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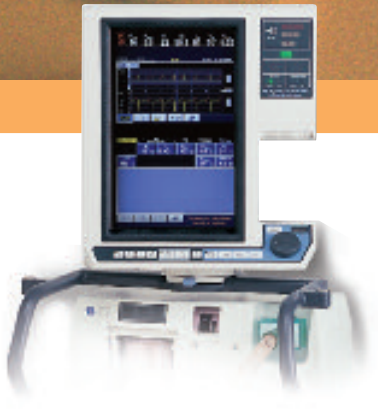

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Editorial

Blowback

At first I thought I would write this editorial about DEHP: If you recall, the use of this PVC was recently deemed potentially harmful to NICU infants. Several hospitals have made an effort to stop using it, including Mercy Hospitals. A hospital in Austria, Glanzing Children's, has virtually phased out PVC plastics from its neonatal unit. While DEHP has been commonly used to soften PVC plastics, certainly a benefit, it can leach into the infusion solution and was found to cause harm to patients receiving IV care, especially male neonatal babies. Of course the PVC industry denied that this posed any health risks, though studies have linked DEHP exposure to multiple problems. A recent article in MCN American Journal of Maternal Child Nursing noted, "Potential toxicities to infants in the NICU are a concern because infants' small body size and compromised physical condition necessitate a multitude of medical interventions, each increasing exposure levels."

But this has been gone over in the literature, I thought, there's nothing new here for an editorial. What struck me, however, was the line about infants' small body size and condition necessitating "a multitude of medical interventions, each increasing exposure levels." And of course the inherent logic of the conundrum reveals itself: if neonatal caregivers weren't practicing multitudes of interventions, there would be no danger of overexposure to PVCs. It's the blowback effect. Every new solution seems to generate its own new problems. Pick up any newspaper or magazine and you'll see the latest warning about the most recent danger de jour. It could kill you just trying to keep up.

To see how this works, you could pick up any issue's news section of this journal and find plenty of confirmation about how good news can turn bad. For instance, in the last issue we reported that C-sections, which are obvious lifesavers, now account for 29% of all births, and have increased attendant risks from anesthesia, infections and blood clots, with excessive bleeding now one of the leading causes of pregnancy-related deaths. You can read in the newspaper that advances in reproductive medicine mean that women in their 30s and 40s have a good shot at giving birth at a time when potential complications and risks are at their greatest. IVF techniques have resulted in more preemies and multiple births. A recent news item on the use of antibiotics in the very young noted, "Doctors should think twice about whether standard drug treatments are doing more harm than good." Another item in our news section noted that babies exposed to chemicals used in nonstick cookware while in the womb are being born at a significantly lower body weight, and reported on an FDA warning that women taking codeine for the pain associated with c-sections risk giving their babies a morphine overdose, as some mothers metabolize the codeine too rapidly and it enters the baby's bloodstream. Well, you get the drift. What's offered with one hand is often taken away with another. Any new practice engenders its own set of risks and new cautions and dangers. Of course neonatologists have long known this, as birth viability has been pushed back to what some say are the limits of common sense. And of course any new possible treatment is going to be tried. There's a certain inevitability in all this. One might, as a parallel comment, note how much easier it was to visit a doctor a couple of decades ago, when you could simply go to your general practitioner. Those days are gone. What can neonatologists do? There's no real solution, except to keep an eye on risks versus benefits, and make cautious and studied and practical judgments accordingly.

Les Plesko, Editor

PS: How to submit editorial material: We are always interested in seeing your papers, case studies, works-in-progress, and abstracts. Neonatal Intensive Care welcomes all submissions. We are not a peer review journal, which means that you get quick notification about the status of your submission. Also, we welcome contributions by all neonatal healthcare professionals, regardless of affiliation. To submit material, all you have to do is send it via e-mail to s.gold@verizon.net, and we will notify you of its status in about a week after we receive it. Please send your submissions in an unformatted word file, and tables and figures as jpegs or pdfs. Neonatal Intensive Care strives to provide an open forum for its readers. As such, all submissions from any segment of the neonatal care community will be considered. Please contact me if you have any questions.

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Editorial Advisory Board

Journey Towards Achieving Healthy People 2010 Breastfeeding Goals in United States

Benamanahalli K. Rajegowda, MD, Muhammad Aslam, MD

Breastfeeding for human infants is natural. It benefits the mothers, the infants and society. It provides economical and ecological benefits, in addition to being healthy for the infant. It also helps the mothers to be closer to their infants to bond and be cuddled. Although it is well known that breastfeeding is beneficial to all, the public, professionals, families and ecologists have not caught up with the breastfeeding recommendation rate in the United States. The American Academy of Pediatrics (AAP) 2001 data on breastfeeding in the United States is shown in the table below.

	Initiation	At 6 months	At One year
All Women	70 %	33 %	18 %
White	72 %	34 %	18 %
Hispanic	73 %	33 %	18 %
Black	53%	22 %	12 %

These figures are all well below the 2010 goals set by Healthy People. In the same study the exclusive breastfeeding rate has not shown any change since 1990, particularly for black women, unmarried, poor, in rural areas and among women younger than 20 years. Healthy People's 2010 goal states that the infant should be exclusively breastfed during the first six months of life and ideally through the first year of life. The national goal of breastfeeding initiation at birth is 75%, exclusive breastfeeding at six months is 50% and the exclusive breastfeeding to continue at one year is 25%. The United States will be nowhere near achieving that level until dramatic changes take place. Breastfeeding information is available everywhere: books, journals, periodicals, committee statements, websites and conferences and meetings; all have been bombarded with information on breastfeeding, but there is still not much improvement in the breastfeeding rate. Many organizations in this country, including AAP, ACOG, LaLeche, and the Surgeon General, along with WHO and UNICEF, have come up with recommendations advocating exclusive breastfeeding up to six months of life. Based on the baby-friendly hospital initiative (BFHI), exclusive breastfeeding is defined as only giving breast milk, with no other supplementation, until six months of life. However, there are many obstacles for women to exclusively breastfeed in an industrialized country like the United States. Some of these are:

Family support for postpartum women is lacking for several reasons.

- Insufficient prenatal education, even though ACOG strongly supports breastfeeding and calls for its fellows, hospital employees and other healthcare professionals taking care of women and their infants to support women who choose to breastfeed their infants.
- Lack of health education in clinics, hospitals and home care services.
- Disruptive, rigid hospital policies and different opinions of the staff, as well as their lack of cooperation.
- Lack of staff education and inability to assist mothers in the immediate postnatal period.
- Drive-in deliveries, birthing center deliveries and discharge home within 48 hours of birth, leaving no time for recuperating women to get help and education.
- Psychosocial and economical conditions that affect many women; some feel that the breast is an organ of physical and sexual beauty and not meant for breastfeeding.
- Lack of public support, though there are legislations stating that mothers can breastfeed their infants in public places.
- Maternal employment; though many institutions and work places have provided help to breastfeeding mothers and there are government policies geared towards helping them.
- Commercialization of infant formula: companies promote exclusive formula feeding by extensive advertisement and by providing free samples and discounts.

WIC supplemental nutritional program for women, infants and children have a long history of educating pregnant women on prenatal nutrition and infant feeding. Despite WIC education about breastfeeding, many mothers ultimately prefer free formula supplies from WIC for nursing their infants. It is the milk formula that is meant to supplement the bottle feeding babies and to some extent supplement the breastfeeding babies,

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but attracts many mothers to enroll who are not willing to breastfeed their infants. It is very important to educate all WIC nutritionists to educate mothers on breastfeeding their infants and also to provide nutritional supplements to breastfeeding mothers to support and enhance milk production.

For mothers who cannot hold their infants to breastfeed or the infant is not within reach (NICU admission), every effort must be made to have an alternative plan to collect breast milk, to feed or store for later use. Modern hand breast pumps as well as commercially available electronic breast pumps are available and accessible within the hospital, home and workplace.

There are only a few contraindications to breastfeeding;

- HIV infected mothers
- Maternal substance abuse
- Untreated active tuberculosis
- Mother on therapeutic or diagnostic radioactive isotopes or chemotherapeutic agents
- Human T-cell lymphocytic virus type 1 and 2.

The baby-friendly hospital initiative (BFHI) established in 1989 has an international initiative implemented by WHO and UNICEF to improve hospital practices known to influence breastfeeding initiation and continuation. BFHI in the United States was founded in 1997 as part of the Healthy People 2000 project. At present, there are about 56 United States hospitals and 1,500 facilities worldwide that are certified by BFHI. To our surprise there are only two in New York State that are certified institutions, but several hospitals have submitted applications to become part of BFHI. BFHI's message is based on ten steps towards successful breastfeeding. These initiatives are geared towards hospital maternity services, for improving skills needed for successful breastfeeding and continuation.

To overcome many of these obstacles, there is a strong effort in this country to win back women to breastfeeding through BFHI, as national breastfeeding is beneficial to all. Education for breastfeeding must be built into the didactic course for all healthcare providers who interact with the women of reproductive age and those who work with infants and children. This curriculum should be included in all the medical, nursing and other healthcare education fields. For many of us who have not received such training there should be an in-service examination and certification.

The New York City Mayor Bloomberg's health commissioner Dr Thomas Frieden has stated: Getting the formula out of the nursery and the baby to breast immediately after birth is a priority. This is easier said than done, but this can be accomplished with BFHI.

Every person who interacts with the mother and the infant should be supportive and encourage breastfeeding. Dr Frieden is correct. He is also allotting funding to educate the staff at the Health and Hospital Corporation (HHC) institutions to encourage women to breastfeed. Money can not buy everything. The system and the culture are to blame for the poor showing of breastfeeding at the HHC facilities but will improve with BFHI.

In summary, breastfeeding offers the best health for the mother, infant, community, society and the country as a whole. The 2010 goal can be achieved by providing information, education to the mothers, acceptance by families and friends, and continued support by everyone involved in maternal child healthcare. The obstetricians and pediatricians along with support from nutritionists and nurses, with help and support from administration and government agencies, will help to improve breastfeeding in the United States. In addition, we should also look into the WIC program to strongly promote only breastfeeding and also to provide lactating mothers with nutritional supplements.

News

☐ January-February 2008

COMMENTARY: WHAT WE ALL KNOW

Healthcare coverage is a mess. It's inarguable. We can have all the debate we want, and it's still a mess. Just so you know where we stand, I'll let the following commentary stand for itself. It is excerpted from a recent article in The Guardian:

No care or concierge care: between two extremes is where America's healthcare system has unraveled. Tens of millions regularly put their health on hold because they cannot afford basic treatment, prescriptions, or even a visit to the doctor. The disparities seem to have brought America to a tipping point. America spends more money on prevention and treatment of disease than ever before, yet it is falling behind on such basic indicators of health as infant mortality and life expectancy. The US spends about 16% of its GDP on healthcare. At $6,700 per capita, it's double what is spent in countries such as France. And yet that still leaves some 47 million Americans entirely without health coverage, and tens of millions of others under-insured and also fails to guarantee a better service to those Americans with access to healthcare. The US ranks last or near the bottom on quality, access, efficiency, equity and healthy lives. Since 2000, there has been a steady decline in the number of employers who offer health coverage. Others are scaling back on the range of coverage. The average cost of insurance premiums rose 7.7% last year, far above the rate of inflation or rise in salaries. The rising costs have shifted the burden of cover on to the individual. By 2003, people were spending almost 20% of their income on insurance premiums and other healthcare costs. For those at the lower end of the income scale, healthcare is not affordable. Healthcare experts say that there is sometimes no rational reason for the rising costs, and that there are huge disparities across the country. None of the current mainstream proposals would move America towards the national healthcare systems of Europe or Canada. That idea remains taboo. – Laszlo Sandor

MONITORING AND MALPRACTICE

The Wall Street Journal recently reported on a controversy surrounding Dr. Barry Schifrin of Yale who has a quarrel with the use of fetal monitoring. In an early experience with a fetal monitor, Schifrin said he was a bystander when an obstetrics team relying on a monitor delivered a baby by C-section, though he thought the baby would be fine and the surgery unnecessary. He said the experience showed him how data could be misinterpreted, and his crusade, ever since, has often put him in the role of testifying against doctors in fetal monitoring-related cases. The Wall Street Journal noted that obstetrics is one of the most-sued specialties, and is often the tipping point in malpractice cases. His resulting testimony, hundreds of times in the last thirty years, has resulted in his censure by ACOG, from which he resigned. In his thirty years as a malpractice consultant, he has given depositions in about 700 cases and testified at 150 trials, earning $2.25 million as an expert witness. In 2002, 85% of fetuses in the US were monitored, but readings are open to interpretation. According to data from ACOG, fetal monitoring has increased C-sections by 53% and diagnosis of fetal distress by 155%, and use of the monitor has also caused an increase in the use of vacuum and forceps. According to Columbia University's Todd Rosen, quoted in the Wall Street Journal article, "It's done more harm than good. We monitor way too much." But many doctors say that the way tracings are used against doctors in malpractice cases is wrong. Schifrin concedes that it's how the monitors are read that's the crux of the problem, and he speaks from a position of some experience, as the son of a prominent obstetrician, and having delivered 6,000 babies. As in one of the first cases he worked on, Schifrin says he has seen many instances where the monitor was detecting the mother's heart rate, elevated by the stresses of labor, rather than the baby's, something that wouldn't occur if a stethoscope was used. But in that first case, the doctor he witnessed against said the death of the infant was due to a pre-existing disorder and

had nothing to do with the delivery. Regardless, Schifrin stood by his diagnosis, and said doctors should simply admit when they're at fault, pointing to how anesthesia has been handled, where the American Society of Anesthesiologists review every case brought against that profession to find out what went wrong, and thus has lower insurance premiums. (The above information is from the Wall Street Journal, October 26, 2007, "Doctor Roils Colleagues...," by Heather Won Tesoriero.)

RUPTURE

A Caesarean section increases the risk by 50-fold that a woman's uterus will rupture during a subsequent vaginal delivery, research suggests. US and Swedish researchers found the condition afflicted nine in every 1,000 mothers who opted to try for a vaginal birth after a previous Caesarean. In contrast, the BJOG study found the rate among women with no history of a Caesarean was just 0.18 per 1,000. The findings were based on a study of more than 300,000 Swedish women by Emory University and the Karolinska Institute in Stockholm. Fourteen of the 274 women who suffered a torn uterus lost their baby, a death rate of 51 per 1,000. In contrast, the neonatal death rate among women who did not develop the condition was just 1.4 per 1,000. Women who gave birth aged 35 or older were nearly three times more vulnerable to a uterine tear than women aged 24 or younger. Clinically obese women had more than twice the risk of women who were not overweight. Inducing labor appeared to double the risk, compared to labor which began spontaneously. The researchers suggested the chemicals used to induce birth weakened previous Caesarean scars, making them more likely to rip. Women who gave birth late were discovered to be more at risk than those who gave birth after a normal-length pregnancy, regardless of whether they had a Caesarean section before. And women who gave birth to babies weighing at least 4kg were at twice the risk than women whose babies were less than 4kg.

NO ROOM AT THE BASSINET

The number of Canadian women from British Columbia being flown across the border for emergency childbirth and neonatal care has shown a large increase, according to a report in the Vancouver Sun. In a recent six month period, there were 35 such transfers to hospitals in Washington State. In 2006 there were none. There are 195 neonatal intensive care beds in British Columbia, 12 more than there were in 2005. Across the province, these beds usually run at about 85-per-cent capacity. When these beds fill up, mothers and babies are transferred to Alberta, and if those beds are full, too, then Washington becomes an option, though it costs more. Most infants stay in hospital for about three weeks, so there isn't a fast turnaround.

FEWER DEAD

The number of children dying around the world has fallen below 10 million a year for the first time since records began in 1960. Figures released by UNICEF showed that global deaths of children fell to an estimated 9.7 million in 2005, down from nearly 13 million in 1990. The drop has been attributed to increased vaccinations, greater use of mosquito nets and vitamin supplements, and more women breastfeeding rather than mixing formula with dirty water. The most important advances included vaccination drives cutting measles deaths by 60% since 1999,women breastfeeding rather than using dirty water, babies sleeping under mosquito nets and babies getting vitamin A drops, which reduce the risk of measles, diarrhea and malaria. Of the 9.7 million children who die each year, 3.1 million are from south Asia, and 4.8 million are from sub-Saharan Africa. West and central Africa have the highest rates of child mortality, with more than 150 deaths per every 1,000 children under five, which compares to six per 1,000 in North America, western Europe and Japan. India and China have shown large improvements, whereas the situation has worsened in southern African countries hit by AIDS, and in war zones, such as Congo and Sierra Leone. The islands of Sao Tome and Principe showed the greatest improvement, cutting child deaths by 48%, mainly due to an anti-malaria campaign which drained swamps and provided mosquito nets. Some questioned the survey, primarily because many information sources for child mortality were either out of date or missing from the UN's database, and because data was provided by governments.

WARNING

Roche and FDA notified healthcare providers that use of CellCept (mycophenolate mofetil) is associated with increased risk of first trimester pregnancy loss and increased risk of congenital malformations, especially external ear and facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney. Based on postmarketing data from the United States National Transplantation Pregnancy Registry and additional postmarketing data collected in women exposed to systemic mycophenolate mofetil during pregnancy, the pregnancy category for CellCept has been changed from Category C (risk of fetal harm cannot be ruled out) to Category D (positive evidence of fetal risk). Labeling changes include the following sections: Boxed Warning, Warnings/Pregnancy and Pregnancy Exposure Prevention, Precautions/Information for Patients, and Adverse Reactions/Postmarketing Experience. Within 1 week of beginning CellCept therapy, women of childbearing potential should have a negative serum or urine pregnancy test. In addition, women of childbearing potential (including pubertal girls and peri-menopausal women) taking CellCept must receive contraceptive counseling and use effective contraception. Healthcare professionals and patients should be aware that CellCept reduces blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness.

LBW & 9/11?

An increase in low birthweight babies born in and around New York in the months after 9/11 has been blamed on stress caused by the attacks. The journal Human Reproduction reported a two-thirds increase in the risk of giving birth to a slightly underweight baby in the week after 9/11. The University of California at Berkeley researchers found it was higher even months later. While many researchers have suggested that the release of stress hormones might, in some circumstances, affect the development of the unborn child, the evidence that it leads to premature birth is not conclusive. The New York study looked at information from more than 1.6 million birth certificates for babies born in the city between 1996 and 2002. They divided the babies into groups depending on how close to Ground Zero their families lived. Compared to the week leading up to 9/11, the following seven days showed a higher risk of babies being born weighing less than 2kg. There was a 67% increase in the risk of a baby weighing between 1.5 and 2kg, and a 44% increase in the chance of a baby weighing less than 1.5kg. In December 2001, the risk of a baby weighing less than 1.5kg was 36% higher than normal, and in January the risk was still 22% higher. The effect was not just confined to the immediate New York City area. In the surrounding areas, or "upstate" New York, the risk of a low

birthweight baby was increased by 46% in January 2002. The researchers said that the initial shock of the attacks may have triggered early labor in some women close to the Twin Towers, while longer-term stresses for women across the whole of New York State may also have interfered with the pregnancy. Many doctors and healthcare providers said, however, that other factors may have come into play, and that the effect of stress on pregnancy is not fully known. Reported by the BBC.

GASP

Twenty to 40% of extremely premature infants suffer abnormal lung development leading to bronchopulmonary dysplasia, a condition addressed by a recent study at Harvard Medical School. Researchers obtained samples from the umbilical cords of 54 surviving infants born at less than 28 weeks gestation and analyzed the activity of all 30,000-odd genes for each infant. The specimens were collected as part of the Extremely Low Gestational Age Newborn (ELGAN) study (elganstudy.org). Twenty of the 54 infants developed BPD after birth; the other 34 did not. In the infants who went on to have BPD, researchers found a difference in a biochemical pathway that's also disrupted in adult COPD. The chromatin remodeling pathway, is responsible for the unwrapping of coiled strands of DNA, which must occur before a gene can act or be expressed. When it is disrupted, certain genes for inflammatory proteins get stuck "on," and the inflammation makes lung tissue degenerate and scar, and other tissue may also be affected. Researchers speculated that histone deacetylase inhibitors directed at this pathway may also prevent or treat BPD. Interrupting the inflammatory process might not only slow or halt infants' progression to BPD directly, but could also avoid the need for them to be on the ventilator for prolonged periods. The researchers didn't find any particular gene to have a different pattern of activity in the infants with BPD. No single gene turned on or off in a statistically different way between the two groups, so researchers realized that it might be an entire pathway that is differentially expressed. But the researchers cautioned that a large sample size would be needed to validate the genetic findings as a reliable predictor of BPD in premature infants. Additionally, researchers found that infants born at younger gestational ages (whether or not they developed BPD) had reduced activity of pathways involved in converting nutrients into energy, a possible explanation for why premature infants require high-calorie intravenous feeding after birth. The study also validated the hypothesis that the umbilical cord makes a good proxy for studying fetal lung physiology. Unlike lung tissue, umbilical cord tissue is readily available to researchers, contains stem cells for many fetal tissues, and appears to reflect the physiology of the fetus and the intrauterine environment.

CUT TO THE CORD

Diagnosing a risk of fatal lung disorders may be possible by analyzing the umbilical cords of premature babies, according to research published in the online open access journal Genome Biology. Researchers at the Children's Hospital, Boston, collected umbilical cord tissue samples from 54 premature infants born at less than 28 weeks of gestation, including 20 samples from infants who later developed BPD. When DNA expression profiles were compared, the researchers found that infants who subsequently developed BPD had distinct gene expression signatures that differed from the ones who did not develop the disease, although the maternal characteristics (for example, the cause of delivery, race, or inflammation of the uterus) were similar. The genes that differed between the two groups involved chromatin remodelling and histone acetylation pathways.

SMOKED OUT

Nine out of ten mothers who lose a baby to cot death smoked while pregnant, according to researchers at Bristol University, who also said the risk increased with every hour babies were exposed to passive smoke after birth. Many studies have shown a clear link between smoking and cot death, but the Bristol research tries to unravel more precisely the cost of smoking both before and after birth. Smoking among pregnant women has fallen from 30% to 20% in the last 15 years. The proportion of babies who went on to die from Sudden Infant Death Syndrome (SIDS) who were born to mothers who smoked during pregnancy had risen from 57% to 86%. A baby exposed to smoke eight hours a day was eight times more likely to die from SIDS than a baby that was never exposed. Researchers said that maternal smoking was the most important avoidable risk factor for SIDS.

PROPAGANDA

The decision to halt an HHS public service campaign that promoted breast-feeding was a matter of politics and economics, according to an editorial in the Los Angeles Times. The campaign was toned down after formula industry representatives hired lobbyists to influence the department. The US House Committee on Oversight and Government reform is investigating whether former Surgeon General Richard Carmona was barred from participating in the breastfeeding advocacy project and if people working on the campaign were overruled by superiors after industry lobbyists pressured the department to weaken the campaign, and the editorial noted that formula companies reframed the debate to be about choice rather than sound nutrition. Reprinted from Kaiser Network via Medical News Today.

CRAZY COMPLICATIONS

Christian Nordqvist, in a copyrighted article published by Medical News Today, wrote that mothers who have severe obstetric complications are more likely to have mental health problems and to die (sooner, one presumes), compared to women who give birth without complications. The London School of Hygiene and Tropical Medicine's study of 1,014 women in Burkina Faso found that of 337 women with SOCs, 199 gave birth to a living baby, 64 lost their baby before completion of pregnancy, and 74 lost their child shortly after birth. Each woman with SOC was compared to two controls whose deliveries had no complications. The researchers followed them all up one year later and found that six in the SOC group died in a year, compared to no one in the control group; babies of moms with complications were 4.5 times more likely to die within 12 months; depression was 82% higher among moms with complications; SOCs were twice as likely to have suicidal thoughts; and half of SOC mothers reported that their pregnancy had a negative impact on their lives.

DO IT NOW

Now is the time to stop neglecting maternal mortality, according to the "Women Deliver" issue of The Lancet. According to the journal, "The Safe Motherhood Initiative was launched by WHO (World Health Organization) and others to help reduce the severe global burden of pregnancy-related illness and death. Sadly, today, most of that burden remains unchanged... The need is known as is the knowledge to fix it. More money exists than

ever, and a range of existing global initiatives has yielded useful experiences and lessons. There can be no more excuses and no further delay. Women's rights are worth fighting for; their lives can and must be saved."

IT'S NOT AIDS

While a recent nationwide poll that said most Americans thought HIV and AIDS was the leading cause of child death in poor countries, the real cause is pneumonia, diarrhea, and neonatal complications. Contributing factors are lack of access to drinking water, malnutrition and preventable diseases associated with conditions of poverty. The survey found that 95% of Americans believe child survival is an important problem facing the world, but that most don't know that the majority of child deaths are preventable. The causes of child death in poor countries are ones no longer faced by richer nations, and two-thirds of the deaths could be preventable with basic services and practices. Reported by Christian Nordqvist in Medical News Today.

MAKE IT SAFER

The Royal Colleges of Anaesthetists (RCOA), Midwives (RCM), Obstetricians and Gynaecologists (RCOG), and Paediatrics and Child Health (RCPCH) have issued new safety standards of care during childbirth. The organizations stressed the need for good working relationships between a multidisciplinary maternity team of midwives, obstetricians, anesthetists, pediatricians, as well as support and managerial staff. Also deemed important was the expansion in the number of midwives and obstetricians. Recommendations are that: women in labor must receive individual one-to-one care from a midwife; consultant obstetricians should conduct physical ward rounds twice a day and review midwifery cases; women requiring conduction or general anesthesia should be seen and assessed by an anesthetist before an elective procedure; and a healthcare professional versed in neonatal life support must be immediately available for all births. For the full report go to rcog.org.uk.

RETENTION

A recent article in BMC Public Health discussed challenges to retention in prenatal care (Retaining women in a prenatal care randomized controlled trial in Canada: implications for program planning, Tough, et al). According to the research, retention of pregnant women in prenatal care is a problem under both universal systems of care, as in Canada, and non-universal systems of care, as in the United States. However, among populations being served by a system of publicly funded healthcare, the barriers are less well understood and universal uptake of prenatal services has not been realized. Determining the characteristics of women who dropped out of a prenatal care randomized controlled trial can help identify those who may need alternate retention and service approaches. In the study, pregnant women were randomized to current standard of care, standard care plus nursing support, or standard care plus a paraprofessional home visitor. Sixteen percent of 2,015 women did not complete all three telephone interviews (197 dropped out and 124 became unreachable). Responders were compared to non-responders on demographics, lifestyle, psychosocial factors, and life events using chi-squared tests. Logistic regression models were constructed using stepwise logistic regression to determine the probability of not completing the prenatal program. Completion rates didn't differ by intervention. In comparison to responders, non-responders were more likely to be younger, less educated, have lower incomes, smoke, have low social support, have a history of depression, and have separated or divorced parents. Unreachable women were more likely to be single, use drugs, report distress and adverse life events. Non-Caucasian women were more likely to drop out. Independent key risk factors for dropping out were: less than high school education, separated or divorced parents, lower social support, and being non-Caucasian. Pregnant women who were single/separated/divorced, less than 25 years old, had less than high school education, earned less than $40,000 in annual household income, and/or smoked had greater odds of becoming unreachable at some point during pregnancy and not completing the study. The article concluded that women at risk due to lifestyle and challenging circumstances were difficult to retain in a prenatal care study, regardless of the intervention. For women with complex health, lifestyle and social issues, lack of retention may reflect incongruence between their needs and the program.

LET'S GET TOGETHER

Mutual European collaboration is important for many clinical trials and essential for trials investigating treatments for rare diseases, according to a report by the European Medical Research Councils (EMRC). The council noted that for many rare conditions, there are insufficient numbers of patients in any single country to allow meaningful clinical trials. The research council's program, called Pan-European Clinical Trials (ECT), has seen the successful launch of two trials into rare bone conditions, osteosarcoma and fibrous dysplasia. While setting up these two trials, the coordinators had to overcome a number of challenges. The osteosarcoma trial involves collaboration across 11 European countries, as well as the US and Canada, recruiting 1,400 patients. The trial has already recruited more patients than any other similar trial. The second collaborative trial is designed to assess the safety, tolerability and efficacy of bisphosphonates in patients with fibrous dysplasia of the bone. Five countries across Europe are involved. Researchers said that the EMRC wants to build on these experiences to develop an in-depth analysis of the current situation in Europe in an international perspective and make recommendations to allow investigator driven clinical trials to be launched as efficiently as possible for the benefit of European patients.

LISTEN UP

A revised policy statement from the Joint Committee on Infant Hearing recommended that pediatricians take the lead in ensuring that all infants are screened for hearing loss by the first month, and if diagnosed with hearing loss by 3 months, engaged in full intervention services by 6 months. Since 2000, when the JCIH first recommended that all infants be screened for hearing loss, the number of screened newborns increased from 38 to 95%. Nonetheless, half the children who failed hearing screening tests did not receive appropriate, timely follow-up care.

PREEMIES AND CHOLESTEROL

Mothers with low serum cholesterol levels are significantly more likely to deliver premature babies, or full-term babies with lower weight, according to the study, "Adverse Birth Outcomes Among Mothers With Low Serum Cholesterol." Researchers studied 118 women with low total cholesterol (less than the 10th percentile) and 940 women with mid-range cholesterol levels. The women were referred to South Carolina clinics for routine second-trimester prenatal care between 1996 and 2001. Among white mothers, the prevalence of preterm delivery was 21% for the low cholesterol mothers, compared to 5% for the mid-cholesterol mothers. There were no significant increases in preterm birth

rates among African American mothers. However, a low maternal serum cholesterol level was associated with lower infant birth weights at term in both racial groups. In addition, a trend was found towards small head size among babies born to mothers with very low cholesterol.

SOMETHING FISHY

Pregnant and breastfeeding women should eat 12 ounces of fish and seafood per week for optimal brain development of fetuses, infants and young children, according to guidelines to be released by the National Healthy Mothers, Healthy Babies Coalition. The coalition's guidelines on consumption of seafood during pregnancy and immediately after pregnancy are at odds with current FDA and EPA guidelines that advise young children, pregnant women, nursing women and women of childbearing age to avoid consuming swordfish, king mackerel, shark and tilefish because of high mercury levels. The warnings also recommend that those groups eat no more than 12 ounces of fish weekly and eat no more than six ounces of canned albacore tuna weekly. Those guidelines were prompted by some studies that showed that high levels of mercury contribute to birth defects and other health problems. Several studies also demonstrated a subtle loss of mental acuity in the offspring of women who consumed fish during pregnancy. However, fish and seafood are the major dietary sources of omega-3 fatty acids, which are important nutrients for the brain and nervous system development. The Healthy Mothers guidelines recommend eating ocean fish, such as salmon, tuna and sardines, which are highest in omega-3s, and noted that the selenium in ocean fish may counteract negative influence of mercury exposure. The guidelines note that women who don't consume enough omega-3s in pregnancy seem to have a higher risk of depression during pregnancy and after giving birth. A study published in The Lancet found that children of women who ate only small amounts of fish during pregnancy had lower IQs and lower academic test scores at age eight and more behavioral and social problems throughout early development than children whose mothers ate 12 or more ounces per week. Other studies also have indicated that consuming low levels of omega-3s can raise the risk of premature birth and low birthweight. The FDA said it's not prepared to change its advice. (Some of the information above is from kaisernetwork.org, © 2005 Advisory Board Company and Kaiser Family Foundation.)

SMEAR IT ON

New data has shown a positive association between the use of vaginal progesterone and infant health at birth. Babies born to women with high-risk pregnancies treated with Prochieve 8% progesterone gel appeared less likely to need intensive care than babies born to mothers treated with a placebo, according to Columbia Laboratories, Inc. Researchers conducted a secondary analysis of phase III data from the largest-ever singleton preterm birth prevention study with progesterone looking specifically at a group of 46 women with high-risk pregnancies because they had a short cervix, and this analysis shows several statistically significant findings: one out of six newborns of mothers treated with vaginal progesterone gel needed to be admitted to neonatal intensive care units compared to one out of two newborns of mothers treated with placebo; and infants born to mothers treated with vaginal progesterone gel who were admitted to intensive care units spent on average only one day in intensive care compared to more than two weeks for those babies of mothers who received placebo. In addition, the analysis provided new insight into which women with high-risk pregnancies respond to treatment with vaginal progesterone gel. When looking at a sample of 46 women with a short cervix of less than 2.8 cm, none of those who were started on vaginal progesterone gel between 18-to-22 weeks of gestational age delivered prior to 32 weeks, while almost one in three women with a shortened cervix given a placebo delivered prior to 32 weeks of gestation. Additionally, the number of admissions and days spent in the NICU by babies whose moms were given vaginal progesterone gel were significantly lower than for those whose moms received placebo. The overall Phase III study, "Progesterone Vaginal Gel for the Reduction of Recurrent Preterm Birth," did not show a beneficial effect of progesterone treatment on reducing the frequency of preterm birth in a larger population of high-risk women identified with only a history of spontaneous preterm birth.

POOR PREEMIES

The University of Illinois at Chicago College of Nursing received a $4.1 million federal grant to develop ways to improve the early growth and development of premature infants who have two or more social-environmental risks such as poverty or minority status. The study will enroll 252 premature infants born between 29 and 34 weeks gestational age at two Chicago medical centers, and will use a clinical model called H-HOPE, Hospital-home transition: optimizing prematures' environment, that combines components from two research programs previously used by researchers. During the audio, tactile, visual and vestibular stimulation component, mothers spend 10 minutes talking to the infant, lightly stroking or massaging it and looking directly in its eyes, followed by five minutes of rocking the baby. In the second program, mothers are taught by a nurse-community advocate team about preterm infant behavior and feeding. This is the first study to simultaneously incorporate programs for both mother and premature infants and evaluate the outcomes for both.

RSV

MedImmune, Inc announced results from two RSV studies presented at the Infectious Diseases Society of America (IDSA) Annual Meeting. The company presented new data regarding motavizumab, a key investigational monoclonal antibody (MAb) being prepared for regulatory submission in the United States. Data was also presented showing the geographical variability of RSV, particularly in the southernmost United States. Data presented includes: Safety, Tolerability, and Immunogenicity of Motavizumab in Young Children After a Second Season of RSV Prophylaxis, which assessed the safety and immunogenicity of motavizumab in young children with a history of prematurity who received two sequential seasons of the antibody. Also presented: RSV Surveillance: Retrospective and Current Data on the Variance in Season Onsets and Offsets.

MUTANT GENE

Why mutations in a single gene can cause infant epilepsy is the subject of research by the Howarld Florey Institute in Melbourne. Infants have protective mechanisms in their brains to control this excitability, but the scientists discovered that a single gene mutation prevents a specific ion channel from functioning correctly, thus causing excitability which results in epilepsy. Researchers noted that the ion channel which carries the mutation is itself naturally protective, as it limits excitability in the infant brain by waiting to fully switch on only in the adult brain. The mutation accelerates this normally delayed development change, leaving the susceptible infant brain with an overly excitable channel and epilepsy. If this switch to a more excitable

state occurs too early during brain development, it is possible that epilepsy and other neurological disorders develop.

PRODUCTS

WITH A TRACE

Children's Medical Ventures, a subsidiary of Respironics, announced that it has received exclusive distribution rights for the NICU Tracer Breast Milk Identification System in the United States and Canada. The system incorporates a handheld scanner that reads and compares barcode labels to ensure that an infant is receiving the correct breast milk from its own mother. NICU Tracer, developed by Kay Medical Concepts, Inc, helps hospitals to reduce critical incidents and avoid serology and med-legal expenses while saving both time and labor. Other significant features of the NICU Tracer Breast Milk Identification System include computerized tracking and auditing of charts that help healthcare professionals to automate these processes. In addition, the system is backed by Children's Medical Ventures' customer service and product support network. Introduced in 2002, NICU Tracer is currently used by more than 35 NICUs throughout the United States. Contact childmed.com.

HAPPY BIRTHDAY

Draeger Medical, Inc celebrated 100 years of ventilation technology in October. In 1907, the company delivered the Pulmotor, the first-ever mobile short-term respirator. As part of its ongoing celebration of these milestones, Draeger Medical showcased an original Pulmotor alongside of its latest respiratory care devices at the annual ASA Annual Meeting in San Francisco and at the AARC. Due to its use in the harsh environments of underground mines and in high altitudes, the reputation of the Pulmotor quickly grew. The first users of the ventilation products were soon dubbed "Draegermen," and ever since, the term has been synonymous with mine rescue teams worldwide. The use of Draeger breathing apparatus quickly spread to other emergency services fields and in 1913, the New York and Pittsburgh city fire departments began equipping their firefighters with the respirators. Today, both cities are still using Dräger self-contained breathing apparatus (SCBA). Draeger has continued to build upon its impressive heritage of breathing innovation. For example, the new SmartCare/PS option for the EvitaXL ventilator is an automated knowledge-based ventilation system developed to improve the efficiency and effectiveness of the weaning process. One of the company's most recent innovations was the introduction of the Oxylog 3000 emergency transport ventilator. In the US, Draeger Medical, Inc also recently released the Carina Home home care ventilator. This system offers clinical-standard ventilation control for patients in the comfort of their own homes. With products such as these, the company is laying the foundation for another 100 years of life-saving success. For a look at Draeger Breathing Milestones, visit draeger.com, and read "The History of Draeger" brochure.

NOT FOR GRANTED

More than 10% of the nation's healthcare facilities are seeking grants from Cardinal Health through a $1 million fund set up by the company to help improve patient safety. More than 700 hospitals, health systems and community health clinics responded to Cardinal's announcement about the grant program, which is the largest and first of its kind in the private sector. To support initiatives that enhance patient safety and quality of care, Cardinal Health will grant up to $50,000 per facility to fund new and innovative programs that establish or implement creative and replicable methods to address challenges in providing quality patient care and to help drive improvements. The company expects to fund up to 40 of the 730 grant requests. In selecting grant recipients, Cardinal Health's selection committee is looking for: projects that respond to a clearly identified, high priority safety issue; projects that apply new thinking and approaches to development of solutions; collaborative programs; demonstrable and sustainable measures to assure that improvements hold up over time; and model programs that can be replicated at other organizations. Contact cardinalhealth.com.

BEHRING STRAIGHT

Siemens is integrating Dade Behring into its existing business of Siemens Medical Solutions Diagnostics, a wholly owned subsidiary of Siemens Medical Solutions USA, Inc, with a transaction that took place this past November. The acquisition allows Siemens to become the leader in the laboratory diagnostics market and enables Siemens to offer its customers a comprehensive portfolio of innovative solutions across the whole healthcare continuum - from prevention to diagnosis, to therapy and care. The company is bringing together the entire medical imaging, laboratory diagnostics and clinical IT value chain under one roof, offering opportunities for the integration of a comprehensive range of technology, workflows and information that will help deliver an improved quality of patient care at reduced costs. According to Siemens, together with Dade Behring, Siemens Medical Solutions Diagnostics is well-positioned to lead the way in bringing new capabilities to the diagnostics industry. Jim Reid-Anderson is leading the Siemens Medical Solutions Diagnostics global business that has nearly 15,000 employees. Jochen Schmitz remains Chief Financial Officer (CFO). Primary offices of the company will be located in Deerfield, IL, the current headquarters of Dade Behring. Siemens has 475,000 employees. Contact siemens.com.

ALL SET TO GO

Masimo, the inventor of Pulse CO-Oximetry and Read-Through Motion and Low Perfusion pulse oximetry, announced the completion of CHN's system-wide implementation of Masimo SET pulse oximetry. Building on a four-year history of superior Masimo SET performance in other areas of its network, CHN expanded the adoption of Masimo SET pulse oximetry technology to virtually every site – making Masimo SET CHN's standard of care for precise, continuous SpO_2 monitoring. Ranked among the top 20 integrated health care networks in the nation, Community Health Network has more than 70 sites of care throughout central Indiana. This includes Community Hospitals East, North and South in Indianapolis and Community Hospital Anderson; The Indiana Heart Hospital, a dedicated heart hospital; Indiana Surgery Centers; Community Physicians of Indiana; Community Home Health Services; MedCheck urgent care centers; occupational health services; nursing homes; and other health care facilities. In 2006, CHN was recognized as a Performance Improvement Leader by Thomson Healthcare and, since 2001, has had fewer adverse patient safety events and discharged patients almost a day earlier. By making the conversion to Masimo, the Community Health Network joins other top hospitals in the United States—including four of the top five—as listed on the US News & World Report Honor Roll, which have all adopted Masimo SET as their primary pulse oximetry platform. Masimo SET is widely recognized as the most

accurate and reliable pulse oximetry technology in the world, clinically proven in more than 100 independent and objective studies to provide the most trustworthy SpO_2 readings even under the most difficult clinical conditions, including patient motion and low peripheral perfusion. These studies prove Masimo SET delivers improvements in outcomes, safety and efficiency. Community Health Network's system-wide conversion included standardizing virtually all of CHN's sites of care to Masimo SET pulse oximeters and sensors. Masimo advanced technology and sensor design increases the durability and longevity of the sensors and cables connecting the patient to the pulse oximeter. Made of a durable, non-absorbent tape material that extends the life of the sensor during single patient use, Masimo adhesive sensors have been shown to reduce sensor usage 49% to 56%. (Holmes M, Thomas A, Vogt J, Gangitano E, Stephenson C, Liberman R. Useful Life of Pulse CO-Oximeter Sensors in the NICU. Respiratory Care 1998;43(10):860; Erler T, Avenarius S, Wichniewski E, Schmidt K, Klaber H. Longevity of Masimo and Nellcor Pulse Oximeter Sensors in the Care of Infants. J. Perinatol., 2003;23:133-135). Contact masimo.com.

CERTIFIED

Vapotherm, the leading developer and manufacturer of high flow oxygen therapy products, has earned an Export Achievement Certificate from the US Department of Commerce. Vapotherm was one of three Maryland companies to receive this designation at a recent ceremony in Wye Mills, MD. The Export Achievement Certificate was created by the DOC to recognize small and medium-sized enterprises that have successfully entered the international marketplace for the first time or that have successfully entered a new market. Vapotherm is now distributed in over 20 countries outside the US, and the company notes that the US Department of Commerce Export Assistance and the State of Maryland Export Assistance has been a valuable resource for use as it expands globally. "With ninety five percent of the world's market outside of the United States, Vapotherm is well positioned in these markets for future growth," said Bill Burwell, Director of the US Commercial Service in Baltimore. Vapotherm, Inc is a privately held manufacturer of respiratory care devices for hospitals and homecare use, specializing in noninvasive technologies for respiratory therapy, especially for the treatment of chronic lung and acute breathing disorders. For more information, visit vtherm.com.

OXIMETRY ROUNDTABLE

Radiometer

Information provided by Jan Weaver, Marketing Services Manager.

How has oximetry changed over the past 5 years, and how has it changed the standard of care in the NICU?

The addition of transcutaneous CO_2 monitoring to pulse oximetry now allows the clinicians a better understanding of the infant's oxygenation and ventilation status. Radiometer's TCM40 uses a CO_2 electrode that allows monitoring ventilation at lower temperatures for longer periods of time. At the same time, the TCM40's pulse oximetry sensor (Nellcor technology) may be a useful tool at the bedside for combating the sudden changes that can arise with duct-dependent congenital heart disease, as well as reducing the frequency of arterial blood gases.

How has your company pursued R&D efforts to continue improving this technology?

Radiometer's newest electrode is designed specifically for use in the NICU. It is smaller in size than conventional sensors and uses a soft, latex-free fixation ring to minimize trauma to the baby's skin. Radiometer has added features to its TCM monitors to deliver stable readings more quickly. A feature called SmartHeat increases electrode temperature by just one degree during the first five minutes of measurement. Without causing any patient discomfort, this feature stabilizes tanscutaneous values faster by increasing the arterialization of capillary blood flow.

How effective is oximetry during low perfusion conditions, and what has been done to improve sat readings during low perfusion?

Radiometer's TOSCA ear clip $tcpCO_2/SpO_2$ electrode incorporates Masimo's SET pulse oximetry technology to warn of potentially erroneous readings under low perfusion conditions. The TCM40 incorporates Nellcor's SatSeconds alarm technology to help manage nuisance alarms caused by low perfusion conditions without sacrificing patient safety.

Nonin

How has oximetry changed over the past 5 years; how has it changed the standard of care in the NICU?

Advances in motion tolerance and ability to read in low perfusion states have been significant in oximetry. Improved algorithms within the oximeter technology and sensor continue to improve performance. For the NICU setting, a device must be able to provide an accurate reading in the presence of both motion and low perfusion. Like many areas of life, wireless technology has reached oximetry. Nonin introduced Avant 4000, the first Bluetooth Wireless oximeter, in 2004. In the NICU, the Avant 4000 allows continuous monitoring without the constraints of wires, providing additional mobility and privacy for parent and child when feeding or conducting kangaroo care.

Has your company pursued R&D efforts to continue improving this technology?

Nonin's dedication to technological leadership, precision manufacturing and uncompromised customer support ensures quality products and service our customers can expect. Nonin's devices are designed to work effectively in all patients at all times. Nonin's history of innovative products began in 1986 and includes the first self-contained fingertip oximeter (Onyx - 1995), first fiber optic sensor for use in magnetic resonance (1991) and the first Bluetooth® Wireless oximeter (Avant 4000 - 2004). New innovative ideas and products continue to flow from our research and development center.

How effective is oximetry during low perfusion conditions; what has been done to improve sat reading during low perfusion?

Pulse oximetry relies on a pulsatile blood flow, therefore low perfusion can create a challenging environment. Nonin addresses the issue of reading in low perfusion from two directions: signal processing within the oximeter and quality of

light in the sensor. It is the combination of these two components that result in optimal performance in low perfusion. Nonin's PureSAT Signal Processing Technology distinguishes "real" pulses from motion artifact resulting in greater use of the most valuable pulse signal waveforms—decreasing the occurrence of false desaturation events and false alarms. Through identification of the best and most reliable signals on a pulse-by-pulse basis, users are provided with accurate information and the fastest response time to physiological changes. Nonin's PureLight Sensor Technology provides only the purest red and infrared LEDs to create unparalleled accuracy. The combination of the Nonin PureSAT Signal Processing Technology with its PureLight Sensor Technology provides a highly responsive and precise system for accurate and reliable readings, even under the most challenging patient conditions.

How has oximetry proven to be cost effective and/or reduced overall costs?
Nonin products have consistently been designed for durability and low power use, which together translate to lower overall costs. The lower power draw of the device provides for fewer batteries. Nonin's 8500 hand-held device requires six double AA batteries for 100 hours of use, while similar devices from a leading competitor require more than 100 AA batteries (Nellcor) for the same amount of use. For research/information about the handheld oximeter see nonin.com/documents/Handheld_Oximeter_Comparison_100hrs.pdf.

What hampers effective use of oximetry?
Pulse oximeters and sensors are designed and tested by oximeter companies to be used together as a system. Each oximeter is programmed with a calibration curve that is calculated in conjunction with specific light characteristics of a sensor. The accuracy of the oximeter therefore depends not just on the oximeter but on the quality and consistency of the lights within the sensor. Unfortunately, a number of non-branded sensors are seen on the market and used interchangeably by end users. Oximeter companies are moving towards proprietary connectors from sensor to oximeter to prevent erroneous use of non-branded sensors.

Covidien: Nellcor Pulse Oximetry

Information provided by Mark Riters, Director of Marketing, Covidien (formerly Tyco Healthcare - Nellcor).

How has oximetry changed over the past 5 years?
Advances in sensor and monitor technology mean patients who were difficult to monitor in the past can now reap the safety benefits of pulse oximetry. Previously, conditions such as low peripheral perfusion, low saturation levels, patient activity and fragile skin were problematic, causing inaccurate or interrupted readings and increased nuisance alarms. However, manufacturers have continually developed better signal processing technology, resulting in more accurate and reliable readings during difficult conditions. New sensor innovations include the LoSat expanded accuracy range in Nellcor's OxiMax adhesive sensors, which improves assessment of patients at low saturation levels (60% - 80% SpO_2). In addition, the presence of a digital memory chip in each OxiMax sensor gives OxiMax monitors the flexibility to operate accurately with a diverse range of sensor designs and opens up a whole new world of pulse oximetry innovation.

How has Nellcor pursued R&D efforts to continue improving oximetry technology?
Nellcor pulse oximeters were introduced in the early 1980s. We have continually driven innovations as applications for the technology have expanded. As part of Covidien (formerly Tyco Healthcare - Nellcor), our R&D efforts are well-supported, and numerous projects are in progress. Our product development is most often based using feedback from the medical community. We identify real patient care issues and work to solve them, rather than indiscriminately adding "bells and whistles" to our products.

How effective is oximetry during low perfusion conditions, and what has been done to improve saturation readings during low perfusion?
Poor perfusion at the extremities can result in weak pulse signals that make it difficult for the oximeter to produce accurate readings. OxiMax pulse oximeters incorporate our latest signal processing methods—sophisticated algorithms that produce accurate, reliable readings even when low perfusion conditions result in weak pulse signals. Selecting the right sensor may also play an important role in monitoring during low perfusion. The OxiMax MAX-FAST forehead sensor is often able to provide SpO_2 readings when digit sensors fail in weak signal conditions. Designed for use on the patient's forehead—a site closer to the heart—the MAX-FAST forehead sensor responds to changes in SpO_2 typically one to two minutes sooner than digit sensors for patients with weak pulses. As a result, hypoxemic events can be detected earlier to maximize patient safety.

How has oximetry proven to be cost effective and/or reduced overall costs?
While pulse oximetry has always been considered a cost-effective tool, choosing the right technology can help reduce costs. For example, clinicians who have difficulty obtaining reliable SpO_2 readings might try switching to another monitor or replacing the sensor, which wastes time and money. Using up-to-date oximetry technology with appropriate, high quality sensors can save time and prevent waste. Because Nellcor OxiMax pulse oximetry is available in most major multi-parameter patient monitoring systems, it's easy to standardize on Nellcor sensors throughout the hospital to save on supply costs.

What type of training and user support programs does Nellcor provide?
Covidien offers an exceptional level of customer support and training resources that include:

- Pulse oximetry in-servicing and additional guidance on best practices for sensor/monitor use in all clinical settings.
- Accredited on-line courses for respiratory care practitioners and nurses offered through our on-line Center for Clinical Excellence (nellcor.com/ccexcellence).
- A variety of educational and product training resource materials including case studies, white papers and reference notes, monographs, competency checklists and protocols.

Technical Services can be reached toll-free. This department is staffed by knowledgeable representatives, who can readily answer questions about product operation and clinical applications, and aid with troubleshooting.

What hampers the effective use of oximetry?
Pulse oximetry has become very common and simple to use, yet caregivers may often fail to properly apply the sensor according to its directions for use. Proper sensor use is critical to oximetry effectiveness. Placing a sensor incorrectly or using it on a site other than the one it was designed for can cause highly inaccurate SpO_2 readings. For example, placing a digit sensor on the forehead can significantly overestimate a patient's saturation level, giving false reassurance. Covidien has materials available free of charge to support on-going clinician education related to sensor selection and application.

Masimo Corporation

Information provide by Joe E. Kiani, CEO and Chairman.

How has oximetry changed over the past 5 years, and how has it changed the standard of care in the NICU?
With the advent of Masimo SET Read-Through Motion and Low Perfusion technology in 1996, and its wide adoption in the past 5 years, pulse oximetry has become a clinically useful tool. The revolutionary performance of Masimo SET pulse oximetry technology has helped clinicians in the NICU save lives, save eyes (from ROP), detect congenital heart defects (CHD), and improve the care of cyanotic babies better than ever before. Even under the most difficult of clinical conditions, where conventional technologies fail, Masimo SET can save lives. For one newborn, admitted with left heart hypoplasia and extremely low perfusion, Masimo SET technology provided the accurate and reliable SpO_2 readings that enabled the neonatal team to continue the resuscitation efforts that saved his life. Without the Masimo SET technology reporting a steady rise in SpO_2 values, "the resuscitative efforts for this baby would have been aborted."[1] False SpO_2 alarms, due to patient motion and low perfusion, are more than an annoyance in the NICU largely because inaccurate SpO_2 values can have devastating and permanent consequences in fragile preemies. Erroneous SpO_2 values often lead to the overuse of supplemental oxygen, which increases the risks of Retinopathy of Prematurity (ROP), a potentially blinding eye disorder that primarily affects premature and low birth weight infants. ROP, which usually develops in both eyes, is one of the most common causes of visual impairment and blindness during childhood. However, because Masimo SET has been proven to have the highest sensitivity (over 97%) and specificity (over 93%) through conditions of motion and low perfusion—the most common source of false alarms with other pulse oximetry technologies—false alarms are reduced by over 90% when compared to conventional pulse oximetry solutions. As a result, the accuracy of Masimo SET read-through motion and low perfusion pulse oximetry, in combination with a strict oxygen management protocol, has been shown to lead to a significant decrease in the incidence of ROP (by 80%) and the need for ROP laser treatment (by 100%) over a three-year period.[2] And, not only has Masimo SET technology been shown superior in helping to reduce ROP—thereby saving the eyesight of babies—research also shows that other pulse oximeters don't provide the same results for ROP reduction as Masimo SET.[3] Another very important application of Masimo SET technology has enabled improved detection of congenital heart disease (CHD) in babies prior to discharge. Each year, 10-30% of deaths due to CHD in the first year are the result of unrecognized cases. By delivering more accurate saturation values, Masimo SET has been shown to improve the sensitivity of screening for CHD.[4] Additionally, when perfusion index (PI), a new measurement in the Masimo Rainbow SET technology platform that reflects real-time changes in peripheral blood flow at the monitored site, was added to the routine screening process, 100% of CHD cases were detected prior to discharge.[5] Clinicians caring for cyanotic children in the pre- and post-op setting face unique patient care challenges, including very low saturation and peripheral perfusion that requires accurate pulse oximetry values for saturation levels below 70% and careful maintenance of these low saturations within very narrow limits. In comparison studies conducted on cyanotic babies, only Masimo SET technology with the Masimo LNOP Blue Sensor delivered accurate SpO_2 readings 100% of the time, while the conventional pulse oximeter failed to obtain readings 15% of the time.[6] Further study results showed that Masimo SET with the LNOP Blue Sensor provided SpO_2 readings that were twice as accurate as other pulse oximetry technology.[7]

How has your company pursued R&D efforts to continue improving this technology?
We have listened carefully to the clinical community to understand what is needed and then we set out to fulfill the need. Since introducing Masimo SET—the first Read-Through Motion and Low Perfusion pulse oximeter—we have continued to champion taking noninvasive monitoring to new sites and new applications by understanding the needs of our customers and their patients. Sometimes that has meant pursuing narrow, but very important solutions that offer better sensor technology enabling a more accurate pulse oximetry system for cyanotic babies, such as the Masimo Blue sensor, the Newborn sensors for neonates in need of resuscitation, or SofTouch sensors for delicate skin conditions. And, sometimes it has meant pursuing broader solutions that offer additional measurement capabilities, such as measuring Methemoglobin for Neonates under iNO therapy with the newly introduced Masimo Rainbow SET. Neonatal, infant, and pediatric patients with congenital heart disease have unique physiology, which has frequently made it impossible for clinicians to obtain reliable pulse oximetry readings. This limitation has impacted the clinicians' ability to rely on continuous SpO_2 measurements to determine the precise cardiac medication and ventilatory management these patients require. After extensive research and development, Masimo introduced LNOP Blue along with a new algorithm that is now featured in all Masimo SET products (since V4.1), as well as, in the new Masimo Rainbow SET platform. LNOP Blue is the first and only adhesive sensor proven accurate on pediatric patients with congenital heart disease with saturations as low as 60%.[8] LNOP Blue provides clinicians with the reliable, continuous pulse oximetry they need to better manage the cardiac medications and ventilation therapy of these critical patients. Another specialty sensor, the LNOP Newborn sensor, was specifically designed with newborn resuscitation in mind. When the Newborn sensor is connected to Masimo-equipped technology (version 4.1 or higher), it automatically enables the fastest SpO_2 readings at maximum sensitivity. In addition to providing optimal performance, the Newborn sensor allows quick application. With a unique combination of a VelAid SofTouch hook-and-loop attachment, and adhesive emitter and detector strip, the sensor stays secure even when the site is wet. In addition, Masimo's SofTouch line of sensors are designed to be used whenever skin sensitivity issues are a concern, such as with extremely low birth weight infants. SofTouch sensors incorporate soft foam and VelAid hook and loop attachment

wraps that come in a variety of configurations to address a wide range of clinical uses.

In terms of broad solutions, Masimo Rainbow SET, our second revolution in pulse oximetry, is a breakthrough noninvasive monitoring platform that uses multiple wavelengths of light to measure many blood constituents that previously required invasive procedures. Masimo Rainbow SET is the first and only technology platform capable of continuously and noninvasively measuring carboxyhemoglobin (SpCO) and methemoglobin (SpMet), in addition to oxyhemoglobin (SpO_2), perfusion index (PI), pleth variability index (PVI) and pulse rate. Masimo's newest measurement, SpMet, provides clinicians with the ability to continuously and noninvasively measure methemoglobin levels. Continuous monitoring of SpMet in neonatal patients has become especially important in light of the elevated risks associated with the use of inhaled nitric oxide (iNO) therapy to treat hypoxic respiratory failure in newborns, which has been shown to induce methemoglobinemia. According to the American Academy of Pediatrics, "infants who receive iNO therapy should be monitored according to institutionally derived protocols designed to avoid the potential toxic effects associated with iNO administration. These effects include methemoglobinemia (secondary to excess nitric oxide concentrations), direct pulmonary injury (attributable to excess levels of nitrogen dioxide), and ambient air contamination".[9] Masimo Rainbow SET provides clinicians with the only way to continuously and noninvasively measure methemoglobin levels in the blood (SpMet), making it an appropriate technology to incorporate into neonatal iNO therapies. By allowing clinicians to monitor methemoglobin noninvasively and continuously, they can be sure they are administering the amount of iNO necessary, without harming the patient. And, we continue to focus on advancing neonatal care and hope, in the near future, to provide more breakthroughs for these very important patients.

How effective is oximetry during low perfusion conditions, and what has been done to improve sat readings during low perfusion?

Before the advent of Masimo SET, pulse oximeters could not measure oxygen saturation when the perfusion levels were under 0.2%. But now with Masimo SET accurate monitoring of patients with perfusions down to 0.02% is a reality. Low perfusion is due to poor peripheral circulation, which is very common on patients in the NICU. Poor peripheral circulation or low perfusion results in a very small amplitude signal, which can become so small that it is difficult to distinguish from the background noise. Detecting the actual SpO_2 signal during low perfusion situations is made more difficult during periods of motion. In effect, the motion raises the background noise level thereby making it even more difficult to distinguish the small amplitude SpO_2 signal during low perfusion. Masimo was the first company to receive FDA clearance for the ability to accurately and continuously read SpO_2 values through motion as well as the first company to receive FDA clearance to claim accuracy in measuring SpO_2 during low peripheral perfusion with the Masimo SET pulse oximeter. We accomplished this through advanced patented technology in hardware, software and sensor design. Through the use of specially designed low noise sensors, cables designed to minimize electrical interference, and circuit boards designed to lower noise, Masimo engineers were able to obtain the SpO_2 signal during very weak pulsations. Masimo SET algorithms assist in picking up the pulsations in the midst of background noise caused by motion and other artifacts. The result is a system that is able to accurately monitor arterial oxygen saturation at low perfusion levels 10-fold lower than the conventional pulse oximeters that were on the market. Masimo SET is still the most sensitive pulse oximeter in accurately measuring arterial oxygen saturation. In fact, Masimo SET is more sensitive than an arterial line in reporting pulse rate in the presence of low perfusion.[10] Today, Masimo continues to be the leader in Read-Through Motion and Low Perfusion technology, documented in more than 10 low perfusion studies specifically on neonates.

How has oximetry proven to be cost effective and/or reduced overall costs?

In a hospital setting, a clinician's ability to use Masimo SET pulse oximetry to help reduce ROP and detect newborns with CHD could save millions of dollars, yet to the patient and their family, the impact that Masimo SET can have on their lives is priceless. Fortunately for hospital administrators, Masimo SET has also been shown to reduce costs. In real-world scenarios, a 250-bed hospital can save up to $300K by using Masimo SET pulse oximetry. These savings are largely attributed to the superior technology and equipment design that is unique to Masimo SET.

- Masimo's performance, with the ability to provide accurate measurements with the first sensor applied, as well as Masimo's unique sensor durability and longevity features lead to direct sensor savings. Multiple studies show a two-fold increase in the useful life of Masimo sensors over other sensors in the NICU.[11,12,13]

- Increased accuracy and reliability means direct medical care savings are realized. By decreasing erroneous oxygen saturation and pulse rate values, Masimo SET reduces the need for investigating the cause of false alarms through additional arterial blood gas testing. Improved accuracy allows for faster weaning of oxygen and ventilator settings with associated cost savings.[14]

- Increased productivity and reduced medical errors lead to indirect medical care savings. Fewer false alarms mean less "staff time" is required to investigate and treat false desaturations so clinicians can focus on caring for patients, not equipment.[15]

What types of training and user support programs do you have in place?

To support best-in-class installations and service, we provide one of the largest teams of pulse oximetry clinical specialists available. Nearly 50 Masimo Clinical Specialists are on staff to support the needs of our customers, including comprehensive "super users" training, flexible shift scheduling and more. In addition, Masimo was one of the first patient monitoring companies to invest in e-learning with Masimo U. Clinicians can sign-up online to get the training they need in a user-friendly, self-paced program. This breadth of customer support provides unparalleled installation processes and resources. In addition, Masimo's Technical Support Team is available 24/7 to answer questions and help resolve clinical issues related to your pulse oximetry equipment and Masimo U is also available to provide 24/7 online instructional and application support. As an added benefit, some Masimo U courses are even accredited for continuing education units.

What hampers the effective use of oximetry?

Perhaps the greatest deterrent to effective use of pulse oximetry is that historical limitations have become current expectations. Many clinicians, who remain unfamiliar with the ability of Masimo SET pulse oximeters to solve the previously "unsolvable" problems of pulse oximetry, believe that accurate Read-Through Motion and Low Perfusion SpO_2 readings are still elusive. As a result, they work with what they have and go through heroic efforts to get a pulse oximetry measurement that can, hopefully, aid them in the care of their patients. With Masimo Rainbow SET, clinicians can finally enjoy the usefulness of pulse oximetry under difficult monitoring conditions, such as patients experiencing shivering, tremors, hypothermia, shock, or in the presence of dyshemoglobins such as methemoglobin. However, like any instrument, proper use provides the best results. Sensor choice and application can dramatically improve the performance of Masimo SET pulse oximetry. Masimo customers can choose between sensors made for patients with fragile skin, patients with CHD, Newborns, or patients requiring methemoglobin monitoring. Additionally, ensuring sensors are properly placed and aligned is crucial to obtaining accurate readings and reducing false alarms. To help identify sensor problems, Masimo developed Signal IQ. When the signal from the sensor is extremely weak or contains excessive artifact and the confidence parameters are violated, the "low Signal IQ" light will flash. This is a cue for the clinician to check the sensor site as part of the evaluation of the patient.

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SPOTLIGHT ON OXIMETRY

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The Changing Epidemiology of Neonatal Sepsis and Meningitis: A Twenty-Eight-Year Experience in a Neonatal Unit

Daniel Hervás, MD; Carmen Masip, MD; Pere Ballíu, MD; Sebastian Albertí, PhD; Juan A. Hervás, MD, PhD

Abstract

Objective: To study the epidemiology of sepsis and/or meningitis in the neonates admitted to a tertiary care neonatal unit during a 28-year period.

Methods: Retrospective review of inborn neonates with culture-proved sepsis and/or meningitis admitted to Son Dureta University Hospital (Mallorca, Spain). Comparison of two birth cohorts (1977-1991 vs 1992-2004) was performed.

Results: There were 809 cases of culture-proved sepsis and/or meningitis. Overall incidence increased from 4.9/1000 live births in the first cohort to 11.3/1000 in the second ($P < 0.0001$), and meningitis rates decreased from 0.65/1000 to 0.56/1000 ($P < 0.6$). In the 1992-2004 period, early-onset infections (EOI) decreased (from 3.2/1000 to 2/1000, $P < 0.001$) and late-onset infections (LOI) increased (from 1.8/1000 to 9.3/1000, $P < 0.0001$); LOI in very low birth weight (VLBW) infants in this period was extremely high (427/1000). Overall case-fatality rate increased from 0.4/1000 to 0.9/1000 ($P < 0.001$), with a significant increase in LOI mortality (from 0.1/1000 to 0.8/1000, $P < 0.001$). In the period 1985-1991, Group B streptococcus (GBS) and S. epidermidis emerged as the most frequent cause of EOI and LOI, respectively. From 1992 to 2004, GBS and non-GBS organisms decreased in EOI, and E. coli was predominant. In LOI, S. epidermidis was predominant most of the time, although Enterobacter and Candida infections notably increased.

Conclusions: Long term historic reviews of neonatal sepsis are useful to analyze epidemiological trends and the factors most probably involved in the changes of microorganisms.

Background

During the last two decades there has been an ongoing interest on the incidence, microbiology and mortality of neonatal sepsis which has resulted in epidemiologic studies mainly from the USA and Europe,[1-11] and less frequently from other parts of the world.[12,13] Although few retrospective studies covering more than 20 years have been reported,[1,2,11] they are of great interest to determine the trends of incidence and outcome of neonatal sepsis, and the changes over time in the predominant microorganisms. The lack of studies covering a long period before and after the implementation of GBS prophylaxis makes it difficult to assess the real impact that this prophylaxis has had on the incidence and microbiology of neonatal infections.

In a previous study we reviewed the neonatal infections in the Island of Mallorca (Spain) during the period 1977-1991.[8] Now, a historic review of the epidemiology of neonatal sepsis and meningitis during the last 28 years (1977-2004) is being presented. An overall retrospective evaluation of the whole period and a cohort comparison of the periods before and after the institution of intrapartum antibiotics for prevention of vertical transmission of GBS infection were performed to analyze variations of neonatal infections.

Patients and Methods

Study population: Hospital records were reviewed for all newborns admitted with the diagnosis of sepsis and/or meningitis to the Department of Neonatology (neonatal intermediary care unit and NICU) of Son Dureta University Hospital, the only tertiary care center in the Balearic Islands (Spain), from January 1977 to December 2004. For comparison with a previous study[8] two birth cohorts were considered, one from 1977 to 1991 and the

Table 1. Infection and mortality rates for 809 inborn neonates with sepsis and meningitis (1977-1991 vs. 1992-2004).

	In patients of indicated birth weight					
	≤ 1500 g			> 1500 g		
	A	B	*P* value	A	B	*P* value
No. of births	364	754		67122	41392	
No. of admissions	364	754		5922	8349	
No. of EOI	25	8		192	76	
No. of LOI	45	322		72	69	
No. of EOI deaths	1	4		16	1	
No. of LOI deaths	3	31		5	4	
EOI rate†	68.6	10.6	< .0001	2.8	1.8	< .01
LOI rate†	123.6	427	< .0001	1.07	1.6	< .01
EOI mortality rate†	2.7	5.3	= .5	0.2	0.02	< .01
LOI mortality rate†	8.2	41.1	< .01	0.07	0.09	= .6

A= 1977-1991; B=1992-2004; EOI= Early-onset infection (0-5 days); LOI= Late-onset infection (≥ 6 days); † per 1000 live births.

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Table 2. Microbiology of neonatal sepsis and/or meningitis (1977-2004).

	No. of cases in which organism was isolated				
	1977-1991*		1992-2004*		Total
Organism isolated in culture	0-5 days†	≥ 6 days†	0-5 days†	≥ 6 days†	
Gram-positive aerobic bacteria					
Coagulase-negative staph.	20	32	3	119	174
Staphylococcus aureus	15	10	3	6	34
Group B *streptococci*	38	2	39	10	89
Group D *streptococci*	15	9	1	30	55
Viridans streptococci	15	5	2	1	23
Listeria monocytogenes	4	2	2	0	8
Other	9	5	1	2	17
Gram-negative aerobic bacteria					
Klebsiella species	34	17	2	34	87
Escherichia coli	26	7	20	32	85
Pseudomonas aeruginosa	8	11	0	20	39
Enterobacter species	12	6	3	65	86
Serratia marcescens	8	0	0	7	15
Other	10	7	7	14	38
Gram-negative anaerobic bacteria					
Bacteroides fragilis	0	1	0	0	1
Other	3	1	0	2	6
Fungi					
Candida	0	2	1	49	52
Total	217	117	84	391	809

*Years of study
†Age at onset of sepsis and/or meningitis

other from 1992 to 2004. In 1992 a written protocol of intrapartum antibiotics for prevention of GBS infection was implemented in our hospital. Only invasive infections occurred in infants born at our hospital were taken into account for this work. The rate of infection was calculated as the number of cases per 1000 live births or the number of infections per 100 admissions to the neonatal unit, as appropriate for comparisons between the two cohorts and other reports.

Microbiologic methods and definitions: Blood cultures were drawn by venipuncture and inoculated into two culture bottles containing aerobic and anaerobic media. Blood and cerebrospinal fluid (CSF) specimens were analyzed by standard methods, and the isolated microorganisms were identified by current techniques. Criteria for diagnosis of sepsis were a single positive blood culture in an infant with clinical signs of infection, and the definition of sepsis due to commensal species established by the Centers for Disease Control and Prevention (CDC, Atlanta).[14] Meningitis was defined by the recovery of a microorganism in the CSF regardless of the result of the cytochemistry of the fluid. Cases were classified by the infant's age when the blood was drawn (or the CSF was cultured) as

Table 3. Relationship between age at onset of sepsis and meningitis, birth weight, and the rates of infection for the most frequently isolated bacteria (1977-2004).

	Patients of indicated birth weight*		
	≤ 1500 g	1501-2500 g	> 2500 g
No. of births	1118	5804	102710
Early-onset infection rate†			
Group B *Streptococcus*	1.7	1.2 (0.3)	0.6 (0.02)
E. coli	5.3	2.5 (0.2)	0.2 (0.01)
Klebsiella species	3.5	2.4 (0.3)	0.2
Late-onset infection rate†			
S. epidermidis	91.2 (5.3)	3.7 (0.2)	0.06 (0.01)
Enterobacter spp	50.9 (4.4)	1.3 (0.2)	0.05
Klebsiella spp	30.4 (1.7)	1.2	0.09
Candida spp	39.3 (8.9)	0.5	0.03 (0.01)
E. coli	25 (4.4)	1	0.05

† per 1000 live births.
* Mortality rate per 1000 live births is shown in parentheses

Table 4. Infection rates (per 1000 live births) of the most prevalent microorganisms in different periods according to the time at onset of infection.

Time at onset/ microorganism	1977-1984	1985-1991	1992-1998	1999-2004
Early-onset infections				
K. pneumoniae	0.8	0.1***	0.04 NS	0.1 NS
E. coli	0.4	0.5 NS	0.4 NS	0.6 NS
S. agalactiae	0.1	1.1****	1.4 NS	0.3***
Late-onset infections				
K. pneumoniae	0.3	0.1 NS	0.4 NS	1.6***
Enterobacter	0.1	0.1 NS	1****	2.6***
E. coli	0.1	0.1 NS	0.4*	1.3**
S. epidermidis	0.1	0.8****	0.9 NS	4.4****
Candida	0.02	0.03 NS	0.4***	2.2****

**** $P < .0001$ for the comparison with the earlier period; *** $P < .001$; ** $P < .01$; * $P < .05$; NS $P \geq .05$

early onset infection (birth to 5 days of age) and late onset infection (≥ 6 days after birth). Death was considered related to infection if it occurred within the time of antimicrobial therapy after the positive culture, and there was no other more probable cause of death due to any underlying disease.

Statistical methods: Statistical analysis was performed with a computerized program (StatView II, Abacus Concepts, Berkeley, CA). The χ^2 test was used for comparison between proportions, and the two-tailed t-test for comparison between age at onset of infection and birth weight. Significance was set at 95% for all analyses.

Results

Descriptive epidemiology: During the 28-year period retrospectively studied, 809 neonates born at our hospital had septicemia and/or meningitis. Figure 1 shows some characteristics of the population studied. The 301 cases of early onset infections occurred at an average age of 1.8 days (range, 1-5 days); and the 508 cases of late onset infections occurred at an average age of 23.5 days (range, 6-60 days). Overall, for 12 patients only cultures of CSF were positive; for 56, cultures of both blood and CSF were positive; and for 741, only cultures of blood were positive.

The rate of very low birth weight (VLBW) infants (< 1500 g of weight) increased from 5.4/1000 live births in the period 1977-1991 to 17.9/1000 in the period 1992-2004 ($P < 0.001$).

Table 1 shows the relationship between birth weight and age at onset of infection for the 809 inborn neonates with sepsis and/or meningitis. Patients of VLBW had a significantly higher rate of early and late-onset infections than did patients whose birth weights were > 1500 g ($P < .0001$).

Microbiology: The microorganisms responsible for sepsis and/or meningitis in neonates in relation to age at the onset of infection between 1977 and 1991 and between 1992 and 2004 are shown in table 2. Overall, Gram-positive bacteria accounted for 49.4% of the cases whereas Gram-negative accounted for 43.3%. Anaerobic bacteria and Candida species accounted for 0.9 and 6.4%, respectively.

In the 301 cases of early onset infection, the most frequent isolates were GBS (25.6%), E. coli (15.3%), and Klebsiella spp (12%). The 508 late onset infections were caused mainly by S. epidermidis (25.8%), Enterobacter spp (14%), Klebsiella spp (10%), and Candida spp (10%).

The rates of infection of the most prevalent microorganisms

causing invasive neonatal infection in relation to the birth weight and age at onset of infection is shown in table 3. S. epidermidis, Enterobacter, Klebsiella, E. coli and Candida infections were significantly more frequent in late-onset infections of VLBW infants (P < .0001). Although 88.3% of the GBS infections occurred in infants weighing more than 2500 g, the rates of GBS infection per 1000 live births in the weights groups studied were not statistically different.

Overall, 59% of the cases of meningitis were caused by Gram-positive bacteria, 40% by Gram-negative and 1% by fungi. GBS was the most frequent cause of meningitis (40%), followed by E. coli (14%), K. pneumoniae (10%), and Listeria (8%).

Incidence: From 1977 to 2004 the overall incidence of sepsis/meningitis for inborn neonates was 7.4 cases per 1000 live births; the rates for early and late-onset infections were 2.7/1000 live births and 4.6/1000 live births, respectively. The overall incidence of meningitis (1977-2004) was 0.6 cases per 1000 live births.

Epidemiologic trends: Figure 2 shows the attack rates of neonatal sepsis and meningitis (total, early onset and late onset) from 1977 to 2004. Although the percentage of overall infection in relation to the number of neonatal admissions was similar in the two periods of study (5.3% and 5.2%, respectively), significant changes in the rates of infection was observed. The rates for total, early and late onset infections during the period 1977 through 1991 were 4.9, 3.2 and 1.8 cases per 1000 live births, respectively. From 1992 to 2004 the total incidence of infection increased to 11.3/1000 (P < .0001); the early onset rate decreased to 2/1000 (P < .001), and the late onset rate increased to 9.3/1000 (P < .0001). As seen in table 1, the greatest variations in infection rates occurred in VLBW infants. The increase in the rate of late onset infection started in 1992 and paralleled a sustained high occupancy rate in our neonatal unit (average 95% in the period 1992-2004).

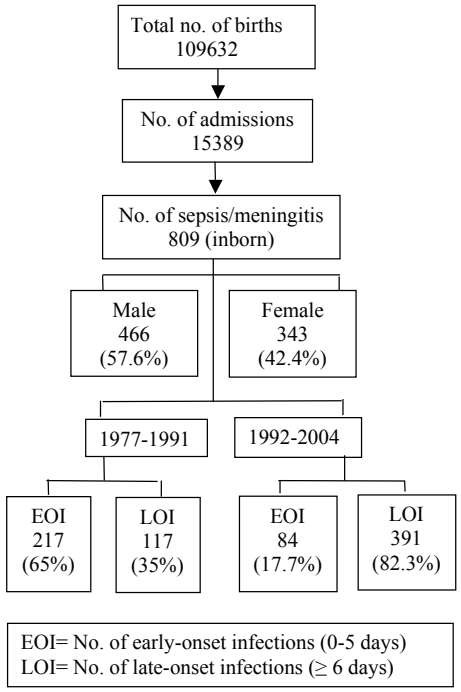

Figure 1. Characteristics of the study population.

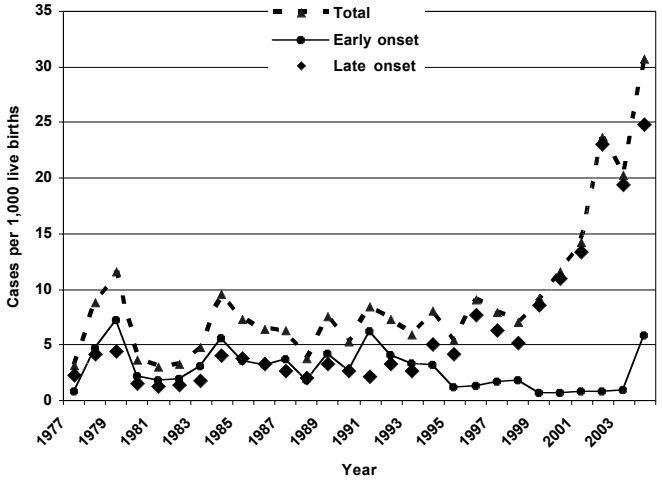

Figure 2. Rates of neonatal sepsis and/or meningitis during 1977 through 2004 for inborn infants. Total rate, early onset and late onset.

Overall, meningitis rate decreased from 0.65/1000 in the period 1977-1991 to 0.56 in the period 1992-2004 (P < .6). Meningitis occurred in 10.5% (34/324) of newborns with bacteremia in the first period and 4.6% (22/473) in the second (P < .01).

The trends in the incidence rates of infection for the most frequent microorganisms causing early and late onset neonatal infection during shorter periods of time within the two main periods of the study are shown in table 4.

The overall infection rates by Gram-negative bacteria in the periods 1977-1991 and 1992-2004 (45.2% and 43.4%, respectively) were not significantly different (P > .5).

Mortality: Tables 1 and 3 show the mortality rates in relation to birth weight, age, and microorganism recovered during the period 1977-2004. Overall mortality rate was significantly higher in the period 1992-2004 than in the period 1977-1991 (0.9/1000 vs. 0.4/1000, P< 0.001). Early onset mortality rate decreased from 0.25/1000 in the first period to 0.1/1000 in the second (P < 0.2). In the same periods, late onset mortality significantly increased from 0.1/1000 to 0.8/1000 (P < 0.001).

Mortality rate was significantly higher among VLBW infants. There was a significant association between the increase in the rate of VLBW infants born at our hospital in the second birth cohort and the increase in the overall neonatal mortality rate (P < 0.001).

The organisms most frequently associated with a fatal outcome in the period 1977-1991 were E. coli (16%), GBS (13%), and Pseudomonas aeruginosa (13%). Of all cases with fatal outcome occurred during this period, 14 (56%) were attributable to gram-positive organisms and 11 (44%) to gram-negative organisms. On the contrary, during the period 1992 through 2004 the organisms most frequently associated with mortality were Candida (27.5%), E. coli (17.5%), and Enterobacter (15%). During the latter period, 18 cases of death (45%) were attributable to gram-negative organisms, 11 (27.5%) to gram-positive organisms and 11 (27.5%) to fungi.

Discussion

During the last thirteen years the overall incidence of neonatal sepsis increased in our neonatal unit up to 11.3 cases per 1000

live births, a rate that is higher than the 1 to 10 cases per 1000 live births reported in the developed countries.[15] The real incidence of sepsis was probably higher, owing to possible false-negative results, a common problem in culturing small blood samples.[9]

As seen in other reports,[2,16,17] during the last decade we have observed a decline of early onset neonatal infections, and an increase in late onset infections. Late onset infections occurred mainly in VLBW infants at a rate (42.7%) higher than that reported in the USA[18,19] (21%) and also in a recent Spanish Collaborative Study (15.6%).[20]

As reported by others,[21] meningitis rates remained relatively stable during the whole period of study, and the decrease observed during the second period was not statistically significant. In recent years, there have been very few papers describing the incidence and microbiology of neonatal meningitis, most probably because so many premature infants are treated with antibiotics long before a lumbar puncture is performed. Stoll et al.[22] consider that meningitis rates may be underdiagnosed in VLBW infants because of the failure to routinely perform LPs in these prematures with suspected sepsis. The reduction in the frequency of meningitis in our neonates with bacteremia during the second period of the study might be the result of a less number of LPs performed. Unfortunately, we do not know the proportion of LPs in infants who underwent a blood culture during the two periods of the study.

In spite of our high rate of neonatal sepsis, the overall case-fatality rate associated with sepsis in our unit during the 28 years of study (8%) has remained lower than the figures reported from other European countries (9-33%),[3,4,9,11] but similar to that of the Spanish Collaborative Study.[20,23] Overall mortality was significantly higher during the second period, and as expected there was a significantly higher mortality rate among VLBW infants.

As shown in a previous study,[8] the microbial pathogens causing early and late onset infections started to change in our hospital in 1985. From 1977 to 1984, K. pneumoniae was the most frequent cause of neonatal sepsis and meningitis, but this frequency decreased in the following years. Remarkably, GBS and S. epidermidis, replaced K. pneumoniae as the predominant pathogens in early and late onset infections, respectively, until 1991. In the period 1992 through 2004 there were new changes in the microbiology of neonatal infections. Since the institution of GBS prophylaxis in our hospital in 1992, early onset GBS disease dropped from 2.4 cases per 1000 live births in 1991 to 0.3/1000 in 2004, and E. coli became the most frequent cause of early onset infection. As regard to late onset infections, Enterobacter became the most frequent pathogen from 1992 through 1998, causing outbreaks by multiresistant strains in our unit.[24] From 1998 to 2004, S. epidermidis has again been the most frequent organism but infections caused by some Gram-negative bacteria (especially Enterobacter and Klebsiella) and fungi (Candida) have notably increased. However, we have not observed a statistically significant increase in the incidence of bacteremia caused by Gram-negative rods as it has been reported by others.[25]

In the majority of cases it is difficult to determine the causes for the emergence and decline of neonatal infections. The decrease of early onset infections during the second period of the study has been most probably related to the institution of GBS prophylaxis. The reasons for the emergence of GBS are unknown, but GBS prophylaxis has clearly caused the decline of this serious neonatal infection.[26] Controversy on the possible increase of non-GBS early onset sepsis with intrapartum antibiotics has been raised, with some reports finding such an increase,[27,28] others finding a decrease,[29] and others finding no effect.[17,30] In our study, during the 1992-2004 period, the decrease of early onset infections equally affected to those caused by GBS and non-GBS organisms.

There are many factors that favor the development of nosocomial infections in neonates.[15] Specific potential causes for sepsis like line catheter days and others have not been analyzed here, but we have observed the following risk factors for infection since the early 1990s: 1) Fertility techniques and other factors have increased the rate of VLBW infants in our population (from 0.5% to 1.8% of the live births), and this increase paralleled the increase in neonatal mortality rate. 2) An important overcrowding of the NICU with an extremely high occupancy rate (average, 95%) occurred during the second period of the study. 3) An overuse of empirical antibiotics, especially third generation cephalosporins, as reported from our unit during the period 1992-1998.[24] All these factors may be involved in the remarkable increase in the rate of late onset sepsis, and are currently being considered in our antibiotic policy and also for planning a new neonatal unit.

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Calcified Fibroids Mimicking Fetal Demise in Pregnancy

Maggie Tetrokalashvili, MD, FACOG; Boris Petrikovsky, MD; Lennox Bryson, MD, FACOG

Introduction

Leiomyomas (fibroids) are common benign smooth muscle uterine tumors, occurring in approximately 20-25% of reproductive age women. The prevalence of uterine leiomyomas among pregnant women ranges from 0.1 to 3.9%.[1] Their sonographic appearance varies widely.[2]

We describe case series of uterine fibroids in pregnancy mimicking fetal demise. These case reports highlight possible limitation of ultrasound in the diagnosis of fibroids in pregnancy.

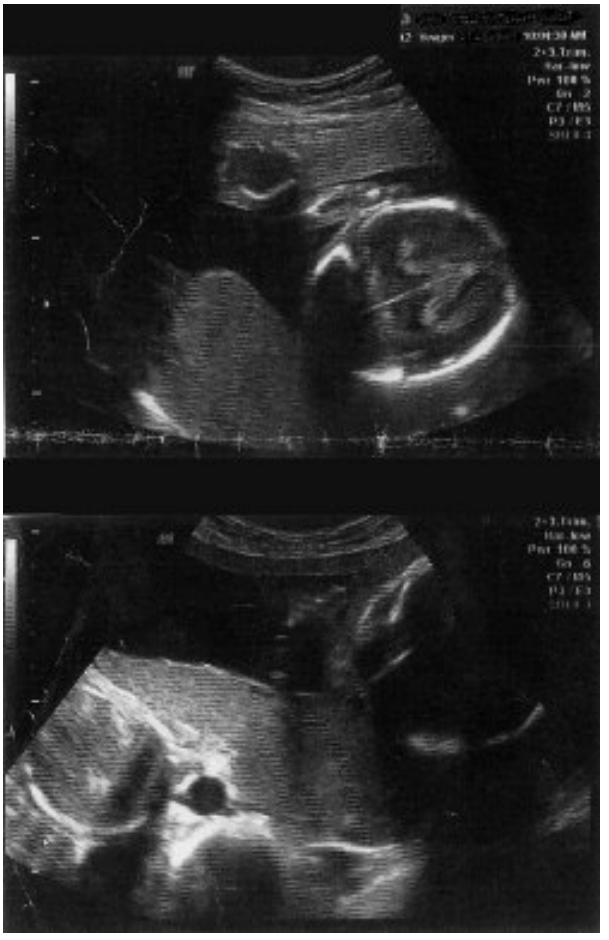
Case 1

27 year old Gravida 2 Para 1 at 27 weeks of pregnancy was sent to fetal testing unit for further management of the triplet gestation with the demise of two fetuses. The provisional diagnosis was made according to the ultrasound films from the referring physician's office (Fig 1A and Fig 1B).

Upon repeating the ultrasound examination at our unit we diagnosed the patient with a viable singleton pregnancy at 27 weeks gestation with two oval-shaped calcified fibroids, the largest measuring 6.8 by 11.4 cm and the smallest measuring 3.2 by 4.8 cm. Patient underwent normal spontaneous vaginal delivery at term without complications.

Case 2

40 year old Gravida 5 Para 2 was referred to the labor and delivery unit for further management of fetal demise at 19 weeks gestation. Diagnosis was made by the ultrasound examination in the referring physician's office. The ultrasound study, repeated in the department of radiology, reported following findings: "single fetus seen, no cardiac activity noted, no amniotic fluid seen, measurements of biparietal diameter correspond to 19 weeks gestation, appearance consistent with intrauterine fetal demise."



Figures 1A and 1B

Attempts to retrieve fetal parts were unsuccessful after prostaglandin E2 induction, laminaria insertion, and dilatation and evacuation under ultrasound guidance. Decision was made to proceed with laparotomy and hysterotomy. During hysterotomy no fetus was identified. Seven submucosal and intramural fibroids ranging from 1.3x1.2x0.9 to 9.0x7.5.x7.0 cm were removed with hemostasis achieved. Pathologic examination confirmed uterine leiomymas with infarction (Fig 2).

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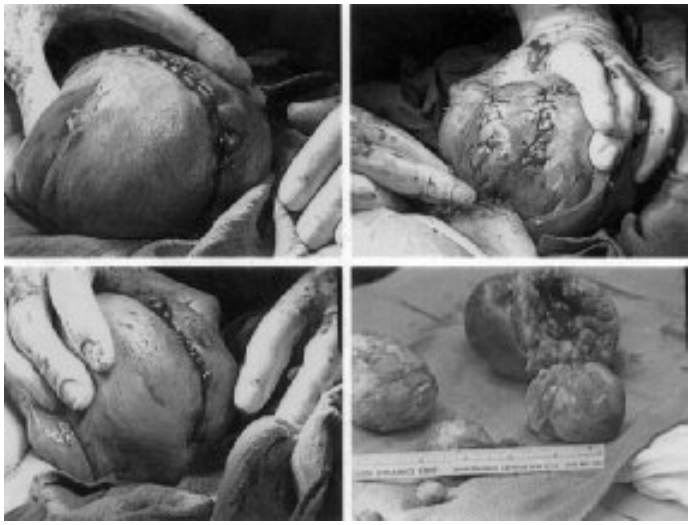

Figure 2

Comment

Uterine leiomyomata are the commonest benign uterine tumors. They can be located within the uterine wall, or cavity, or even completely separate from the uterus.[3] The typical ultrasonographic appearance of the fibroid is homogenous, hypoechoic area within the uterine wall causing deformity in contour. However occasionally, in cases of degeneration or calcification, differential diagnosis may include uterine malignancy, gestational trophoblastic disease, ovarian tumors and even fetal head or fetal parts.[4,5]

The diagnosis of leiomyomata is best made in the non-pregnant state, because, as pregnancy progresses, the fibroids may become inaccessible as they become soft, flatten out and become indistinct due to interstitial edema and they are often confused with fetal parts.[6]

In 98% of patients, fibroids are multiple. This is a first report when multiple fibroids were mimicking in utero demise of two fetuses.

Conclusion

In spite of recent developments in ultrasound expertise and equipment, accurate diagnosis is sometimes difficult. In pregnancy, unusual appearance of uterine fibroids can lend to erroneous diagnosis.

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Medicine Is War and Other Medical Metaphors

Paul Hodgkin

When I worked in a paediatric casualty department children were forever being told that after being stitched, x-rayed, or covered in plaster, they would be "bionic." The desire to be more machine-like is apparently widespread—inevitably perhaps, in an age when technology is both idolised and feared. Medicine is strewn with mechanistic language and concepts, and the metaphor "the body is a machine" suffused much of the language of pathology and physiology. I write here about some of the linguistic forms that underline the way we talk about medicine and the way that they limit as well as advance our thinking.

Examining the metaphors behind language is worthwhile because it clarifies our assumptions. Seeing the body as a machine, for example, has been useful—the heart, after all, is much like a pump and treating it as one has provided many insights. The success of the mechanistic approach, however, has meant that we have often imbued the body with other machine-like attributes. All too easily patients become—like machines—identical, passive and "fixable." Medicine, as has often been pointed out, has become dominated by a mechanistic hubris, which sees machines and engineered solutions to ill health as the favourite way forward.

All this, of course, begs the question of the relation between the language we use and the things it describes. Some have felt that any language may actually prevent its native speakers from perceiving the world in ways that are quite "normal" in other tongues.[1] According to this view, language more or less determines reality. A world and language evolve together, both influencing each other. The particular vocabulary and syntax of any given language "do not make it impossible to express certain things, they merely make it more difficult to express them."[2]

The vocabulary of medicine is certainly one example of the way linguistic forms affect our perception of the world. As Dixon has pointed out, we have 20 rubrics for different types of respiratory infection, but only one word for poverty.[3] Differentiating respiratory syncytial virus from mycoplasma thus becomes possible, but we still have only general terms with which to express, say, overcrowding. Our language thus drives important factors to the margins of consciousness.

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Most common themes

Much medical language is built around a few metaphors. Phrases such as "he sank into a coma," "You're in tip-top condition," and "falling ill" are constructed around the idea that health is up and illness is down. (This particular example is taken from an excellent book by Lackoff and Johnson,[4] which describes in detail the importance of metaphors in organizing our thoughts and language.)

That health is up is hardly surprising. We are after all up and about when well and horizontal when dead or ill. A meatier medical metaphor is "medicine is war." The language that we use about our role as doctors is cast almost entirely by this metaphor and military images also appear in every aspect of medical language and jargon

It's an *overwhelming* infection; she's got an *infiltrating* carcinoma; the body's *defenses*; he's having a heart *attack*; *killer* T-cells; we must treat him *aggressively* and use everything in therapeutic *armamentarium*; we've *wiped out* smallpox; go to *casualty* and the house *officer* will deal with you;

A common variant of this is the medicine is a "detective story" metaphor, in which the disease is the villain and making the diagnosis approximates making the arrest:

This *sinister* disease requires a rigorous history to be taken plus *searching examination* together with a high index of *suspicion* in order to spot *the telltale clues* and make the correct diagnosis.

The "medicine is war" metaphor also has more serious implications as it emphasizes that taking action is a virtue, patients are passive, the main protagonists in this drama are doctors and diseases (patients are not the "real" focus), technologies are weapons (and thus, implicitly, the more the better), and we doctors know best as we are the ones in control. These attitudes clearly have some advantages—for example, it is easier for doctors to bear the failures of medicine if the "real" enemy is construed to be the disease. For many specialties,

however, including geriatrics, psychiatry, and general practice, using the "medicine is war" metaphor can be counterproductive. In addition, the doctor's self image of battling against disease may not be in the patient's best interest. The cost of our inappropriately aggressive attitude to fighting disease has often been borne by our patients as they have suffered, among other things, tonsillectomy, hospital delivery, and the overprescription of psychotropic drugs.

Roles of doctors, patients, and disease

The concept that patients are in part just the "clinical material" with which doctors fight the great battle against disease takes subtle forms. The word cohort, for example, was originally part of a Roman battalion—a set of identical and ultimately expendable soldiers to be used to the most useful advantage in winning the battle.

Fighting wars is usually an unpleasant, boring, and masculine activity. The "medicine is war" metaphor perhaps encourages the virtues required to survive the long hours and intense hierarchies of hospital life. Unfortunately, it also discriminates against feeling and reflection and makes it harder to strike the right balance between work and personal life.

Another curious twist of medical language is the way that we habitually talk about diseases as if they were objects rather than processes, saying, for example, "He's got mumps" and not "He's mumping." Cassells pointed out how widely both patients and doctors view disease as an "it," with an independent existence.[5] After all, this is the main way in which we have classified and studied illness. But to see disease as an object and not a process is to emphasise that one can indeed "get rid" of "it," that its arrival was probably unbidden and that cure is equivalent to physical removal. As patients we can draw tight comfortable lines around the disease and say that the rest is normal. For doctors the disease, rather than the context in which it occurs or its meaning for the patient, becomes the most important level of study. The corollary of the "diseases are objects" metaphor is that patients are naturally seen as containers for those objects: He's *full of* cancer; we've just got to *get in there* and control the bleeding; I'm taking so many pills I'm beginning to rattle; we must *get to the bottom* of the problem. Again this is widespread and useful because in many ways we are containers that we can physically put tablets into and take gall bladders out of. To the extent that patients are seen as mere vessels for disease, however, they will also be assumed to be passive and less important than the disease itself.

Medicine and emotions

There is one last, intriguing aspect of language that is relevant to medicine, which is the way in which we talk about emotions. Many of the phrases we use to talk about feelings depend on two assumptions: emotions are fluids and intensity is temperature. He was *swamped* with feeling; she was *bubbling over* with joy; I nearly *exploded* with rage; they were *boiling over* with excitement; they've *channelled* their feelings into other things; he's emotionally *volatile*. The language of feeling implies an extensive network of subterranean piping. The purpose of this subconscious plumbing is to prevent the unseemly spilling of emotions into the open, and indeed many of the phrases we use imply plumbing failures of one kind or another. If we do, heaven forbid, actually begin to feel something all kinds of ills apparently lie in wait. The emotional fluids may even vaporize under the heat of our feelings and end up *clouding* our judgment. Within medicine, at least, emotions and feelings are actually thought of as dangerous and contaminating fluids.

The traditional way of dealing with this problem is by trying to keep the emotional temperature as low as possible. Exactly how this is to be achieved is rarely explained but it is certainly the method implicitly recommended in most teaching on medical and surgical wards. Apparently the mature doctor should be able to control the emotional temperature of even the most tragic situations so that at least his or her feelings remain nicely controllable as frigid blocks of ice. Such assumptions, of course, do little to help patients—or for that matter, doctors.

Problems arise not because these ways of thinking are not valid—at times all these metaphors are useful—but because their pervasiveness excludes other equally true ways of seeing health and illness. The metaphors underlying our language create a subtle pressure that is perhaps part of the reason that we find it so difficult to think of people as wholes, as having a reality much greater than the sum of their organs, diseases, or economic value. Having such a restricted choice of language, we are all too often forced, inadvertently, into useless, harmful, or insensitive ways of thinking.

Alternative metaphors

It is, of course, possible to try to create new metaphors with which to weave a richer understanding of both illness and disease but this is not easy. The old metaphors are hard to dislodge, while new ones inevitably seem precocious.

Still, it is interesting to see what other metaphors might be available and the kinds of thinking they imply. An alternative to "medicine is war," for example, might be "medicine is a collaborative exploration." This recognises that what we are engaged on is exploratory—by its nature it is intrinsically uncertain. Although some people may have more expertise in particular aspects of medicine than others, neither doctors nor patients have a direct line to the truth. It also implies that medicine is cooperative and many people are involved: patients, their family, health workers, and researchers. Success depends on working together. Neither success nor failure is the sole responsibility of any one person; in other words, it is not the surgeon alone who "cured" the patient, but just as importantly the patient's own ability to heal himself together with the other members of staff, family, and so on. Embedded in the metaphor too, is "labor," reminding us that medicine depends on hard work by both patient and doctor.

Our bodies often replace almost all of their physical constituents. Metaphors such as "the body is an enduring pattern" or" the body is a biochemical dance" might profitably supplement the currently overwhelming view of bodies as machines.[6] These metaphors are just as true as a mechanistic way of looking at physiology but would emphasise, for example, the processes of keeping healthy and the importance of nutrition. They assert our vitality and the shimmering complexity of living processes rather than the predictability of the machine.

There are many other subjects that might yield additional new metaphors and insights. We could, for example, reacquaint ourselves with the word "healing" and all the many meanings

Continued on page 35…

A Systematic Review of Cooling for Neuroprotection in Neonates with Hypoxic Ischemic Encephalopathy – Are We There Yet?

Sven M. Schulzke, Shripada Rao, Sanjay K. Patole

Abstract

Background: The objective of this study was to systematically review randomized trials assessing therapeutic hypothermia as a treatment for term neonates with hypoxic ischemic encephalopathy. Methods: The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL databases, reference lists of identified studies, and proceedings of the Pediatric Academic Societies were searched in July 2006. Randomized trials assessing the effect of therapeutic hypothermia by either selective head cooling or whole body cooling in term neonates were eligible for inclusion in the meta-analysis. The primary outcome was death or neurodevelopmental disability at ≥18 months.

Results: Five trials involving 552 neonates were included in the analysis. Cooling techniques and the definition and severity of neurodevelopmental disability differed between studies. Overall, there is evidence of a significant effect of therapeutic hypothermia on the primary composite outcome of death or disability (RR: 0.78, 95% CI: 0.66, 0.92, NNT: 8, 95% CI: 5, 20) as well as on the single outcomes of mortality (RR: 0.75, 95% CI: 0.59, 0.96) and neurodevelopmental disability at 18 to 22 months (RR: 0.72, 95% CI: 0.53, 0.98). Adverse effects include benign sinus bradycardia (RR: 7.42, 95% CI: 2.52, 21.87) and thrombocytopenia (RR: 1.47, 95% CI: 1.07, 2.03, NNH: 8) without deleterious consequences.

Conclusions: In general, therapeutic hypothermia seems to have a beneficial effect on the outcome of term neonates with moderate to severe hypoxic ischemic encephalopathy. Despite the methodological differences between trials, wide confidence intervals, and the lack of follow-up data beyond the second year of life, the consistency of the results is encouraging. Further research is necessary to minimize the uncertainty regarding efficacy and safety of any specific technique of cooling for any specific population.

The authors are with the Department of Neonatal Paediatrics, Women's and Children's Health Service; Schulzke and Patole are also with the University of Western Australia, Perth. The authors wish to thank Prof Douglas Altman for advice on composite outcomes. Reprinted from BMC Pediatrics, BioMed Central,

Background

Hypoxic ischemic encephalopathy (HIE) following perinatal asphyxia contributes significantly to neonatal mortality and morbidity including long-term neurodevelopmental sequelae in up to 25%-60% of survivors.[1-3] Despite significant research there is still no proven intervention for neuroprotection in HIE.[4] The literature on therapeutic hypothermia as a treatment for "white asphyxia" dates as far back as early 60s.[5,6] Experimental studies have shown that mild to moderate hypothermia (33-34°C), applied within the first hours of an acute hypoxic event, is neuroprotective.[7-9] A Cochrane review incorporating two small randomized controlled trials (RCT) has reported no evidence of benefit or harm related to therapeutic hypothermia in term neonates (N=50) with HIE.[4] Three large RCTs have been published since the last substantive amendment of this systematic review in July 2003.[10-12] Given the significance of the condition, and the encouraging results of the recent RCTs, an up to date systematic review was conducted to evaluate the efficacy and safety of therapeutic hypothermia in term neonates with HIE.[13,14]

Methods

RCTs comparing therapeutic hypothermia, by either selective head cooling or whole body cooling, with normothermia in term neonates with perinatal asphyxia and HIE were eligible. Asphyxia was considered to be present if at least one of the following criteria was met: Apgar score of ≤5 at 10 minutes, at least one cord pH or arterial pH ≤7.1 or base deficit ≥12 within the first hour of life, ongoing resuscitation or mechanical ventilation at 10 minutes of life. HIE had to be defined by standardized neurological examination.[15,16] Neonates with major congenital abnormalities were excluded.

The primary outcome was a composite of death or neurodevelopmental disability at ≥18 months of life. Disability included cerebral palsy (CP) according to the Gross Motor Function Classification System (GMF)[17] or another validated scale, developmental delay as measured by Griffiths or Bayley assessment,[18,19] intellectual impairment (IQ >2 SD below the mean), blindness (vision <6/60 in both eyes), and hearing loss requiring amplification. Secondary outcomes included individual components of the primary composite outcome and adverse events such as sinus bradycardia, arrhythmia, arterial

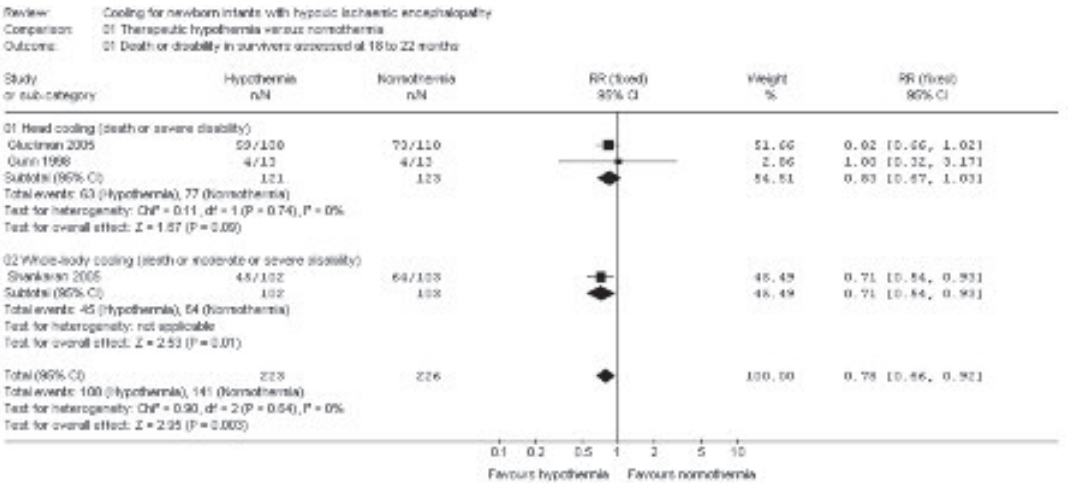

Figure 1

hypotension (mean arterial pressure <40 mm Hg), thrombocytopenia, coagulopathy, anemia, hypoglycemia, abnormal renal function (urine output 0.5ml/kg/hour and/or serum creatinine > 0.09 mmol/l), hepatic dysfunction (aspartate aminotransferase > 200 IU/l, alanine aminotransferase >100 IU/l), sepsis, seizures and hypokalemia.

A systematic literature search was conducted in July 2006 according to the methodology of the Cochrane Neonatal Review Group. The databases searched included the Cochrane Database of Systematic Reviews (Issue 3, 2006), the Cochrane Central Register of Controlled Trials, EMBASE, CINAHL, and MEDLINE databases using the following search strategy: "Infant, Newborn"[MeSH] AND ("Hypothermia"[MeSH] OR "Hypothermia, Induced"[MeSH]) AND ("Asphyxia"[MeSH] OR "Asphyxia Neonatorum"[MeSH] OR "Hypoxia-Ischemia, Brain"[MeSH] OR "hypoxic ischemic encephalopathy" OR "hypoxic ischemic encephalopathy"). Cross-references of publications were checked. A hand search of the proceedings of the Pediatric Academic Societies published in Pediatric Research from 1980 was conducted. No language restrictions were applied. SKP and SMS designed the review protocol. All authors searched the literature independently and assessed inclusion criteria and quality of the trials. SMS and SR independently extracted the data. Inconsistencies were sorted out by discussion. Trial quality was assessed by method of randomization, concealment of patient allocation, blinding of intervention, blinding of outcome assessors, and completeness of follow-up.

Meta-analysis was performed using Review Manager software (RevMan, version 4.2.7 for Windows, Oxford, England: The Cochrane Collaboration, 2003). Relative risk (RR) and risk difference (RD) were calculated with 95% confidence intervals (CI). Preplanned subgroup analysis for selective head cooling and whole body cooling was carried out. The number needed to treat (NNT) or harm (NNH) was calculated for significant comparisons. Heterogeneity was estimated by the I2 statistic. A fixed effects model was used. Reporting follows the QUOROM guidelines.[20]

Results

187 abstracts were identified. Twelve potentially relevant reports were retrieved for detailed evaluation. A total of eight reports[10-12,21-25] of five RCTs involving 552 neonates were eligible for inclusion in the analysis. Two RCTs involved selective head cooling by a cooling cap,[10, 21] the other three involved whole body cooling.[11,12,24] Tables 1-3 summarize their characteristics and quality assessment. No significant heterogeneity was noted using the I2 statistic. Gunn et al published their results as 3 different reports using 4 sequential temperature ranges for cooled infants.[21-23] From these 3 reports, we present the

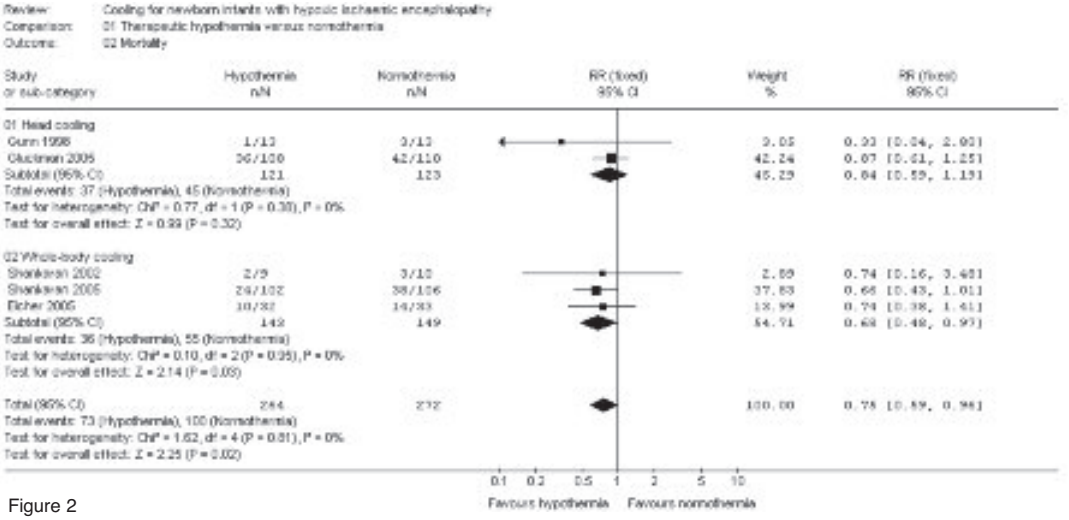

Figure 2

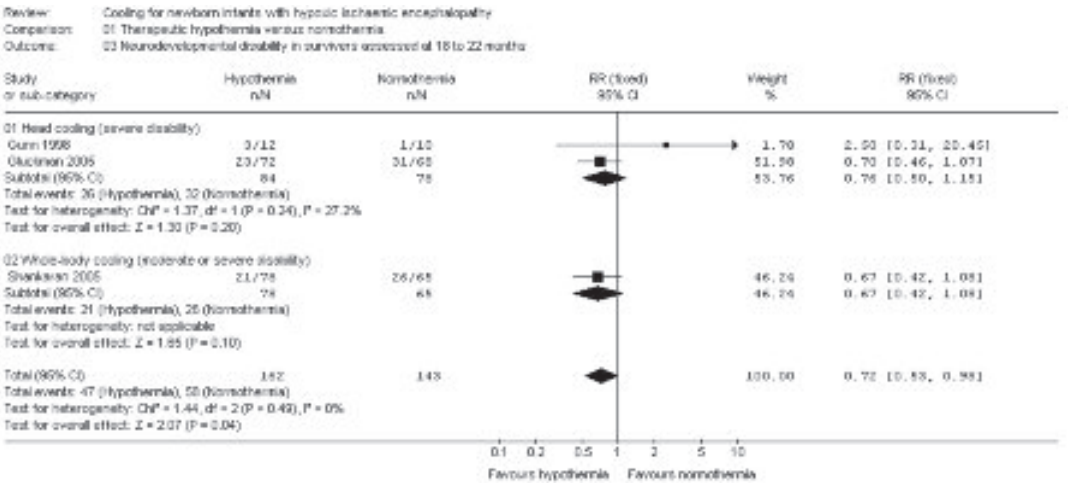

Figure 3

combined data on all neonates randomized to a rectal temperature of 34.0-35.5°C and refer to the trial as Gunn et al 1998. Eicher et al reported the safety[25] and efficacy[12] outcomes of therapeutic hypothermia in two separate publications. For the purpose of this meta-analysis their study is referred to as Eicher et al 2005. The studies Eicher et al 2005 and Shankaran et al 2002[24] were included in the review only for analysis of mortality and adverse events because the follow-up rate in Eicher et al 2005 was low (68%) and Shankaran et al 2002 did not report long-term follow up. The reasons for excluding four trials[26-29] from the metaanalysis and their characteristics are summarized in Table 4.

Results of the meta-analysis

(1) Death or neurodevelopmental disability at ≥18 months (Figure 1): Three trials[10,11,21] involving 449 neonates assessed the primary composite outcome of death or neurodevelopmental disability at 18 to 22 months of life. The trials by Gunn et al 1998 and Gluckman et al 2005 (selective head cooling by a cooling cap) had primary composite outcome of death or severe neurodevelopmental disability at 18 months defined as severe CP (equivalent to GMF level 3 to 5 in Gluckman et al 2005), Bayley mental developmental index (MDI) <70, or bilateral cortical visual impairment.

The trial of Shankaran et al 2005 (whole body cooling) had a primary composite outcome as death or moderate or severe neurodevelopmental disability at 18 to 22 months. Moderate disability was defined as Bayley MDI of 70 to 84 in addition to one or more of the following: GMF level 2, hearing impairment with no amplification, or a persistent seizure disorder. Severe disability was defined as any of the following: GMF level 3 to 5, Bayley MDI <70, hearing impairment requiring hearing aids, or blindness.

There is evidence of a significant effect of therapeutic hypothermia on the primary composite outcome of death or disability (RR: 0.78, 95% CI: 0.66, 0.92, NNT: 8, 95% CI: 5, 20) on pooling the data from these 3 trials. Analysis of the data from Shankaran et al 2005 showed evidence of benefit of whole body cooling in reducing death or moderate or severe disability (RR: 0.71, 95% CI: 0.54, 0.93, NNT: 6, 95% CI: 3, 20). Analysis of data from Gunn et al 1998 and Gluckman et al 2005 (selective head cooling) did not indicate such an effect on death or severe disability considering the 95% CI (RR: 0.83, 95% CI: 0.67, 1.03).

Included trials	Selective head cooling		Whole body cooling		
	Gunn 1998	Gluckman 2005	Shankaran 2002	Shankaran 2005	Eicher 2005
Design	RCT	RCT Multicenter	RCT Multicenter	RCT Multicenter	RCT Multicenter
Number of participants	26	234	19	208	65
Gestation	≥ 37 wks	≥ 37 wks	≥ 36 wks	≥ 37 wks	≥ 35 wks
Inclusion criteria (details see Table 2)	Asphyxia and moderate to severe HIE	Asphyxia and moderate to severe HIE	Asphyxia and moderate to severe HIE	Asphyxia and moderate to severe HIE	Asphyxia and HIE
Target temperature treatment group (°C)	34.5-35.5 (n=6) 34.0-35.0 (n=7) Not analyzed: 36.0-36.5 (n=6) 35.5-35.9 (n=6)	34.0-35.0	34.5	33.5	32.5-33.5
Target temperature control group (°C)	36.8-37.2	36.5-37.5	36.5	36.5-37.0	36.5-37.5
Site of temperature probe	Rectal	Rectal	Esophageal	Esophageal	Rectal
Average age at start of cooling (min)	294	330	318	302	120
Duration of cooling (h)	48-72	72	72	72	48
Cooling device	Servo-controlled cooling cap	Servo-controlled cooling cap	Two servo-controlled cooling blankets	Two servo-controlled cooling blankets	Ice bags followed by one servo-controlled cooling blanket
Primary outcome	Adverse events	Composite of death/severe disability	Adverse events	Composite of death/moderate or severe disability	Adverse events
Latest follow-up (months)	18	18	Follow-up not reported	18-22	12
Follow-up tools	Bayley II	Bayley II GMF	-	Bayley II GMF	Bayley II Vineland

Table 1 - Characteristics of included trials

The results for the primary composite outcome did not change significantly on analysis by a random effects model.

(2) Mortality (Figure 2): Overall, analysis of data from five trials[10-12,21,24] demonstrated a beneficial effect of therapeutic hypothermia on mortality (RR: 0.75, 95% CI: 0.59, 0.96, NNT: 11, 95% CI: 6, 100). Subgroup analysis indicated no significant reduction of mortality after selective head cooling (RR: 0.84, 95% CI: 0.59, 1.19). However, whole body cooling did have a protective effect (RR: 0.68, 95% CI: 0.48, 0.97, NNT: 8, 95% CI: 5, 100).

	Selective head cooling		Whole body cooling		
	Gunn 1998	**Gluckman 2005**	**Shankaran 2002**	**Shankaran 2005**	**Eicher 2005**
Definition of asphyxia	5 min Apgar < 7 or pH < 7,1 (first hour)	10 min Apgar < 6 or resuscitation or pH < 7.0 or BD[#] > 16 mmol (first hour)	pH <7.0 or BD > 16 or (if no blood gas or pH 7.01-7.15 or BD[#] 10-15 mmol: acute perinatal event and seizures or HIE[*])	10 min Apgar < 6 or resuscitation or pH <7.0 or BD[#] > 16 or (if no blood gas or pH 7.01-7.15 or BD[#] 10-15 mmol: acute perinatal event and seizures or HIE[*])	10 min Apgar < 6 or resuscitation or pH <7.0 or BD[#] > 13 or acute perinatal event
Definition of HIE[*]	Sarnat stage 2-3	Pre-randomisation EEG and Sarnat stage 2-3	Modified Sarnat stage 2-3	Modified Sarnat stage 2-3	Sarnat stage 1-3

[#]BD base deficit [*] Hypoxic ischemic encephalopathy

Table 2 - Inclusion criteria of included trials

Included Trial	**Gunn 1998**	**Gluckman 2005**	**Shankaran 2002**	**Shankaran 2005**	**Eicher 2005**
Adequacy of method of randomisation	Yes Computer generated	Yes Computer generated, block	Yes Computer generated, block	Yes Computer generated, block	Yes Central website, block
Concealment of allocation	Yes Sealed opaque envelopes	Yes Sealed opaque envelopes	Yes Central data-coordinating center	Yes Central data-coordinating center	Yes Central website
Blinding of intervention	None Due to nature of intervention	None Due to nature of intervention	None Due to nature of intervention	None Due to nature of intervention	None Due to nature of intervention
Blinding of outcome assessors	Not robustly	Yes	No	Yes	Unknown
Completeness of follow-up	Yes (96%)	Yes (93%)	Follow-up not reported[#]	Yes (98%)	No (68%)[#]

[#] Data from this trial was only pooled for analysis of mortality and adverse events

Table 3 - Quality assessment of included trials

(3) Neurodevelopmental disability at ≥18 months (Figure 3): Analysis of data from three trials[10,11,21] showed a significant effect of therapeutic hypothermia on neurodevelopmental disability at 18 to 22 months (RR: 0.72, 95% CI: 0.53, 0.98, NNT: 9, 95% CI: 5, 100). Subgroup analysis of trials of neither selective head cooling assessing severe disability (RR: 0.76, 95% CI: 0.50, 1.15) nor whole body cooling assessing moderate or severe disability (RR: 0.67, 95% CI: 0.42, 1.08) showed a significant benefit.

(4) Disabling CP (GMF level 3 to 5) at ≥18 months: Pooled data from three trials[10,11,21] didn't show a significant effect of therapeutic hypothermia on disabling CP at 18 to 22 months (RR: 0.69, 95% CI: 0.46, 1.03). Subgroup analysis of selective head cooling (RR: 0.72, 95% CI: 0.41, 1.26) or whole body cooling (RR: 0.66, 95% CI: 0.36, 1.18) also did not indicate a significant effect.

(5) Developmental delay (Bayley MDI <70) at ≥18 months: Analysis of data from three trials[10,11,21] didn't demonstrate a significant effect of therapeutic hypothermia on developmental delay at 18 to 22 months (RR: 0.76, 95% CI: 0.54, 1.06). Subgroup analysis of selective head cooling (RR: 0.86, 95% CI: 0.54, 1.37) or whole body cooling (RR: 0.65, 95% CI: 0.40, 1.08) also did not indicate a significant benefit.

(6) Blindness at ≥18 months: Pooled data from three trials[10,11,21] didn't indicate a significant effect of therapeutic hypothermia on blindness assessed at 18 to 22 months (RR: 0.52, 95% CI: 0.27, 1.02). Subgroup analysis of selective head cooling (RR: 0.57, 95% CI: 0.23, 1.37) or whole body cooling (RR: 0.47, 95% CI: 0.16, 1.32) also did not indicate a significant benefit.

(7) Hearing loss requiring amplification assessed at ≥18 months: Analysis of data from three trials[10,11,21] didn't indicate a significant effect of therapeutic hypothermia on severe hearing loss at 18 to 22 months (RR: 0.97, 95% CI: 0.36, 2.59). Subgroup analysis of selective head cooling (RR: 1.43, 95% CI: 0.36, 5.72) or whole body cooling (RR: 0.62, 95% CI: 0.14, 2.68) also did not indicate a significant effect.

(8) Adverse events: Sinus bradycardia[12,15,17,30] (RR: 7.42, 95% CI: 2.52, 21.87, NNH: 13, 95% CI: 8, 20) and thrombocytopenia[12,15,17] (RR: 1.47, 95% CI: 1.07, 2.03, NNH: 8, 95% CI: 5, 50) were reported as significant adverse events (Thrombocytopenia: Gunn et al 1998 and Eicher et al 2005: platelet count <150000/µl, Gluckman et al 2005: <100000/µl). Only Gluckman et al 2005 reported higher mean plasma glucose concentrations between 4 h and 24 h in cooled vs control infants which resolved spontaneously.[10] There were no other significant adverse effects (Table 5).

Discussion

Our results suggest that in general, cooling of neonates with HIE has a beneficial effect on the primary composite outcome of death or disability at 18-22 months. The similarity of outcomes between trials despite the heterogeneity related to various factors including methodology of cooling (head vs. body, devices, target temperatures, site of monitoring, duration of intervention etc.), patient characteristics (place of birth, temperature and age at enrolment etc.), and the definition and degree (moderate and/or severe) of neurodevelopmental disability (Table 1) is reassuring for the generalisability of the findings. Differences in the behavior of the composite outcome vs. its individual components are an important consideration.[30] The selection of death and neurodevelopmental disability as components of the prespecified primary composite outcome is justified. The frequency of the components of the primary composite outcome is significant and comparable, assuring that no individual component is driving it in any specific direction. The data show reasonably convincingly that the benefit for the primary composite outcome is significant and is probably a fair reflection of benefit for its individual components. Individual components of the primary composite outcome show significant benefits of cooling but have wide CIs suggesting that more data is needed to minimize the uncertainty. However, it is important to note that interpretation of CI is a personal and subjective issue. Overall, there seems to be reasonably good evidence of a real benefit of cooling on the primary composite outcome and its components.

The definition of disability in the whole body cooling trial by Shankaran et al is quite different from that in the selective head cooling trials by Gluckman et al and Gunn et al (moderate/severe vs. only severe disability). However the effect of this difference in definitions on the results of the meta-analysis is limited because the proportion of infants with moderate disability is low in all trials. Subgroup analysis seems to suggest that the results of the selective head cooling trials are not as convincing as those of the whole body cooling trials. However,

Study	Description of the trial	Reason for exclusion
Akisu 2003 [26]	Randomized trial of 21 neonates with asphyxia, 10 assigned to head cooling for 72 h, 11 assigned to normothermia. Primary outcomes were electroencephalographic changes and concentrations of platelet activating factor in cerebrospinal fluid during the time of treatment	1. Enrolment based on presence of asphyxia only, not HIE* 2. Target temperature in hypothermia group 36.0-36.5°C 3. Time of start of intervention not standardized 4. No clinical follow-up data available
Zhou 2003 [27]	Randomized trial of 50 term neonates with asphyxia, 27 assigned to head cooling for 72 h, 23 assigned to normothermia. Primary outcomes were echocardiographic changes at the end of the intervention	1. Inclusion based on presence of asphyxia only, not HIE* 2. No clinical follow-up data available
Shao 2005 [28]	Multicenter randomized trial. 206 term neonates with HIE*, 127 allocated to head cooling via cooling cap for 72 h, 79 assigned to normothermia. Primary outcome was a composite of death or severe disability at 18 months	1. Concerns about randomization: Large difference in group sizes, method of randomization unknown, concealment of allocation unknown 2. Ongoing follow-up, currently 45% of survivors assessed at 18 months
Lin 2006 [29]	Singlecenter trial. 58 term neonates with HIE*, 30 assigned to head cooling via cooling cap for 72 h, 28 controls allocated to normothermia. Primary outcomes were changes on head computed tomography scans after one week and a behavioral assessment at 7-10 days	1. Not randomized, group allocation based on odd or even date of admission 2. Mean temperature in control group at begin of trial 35.7°C (all neonates outborn, no transport cot available), timing of enrolment and rewarming of control group unclear 3. No follow-up data available

* Hypoxic ischemic encephalopathy

Table 4 - Trials excluded from the analysis

Number of included trials	Number of participants	Adverse event	Relative risk (95% CI)
4 [10,11,21,25]	526	Sinus bradycardia	7.42 (2.52, 21.87) Number needed to harm: 13 (95% CI: 8, 20)
3 [10,11,21]	464	Arrhythmia requiring treatment	1.04 (0.07, 16.39)
4 [10,11,21,24]	483	Hypotension	1.17 (0.96, 1.42)
3 [10,21,25]	318	Thrombocytopenia	1.47 (1.07, 2.03) Number needed to harm: 8 (95% CI: 5, 50)
3 [10,11,25]	500	Coagulopathy	1.28 (0.94, 1.75)
2 [10,25]	292	Anemia	1.75 (0.86, 3.57)
3 [10,11,21]	464	Hypoglycemia	0.76 (0.49 to 1.17)
5 [10,11,21,24,25]	545	Abnormal renal function	0.91 (0.79 to 1.05)
2 [10,11]	448	Hepatic dysfunction	0.83 (0.64, 1.09)
4 [10,11,21,25]	526	Sepsis	1.04 (0.45 to 2.39)
5 [10,11,21,24,25]	545	Seizures	1.04 (0.91 to 1.18)
2 [10,25]	292	Hypokalemia	1.02 (0.84 to 1.25)

Table 5 - Analysis of adverse effects of therapeutic hypothermia

there might be no clinically important difference between these cooling techniques for several reasons: Firstly, this subgroup analysis is clearly dominated by the two major trials Gluckman et al and Shankaran et al, and therefore of limited value. The overall trend for both cooling techniques is towards a benefit (Figure 1). Secondly, differences in the severity of neuronal injury may explain these findings considering the differences in the inclusion criteria of those two trials (Table 2). The proportion of neonates with very low Apgar scores, severe aEEG background activity and severe clinical encephalopathy was higher in the intervention group in Gluckman et al, possibly reducing the chances to demonstrate selective head cooling benefits. A significant reduction in death or major disability was however noted in the prespecified subgroup analysis of neonates with only moderate injury defined by aEEG criteria.[10,31] Thirdly, palliation bias in the form of a higher rate of withdrawal of treatment (27 vs. 12) in the control group may also have played a role in the significant benefit reported in the whole body cooling trial by Shankaran et al.[32] In addition, 41/106 neonates in the control group of Shankaran et al, at least once had a temperature >38°C within the 72 hours of the intervention, which may have influenced for their outcome.[32]

The frequency of sinus bradycardia following therapeutic hypothermia was significant. A borderline effect on thrombocytopenia was noted and there was a trend towards a higher risk of anemia, coagulopathy, and hypotension (Table 5). However, sinus bradycardia is a physiological response rather than a true adverse event and did not compromise perfusion, and thrombocytopenia was not reported as of clinical importance. The adverse events therefore may be outweighed by the potential benefits.

Given the overall encouraging results without significant adverse effects it is not surprising that some centers may now consider therapeutic hypothermia as a standard treatment for HIE.[33] However, many experts including a commission of the American Academy of Pediatrics[34] have suggested that further research should continue and therapeutic hypothermia should not be offered outside RCTs. Their suggestions are based on heterogeneity as discussed above and the possibility that neurological outcomes at 18 to 22 months may not reflect the true long-term benefits.[35, 36] The rate of severe disability is very unlikely to change, however, more subtle neurodevelopmental problems that cannot be assessed at the age of 18 months may become apparent by school age.[1] The unaddressed issues include the specific target population that is most likely to benefit, the most effective and safe method for cooling, the optimal age at onset and duration of cooling, and the field difficulties in applying any specific method for cooling, particularly for outborn neonates.[34] In practice, hypothermia is quite frequent in asphyxiated neonates, whereas guidelines for rewarming are not standardised/uniform. The targets, methods as well as the speed of rewarming may influence the neuronal recovery/damage following HIE. This issue is especially important during transport of hypothermic neonates with HIE. The field difficulties have been addressed to some extent by Eicher et al who showed that it is feasible to cool outborn neonates with ice bags followed by cooling with a blanket on reaching the receiving hospital. This approach can help to reduce the time between birth asphyxia and initiation of cooling. Animal studies have clearly shown that there is a correlation between early onset of cooling and treatment effect.[37]

Experts have advised that centers wishing to offer therapeutic hypothermia outside RCTs should adhere strictly to a trial protocol and have established the substantial resources required to cool neonates with HIE. The minimum resources include a transport team to retrieve neonates and start cooling before four to six hours of life and a multidisciplinary team for long-term neurodevelopmental follow-up.[33]

At least three more RCTs of therapeutic hypothermia aiming at a combined total of over 650 neonates are currently in progress.[38-40] The long-term outcomes ≥18 months of age of the single trial with complete recruitment (according to the TOBY trial website) will not be ready for publication until end of 2008 at the earliest.[38] Ideally it is preferable to include the long-term results of those ongoing studies in this systematic review to

have definitive answers. However, those studies are not designed to answer all the unaddressed issues listed earlier, therefore waiting for their results is ethically complex. They may show beneficial effects of therapeutic hypothermia while narrowing the CI. In that case it is disturbing to think that while waiting for the CI to narrow the purists may have denied a beneficial intervention to neonates with HIE. Obviously ethics,[41] resources, parents' wishes, and last but not the least, the anxiety related to future medicolegal challenges, will have to be balanced before deciding whether therapeutic hypothermia can be offered as a standard treatment for HIE. Continuing to participate in a trial of therapeutic hypothermia while offering it to neonates whose parents insist on it probably violates the principle of equipoise, the very justification for conducting a RCT.

Conclusions

Evidence from high quality RCTs indicates that overall, cooling of neonates with moderate to severe HIE reduces the risk of death or disability at 18 to 22 months without significant adverse effects. Despite the methodological differences, wide CIs, and lack of long-term follow-up data, the consistency of benefits and its sound scientific basis indicate that cooling may be an attractive option for neuroprotection in HIE – a condition that lacks any effective treatment at present.

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that it has for both lay people and alternative practitioners. There is also a widespread lay metaphor "illness is imbalance." This is little used by doctors but might form the basis on which some of the insights of modern medicine may be reconstructed for both patients and doctors. New scientific understandings are themselves a potent source of new metaphors. The image of the hologram, which influences current researchers in neurophysiology, is an example of a new metaphor that emphasises the wholeness and interrelationship of organisms.[7]

Finally, there is the fact that medicine has grown out of a science governed and dominated by men and masculine patterns of thought.[8]

If we are to humanize medicine and create institutions that encourage the full participation of patients, while offering them the best of traditional medicine, we need to incorporate new images into our thinking. Essential to this process would be new metaphors around which we can reconstrue both our present and our emerging knowledge. In the face of the further drive to reductionism that will flow from bioengineering such unifying and believable metaphors will be essential if we are to continue in any way to be healers as well as technocrats.

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Proximity Morality in Medical School – Medical Students Forming Physician Morality "On The Job"

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Abstract

Background: The value of ethics education has been questioned. Therefore we did a student survey on attitudes about the teaching of ethics in Swedish medical schools.

Methods: Questionnaire survey on attitudes to ethics education with 409 Swedish medical students participating. We analyzed > 8000 words of open-ended responses and multiple-choice questions using classic grounded theory procedures.

Results: In this paper we suggest that medical students take a proximity morality stance towards their ethics education meaning that they want to form physician morality "on the job." This involves comprehensive ethics courses in which quality lectures provide "ethics grammar" and together with attitude exercises and vignette reflections nurture tutored group discussions. Goals of forming physician morality are to develop a professional identity, handling diversity of religious and existential worldviews, training students described as ethically naive, processing difficult clinical experiences, and desisting negative role modeling from physicians in clinical or teaching situations, some engaging in "ethics suppression" by controlling sensitive topic discussions and serving students politically correct attitudes.

Conclusion: We found that medical students have a proximity morality attitude towards ethics education. Rather than being taught ethics they want to form their own physician morality through tutored group discussions in comprehensive ethics courses.

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Background

Medical ethics education differs from other subjects and the importance of formal courses in ethics has been questioned. Some medical schools combine instruction in bioethical principles with teaching of humanities programs. The teaching of ethics varies in Swedish medical schools from interspersed lectures to formal ethics courses. Lately, teachers are developing a common national curriculum in the view of a new Swedish university regulation in 2007 to align with European higher education in the Bologna Process. One of three main outcomes of medical education according to the new regulation is ability to understand and assess values and attitudes. Thus, there is a change process underway regarding medical ethics education in Sweden.

We designed a questionnaire survey in order to elucidate how medical students view the ethics education in medical schools. Many students gave input on the ethics course curriculum: Should ethics be taught in lectures or learned through group discussions? Should the ethics course be a separate course among others, or should it be part of other courses with lectures and group discussions interspersed? Should it come early or late in the medical school curriculum? Should the literature be specific ethics literature or novels and short stories with relevant ethical content? From multiple-choice responses we found that strong ethics interest was associated with frequent experiences of physician teachers as good role-models and an absence of poor role models. In the present study we wanted to explore what was going on in medical schools regarding the medical ethics education by analyzing open-ended survey responses together with response data from multiple-choice items.

Methods

We did a survey on attitudes towards the medical ethics education during 2005 as a request from the delegation of medical ethics of the Swedish Society of Medicine. Swedish medical students from the 1st, 5th and 11th (last) term participated. The survey consisted of 14 items of which 10 had a total of 59 multiple-choice response options and generous space

Table 1: The survey items and numbers of multiple-choice options and open-ended response word count.

Survey items 1–14	Number of multiple choice items	Number of open-ended responses*	Open-ended responses, word count
1. The general outline of the ethics education was valuable	5	36	251
2. The following modes of education were valuable	6	13	76
3. The education was valuable within the following specific fields	18	34	468
4. The education was valuable within the following general fields	7	22	252
5. Which specific or general areas were valuable? Please give examples!	0	55	410
6. This is my general attitude to ethics education	3	66	960
7. Have you experienced the following (regarding physicians/teachers)	4	24	238
8. Have you encountered (good and/or poor role models/situations that affected you)?	2	27	289
9. The following forms of examination were valuable	8	15	108
10. What was your required course literature (in the ethics education)?	0	94	560
11. How important was medical ethics education for you?	6	46	685
12. Please offer suggestions for changes of the design of the ethics course that would improve it	0	110	1352
13. Should ethics education continue during intership and residency? If yes, then how?	2	156	1422
14. Please supply further comments to the questions above.	0	38	1135
TOTAL	**59**	**736**	**8206**

*Total number of responders to open-ended items: 220

for open-ended comments, and 4 items were open-ended only, see Table 1.

Sample: The overall response rate to the questionnaire survey was 36%, and varied between different centers from 13% to 83%, with a total of 409 respondents, 308 women (75%) and 101 men (25%). More than half (220/409) of the respondents gave one or more written open comments amounting to > 8000 words. These comments were transcribed into Word from handwritten text.

At some centers a whole term would drop out since the responsible teacher failed to hand out the survey. Yet, the response patterns of the different questionnaire items did not differ significantly between schools with low and high response rates when different logistic regression models were applied to the data. The most comprehensive open responses came from last term students. Thus the most experienced students gave the biggest input to the analysis of the qualitative data – the main data source for this study.

Analysis: We analyzed open-ended comments and multiple-choice responses by classic grounded theory (GT) procedures. Since classic GT is rarely used and differs from other methods analyzing qualitative and quantitative data we describe and discuss GT a lot in this paper. The GT dictum "all is data" means that we compared both qualitative responses and quantified multiple-choice items in the same analysis. Multiple-choice results were dichotomized, analyzed in logistic regression models, and compared with open-ended responses. GT analysis begins with open coding of data line by line. Codes answer the questions "what is going on?" and "what concept does this data represent" or "what concept that explains what is going on catches the latent pattern in this data?" and most important: "what are the participants main concern and how are they continually trying to resolve it?" Theoretical memos, in the shapes of text, diagrams, and figures, were written, typed, or drawn in the comparative process as soon as open coding started. This paper was sorted and written up from more than 4,000 words and many dozens of pages of typed and handwritten memos. "Memos are the theorizing write-up of ideas about substantive codes and their theoretically coded relationships as they emerge during coding, collecting and analyzing data, and during memoing." Memoing is "the core stage of grounded theory methodology," and should be done at any time and place in order to capture creative ideas. The analytic procedures were done with experience from earlier GT studies.

Discovery of Grounded Theory from 1967 is the most quoted reference for any single method analyzing qualitative data according to Google scholar search (7884 citations August 2007). GT has the inductive approach to generate hypotheses explaining how participants in a studied substantive area resolve their main concern. Thus, GT conceptualizes "what is going on" in the field of study by the "constant comparative method," another name for GT. This indicates a constant comparison of data during an iterative research process, which involves open coding, memoing, theoretical sampling (data collection based on hypotheses from the ongoing analysis), selective coding (recoding data based on concepts from the ongoing analysis), sorting and writing up (sorting memos in piles based on concepts in the theory and then writing up the sorted piles into a paper or book). GT analysis aims at conceptual theories abstract of time, place and people and differs from most studies using qualitative data by presenting explanatory concepts instead of descriptions. Many clinical research methods consider persons or patients as units of analysis, whereas in GT the unit of analysis is the incident not the person(s) involved (incident = a distinct piece of action, or an episode, as in a story or play). The number of incidents being coded and compared typically amounts to several hundred in a GT study since every participant often reports many incidents. When comparing many incidents in a certain field, the emerging concepts and the relationship between them are in reality probability statements and therefore GT should not be considered a qualitative method but a general method that can use any type of data. The results of GT are not reports of facts but an integrated set of conceptual hypotheses. Validity in its traditional sense is consequently not an issue in GT research, which instead should be judged by fit, relevance, workability, and modifiability. Fit has to do with how close concepts fit with the incidents they are representing, and this is related to how thorough the constant comparison of incidents to concepts was done. A relevant study deals with the real concern of participants and captures attention. The theory works when it explains how the problem is being solved with much variation.

A modifiable theory can be altered when new relevant data is compared to existing data. A GT is never right or wrong, it just has more or less fit, relevance, workability and modifiability, and readers of this article are asked to try its quality according to these principles.

Results

In this study we analyzed student attitudes and "what was going on" in the medical ethics education based on survey data. The medical students argued for a proximity morality stance, or forming morality "on the job." This morality forming is ideally done in comprehensive ethics courses with tutored small groups. Forming physician morality requires "ethics grammar" provided by selected high quality lectures, and impulses from attitude exercises and vignette reflections in "ethics labs". Patient cases and clinical issues are thus discussed in interactive groups that help to deal with emotionally difficult clinical situations. To desist negative role modeling is another function of the ethics courses where reflected professionalism is developed for diverse medical students in a heterogeneous world.

Proximity morality in medical school – How?: On the job morality forming in medical school is typically done in interactive discussion groups. These groups have a support network function where medical students are allowed professional role growth within a permissive context where ethical and value-laden issues are discussed and tried. The structure ideally consists of tutored groups that repeatedly work with case study approaches, discuss ethical principles, and continue during internship. Within a frame resembling the clinical setting students grow their own ethical attitudes and shape their individual physician morality. Group discussions provide good training for handling ethical difficulties since real world medical ethics consist of unique complex situations often involving several people. One goal of interactive ethics group discussions is to understand what appropriate physician behavior is.

• *Ethics discussion forums should be based on tutored small groups to prevent people with strong views from dominating* - last term student.

• *We need group discussions with teachers making sure that everyone develops decent ethical values as physicians* - fifth term student

• *Every section could end with ethical discussions related to the specific subject, psychiatry/internal medicine/surgery* - last term student

Forming physician morality also includes quality lectures on ethics, preferably by professional ethicists. These lectures provide students with a basic "ethics grammar" about ethical principles and concepts. This feeds the interactive group discussions and improves their quality concerning ethical issues.

• *Professional lecturers from the faculty of arts (are wanted)* - first term student

In the ethics lab, students work with practical, sometimes challenging attitude exercises and vignette reflections. These stimulate critical thinking about current ethical problems in clinical training. It requires that participants position themselves ideologically, and for some attitude exercises also physically. Attitude exercises are often done in case studies.

• *A case is presented and different opinions (re the case) represented by four different corners. One can go to any corner and argue against the other corners and eventually change corners* - last term student.

Proximity morality in medical school – Why?: Why would medical students want to form physician morality on the job? The deliberate forming of a physician morality is necessary for several reasons. A number of student responses dealt with arguments for ethics education in general and forming physician morality on the job in particular:

The professional identity of future physicians requires moral reflection.

• *An open discussion forum on difficult issues and professional identity conflicts would make us better physicians* - last term student

• Small groups during clinical training – discussing the professional physician role and work issues *" (on suggested ethics education during later internship)* - last term student

Medical students are different. Some are ethically naive, or not interested in ethics, and others even described as socially "autistic." The importance of ethics education is obvious for these groups.

• *Only autistic people need ethics education* - last term student

Diversity. We live in a society with increasing diversity and multiple religious views.

• *What is it really like in our secularized country? How can we say something is right when we don't share the same values* - fifth term student

Processing difficulties. A group discussion format of ethics education helps in processing tough experiences from the clinical setting.

• *We underestimate the power of what we can do for each other during the education* - last term student

• *Small groups discussing everyday problems and ethical issues in the workplace* (on suggested ethics education during later internship) - first term student

Desisting negative role modeling. By defying ethics suppression and politically corrected ethics the influences of physicians/teachers as poor role models may be addressed and negative role modeling dealt with in the interactive groups. Some teachers and physicians were described as being "masters of opinion control" trying to neutralize discussions about ethically sensitive topics by putting the lid on discussions, and defending politically correct opinions.

• *I prefer a good (neutral) clinician instead of zealous, ideologically motivated people* - fifth term student.

• *Teachers gave too little space for own views – there was a correct key for the discussion* - last term student

In a statistical analysis of the survey presented elsewhere we saw a significant relationship between a low interest in ethics and frequent experiences of poor role models and the absence of good ones in all three terms. For final-term students, there was a significant association between a high interest in ethics and experiences of good role models and a preference for discussions in small groups.

Discussion

"Personally I'm always ready to learn, although I do not always like being taught." – Winston Churchill

The quote illustrates the students' attitudes towards medical ethics education in this study. We propose that medical students by a proximity morality stance want ethics education on the job to help them in the learning process of becoming physicians. In this process they form their own physician morality rather than being taught ethics. This ideally takes place in comprehensive ethics courses where tutored groups openly discuss and reflect on difficult ethical topics and moral dilemmas. High quality lectures are interwoven to give an ethics grammar. These lectures provide default ethical principles nurturing group discussions together with attitude exercises and vignette reflections in ethics labs. These interactive discussion groups also have a support network function. Here students process ethical problems in an environment where physician morality is allowed to form and grow on the job. Hence, rather than being served ideologically stained opinions students prefer to reflect and discuss different ethical attitudes. As an example of their proximity morality one could say they want to bake their own moral cakes instead of being served ethical cookies.

In a British study of university students' expectations of teaching the students hoped for more interaction between students and teachers. They also suggested that groups provide effective learning, and this view was most prominent among medical students. These findings resemble ours when it comes to preferences for teaching structures. In a Swedish study the authors suggested that interactive lecturing was a stimulant to a problem-based learning (PBL) program. This is in line with our proposition of the need for good quality lectures to feed ethical discussions with ethics grammar and input from ethics labs. In a review of ethics teaching the authors were nihilistic about its effects and suggested that critical determinants of physician identity operate not within the formal curriculum but in a subtler, less officially recognized "hidden curriculum". Also, medical education could be seen as a form of moral training of which formal instruction in ethics constitutes only a small piece. In a study investigating the effect of ethics education on physician morality it was concluded that moral development and ethical confidence were unaffected by ethics education. The goals of ethics education was conceptualized as having cognitive, behavior and attitudinal dimensions. Ethics was supposedly studied for its own sake contributing to "one's all around character". We agree with this author's conclusions, and our analysis suggests that instead of an emphasis on teaching, ethics and morality has to be learned on the job as discovered in a neonatal unit study of proximity ethics. As a reference to oneself's morality Levinas talks about "the other." Similarly "the others" (fellow students and teachers/physicians) are necessary for understanding the suggested "on the job" morality development in our study.

The method for this study was classic grounded theory (GT) aiming at generating conceptual hypotheses of the resolution of a main concern and not describing a studied area. Yet, most studies citing GT fail to fulfill its aims. In a Biomedcentral "grounded theory" search in 2006 the first author (HT) reviewed 35 consecutive articles. Some presented a core variable – a fundamental part of GT, but most studies were descriptive and lacked explanatory integration. In this study we did GT analysis of written open and multiple-choice survey responses. We did not theoretically sample data outside of the survey. Yet we conceptualized a tentative model, a preliminary core variable theory, of how medical students want their education in medical ethics. This model is, according to the GT paradigm, not right or wrong. It is just a set of probability statements from which hypotheses are generated by constantly comparing available data. When presenting this proximity morality model of ethics teaching to physician colleagues and ethics teachers the reactions have been mostly positive. The model makes sense and seems to fit with experience.

Limitations: This paper suggests a proximity morality model showing how medical students want their ethics education in medical school, but does not take into account their teachers' views. Also, our study is limited by the qualitative data being only written comments in an otherwise multiple-choice survey with a partial response rate. As for the low response rates, the centers with the highest response rates (83%) had the same attitude pattern as those with low response rates (13%). Thus the data seems generalizable enough to fit the requirements for an inductive study. The 11th term students gave the largest quantitative input of qualitative data and thus had a comparatively larger impact on theory generation. Whether this was a limitation is questionable. In our view it gave us more valuable longitudinal data. To use interview data by theoretically sampling outside of the survey might improve the model. We tried to compensate for this by also sampling dichotomized multiple-choice survey data in accordance with the GT maxim "all is data." The survey data consisted of structured responses, which is not recommended in classic GT. This is another argument for expanding the theoretical model with interview data. For possible future application in medical schools we thus intend to refine and modify the model and develop it through interaction with medical students and teachers.

Conclusion

In this study we present a tentative conceptual model of proximity morality guiding medical students to shape their own medical ethics education "on the job". We suggest that medical students rather than being taught ethics want to form their own physician morality. This is typically done in comprehensive ethics courses with tutored group discussions. Here high quality lectures supply "ethics grammar" and together with attitude exercises and vignette reflections in "ethics labs" nurture discussions on different ethical issues. This helps students to develop a professional physician identity, handling diversity of religious and existential worldviews, training students described as ethically naive, processing difficult clinical experiences, and desisting negative role modeling.

Hypoplastic Left Heart Syndrome

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Abstract

Hypoplastic left heart syndrome (HLHS) refers to the abnormal development of the left-sided cardiac structures, resulting in obstruction to blood flow from the left ventricular outflow tract. In addition, the syndrome includes underdevelopment of the left ventricle, aorta, and aortic arch, as well as mitral atresia or stenosis. HLHS has been reported to occur in approximately 0.016 to 0.036% of all live births. Newborn infants with the condition generally are born at full term and initially appear healthy. As the arterial duct closes, the systemic perfusion becomes decreased, resulting in hypoxemia, acidosis, and shock. Usually, no heart murmur, or a non-specific heart murmur, may be detected. The second heart sound is loud and single because of aortic atresia. Often the liver is enlarged secondary to congestive heart failure. The embryologic cause of the disease, as in the case of most congenital cardiac defects, is not fully known. The most useful diagnostic modality is the echocardiogram. The syndrome can be diagnosed by fetal echocardiography between 18 and 22 weeks of gestation. Differential diagnosis includes other left-sided obstructive lesions where the systemic circulation is dependent on ductal flow (critical aortic stenosis, coarctation of the aorta, interrupted aortic arch). Children with the syndrome require surgery as neonates, as they have duct-dependent systemic circulation. Currently, there are two major modalities, primary cardiac transplantation or a series of staged functionally univentricular palliations. The treatment chosen is dependent on the preference of the institution, its experience, and also preference. Although survival following initial surgical intervention has improved significantly over the last 20 years, significant mortality and morbidity are present for both surgical strategies. As a result pediatric cardiologists continue to be challenged by discussions with families regarding initial decision relative to treatment, and long-term prognosis as information on long-term survival and quality of life for those born with the syndrome is limited.

Disease name and symptoms

The congenital heart lesion more commonly known today as hypoplastic left heart syndrome (HLHS) was initially termed hypoplasia of the aortic tract complex by Lev in 1952.[1] This initial description resulted from examination of a series of specimens found to have isolated hypoplasia of the aorta, hypoplasia of the aorta and ventricular septal defect, and hypoplasia of the aorta with aortic stenosis or atresia, with and without mitral stenosis or atresia. The series of Lev was followed by the study of Noonan and Nadas, who in 1958 first used the term hypoplastic left heart syndrome collectively to describe their series of specimens with multiple malformations involving left-sided structures of the heart.[2]

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Definition and Diagnostic criteria

Hypoplastic left heart syndrome refers to the abnormal development of the left-sided cardiac structures, resulting in obstruction to blood flow from the left ventricular outflow tract. In addition, the syndrome includes underdevelopment of the left ventricle, aorta, and aortic arch, as well as mitral atresia or stenosis. The severity of outflow obstruction, the left heart structures involved, and the degree of left ventricular and aortic hypoplasia, may vary among patients, resulting in a spectrum of patients with varying levels of severity.[3]

Epidemiology

The syndrome has been reported to occur in approximately 0.016 to 0.036% of all live births.[4-7] It accounts for 1 to 3.8 % of all congenital cardiac malformations.[8] Up to seven-tenths of cases are reported to occur in males.[4] The recurrence risk in siblings is 0.5%, with other forms of congenitally malformed hearts seen in 13.5%.[9]

Clinical Description

Newborn infants generally are born at full term, and initially appear healthy. With closure of the arterial duct, the systemic perfusion becomes decreased, resulting in hypoxemia, acidosis, and shock. Usually, no heart murmur, or a non-specific heart murmur, may be detected. The second heart sound is loud and single because of aortic atresia. Often the liver is enlarged secondary to congestive heart failure.

A small subset of patients have restriction of blood flow from the left to right atrium because of an inadequate or absent atrial communication. Such restriction to flow of blood from the left to right atrium can result in severe left atrial hypertension, and decreased blood flow into the right atrium and the dominant right ventricle, resulting in decreased flows into both the systemic and pulmonary circulations. These patients present with cardiogenic shock and profound cyanosis at birth, and are likely to die in the absence of an intervention, such as catheter-based or surgical septostomy, performed soon after birth, to relieve obstruction or to create a means of communication in the atrial septum, allowing decompression of the left atrium and free flow of blood from the left atrium into the right atrium.

Etiology

The embryologic cause, as in the case of most congenitally malformed hearts, is not fully known. Early epidemiologic

studies report a multifactorial influence to be the cause of up to 90% of cardiac anomalies, with a recurrence rate in further offspring of 2% to 6%.[10] Associated risk factors include maternal, gestational, and familial conditions. Fetal exposure to teratogens may also be a risk factor. Likewise, fetal exposure to active maternal infections, such as rubella, herpesvirus, coxsackievirus B5, and cytomegalovirus, may be a risk.

Chromosomal aberrations account for about 6% of all congenitally malformed hearts. Many genetic and hereditary diseases are associated with such congenital malformations, although the causative mechanism is unknown. Prospective studies using chromosomal analysis have suggested that some malformations may be the result of a single gene defect.[11]

In the case of hypoplasia of the left heart, the resulting multiple anomalies may result from either the multifactorial factors described above, or from a reduction of left ventricular inflow or outflow during fetal development.

Diagnostic methods

The most useful diagnostic modality is the echocardiogram, which may help confirm the diagnosis, and as well as diagnose basic variability in anatomic structures within this anatomically heterogenous population. Information collected should include the size of the inter-atrial communication, function of the atrioventricular valve, and the size of the ascending aorta, as these are useful measurements for stratifying the options for treatment. Although the electrocardiogram is non-specific, many patients display right ventricular hypertrophy, and have paucity of left ventricular forces. Chest radiographs are not diagnostic, and cardiac catheterization is only needed if an intervention such as creation or enlargement of the inter-atrial communication is required.[12]

Differential diagnosis

The clinical presentation may resemble those of neonates with other left-sided obstructive lesions where the systemic circulation is dependent on ductal flow. These conditions may include critical aortic stenosis, coarctation of the aorta, interrupted aortic arch. As with hypoplasia of the left heart, their clinical presentation is cardiogenic shock following closure of the arterial duct. Other non-structural cardiac diseases, with clinical presentation in a shock-like state, such as neonatal myocarditis and neonatal sepsis, should also be included in the differential diagnosis. These conditions can be easily differentiated by echocardiography.

Genetic counseling

Upon diagnosis, both genetic counseling and testing should be offered to both parents. Multiple genetic syndromes have been reported, including Turner's syndrome, Noonan's syndrome, Smith-Lemli-Opitz syndrome, Holt-Oram syndrome, and many others.[13,14] Overall, one-quarter of all patients have an associated genetic disorder or major extracardiac abnormality.

Antenatal diagnosis

The syndrome can be diagnosed by fetal echocardiography between 18 and 22 weeks of gestation.[14-16] Further evaluation should include genetic testing, and the examination for other extracardiac malformations. Once the diagnosis is made, the perinatal team should monitor growth and development of the other fetal organs. Vaginal delivery is often recommended, as long as the fetus has no signs of cardiac failure. Although the syndrome has not been found to have deleterious effects on labor and delivery, most health care professionals advise that the birth of the infant should occur in a cardiac surgical center.

Management including treatment

Afflicted children require surgery as neonates, as they have duct-dependent systemic circulation. Currently, there are two major treatment modalities. These are primary cardiac transplantation, or a series of staged functionally univentricular palliations.[17] The functionally univentricular palliation typically includes three operations. The first stage of palliation, or the Norwood operation, is performed at birth. The second stage is a bi-directional Glenn operation, usually undertaken at 6 to 8 months of age. The third, and final, stage is the Fontan operation, which can be performed between the ages of 18 months and 4 years. The treatment chosen is dependent on the preference of the institution, its experience, and also preference. Connor et al., recently evaluated outcomes for 251 children during 1997, with 17 managed by primary cardiac transplantation, and 234 by stages palliation, and showed that death occurred more frequently in those undergoing primary cardiac transplantation, with 42% dying, compared with those undergoing the Norwood operation, of whom 35% died.[18] The mortality rate for children managed through primary cardiac transplantation does not include children who died waiting prior to cardiac transplantation. The increased risk of death in children waiting for transplantation, and the scarcity of donor organs during the neonatal period, has made this modality less favorable, but is still offered in a few centers in the United States of America.[19]

For patients undergoing functionally univentricular palliation, leading to creation of the Fontan circulation, the highest risk of mortality is following the initial operation, with up to three-tenths of patients dying in some reported series.[20] The Norwood operation consists of constructing a new aortic root and arch, disconnecting the pulmonary trunk from the pulmonary circulation, and incorporating it into the systemic outflow tract. A modified Blalock-Taussig shunt, of 3 to 4 millimeters in diameter, is constructed to supply blood to the lungs. As pulmonary vascular resistance is lower than systemic vascular resistance, blood flows from the aortic root to the pulmonary circulation during diastole. This results in decreased diastolic blood pressure in the aortic root, and thus decreased coronary arterial perfusion. As a result, these children may suffer from myocardial ischemia, causing cardiac failure and sudden death after discharge from hospital following successful initial surgical palliation. Since blood flows into the pulmonary circulation in diastole, the fraction of cardiac output distributed to the pulmonary circulation is higher than the systemic circulation, and the blood returning from the pulmonary circulation creates a volume load to the dominant right ventricle.[21] Recent modifications of the Norwood operation, involving replacement of the systemic-to-pulmonary arterial shunt with placement of a cyro-preserved non-valved conduit directly from the right ventricle to pulmonary arteries, have resulted in better maintenance of diastolic blood pressure, and in some centers have improved both hospital mortality and mortality after discharge for children undergoing the initial stage of palliation.[22] The advantage of placement of a conduit, however, has still to be proven in a randomized control trial.

The second stage of palliation is called the bi-directional Glenn operation. This consists of anastomosis of the superior caval vein to the right pulmonary artery, and takedown of the systemic-

to-pulmonary arterial shunt or conduit.[23] Results following the venous shunt are very good, and the overall operative mortality is reported to be from 2 to 5.4%. The third stage of palliation is construction of the Fontan circulation, which consists of routing the inferior caval venous blood through a conduit placed in the lateral wall of the right atrium into the pulmonary arteries, or through an extracardiac conduit. A fenestration is usually created between the medial wall of the baffle and the systemic atrium to allow decompression of the atrial conduit pathway into the systemic atrium. The fenestration is usually closed in the catheterization laboratory up to 1 or 2 years after the Fontan operation. Nowadays, the operative mortality for conversion to the Fontan circulation is also less than 5%. Cardiac catheterization is usually undertaken prior to both the second and third stages of palliation to study anatomical and physiological details, and to perform corrective interventions. Long-term and functional outcome data following the functionally univentricular palliation is currently being evaluated.

Unresolved questions

A number of unresolved questions continue to surround management and treatment.[24] Despite advances in surgical techniques and medical therapies, those with the syndrome continue to have the highest mortality of all congenital cardiac malformations for infants less than one year of age,[25] rivaling in this regard those with pulmonary atresia and intact ventricular septum, and those with isomerism of the right atrial appendages, or asplenia syndrome. Although survival following initial surgical intervention has improved over the last 20 years, pediatric cardiologists continue to be challenged by discussions with families regarding initial decision relative to treatment, and long-term prognosis.[26-28] This is due in part to the limited information available in short-term and long-term functional and cognitive behavior in these children. The information that is available suggests that, regardless of surgical approach, staged surgical reconstruction or transplantation, long-term functional and cognitive behavior is strongly related to initial condition at diagnosis, and hence is variable.[29-31] Prenatal diagnosis, fetal intervention, and its impact on survival after the first stage of palliation, are areas of current study.[32-34] The limited information available has suggested that infants diagnosed during the prenatal period are more likely to survive the initial stage of palliation as compared to those that are not diagnosed during the prenatal period.[35] Small controlled clinical studies are investigating intervention in the fetal period to prevent the development of the syndrome through the use of balloon dilation and placement of stents in areas of restriction or hypoplasia. Short-term outcomes for this prenatal intervention are variable, and continue to be studied.[36,37]

Another ongoing discussion, less in the United States of America than in Europe, involves the option of no intervention, known as compassionate care, and otherwise described as passive euthanasia. Until 1980, when the Norwood procedure was introduced, compassionate care was the only option available to infants born with the syndrome. Recent studies seem to suggest most diagnosed infants now initially undergo a surgical intervention, but it is not clear if the option of lack of intervention is discussed with families at the time of initial pre- or postnatal diagnosis.[38-49]

Psychosocial concerns

Comprehensive counseling by the health care team is a critical component of care for the family of a child born with hypoplastic left heart syndrome. A review of the current outcomes of surgical intervention, as well as studies describing neurological and developmental outcomes, will guide families in their choice of treatment, or lack of treatment. For families who elect to have surgical intervention, care for their afflicted child is associated with numerous hospitalizations, services of a multidisciplinary team of specialists, and use of both advanced and innovative technology. The significant financial burden, or out of pocket expenses, that the family will incur should also be part of the preparation. Additional outside support can be provided by directing families to support groups available for families who have a child with congenital cardiac disease, and other online resources.

Conclusion

As a result of advanced technology, refined surgical techniques, and catheter-based interventions, the mortality in the short term has improved dramatically for children born with hypoplasia of the left heart. The syndrome, nonetheless, it is still considered one of the most complex congenital cardiac malformations to manage. Many unresolved questions regarding treatment, and long-term functional and cognitive outcomes, remain for these children. Further information on these topics is required appropriately to guide discussions with families regarding initial options for treatment, long-term survival, and quality of life.

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Support to a Woman by a Companion of Her Choice During Childbirth: A Randomized Controlled Trial

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Abstract

Background: To evaluate the effectiveness and safety of the support given to women by a companion of their choice during labor and delivery.

Methods: A total of 212 primiparous women were enrolled in a randomized controlled clinical trial carried out between February 2004 and March 2005. One hundred and five women were allocated to the group in which support was permitted and 107 to the group in which there was no support. Variables regarding patient satisfaction and events related to obstetrical care, neonatal results and breastfeeding were evaluated. Student's t-test or Wilcoxon's test, chi-square or Fisher's exact test, risk ratios, and their respective 95% confidence intervals were used in the statistical analysis.

Results: Overall, the women in the support group were more satisfied with labor (median 88.0 versus 76.0, $p < 0.0001$) and delivery (median 91.4 versus 77.1, $p < 0.0001$). During labor, patient satisfaction was associated with the presence of a companion (RR 8.06; 95%CI: 4.84 – 13.43), with care received (RR 1.11; 95%CI: 1.01 – 1.22) and with medical guidance (RR 1.14 95%CI: 1.01 – 1.28). During delivery, satisfaction was associated with having a companion (RR 5.57, 95%CI: 3.70 – 8.38), with care received (RR 1.11 95%CI: 1.01 – 1.22) and with vaginal delivery (RR 1.33 95%CI:1.02 – 1.74). The only factor that was significantly lower in the support group was the occurrence of meconium-stained amniotic fluid (RR 0.51; 95%CI: 0.28 – 0.94). There was no statistically significant difference between the two groups with respect to any of the other variables.

Conclusion: The presence of a companion of the woman's choice had a positive influence on her satisfaction with the birth process and did not interfere with other events and interventions, with neonatal outcome or breastfeeding.

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Background

The rates of maternal and neonatal mortality and morbidity decreased as a consequence of the adoption of modern obstetric practices, especially during labor and delivery. However, obstetrical interventions continued to increase, particularly the rate of Caesarean sections. Active management is based on the assumption that the preventive management of events that may potentially result in adverse effects in the mother or the fetus reduces the morbidity rates of both.

Support provided during labor and delivery by professional healthcare workers, non-medical female attendants and trained women (doulas) assigned to this task has been evaluated in controlled studies. Data suggest that the effects of support are associated with a reduction in the dissatisfaction or negative perception of women towards giving birth, in the use of analgesia/anesthesia, and in the frequency of instrumental vaginal delivery (forceps and vacuum extraction) and Caesarean section.

Based on scientific evidence, the World Health Organization recommends that the parturient should be accompanied by people she trusts and with whom she feels at ease, possibly her partner, a friend, a doula, a nurse or midwife. However, the effects of the support provided by the presence of the woman's chosen companion on her satisfaction, on the events of labor and delivery and on perinatal results have not yet been fully evaluated in controlled studies. The usefulness of support and the type of support provided by family members, a partner or by friends of the woman have only been evaluated in observational studies.

It is important to recognize and understand the influence of such support not only because of its effect on obstetrical and

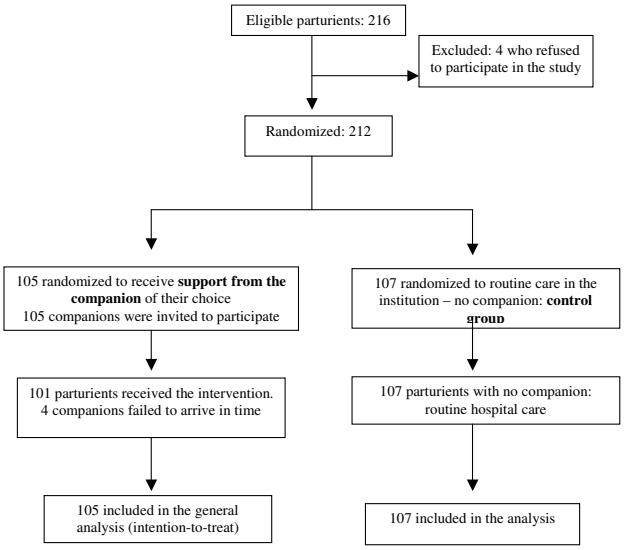

Figure 1
Flowchart of participants through trial.

Table 1: Baseline sociodemographic and obstetrical characteristics of the women, according to group

Characteristic	Support (n = 105)	Control (n = 107)
Age [mean in years (range)]	20.6 (13–42)	20.1 (14–36)
In a stable union (n)	80 (76.2%)	92 (85.9%)
Secondary education (n)	103 (98.1%)	106 (99.1%)
Religious (n)	96 (91.4%)	100 (93.4%)
Non-white skin color (n)	79 (75.2%)	75 (70.1%)
Housewife (n)	63 (60.0%)	67 (62.6%)
Start of prenatal care (GA < 28 weeks) (n)	101 (96.2%)	103 (96.3%)
Number of prenatal visits ≥ 6 (n)	84 (85.0%)	84 (78.5%)
Accompanied during prenatal care (n)	44 (41.9%)	54 (50.5%)
Participated in classes for pregnant women (n)	16 (15.2%)	16 (14.9%)
Gestational age at delivery [mean in weeks (range)]	39.2 (37–42)	39.0 (37–42)
Cervical dilation at admission [mean in cm (range)]	3.9 (3–6)	3.9 (3–6)
Cervical effacement ≥ 80% (n)	75 (71.4%)	68 (63.6%)
Intact amniotic membrane (n)	82 (78.1%)	83 (77.6%)

There were no statistically significant differences between the groups.

perinatal events but also on the patient's attitude towards the birth experience itself. Although, since 2005, following some initial isolated state initiatives, it is guaranteed by national law to all Brazilian women to have a companion of her choice present during labor, it is not respected by many services and providers. Due to the paucity of evidence-based data available on the effects of the presence of a companion of the woman's choice during the birth process, especially in developing countries, this study was developed to evaluate the influence of this support provider on the satisfaction of the parturient with labor and delivery and on perinatal and breastfeeding outcomes in the twelve hours following delivery.

Methods

A randomized controlled trial was carried out between February, 2004 and March, 2005 at the Sumare maternity hospital linked with the University of Campinas, São Paulo, Brazil. Sample size was based on a previous study in which the support given by nurses during delivery was evaluated. Considering a difference of 15.1% between the groups regarding patient satisfaction, a significance level of 5% and a power of 80%, minimum sample size was calculated at 96 patients in each group. Considering a possible loss of information or discontinuation of up to 10%, total sample size was calculated at 212 women.

Inclusion criteria were: primiparous pregnant women with a single, term live cephalic fetus; in active labor – cervical dilation ≤3 cm and ≤6 cm; intact membranes or amniorrhexis of ≤2 hours; uterine height < 40 cm; no evidence of cephalic-pelvic disproportion or fetal distress. Exclusion criteria were: unavailability of a companion; fetal malformation; maternal disease and/or indication for elective Caesarean section.

The study was approved by the Institutional Review Board and by the director of the hospital. At the time of the study for women to have a companion during labor was not a policy at that institution, as it is still not for the majority of institutions in Brazil. Therefore, to participate in such study would theoretically represent a potential benefit for the women. The eligible women and their chosen companions were supplied with information on the objectives and design of the study, and agreed to participate by signing an informed consent form.

Randomization was carried out using a computer-generated sequence of 212 random numbers. The individual assignment numbers were all placed in an opaque container to assure the concealment. The eligible women who had agreed to participate in the study selected one of the numbers once, and were therefore allocated either to the intervention group (with support) or to the control group (no support) according to the list. Support was defined as presence of a chosen companion during labor and delivery.

In both groups, care during labor and delivery was provided according to the routine protocol of the institution, including active management of labor, a relatively common procedure in Brazilian maternities: early amniotomy, use of oxytocin, intermittent electronic fetal monitoring, and systematic analgesia. At this institution, a companion during labor and delivery had not previously been permitted. This was the only difference between the two groups.

The companions received standardized verbal and written instructions provided by the principal investigator, containing information on: the activities involved in providing support to the woman (stay beside her, provide support, be affectionate, keep her calm, massage her, stimulate and encourage her), expected behavior when confronted with signs of tiredness, anxiety, concern, crying, screaming and/or the woman's feelings of inability to cope; compliance with regulations (use of standardized clothing, no eating, no smoking, no touching the equipment or material, contact the nursing staff if need to leave); and the possibility of requesting information from staff. The need to preserve the privacy of the other women was also emphasized. There were no specific instructions for the health professionals.

Table 2: Risk ratios and 95% confidence intervals for satisfaction ("well satisfied" or "very satisfied") during labor and delivery, according to group

Variable	Support (n = 105)	Control (n = 107)	RR (95%CI)	p value
Labor				
Evolution of labor	56	49	1.16 (0.89–1.53)	0.272
Having a companion	96	13	10.08 (5.38–18.89)	<0.0001*
Care received	98	90	1.11 (1.01–1.22)	0.034
Medical guidance	94	84	1.14 (1.01–1.28)	0.028
Guidance from nursing staff	94	89	1.08 (0.97–1.20)	0.178
Delivery				
Evolution	73	60	1.24 (1.00–1.53)	0.042
Having a companion	95	19	8.17 (4.51–14.78)	<0.0001*
Care received	98	90	1.11 (1.01–1.22)	0.034
Medical guidance	91	86	1.08 (0.96–1.22)	0.217
Guidance from nursing staff	93	92	1.13 (0.72–1.77)	0.571
Type of delivery				
Vaginal	58	44	1.33 (1.02–1.74)	0.033
Caesarean	2	6	0.40 (0.10–1.40)	0.193*

Chi-squared test, *Fisher's Exact Test

The outcomes included satisfaction, assessed by asking the woman about how she felt during labor and delivery (evolution of labor, having a companion or not, instructions received from doctors and nursing staff, healthcare provided and type of delivery). These questions were answered by choosing one of a sequence of five symbols with facial expressions corresponding to "very dissatisfied", "dissatisfied", "satisfied", "well satisfied" and "very satisfied". Satisfaction assessment was carried out between 12–24 hours post delivery at rooming-in care unit. For the purpose of analysis, satisfaction was considered to have been achieved whenever the answers of "well satisfied" or "very satisfied" were given. We collected data on the following outcomes: duration of first stage of labor; amniotomy in relation to the time of hospital admission and cervical dilation; color of amniotic fluid; use of oxytocin in relation to cervical dilation; time of analgesia in relation to cervical dilation and time of admission to hospital; presence of functional dystocia and changes in fetal wellbeing; length of the second stage; time between hospital admission and delivery; time from analgesia until delivery; type of delivery (vaginal/Caesarean). Neonatal outcomes were: Apgar score at 1 and 5 minutes, birthweight, admission to the neonatal intensive care unit (NICU), and immediate mother-infant contact following delivery. Variables regarding breastfeeding were: the ability of the infant to take the breast and suckling in the delivery room and in the 12 hours following delivery, cracked nipples and the number of breast-feeds in the first 12 hours.

We used SAS software program, version 8.2 for statistical analysis. An intention-to treat-analysis was performed. Mean and medians were calculated for continuous variables, while Student's t and Wilcoxon tests were used to assess differences between groups. For categorical variables, chi-square or Fisher's exact tests were used. Risk ratios and their respective 95% confidence intervals were calculated for the main outcomes. Significance was established as $p < 0.05$.

Results

A total of 212 parturients participated in the study, 105 in the intervention group and 107 in the control group (Figure 1). From a total of 105 companions, most common was the woman's partner/father of the child (47.6%), followed by the woman's mother (29.5%) or another female relative (aunt, mother-in-law, sister, cousin, sister-in-law, grandmother) or friend (22.8%). A total of 49.5% of companions were already present when the parturient was admitted to hospital, while 50.5% were located and invited to participate by telephone. The mean age of companions in this study was 33.5 years (range 18–62 years). Most (68.3%) had primary education and 71.3% had paid employment. Their support was provided continuously and they left the woman's side only sporadically.

Table 1 shows that there were no significant differences between the groups in sociodemographic and obstetrical characteristics of women at the time of hospital admission. Regarding satisfaction with the birth experience, having a companion during labor and delivery were strongly associated with higher satisfaction in the intervention group. The women of this group were also more satisfied with the care they received during labor, with the medical guidance given during labor, with care received during delivery, and with vaginal delivery, than women in the control group (Table 2).

The occurrence of meconium-stained amniotic fluid was the only obstetrical outcome related to labor or delivery that was statistically significantly lower in the intervention compared to the control group (RR 0.51; 95%CI: 0.28 – 0.94), (Table 3). Regarding the newborn and breastfeeding outcome, there were no statistically significant differences between the intervention and control groups (Table 4).

Discussion

These results show that the support provided by a companion of the woman's choice during labor and delivery had a positive effect on her satisfaction with the birth experience. Although the opinion of the health professionals were not assessed systematically, it seems that this intervention was well-accepted by them. No previous training was offered to the health workers, and the companions underwent no prior preparation. Therefore, the assistance the women in both groups received during labor and delivery was the standard care routinely provided in that hospital, and there were no changes in management. It is important to emphasize that this is not a study about doulas and if on one hand there is a general belief that a labor companion has always positive effects, there are, on the other hand still a lot of health facilities where companions are not allowed, especially in developing settings. It was and still it is expected that the results of this study could help providers to acknowledge and respect women's rights during birth.

Satisfaction may have been influenced by assessment in the first 12–24 hours postpartum, in which feelings of dependency and benevolence and a halo effect are common. This effect describes a lack of criticism due to social ability and/or fear of reprisals, or because of a sensation of relief at having gone through a safe experience and having a healthy baby. However,

Table 3: Effects of intervention on the events of labor and delivery, according to group

Event	Support (n = 105)	Control (N = 107)	RR (95% CI)	p value
Cervical dilation [median (range)]				
Amniotomy	5 (3–8)	5 (3–10)	-	0.958†
Oxytocin	4 (3–9)	4 (3–9)	-	0.653†
Analgesia	5 (3–10)	5 (3–10)	-	0.253†
Functional Dystocia				
Absent	99	97	-	0.655
Tachysystole	2	3	0.66 (0.11–3.87)	
Hypo/oligo-systole	4	7	0.58 (0.17–1.91)	
Color of amniotic fluid				
Clear	91	80	-	0.020
Meconium-stained	13	26	0.51 (0.28–0.94)	
Fetal heart rate				
Unaltered	81	76	-	
Altered	24	31	1.18 (0.84–1.66)	0.309
Type of delivery				
Vaginal	94	95	-	
Caesarean	11	12	0.93 (0.43–2.02)	0.862
Time [median (range)]				
First stage of labor§ (h)	3.4 (1.2–15.5)	3.8 (1.4–11.8)	-	0.123†
Admission – amniotomy (h)	1.1 (0–6.9)	1.2 (0–9.0)	-	0.639†
Admission – analgesia (h)	1.7 (0.1–7.8)	1.8 (0.3–9.3)	-	0.283†
Second stage of labor§ (min)	18 (4.8 – 75)	16.2 (1.2–48)	-	0.368†
Analgesia – birth (h)	2.3 (0.1–14.6)	2.3 (0.1–8.6)	-	0.605†
Hospital admission – birth (h)	3.8 (1–16)	4.3 (1.3–12.2)	-	0.284†

†Wilcoxon test, §Caesarean sections excluded, Chi-square test

this effect would probably be the same for both groups and could not explain the difference between them.

Experience during birth has been evaluated in controlled studies in which the type of care provider (doula, nurse or lay-person) varied. In most cases, anxiety, self-esteem, feelings of failure and difficulty, as well as levels of personal control and pain were assessed. In the present study, a chosen companion was the most important factor affecting the satisfaction of the parturient with labor and delivery, similar to what was found by Bertsch et al. In other controlled studies the presence of a partner or other family member was not permitted or it was already a common practice in the institution and was therefore not evaluated. These findings differ from those of Langer et al., who reported that support had no influence on women's satisfaction in a study in which the presence of family members was not allowed and the majority of doulas were retired nurses.

In the intervention group, women's greater satisfaction with the guidance received from the doctors during labor has also been identified in another study with a different population, evaluated when the woman was accompanied by a person of her choosing. When doulas or professional healthcare workers are the support providers, instructions are generally supplied by these individuals. Support also increased satisfaction with the care received during labor and delivery, and this finding is in agreement with data already reported when the women received support from nurses.

Support also contributed towards satisfaction with vaginal delivery. Similar results were reported in other studies where women in the control group considered the experience of giving birth worse than they had imagined, compared to those in the intervention group. Therefore, it would appear that the presence of a person specifically designated to provide support positively influences the woman's perception of the birth experience itself, as seen in some meta-analysis and systematic reviews. This higher level of satisfaction may have been influenced by the woman's expectations and the way in which she perceived her care and by having a companion in a setting in which normally this would not be permitted.

Similar conclusions may also be drawn with respect to pain, which is considered a great generator of dissatisfaction. In our study, however, all the women were submitted to analgesia during labor. It would appear that the influence of pain and pain relief on satisfaction is not as obvious, direct or beneficial as the influence of the attitudes and behavior of professional health workers. Further studies are required to investigate the influence of pain on satisfaction.

The finding of a lower occurrence of meconium-stained amniotic fluid may be due to a possible reduction in the anxiety of women who received support, although this was not measured. It is known that an elevated level of maternal epinephrine resulting from stress affects blood flow to the fetus through an α-adrenergic constrictive effect on uterine vascularization, causing transitory hypoxia. On the other hand, emotional support and the measures of comfort and information provided to the woman may reduce her anxiety and fear.

The lack of effect of support on any of the other events may have been due to the nature of the study protocol, in which active management of labor was adopted, as it is relatively common in a great proportion of Brazilian maternities, although not confirmed as a real effective intervention. This possible bias

Table 4: Effects on the newborn infant and breastfeeding outcomes, according to group

Outcomes	Support (N = 105)	Control (N = 107)	RR (95%CI)	p value
Apgar score at 1 minute < 7	20	21	0.97 (0.56–1.68)	0.915
Apgar score at 5 minutes < 7	3	2	1.53 (0.26–8.96)	0.681*
Birthweight (g) (mean ± SD 95%)	3.197 (2.360–4.245)	3.246 (2.410–4.145)	-	0.370¶
Admission to NICU	5	6	0.91 (0.47–1.77)	0.781
Immediate contact mother/newborn	52	41	1.29 (0.95–1.76)	0.100
Time of contact mother/newborn (min) (mean ± 95% SD)	25.1 (10–55)	22.7 (10–40)	-	0.360†
Takes breast/suckles in delivery room	12	7	1.75 (0.72–4.26)	0.213
Takes breast/suckles (12 h following birth)	99	100	1.08 (0.59–1.97)	0.801
Breast fissure	7	6	1.19 (0.41–3.42)	0.747
Number of breast-feeds 12 hours following birth (mean)	4.3 (0–12)	4.4 (0–10)	-	0.589†

Chi-squared test, * Fisher's Exact Test, ¶Student's t-test, † Wilcoxon's test

may have minimized the positive effects of support on some of the outcomes. This makes the finding of less lower occurrence of meconium-stained fluid even more important, possibly reflecting the positive stress-prevention aspect of support in labor in its potential impact over the newborn. This data is in agreement with results from a multicentric study carried out by Hodnett et al. in which support was provided by nurses. The benefits of support may be surpassed by the rates of intervention carried out in the environment in which delivery occurs; routine analgesia being the factor that most reduces the effect of support on obstetrical interventions.

The results regarding the duration of the first stage of labor are contradictory to data reported from studies in which support was provided by lay-women, doulas and midwives, where it was reduced. However, it must be considered that in our study first stage of labor was short in both groups. With respect to Caesarean section, it is noteworthy that rates were low in both groups, and there was no effect of labor support on these rates. This finding is in conflict with reports from other studies in which the rate of Caesarean section was lower in the group receiving support.

In general, support had no effect on the management of labor in the institution. Interventions such as the use of oxytocin, amniotomy and analgesia, when evaluated in relation to cervical dilation, were carried out early in both groups, and the time between hospital admission, analgesia and amniotomy was less than two hours. Intervention had also no influence on neonatal outcomes and these data are in agreement with other trials. In this study, results regarding breastfeeding were similar in the two groups; however, breastfeeding was only analyzed in the first twelve hours following delivery, while ideally it should be evaluated the first months following delivery.

Conclusion

One important finding of this study is that a lay-companion in places where its presence had not previously been permitted has no effect on the routine of care. The fact that the women with support reported higher levels of satisfaction with the medical information/guidance they received indicates that perhaps there was a change in attitude. Perhaps because there was someone else in the room, medical staff were more forthcoming and user-friendly than when no support person was present. These findings of higher patient satisfaction may also encourage and sensitize healthcare providers to adopt this practice in health institutions where such a support companion is not permitted, or even where doulas, lay-persons or professional healthcare providers are designated to this role.

In this context, this study may provide a basis for the planning and execution of actions aimed at implementing this practice. Moreover, it may contribute towards increasing the value of the presence of a companion of the woman's choice. Additionally this type of support incurs no extra onus to the institution or to the woman. Therefore, socioeconomic status is not a factor that would limit or impede the implementation of this action. Both the women and the healthcare providers may benefit from this practice, since support improved maternal satisfaction with the birth process, and consequently benefits all those involved in this process. This hopefully could be an advertisement to all places where women still deliver alone.

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Patent #US 6,502,573 B1 Other Patents Pending
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Antenatal Screening and the Gendering of Genetic Responsibility

Kate Reed

Abstract

Background: The objective of this study is to explore men's and women's perceptions of antenatal blood screening. The study will assess the impact of these perceptions on decision making regarding diagnostic testing and selective abortion, and on parental feelings of genetic responsibility. By exploring gender and antenatal screening in this way, the research aims to contribute to our understanding of lay perceptions of genetic screening and increase our knowledge of the decision-making process in screening.

Research design: This qualitative study will be based on semi-structured interviews with twenty pregnant women and twenty male partners in the post-industrial city of Sheffield, UK. All interviews will be taped, transcribed and analysed thematically using NVIVO, a qualitative software package.

Discussion: The findings of this study have relevance to existing debates on the social and ethical implications of reproductive genetics. A better understanding of male and female perceptions of the screening process could improve guidance and practice in antenatal screening and genetic counselling. It will also inform and contribute to the development of theory on gender and genetic screening.

Background

Within the UK, antenatal blood tests are routinely offered to women in pregnancy during the first NHS dating scan at around 12 weeks gestation. At this time pregnant women are offered a range of tests which include screening for maternal diseases and screening for fetal health. These include tests that identify those who are affected by or at an increased risk of developing a genetic disorder. Such tests include hemoglobinopathy screening for genetic conditions such as sickle cell anemia and thalassemia.[1] Blood tests for the hormone human chorionic gonadotrophin (hCG), the protein alpha-feto (AFP) and the protein unconjugated oestriol (uE3) are also offered at this time.[2] This is often known as the triple test and is used to estimate the risk of spina bifida, Down syndrome and anencephaly.[3] Screening takes place at the first dating appointment with the exception of the triple test that takes place after week 14 of the pregnancy. The study on which this protocol is based will be concerned with both hemoglobinopathy screening and with the triple test.

During the screening process the emphasis is on testing women. Male partners are tested only where a combined positive male and female test could detect fetal abnormality, such as sickle cell anemia. Little is known about male partners' views and involvement in antenatal blood screening and their impact on parental feelings of genetic responsibility. Existing research has tended to focus on women as the main recipients of screening and on women's feelings of maternal responsibility.[4] While existing research does acknowledge that factors such as partners, family and peers may play a role in women's screening choices and decisions in antenatal screening, little research focuses in detail on men's roles in screening and antenatal care. For example, little work has been conducted on expectant fatherhood and ultrasoundography.[5] This lack of focus on men's roles can be related to two issues: first, research tends to focus on pregnant women because pregnancy takes place in the female body and thus women are automatically connected to the fetus.[6] Secondly, men are often reticent to take part in research on pregnancy because it is perceived to be a women's issue.[7] However, the nature and optimal level of father involvement continue to interest researchers.[8] Furthermore, researchers often highlight the importance of including men in research on antenatal screening. An American study on amniocentesis found that male partners of pregnant women deeply influenced their partners' decisions to use or refuse antenatal diagnosis and selective abortion.[7] This study highlights the need for more research on gender that includes a focus on both men's and women's perceptions of antenatal screening. A better understanding of the impact of gender on this process will contribute to guidance and practice in antenatal screening and genetic counselling.

Through empirical research with twenty pregnant women and their male partners in Sheffield, UK, this study aims to explore the impact of gender on antenatal blood screening. The study will

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take an inductive approach to research not a deductive one, with research problems being explored empirically. The two main research problems to be addressed here are: first, does gender influence choice and decision-making in antenatal screening and, if so, in what ways does it do so? For the purposes of this study gender will be defined as the socially structured differentiation of the sexes.[9] Secondly, does gender affect potential parental feelings of genetic responsibility and, if so, how? What this refers to is an exploration into whether one parent feels more responsible than the other for the genetic status of the fetus. If so, how does this affect decisions made about screening and diagnostic testing?

In order to address these two main research problems, the following subsidiary research questions will be asked within the study:

- How involved are men in the screening process?
- How far do women consult their partners about which tests to opt for and why?
- Do women and men feel equally responsible for the genetic status of the fetus?
- Does the screening process enhance a traditional gendered division of labour whereby women take the major responsibility for the fetus -or does it challenge traditional gender divisions?
- Finally, how does the gendered nature of the screening process affect any decisions made about the fetus?

In asking such questions, the study aims to explore the impact of gender on antenatal screening, on decision-making and on feelings of parental genetic responsibility.

Method

In order to assess women's and men's attitudes to antenatal blood screening, a method is needed which generates 'open' data rather then imposing a formalised set of questions.[10] Thus the method chosen for this research is semi-structured interviewing. This method involves posing open ended questions to respondents and following the responses with further questions. This method is often used in qualitative research because it enables the researcher to explore issues in detail.[11] Researchers who take this approach often use a semi-structured guide as a basis for this type of interviews.[12] Within this study an open ended interview schedule will be used. In order to obtain data relating to the research questions stated in this protocol, the interview schedule will be based around screening procedures themselves and the decision- making process. Examples of the types of interview questions to be asked include: which blood tests are opted for and why? Do couples decide which tests to opt for together or does one partner take a more active role in making decisions about screening? Do men and women make decisions about diagnostic tests as a couple or does one partner take more responsibility? The same interview questions will be used for both men and women.

Sampling: Twenty pregnant women and their male partners will be interviewed within the study, making 40 respondents overall. The primary investigator has substantial experience of conducting small scale studies such as this one.[13-15] Based on previous experience the primary investigator felt that this number of respondents would elicit a substantial but manageable amount of data. However, we will use a flexible approach to sampling, which is common in qualitative research.[16] Should forty respondents yield little data then more interviewing will be conducted. If research categories become saturated at an early stage (see analysis) then fewer interviews will be conducted. This is what is known as an iterative approach to research- that is there is a repetitive interplay between the collection and analysis of data.[11]

Research on antenatal screening has highlighted the importance of variations according to social class and ethnicity.[17-18] The sample will therefore be stratified according to ethnicity and social class. Ethnicity will be measured here using respondents own selfdefinition.[19] Social class will be measured using the NS-SEC occupational classification system.[20] In order to access a diverse sample respondents will be recruited from two distinct localities in Sheffield. Ten women and their partners will be recruited from location 1. This is an electoral ward with a non white population of 30% and where average weekly earnings are below the national average. The second group will be recruited through local midwives in location 2. This is an electoral ward which has a white population of 95% and where the average income is above the national average.

In order to adequately explore the screening process, pregnant women in the study will be at the point of at least 17 weeks' gestation. The reason for selecting this phase of the pregnancy relates to the dates at which blood screening occurs. Hemoglobinopathy screening normally takes place during the first dating scan at 12 weeks with the 'triple test' being offered at around 16 weeks. In order to gain respondents views on these tests women and their partners will be interviewed after they have taken place. To access a wide range of views on screening, respondents will include women and men who are experiencing first, second and third pregnancies. Respondents will have to be between 18 to 40 years of age. These variables will be used as criteria for recruitment and will also be used during data analysis to see if there are any patterns in the effects of gender according to age and number of pregnancy.

Recruitment: Respondents will be recruited through local NHS community and hospital midwives in Sheffield, UK. Midwives practicing in the hospital and in the two relevant community locations will initially be approached by the primary investigator. Information sheets about the research will be given to the midwives and they will be briefed on recruitment criteria. Once their cooperation has been obtained, the midwives will be asked to disseminate this information to pregnant women who meet recruitment criteria and ask women if they and their partners would be willing to participate in the study. If interested in participating, women can either confirm this with their midwife or alternatively contact the research team directly using a stamped self-addressed envelope. The research team will then wait to hear from the midwife and potential respondents and they will then approach those who have left their contact details.

Male partners will be recruited in two different ways. Where possible, they will be recruited during their attendance with partners to screening appointments. However, as men do not always attend routine antenatal appointments, they will also be recruited through pregnant partners. Once pregnant women have agreed to take part in the study, they will be asked if it would be possible to invite their male partners to participate. Another patient information sheet will be given to the women to pass onto the male partner with the same contact options as those outlined above.

As argued by many researchers, it is often difficult to recruit women of color and working class women in research on pregnant women and antenatal care.[17-18] It has often been argued that qualitative research on women tends to reflect the views of white middle class women because they tend to volunteer to participate in research more than any other group. This often leads to a self-selecting and biased sample. In order to try and address this issue social researchers tend to advocate the use of more labour intensive strategies such as verbal face-to-face contact, ethnicity matching and snowballing.[21] Within this study on gender and antenatal screening, two different geographical areas will be chosen in order to avoid a self-selecting sample. Should it prove difficult to elicit a diverse sample in this study, then more labour intensive strategies will be employed. This would probably involve contacting various pregnancy groups and local government initiatives in the relevant locations.

Data collection: Data will be collected by the primary investigator and one researcher through the use of an agreed interview schedule. The interviews will be conducted in antenatal clinics. Where possible interviews will take place in private rooms within clinics. If respondents are not happy with being interviewed in this environment, interviews will take place in respondents' homes or in a location suitable to them.

All interviews will last approximately 1 hour and will be tape-recorded. As with much social science research, issues may be raised relating to the reliability and validity of the project.[11] Semi-structured interviews, because of their subjective nature can be affected by interviewer bias. Issues of reliability are also called into question due to the fact that two people will be interviewing on this project rather than one person which may lend it further to interviewer bias. Furthermore, the subjective nature of the research also brings into question issues of validity as research accounts may be subject to misinterpretation and misrepresentation by the researcher. Within the study these problems will be counteracted by firstly providing a very clear interview schedule for both researchers to follow. The same questions will be asked of all respondents. In order to ensure validity, the interviewees' answers will be relayed back to them for verification after each interview.[22] In order to maintain reliability using two interviewers, some joint interviews will be conducted with both researchers present (at the start of fieldwork).

Ethical approval to conduct the study was granted by the South Sheffield Research Ethics Committee on 08/10/2006 Reference number 06/Q2305/155. All respondents will provide written consent prior to each interview. Respondents and interview transcripts will all remain anonymous.

Transcription and analysis of data: Having collected the data, it will be transcribed and analysed. In order to explore potential differences in social class and ethnicity the data from the two different locations will be analysed separately and then compared. The data will be analysed drawing on a grounded theory approach which means that the research will not start with a hypothesis, but rather, data will be used to inform existing social theories and also to develop new ones.[23]The process of data analysis will take several stages: First, interview transcripts will be reviewed and coded. Codes serve as shorthand devices to label, separate, compile and organize data.[24] NVIVO, a qualitative software package will be used to assist the coding process through the identification of commonly used words and phrases in the transcripts. After coding, data will then be organized into themes and categories. Social theories will then be developed using these themes and research categories.

Discussion

It is important to remember that this is only a small scale study and therefore the findings are not generalizable to the population at large. However, the findings of the research will offer a modest contribution to academic debates in the area of reproductive genetics. There has been much debate about the social and ethical issues of genetic antenatal screening, particularly because of the spectre of eugenics that hangs over genetic testing.[25] This research project will contribute to our understanding of the social implications of genetic screening by evaluating lay perceptions of men and women's roles in antenatal screening. Furthermore, the concepts and categories developed from the research will be used to inform existing social theories on gender, genetics and screening.

The research also has implications for health practitioners. Genetic counselling in antenatal screening is generally

considered to be of a high standard in the UK. According to recent reports however, the screening setting is often highly pressurized with too much emphasis on routine and not enough time to explore patient feelings towards screening and diagnostic tests.[26] Through increasing our understanding of people's perceptions of genetic testing, this qualitative study aims to offer a modest contribution towards enhancing screening practice. In particular, the study will provide us with a better understanding of screening among diverse populations. Thus it will enhance sensitivity to diverse populations in screening practices and genetic counselling. The research is also relevant to policy-makers who are attempting to make screening procedures more sensitive to the needs of potential parents.

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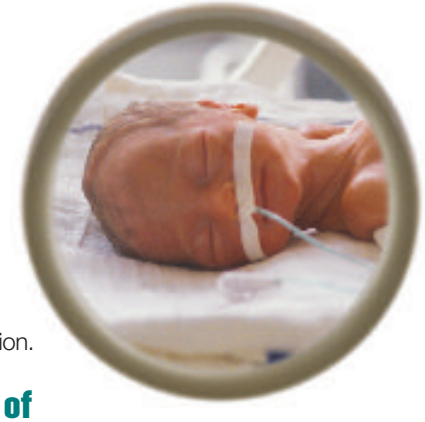
- ***RSV continues to be the most frequent cause of lower respiratory tract infections such as bronchiolitis and pneumonia among infants less than 1 year of age***[2]

Premature lungs are more vulnerable to severe RSV disease

Compared to full-term infants, 34-week gestational age (GA) infants have:

- ***Only 52% of the calculated lung volume***[3]
- ***About 35% thicker airway walls***[3]

This means that the lungs of 34-week GA infants have less volume to accommodate gas exchange.



At 1 year, prematurity continues to impact lung function. Results from a study conducted in premature infants (<36 weeks' GA) who had no history of respiratory disease during the neonatal period demonstrated:

- ***<50% of predicted lung function compared to the normal predicted value***[4,5]

Therefore, even healthy-looking premature infants may be susceptible to infection.

RSV disease can affect all premature infants regardless of degree of prematurity[6]

A study of infants hospitalized with RSV disease compared 33–35 week GA infants with those ≤32 weeks' GA. Hospital outcomes were found to be at least as severe in the 33–35 week GA group. These late preterm infants (33–35 weeks' GA) had a(n)[7]*:

- ***24% longer hospital length of stay***
- ***33% longer ICU length of stay***
- ***81% greater rate of intubation***

*These endpoints were not analyzed for statistical significance between the ≤32 week GA and 33–35 week GA groups.

The need for RSV prevention is critical

Unfortunately, RSV is highly contagious. And because even healthy-looking 33–35 week GA infants face severe consequences from RSV disease,[7] it is important to consider preventive measures for all at-risk infants.[6†]

†Infants with bronchopulmonary dysplasia or a history of premature birth (≤35 weeks' GA) and children with hemodynamically significant congenital heart disease.

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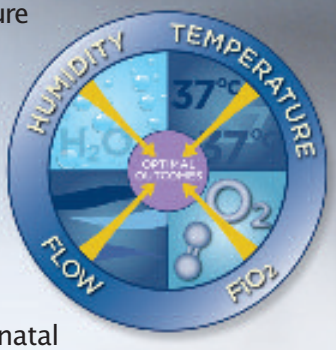

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[1]Brian Walsh, Comparison of high flow nasal cannula (HNC) devices. Respiratory Care 2006; Vol 51 No 11.

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