 1.6), 1.0 (0.7, 1.6), and 1.2 (0.8, 1.8). RRs were slightly larger following adjustment for confounding: 1.2 (0.7, 1.9), 1.1 (0.7, 1.8), and 1.4 (0.9, 2.2), respectively. RRs and 95% CIs for PTD for the cold tap and total tap water quartiles were generally below 1.0 compared to the lowest quartile for follow-up data and average follow-up and baseline data. Relative to women not drinking bottled water, the adjusted RR for any bottled water intake was 1.2 (95% CI: 0.8, 1.8) for the follow-up data and 0.8 (95% CI: 0.5, 1.4) based on the average baseline and follow-up data.

Discussion

Previous epidemiological studies of disinfection by-products in drinking water have shown a possible increased risk of impaired fetal growth with increasing exposure but a decreased risk of PTD.¹²⁻¹⁶ Hoffman et al¹³ postulated that the decreased risk of PTD may be partially due to a protective effect of higher water intake on pregnancy outcomes, but this has rarely been examined. Overall, the adjusted SGA results in our study were largely null although the RRs for follow-up data on total tap water and total water intake were consistently below 1.0 (range 0.6-0.9) for the higher water exposure categories. The adjusted PTD findings were also largely null with most RRs below the null value of 1.0. For both the follow-up and average of follow-up

and baseline data analyses, we observed a slight increased risk of PTD in the high total water intake group (RRs=1.2 and 1.4) relative to those in the low intake category.

To the best of our knowledge, this is the first study to examine the relationship between water intake and birth weight in a prospective epidemiological study. We saw some evidence of an exposure-response relationship with mean birth weight differences ranging from 27-50 grams with increasing total water intake compared to the lowest quartile after adjustment. We found results similar in magnitude for the cold tap water and total tap water intake measures based on the follow-up data. Similar results were found for all three exposure measures based on an average of baseline and follow-up questionnaire data including suggestion of an exposure-response relationship for cold tap and total tap water intake.

One of the strengths of the study was the detailed individual-level information on water intake and potential confounding factors collected for this pregnancy cohort. Several of these confounders had considerable impact on the association between water intake and birth weight. For example, established risk factors for fetal growth measures such as maternal race, age, education, and household income attenuated the mean birth weight by 17-39% compared to the univariate total water intake model results. Although we did not find evidence that diabetes was a strong confounder in this analysis, results were slightly stronger when the birth weight data were restricted to non-diabetics (data not shown). We recognize that even after adjustment for confounding factors, there may be unmeasured aspects of maternal physiology or behavior that affect both water intake and pregnancy outcome so that the water intake

itself is not causally related to the outcomes. For example, previous research suggests that participants reporting no water intake also reported increased soft drink consumption and less fruit, vegetable and low- and medium-fat dairy product intake.¹⁷ Although dietary information was not collected on this population, our detailed analysis of confounding likely led to indirect control of nutritional status to some degree through adjustment of confounders such as household income, education, and prenatal vitamin use. In addition, very few study participants (0.3%) in our study population reported no water intake which should minimize the potential for confounding due to unhealthy lifestyles during pregnancy.

An additional study strength was the collection of multiple measures of water use during pregnancy which allowed for examination of water intake measures. This is potentially important for exposure assessment as previous studies have indicated that water use changes may occur during pregnancy.¹⁸ It is not entirely clear, however, whether these changes are due to behavioral decisions related to perceived health benefits, physiologic changes such as increased thirst, or variation due to measurement error. Since 95% of foetal growth occurs after the 20th gestational week,¹⁹ we considered the follow-up data (collected during 20-24 gestational weeks) to be the most relevant data for examination of fetal growth measures and prematurity. However, we also examined water intake results based on a measure of the average follow-up/baseline data, but saw little difference in comparison to the follow-up data.

Although these data represent one of the most extensive water use data collective efforts to date in a reproductive epidemiological study, self-reported data are subject to recall error. Given the prospective nature of the data collection, differential error could not have occurred since the birth outcomes were unknown at the time the pregnant subjects reported the water consumption and information on confounding factors. Nonetheless, water intake is difficult to measure and may be subject to non-differential error. This may have reduced our statistical power and limited the ability to detect exposure-response relationships and effects small in magnitude (e.g., small changes in mean birth weight). Another limitation of the study was a narrow exposure gradient for bottled water intake which precluded examination of multiple exposure categories. In contrast, there was considerable variability in reported tap and total water intake across study subjects, but we did not have a truly unexposed (ie, those not consuming any water) reference group for the total tap and total water categories. The number of subjects (0.3%) reporting no water intake in this population is less than that from other studies (50Our study subjects were highly motivated, highly educated, and represented a low risk population, since they were actively seeking prenatal care during pregnancy and volunteered for this study. This may limit the generalizability of study findings and also raises the potential for bias among this highly motivated population if drinking water or other "healthful behaviors" are related to self-selection. The overall proportion of preterm births in the study population is lower than (9% vs. 13%) that reported in the United States in 2005.²¹ The prevalence of SGA (5%) in our population based on birth weight deciles from United States population estimates was also lower than would be expected for the general population. This low risk population, therefore, limited our statistical power to detect associations due to the decreased frequency of adverse health outcomes (eg, SGA) being considered. SGA may also include small births that are both pathologically growth restricted

and some that are constitutionally small due to a variety of factors such as maternal ethnicity, parity, weight, height, etc. Therefore, the examination of SGA births is a potential limitation that could limit our ability to detect associations that may be present if some of these births represent constitutionally small births that are not truly growth restricted.

Conclusions

In conclusion, we found limited evidence of an association between specific measures of water intake and risk of adverse pregnancy outcomes such as SGA and PTD. This is in contrast to a previous study which reported an inverse association with water intake and risk of both SGA and PTD,² but is consistent with another study which found no association between water intake and risk of either PTD or low birth weight.³ Despite limited statistical power, we did see some evidence of small increases in mean birth weight for higher levels of total water intake during pregnancy. This might warrant further examination in higher risk populations as this was the first study to examine this endpoint in relation to water intake.

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Continued on page 51...

Chest Physiotherapy in Preterm Infants with Lung Diseases

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Abstract

Background: In neonatology the role of chest physiotherapy is still uncertain because of the controversial outcomes.

Methods: The aim of this study was to test the applicability in preterm infants of “reflex rolling,” from the Vojta method, in preterm neonates with lung pathology, with particular attention to the effects on blood gases and oxygen saturation, on the spontaneous breathing, on the onset of stress or pain. The study included 34 preterm newborns with mean gestational age of 30.5 (1.6) weeks – mean (DS) – and birth weight of 1430 (423) g – mean (DS) –, who suffered from hyaline membrane disease, under treatment with nasal CPAP (continuous positive airways pressure), or from pneumonia, under treatment with oxygen-therapy. The neonates underwent phase 1 of reflex rolling according to Vojta method three times daily. Respiratory rate, SatO_2 , transcutaneous PtcCO_2 e PtcO_2 were monitored; in order to evaluate the onset of stress or pain following the stimulations, the NIPS score and the PIPP score were recorded; cerebral ultrasound scans were performed on postnatal days 1-3-5-7, and then weekly.

Results: In this population the first phase of Vojta’s reflex rolling caused an increase of PtcO_2 and SatO_2 values. No negative effects on PtcCO_2 and respiratory rate were observed, NIPS and PIPP stress scores remained unmodified during the treatment; in no patient the intraventricular haemorrhage worsened in time and none of the infants developed periventricular leucomalacia.

Conclusions: Our experience, using the Vojta method, allows to affirm that this method is safe for preterm neonates, but further investigations are necessary to confirm its positive effects and to evaluate long-term respiratory outcomes.

Background

Chest physiotherapy (CPT) has been used to clear secretions, to reduce post-extubation atelectasis, to reduce the use of reintubation, and also to help lung ventilation in newborns with respiratory problems.¹⁻³ However, concerns about the safety of some forms of chest physiotherapy have been raised, especially

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for very low birth weight infants (VLBW), due to the risk of brain damage related to some CPT techniques.⁴

The forms of CPT more commonly used during the neonatal period are active chest physiotherapy (tapping or vibration delivered on the chest) and non-active techniques (e.g. positioning and suction alone), but caution is required also when interpreting the possible positive effects of these chest physiotherapy treatments.⁵⁻⁸

With regard to the different CPT techniques and the controversial outcomes they yield, we decided to test the applicability in preterm infants of ‘reflex rolling’, from the Vojta method.

The Vojta method is a physical therapy, initially developed in the 1960 s for the treatment of children with or at risk of cerebral palsy. It is a program that employs isometric strengthening techniques through tactile stimulation, to encourage the development of normal movement patterns and therefore to improve respiration. The aim of this study was to evaluate the ‘safety’ of Vojta reflex stimulations in preterm neonates with lung diseases, investigating particularly the effects on blood gases and on oxygen saturation, the effects on spontaneous breathing and the presence of stress/pain.

Methods

Subjects: The study included preterm newborns with gestational age ranging from 28 to 34 weeks, admitted to the Neonatal Intensive Care Unit of “A. Gemelli” Hospital (Sacro Cuore Catholic University, Rome), from 1 January 2008, to 30 September 2008, who suffered from hyaline membrane disease, under treatment with NCPAP (nasal continuous positive airways pressure), or from pneumonia, who received oxygen-therapy.

Newborns with congenital malformations, asphyxia at time of birth, under treatment with neurotropic drugs, or with intraventricular hemorrhage >2nd grade according to Papile’s classification, were excluded from the study.⁹

All newborns breathed spontaneously, and were treated with:
1. Continuous positive pressure ventilation delivered by nasal cannula (maximum CPAP=6 cm H_2O and maximum $\text{FiO}_2=0.40$);
2. Oxygen-therapy with maximum $\text{FiO}_2=0.40$. After birth, the newborns received citrate caffeine as prophylaxis of apnoea of prematurity. Antibiotic therapy was administered when diagnosis of pneumonia (clinical and radiological) was made.

Table 1 - Clinical Characteristics of the two study groups

	Group 1	Group 2
Number of patients	21	13
Gestational Age (weeks) mean± SD	30.3 ± 1.0	30.8 ± 2.3
Birth Weight (g) mean± SD (range)	1340 ± 180 (1010 - 1640)	1575 ± 635 (565 - 2480)
Sex ratio (male/female)	1.1	0.44
Postnatal Age (days) mean± SD (range)	6 ± 1 (2 - 7)	10.6 ± 3.5 (8 - 20)
IVH <3 grade (n°)	2	4
CLD n°(%)	3 (14,3)	3 (23,1)

Table 2 - Blood gases, SatO₂ and respiratory rate (RR) in group 1

	pre stim.	end II stim.	end IV stim.	5 min	15 min	25 min
PtcO₂ (mmHg)						
Mean (±SD)	61.7 (12.9)	61.3 (12.9)	63.2 (12.7)	68.6 (13.7)	70.9 (13.9)	73.1 (13.6)
SatO₂ (%)						
Mean (±SD)	92.2 (3.9)	92.0 (2.8)	92.5 (3.8)	93.6 (3.3)	94.3 (3.1)	94.0 (3.2)
PtcCO₂ (mmHg)						
Mean (±SD)	42.1 (6.4)	42.2 (7.2)	42.6 (7.7)	43.0 (6.7)	43.6 (6.4)	44.2 (6.9)
RR (b/min)						
Mean (±SD)	42 (10)	48 (13)	47 (15)	45 (10)	45 (11)	46 (12)

Table 3 - Blood gases, SatO₂ and respiratory rate (RR) in group 2

	pre stim.	end II stim.	end IV stim.	5 min	15 min	25 min
PtcO₂ (mmHg)						
Mean (±SD)	65.8 (12.9)	63.9 (9.6)	64.1 (11.6)	66.8 (10.8)	69.6 (14.5)	73.6 (15.0)
SatO₂ (%)						
Mean(±SD)	94.7 (3.0)	95.6 (3.2)	95.7 (4.0)	96.8 (2.8)	97.4 (2.6)	97.5 (2.9)
PtcCO₂ (mmHg)						
Mean(±SD)	45.9 (5.9)	45.8 (6.2)	45.5 (5.2)	44.9 (4.9)	44.8 (4.1)	44.9 (4.0)
RR (b/min)						
Mean(±SD)	46 (15)	41 (11)	42 (16)	41 (12)	45 (18)	47 (13)

The “reflex rolling” according to Vojta: The neonates underwent phase 1 of reflex rolling according to Vojta. This manoeuvre does not require the newborn to be moved, but only a slight rotation of the head towards the side from which the stimulus is delivered. The starting position for performing the first phase of reflex rolling is the asymmetric supine position, with the limbs freely lying on the resting surface.

A digitopressure was exerted on the chest area, where the mammillary line crosses the insertion of the diaphragm, either at the level of the 6th rib, or between the 5th and the 6th, or between the 6th and the 7th.

Each treatment consisted in delivering four stimuli, two to the left half of the chest (stimulations I and II) and two to the right half of the chest (stimulations III and IV). Each stimulus consisted of a slight pressure, progressively oriented in dorsal, medial and cranial directions, diagonally to the spine. The

treatment was repeated three times a day, at time intervals of 0, 2 and 4 hours.

Monitoring and controls: The tests performed were the following: a. Respiratory rate (RR) and SatO₂ were monitored by Hewlett-Packard HP monitor (Hewlett Packard M1205A Omni Care model, Andover, Germany); b. Transcutaneous monitoring of PtcCO₂ e PtcO₂ by TINA (Radiometer Medical, Copenhagen, Denmark). The tests were performed before the reflex stimulation, at the end of stimulation II, at the end of stimulation IV and at 5, 15, 25 minutes after the whole series of stimulations, during each of the three daily treatments; c. Cerebral ultrasound scan on postnatal days 1-3-5-7, and weekly, using a color Doppler unit. (Hewlett-Packard “Image Point” Doppler).

Monitoring of stress or pain: In order to evaluate the onset of stress or pain following the stimulations, two pain and stress evaluation scales were adopted: the NIPS score (Neonatal Infant Pain Scale) and the PIPP (Premature Infant Pain Profile) Score.^{10,11} The NIPS scores were recorded before the reflex stimulation, at the end of the second stimulation, at the end of the fourth stimulation and at 5, 15, 25 minutes after the stimulation, during all three sessions. The PIPP scores were recorded only once in each session during stimulation.

Statistical Analysis: Continuous data are presented as mean ± standard deviation. To compare each parameter at each time point, Repeated Measures One-way ANOVA with Bonferroni’s Multiple Comparison Test was performed using GraphPad Prism version 4.00 for Windows (GraphPad Software, San Diego CA.) A score of p<0.05 was considered significant.

Results

Over the time of study, 60 neonates showed criteria of eligibility; 7 newborns with severe congenital malformation and 19 newborns who required mechanical ventilation were excluded. Therefore, the neonates included in the study were 34, 19 female and 15 male. The gestational age of the newborns included in the study was 30.5 (1.6) weeks – mean (DS) – and the neonatal weight was 1430 (423) g – mean (DS) –.

We studied the effects of the application of reflex rolling during the first week of life and after the first week of life. Therefore, two groups of newborns were observed (Table 1): GROUP 1: 21 newborns with hyaline membrane disease during the first week of life. All newborns were treated with NCPAP. GROUP 2: 13 newborns with a respiratory disease persisting after the first week of life, who were spontaneously breathing and on oxygen-therapy.

In any case, the IVH (intraventricular hemorrhage) diagnosis was made during the infant’s first day of life; in no patient the intraventricular hemorrhage worsened in time. None of the infants we observed developed periventricular leucomalacia.

Monitoring of blood gases and respiratory rate: In group 1, PtcO₂ was found to be significantly different across the time points (p<0.0001); post-hoc analysis according to Bonferroni showed a significant difference (p<0.05) among the mean values of pO₂: before the stimulation and at 5', 15' e 25'; at the end of stimulation II and at 5', 15' e 25'; at the end of stimulation IV and at 15' and 25'. In a similar way, SatO₂ was found to be significantly different across the time points (p<0.001); post-hoc analysis according to Bonferroni showed a significant

difference ($p < 0.05$) among the mean values of SatO_2 : before the stimulation and at 5'; at the end of stimulation II and at 15' and 25'. No statistically significant difference was found for ptcCO_2 . No increase in RR was recorded; therefore, it is possible that the improved oxygenation induced by this method may be due to an increased tidal volume. (Table 2).

In group 2, PtcO_2 was found to be significantly different across the time points ($p < 0.01$); post-hoc analysis according to Bonferroni showed a significant difference ($p < 0.05$) among the mean values of pO_2 : before the stimulation and at 25'; at the end of stimulation II and at 25'; at the end of stimulation IV and at 25'. SatO_2 was found to be significantly different across the time points ($p < 0.05$); but Bonferroni's multiple comparison test did not show any significant difference among individual evaluations. No statistically significant difference was found for ptcCO_2 , nor for RR (Table 3).

Monitoring of stress/pain: The NIPS scores for the two study groups did not show pain nor stress signs during stimulation, in any of the daily settings. Moreover, the PIPP scores showed no stress. The values found in group 1 were: 6.1 (1.9) – mean (SD) – with the first recording; 6.0 (2.0) with the second recording; 6.2 (1.5) with the third recording and in group 2 they were 6.3 (1.6) with the first recording; 6.2 (1.7) with the second recording and 6.4 (1.8) with the third recording.

Discussion

In neonatology, respiratory physiotherapy is still controversial.⁵ In treating neonates, the most renowned methods are mechanical techniques such as percussion and vibrations, which represent the so-called active respiratory physiotherapy (ARP), postural drainage, tracheal aspiration, elicitation of the cough reflex, respiratory modifications induced by means of posture. The specialized literature concerning neonates mainly sets its focus on active respiratory physiotherapy and on the specific aspect of preventing post-extubation atelectasis.

With regard to the prevention of post-extubation atelectasis, the strong doubts concerning the actual utility of active respiratory physiotherapy seem to be confirmed; in fact, there is no evidence of a clear benefit in terms of a decreased rate of post-extubation lobar collapse.^{5-7,12,13} Besides the scarce benefits, some authors have suggested that ARP might entail the risk of a neurologic damage, especially in neonates whose weight is < 1500 grams, a risk which other studies did not confirm.^{4,8,13-18}

It is not surprising; however, that active respiratory physiotherapy might prove to be an invasive technique for preterm newborns. In fact, it has been stressed that ventilated patients may show irritability, an increased consumption of oxygen, an increased heart rate and arterial blood pressure, a higher rate of gastro-oesophageal reflux and, what represents a high risk for preterm newborns, an increased intracranial pressure.^{19,20}

In any case, active respiratory physiotherapy and particularly vibrations and percussion are unsuitable for VLBW neonates, due to their physical features; in fact, in these patients the anatomical and physiological features of the ribcage subdue and cancel the effect of the aforesaid techniques, which nevertheless maintain their effectiveness in childhood and in adult age.

Therefore, non-active respiratory physiotherapy (ie postural

therapy and postural drainage) seems to be the only respiratory physiotherapeutic technique available for VLBW neonates.

In 1967 Václav Vojta developed and made public the reflex rolling model, defining the chest as a crucial area. By stimulating the chest of a child suffering from athetosis and relapsing episodes of pneumonia and atelectasia unaffected by other active respiratory physiotherapeutic treatments, Vojta noticed a global reaction, consisting of a rotation of the head with flexion of the lower limbs and rotation of the pelvis, opening of the hands and, what is most important, an increase in depth of costal respiration, with an expansion of the ribcage.²¹

The importance of these stimulations, especially if repeated, lies in the fact that the afferences due to induced physiologic muscle activity are imprinted in the central nervous system (CNS) and memorized. The CNS is set in an activated state, and the duration of such activation persists for at least half an hour after the stimulation has ended.

Our study aimed at evaluating the use of reflex rolling in preterm neonates suffering from respiratory diseases. In the neonates we studied, the first phase of Vojta's 'reflex rolling' caused an increase of PtcO_2 and SatO_2 values, showing a positive action on oxygenation.

No negative effects on PtcCO_2 were observed, as these values remained constant over the treatment period, and within the normal range. A further confirmation of this technique's safety came from the negative results of the NIPS e PIPP stress scores, which remained substantially unmodified over the treatment.

The positive results obtained should be followed by a further investigation concerning the efficacy of the 'reflex rolling' technique in preterm newborns, by means of a randomized controlled study. The positive effects may be confirmed by the evaluation of respiratory functionality tests and by long-term respiratory outcomes.

Conclusion

Although the role of CPT in neonates with respiratory diseases remains debated and needs further evaluation, our experience concerning the use of Vojta's method provides a different perspective and takes again into consideration respiratory physiotherapy as a resource for the treatment of neonatal lung diseases. Studies performed on larger series of patients may be able to definitively confirm the effectiveness of Vojta's method as a suitable treatment for neonates, particularly in order to provide a support for all other therapeutic measures based on the use of drugs and ventilation.

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Maternal and Neonatal Factors Associated With Mode of Delivery Under a Universal Newborn Hearing Screening Program in Lagos, Nigeria

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Abstract

Background: Emerging evidence from a recent pilot universal newborn hearing screening (UNHS) program suggests that the burden of obstetric complications associated with mode of delivery is not limited to maternal and perinatal mortality but may also undermine optimal early childhood development of the surviving newborns. However, the potential pathways for this association have not been reported particularly in the context of a resource-poor setting. This study therefore set out to establish the pattern of delivery and the associated neonatal outcomes under a UNHS program.

Methods: A cross-sectional study in which all consenting mothers who delivered in an inner-city tertiary maternity hospital in Lagos, Nigeria from May 2005 to December 2007 were enrolled during the UNHS program. Socio-demographic, obstetric and neonatal factors independently associated with vaginal, elective, and emergency cesarean deliveries were determined using multinomial logistic regression analyses. The instruments for the substantive newborn hearing screening project that formed the basis of this work were provided by Natus Medical Inc, USA, Otodynamics (UK) Ltd and Oticon Foundation, Denmark.

Results: Of the 4,615 mothers enrolled, 2,584 (56.0%) deliveries were vaginal, 1,590 (34.4%) emergency cesarean and 441 (9.6%) elective cesarean section. Maternal age, parity, social class and all obstetric factors including lack of antenatal care, maternal HIV and multiple gestations were associated with increased risk of emergency cesarean delivery compared with vaginal delivery. Only parity, lack of antenatal care and prolonged/obstructed labor were associated with increased risk of emergency compared with elective cesarean delivery. Infants delivered by vaginal method or by emergency cesarean section were more likely to be associated with the risk of sensorineural hearing loss but less likely to be associated with hyperbilirubinemia compared with infants delivered by elective cesarean section. Emergency cesarean delivery was also associated with male gender, low five-minute Apgar scores and admission into special care baby unit compared with vaginal or elective cesarean delivery.

Conclusions: The vast majority of cesarean delivery in this population occur as emergencies and are associated with socio-demographic factors as well as several obstetric complications. Mode of delivery is also associated with the risk of sensorineural hearing loss and other adverse birth outcomes that lie on the causal pathways for potential developmental deficits.

Background

It is now widely acknowledged that effective efforts aimed at improving child health in resource poor countries must be preceded and underpinned by improvement in maternal health within a continuum of care from pregnancy to adolescence.¹ This is corroborated by substantial evidence showing that regions such as sub-Saharan Africa and South Asia with the highest rates of maternal mortality also have the highest burden of infant and child mortality worldwide.²⁻⁵ Maternal deaths in these regions are predominantly attributable to obstetric complications during pregnancy and childbirth,³ and can be averted or substantially curtailed through availability and access/proximity to modern obstetric services by skilled attendants.⁶ In many developing countries, such services are found mostly in urban areas, but they are increasingly being directed to rural areas under various global health initiatives.⁷

In many developing countries undue delays in initiating life-saving surgical intervention for women at risk of severe complications among other factors may undermine the envisaged outcomes from facility-based services.^{3,8} Such delays must be due to delay in seeking essential obstetric care; in reaching the hospital or appropriate health facility; or in receiving adequate care in the hospital.⁸ For example, barring the absence of other barriers such as cost and accessibility, refusal of life-saving cesarean section is not uncommon among women in urban settings in sub-Saharan Africa particularly in a country like Nigeria which is a leading contributor to regional and global burden of maternal mortality.⁹⁻¹³

Typically, in secondary and tertiary maternity hospitals many mothers arrive in a moribund state or with complications that may either lead to death or severe morbidity and disability in the mother after emergency surgical intervention.^{3,14,15} While perinatal mortality associated with complications during pregnancy and childbirth has been extensively reported in the literature, evidence linking mode of delivery (with or without obstetric complications) to the risk of developmental disabilities in the surviving newborns in developing countries is rare.¹⁶

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Table 1. Socio-demographic factors of mothers by mode of delivery

Factors	Total deliveries (%) n=4615	Vaginal delivery (%) n=2584	Emergency caesarean section (%) n=1590	Elective caesarean section (%) n=441
Age (Years) [a]				
< 20	77 (1.7)	41 (1.6)	32 (2.0)	4 (0.9)
20 – 35	4011 (87.1)	2275 (88.1)	1379 (87.1)	357 (81.0)
> 35	519 (11.3)	266 (10.3)	173 (10.9)	80 (18.1)
Marital status				
Married	4519 (97.9)	2530 (97.9)	1555 (97.8)	434 (98.4)
Not married	96 (2.1)	54 (2.1)	35 (2.2)	7 (1.6)
Parity				
Primiparous	2316 (50.2)	1290 (49.9)	861 (54.2)	165 (37.4)
Multiparous	2299 (49.8)	1294 (50.1)	729 (45.8)	276 (62.6)
Ethnicity				
Yoruba	3478 (75.4)	2055 (79.5)	1107 (69.6)	316 (71.7)
Hausa	128 (2.8)	77 (3.0)	43 (2.7)	8 (1.8)
Ibo & Others	1009 (21.9)	452 (17.5)	440 (27.7)	117 (26.5)
Religion				
Muslim	1888 (40.9)	1173 (45.4)	555 (34.9)	160 (36.3)
Christianity	2727 (59.1)	1411 (54.6)	1035 (65.1)	281 (63.7)
Education				
Primary or none	420 (9.1)	244 (9.5)	147 (9.3)	29 (6.5)
Secondary	2419 (52.4)	1344 (52.0)	872 (54.8)	203 (46.0)
Tertiary	1776 (38.5)	996 (38.5)	571 (35.9)	209 (47.4)
Occupation				
None	899 (19.5)	534 (20.7)	309 (19.4)	56 (12.7)
Small trade/casual job	2309 (50)	1296 (49.3)	803 (50.5)	210 (47.7)
Full-time job	1407 (30.5)	754 (29.2)	478 (30.1)	175 (39.7)
Social class				
High	808 (17.5)	441 (17.1)	244 (15.3)	123 (27.9)
Middle	3231 (70.0)	1791 (69.3)	1164 (73.2)	276 (62.6)
Low	576 (12.5)	352 (13.6)	182 (11.4)	42 (9.5)
Accommodation				
Owned	228 (4.9)	150 (5.8)	63 (4.0)	15 (3.4)
Rented	4387 (95.1)	2434 (94.2)	1527 (96.0)	426 (96.6)
Housing sanitation facilities				
Not Shared	2391 (51.8)	1321 (51.1)	792 (49.8)	278 (63.0)
Shared	2224 (48.2)	1263 (48.9)	798 (50.2)	163 (37.0)

Missing data: [a] = 8 (0.2%).

Emerging evidence from a recently concluded pilot universal newborn hearing screening (UNHS) program in a maternity hospital in Nigeria for example suggests that mode of delivery may be associated with sensorineural hearing loss in the surviving newborns.¹⁷ This is consistent with existing reports associating the greatest burden of developmental disabilities worldwide with countries such as Nigeria, India and Pakistan besides having the highest rates of maternal and child mortality.¹⁸ However, the potential pathways for this association have not been reported. We hypothesized that adverse neonatal outcomes commonly associated with mode of delivery in a resource-poor country are directly associated with or lie on the causal pathway of developmental disabilities such as sensorineural hearing loss. This study therefore set out to establish the pattern of delivery and the associated maternal factors; determine infant factors/neonatal outcomes associated with mode of delivery; as well as identify possible direct or indirect links between mode of delivery and developmental deficits in early infancy under a UNHS program in a developing country.

Methods

Study design and population: This cross-sectional study was conducted in an inner-city tertiary maternity hospital in Lagos, Nigeria from May 2005 to December 2007. Lagos is the most populous city in sub-Saharan Africa and the hospital is the oldest maternity hospital in metropolitan Lagos providing specialist services to several private and public hospitals within and outside its catchment area. The hospital is owned and managed by the state government as a public health institution. All live births over the study period were eligible for enrollment into the study, excluding those who did not survive 24 hours after

Table 2. Obstetric factors by with mode of delivery

Maternal profile	Total deliveries (%) n=4615	Vaginal delivery (%) n=2584	Emergency caesarean section (%) n=1590	Elective caesarean section (%) n=441
Antenatal care				
One or more visits	3006 (65.1)	1910 (73.9)	745 (46.9)	351 (79.6)
None	1609 (34.9)	674 (26.1)	845 (53.1)	90 (20.4)
Herbal drug in pregnancy				
None	3732 (80.9)	2020 (78.2)	1329 (83.6)	383 (86.8)
Yes	883 (19.1)	564 (21.8)	261 (16.4)	58 (13.2)
Hypertensive conditions				
No	4317 (93.5)	2499 (96.7)	1415 (89.0)	403 (91.4)
Yes	298 (6.5)	85 (3.3)	175 (11.0)	38 (8.6)
Ante-partum haemorrhage				
No	4566 (98.9)	2582 (99.9)	1546 (97.2)	438 (99.3)
Yes	49 (1.1)	2 (0.1)	44 (2.8)	3 (0.7)
Cephalopelvic disproportion				
No	4433 (96.1)	2580 (99.8)	1443 (90.8)	410 (93.0)
Yes	182 (3.9)	4 (0.2)	147 (9.2)	31 (7.0)
Premature rupture of membranes				
No	4565 (98.9)	2568 (99.4)	1561 (98.2)	436 (98.9)
Yes	50 (1.1)	16 (0.6)	29 (1.8)	5 (1.1)
Prolonged/obstructed labour				
No	4190 (90.8)	2565 (99.3)	1205 (75.8)	420 (95.2)
Yes	425 (9.2)	19 (0.7)	385 (24.2)	21* (4.8)
Malpresentation				
No	4338 (94.0)	2521 (97.6)	1425 (89.6)	392 (89.9)
Yes	277 (6.0)	63 (2.4)	165 (10.4)	49 (11.1)
Previous caesarean section				
No	4152 (90.0)	2569 (99.4)	1325 (83.3)	258 (58.5)
Yes	463 (10.0)	15 (0.6)	265 (16.7)	183 (41.5)
Maternal HIV				
No	4350 (94.3)	2441 (94.5)	1507 (94.8)	402 (91.2)
Yes	265 (5.7)	143 (5.5)	83 (5.2)	39 (8.8)
Multiple gestations				
No	4314 (93.5)	2454 (95.0)	1458 (91.7)	402 (91.2)
Yes	301 (6.5)	130 (5.0)	132 (8.3)	39 (8.8)
Fetal distress				
No	4485 (97.2)	2581 (99.9)	1465 (92.1)	439 (99.5)
Yes	130 (2.8)	3 (0.1)	125 (7.9)	2 (0.5)

*possible error in patient records due to prior consent for elective caesarean section at booking. However no material effect was observed when reflected in the analysis

delivery. Newborns whose mothers were too ill to be interviewed including near misses and those who died during childbirth were also excluded. Ethical approvals were obtained from Lagos State Health Management Board, Nigeria and University College London, UK as part of a wider UNHS pilot project.¹⁷

Main outcome variables: Three modes of delivery were considered as outcome measures namely: vaginal delivery, elective and emergency caesarean section. Vaginal delivery included spontaneous vertex and assisted/instrumental delivery such as breech, forceps and vacuum. Caesarean section was termed elective if the decision for the operation was made before onset of labor because the pregnancy was considered to be high-risk and/or mother was referred from antenatal clinic. Elective cesarean section in this population was rarely based on nonmedical reasons. Emergency cesarean section refers to operations prompted by a diagnosis of fetal distress, vaginal bleeding, premature rupture of membrane, antepartum hemorrhage or hypertensive conditions. The term also embraces emergency intrapartum cesarean section initiated during labor.

Maternal factors: The factors of interest were guided by evidence from published literature¹⁹⁻²¹ and the available data from hospital records of the participants. These included socio-demographic factors such as age, marital status, parity, ethnicity, religion, education, occupation, social class, type of residential accommodation (rented or owned) and sanitation facilities (shared or self-contained). Social classes were determined based on mother's education and father's occupation.²² Social class I termed as "high," II or III as "middle" and IV or V as "low." Maternal factors also included variables reflecting health-seeking

Table 3. Socio-demographic predictors of mode of delivery after multinomial logistic regression[§]

Factor	Emergency c-section vs vaginal delivery Adjusted odds ratio (95% Confidence interval)	Emergency c-section vs elective c-section Adjusted odds ratio (95% Confidence interval)	Vaginal delivery vs elective c-section Adjusted odds ratio (95% Confidence interval)
Age (Years)			
< 20	1.18 (0.62 – 2.22)	1.09 (0.35 – 3.38)	0.93 (0.30 – 2.86)
20 – 35	1.0	1.0	1.0
> 35	1.58 (1.22 – 2.06)**	0.69 (0.50 – 0.95)*	0.44 (0.31 – 0.61)***
Marital status			
Married	1.17 (0.64 – 2.14)	1.61 (0.63 – 4.10)	1.38 (0.54 – 3.48)
Not married	1.0	1.0	1.0
Parity			
Primiparous	1.51 (1.26 – 1.81)***	1.27 (0.98 – 1.66)	0.84 (0.65 – 1.10)
Multiparous	1.0	1.0	1.0
Ethnicity			
Yoruba	0.76 (0.61 – 0.95)**	1.07 (0.79 – 1.45)	1.40 (1.03 – 1.91)*
Hausa	0.68 (0.40 – 1.16)	1.40 (0.60 – 3.29)	2.07 (0.87 – 4.91)
Ibo & Others	1.0	1.0	1.0
Religion			
Muslim	0.90 (0.74 – 1.09)	0.85 (0.64 – 1.13)	0.95 (0.71 – 1.26)
Christianity	1.0	1.0	1.0
Education			
Primary or none	1.15 (0.78 – 1.69)	1.27 (0.72 – 2.25)	1.10 (0.62 – 1.97)
Secondary	1.08 (0.85 – 1.39)	1.10 (0.78 – 1.57)	1.02 (0.71 – 1.46)
Tertiary	1.0	1.0	1.0
Occupation			
None	0.84 (0.66 – 1.08)	1.45 (1.00 – 2.11)*	1.72 (1.19 – 2.50)**
Small trade/casual job	0.95 (0.76 – 1.20)	0.97 (0.71 – 1.34)	1.02 (0.74 – 1.41)
Full-time job	1.0	1.0	1.0
Social class			
High	1.28 (0.86 – 1.89)	0.66 (0.38 – 1.13)	0.51 (0.30 – 0.89)*
Middle	1.37 (1.03 – 1.83)*	1.22 (0.80 – 1.85)	0.89 (0.58 – 1.35)
Low	1.0	1.0	1.0
Accommodation			
Owned	0.64 (0.43 – 0.98)*	1.33 (0.70 – 2.50)	2.06 (1.09 – 3.88)*
Rented	1.0	1.0	1.0
Housing sanitation facilities			
Not Shared	1.14 (0.94 – 1.38)	0.84 (0.64 – 1.11)	0.74 (0.56 – 0.98)*
Shared	1.0	1.0	1.0

[§]After adjusting for all obstetric factors; *p<0.05; ** p<0.01; ***p<0.001. c-section=caesarean section; vs=versus/compared with

Table 4. Obstetric predictors of mode of delivery after multinomial logistic regression[§]

Factor	Emergency c-section vs vaginal delivery Adjusted odds ratio (95% Confidence interval)	Emergency c-section vs elective c-section Adjusted odds ratio (95% Confidence interval)	Vaginal delivery vs elective c-section Adjusted odds ratio (95% Confidence interval)
Antenatal care			
One or more visits	1.0	1.0	1.0
None	2.54 (2.14 – 3.03)***	3.23 (2.46 – 4.24)***	1.27 (0.96 – 1.68)
Herbal drug in pregnancy			
None	1.0	1.0	1.0
Yes	0.76 (0.60 – 0.95)*	1.06 (0.75 – 1.51)	1.40 (0.99 – 1.99)
Hypertensive conditions			
No	1.0	1.0	1.0
Yes	4.80 (3.52 – 6.52)***	1.12 (0.75 – 1.68)	0.23 (0.15 – 0.36)***
Ante-partum haemorrhage			
No	1.0	1.0	1.0
Yes	72.58 (17.08 – 308.47)***	3.49 (1.04 – 11.72)*	0.05 (0.01 – 0.30)**
Cephalopelvic disproportion			
No	1.0	1.0	1.0
Yes	79.83 (29.00 – 219.78)***	1.36 (0.87 – 2.13)	0.02 (0.01 – 0.05)***
Premature rupture of membranes			
No	1.0	1.0	1.0
Yes	3.38 (1.66 – 6.87)***	1.93 (0.70 – 5.31)	0.57 (0.19 – 1.75)
Prolonged/obstructed labour			
No	1.0	1.0	1.0
Yes	59.95 (37.11 – 96.84)***	5.06 (3.16 – 8.10)***	0.08 (0.04 – 0.16)***
Malpresentation			
No	1.0	1.0	1.0
Yes	6.70 (4.82 – 9.32)***	0.91 (0.63 – 1.32)	0.14 (0.09 – 0.21)***
Previous caesarean section			
No	1.0	1.0	1.0
Yes	59.41 (34.46 – 102.42)***	0.41 (0.31 – 0.54)***	0.01 (0.00 – 0.01)***
Maternal HIV			
No	1.0	1.0	1.0
Yes	1.40 (1.00 – 1.97)*	0.45 (0.29 – 0.69)***	0.32 (0.21 – 0.49)***
Multiple gestations			
No	1.0	1.0	1.0
Yes	2.39 (1.75 – 3.26)***	1.08 (0.71 – 1.64)	0.45 (0.29 – 0.70)***
Fetal distress			
No	1.0	1.0	1.0
Yes	116.25 (36.28 – 372.50)***	16.61 (4.04 – 68.29)***	0.14 (0.02 – 0.87)*

[§]After adjusting for all socio-demographic factors; *p<0.05; ** p<0.01; ***p<0.001. c-section=caesarean section; vs=versus/compared with

behaviors such as antenatal care and traditional herbal drug use in pregnancy; obstetric indications for caesarean delivery such as hypertensive conditions (including pre-eclampsia, eclampsia and pregnancy induced hypertension), antepartum hemorrhage, cephalopelvic disproportion, premature rupture of membranes, prolonged and/or obstructed labor, malpresentation, previous caesarean delivery, fetal distress and other obstetric conditions such as maternal HIV status and multiple pregnancies.

Infant factors/outcomes: The neonatal factors or outcomes of interest were infant's gender, gestational age, birthweight, Apgar scores at one minute and five minutes, hyperbilirubinaemia, admission into special care baby unit (SCBU) and hearing screening outcomes. SCBU admission is a helpful surrogate for a range of adverse perinatal conditions that cannot be readily ascertained in hospitals with limited diagnostic facilities. Hearing screening outcomes were based on a two-stage hearing screening protocol consisting of a first-stage screening with transient evoked otoacoustic emissions followed by a second-stage of automated auditory brainstem response test as previously reported.¹⁷ Maternal and neonatal mortality associated with mode of delivery were not considered in this study due to incomplete data for the entire period of this study.

Statistical Analysis: Cross-tabulation of the outcome and explanatory variables was done to provide a descriptive overview of our study population. Multinomial logistic regression model was used as it is an appropriate modeling tool where there are more than two discrete outcomes. It estimates the effect of the independent variables on the probability of a particular method of delivery. The three categories of delivery (vaginal, elective and emergency caesarean section) as specified in this study are sufficiently distinct to satisfy the assumption of independent alternatives. Unconditional univariable multinomial logistic regression analysis was first performed for each independent variable against the dependent variable (mode of delivery) to examine the unadjusted association with the three

modes of delivery. The strength of association was estimated by odds ratios (OR) and the corresponding 95% confidence intervals (CI). All biologically plausible factors and those with significance or borderline significance at p<0.05 were entered into the multinomial multivariable logistic model to assess the effect of each variable independently on the mode of delivery while controlling for the potential confounding effects of covariates. There were no a priori hypotheses for interaction terms so these were not investigated. Finally, neonatal factors or outcomes significantly associated with mode of delivery were determined after adjusting for all socio-demographic and obstetric factors. Model performance was estimated with the Nagelkerke Pseudo-R² statistic (a measure of explained variation in the model). Missing data were managed by exclusion in all of the analyses. All statistical analyses were done with SPSS Windows version 16.0 (SPSS Inc, Chicago IL).

Results

A total of 4,615 (81.9%) consenting mothers with live births out of 5,636 recorded deliveries (including perinatal deaths) at the hospital over the study period were enrolled. In all, 2,584 (56.0%) mothers had vaginal delivery, 1590 (34.4%) emergency cesarean section and 441 (9.6%) elective cesarean section. Majority of the mothers were between the ages of 20-35 years, married, of the Yoruba ethnic group, had a minimum of secondary education, belonged to the middle social class and lived in rented accommodation with almost half (48.2%) having shared sanitation facilities (Table 1). Emergency cesarean section rate was highest among Yoruba tribe (69.6%), Christian mothers (65.1%), those living in rented accommodation (96%) and those in the middle social class (73.2%). More than half (54.2%) of mothers who had emergency cesarean section were primiparous. The obstetric profile of the mothers showed that about a third (34.9%) did not attend antenatal clinics for their current delivery and almost one-fifth (19.1%) reported using herbal medication during pregnancy (Table 2). A total of 1,544 (33.5%) from the total study population had at least one medical indication for

Table 5. Neonatal factors associated with mode of delivery after multinomial logistic regression[§]

Factor	Total (%) n=4615	Emergency c-section vs vaginal delivery Adjusted odds ratio (95% Confidence interval)	Emergency c-section vs elective c-section Adjusted odds ratio (95% Confidence interval)	Vaginal delivery vs elective c-section Adjusted odds ratio (95% Confidence interval)
Gender				
Female	2229 (48.3)	1.0	1.0	1.0
Male	2386 (51.7)	1.23 (1.03 – 1.45)*	1.04 (0.82 – 1.33)	0.85 (0.67 – 1.09)
Gestational age				
37 weeks and above	3678 (79.7)	1.0	1.0	1.0
Less than 37 weeks	937 (20.3)	0.86 (0.69 – 1.07)*	0.72 (0.53 – 0.99)*	0.85 (0.62 – 1.14)
Birthweight				
2500g and above	4044 (87.6)	1.0	1.0	1.0
Less than 2500g	571 (12.4)	0.79 (0.60 – 1.03)	1.36 (0.88 – 2.10)	1.73 (1.12 – 2.67)*
Apgar score at 1 minute [a]				
0 - 6	3956 (90.4)	1.15 (0.84 – 1.56)	0.82 (0.53 – 1.27)	0.72 (0.47 – 1.09)
7 - 10	419 (9.6)	1.0	1.0	1.0
Apgar score at 5 minutes [b]				
0 - 6	1244 (28.4)	1.73 (1.42 – 2.11)***	1.69 (1.27 – 2.26)*	0.98 (0.73 – 1.32)
7 - 10	3131 (71.6)	1.0	1.0	1.0
Hyperbilirubinaemia				
No	4423 (95.8)	1.0	1.0	1.0
Yes	192 (4.2)	1.39 (0.90 – 2.16)	0.42 (0.24 – 0.74)*	0.30 (0.17 – 0.55)***
Admission into SCBU				
No	4148 (89.9)	1.0	1.0	1.0
Yes	467 (10.1)	1.56 (1.16 – 2.11)**	2.19 (1.30 – 3.70)	1.40 (0.82 – 2.41)
Hearing screening tests				
Pass	4296 (93.1)	1.0	1.0	1.0
Refer	119 (2.6)	0.77 (0.46 – 1.32)	3.74 (1.10 – 12.72)*	4.83 (1.42 – 16.46)*
Incomplete	200 (4.3)	0.80 (0.52 – 1.22)	1.53 (0.73 – 3.20)	1.92 (0.92 – 4.00)

Missing data: [a],[b] = 240 (5.2%); *p<0.05; ** p<0.01; ***p<0.001;

[§]After adjusting for all maternal factors as well as all covariates. SCBU=special care baby unit; C-section=caesarean section; vs=versus/compared with

caesarean section and 1,352 (87.6%) of this group had caesarean section. Conversely, cesarean section was medically indicated in 66.6% of all those who had such intervention. Previous cesarean section and prolonged/obstructed labor were the commonest maternal obstetric indications in the total population. Emergency cesarean section rate was highest among mothers who did not attend antenatal clinics (53.1%). About 6% of the mothers were diagnosed with HIV.

The univariate multinomial analyses showed that apart from marital status and religion all sociodemographic and obstetric factors were significantly associated with mode of delivery.

Nonetheless, all factors were entered into the multivariable regression models in deriving the final prediction models. While the model consisting only of the socio-demographic factors (Table 3) explained only 6% (Nagelkerke R²=0.058) of the variation in mode of delivery, the model for obstetric factors (Table 4) explained about 52% (Nagelkerke R²=0.517). The addition of socio-demographic factors marginally increased the explained variations in the model for obstetric factors by 1% to about 53% (Nagelkerke R²=0.534). No evidence of any collinearity among the factors was found in the final models.

Emergency cesarean section compared with vaginal delivery:

Older mothers, those who were first-time mothers or in the middle social class had increased odds of emergency cesarean section although 24% lower odds were observed among Yoruba mothers. As expected, all the obstetric factors increased the odds of emergency cesarean section with antepartum hemorrhage, cephalopelvic disproportion, prolonged/obstructed labor, previous cesarean section and fetal distress showing the highest odds. Although maternal HIV was associated with 40% increased odds for emergency cesarean section, the difference was only marginally significant (p=0.054). Mothers who used herbal medications in pregnancy were found to have 24% lower odds for emergency cesarean section.

Emergency cesarean section compared with elective cesarean section:

Maternal age and occupation were the only

socio-demographic factors predictive of emergency caesarean section among those who required surgical intervention. Fetal distress was associated with the largest odds for emergency cesarean section while HIV-positive status and previous cesarean section were associated with over 50% decreased odds of emergency cesarean section. Hypertensive disorders, cephalopelvic disproportion, premature rupture of membranes and malpresentation were not discriminatory among mothers who had cesarean section.

Vaginal delivery compared with elective cesarean section:

Compared to women in the active childbearing age (20-35 years), women older than 25 years had 56% lower odds of vaginal delivery while being a Yoruba woman or having no occupation was associated with increased odds of vaginal delivery. Similarly, living in owned residential accommodation increased the odds of vaginal delivery by two-fold compared to those in rented accommodation while expectedly, living in an apartment without shared sanitation facilities decreased the odds of vaginal delivery by 26%. Almost all the obstetric factors including multiple pregnancies but excluding premature rupture of membranes were associated with decreased odds for vaginal delivery. Lack of antenatal care and use of herbal drug in pregnancy were not significantly associated with vaginal delivery. Overall, marital status, religion and education were not associated with any mode of delivery while maternal age was a consistent socio-demographic predictor for vaginal delivery or cesarean section.

Neonatal outcomes/factors by mode of delivery:

Neonatal factors associated with mode of delivery after adjusting for all maternal factors are presented in Table 5. Infants delivered by vaginal method or emergency cesarean section were more likely to be associated with the risk of sensorineural hearing loss but less likely to be associated with hyperbilirubinaemia compared with infants delivered by elective cesarean section. Emergency cesarean delivery was also associated with male gender, low five-minute Apgar scores and admission into special care baby unit (SCBU) compared with vaginal or elective cesarean delivery. Infants delivered by emergency cesarean section were less likely to be preterm while those delivered by vaginal method were more likely to have low birthweight compared to infants delivered by elective cesarean section.

Discussion

The study has shown that the rate of cesarean section in this tertiary maternity hospital is high and the substantial proportion was by emergency surgical intervention. Our study has also shown that emergency cesarean section in this hospital is associated with a wide range of obstetric complications resulting in adverse outcomes for the surviving newborns. These findings need to be set against the backdrop of the fact that the study was conducted in an inner-city community where the vast majority of mothers belonged to the middle or high social class but over half (52%) still delivered outside hospital facilities despite access to several private and public hospitals.²³ About 57% were attended by skilled health personnel suggesting that a few mothers who delivered outside hospital were still attended by skilled health personnel. Traditional maternity homes accounted for the largest proportion (40%) of all deliveries or 77.5% of all non-hospital deliveries.²³ Our hospital is the only tertiary maternity hospital serving this population and possibly reflects the settings in many countries in sub-Saharan Africa. Evidently, maternal health-seeking behavior in this urban setting is likely to reflect a complex interaction between socio-demographic, cultural and

medical factors similar in some ways to those of mothers in rural communities.^{24,25}

The observed cesarean section rate in this study is comparable to other local studies²⁶ but higher than the reported rates from other public health institutions which are usually in the range of 5% to 43% where rates closer to the upper end are more typical in Latin America.^{9,14,27} This high rate of cesarean section is not an indication of an indiscriminate preference by health professionals or mothers as has been observed in some developing countries^{14,27} but of the referral status of the hospital in a community where a majority of mothers prefer non-facility based delivery with a high probability of late presentation requiring surgical intervention during labor. Non-vaginal delivery is generally viewed as a sign of maternal laziness, reproductive failure or a curse from perceived enemies or deity in this population. It was therefore not uncommon even where cesarean section was indicated by past pregnancy history for women to attempt vaginal delivery until there was a glaring failure with obvious threat to the life of the mother or unborn child.²⁸

Qualitative studies have in fact established that some women will not even accept cesarean section under any circumstances for reasons such as the fear of pain or death, financial cost, embarrassment by friends, religious beliefs and husband's disapproval.^{13,25} The delays associated with these and other factors^{8,12,29} may have contributed to the high proportion of emergency cesarean section (more than three-quarters of all cesarean sections). It may be worthwhile to undertake an audit to establish the relative contributions of the various types of delays to the high rate of emergency cesarean section and cases of near-misses in this setting.

Undoubtedly, a major pathway to the high rate of emergency cesarean section in this population was the lack of antenatal care which was associated with more than two-fold risk compared to those who received antenatal care. Over half of the mothers who delivered by emergency cesarean section had no antenatal care. It was also not uncommon for some mothers who had received antenatal care to end up with emergency cesarean section if they were culturally averse to the potential for surgical intervention and had unsuccessfully attempted vaginal delivery within or outside a hospital setting.^{13,30,31} Lack of antenatal care therefore remains a vital link between socio-demographic or obstetric risk factors and adverse pregnancy outcomes and perhaps the most modifiable of all risk factors.³²

A majority of the socio-demographic and obstetric factors associated with mode of delivery in this study accord with findings from studies in both developing and developed countries.^{9,14,20,21} Factors less commonly reported are type of residential accommodation, sanitation facilities and use of herbal drug in pregnancy. These may be worth exploring more appropriately through future qualitative studies especially. These may be worth exploring more appropriately through future qualitative studies especially the use of herbal drug in pregnancy which perhaps mirrors the trend in both developed and developing countries towards the combined use of alternative/complementary medicine and orthodox medicine to prevent adverse health outcomes or maximize treatment benefits.³³ The risks associated with obstetric complications and different modes of delivery are more commonly measured in terms of maternal and perinatal mortality,³ and this practice tends to underestimate the overall burden of the adverse health

outcomes.³⁴ The current study provides further evidence that mode of delivery is associated with the risk of sensorineural hearing loss and complements our earlier report in which emergency caesarean section and vaginal delivery were associated with at least two-fold risk of sensorineural hearing loss in surviving newborns compared with elective cesarean section.¹⁷ Our findings also suggest that while all cesarean sections combined may portend lesser risk for sensorineural hearing loss compared with vaginal delivery as reported by studies from countries with higher standards of obstetric practice,^{35,36} infants delivered by emergency cesarean section were likely to be at a greater risk than those delivered by elective cesarean section in this resource-poor setting.

It is in fact common in our population for emergency cesarean section to be initiated after prolonged and unsuccessful trial of labor due to several factors including cultural aversion to surgical intervention and financial constraints. In contrast, a related study among mothers with previous cesarean section found no association between mode of delivery and sensorineural hearing loss,²⁸ which leads us to speculate that the incidence of fetal distress and the associated risks are less likely to be pronounced in pregnancies already considered as high risk as trial of labor in this group of women is likely to be more closely monitored for cesarean section than those without such obstetric indications. Although further confirmatory tests could not be provided for the majority of infants who failed the screening tests due to a high rate of follow-up default, our two-stage screening protocol typically has a test sensitivity of 92%, specificity of 98% and positive likelihood ratio of 61 in hospital-based settings³⁷ and is currently the protocol of choice in many UNHS programs worldwide.

Birth asphyxia (as indexed by low five-minute Apgar scores), hyperbilirubinemia and SCBU admission are established risk factors for a broad range of developmental disabilities such as cerebral palsy, mental retardation and specific language/attention deficient disorders,³⁸ and the observed increased risks accord with existing extensive data on the respiratory morbidity associated with mode of delivery.^{26,39-41} Other studies have also found that cesarean section is associated with adverse long-term health of survivors through reduced rates of breastfeeding.⁴² While the increased risk of hyperbilirubinemia associated with elective cesarean section warrants further investigation, the overall evidence from the current study would nonetheless suggest that the benchmark for evaluating the effectiveness of any mode of delivery should not be limited to the number of deaths averted but also the risks of developmental disabilities in surviving newborns particularly when emergency cesarean section is necessitated in already compromised infants. Mothers and healthcare providers need to appreciate this added dimension to obstetric care in developing countries. The association between infant's gender and mode of delivery was an unusual finding that needs to be explored further in future studies.

Major advantages of this study include the comparative analysis of three modes of delivery simultaneously with the associated neonatal outcomes seldom found in similar studies from developing countries. This study has also demonstrated that newborn screening programs offer unique platforms for establishing interrelationships among various determinants of maternal and neonatal outcomes besides the benefits of early detection for timely intervention. However, a number

of limitations of this retrospective cross-sectional study are worth noting. It is uncertain how the findings in this study can be generalized for other tertiary health institutions within different cultural settings outside sub-Saharan Africa in view of the selection bias. Adverse outcomes considered in this study excluded maternal and perinatal mortality associated with the obstetric practices but this burden is already well documented in existing literature. The potential impact of the cost of cesarean section on maternal decision was not ascertained although this was less likely to be a major factor in this state-funded public hospital compared with fees charged by private hospitals. Data on the number of antenatal visits made or the number of previous cesarean sections among those with this history was also not considered. Prospective studies addressing these limitations as well as exploring the interaction effects of parity are necessary to support the findings in this study.¹⁹ Analysis of time interval between admission and caesarean section (to indicate degree of urgency) and analysis of subsequent length of hospital stay (to indicate severity of outcome) as well as a study of the long-term outcomes for these “near-miss” obstetric events would be valuable.

Conclusions

This study has shown that the rate of emergency cesarean section in a tertiary referral hospital is likely to be high in a community where a high proportion of women prefer to deliver outside hospitals. This pattern of delivery is associated with several obstetric complications and adverse neonatal outcomes which portend substantial risks of developmental deficits such as sensorineural hearing loss in the surviving newborns. Efforts aimed at improving maternal and child mortality in this and similar settings must recognize the broader dimensions of the burden of obstetric complications associated with emergency cesarean section.

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Aerogen nebulizers deliver an incredible four times more medication than traditional jet nebulizers, offering you unsurpassed efficiency and allowing you to give your patients the very best care available. They work independently to the ventilator settings meaning there's no added flow, no nuisance alarms, no loss of PEEP when opened for refill and no drug wastage. Aerogen truly sets a new standard.



**Breathe easy.
You're giving the
best care.**

