Vol. 20 No. 6
October 2007

neonatal INTENSIVE CARE

The Journal of Perinatology-Neonatology

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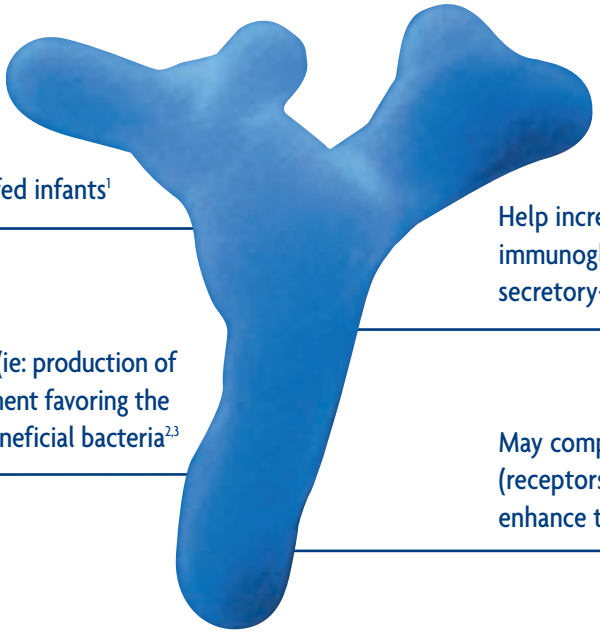

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Editorial

Emergent Issues

The following review, "Cradle or Grave," by Michelle Pridmore-Brown, appeared in the Times Literary Supplement, May 30, 2007. Pridmore-Brown reviewed the books Birth, by Tina Cassidy, Born in the USA, by Marsden Wagner and Bioethics and Women, by Mary Briody Mahowald. Here are some excerpts of what she had to say:

Much of birthing women's misery can be traced to "cephalo-pelvic disproportion." Bipedalism severely constrains our hip size – and big brains mean that even though babies are born too early in their development for anyone's comfort, they are still likely to get stuck in the birth canal. Rather aptly known as Eve's curse, the brain–pelvis stand-off is an evolutionary compromise that leaves little margin for error. This stand-off accounts for the fact that most women experience far more pain during childbirth than their primate cousins; for an African proverb stating that pregnant women have one foot in the grave; and for the fact that the skill of an attendant can easily make the difference between life and death. Up to the 1930s or so, it is estimated that about 1 per cent of birthing women died (and far more of their babies). The journalist Tina Cassidy's book on birth describes the diverse ways in which humans have addressed, rationalized and assigned blame for the perils of birth. She motivates her excavation by using her own twenty-first-century experience with cephalopelvic disproportion as a point of departure; what was to be her "planned" "natural" "birth experience" (each word semantically loaded in her telling) ended up being quite the opposite, thanks to her small pelvis, induction, an epidural and ultimately an emergency Caesarean section.

Cassidy unpacks various notions of the "natural" and shows the extent to which birth is in fact not just some timeless event, but culture- and class-mediated – whether it occurs among the !Kung San of the Kalahari (women give birth alone) or in Marco Polo's China (where fathers were put to bed for forty days with their newborns) or seventeenth-century Europe, when "barber surgeons" wrested the practice from persecuted but far more competent midwives, or early twenty-first-century Brazil, where up to 90 per cent of wealthy women opt for an elective C-section. Religious beliefs, too, have obviously had a significant role in birth – in persecuting midwives as witches, in adjudicating who was most worth saving (mother or baby), and in interpretations of pain. Cassidy's romp through modern history bears repeating because it also reminds us that "science," or at least medical obstetrics, is often a vigilante affair. For instance, after the move from midwives to doctors, mortality rates initially shot up, as did rates of postpartum debility. Hospital births starting in the eighteenth century were a huge liability; impatient obstetricians zealously used their instruments to wrest babies from only partially opened wombs; and doctors often did not wash their hands and so transmitted deadly puerperal fever from woman to woman – or, indeed, from corpse to woman. Even in the early twentieth century, after germ theory was known about, hospitals were still the worst places to give birth and yet, paradoxically, they became the birthing place of choice for an ever-increasing number of women; infant mortality jumped 50 per cent between 1915 and 1929 in the United States in lockstep with the widespread across-class shift from home to hospital.

Where Cassidy is a wide-eyed outsider with a lively style, Wagner is a pediatrician, perinatologist, policy wonk, expert witness at countless trials, and World Health Organization (WHO) adviser, he is a whistleblower with a clear agenda: namely, to convince his public that, in the US, obstetrics is still a vigilante practice and that the public is being duped in much the same way as it was in previous eras. In a nutshell, the birthing industry is in the midst of yet another dangerous fad: too much medical intervention in the names of two cultural values: convenience and control. Wagner believes these values are dangerous in the obstetrical context. Proof that things are amiss in the US: it has the second worst newborn mortality figures in the industrialized world, despite having the most expensive maternity system. Women are 70 per cent more likely to die in childbirth in the US than in Europe.
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neonatal INTENSIVE CARE

Published seven times each year by
Goldstein and Associates, Inc.
10940 Wilshire Blvd., Suite 600
Los Angeles CA 90024
Phone: 310-443-4109
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Circulation, Coverage, Advertising Rates: Complete details regarding circulation, coverage, advertising rates, space sizes, and similar information are available to prospective advertisers. Closing date is 45 days preceding date of issue.

Change of Address notices should be sent promptly to Circulation Department: provide old mailing label as well as new address: include zip code or postal code. Allow two months for change.

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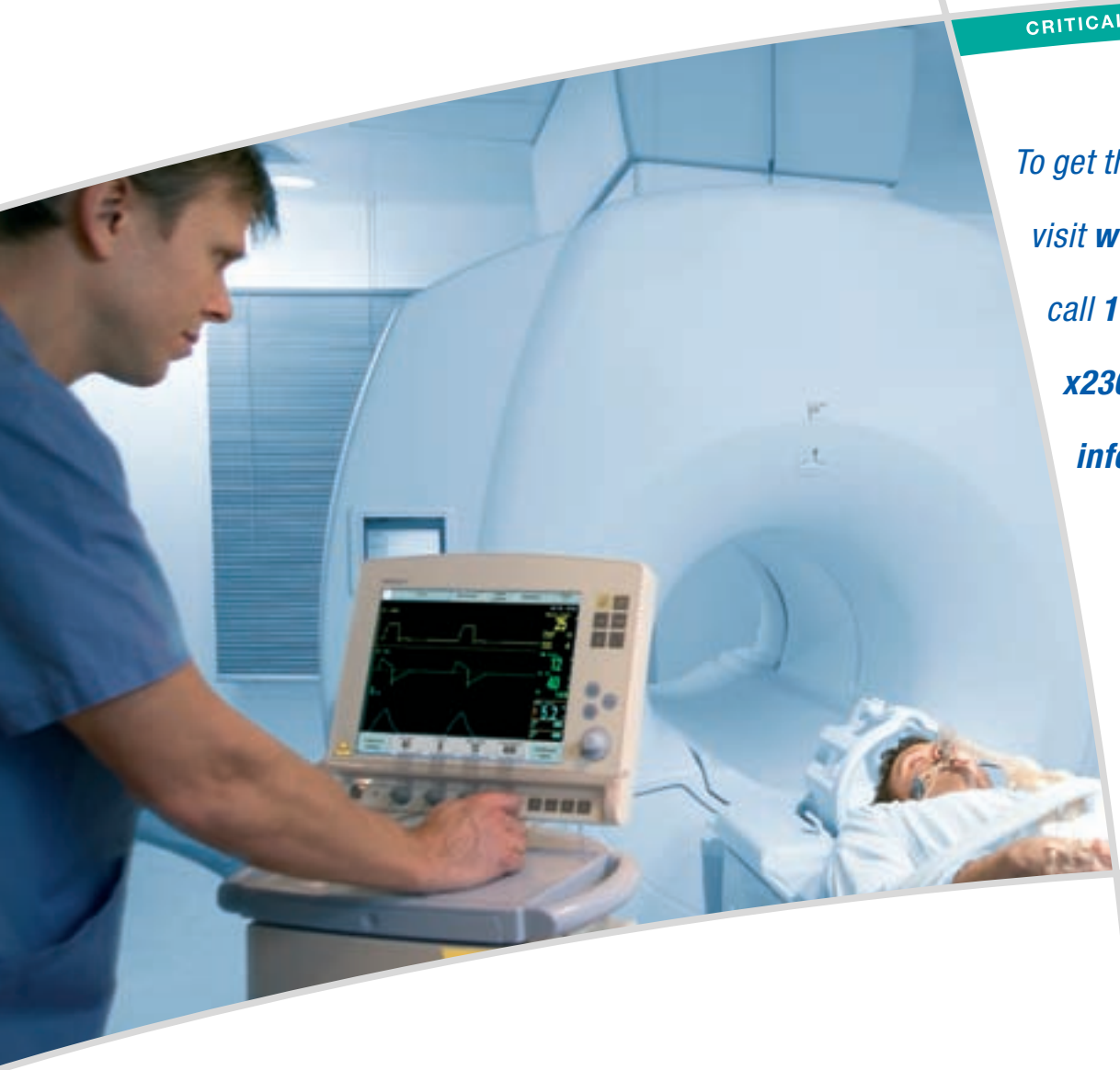

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News

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WOMB ROOMS

The New York Times reports on the latest trend in NICUs, so-called womb rooms where preemies and other neonates can have some privacy designed to mimic the environment of the womb. Such rooms are designed to offer the opportunity for uninterrupted sleep, indirect light, skin-to-skin contact and the assuring sound of parents' voices. Such care is meant to promote recovery after the rough experience of a premature birth. The Times references various studies which demonstrate that a womb-like environment promotes "a faster transition to independent feeding, fewer days needing extra oxygen, better growth and fewer days in the hospital. Once home, the infants show improved attention and motor skills, and better cognitive and social skills." According to the Times, "The science has been slow to materialize into square feet. Some hospitals are concerned about the space and the cost. Doctors and nurses ask whether they would have a good view of the babies if they were divided by walls, and have had to adapt to a cultural change that allows greater parental access." According to a professor of pediatrics at Stanford University, "It is an idea that should be carefully studied with multisite randomized trials before we spend millions redesigning NICUs." The Times noted that about 20 of the at least 800 neonatal intensive care units in the United States have completed projects where most or all of the rooms are private. About 40 are planning or building private rooms. Some welcome the trend, with one doctor remarking, "Our N.I.C.U. is like a casino. You walk in, and there are monitors going off, ventilators. Imagine weighing a few pounds and you are subjected to that for 120 days." The Times article barely alluded to the cost of such units, merely noting that neonatal intensive care, in general, was expensive.

GOING FAST

Half of the sextuplets recently born prematurely to a Minnesota couple have now died. The four boys and two girls were born about 4 months early at a Minneapolis hospital. Doctors had advised the couple to selectively reduce the number of viable fetuses to two, but they declined. The four boys and two girls were born in the 22nd week of pregnancy and weighed from 11 ounces to 1 pound, 3 ounces. The parents spent more than a year trying to conceive, using fertility drugs.

TAKE TWO

Taking aspirin throughout pregnancy could reduce the risk of the potentially dangerous condition preeclampsia, according to a study at the University of Sydney. The results suggested cases of preeclampsia could fall by 10% if aspirin was taken widely. Experts urged caution, given the small risks linked to long-term aspirin use. However, the study found no evidence that taking aspirin long term might be linked to bleeding problems at any stage, although the researchers said that their evidence was not

strong enough to rule this out entirely. The research used information gathered by dozens of smaller research projects to try to come up with a reliable verdict on the risks and benefits of the treatment. It found that taking low-dose aspirin during pregnancy reduced the risk not only of preeclampsia, but also premature birth, and of poor pregnancy outcome in general. However, some doctors cautioned that while some women were so obviously at high risk that aspirin was justified, it was harder to balance whether the potential harm caused by aspirin was a price worth paying in pregnancies where pre-eclampsia was less likely, and wondered if treating 50 women to prevent one case of pre-eclampsia or one pre-term birth was worthwhile.

BABY BRAIN

Dr Joe Dispenza discussed life-long implications of maternal stress at the Gentle Birth World Congress in Portland, OR. Dispenza was recently featured in the new age film, "What the %$!* Do We Know." He said there's scientific proof that the mind-state of a pregnant mother affects the growth of her baby's brain, especially in the area of its forebrain, where the centers of logic, impulse and emotion reside. Scientists have known for years that chronically high levels of maternal stress negatively influence the birth weight and gestational age of the fetus, but studies done at the University of Kentucky's Chandler Medical Center in the late 90s suggested that maternal stress and stress hormones directly influence fetal brain development as well. Inadequate development of the forebrain has been suggested as a possible explanation for aggressive and antisocial behavior in children. Barbara Harper, founder of Waterbirth International, sponsor of the Congress, stated that an expectant woman's thoughts and emotions have a direct effect on her health, "which in turn impacts her birth experience." Similarly, her mental state alters the physical environment of the womb through increased or decreased blood flow and varying levels of hormones crossing the placenta, " which in turn directly affects the health of her baby."

BORN AGAIN

Born in Bradford is one of the world's biggest research studies into the reasons behind why some children fall ill while others do not. It will track the lives of more than 10,000 babies born in the city over three years from pregnancy, through childhood, until they become adults. Born in Bradford is the latest in the 60-year history of post-war birth "cohort" studies of society in Britain. Factors recorded by Born in Bradford researchers in pregnancy or early life may prove to cause illnesses or other problems later on. Blood samples will be taken from mothers and fathers before the birth and a sample will also be taken from the newborn baby. The family will also fill in a detailed lifestyle form asking about issues such as diet, living conditions and exercise. The families will be monitored annually and their profiles updated. The blood samples will provide a DNA profile of each person. That along with the questionnaires will allow researchers to assess how health is impacted by environmental conditions as well as genetic make-up. It will also become a valuable research tool for those looking at specific diseases such as epilepsy or asthma. Why Bradford? Despite being the fifth largest city in the UK the city's health is cause for concern. Bradford has higher than average levels of deprivation and child poverty. Life expectancy for both adult males and females is lower than the national average too. But one of the biggest causes for concern is the high infant mortality rate. The number of babies who die before reaching their first birthday is among the highest in the country.

TOO OLD?

A woman who gave birth to twin boys at age 60 said she was on a mission to let women know they have choices. Freida Birnbaum underwent in-vitro fertilization at a South African clinic that specializes in older women and gave birth by C-section. "I don't feel like I went through a lot of trauma during delivery or even through the process of being pregnant," she said. The hospital said she was the nation's oldest mother of twins. She already has three other children, but she said she wanted another child closer in age to their youngest son, and didn't want to adopt. Reported by the Associated Press via ABC News Internet Ventures.

BUSIER THAN YOU THINK

Midwives in the UK are delivering almost 25% more babies than some Tory experts believe is appropriate, figures released by the Conservative Party suggest. The Tories say the government's failure to anticipate a big rise in the birth rate in England has left midwives under intense pressure. They argue this could derail ministers' commitment to offering all women a choice of where to give birth by 2009. But ministers dismissed the claim as "scaremongering". Since 2001, the number of live births in England has increased by almost 71,000 (12.5%), and is now at a 26-year high. In 2006, 635,679 live births were recorded. However, the increase in the number of midwives has not kept pace, rising by 4.5% over the same period. The Royal College of Midwives recommends that each midwife should deliver 27.5 babies a year. The surge in live births meant that on average each midwife in England delivered 33.7 babies last year.

The Conservatives said government experts had under-estimated the actual number of live births last year by nearly 40,000. They said the intense pressure being placed on midwives explained why the rate of home births, which are time consuming and labor intensive, is relatively low. The health secretary argued that a shortage of midwives was jeopardizing the future of some maternity-led units as midwives were being deployed to larger consultant-led units to ensure safe staffing levels. A Department of Health spokesperson accused the Conservatives of "irresponsible scaremongering," noting that there are now 2,423 more midwives than there were 10 years ago.

RESEARCH AWARD

Professor Frank A. Manning MD is the recipient of the 2007 Fetal Research Award. He is a graduate of the School of Medicine at the University of Manitoba in Winnipeg, Manitoba Canada. After completing a rotating internship at University of Southern California he returned to Manitoba and completed a 4 year residency in Obstetrics and Gynecology. He was awarded a Queen's scholarship to Oxford University culminating in a Master of Science. While at Oxford he studied fetal breathing and published his seminal work on the regulation of human fetal breathing and the effects of smoking and hypoxia on fetal breathing. From Oxford he returned to the University of Southern California and began his groundbreaking work on the application of dynamic ultrasound in the assessment of the fetus. He published the original research on the nature and character of fetal movements, on defining fetal tone and on the measurement of amniotic fluid volume in health and disease. He devised and in 1981 reported on fetal biophysical profile scoring, a method of fetal assessment that has become the gold standard. By 2007 fetal biophysical profile scoring and its various iterations were in use all throughout the world and an

Dr F. Manning receiving Fetal Research Award (Golden Fetus) from Dr B. Petrikovsky (right), Scientific Director of the Foundation. Photo by Dr. Emil Gurshumov.

estimated 20,000,000 pregnancies are evaluated by this method annually worldwide. In 1983 he was among the first clinical scientists to devise and apply ultrasound-guided techniques for intrauterine surgery. His team reported on in utero treatments of fetal obstructive uropathy, pleural effusions and critical aortic stenosis. He is the founding member and past president of the Fetal Medicine and Surgery Society. For this groundbreaking work in the fields of dynamic ultrasound, fetal assessment and fetal therapy he received numerous honors including research awards from the Society of Obstetricians and Gynecologists of Canada, the Rh Society, among others. He has published 190 peer review articles, 270 abstracts, more than 200 invited submissions and 7 books. He remains in active practice and is a Professor at the School of Medicine at New York University. (See photo this page.)

NOT A CHANCE

The chances of your second child dying of cot death after losing your first have been overestimated, according to a new study set to reignite the debate. Failure to hold a postmortem, rule out murder or check for familial causes meant eight studies into the condition were defective, the UK research said. The authors of the report, published in Archives of Disease in Childhood, hope to reassure those who had lost a child.

But implying that murder may sometimes be involved will prove controversial. Researchers looked at eight studies produced in English since 1970 which had reported relative risks of cot death recurring ranging from 1.7 to 10.1 times that of the general population. The convictions of several mothers accused of murdering their young children have been overturned on appeal, mainly on the grounds that after losing one child to cot death there is a much higher chance of losing a second. Murder convictions have been overturned based on previous statistics about the chances for a second cot death. One doctor told a court that the chances of losing two children to cot death were 73m to one, but the Royal Statistical Society disputed those odds, saying there were closer to 200 to 1. Some experts said there was no evidence to back up the 1 in 200 assertion.

GET OUT OF THE STREET

Exposure of pregnant women to fine particulate matter from traffic may reduce their children's birth weight, according to researchers at INSERM in France and the National Research Center for Environment and Health in Germany. The study of

1,106 mothers and children collected information on the influence of living conditions and behaviors and its relation to the development of the immune system and allergies. On the basis of a measuring campaign at 40 locations in the city of Munich, the concentrations of traffic-related atmospheric pollutants during pregnancy, including fine particulate matter (those with a diameter of less than 2.5 micrometers, PM2,5), could be modeled at the home address of the pregnant women. The model took into account the distance of each home from streets, the population density near the home as well as the fluctuations in the concentration of the air pollutants over time during the pregnancies. The proportion of newborns with a birth weight below 3,000 grams increased with increasing concentrations of fine particulate matter during pregnancy. A similar association was observed between the absorbance of fine particulate matter and birth weight. The absorbance of particulate matter is considered to be a marker of the particles originating from traffic, and in particular from diesel vehicles. Researchers noted that the biological mechanisms which could explain the influence of air pollutants on the growth of fetuses are not known as yet. Fine particulate matter consists of hundreds of chemical substances. It is conceivable that a minor fraction of the fine particulate matter reaches the blood through the lungs and influences the placenta or other organs which are responsible for regulating the growth of the fetus. Studies from the US and Poland have for example shown that polycyclic aromatic hydrocarbons (PAH), which are produced during incomplete combustion processes, can reach the fetus and influence its growth.

FROZEN FIRST

The first baby created from an egg matured in the lab, frozen, thawed and then fertilized, has been born. Until now it was not known whether eggs obtained by in vitro maturation could survive thawing to be fertilized. The advance spares women from taking risky fertility drugs that can cause ovarian hyperstimulation syndrome (OHSS). The findings hold particular hope for patients with cancer-related fertility problems caused by chemotherapy, which can lead to infertility. Four successful pregnancies were achieved with the method, with one leading to birth. The scientists who performed the procedure, at McGill Reproductive Center, Montreal, cautioned that the procedure hasn't yet been tried on women with cancer. They also noted that the pregnancy rate is very low and therefore large numbers of eggs would be needed. It was also stressed that the treatment was suitable for people with fertility problems linked to conditions such as PCOS or cancer, and not for women who merely wanted to delay having a family.

APPLE A DAY

Children of mothers who eat apples during pregnancy are less likely to develop asthma, according to research at The University of Aberdeen, where 2,000 expectant mothers were questioned about their eating habits, and their children's health evaluated over five years after the kids were born. Researchers found that moms who ate four or more apples a week were half as likely to have an asthmatic child, compared with those who ate no apples or just one. No-one could say why apples produced this benefit, but the fruit has been linked to better lung health when eaten by adults, perhaps because of its antioxidant properties. The project has also linked vitamin consumption in pregnancy to lower levels of asthma. Researchers cautioned that eating apples doesn't guarantee lower asthma rates in children, since other factors may be at play.

TENDERED

Cardinal Health Care has completed its initial tender offer for Viasys Healthcare, with more than 80% of Viasys common stock tendered. The move makes Viasys a majority-owned subsidiary of Cardinal Health. "Now that Viasys is part of Cardinal Health, we are ready to move forward and bring our combined offerings to global customers," said R. Kerry Clark, chief executive officer of Cardinal Health. The tender offer and merger plans are valued at approximately $1.5 billion including the assumption of outstanding debt. Viasys had revenue of $610 million in 2006. The acquisition expands Cardinal Health's clinical and medical product offerings for acute-care customers and the business will be integrated into Cardinal Health's Medical Products Manufacturing segment.

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Adaptive Pressure Control Ventilation: One Size Fits All?

Melissa Turner, BA, RRT; Paul Garbarini MS, RRT

The authors are with Hamilton Medical, which provided this article.

As advances are made in the science of mechanical ventilation, clinicians are faced with a plethora of mode choices when initiating mechanical ventilation of a patient. There have always been arguments for and against the different modes that are available. One certain fact is that a patient's lung condition is dynamic and therefore parameters of ventilation may require modification in order to keep the lungs safe and provide comfort when appropriate. In a recent article by Branson and Chatburn,[1] volume control, pressure control and adaptive pressure control were reviewed while visiting the question, "Should Adaptive Pressure Control Modes Be Utilized for Virtually All Patients Receiving Mechanical Ventilation?" With respect to Chatburn's classification of ventilation modes,[2] volume control, pressure control, and adaptive pressure control are all breath types that can be delivered through continuous mandatory ventilation (CMV), intermittent mandatory ventilation (IMV), and continuous spontaneous ventilation (CSV).

Volume controlled breaths are described as breaths with a set point that limits flow or volume. During volume control, peak inspiratory pressure is varied dependent on lung mechanics and patient interaction with the breath.

Pressure control delivered breaths use a constant pressure as a set point. The flow rate is variable in order to meet the pressure set point. Tidal volume and flow varies with changes in lung mechanics and patient effort.

Adaptive pressure control breaths use some advantages of both previous breath types. This breath is delivered using a pressure set point during the inspiratory phase while "adapting" pressure between breaths to maintain a target tidal volume. If the breath cannot be delivered within the specified pressure limits an alarm will be activated. As such, the targeted tidal volume may not be reached if, for example, the patient's respiratory system compliance is too low and the pressure limit is set too low. It is important to realize that tidal volume may be higher or lower than expected on a breath by breath basis as the ventilator needs time to adjust/adapt pressure over the course of several breaths to maintain the target Vt.

As pointed out by Branson and Chatburn, no randomized controlled trials using large numbers of patients have been done to study adaptive pressure control. There have been several smaller trials that have suggested some advantages of adaptive pressure control. Piotrowski et al[3] found that adaptive pressure control ventilation compared to volume control, had a lower incidence of intraventricular hemorrhage grade II and higher in neonates and that the duration of ventilation was shorter along with a lower incidence of hypotension in infants who weighed less than 1kg. Alvarez et al[4] found a lower peak airway pressure as well as a slight improvement in carbon dioxide elimination using adaptive pressure control as compared to volume control ventilation. Peak pressures were also lower compared to volume control as noted by Guldager et al.[5] Kocis et al[6] also note the lower peak airway pressures using adaptive pressure control compared to volume control in infants post congenital heart disease surgeries. Considering all of the above studies in support of using adaptive pressure control ventilation, it is shown that peak airway pressures are consistently lower than with volume control ventilation. These studies were unable, however, to show any reduction in the duration of mechanical ventilation, reduction of complications, improvement in patient-ventilator asynchrony, or improvements in rate of survival.

There are several potential advantages to using adaptive pressure control ventilation although those advantages could be seen as a disadvantage in some perspectives. A targeted set tidal volume is achieved using the lowest possible peak airway pressures. Pressures are titrated on a breath to breath basis to the target tidal volume without clinician intervention. Some clinicians note that the "peak" pressure is lower than in volume control mode, but this is misleading as the lower peak pressure to achieve the same tidal volume is due to the resistive effects of a fixed flow pattern vs. a variable flow pattern. The plateau pressure will be the same if the tidal volume and PEEP targets are the same regardless of mode (assuming there's no differences in potential autopeep).

Indeed, as the flow is variable, patients can generate whatever tidal volume they want if they're capable, so the volume target is really a minimum tidal volume guarantee. Therefore, the inspired tidal volume may be much higher than the targeted tidal volume if the inspiratory effort generated by an active patient is great. Some clinicians may consider this harmful. (This is subject to much debate.) Another potential advantage to the variable tidal volume that could be produced with adaptive pressure control ventilation is a possible increase in surfactant production, which can improve lung mechanics and gas exchange as evidenced in studies done by Arnold et al.[7,8] (However, as a counterpoint, this assumes that the Vt can vary during adaptive pressure control to mimic the normal variation in spontaneous breathing pattern, which is the opposite of what the adaptive pressure algorithm is trying to do.)

When considering better patient-ventilator synchrony, proponents of adaptive pressure control point out that both tidal volume and flow can vary to meet patient demand while guaranteeing a minimum tidal volume. Pressure control does not guarantee a tidal volume minimum. During volume control, both tidal volume and flowrate are fixed values and do not change with patient demand. For this reason, if patient demand is increased, work of breathing (WOB) may also be increased. The disadvantage with adaptive control ventilation lies within human decision making about where to set the target tidal volume. If the patient's demand is not met because of an inappropriate target tidal volume setting or inappropriate pressure limit setting, then better patient-ventilator synchrony cannot be guaranteed. Ventilator-induced lung injury could be caused or exacerbated if tidal volumes are not reduced (indexed to ideal body weight) in ALI/ARDS.

Less clinician intervention and automated weaning are also identified by Branson and Chatburn as potential advantages of adaptive pressure control ventilation. Studies have suggested that there are fewer alarms and interventions needed from staff when using adaptive pressure control ventilation as compared to conventional modes. As a patient is able to maintain the target tidal volume or exceeds it, the pressure is decreased during adaptive pressure control, which helps to automate the weaning process. When considering weaning, the process can only be automated when the work of breathing is transferred appropriately from the ventilator to the patient as the patient's ability to breathe spontaneously improves. Also, it is important to point out that adaptive pressure control does not distinguish between improving lung mechanics and an increase in demand and drive due to such things as anxiety, fever or other factors that may cause that increase. In that situation the ventilator could decrease support to the patient and exacerbate the condition.

Branson and Chatburn state the only clear advantages of adaptive pressure control seem to be "more stable gas exchange than conventional pressure-controlled ventilation, better patient-ventilator synchrony than conventional VCV, and probably less human time spent at the bedside making sure the ventilator is meeting the patient's needs."[1] Branson and Chatburn also state, "Modes that use this strategy are a step above tactical control (ie, that require the operator to select and adjust all ventilator output set points), they are still a step below intelligent control (ie, those that allow the ventilator to mimic human decision making)."[1]

Adaptive support ventilation (ASV) is an intelligent control ventilation system. It delivers breaths in the same fashion that adaptive pressure control delivers breaths. However, human decision is not required for setting the target tidal volume, as the Vt is adapted to the patients lung mechanics. ASV employs the Otis Least Work equation to find the optimal tidal volume target and rate for each individual patient. The ASV algorithm takes in to consideration the patient's pulmonary mechanics and

expiratory time constants in order to target an optimal tidal volume and rate to meet a target minute ventilation. The pressure, target tidal volume, target rate and I:E ratio all adapt to changes in the patient's lung mechanics and respiratory drive. The tidal volume and rate are also a function of the minute ventilation which is input by the clinician and is expressed as percent of normal minute ventilation for a patient of a particular ideal body weight. With ASV, the tidal volume is no longer an arbitrary clinician selected set-point. Lung protective strategies are incorporated into ASV based on pressure limitations that are clinician set, as well as by other limitations on tidal volume and rate which are dynamically modified as changes occur in the patient's respiratory system. ASV represents the dawn of the intelligent ventilation era and may be adaptive pressure control ventilation's answer to the "one size does not fit all" theory.

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PRODUCTS

TO THE MAXTEC

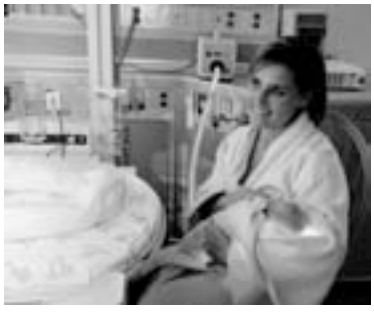
Maxtec Inc, Salt Lake City, announces the release of the all new **Pulsox-300i** pulse oximeter from Konica Minolta Sensing. For years, the Pulsox-3 series provided the perfect solution for spot checking and recording heart rate and blood-oxygen saturation. Now, the Pulsox-300i offers even more. The Pulsox-300i comes complete with 300 hours of non-volatile data storage, 30 hours of battery life on one AAA battery and provides connection to a PC via USB port for faster downloading and report printing. The company also announced the release of its new **OptiVenturi**. This unique product offers Fisher & Paykel humidifier and OPTIFLOW users the ability to mix ambient air and oxygen without the need of piped medical grade air. This unit also includes the company's Maxtec analyzer technology, providing 5,000 hours of battery life and a simple one touch calibration. The OptiVenturi is also equipped with a high-flow flow meter, making this combination a perfect solution with all the features you want in a high flow delivery system. Maxtec offers this product with either the MAX-250ESF fast response sensor, or the MAX-250E long life sensor. Contact the company at (866) 4-MAXTEC or maxtecinc.com.

TAKING CARE

Invacare Corporation announced today that Joseph S. Lewarski is joining the company as vice president, respiratory products group. Lewarski will be responsible for all of the Company's respiratory and sleep related activities, including new product development, business development, and creation of sales and marketing programs. Lewarski has served in numerous management and leadership roles in both the acute care and alternate healthcare settings. Contact invacare.com.

BLUE FOR YELLOW

GE Healthcare released today the BiliSoft LED Phototherapy System, a revolutionary blue LED and fiber optic based technology for the treatment of indirect hyperbilirubinemia. This innovative product responds to clinical guidelines at the same time that it promotes the natural developmental care of newborns. BiliSoft delivers phototherapy anywhere – in the Neonatal ICU, Pediatrics, Well Baby Nursery or at home. BiliSoft can be used in any environment – in a radiant warmer, incubator, bassinet, crib, or in a caregiver's arms. Designed with the feedback of neonatal nurses around the globe, BiliSoft provides distinct improvements over existing technologies. BiliSoft utilizes six blue LEDs with a "soft" large light pad, in two sizes, for use with premature infants or full-term babies. BiliSoft meets the guidelines of the American Academy of Pediatrics Guidelines on Jaundice Management, which specify irradiance levels of at least 30µW•cm-2•nm-1 and a narrow bandwidth of 430-490 nm to match bilirubin response curve. With a larger surface area, and more intensive light, BiliSoft also creates the opportunity for developmental positioning or swaddling of infants during treatment. A new soft, flexible fiber optic light pad allows the swaddling or wrapping of full-term babies to further enable feeding and holding during jaundice treatment. BiliSoft operates quietly, contributing to a soothing, comfortable environment for the newborn wherever it's needed-in the hospital or at home. Contact gehealthcare.com.



TUBULAR

A new neonatal-infant tracheostomy tube holder that features a friendly duck pattern, easy fastener tabs, and a moisture repellent lining is being introduced by Dale Medical Products,

Inc of Plainville, MA. The Dale PediDucks Tracheostomy Tube Holder is ready to use and provides fastener tabs that are shaped to easily fit into the flange of any size trach tube and has a rounded hook-and-loop back tab fastener for sizing. Featuring a neck band with a joyful duck pattern that comforts parents, children, and clinicians, this latex-free holder has a moisture repellent lining and is a very effective way to secure tracheostomy tubes. Designed to prevent accidental dislodgment or displacement of the trach tube, trachesophogeal fistula, tracheal stenosis, or airway ganuloma, the Dale PediDucks Tracheostomy Tube Holder eliminates the frustrations of using twill ties and other types of holders while minimizing secondary complications. The two-piece neckband adjusts from neonate to infant. Dale PediDucks Tracheostomy Tube Holders sell for $ 2.75 each, individually packaged 10 per box. Free samples are available upon request. Contact dalemed.com, (800) 343-3980.

LEGENDARY

nSpire Health's all-inclusive KoKo Legend portable spirometer exceeds ATS/ERS 2005 standards. KoKo Legend redefines accuracy through technology and simplicity with Legend's intuitive color touch screen walking both patient and physician through standard testing procedures promoting superior patient test results. KoKo Legend utilizes a unique flexible orifice pneumotach which is extraordinarily precise at the low flow rates common in both pediatric and COPD patients. Choose built-in-printing or external office printing for 8.5 x 11 reports. Easily transfer data into our KoKo PFT Spirometry software via a standard USB cable. For more information call (800) 574-7374, nspirehealth.com.

PRODUCT REVIEW

CULTURED

Nestlé Nutrition is launching Good Start Natural Cultures, the first and only US infant formula that contains probiotics to help support a healthy immune system. A balanced intestinal microflora is a key factor in the development of an infant's immune response. Many experts credit the predominance of bifidobacteria, a type of good bacteria, in the intestinal flora of breastfed infants as one of the reasons for their general good health. In formula-fed infants, the amount of bifidobacteria is, in general, significantly lower than in breastfed infants. Good Start Natural Cultures is designed to help infants fed routine infant formula achieve higher levels of these beneficial bacteria, improve the balance of microflora in their gastrointestinal (GI) tract, and support a healthy immune system. The probiotic in Good Start Natural Cultures is Bifidobacterium lactis (designated Bifidus BL). "Nestlé is dedicated to advancing infant nutrition through innovation and research," said José Saavedra, MD, Medical and Scientific Director, Nestlé Nutrition. "Good Start Natural Cultures is a first-of-its-kind infant formula in the United States. The inclusion of probiotics clearly goes a step further than providing basic nutrients for growth and development by adding a functional component which addresses an important objective of nutrition: supporting and modulating an infant's immune system. It is truly the next generation of infant formula."

Probiotics are safe and beneficial for the pediatric population. Bifidobacteria are among the most widely used microorganisms in the food supply and one of the most widely studied for functionality. Supplementation with specific strains of dietary bifidobacteria in infants has been shown, among other positive effects, to help balance the flora in the GI tract, acidify the intestinal lumen (creating an environment unfavorable to less beneficial species), support gut barrier function, and modulate immune system response.

Numerous peer-reviewed, published clinical studies also have demonstrated the benefit and safety of B. lactis in infants and young children and have noted no adverse reports from this oral supplementation. In addition, the US Food and Drug Administration has authorized the use of B lactis in Good Start Natural Cultures.

"The safety and immune enhancing effects of certain strains of Bifidobacterium have long been studied. It's an exciting time for probiotics in the US with the introduction of food products similar to those that have been available for years in Europe and Asia containing strains with documented health benefits," said Mary Ellen Sanders, Executive Director, International Scientific Association for Probiotics and Prebiotics. "Breastmilk is the ideal food for infants, and exclusive breastfeeding, for as long as possible, supports an infant's immunity in many ways," said Dr Saavedra. For mothers who cannot or choose not to breastfeed, or those who choose to supplement, Good Start Natural Cultures offers clinicians an important innovation in infant formula. "The inclusion of probiotics in infant formula is a major step toward providing infants a small part of the immune-related benefits that only breastfeeding can provide."

As with Nestlé's other Good Start milk-based formulas, Good Start Natural Cultures is made with easy-to-digest 100% whey protein, partially hydrolyzed through a patented process and it contains DHA&ARA for brain and eye development. Each 4 oz serving of Good Start Natural Cultures contains 107 colony forming units of viable B lactis. For more than 15 years and in 30 countries, Nestlé has been safely nourishing infants with B lactis-containing formulas. Good Start Natural Cultures is available in powder form in two sizes, 12 oz and 24 oz, and can be found at Wal-Mart, Target, and Babies R Us stores and other retailers. Contact nestleinfantnutrition.com, (800) 510-7494.

FREQUENTLY ASKED QUESTIONS ABOUT PROBIOTICS

What are probiotics?

Probiotics are defined as nonpathogenic organisms in the food supply that are capable of conferring a health benefit. The definition of probiotics has evolved as knowledge in this area has increased, but it is generally accepted that probiotics: 1 - are microbial organisms; 2 - remain viable and stable during use and storage prior to consumption; 3 - are able to induce change in a human's intestinal ecosystem; 4 - yield a health benefit when consumed in adequate amounts. There are a variety of strains of probiotics, particularly in the Bifidobacteria and Lactobacilli families, that have been shown to confer different and specific benefits.

Why do we need bacteria? Aren't all bacteria bad?

Bacteria are a major part of our environment. While some bacteria can cause disease, others can have health benefits. Bacteria are in constant interaction with our immune system, particularly via the respiratory tract, and the intestinal mucosa. Rather than completely avoiding bacteria, or unsuccessfully

attempting to sterilize our world, a healthy future involving the use of select bacteria to create a favorable interaction may result in better health. The human gastrointestinal (GI) tract is the primary and largest interface between the human body and its environment. As such, it is both the largest immune organ in the body and home to a microbial flora, important for the function of the gastrointestinal tract. Microflora are the community of bacteria which naturally occur in a person's digestive system. They are composed of more than 400 different species of microorganisms and are important for the function of the gastrointestinal tract. The intestinal microflora significantly influences the health of the human host. This microbial ecosystem is unique to each individual, changing throughout a person's lifetime in response to changes in diet, health, medications and the environment. Among other functions, the bacteria of the intestinal microflora are responsible for the production of nutrients (such as vitamins) and for fermentation of complex foods not digested by human enzymes such as fiber. A balanced microflora can also provide important support for a healthy immune system, strengthening the natural intestinal barrier against undesirable outside elements.

What benefits do probiotics provide?
A growing body of literature reports potential clinical applications for probiotics, with results that confirm their usefulness for immune-system support and general well-being. Maintaining the natural bacterial equilibrium of the GI tract helps to create an environment unfavorable to less desirable microorganisms.

Lactic-acid producing bacteria, including Bifidobacteria and Lactobacilli, are the most widely used probiotic organisms and hence some of the most widely studied. Since many probiotics are provided in a food, it would be inappropriate to recommend them for the prevention or treatment of a specific disease. However, an important part of the evidence for the beneficial role of probiotics in supporting a healthy immune system, specifically in the pediatric population comes from clinical trials studying their effect in various clinical conditions. These include management and prevention of acute diarrhea and antibiotic-associated diarrhea. Other emerging research has studied the potential effect of specific probiotics in treating or preventing allergic diseases, reducing gut inflammation, and preventing, treating, or decreasing the duration of infectious diarrhea.

How do probiotics work?
Research indicates that probiotics exert their effects both by promoting the gut's barrier function and by regulating the immune system. When probiotics are ingested, they become part of the intestinal microflora and help promote a healthy balance of beneficial versus less desirable species of bacteria. Various probiotic bacteria have been shown to improve gut barrier function by increasing mucin secretion (a major component of intestinal mucus, which acts as a defense barrier) and improving intestinal permeability. Probiotics have also been shown to enhance immunoglobulin response (specifically secretory IgA), and modulate immune response towards antigen tolerance.

Are probiotics safe? Are they safe for infants and children?
To date there have been more than 70 clinical studies, involving more than 4,000 children and infants consuming infant formula or foods containing microbial ingredients. Of particular interest are clinical trials with bifidobacteria used as probiotics. Bifidobacteria species are indigenous to the intestinal tract of both infants and adults. They are the most prevalent of all bacterial species that colonize the intestine of breastfed infants and are thought to be associated with some of the health benefits of breastfeeding. Formula fed infants do not show this general predominance of bifidobacteria. Thus, bifidobacteria are uniquely appropriate for use in infants and children as a probiotic, and supplementation with bifidobacteria, particularly Bifidobacterium lactis (B. lactis), has been increasingly studied in these groups. Extensive use in clinical trials in infant feeding documents safety, and research increasingly indicates that the incorporation of several of these microorganisms, including B. lactis in the feeding of infants can exert a positive effect, mainly by supporting a healthy immune system and improving intestinal barrier function as described above. Studies in infants, children and adults have also confirmed that administration of bifidobacteria used as a probiotic is safe and well tolerated. The safety of bifidobacteria in general and B. lactis specifically has been well documented and no significant adverse events have been reported in clinical trials in which these microorganisms were fed. Infant formulas supplemented with B. lactis have also been marketed for more than 15 years in 30 countries with an excellent safety record. B. lactis is Generally Recognized As Safe (GRAS) for use in infant formula from birth. After extensive evaluation of epidemiologic, toxicologic, microbiologic and other pertinent information, the FDA has authorized the commercialization of Nestlé Good Start Natural Cultures as a starter infant formula in the United States.

How often should people take probiotics?
Probiotics can be consumed on a regular, daily basis to promote the benefits of general well-being and immune-system support.

Head Lag and Sleep Time as Risk Factors for Car Safety Seat Related Oxygen Desaturation Events

Michele DeGrazia RNC, PhD, NNP

Abstract

Objectives: To explore premature infants' sleep time in their car safety seat and head control as risk factors for car safety seat-related oxygen desaturation events.

Design, Setting, and Participants: This descriptive, non-experimental, observational study of 49 premature infants was conducted at a tertiary healthcare institution.

Main Outcome Measures: Head control (measured as head lag by the pull-to-sit maneuver) of premature infants, the duration of sleep/wake activity and oxygen desaturation events during two 90-minute Infant Car Seat Challenges were measured. Also the association of oxygen desaturation events with head lag and time spent sleeping in their car safety seat was analyzed. Data were analyzed by descriptive and nonparametric statistics.

Results: Neither head lag nor sleep time influenced car safety seat-related oxygen desaturation events.

Conclusions: This study's findings increase neonatal healthcare providers' understanding of car safety seat-related oxygen desaturation events and provide direction for further investigation of this phenomenon.

Key words: car seat, prematurity, sleep, head lag, and NICU Network Neurobehavioral Scale (NNNS), oxygen desaturation

Background

Oxygen desaturation events are manifested as symptoms of apnea, bradycardia, periodic breathing and oxygen desaturation in approximately one-third of premature infants placed in the semi-reclined seating position of a car safety seat (DeGrazia, 2007). Due to these difficulties, the American Academy of Pediatrics (1999) has recommended that all infants born at less than 37 weeks gestation undergo a period of observation in their car safety seat, called the Infant Car Seat Challenge (ICSC), prior to hospital discharge. However, little is known regarding risk factors for car safety seat-related oxygen desaturation events.

The known risk factors for car safety seat-related oxygen desaturation events include gestational age (Willett, Leuschen, Nelson, & Nelson, 1986), semi-reclined seating position or angle of recline (Smith & Turner, 1990), sleep time (Hertz, Aggarwal, Rosenfeld, & Greensher, 1994; Nagase, Yonetani, Uetani, & Nakamura, 2002) genetic disorders (Bass & Mehta, 1995), and the time spent in the car safety seat (Merchant, Worwa, Porter, Coleman, & deRegnier, 2001). Head control and sleep time in the seat are two factors that may be associated with car safety seat-related oxygen desaturation events, but head control has not been investigated and only two studies have examined sleep as a risk factor (Hertz et al, 1994; Nagase et al, 2002).

Head lag, a measure of head control, is important to assess in premature infants because they are more likely to have diminished head/upper torso control (Mercuri et al, 2003), which prevents infants from repositioning their heads when experiencing impaired oxygenation. Infants' degree of maturation depends on the time spent outside the womb (Forslund & Bjerre, 1983; Mercuri et al, 2003). Sleep time in a semi-reclined position is also important to investigate further since sleep may compromise head control by allowing the infant's body to relax into a more slouched position (Hertz et al, 1994; Nagase et al, 2002). During sleep, premature infants are also more prone to periodic breathing, and apnea and are less likely to respond to the body's biofeedback mechanisms that would normally signal infants to readjust their body position (Hertz et al, 1994; Holditch-Davis, Edwards, & Wigger, 1994). Therefore, this study was undertaken to explore head lag and sleep time as risk factors for car safety seat-related oxygen desaturation events.

Methods

Design and Setting: This descriptive, non-experimental, observational study was part of a larger study on stability of the ICSC (DeGrazia, 2007) conducted between 12/31/04 and 06/02/05 at a tertiary healthcare institution with a level I newborn nursery and a level III neonatal intensive care unit (NICU).

Sample: A convenience sample of 50 premature infants, born to English-speaking parents preparing for their initial discharge from the NICU or newborn nursery, received medical clearance by their healthcare team to participate. The NICU infant

Michele DeGrazia is with Children's Hospital, Boston. This article has been peer-reviewed for publication by Muhammad Aslam, MD, clinical fellow at the Harvard Neonatal-Perinatal Fellowship Program and a member of editorial advisory board of Neonatal Intensive Care. The author wants to pay sincere thanks to her scientific advisors at the University of Massachusetts, Worcester: Drs. Susan Sullivan-Bolyai, Carol Bova and Carol Bigelow.

participants had been free of apnea, bradycardia, and oxygen desaturation for at least 48 hours. Infants who had not been monitored in the nursery were monitored in their crib for 30 minutes before the initial ICSC to ensure that the infants' baseline oxygenation was stable (> 93%). Infants were excluded from the study if they 1) required an orthopedic support or brace (n = 0), 2) were in state custody (n = 1), 3) required oxygen or methylxanthine treatment (n = 0), 4) failed the 30-minute oxygen saturation pre-screen in their crib, or 5) were born to non-English-speaking parents (n = 0).

Study Variables: Parent(s) of participants were informed that their infant would undergo two ICSCs, a single pull-to-sit maneuver, and that the infant's medical record would be reviewed. The study variables were premature infants' head control as measured by head lag, sleep/wake activity and oxygen desaturation events during two 90-minute ICSCs.

Head lag: One of 3 research assistants (RAs) measured head lag by the pull-to-sit maneuver (Lester & Tronick, 2002). This maneuver involves placing one's thumbs in both of the infant's palms while holding onto the infant's wrists as he/she lies supine in the crib. The examiner then pulls to extend the infant's arms, initiating the infant's automatic grasp of the examiner's thumbs, and pulls the infant to a sitting position (Lester & Tronick, 2002). Since the accuracy of this maneuver requires the infant to be in sleep/wake state 4-5, infants were assessed for the appropriate state immediately before head lag was measured.

Head lag during the pull-to-sit maneuver was easily scored from 1-11 (ordinal scale) on the NICU Network Neurobehavioral Scale (NNNS) according to the infant movement observed (Lester & Tronick, 2002). Lower scores (1-4) indicate less mature responses (head can be lifted to but not maintained in an upright position), median scores (5-7) indicate increasingly mature responses (able to hold head upright briefly) and higher scores (8-9) indicate more mature responses (able to maintain head in upright position). Scores of 10-11 suggest abnormal or hypertonic responses. These scores were not made known to the researcher, who was performing the ICSCs.

Sleep time: Sleep time was determined by continuously observing infants' sleep/wake state during each ICSC. Sleep/wake activity was scored on the appropriate subscale of the NNNS (Lester & Tronick, 2002), which has 6 state observations: 1 indicates deep sleep, 2-5 indicate increasing alertness, and 6 indicates inconsolable crying.

Oxygen desaturation events: Participants' blood oxygenation levels were continuously monitored during two 90-minute ICSCs in their infant-style car safety seats. An oxygen desaturation event was defined as one or all of the following: 1) apnea for > 20 seconds, 2) more than two consecutive episodes of periodic breathing (lasting 3-20 seconds and interrupted by respiratory rate >70) that were associated with oxygen desaturation of < 93%, 3) heart rate of < 80 beats per minute without spontaneous recovery, and 4) oxygen saturation of < 93 % without spontaneous recovery. Spontaneous recovery was defined as a consistent rise in heart rate or oxygen saturation within 10 seconds without intervention. This time was chosen because brief (< 4 seconds) decreases in oxygen saturation may be normal for older premature infants and not clinically significant unless repeated (Poets et al., 1991). For premature infants with a persistently low resting heart rate (<100 beats per minute), a fall in heart rate greater than 20% without spontaneous recovery was considered a bradycardic episode.

Table 1

Time Participants Spent Sleeping in their Car Safety Seats (N = 49)

Group	N		Percent Sleep Time ICSC #1	Percent Sleep Time ICSC #2
All	49	Range	0-100	0-100
		Mean	65.82	68.14
		SD	31.82	35.61
1	37	Range	0-100	0-100
		Mean	68.78	73.89
		SD	30.47	30.49
2	5	Range	0-100	0-100
		Mean	48.80	54.60
		SD	41.07	50.69
3	7	Range	12-100	0-98
		Mean	62.29	47.43
		SD	33.10	44.67

Reliability and Validity of Head Lag Measurements: Reliability of the head lag measurements was assured by having the researcher, a certified NNNS trainer, educate the RAs to perform and score the pull-to-sit maneuver and participants' sleep/wake activity before that maneuver. The researcher and each RA worked in dyads to examine several infants until they assigned the same sleep/wake activities and pull-to-sit scores 8/10 times. The 3 RAs also worked together in dyads 4 times during the study to ensure that they scored infants in the same manner.

Study Procedures : The study was approved by the study site's institutional review board. The first part of this study examined sleep time during two 90-minute ICSCs. During the ICSCs, the infants' heart rate, respiratory rate, respiratory effort, oxygen saturation and sleep time were recorded by the researcher. During the second part of this study, the infants' head lag (a measure of head/upper torso control) was measured by one of three RAs. Once a prospective discharge date was secured, the researcher notified an RA and the participant's parent(s) of the schedule for the two ICSCs (24 hours ± 12 hours between tests) and the pull-to-sit maneuver. Each participant's pull-to-sit maneuver was to be completed within the same timeframe as the two ICSCs.

Data Analysis

All data except those from the pull-to-sit maneuver were entered by the researcher into the Statistical Package for the

Table 2

Sleep/Wake State and Head Lag Scores (N = 49)

Group	n		Sleep/Wake State Score	Head Lag
All	49	Range	3-6	1-11
		Mean	4.04	4.53
		SD	0.71	1.86
1	37	Range	3-5	1-11
		Mean	4.03	4.54
		SD	0.73	1.91
2	5	Range	3-5	3-5
		Mean	3.80	4
		SD	0.84	1
3	7	Range	4-7	1-7
		Mean	4.29	4.86
		SD	0.49	2.19

Social Sciences (SPSS), version 11. The pull-to-sit data were entered by a graduate student. Data were analyzed by descriptive and nonparametric statistics (p value significant = < 0.05). Nonparametric statistical methods were used instead of data transformations because nonparametric analyses always provide valid inferences and do not rely on the underlying shape of the distribution, and they curtail the burden of meeting assumptions and analyzing data on a transformed landscape (DeGrazia, 2007). The need for nonparametric analyses was further dictated by a small sample size and irregular data distributions.

Recording data: To assess whether sleep time in the car safety seat was a risk factor for oxygen desaturation events, it was normalized as a percentage of total time in the car safety seat. Percent of sleep time was recoded into 2 categories: < 80% and > 80% of the total time in the car safety seat. This categorization was dictated by the median percent sleep time for ICSC 1 (78%) and ICSC 2 (83%). Median was chosen instead of mean sleep time because the data distributions were multimodal. This recoding identified which infants slept for a longer period of time (ie > 80%) in their car safety seat versus those who slept less (< 80%). Therefore comparisons could be made between sleep time and occurrence of oxygen desaturation events. Head lag was also recoded into two categories: head lag < 5 and ≥ 5. This cut point was dictated by the mean head lag scores (M = 4.5 or 5.0). Re-categorization enabled infants with immature head control (< 5), to be differentiated from those with moderate to mature head control (≥ 5).

Results

Participants: The 49 participating infants were approximately evenly divided by gender: 23 (47%) males and 26 (53%) females. Their birth weights ranged from 740 to 3565 grams (M= 2226.59; SD= 667.59), and their weight at discharge ranged from 1705 to 3580 grams (M= 2413.33; SD= 392.83). Most participants (78%) were white. Two-thirds of the infants (67%) were born by Caesarean section; the rest were delivered vaginally (32%). The sample's gestational ages were between 24 and 36 weeks. At the time of ICSC (hospital discharge), the participants' corrected gestational ages ranged between 34 and 40 weeks. Infant diagnoses were similar to most NICU patient populations, such as hyperbilirubinemia (43%), anemia (43%), respiratory distress syndrome (22%), apnea (19%), and chronic lung disease (11%) among others.

Infant Car Seat Challenge: Infants who experienced at least one oxygen desaturation event during each ICSC failed the test, resulting in 3 outcome groups: pass/pass (n = 37; 76%), fail/fail (n = 5, 10%), and pass/fail (n = 4; 8%) or fail/pass (n = 3; 6%) (DeGrazia, 2007). The 3 outcome groups did not differ significantly in gender, birth route, race/ethnicity age or illness. Any infant failing at least one ICSC was recommended to be sent home in a car bed.

Sleep Time: Sleep time varied widely among participants, but mean sleep time for ICSC 1 and 2 did not differ significantly among the 3 outcome groups (p = 0.416 and 0.546, respectively; Kruskal-Wallis test) (Table 1). Furthermore, when groups 2 and 3 were combined, sleep time for ICSC 1 and 2 did not differ between infants who passed both ICSCs (group 1) and those who did not (groups 2 and 3) (p = 0.282 and 0.287, respectively; Kruskal-Wallis test). More importantly, some infants experienced oxygen desaturation events when they were awake, while others were sleeping during their events.

Head Lag: Sleep/wake state of all participants was measured by the RAs before each pull-to-sit maneuver to ensure that infants were in an optimal sleep/wake state (state 4 or 5) to assess head lag (Table 2). This goal was sometimes difficult to meet due to frequent changes in sleep/wake activity. The pull-to-sit exams for 2 infants were completed outside the 36-hour time frame for the ICSCs; one infant was assessed 8 hours afterwards and the other was 2 days later. Of the 49 participants, 77% were in an optimal state (4 or 5) for scoring head lag, while 23% were in a sub-optimal state. Despite this difficulty, no significant difference was found in sleep/wake state among the 3 outcome groups (p = 0.44; Kruskal-Wallis test).

The mean head lag score for all participants was 4.53 (SD= 1.86, range = 1-11). Head lag scores did not differ significantly among infants in the 3 ICSC outcome groups (p = 0.778, Kruskal-Wallis test). This finding did not change when the data were analyzed without the outliers, i.e., infants with suboptimal sleep/wake states, infants measured outside the 36-hour time frame, and one hypertonic infant (p = 0.907, 0.951 and 0.799, respectively; Kruskal-Wallis test). While many participants (n = 22, 45%) showed less mature head control responses (scores of 1-4, ability to lift but not maintain the head in an upright position), over half (n= 25, 51%) demonstrated moderately mature responses to the pull-to-sit maneuver (scores of 5-7, indicating an ability to briefly hold the head upright). Only 1 participant exhibited a more mature response (scores of 8-9, indicating an ability to maintain the head in an upright position), while 1 other demonstrated an abnormal or hypertonic response to the maneuver (scores of 10-11). Furthermore, when participants were divided into those who passed both ICSCs (n = 37) and those who did not (n = 12), there was still no statistical difference in head lag scores (p = 0.686; Kruskal-Wallis test).

Odds for Experiencing an Oxygen Desaturation Event: When the odds for experiencing an oxygen desaturation event was examined by unadjusted bivariate analysis, no difference was found between infants in the two sleep categories. In other words, sleeping > 80% of the time was not associated with oxygen desaturation. In this analysis, the 95% confidence interval includes "1"; therefore, the findings are not statistically significant. Also, the large width of the confidence intervals indicated that the sample size was too small.

The unadjusted bivariate analysis also demonstrated that the odds for experiencing an oxygen desaturation event were 30% greater for infants with increased head lag scores (> 5.0), or those infants with a greater degree of head control. However, this result must be interpreted with caution since no difference was previously detected among the three groups of infants with different ICSC outcomes. Thus, this finding may be an artifact of data categorization. Also, in this analysis, the 95% confidence interval includes "1"; therefore, the findings are not statistically significant. Furthermore, adjusted analysis could not be completed because of the discrepancy in group sizes.

Discussion

This study found that neither head lag nor sleep time influenced car safety seat-related oxygen desaturation events. However, the findings increase neonatal healthcare providers' understanding of car safety seat-related oxygen desaturation events and provide direction for further investigation. The results are discussed in detail below.

Sleep/Wake Activity: Sleep/wake activity was measured by observing 49 premature infant participants during two ICSCs in their car safety seats. When grouped by ICSC outcome, the participants in each group slept from 0 to 100% of the time in their car safety seats. During 48 of 98 ICSCs, infants slept > 80% of the time, whereas during 14 ICSCs infants did not sleep at all. Sleep/wake activity was difficult to measure for some infants due to frequent transitions between sleep and wakefulness. Similar methodological difficulties in coding sleep/wake activity by observation have been overcome by using electroencephalograms (Sahni, Schulze, Stefanski, Myers, & Fifer, 2004). Therefore, the use of advanced recording techniques for measuring sleep/wake activity is recommended for future investigation of this phenomenon.

Head Lag: The head lag of the majority of premature infant participants (53%) was scored as moderately mature or mature, whereas 45% were scored as immature in the pull-to-sit exam. However, 22% of infants were not in the correct sleep/wake state at the time of their pull-to-sit exams, compromising the accuracy of their head lag score. Nonetheless, removing these infants from the analysis had little effect on the distribution of scores; 55% of infants had moderately mature or mature scores, and 24% had immature scores. Furthermore, both the sample and sample subset had a corrected gestational age range of 34-40 weeks.

These findings of varied head lag measures are consistent with previous reports in the preterm infant population (Allen & Capute, 1990; Forslund & Bjerre, 1983; Mercuri et al, 2003). Some found a wide range of responses to an exam of head control, but none were mature on exam (Mercuri et al, 2003). Similarly, others reported that more than half of premature infants studied at term continued to demonstrate head lag (Allen & Capute, 1990). In addition, when studying a cohort of formerly premature infants corrected to term, there was a greater tendency toward head lag when compared to infants born at term gestation (Forslund & Bjerre, 1983).

Sleep Time and Oxygen Desaturation: This study found no significant relationship between sleep time and car safety seat-related oxygen desaturation events. However, this finding is limited by inconsistencies in ICSC time (and therefore sleep time) due to removal of infants from their car safety seat if they failed their ICSC. Despite this limitation, some important observations were made. First, sleep time varied widely for infants in all three ICSC outcome groups, indicating a lack of association between sleep and oxygen desaturation events. Second, some infants experienced oxygen desaturation events when they were awake, whereas others were sleeping during their events. These observations and lack of statistically significant findings suggest that sleep is not a risk factor for oxygen desaturation events in car safety seats.

Despite these findings, however, it can be argued that more information is needed regarding the relationship between sleep and oxygen desaturation events in car safety seats. First, this study's small sample and the unsophisticated method for measuring sleep time may have contributed to the lack of association between sleep and oxygen desaturation events. Second, sleeping infants' ability to maintain stable blood oxygenation is affected by physical and physiological changes: 1) the body relaxes and can slump over, resulting in poor positioning (Hertz et al, 1994; Nagase et al, 2002), 2) posterior mandibular movement can lead to airway occlusion (S. Tonkin, L., 1998), and 3) prolonged breathing pauses can contribute to a hypoventilatory state (Holditch-Davis et al, 1994). Moreover, sleeping infants are less likely to respond to biofeedback mechanisms that enable them to correct poor alignment of the body and breathing problems (Hertz et al., 1994; Nagase et al, 2002).

Third, although anecdotal evidence from parents indicates that infants sleep better in their car safety seats, some infants in this study were noted to have frequent state transitions. Such frequent transitions in the supine position have been hypothesized to protect infants from sudden infant death syndrome (Goto et al., 1999). The rationale for this hypothesis is that premature infants have more frequent changes in sleep/wake activity and more heart rate variability when positioned supine than when prone, resulting in less time spent in sleep states associated with breathing irregularities (Goto et al, 1999). Fourth, the association between sleep and oxygen desaturation events has important implications for current US child care practices. Parents use seating devices as a replacement for holding infants or placing them in a crib (Callahan & Sisler, 1997; Cote, Bairam, Deschesne, & Hatzakis, 2007; Salhab et al, 2007). These car safety seat-bound infants are sometimes left sleeping in these devices for prolonged periods; sometimes even throughout the night. These important facts indicate the need for additional investigations on the relationship between sleep time and car safety seat-related oxygen desaturation events.

Head Lag and Oxygen Desaturation: Premature infants with head lag scores > 5 were found to be at 30% greater odds for experiencing oxygen desaturation events in their car safety seats. However, this finding did not reach statistical significance

and may be spurious due to categorization of the data, indicating the need for additional investigation. Moreover, evidence suggests that decreased head control may compromise premature infants' airway. For example, infants' airway space is known to be narrowed due to a prominent occiput, an unstable temporomandibular joint, and a toothless jaw (Tonkin, 1998; Tonkin et al, 2003). When the back of infants' shoulders and occiput are forced into a straight line, such as when they are placed into a car safety seat, the head is flexed forward on the neck and chest (Tonkin, 1998; Tonkin et al, 2003). Since truncal tone and ventral suspension emerge closer to term, many premature infants evaluated at term gestation demonstrate persistent head lag when pulled to the sitting (Allen & Capute, 1990; Forslund & Bjerre, 1983; Mercuri et al, 2003). Therefore, greater head lag in many premature infants may make them unable to reposition themselves to keep their small airways patent and place them at risk for airway compromise and impaired oxygen saturation.

Study Limitations: This study had several limitations. First, the sample of premature infants was recruited by convenience, which does not ensure that the sample is representative of the premature infant population at large. Second, differences in CSS design (harness mechanisms and seat contours) may have affected the ICSC results, thereby limiting the study's reproducibility. Third, although sample size and power calculations were considered in the study design, the study was terminated early because the main study question was answered (DeGrazia, 2007). Early termination of this study may have precluded achieving statistical significance. Fourth, an unsophisticated method (observation) was used to measure sleep time, whereas a more objective measure would have been polysomnographic recordings (Salmi 2004). Using a subjective measure such as observation may have affected the study results. Fifth, because this study was only partially funded, the researcher participated in data collection and analysis. Therefore, the researcher was not blinded to the ICSC study results, possibly introducing investigator bias.

Conclusions

Evidence suggests that premature infants spend long periods sleeping in their car safety seat (Callahan & Sisler, 1997; Littlefield, 2003; Myers, Yuen, & Walker, 2006; Salhab et al, 2007). Although these infants are at risk for car safety seat-related oxygen desaturation events, it remains unclear whether sleep time and/or head lag (a measure of head and upper torso control) are risk factors for these events. Until these phenomena can be studied further, healthcare providers should exercise caution when selecting a car restraint device for infants exhibiting increased head lag. Moreover, until larger studies have established the relationship between sleep time and car safety seat-related oxygen desaturation events, parents should be told to limit the time infants spend in a car safety seat to travel time only, unless the semi-reclined position is required for treatment of medical conditions (Salhab et al, 2007).

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Neonatal Seizures in Delivery Room: A Diagnostic Dilemma

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Introduction
Seizures in the neonatal period can arise from a vast array of causes but they are very rare to manifest immediately after birth. The major differential diagnoses include structural brain anomalies, metabolic disturbances, hypoxia-ischemia, maternal drug use and infection. We present the case of a newborn with seizures in the delivery room. She was noted to have major anatomical brain anomalies consistent with pontocerebellar hypoplasia demonstrated on neuroimaging studies. Infant died in the neonatal period due to complications. We present this case with a brief review of the literature.

Case Report
A full term female infant was delivered by spontaneous vaginal delivery at 40 weeks' gestation to a 19-year-old Hispanic, primigravid mother. She had no medical problems before or during pregnancy. She had regular prenatal care and fetal sonogram at 20 weeks' gestation reported normal anatomic survey. Her second stage of labor was prolonged, requiring an episiotomy to deliver the infant. At the time of delivery, she had no fever, rash, or any other symptoms of a viral illness. She required no sedation or anesthetic agent intrapartum. APGAR was 9 and 9 at one and five minutes respectively. Infant was immediately noted to be breathing shallow and fast with a tremulousness of all extremities along with tonic posturing and rigidity of lower limbs. Gross examination of the infant in the delivery room showed no anatomical abnormalities except for a left preauricular skin tag. Mother denied use of drugs, alcohol, smoking or any febrile illness during pregnancy. The infant was transferred to the neonatal intensive care unit for further evaluation and management.

In the NICU, her weight (3450g at 50th percentile), length (47cm at 50th percentile) and head circumference (33cm at 50th percentile) were recorded. Her initial vital signs were as follows; Temp 36.60C, HR 140 beats per minute and regular, RR 38 breaths per minute and shallow, BP 82/50 (55) and O_2 sat 96% RA.

She continued to have tonic posturing in lower limbs and seizure-like clinical picture as noted in the DR along with weak cry, occasional irritability, hypersensitivity to touch, exaggerated reflexes, hypertonia in all four extremities with flexion contractures of the lower limbs, no suck or swallow reflex and drooling from the mouth. She was responsive to sound and light. She was also noted to have tremulousness of the tongue with stiffness of the jaw. A preliminary diagnosis of seizure disorder was made and routine laboratory evaluation including an arterial blood gas, glucose, electrolytes, TORCH studies, complete blood count, blood culture and urine for toxicology screen was obtained. She was also loaded with intravenous Phenobarbital and started on antibiotics. After the Phenobarbital she was noted to have a decrease in tremors and irritability, with no change in tonic posturing.

She remained conscious and breathing room air all the time. Neurology, genetics, orthopedics and ophthalmology consultations were obtained. Genetics recommended chromosome studies, which showed normal female karyotype. Neurologist suggested imaging studies of the brain and CPK levels. By this time all the blood and urine workup as reported above was normal. Her eye examination was significant for no corneal sensation, fixed pupils and small macular hemorrhages on fundi. The orthopedic consultation documented contraction deformities and recommended brain imaging to rule out brain anomalies.

Head ultrasound at 4 hours of life demonstrated bilateral

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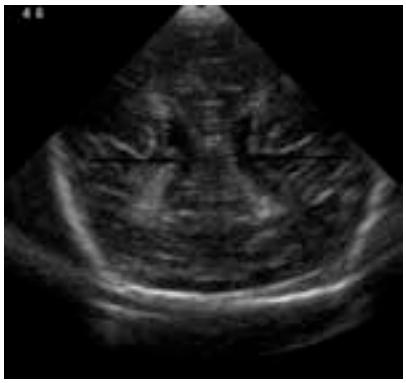

Figure 1. Head ultrasound performed at 4 hours of life demonstrating bilateral germinal matrix hemorrhage with ventriculomegaly (arrows).

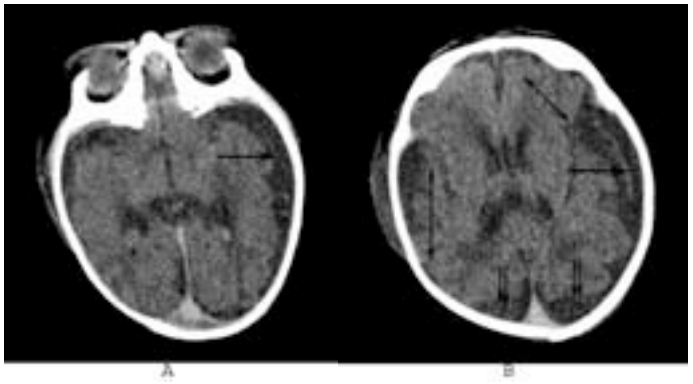

Figure 2. CT scan without contrast at 12 hours of life demonstrating pachygyria (double-head arrows), right parietal hematoma (large single-head arrows) and bilateral occipital hematomas (single-head double arrows).

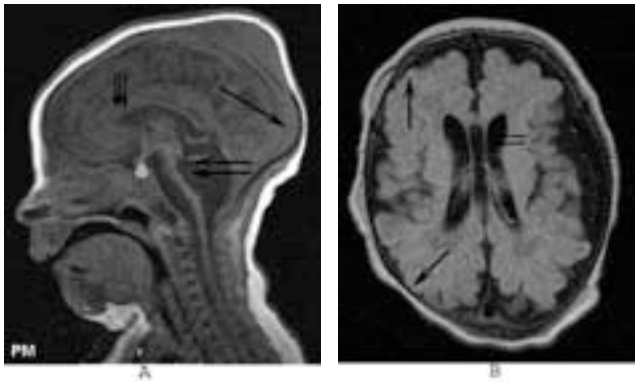

Figure 3. MRI of the brain without gadolinium at 24 hours of life.
A: Diminution in size of pons (large double arrows), virtually nonexistent cerebellum with only the superior portion visualized with most of the posterior fossa filled with CSF (large arrow). Anterior portion of the corpus callosum is incompletely formed and the entire corpus callosum is thin (small tripple arrows). B: Ventricles are enlarged with resolving bilateral germinal matrix hemorrhage (double arrows). The sulci and cisterns are prominent and the gyri appear thickened (large arrows).

germinal matrix hemorrhage with ventriculomegaly, which was not conclusive of a clinical picture necessitating further neuroimaging (Figure 1). Head CT scan at 12 hours of life demonstrated right parietal and bilateral occipital hematomas and concern for pachygyria (Figure 2). She continued to have all the symptomatology along with difficulty in sucking, swallowing and absent gag reflexes. Brain MRI was obtained at 24 hours of life to further delineate the CT scan findings. It demonstrated pontocerebellar hypoplasia, partial agenesis of corpus callosum and pachygyria (Figure 3).

The family was updated regarding the lethal brain malformations and future neuro-developmental outcome. Parents refused redirection of care and she was continued on gavage feeding with good tolerance. She was also considered for chronic care facility placement. While awaiting chronic care placement, she developed aspiration pneumonia requiring ventilator care and died of respiratory failure. Parents refused autopsy and the case was denied also by city medical examiner.

Discussion

The clinical picture presented in this full term infant was a dilemma and shock for parents who were expecting a normal baby. It represented a period of anxiety for obstetricians who are concerned about the outcome of the infants in this litigious society where their care is scrutinized by the legal community. It was also a surprise for the neonatologists who were handling this baby. Limited literature exists for a baby to have seizure-like activity immediately after birth. It is the responsibility of the neonatologist what to tell the anxious parents and obstetrician in such a situation in addition to the challenging job of working up this baby for cause of this seizure-like activity. The clinical picture suggested an immediate perinatal event like hypoxia, metabolic disturbances, maternal analgesia and/or anesthesia, and inborn errors of metabolism (IEMs) including Pyridoxine dependency.[1] Neonatal narcotic withdrawal convulsions, intracranial bleed and infection with bacterial and viral agents have to be ruled out as well.

The common metabolic problems like hypoglycemia, hypocalcemia, hyponatremia, hypomagnesemia and IEMs were ruled out. Infections including TORCH screen was negative. A drug withdrawal was unlikely since urine toxicology screen was negative. In utero hypoxic event was also unlikely as there were no signs of depression at birth and cord and neonatal blood gas results were normal. Three major causes, intracranial bleed, CNS anomalies and a Pyridoxine dependency syndrome were considered causative.[2,3] The neuroimaging studies of the brain demonstrated developmental brain anomalies in this case. Head ultrasound and CT provided limited information. In this situation, brain MRI is a useful tool to differentiate structural anomalies and also to detect tumors or space occupying lesions and dysplasias.[4] Brain MRI clearly demonstrated structural anomalies including pachygyria, hypoplasia of the corpus callosum, and hypoplasia of the pons and cerebellum. MRI brain is emerging as an important diagnostic tool in neuroimaging of neonatal brain anomalies.[5] These anomalies do occur as a single entity or as a group with lissencephaly or schizencephaly. They manifest clinically as tremors and paucity of movements, feeding problems and seizures or infantile spasms. This infant had typical clinical features of multiple brain anomalies; one should differentiate it from Aicardi syndrome, Arnold-Chiari malformation and holoprosencephaly. Due to these unique structural brain anomalies and clinical picture a diagnosis of Pontocerebellar hypoplasia was made.

Pontocerebellar hypoplasias are congenital disorders of diverse spectrum and include carbohydrate-deficient glycoprotein syndrome type 1, cerebromuscular dystrophies (Walker-Warburg syndrome, Fukuyama syndrome, muscle-eye-brain disease) and at least two types of autosomal recessive neurodegenerations known as pontocerebellar hypoplasia type I and II.[6,7] Pontocerebellar hypoplasia type 1 is a lethal phenotype with death in the first year of life. Clinical features include congenital contractures, respiratory insufficiency, central and peripheral

motor dysfunction and spinal anterior horn degeneration.[8] Pontocerebellar hypoplasia type 2 is characterized by progressive microcephaly, extrapyramidal dyskinesia and normal spinal cord findings. Such infants frequently die during childhood.[9,10] The workup for pontocerebellar hypoplasia includes imaging of the brain to differentiate other less invasive pathologies and treatment is supportive with seizure control and nutrition.[11,12] Pregnancy counseling is advisable and a detailed fetal MRI should be performed in all subsequent pregnancies to rule out this condition.[12]

Prognosis of the infant is guarded due to progressive neuromuscular handicap and infections, and redirection of care is recommended as no meaningful survival is expected. Support and bereavement counseling should be provided to the family. In our case parents refused redirection and this decision should be respected as well. Majority of these die in neonatal period regardless of the level of care provided.

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Editorial…Continued from 7

Wagner enjoins pregnant women to shun any birth book that advises "trusting your doctor" or "listening to your doctor." Such phrases are red flags. Instead, they should trust the scientific evidence and "trust their bodies." A call to action, Born in the USA includes a list of sensible recommendations: for a national health care system that would provide care to all pregnant women, for more home deliveries, for increased use of midwives, and, of course, for increased scrutiny, transparency and accountability of the health care system.

Mary Briody Mahowald's Bioethics and Women takes a similar moral stance to that of Wagner and also promulgates the adjudicating power of evidentiary medicine. A bioethicist and professor emerita at the University of Chicago, Mahowald offers no clear recipes or conclusions. Where Wagner's tone is often inflammatory, hers is earnest, at once less entertaining and more nuanced. Mahowald applies "standpoint theory" (a kind of postmodern counter-hegemonic ethics par excellence that privileges the standpoints of multiple and especially non-politically dominant perspectives) to the clinical setting – but with the caveat that, in the case of birth, the pregnant woman's perspective must be prioritized because she has the greatest stake in the matter. The problem here is that a shifting tapestry of interests, stakes, knowledge claims and power relations means that medical decisions must be made on a case-by-case basis. This makes medical decision-making an art, and messy. Mary Briody Mahowald offers no recipes for balancing competing claims – of groups and individuals, for instance – or for adjudicating pesky moral dilemmas like sex selection. She is more hopeful than Marsden Wagner about the clinician, believing that the obstetrician, with the right incentives and information, can be transformed into a consistently virtuous practitioner. Her ethics stands as a postmodern ideal.

This review has been abridged and edited for the readers of Neonatal Intensive Care. Please see the Times Literary Supplement for the complete review.

Tailored Procedures – A New Approach to Prenatal Diagnosis

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Introduction

Chorionic villus sampling (CVS) and amniocentesis are prenatal diagnostic procedures used to detect certain fetal genetic abnormalities. Both procedures increase the risk of miscarriage.[19]

CVS is done at 10-12 weeks gestation, and amniocentesis is done at 15-18 weeks gestation.

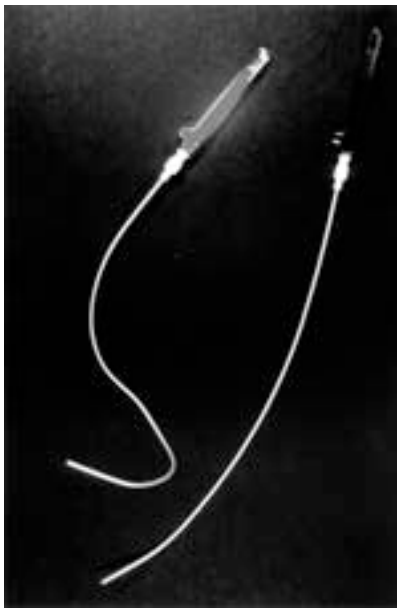

Figure 1. CVS catheters: on the left-abnormally shaped due to difficult procedure, on the right-CVS catheter after an "easy" procedure.

The current standard of care in the United States is to offer either CVS or amniocentesis to women who will be 35 years of age or older when they give birth, because these women are at increased risk of giving birth to infants with Down syndrome and certain other types of aneuploidy.[9,12,14,17] Several controlled studies were conducted to evaluate the safety of amniocentesis before its widespread use.[4,15] The major finding from these studies was that amniocentesis increases the rate of miscarriage by approximately 0.5%. Amniocentesis became an accepted standard of care in the 1970s. In 1990, more than 200,000 amniocentesis procedures were performed in the United States.[16] Later studies have demonstrated less than 0.5% risk of miscarriage with the procedure. The risk of an amniocentesis depends on the experience of the operator.

CVS has become widely used worldwide in the 1980s. The World Health Organization (WHO) sponsors an International Registry of CVS procedures; data in the International Registry probably represents less than half of all procedures performed worldwide. More than 80,000 CVS procedures were reported to the International Registry from 1983–1992. According to the U.S. Department of Health and Human Services report the risk of miscarriage with CVS or amniocentesis is operator dependent.[1,5,6] Most procedures are performed in specialized centers by experienced operators with up to 10,000 CVS performed by single operator.[7] Most practitioners do not have the experience; therefore, the quoted complication rate is not applicable to them.[3]

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Purpose and hypothesis

The purpose of our study is to offer the patients with increased risk of fetal chromosomal abnormalities definitive and safe diagnostic procedure during the first trimester.

CVS is largely underutilized in the USA. In some institutions the ratio of amniocentesis to CVS is 500 to 1.[2,8,10] CVS or amniocentesis may be technically difficult or easy depending on many factors (maternal body habitus, location of the chorion, presence of fibroids, uterine position, etc).

The purpose of this report is to consider the prenatal screening procedure tailored to anatomical features of the individual patient.[11,12,18]

We evaluated the hypothesis that tailoring CVS or amniocentesis to its technical difficulty will increase the number of first trimester diagnosis of fetal chromosomal abnormalities, and will have acceptable and comparable diagnostic accuracy and complication rate, when performed by moderately experienced operator.

Materials and methods

513 patients between 10 and 20 weeks gestation with increased risk of fetal chromosomal abnormalities were evaluated at Nassau University Medical Center and Moscow University School of Medicine.

Patients underwent genetics counseling, transabdominal and transvaginal ultrasounds, and were offered either CVS or amniocentesis for the diagnosis of fetal chromosomal abnormalities.

After obtaining informed consent CVS or amniocentesis was performed based on ease of accessibility of chorion (for CVS) or amniotic fluid (for amniocentesis), determined by physical exam and ultrasound.

Patients with anterior and low-lying placentas (easy access for transcervical CVS) had transcervical CVS, whereas ones with posterior or fundal placentas had amniocentesis or transabdominal CVS (Fig1).

Number of attempts per procedure, number of successful procedures, and pregnancy loss rate were calculated. Both operators (BP, LS) had moderate experience with prenatal procedures (over 3000 amniocentesis and 500 CVS total).

Results

Adequate samples for chromosomal analysis were obtained in 511 out of 513 patients (99.8%).

First trimester diagnosis for the fetal chromosomal abnormality was established in 64 % of the patients.

Diagnosis was established in 99.5% of transabdominal CVS, 99% of transvaginal CVS and 100% of amniocentesis. Diagnostic sample was obtained from the first pass of the needle or catheter in 94% of transabdominal CVS, 93% of transvaginal CVS and 98% of amniocentesis procedures.

Miscarriage rate remained less then 1% with CVS and less then 0.5% with amniocentesis. CVS-related complication rate was 0.6%. Combined pregnancy loss including terminations of pregnancy was 2.1%.

Distribution of Procedures

Transabdominal CVS	211
Transvaginal CVS	119
Amniocentesis	183

Procedure Success Data

Attempts per Amniocentesis Transabdominal	Transvaginal Patient	CVS	CVS
1	198	111	179
2 or more	12	7	4

Conclusions

Both CVS and amniocentesis are acceptable procedures for the diagnosis of fetal chromosomal abnormalities.Tailoring of these diagnostic techniques to the difficulty or ease of the procedure may result in more first trimester diagnoses of fetal chromosomal abnormalities in high-risk patients.

Diagnostic accuracy of the procedures tailored to anatomical features of the individual patient is superior to the historical controls, with less needle or catheter insertion attempts per procedure and improved success in specimen retrieval. The miscarriage rate with tailored CVS and amniocentesis remains comparable to the historical controls.

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Falling Birth Rates and Fertility Management in Russia

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In 1990, we reported on the status of obstetrical services in the USSR.[1] Many things have changed since. The USSR ceased to exist after the difficult times of perestroika. The former Soviet Republics, (Ukraine, Belarus, Georgia, etc) became independent countries; local wars raged; some of the former republics' healthcare had deteriorated.

Russia's birthrate has been on the decline for decades and, in 2004, the rate was at just 1.17 babies per woman. It had been twice as much in 1990, according to the Federal State Statistics Service. Population demographers say that 2.4 children per woman are necessary for any nation to sustain its population.

The numbers are exacerbated by the nation's high abortion rates, as abortion is considered a primary means of birth control. The results of these changes are seen in a recent UN report, which indicates that the Russian population will shrink by one-third by 2050. This could leave the nation unable to defend itself, man maintained factories and other labor-intensive businesses and provide for older Russians in their retirement years. Table I, below, reflects the birth rate in other countries, in comparison to the 1.17 per woman in the Russian Federation.

Russia is trying financial incentives to try to stem the tide of under-population. President Vladimir Putin defined the crisis as the nation's biggest problem and the government is offering bonuses to women who have a second child. Women who choose to have a second child can qualify for $9,200 – a huge sum in a country where the average monthly salary is $330. Putin ordered the Russian parliament to more than double the monthly child support payments to about $55 US monthly. Adoption out of the country has also become more difficult. Putin has also focused on adoption to promote the population and foreign adoptions of Russian children are on the decline. He has asked parliament to increase to the stipend given, $166 per month, to families that adopt children.

Table I – Birth Rate Comparisons

Country	Current Birth Rate
Czech Republic	1.23
Finland	1.80
France	1.90
Germany	1.37
Iceland	2.03
Ireland	1.99
Italy	1.24
Latvia	1.16
Norway	1.81
Portugal	1.5
Poland	1.23
Slovenia	1.22
Spain	1.15
Sweden	1.75

*A fertility rate of 2.1 makes population stable.

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As evident from Table I, the Russian Federation is not the only country experiencing declining birthrate and trying to change the trend. Various positive and negative reinforcements by various governments are reflected in Table 2.

The campaign takes effect this year, and is expected to last at least 10 years. Russian government incentives should be viewed taking into consideration the fact that Russia's gross domestic product per capita in 2005 was $10,700, compared with $42,000 in the United States. Therefore giving a Russian $9,200 in cash is like giving an American $36,112. Would this be enough to convince Americans to assume the financial responsibilities associated with an additional child? For most, probably not. Financial incentives are not the only solution to increase the

Table II – Benefits for Babies

Country	Benefits/taxes
Austria	Monthly $547 for the youngest child until age of 3. Tax benefits of $64 per month per child. Free textbooks and school buses 4 months of maternity benefits.
Estonia	Monthly income for up to 15 months up to a ceiling of $1,560. Non-wage-earners get $200 a month.
France	$940 per month for one year after 3rd child. On top of 3 years stipend of $642.
Germany	67% net pay (maternity leisure) for one year not exceeding $1,800 euros per month. Two months of paid leave for husbands.
Spain	Tax rates for pensions are tied to the number of children a worker has. Rates for those with two kids remain constant, and fall for those with more than two, and rise with fewer than two.
Russia	$9,232 for a second child. The benefit would be paid in vouchers that could be spent on accommodation, childrens education, or their own pension once a child has turned three. In addition, the government would pay families with one child $55 a month, doubling the amount for a second child.

birthrate. In actuality, rich people tend to have fewer kids while people in poor countries usually have more.

For centuries, the Russian Empire expanded at an average rate of 55 square miles per day, fueled by rapid population growth. By the year 1900, Russian women were still bearing, on average, more than seven children in a lifetime.

P. Longman the author of "The Empty Cradle" (Basic Books, 2000) presented a detailed review of the Russian fertility rate from the times of Stalin's purges through the Brezhnev's stagnation; Gorbachev's perestroika to Putin's capitalism.

In 1920, Russia's law on abortion allowed termination of pregnancies at state hospitals without cost. This policy was maintained until 1936, when abortions were banned. Stalin's attempt to increase the birthrate failed: illegal abortions flourished. During the 1960s the Russian family began to break apart. The marriage rate dropped by 19%, the divorce rate doubled, and the number of Russian babies born each year declined by 34%. By 1964, Soviet women no longer produced enough children to replace the population. Between 1965 and 1975, the percentage of Russians under the age of 15 dropped from 30 to 23%. By the early 1980s, with the birthrate continuing to slip, and with deaths exceeding births by well over half, current projections show the Russian population will fall by 29% by 2050. In 1992, there were an estimated 224.6 abortions for every 100 live births. In order to preserve the current ratio of workers to retirees, Russia would have to either raise the average retirement age to 73, or import 308 million immigrants by 2050, which would leave native Russians a minority group constituting only 27% of the population. President Putin has addressed this problem in apocalyptic terms, telling his government, "We are facing the serious threat of turning into a decaying nation."

Preliminary Results of the Incentives Worldwide

Although many of the incentives are recent, making their effect difficult to assess, we put together some of the preliminary results. France's birth rate of about 1.8 children per woman makes it the only European country with the possibility of maintaining its current population through births (Kaiser Daily Women's Health Policy Report, 9/6). According to the organization APM, France has Europe's second-highest birth rate in part because of incentives offered by the government. Juliette LaFont, spokesperson for the French Ministry of Family Affairs, said that what distinguishes France from other European countries is its "policy of giving women the choice to work or not by giving them all of the services and means." APM reports that France spends $57 billion annually, nearly 15% of its total budget, for family and children. In Estonia, two years into the program, the government is seeing some of the first tentative results. Since the adoption of the new benefits, Estonia's fertility rate has improved from 1.5 to 1.3 in the late 1990's. Estonia was one of the fastest-shrinking nations on earth, at risk of losing nearly half its 1.4 million people by mid-century (M.Walker, the Wall Street Journal, Oct. 2006). But the experience in places such as France and the Nordic countries suggests that incentives can make an impact. For example, women in Sweden and Norway, which support families with generous benefits, labor laws and childcare, have close to two children on average. However, cash and other incentives may have some impact but probably are not enough to lift fertility (M. Fritz, Aug 2006, The Wall Street Journal).

Just since March 16 countries ranging from Bulgaria to Taiwan have increased incentives. The results of such incentives have been mixed. In 2004, Australia began offering bonuses increasing the bounty to about $3,000 this year. The government has credited the bonus with pushing the average number of births per female to 1.82 from 1.76. Japan has been extending maternity leaves and providing other incentives, but its fertility rate has continued to decline, hitting a post-World War II low of 1.3 births per female.

Some Japanese localities, facing near catastrophic population loss, are offering rich incentives. Yamatsuri, a town of 7,000 just north of Tokyo, offers parents $4,600 for the birth of a child and $460 a year for 10 years. Singapore has a particularly lavish plan: $3,000 for the first child, $9,000 in cash and savings for the second; and up to $18,000 each for the third and fourth. It is becoming clear that financial incentives should be part of the plan but not a plan itself. Our review of birth rates in "traditional" or religious communities are significantly higher than in the liberal ones.

Just as the statistics alert us to the problem, they may also alert us to the solution. It is interesting and important to note that the conservative, deeply religious state of Utah has a much higher birth rate (2.76 per women in 2000) than the ultra-liberal state of Vermont (1.57 per women). In other words, women in Utah produce 73% more children per woman than Vermont. Similar trends can be observed in studies comparing birth rates among Orthodox Jews versus secular Jews.The Journal Mishpacha (November 16, 2006) reports statistics for the Orthodox community in Israel based on a Housing Ministry.

The Orthodox community has an annual growth rate of 6.6% compared to 1.4% for the general Jewish community; 60% of all Orthodox are under the age of 18.

Incentives for increased birthrate are an old concept. Echoing old fears about the declining German birth rate, Nazi officials implemented "positive" eugenic measures, promoting large ("child-rich") families by setting aside houses in new subdivisions for qualified families and issuing the Honor Cross of German Motherhood to healthy, "German-blooded" women who had at least four children. Public health campaigns advised pregnant women to eschew alcohol and nicotine and "genetic poisons" that were harmful to the fetus" (reported by S. Bachrach in the New England Journal of Medicine, July 2004).

In summary, it appears too early to assess the effectiveness of government efforts to increase birthrates. We will provide and update in a 1-2 year period.

Addendum

After this manuscript had been submitted,, The New York Times World briefing reported: "Spain: Bonus For Babies. Families will get $3.400 for each baby born in Spain as a reward for helping to raise the country's low birthrate, Prime Minister Jose Luis Rodriguez Zapatero told Congress in his State of the Nation address. Spain's birthrate for 2006 was 1.37 lifetime births per woman, among the lowest in Europe."

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Breastfeeding Pattern In An Urban City Hospital

Meena Narasimhan, MD; Poornima Chintalapalli, MD; Maria P. Pablo-Prino, MD; Muhammad Aslam, MD; Anasuya Nagaraj, MD; Benamanahalli K. Rajegowda, MD

Abstract

Introduction: Breastfeeding has lots of advantages to the mother and the baby. As the saying goes "human milk is for humans and cow milk is for cows." Recent trends in breastfeeding and the Surgeon General's statement for "Healthy People 2010" urge that at least 50% of women should exclusively breastfeed for 6 months. Although a majority of organizations have supported breastfeeding, rates are still not optimal in the United States. A wide array of issues, particularly amongst the lower socioeconomic population in urban areas, as well as promotion of formula feeding is responsible.

Objectives: Lincoln Medical and Mental Health Center is an inner-city hospital serving mainly a low socioeconomic population with diverse ethnic backgrounds. We have reviewed the obstacles in breastfeeding among this group and how to overcome them.

Methods: We interviewed 272 mothers in the immediate postpartum period from October through December 2005. We also reviewed the medical records to assess the age, race, parity, nationality, time of initiation and number of breastfeedings in full term newborn babies.

Results: The breastfeeding rate in our population was 49.2%. Breastfeeding was almost uniform in all age groups and all races. It was higher among multiparous and foreign-born mothers. Initiation of breastfeeding in the delivery room was 14.9%. Only 3.6% of mothers exclusively breastfed and the rest were constituted as any breast-feeding group, which varied from 1-5 feedings in 77.4% of the cases and more than 5 feedings in 22.6 % of the cases over a 48-hour period.

Conclusions: The rate for any type of breastfeeding was 50%, which is still way below the target of 75% set by "Healthy People 2010" for breastfeeding in the early postpartum period. Majority of study population desired to breastfeed their infants but there appeared to be obstacles to breastfeeding initiation, including system-based practices not conducive to breastfeeding. This can be overcome by appropriate training of all those who work in the perinatal area along with simplified patient friendly hospital breastfeeding policy. Education of prospective mothers should begin in the early prenatal period to facilitate smooth transition to breastfeeding in the intrapartum to postpartum period.

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Introduction

Extensive research using improved epidemiologic methods and modern laboratory techniques have documented diverse and compelling advantages for infants, families and society from breastfeeding and use of human milk. These advantages include health, nutritional, immunologic, developmental, psychological, social, economic and environmental benefits. Significant advances in science and clinical medicine have occurred in regard to an initiative towards breastfeeding.

Promotion of breastfeeding has become a national priority. United States Department of Health and Human Services in "Healthy People 2010" stated: Infants should be exclusively breastfed during the first six months and ideally through the first year of life. The national goal is initiation of breastfeeding in 75% at birth, exclusive breastfeeding in 50% at 6 months and exclusive breastfeeding to continue in 25% at one year.[1] In 1997, the American Academy of Pediatrics (AAP) published the policy statement "Breastfeeding and the use of human milk."[2] Several other organizations including the World Health Organization (WHO) have advocated exclusive breastfeeding for human infants.[3] Pediatric house staff in training at Lincoln Medical and Mental Health Center (LMMHC), spend a month of clinical experience in the newborn nursery and are taught best practices regarding breastfeeding. Our hospital is an inner-city urban hospital serving mainly low socioeconomic population with varied ethnic background. It is part of eleven Health and Hospital Corporation (HHC) hospitals caring for mother-infant

Table 1. Comparison of Breastfeeding vs. Non-Breastfeeding Data

TYPE	ATTRIBUTE	BREASTFEEDING MOTHERS	NON BREASTFEEDING MOTHERS
		134 (49.2 %)	138 (50.7%)
Race	African (78)	38 (48.7%)	40 (51.3%)
	Hispanic (186)	93 (50%)	93 (50%)
	Others (8)	3 (37.5%)	5 (62.5%)
Age group (Years)	15-20 (55)	26 (47.2%)	29 (52.7%)
	21-30 (162)	85 (50.9%)	77 (49.1%)
	31-40 (51)	21 (41.1%)	30 (58.8%)
	≥ 41 (4)	2 (50%)	2 (50%)
Parity	Primiparous (64)	24 (37.5%)	40 (62.5%)
	Multiparous (208)	110 (52.9%)	98 (47.1%)
Social Environment	Living With Family (160)	86 (53.8%)	74 (46.3%)
	Living With Boyfriend (21)	7 (33.3%)	14 (66.7%)
	Living Alone (13)	3 (23%)	10 (77%)

pairs. HHC compiled data for all eleven hospitals in 2003 showed an exclusive breastfeeding rate of 15% which is far lower than the national target. Any breastfeeding rate was 45%, while formula fed infants comprised the remaining 40%.

Objectives

- To determine the relationship of breastfeeding in our population to age, race, parity, social environment, marital status, level of education and maternal smoking influence.
- To determine the time of initiation of breastfeeding and the percentage of exclusive breastfeeding.
- Education of hospital staff and mothers to improve future breastfeeding rates.

Materials and Methods

An observational, cross-sectional study was conducted for a three month period at LMMHC from October to December 2005. We interviewed 272 mothers in the postpartum rooms individually on the day of discharge as part of our training and to gather data on breastfeeding to improve future breastfeeding rates at our institution. Inclusion criteria included mothers of infants who were full term, have normal newborn nursery care with no perinatal complications. Exclusion criteria included preterm infants and full term infants requiring neonatal intensive care. Full term was defined as all infants born > 37 weeks of gestation. The study was explained to the mothers and informed verbal consent obtained. Breastfeeding was defined as exclusive vs. any in our study. Exclusive breastfeeding included all infants who had received only breast milk with no other liquids including water. Any breastfeeding included infants who had at least two breastfeedings during the hospital stay.

Results

The overall rate of any breastfeeding in our population was 49.2% versus non-breastfeeding 50.7 % .The comparison of data is presented in table 1.

a. Patterns by type of milk: 3.6% of the mothers were exclusively breastfeeding and 45.5% were both breast and bottle-feeding. About half of the mothers (50.7%) did not initiate any breastfeeding throughout the hospital stay.

b. Breastfeeding pattern in relation to socio-demographic characteristics: The socio-demographic data in our study has shown no significant differences in breastfeeding between maternal race and age. Multiparous women (52.8%) were more likely to breastfeed than primiparous women (37.5%). We also found that breastfeeding a previous child had a positive outcome on breastfeeding the present child. Women who lived with other family members had significantly higher breastfeeding rates (53.8%) compared to women who lived alone (23%) or with a boyfriend (33.3%).

c. Attitude towards breastfeeding in the prenatal period: 90% of the mothers surveyed received prenatal education through Women, Infant and Child (WIC) program, prenatal care

providers and lactation coordinators, and a majority of them expressed a desire to breastfeed at the time of delivery. Despite prenatal education and decision to breastfeed only 49.2% of mothers were breastfeeding and others were breastfeeding with combination of formula feeding.

d. Initiation of Breastfeeding: 14.9 % of the mothers initiated breastfeeding in the delivery room and only 2.2% had given the first feed in less than 4 hours of the newborn's life. Majority of the women (74.6%) had initiated breastfeeding by 24 hrs after birth. 77.4% of mothers gave 1 to 5 feedings during hospital stay where as 22.6 % had given > 5 feedings.

Discussion

Breastfeeding is one of the oldest practices recommended by all cultures and religions worldwide. It is natural, species-specific and easy to initiate. However, it is concerning that there has been a change in the pattern of breastfeeding particularly in our community. A downward trend in breastfeeding has been noted worldwide.[4,5,67,8,9,10,11,12] Even in the Middle East where the practice was very common, reports from previous studies have shown that the vast majority of women do breastfeed their children for some time, but they often cease breastfeeding exclusively too early to give the maximum benefit, especially in urban areas where there is easy availability of formula.[13] Despite this some mothers still cling to the old practice and want to breastfeed even if they have no latching, and cases of induced lactation have been documented in literature.[14] Developing countries have higher rates of breastfeeding even though WHO is helping to provide formula feeding in starvation countries.[15,16,17] In the United States, the same downward trend for breastfeeding has been documented.[18,19]

The exclusive breastfeeding rate for HHC in 2003 was about 15%, whereas formula and breastfeeding rate was 45%; the rest were using formula feeding. The results from our study showed only 3.6% of mothers were breastfeeding, which is still below the target of 75% set forth by Healthy People 2010 for breastfeeding in the early postpartum period and also way below the HHC data for 2003. Maternal age and other socio-demographic factors have been shown repeatedly to be positively associated with breastfeeding initiation and duration. In our study we found no significant difference in maternal age, parity, ethnicity and social support systems regarding initiation of breastfeeding. Most of our study population desired to breastfeed initially and received prenatal education but there appeared to be obstacles to breastfeeding initiation including system-based practices not conducive to breastfeeding.[20,21] Mode of delivery, vaginal vs cesarean section, also influences the initiation of breastfeeding.[22]

Lawson and Tulloch, in an earlier study of Australian women, showed that breastfeeding duration up to 3 months was related to the timing of the first breastfeeding and the extent of mother-infant contact in the 72 hours after birth.[23] In our study we found a low number of mothers who initiated breastfeeding at the delivery room and less than 4 hours postpartum, which could be one of the factors that influenced our low rate of breastfeeding. This is because mother and infant were separated soon after birth. This practice should be avoided in a healthy term newborn in order for the mother to establish bonding and to initiate breastfeeding. The mother-infant dyad must be continued in the postpartum unit. Breastfeeding is also reinforced by the baby-friendly hospital initiative, which promotes practices as part of the ten steps to successful breastfeeding and can increase both the duration and the exclusivity of breastfeeding in the first year of life.

It has also been proven that prelacteal feeds and the early supplementation of breastfeeding with infant formula have been associated with shorter duration of breastfeeding.[24] In a study of Swedish women, it was found that supplementation in the hospital while breastfeeding had no significant influence on breastfeeding duration; however, it was negatively associated with a shorter duration of exclusivity.[18,25,26,27] We have similar comparable results in our study. Despite 15% having initiated breastfeeding in the delivery room, only 3.6% were exclusively breastfeeding. Based on our study we have found a major breakdown in system-based practices from labor and delivery to the postpartum unit which need to be addressed for further improvement in breastfeeding rates.

Organizations like WIC, though advocating breastfeeding, are also providing formula free of cost. The majority of women listen to the breastfeeding initiatives and then ultimately get free formula and practice formula feeding. Several studies have documented lower rates of breastfeeding in WIC participant mothers.[28] A change in culture may also play a role as women who breastfed their first child when they were outside the United States are known to start formula feeding in subsequent children due to a multitude of reasons including poverty, family influence, media promotion, need for a job, easy access to formula feeding and other environmental factors.

System-based practices can be improved by appropriate training of all those who work in the perinatal area, along with simplified baby friendly hospital breastfeeding policies. Education of prospective mothers should begin in the early prenatal period to facilitate smooth transition to breastfeeding in the intrapartum to postpartum period.[29] The obstetrician should play an important role in educating mothers, starting with first prenatal visit and stressing the importance in subsequent visits. They should work as a team with WIC, nursing staff, and the breastfeeding coordinator to develop a simple, comprehensive educational program to help mothers and their families understand the simplicity of breastfeeding. This is easily said but hard to implement, as it requires motivation of healthcare and non-healthcare staff towards teaching of prospective mothers, as well as commitment and support. Most hospitals have policies for breastfeeding awareness and education, but methods to implement them are lacking. Having a policy is not enough; a collaborative effort of all those involved in the care of mother-infant dyad with one to one support is the most feasible solution and should be addressed at each institution. An extensive effort by the HHC, with a grant from the Department of Health, has begun to train staff to help mothers to increase the breastfeeding rate at all HHC facilities and we will be evaluating the progress in the coming years.

Media also plays a vital role in the conflict of breast vs formula feeding, and the total hijack of the media by multinational infant formula producing companies has changed the balance towards formula feeding as it is presented as safe, nutritious, and a symbol of high society. Studies on the role of media and promotion of formula feeding have been well documented.[30] The role of the media towards breastfeeding and formula feeding should be balanced, as there is still need of formula feeding for

women where breastfeeding is contraindicated and for those who wish to continue formula feeding despite education and support on breastfeeding.

It is the patient and her healthcare providers, with support from family, that would make breastfeeding a successful event for the mother and the baby. The mother needs continued support and education on breastfeeding after discharge from the hospital by a pediatrician and the outreach staff. We have incorporated AAP guidelines at LMMHC for providing one week follow-up clinic appointments to all those who breastfeed to evaluate the baby and to continue support to the mother. The HHC mandates to increase breastfeeding rate at HHC hospitals; it is a priority and full support at each institution definitely show much progress in the coming years.

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Antenatal Screening and Its Possible Meaning From an Unborn Baby's Perspective

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Abstract
In recent decades antenatal screening has become one of the most routine procedures of pregnancy-follow up and the subject of hot debate in bioethics circles. In this paper the rationale behind doing antenatal screening and the actual and potential problems that it may cause will be discussed. The paper will examine the issue from the point of view of parents, health care professionals and, most importantly, the child-to-be. It will show how unthoughtfully antenatal screening is performed and how pregnancy is treated almost as a disease just since the emergence of antenatal screening. Genetic screening and ethical problems caused by the procedure will also be addressed and I will suggest that screening is more to do with the interests of others rather than those of the child-to be.

Introduction

Antenatal testing (ANT) is widely used in modern obstetrics and gynecology. I shall discuss the procedures involved in ANT from different perspectives, beginning with definitions of antenatal screening and antenatal diagnosis, the main objectives and indications for their use. Secondly, I will discuss the risks and complications of ANT, the concerns, doubts and moral controversies it raises. Thirdly, since counseling is an integral part of ANT, I shall try to determine what the ideal of counseling before and after ANT is meant to be. Finally, with particular reference to some relevant concepts like responsibility, suffering and interest, I attempt to describe the whole issue more comprehensively.

Recent studies have indicated that the major pediatric health problems are handicaps due to genetic disorder or congenital malformation. When it was noticed that more than a quarter of all deaths in the first year of life were due to fetal abnormalities,[1] scientists were alarmed and parents sought a remedy for the problem. Although antenatal diagnostic techniques were initially described in the nineteenth century, it was not until the middle of 20th century that the techniques were applied to AND and management of various genetic disorders and congenital malformations. And, at the present time, antenatal screening and diagnostic techniques are almost the norm. It has been said that, probably around 90% of women in the UK have undergone one of these at some time during pregnancy.[2] Although there is only a slight difference between the two procedures, the authorities do distinguish between antenatal screening (ANS) and antenatal diagnosis (AND).

Aims of antenatal testing

ANS services are based on population screening to identify people with a genetic risk, or a risk of having a child with a congenital or genetic disorder.[3] In the Dutch Health Council report on genetic screening, the major aim is defined as: "To enable people to decide upon a course of action that is acceptable for them".[3] ANS includes:

1. Screening for sporadic conditions affecting the fetus (infections, chromosomal disorders, malformations, maternal diabetes);
2. Family history for genetic risks;
3. Population screening for carriers of common recessively inherited diseases.

Different health authorities in different countries have pointed out various aspects of ANS. While the Danish Health Council considers screening as a community-based form of help based on the obligation to help the weak, the Nuffield Council on Bioethics (in Britain) points out that, although the primary aim seems to be to improve the health of persons suffering from genetic disorders, the benefits should include enabling individuals to take account of the information for their own lives, and empowering them as prospective parents to make informed choices about having children.[3]

Although the screening test is not usually in itself diagnostic, it detects a subgroup of those tested who are at higher risk of having the disease or disorder than the original population

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Table 1: Antenatal Tests

Type of test	Detectable conditions	Stage of pregnancy
Invasive: mother only		
MSAFP		
Estimation of maternal serum alphafetoprotein in maternal blood.	Neural tube defects; Down's syndrome.	16th-18th week.
Combined maternal blood test		
Estimation of MSAFP, chorionic gonadotropin and/or unconjugated oestriol.	Down's syndrome.	16th-18th week.
Invasive: both fetus and mother		
Amniocentesis		
A test involving the insertion, through the mother's abdomen, of a fine needle into the amniotic sac and the removal of amniotic fluid.	Chromosomal disorders; a number of hereditary disorders caused by a single gene; neural tube disorders.	12th-14th week.
Chorion biopsy		
A test involving the introduction through the mother's vagina or abdomen of a needle into the womb and the removal of tissue surrounding the fetus.	Chromosomal disorders; a number of hereditary disorders caused by a single gene.	8th-12th week.
Fetoscopy		
A test involving the introduction through the mother's abdomen of an instrument enabling the examiner to see the fetus.	Chromosomal disorders; disorders detectable by fetal blood sampling; malformations.	16th-18th week.
Cordocentesis		
A test involving the insertion of a needle through the mother's abdomen (where the umbilical cord of the fetus is attached to the placenta) and then the removal of fetal blood.	Chromosomal disorders; disorders detectable by fetal blood sampling.	15th week onwards.
Non-invasive		
Ultrasound scan		
An instrument is passed over the mother's bare abdomen and a picture of the fetus is produced on a screen.	Fetal growth and development; multiple pregnancy; malformations, including neural tube defects.	Any time but often about the 16th week to check dates and development.
Radiography		
The mother's abdomen is X-rayed. This is hardly ever done today.	Skeletal abnormalities requiring a picture of the whole skeleton.	20th week onwards.

screened, in many cases it is possible to make diagnoses with considerable accuracy.

Three different types of ANS methods are widely used;

1. **Biochemical Screening:** In this technique, a single specimen of blood taken from a pregnant woman at about 16-18 weeks of pregnancy, can be used to screen for Down's Syndrome and open neural-tube defects. This can detect about 60% of pregnancies with Down's Syndrome, about 90% of pregnancies with open spina bifida, and virtually all cases of anencephaly.[4] Biochemical screening tests are used to identify those women who are at high enough risk to justify the hazards and costs of the diagnostic procedures.

2. **Genetic Screening:** The sensitivity and the specificity of genetic screening is fairly high. The test is carried out either by amniocentesis or by Chorionic Villus Sampling (CVS) at 14-16 weeks and 8-9 weeks respectively. Using standard cytogenetic techniques it is possible to culture amniotic fluid cells from as little as 10 ml. of amniotic fluid at 12 weeks, although successful culture before this time is currently less reliable. In CVS chorionic tissue obtained via endoscopic biopsy is used to make the types of fetal diagnoses by culture of amniotic fluid cells. The objectives of genetic screening developed by the Royal College of Physicians (London) are: to allow the widest possible range of informed choice to women and couples at risk of having children with an abnormality; to allow couples to embark on having a family knowing that they may avoid the birth of seriously affected children through selective abortion; to ensure optimal treatment of affected infants through early diagnosis.[4]

3. **Ultrasound Screening:** The objectives of ultrasound screening are defined as: to reduce the prenatal mortality

Table 2: Costs and benefits of antenatal diagnosis typically noted by the medical profession

Costs	Benefits
	For hospital and health authorities
1) Costs in connection with diagnosis,	1) Scarce resources allocated to children with good prognosis (rather than to severely handicapped children).
2) Costs involved in performing termination.	
3) Costs in connection with counseling services.	
	For pregnant women and fathers-to-be
	Availability of prenatal diagnosis
	1) Increase in the number of healthy children born to parents at risk who, had prenatal diagnosis not been available, would have avoided becoming pregnant.
	Diagnostic procedures
1) Risk of fetal loss or injury,	
2) Maternal hazards,	
3) Maternal anxiety.	
	Result:
	true negative
	2) Reassurance,
	3) An increase in the number of healthy children born to parents at risk who, had the test result not been negative, would have terminated pregnancy on grounds of risk.
	false negative
4) False reassurance.	
	false positive
5) Abortion of healthy fetus,	
6) Grief and adverse psychological consequences of termination of non-affected pregnancy.	
	true positive
	-followed by abortion-
7) Grief and adverse psychological consequences of termination of affected pregnancy.	4) Averted parental distress and burden of care for disabled child,
	5) Additional non-disabled children.
	-not followed by abortion-
	6) Time to prepare for the birth of the disabled child.

and morbidity; and to allow the identification of a group of babies for whom treatment in utero may be appropriate by defining structural abnormalities.

Antenatal Diagnosis

AND has four main purposes: to inform and prepare parents for the birth of an affected infant; to allow in utero treatment, or delivery at a specialist centre for immediate postnatal treatment; to allow termination of an affected fetus; and to provide information so that parents may choose between 1, 2 and 3.

Evidently, the goal of AND is to help couples make an informed choice, one which they feel is best for themselves and their families. AND tests can be divided into those involving measurements of chemicals in maternal blood, imaging the fetus, and invasive tests to remove tissue of fetal origin. The tests in the last group may be carried out before 14 weeks' gestational age but after implantation, beyond 14 weeks' gestational age, or in the pre-implantation period. The tests, which are carried out in the preimplantation period are embryo biopsy and polar body analysis. The tests in the second group are fetal blood sampling, fetal tissue biopsy, amniocentesis, and transabdominal chorion biopsy. The tests in the first group, that are the most widely used at present, are early amniocentesis, transabdominal chorion villus biopsy or sampling (CVS) and transcervical CVS. Table 1[5] indicated some of these antenatal tests with their time of application, and detectable conditions.

Preimplantation Diagnosis (PID)

Among other ANTs PID has a special feature. It aims to avoid the possibility of an affected pregnancy completely. It is based on the simple strategy of sampling genetic material from eggs or embryos within the first week of their development following fertilization. The genetic material is used to detect whether a particular genetic defect is present and whether the embryo will be affected by it. This procedure theoretically enables the selection of only healthy embryos for implantation, or the genetic modification of embryos with disabilities or genetic defect prior to implantation. Beside other advantages PID is more abstract and less invasive than other AND technologies. PID is done at an earlier time than AND-up to five days as against ten-sixteen weeks. This may lessen feelings of emotional attachment in that PID can prevent termination of a pregnancy diagnosed as affected at later stages of gestation. It is argued that the earlier the diagnosis of genetic conditions, the easier the moral choices for many women or couples. For those who hold that the early fetus (ie pre-sentient or not yet a person) is morally different from the older fetus, early identification of fetal genetic conditions will diminish the moral confusion of abortion. R. G. Edwards, the pioneer of in vitro embryology, observed that, "Identifying embryos with genetic abnormalities would offer an alternative to amniocentesis during the second trimester of pregnancy, and the 'abortion in vitro', of a defective preimplantation embryo would be infinitely preferable to abortion in vivo at twenty weeks of pregnancy or thereabouts as the result of amniocentesis are obtained."[7]

Although it seems emotionally (perhaps also ethically) less problematic, there are still objections to the manipulation of human preimplantation embryos.[8] The objections are generally based on the view that there is, in principle, no difference between an eight-cell embryo, and a fetus or a child. In this view, they are all human individuals and, since informed

consent is not possible, they should not be interfered with. On this basis, terminating an affected pregnancy halfway through the pregnancy is no more or less acceptable than discarding affected preimplantation embryos. The opposing view draws a sharp distinction between these stages of a human being's development and consequently argues that the ethical constraints are different at each stage. In this case, manipulation of early embryos to remove cells for genetic analysis is acceptable and some would argue that discarding affected embryos is preferable to doing so at later stages. Another concern about PID is that, after prenatal diagnosis, there is at least a theoretical possibility that a couple will decide to carry a genetically abnormal fetus to full-term. In the context of preimplantation diagnosis and IVF, the decision-making process is eliminated; the genetically abnormal embryo will not be implanted.[9]

Benefits of antenatal testing

There can be a little doubt, on the face of it, that the techniques just described were devised to help people, and aim to enable parents to plan their future family knowledgeably. However, many authorities from various fields have expressed some serious concerns about them. It is important to define the real aims of these techniques, and see how they work in practice. It is thought that these techniques may not necessarily have been developed with the interests of women primarily in mind, nor are necessarily applied to further women's interests.[10] A governmental document from DHSS (in United Kingdom) may help us to clarify our thinking about the real aim of these technologies. It reads: "...because caring for the handicapped can impose great burdens on our society the prevention of handicaps...in addition to its other benefits may save money. The costs of providing amniocentesis for all expectant mothers over the age of 40 years, and maternal serum AFP screening for all pregnant women, would be more than offset by the economic benefits in terms of savings of expenditure on children and adults with Down's Syndrome and spina bifida".[11]

Rational as this sounds, this kind of rational-economic thinking may degrade society's willingness to accept and care for abnormal children, while at the same time enlarging the category of unacceptable abnormality and narrowing the range of acceptable normality. If Down's syndrome and spina bifida are 'too' expensive today, what will become too expensive if the economic climate becomes gloomy?[12]

Whether and how far it is right to accommodate cost-benefit analysis in the medical field has always been problematical. As has the question of whether economical considerations should affect clinical decisions.[13] Some reports have compared, for populations with varying incidence of neural tube defects, the benefits of a antenatal screening program (in terms of number of births with neural tube defects prevented) against the physical costs (in terms of the number of normal fetuses harmed by amniocentesis) the cost-benefit ratio becomes progressively less favorable as the population incidence of neural tube defects decreases. This, together with the fact that around 85 per cent of babies with neural tube defects are either still-born or die within the first year of life, means that, in regions with a low incidence of neural tube defects, it is possible that more unaffected pregnancies may be harmed than handicapped children avoided.[14] Another recent report has also indicated the 'possible cost' of antenatal diagnosis. With its annual report, the Danish Council of Ethics has published a debate outline on ethical issues in fetal diagnostics. It consists of a report on the past, present and future of fetal diagnostics, commissioned from a Danish science writer, and a discussion of the Council's deliberations on the issue. The report reads, "Just under 120,000 fetuses examined. Over 2,200 sick or deviant fetuses identified and aborted. Loss of some 1,100 presumably healthy fetuses as a side-effect of the examination used."[15] The council sums up that "it is essential to stress that, irrespective of the stance taken on fetal diagnostics, it will be problematic for either one or the other party involved in fetal diagnostics." Table 2[5] outlines the costs and benefits of AND typically noted by medical practitioners involved in AND. The table makes it clear that medical practitioners usually focus on the pregnant woman rather than on the fetus when they assess the advantages and disadvantages of antenatal diagnosis.

As the table shows, it is possible to argue that AND tests can benefit everyone but the prenate. However, there is no denying that AND can be a vital aid in monitoring pregnancies for therapeutic reasons with a view to safe deliveries, and most AND is performed in order to prevent the birth (or conception) of disabled children. This motivation is clearly expressed in the report of the Royal College of Physicians: "Unless prenatal diagnosis is to be devoid of practical application when it reveals a major defect in the fetus, a responsible doctor must discuss with the parents the option of terminating that pregnancy and must in some circumstances provide information that may deter them from further reproduction."[16] The termination of pregnancy and its acceptability is taken elsewhere,[17] but it is worth mentioning here that it is highly questionable to claim termination of pregnancy as in the child's best interest.

It has been argued that the availability of antenatal screening and diagnostic testing has changed the experience of pregnancy. Before the development of antenatal testing for fetal abnormality, the fetus was assumed to be healthy, unless there was evidence to the contrary. The presence of antenatal testing and monitoring shifts the balance towards having to prove the health or normality of a fetus.[18] Pregnancy has come under medical control to such a degree that it is almost treated as a disease, and pregnant women have accepted their role as patients in need of medical help. Both the medical profession and pregnant women now regard antenatal diagnosis as a necessary part of prenatal care.

Barbara Rothman, in her book The Tentative Pregnancy, maintains that it is the medical profession that has created a need for antenatal diagnosis for 'reassurance' by creating what she calls "genetic anxiety," thereby capitalizing on women's normal fear of having a defective, socially unacceptable, child, just as deodorant and mouthwash companies first had to create anxiety about socially unacceptable body odor before they could market their product.[19] However, if there really is a normal fear of having a 'defective', socially unacceptable child, then it is the duty of health care professionals to find a solution. Rothman's critique may well be a response to a certain paternalism in the attitudes of the medical vis-à-vis ANT. As in many other medical interventions, informed consent and intelligent counseling are of prime importance in ANT procedure.

Effect of counseling

Counseling before and after ANT is crucial.[20] It is suggested that, in an ideal counseling, the parents should be told that there

is no 'right' decision to be made, and it should be made clear that whatever their decision is, it will be supported. They must also be clear about whether it is a screening test or a diagnostic test, and how accurate it is in their particular situation. They need to be aware of the risks involved to the pregnancy and the possible consequences of dealing with the information the test provides.[21] Normally, medical professionals should not offer antenatal diagnosis, because it is known that it is very difficult for a woman to decline AND when offered.[22] Instead, they should discuss the feasibility, accuracy and clear-cut details of any such tests, including the dangers of it.

Three pieces of information which women tend to cite as reasons for changing their minds about tests are: the level of risk they have for the condition in question; the miscarriage risk of the test being considered; the method of termination which would be offered if they chose to terminate the pregnancy following an abnormal result from the test in question.[21]

To provide this kind of ideal counseling, firstly there must be enough well-trained health care professionals. The units that provide these services must also provide suitable training opportunities and satisfy the expectations of users of ANT services.

Chadwick suggests that 'genetic counseling' includes the following kinds of activity: advising adults, pre-conception, of the probability of their conceiving a child with a genetic disorder;advising adults, post-conception, and as a result of some method of fetal screening, as to whether or not the fetus is suffering from a genetic disorder; alerting them to the options open to them.[23]

Clearly, it is important to leave the final decision to the parents. Doctors are supposed to not impose their own moral attitudes upon their patients. If they find themselves disagreeing with the moral stance of their patients over these issues they should explain their situation and advise the patients to consult a clinical geneticist.[24]

However, it seems it does not work like this in practice, because, making rules does not mean everything. The most important and difficult thing is applying them. And this depends on the development of public awareness and education.[25] It is argued that the conflict of interests between providers and users of antenatal screening services is clearly reflected in the counseling process. At all stages of screening, counseling is systematically biased towards encouraging women to take up the tests and have an abortion if an abnormality is detected, rather than providing women with the information and support they require to make an informed choice and to avoid unnecessary distress.[10] The Medical Research Council (MRC) stated in its report that, "Of the 112 women (including high risk women) interviewed after they had had an amniocentesis, 28 (24 per cent) were unaware that amniocentesis carried a risk of miscarriage, and 96 (86 per cent) were unaware of any other possible hazards. Of the 16 women aware of the possible risks to the newborn infant, 12 had obtained this information from sources other than the medical staff who had counseled them about amniocentesis."[14] There is literature available which is compatible with the MRC's report. For example: "Women undergoing routine antenatal screening are generally under-informed about the tests they are being offered and may subsequently undergo. For example, 39 per cent of women who had recently undergone maternal serum alphaprotein (MS-AFP) screening for open neural tube defects were unaware that they had even had the test".[26]

Self-evidently, this is not an ideal situation for any health care service. Apart from the failure to provide enough information, the bias toward termination of pregnancy in the event of abnormality detection is another controversy in AND procedure. It is generally conceded by the medical profession that the primary aim of antenatal diagnosis is the detection, and subsequent abortion, of abnormal fetuses. Because of the procedural risks to the fetus and the lack of effective methods of fetal therapy for most malformations, antenatal diagnosis is a rational activity only if abortion is seen as an acceptable alternative.[27] However, this kind of approach to prenatal diagnosis may be considered not only unfair, but also rather unethical, by some people.

In order to describe the feelings of parents who are pushed to have a termination, one needs to have experienced it. But it is not too hard to comprehend the difficulty for parents who decide not to terminate a pregnancy with a diagnosed fetal abnormality-they must face, as well as the distress of coping with a handicapped child, the mental and emotional struggle of defending their decision before health professionals.[28] In an ideal ANT procedure, health care professionals are expected to strengthen their role as providers of support to the families for whom they care. They should provide moral support and practical help both to those who terminate fetuses at risk of malformation or disease and to those who choose not to do so. Furthermore, ANT providers in this field are expected to prevent any possibility that financial considerations might affect clinical behavior. Angus Clarke, a clinical geneticist, makes a distinction between giving advice-a prescriptive activity, often subtly authoritarian when applied to the field of personal reproductive decisions-and the informing, supportive, and 'enabling' process of counseling.[29] And he adds, "We do not tell people what to do but support them in reaching decisions, with the consequences of which they then have to live for the rest of their lives. We may have to inform clients about the disadvantages of their preferred course of action so that they can examine all options (such as a permanently handicapped child, or permanent remorse at a termination), but, when the decision is genuinely their own, the parents are much more likely to be able to live with it."[29]

Another counseling issue related to ANT is that of directiveness. It has been argued that pre-test counseling should be non-directive since it is counselee and not the counselor whose entire future life may be affected by decisions made at the sessions. However, those present at the Third European Meeting on Psycho-social Aspects of Genetics (1992) voted by a narrow majority that non-directive genetic counseling was not achievable in practice. This is partly due to the fact that counselors come to sessions with their own views about what they think they would do in the situation or what they think a responsible person should do. These views may be held consciously or unconsciously but they will influence the counselors' choice of words in describing conditions, tests and probabilities, their facial expression, body language, and the order in which things are explained and the amount of time spent on different topics. For this reason non-directive counseling is thought to be an unattainable ideal. It is not because of a personal failure on the part of the genetic

counselor but as a direct result of the structure of the encounter between counselor and client.[30] Clarke argues that the counselor's conscious or even unconscious motives are irrelevant; the offer and acceptance of genetic counseling has already set up a likely chain of events in everyone's mind.[30]

From all these discussions it becomes apparent that non-directive counseling is a myth. Today, counseling is directive, and its direction is towards having ANT and going to termination if something is wrong with the baby in the womb. Let us now discuss (in terms of its benefits to different parties) the consequences of ANT.

Consequences of antenatal testing

The primary purpose of AND is to relieve parents of anxiety over inheriting a genetic disease, or giving birth to a child with congenital abnormalities (eg, for older women), and this is the major outcome. AND is defined as intended to inform parents of the birth of an affected infant, to allow in utero treatment, or delivery at a special centre for immediate postnatal treatment, or to allow termination of an affected fetus; in practice the last of these three has become the most used course of action. Many writers have criticized this attitude as wrong. Among the arguments put forward is that wide acceptance of selective abortion diminishes the importance of and the motivation for, research on cures for genetic disorders, whether in utero or after birth to be taken up.

There is a little doubt that relatively non-invasive technology whose primary purpose is to diagnosis treatable disorders and cure them before or after birth would be warmly welcomed by parents and ethicist alike. However, the present reality is that antenatal diagnosis rarely leads to fetal therapy. In fact, in many cases normal fetuses are negatively effected from the CVS procedure.[31] There is also evidence that the availability of AND may be leading scientists to leave research on cures of genetic disorders in favor of selective abortion. During the 1960s there were two to three times as many people working on a cure for Tay-Sachs disease than at present. The emphasis now is put on an antenatal diagnosis for Tay-Sachs disease, followed by abortion in the case of a test positive. Similarly, as soon as an antenatal diagnostic test for Huntington disease became available in the early 1980s, funds began to disappear for research to find a cure.[31] Beside these trends, the greater social acceptability of abortion, and increased pressure on women to undergo AND from health insurance companies medical professionals and government agencies, are all possible negative consequences of AND. Alongside the benefits of diagnosing abnormalities in early stages of pregnancy, there are some potential psychological costs. These include anxiety, loss of confidence about the pregnancy and negative attitudes towards the baby. A major worry is, or ought to be, that the availability of AND may make people increasingly intolerant of the disabled and hostile towards parents who choose not to abort affected fetuses.[5]

The use of AND for sex selection and termination of pregnancy if the fetus is of the undesired sex is, rightly, described as an atrociously unethical practice.[32] However, it is also easy enough to see the wish to have a boy or a girl as simply satisfying the desires or needs of the future parent(s) or other relatives. Strictly argued, sex preference could be regarded in the same way as exercising a preference for a normal, healthy child, rather than an unhealthy one. If someone has the right to do something to have (or not to have) a disabled child, he or she could argue the same right to have (or not to have) a child of particular sex. Strictly speaking, both properties, being healthy/disabled or male/female are morally, neutral. The reasoning follows: if it is right to terminate the pregnancy in case of disability, is it not equally right to terminate it in case of undesired sex, or vice versa. Mahoney observed that parents are necessarily determining a child's genetic constitution, its environment, its character and its entire future by the unavoidable choices they make, whether consciously or not: the choice to have a child, the choice to do so in a particular country or town or climate, the choice to send it to a particular school, the choice to encourage it or discourage it in certain forms of behavior, and so on. He went on to conclude, "I do not see why, within such a chain of choices, the choice of sex should be singled out for particular moral disapproval."[33] It is wrong, it could be argued, to differentiate undergoing an AND with the intention of finding out the health condition of the fetus with termination as a possibility, from undergoing an AND to check the sex of the fetus with, again, termination as a possibility. In principle, both can be seen as equally morally acceptable or unacceptable.

In 1883 Francis Galton started using the word eugenics, defined as the science of improving stock, not only by judicious mating, but whatever tends to give the more suitable races or strains of blood a better chance of prevailing over the less suitable than they otherwise would have had.[34] However, later the social policy intervention, along with genetics measures exists in many countries.[34] These policies do not aim to coerce or make mandatory who will be conceived and born, they emphasize the elimination of hereditary disease and handicaps through antenatal testing. This eugenics thinking is justified by some, since it is not a science based on Nazism, racism, discrimination to minorities and genetic determinism. It is a science which is inherent in the core eugenic doctrine of improving the stock of humankind by application of the science of human heredity. This science can be called "negative eugenics."

Despite all improvements, still ANT is not 100 per cent accurate. It is reported that, "Routine screening tests do not detect all cases. MS-AFP detects about 80 percent of cases of spina bifida. Although smaller, there is a false negative rate from both CVS and amniocentesis. Inherent in all screening tests is the possibility of a false positive result."[26] The routine use of ultrasound may result in the detection of symptomless minor anomalies, the incidence and natural history of which are unknown. Although these are not indications for a termination, their detection means that women face the rest of their pregnancies with the knowledge that their child has an abnormality where implications are unknown. This may have two different consequences: the diagnosis of a possible abnormality may affect the acceptance of the baby by the parents and create negative attitudes in them towards it; or it may alert parents to prepare emotionally and psychologically for their (possibly) handicapped baby. In either case parents have 5-6 months to make up their minds-which is better than being surprised in the labor room.

For all couples with an abnormal result, there may be moral or religious objections or social pressures about termination, there may be disagreements between the couple as to the correct course of action and it is not always possible to give the couple a clear idea of the particular disability of that particular fetus.

There is also the extremely important emotional consequence of the decision-the feeling of responsibility for the loss of a wanted child, which many couples describe as guilt. Clearly, in these situations, the decision making is more difficult, and for those couples who choose to terminate a pregnancy at less than 100 per cent risk of the fetus being affected, there will be lingering doubts about whether the baby might, after all, have been normal. A study has shown that in 38 per cent of the cases there are differences between the attitudes of parents towards AND.[22] While discussing the harms and the benefits of the antenatal screening programmers Atkins and Hey suggested that, "It is possible that some screening programmers currently do more harm than good. Antenatal diagnosis does not always increase a child's chance of survival. Liveborn children with an uncomplicated abdominal wall defect, for example, have an excellent chance of survival and a negligible risk of long-term disability, but antenatal diagnosis can bring with it ill-justified pressure for the pregnancy to be terminated."[1]

In Whose Interest?

There can be no objection if the aim of ANT procedure is to diagnose abnormality and cure it, if that is possible. However, many people are uneasy about terminating the life of the fetus. At this stage the question arises: Whose interest does ANT serve-the interest of the child-to-be, or of the parents, or of the siblings' and/or of the society as a whole? In the event of an abnormality being diagnosed, treatment before birth, or birth in a centre where the necessary interventions are possible, the child-to-be would definitely benefit from ANT. In this case everyone will have tried their best to give the unborn a (better) life. There is a question whether having a child with an abnormality is good for parents, siblings, or the society. In fact the interest of the child/person vis-à-vis having a life at all, overweighs others' comparatively trivial interests, for almost any interest is trivial compared to life. Of course, it is not convenient to have a disabled child/sibling/citizen; of course, everyone would prefer to have a healthy one. However, in AND and subsequent termination, the choice is not between being born with health or being born without it; rather, the choice is between a worldly existence or none at all. And the difference between existence and non-existence is beyond comparison.[35]

Should we then admit that, except where pre- or post-natal treatment is the aim, AND has nothing to do with the prenate's interest, but with parents', siblings' and/or society's interest? Several authors have said that much antenatal diagnosis is for the benefit of the parents rather than the fetus.[36] But is it that straightforward?

Does the birth of a disabled child not add to the suffering in the world? Harris has argued on one occasion that: "We have an obligation to prevent suffering and disability, or, more abstractly that we should try to produce a world with less rather than more suffering in it, that we should try to produce a happier world. So indeed there is clearly a moral obligation to provide such screening where possible so that parents can have the opportunity to choose not to bring suffering or disability into the world."[37] A counterargument was put by Galjaard, a professor of cell biology: "Parents who have integrated their suffering, having had one or more handicapped children now stand up and defend the birth and the experience of these handicapped children as having made them happier, their marriage better, and so on."[37] To this Harris replied with an analogy: "Imagine a pregnant woman has a condition. The fetus is damaged, but there is a simple risk-free procedure which will remove the damage. She just has to imbibe orange juice and the handicap will be removed. But she says no, she does not want to do it, she does not want this therapy because the last handicapped child she had made her so happy she intends to have another. What one would feel about such a decision gives the key to the respectability of the happiness argument from other people's misery."[37] As I have argued elsewhere in discussing this analogy, if all that is needed is to imbibe orange juice and remove the handicap, then drinking orange juice is the only course of action that any sensible person would take.[38] But in reality there is rather more involved, and rather more at stake, than a simple drink of orange. The ANT procedure is not risk free (as we saw, above). Thereafter, the choice is not 'drink orange juice and have a healthy baby', which the mother perversely refuses because she 'prefers' to have a disabled child. Rather, the choice is (after the risk of ANT): have a child who may have disability or not have the child, i.e. terminate your pregnancy.

Furthermore, some genetic disorders are diagnosed antenatally which may not surface for many years after birth, and possibly only after the parents themselves are deceased. Huntington's chorea would be a case in point. In this circumstance, should termination follow ANT, although there is 20 or 30 years of happy, normal life expectancy? Harris answered the question in this way: "I think it would be better not to bring that degree of suffering, albeit postponed, into the world. Taking a decision when no person is in being is quite different from saying to a 20 year-old who has Huntingdon's and who will die from it that their life has not been worth having. When it is an embryo or a fetus, before it has a conscious life, the calculation to be made is which action causes the least suffering, and I think termination is the answer to that question."[37] First of all we must admit that the comparison to be made is not that between nonexistence and a deprived life but that between a defective life and the life of a normal child. Of course it would be better not to bring that degree of suffering into the world. And, it is absolutely preferable to take a decision when there is as yet, 'no person in being'. However as soon as an individual life is being, there is no point in comparing that life, however deprived it may be, with non-existence. This does not mean rejecting outright the possibility that there are some situations in which it is better to be dead. But that is a decision for the individual concerned, not a decision for others to take, whoever they are.

In sum, there are two questions before us: 1) determine the 'morally safe' period to manipulate the prenate, and 2) to improve AND techniques to in order to detect abnormalities within the 'safe' period. As was argued elsewhere, the 'morally safe' period could be up to the eighth week after conception,[39] unless the zygote's normal development has been prevented by some measure such as freezing. During this period it is morally less problematic to check the prenate's state of health because, should we decide not to carry on the prenate's life, we would not be intervening in and terminating an individual human life, a distinct person. Now the only AND technique currently available to enable us to test the prenate's state of health during the 'safe' period is preimplantation diagnosis (PID). It is carried out in the first week of gestation and before implantation; it does not pose any medical or moral problem. PID is therefore the most reliable and morally acceptable of the current ANT techniques.[12]

Conclusion

In conclusion we can say that, although there are different views in the wide bioethics community, antenatal screening and antenatal diagnosis are new technologies developed to contribute to our happiness and welfare, but like many other new technologies, they are accompanied by new moral controversies. It is not proper to conclude that "ANT is good" or "ANT is evil." Deciding this issue is firmly attached to a number of ethical dilemmas at the heart of which is the moral status of the prenate. So, deciding the issue is dependent upon the views of the person, and a case-by-case approach can be suggested. If any embryological stage is defined as the beginning of a human individual, only testing but not termination may be allowed. We have stressed the vital importance of providing the parents with good counseling before and after ANTs. The aim of good counseling is to inform and enable parental understanding and choices with respect to their unborn child; health care professionals should not impose their own beliefs upon the parents.[40] What they can and must do is to debate the issues among themselves, to review their criteria for advising ANT procedures, and for the choices that may follow, so that they are providing the best possible service to their patients who are, of course, 'persons', a category which the prenates may also belong, at least in the minds and hearts of their parents.

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Fetal and Neonatal Alloimmune Thrombocytopenia

Cecile Kaplan

Abstract

Fetal/neonatal alloimmune thrombocytopaenia (NAIT) results from maternal alloimmunization against fetal platelet antigens inherited from the father and different from those present in the mother, and usually presents as a severe isolated thrombocytopenia in otherwise healthy newborns. The incidence has been estimated at 1/800 to 1/1,000 live births. NAIT has been considered to be the platelet counterpart of Rh Haemolytic Disease of the Newborn (RHD). Unlike RHD, NAIT can occur during a first pregnancy. The spectrum of the disease may range from sub-clinical moderate thrombocytopenia to life-threatening bleeding in the neonatal period. Mildly affected infants may be asymptomatic. In those with severe thrombocytoaenia, the most common presentations are petechiae, purpura or cephalohematoma at birth, associated with major risk of intracranial hemorrhage (up to 20% of reported cases), which leads to death or neurological sequelae. Alloimmune thrombocytopenia is more often unexpected and is usually diagnosed after birth. Once suspected, the diagnosis is confirmed by demonstration of maternal antiplatelet alloantibodies directed against a paternal antigen inherited by the fetus/neonate. Postnatal management involves transfusion of platelets devoid of this antigen, and should not be delayed by biological confirmation of the diagnosis (once the diagnosis is suspected), especially in case of severe thrombocytopaenia. Prompt diagnosis and treatment are essential to reduce the chances of death and disability due to haemorrhage. Due to the high rate of recurrence and increased severity of the fetal thrombocytopenia in successive pregnancies, antenatal therapy should be offered. However, management of high-risk pregnancies is still a matter of discussion.

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Disease name/synonyms: Fetal/neonatal alloimmune thrombocytopenia (FAIT/NAIT)[1] or foeto-maternal alloimmunisation thrombocytopenia (FMAIT).[2]

Definition/diagnostic criteria: Fetal/neonatal alloimmune thrombocytopenia (NAIT) is a disorder caused by fetomaternal platelet incompatibility that usually presents as severe isolated thrombocytopenia in otherwise healthy newborns. It results from destruction of the fetal platelets by maternal immunoglobulin G (IgG) antibodies elicited during pregnancy and directed against foetus-specific platelet antigens that are inherited from the father and are different from those present in the mother.[1]

Clinically, the diagnosis is suspected when an otherwise healthy neonate, born after an uneventful pregnancy and delivery, exhibits petechie or widespread purpura at birth or a few hours after birth. Visceral hemorrhages are less common. The mother is typically healthy, with no previous history of thrombocytopenia, auto-immune disorders or ingestion of drugs. The infant has no clinical signs of infection or malformations (see Differential diagnosis). Approximately 20% of these infants show evidence of intracranial hemorrhage (ICH) leading to death or neurological sequelae (see Prognosis). The platelet count is low at birth and may be associated with anemia, secondary to bleeding. Platelet immunological investigations will confirm the maternal specific alloimmunisation.

Epidemiology

NAIT is the commonest cause of severe isolated thrombocytopenia in the fetus and newborn. Prospective studies showed that it occurs in about 1 in 800 or 1000 live births.[3,4] Unselected cohort of neonates reported 0.9% frequency of neonatal thrombocytopenia.[5] Immune etiology was demonstrated in one third of these cases. As thrombocytopenia when moderate (whatever its cause) is often silent, systematic neonatal blood sampling for a platelet count is the only possible way to detect neonatal thrombocytopenia and to provide better management of the infant and subsequent pregnancies.[5]

Clinical description

In the foetus, alloimmune thrombocytopaenia is considered to be the most severe thrombocytopaenia. It may occur very early during pregnancy, and in several studies, ICH has been documented before 20 weeks of gestation.[6-8] In utero, ICH accounts for approximately 50% of the reported cases of ICH in NAIT. Therefore, NAIT should be considered as a potential aetiological factor in all cases where porencephaly, ventriculomegaly and, in fact, any type of ICH is discovered during the fetal life.

In the neonate, purpura or hematoma are the most common clinical manifestations. Visceral hemorrhages, such as gastrointestinal bleeding or hematuria, occur less frequently. ICH has been reported in NAIT (whatever the platelet antigen involved, see Aetiology) and is usually present at birth. ICH may also occur later, if the thrombocytopenia persists. Mildly affected infants may be asymptomatic.

Anti HPA-1a and -3a immunization induce severe neonatal thrombocytopenia (see Etiology).[9] NAIT linked to HPA-5b incompatibility seems to be less severe than HPA-1a NAIT.[10] However, the infant may be symptomless, with thrombocytoaenia discovered incidentally, even in case of HPA-1a alloimmunization. Therefore, unexpected or unexplained neonatal thrombocytopenia or early onset of severe thrombocytopaenia in both pre-term and term babies should raise the possibility of NAIT and guide investigations accordingly.

Etiology

NAIT results from maternal immunization against fetus-specific platelet antigens. The exact mechanism underlying maternal sensitisation remains unknown. A prospective study detected antibodies at 16 weeks of gestation in primipara primigravida women.[3] The maternal IgG alloantibodies can cross the placenta as early as the 14th week of pregnancy. The fetal alloantigens are fully expressed as early as the 18th week of gestation.[11,12] In these circumstances, fetal thrombocytopenia (platelet counts below 150.10^9/L) can occur very early during pregnancy and there is no spontaneous correction.[3]

Although platelets express human leukocyte antigen (HLA) Class I and ABO blood group antigens at their surface, NAIT is mainly due to alloantibodies directed against platelet-specific alloantigens. A prospective study analysis showed that HLA antibodies did not cause thrombocytopenia,[14] unless there is an association with neutropenia.[15] Casual observations suggest that NAIT is sometimes due to ABO incompatibility, although the particular features of these cases are not well established.

The so-called platelet-specific alloantigens, conventionally defined by their exclusive presence on the megakaryocyte lineage, have a phenotype frequency that varies between ethnic groups.[16,17] Since 1990, the Human Platelet Antigen (HPA) nomenclature has been adopted.[18,19] The platelet-specific antigen systems have been numbered chronologically in order of publication, and the allelic antigens designated alphabetically in order of frequency in the population: "a" designating the higher frequency allele, "b" the lower frequency allele. Polymorphism responsible for several of the platelet allotypes has been identified and a new nomenclature proposed.[20] Among the platelet-specific alloantigens, HPA-1a antigen is the form most commonly involved in NAIT in Caucasians,[21] followed (at much lower frequency) by HPA-5b.[10] In Asians, NAIT is essentially linked to the HPA-4 system. Maternal immunization against rare or private alloantigens has been reported.[22-26]

Retrospective and prospective studies highlighted the importance of immunogenetic factors in platelet alloimmunization. The HLA class II DRB3*0101 allele in mothers could be implicated in anti HPA-1a immunization,[27-29] whereas anti HPA-5b alloimmunization was reported to be associated with a cluster of HLA DR molecules, sharing a particular polymorphic amino-acid sequence at position 69–70 in the DR,1 chain.[30] A better understanding of the immune response to platelet alloantigens would allow for a better definition and thus appropriate management of pregnant women at high risk.

Diagnostic methods

The first step in the diagnosis is to confirm the isolated thrombocytopenia in the newborn, and the absence of thrombocytopenia in the mother. The platelet count is variable, usually as low at birth as $<50.\ 10^9$/L. Anaemia occurs secondary to bleeding. Platelet immunological tests require expertise in the field. The therapy should be started as soon as a provisional diagnosis has been made. Any difficulties in confirming the diagnosis should not delay the therapy.

Testing involves the detection of maternal circulating antibodies and identification of the targeted platelet antigen, with determination of the platelet phenotype and genotype of both parents. Antibodies are usually detected with antigen capture enzyme-linked immunosorbent assay (ELISA) and the microplate enzyme-linked assay.[31] Molecular techniques are used for genotyping.[32] If the father is heterozygous for the considered antigen or if the paternity is uncertain, the platelet typing of the infant should be performed to confirm the diagnosis. Diagnosis is certain when parental antigen incompatibility with a corresponding maternal antibody is demonstrated. The biological diagnosis is unclear in the absence of such an antibody (in this case, a repeat testing may substantiate the diagnosis), or when a new, rare or private antigen is involved. Diagnosis should be unequivocally established before a subsequent pregnancy for a better management. Diagnosis of fetal ICH is made by ultrasonography and magnetic resonance imaging (MRI).

Differential diagnosis: Careful examination of the infant and consideration of the maternal history should exclude most of the other causes of neonatal thrombocytopaenia.[33] However, NAIT may also be associated with other causes of thrombocytopaenia, especially maternal antiplatelet autoimmunity.[5]

The main other causes of neonatal thrombocytopaenia are:

- Infection: Bacterial, viral or parasitic infections that may occur in intensive care units
- Disseminated intravascular coagulation is most often secondary to acute fetal distress or sepsis
- Immune destruction
- Maternal autoimmunity: autoimmune thrombocytopaenic purpura, lupus erythematosus; maternal use of drugs
- Platelet consumption
- Hemangioma, extensive thrombosis
- Megakaryocytopoiesis impairment
- Chromosomal abnormalities
- Bone marrow metastases

- Congenital leukemia
- Down-regulation of megakaryocytopoiesis during the course of Rh haemolytic disease or chronic hypoxia

Inherited causes are:
- Constitutional thrombocytopaenia such as thrombocytopaenia associated with absent radii (TAR syndrome), Congenital Amegacaryocytopenia (CAMT), Wiskott-Aldrich Syndrome, Bernard Soulier Syndrome (BSS)
- Thrombocytopenia due to inherited disorders such as von Willebrand 2B disease or constitutional deficiency in ADAMTS 13, leading to thrombotic thrombocytopenic purpura.

Genetic counseling

The recurrence of thrombocytopenia is very high and its severity usually increases in subsequent pregnancies. The risk depends on whether the father's platelet genotype is homozygous or heterozygous for the targeted antigen. Therefore, in case of heterozygosity or if the paternity is uncertain, the fetus platelet genotype must be determined with molecular biology techniques using amniocytes, microvilli or fetal blood sampling. Noninvasive typing from maternal blood is under investigation.

Platelet typing can be proposed to the sisters of an affected woman, in order to detect high-risk pregnant women. In our experience, antenatal management for the first affected pregnancy depends on the detection of maternal alloantibodies.

Antenatal diagnosis: In cases of women already identified as at risk of having or developing HPA alloimmunization (first child with NAIT or previous history of NAIT in the family), fetal genotyping may be performed either on chorionic villi or on amniotic cells.

Alloimmune thrombocytopenia can be suspected in case of fetal ICH. Fetomaternal alloimmune thrombocytopenia presenting antenatally as hydrops fetalis[34] has also been reported as a complication of foetomaternal platelet alloimmunisation. Recurrent miscarriages should be taken into account.

When incidental, thrombocytopenia is discovered by fetal blood sampling and careful determination of contamination with amniotic fluid should be included. Considerations in the differential diagnosis of fetal alloimmune thrombocytopenia include both maternal and fetal factors, among which thrombocytopenia in fetuses small for date with the risk of intraventricular hemorrhage[35] and fetal hypoxia,[36] infection, chromosomal abnormalities, but associations should not be ignored. In other causes of thrombocytopenia, alloimmunization should be studied when thrombocytopaenia is atypically severe.

Management

Neonatal management: Throughout the thrombocytopenic period, the infant is at risk of hemorrhage, especially ICH. Optimal management should be initiated on the basis of the clinical situation, even before the diagnosis has been confirmed by platelet immunological testing.

For infants with hemorrhages or platelet counts below 30. 10^9/L during the first 24 hours of life, the treatment of choice is the transfusion of platelets, which will not be destroyed by the maternal antibodies present in the circulation of the newborn. The mother is the best donor. After maternal transfusion, the infant's platelet count usually increases promptly, which itself argues in favour of alloimmunization. The maternal platelets must be washed to remove the antiplatelet antibody and irradiated to prevent graft versus host disease. If the mother is not available, blood banks can provide HPA1b/1b donors' platelets, since HPA-1a incompatibility is the most frequent cause of NAIT. When private or rare platelet antigens are considered, members of the family can be genotyped. When compatible platelets are not available or their delivery is delayed, transfusion of random platelets with or without intravenous immunoglobulins may be performed.[37] Intravenous immunoglobulins alone should not be given in this situation, because of the delayed onset of their effect (18–24 hours after injection).[38]

Infants without hemorrhage and a platelet count above 30. 10^9/L: These cases require close monitoring until an adequate platelet count is reached. Usually, platelet transfusion is not necessary, as the platelet count increases rapidly. Alternatively, in case of severe drop in the platelet count, the management described above should be considered. In some cases, intravenous IgG (1g/kg/day for 2 days) may be used to raise the platelet count.

Outcome and prognosis

The outcome depends on the severity of thrombocytopenia at birth and the promptness of diagnosis and treatment. The need of immediate treatment depends on the presence of bleeding and the severity of thrombocytopenia. If treatment is required, then it should not be delayed. In all cases, platelet counts should be closely monitored until a normal platelet count is obtained. The duration of the postnatal thrombocytopenia is usually one to two weeks, but it may occasionally persist for longer. Radiological evaluation of the head (ultrasonography, MRI) is required to detect/exclude ICH. In absence of severe bleeding, the outcome is favorable. When ICH has occurred, retrospective studies in series of anti HPA-1a NAIT report a mortality of 10%, and a 20% rate of neurological sequelae.[21,28,39]

Management of subsequent pregnancies: The current management of pregnancies subsequent to a delivery of an affected child is aimed at preventing ICH during pregnancy and delivery. Currently, there are no techniques for evaluating the fetal status that do not involve invasive procedures (ie percutaneous umbilical blood sampling) and that do not carry risks. However, in subsequent pregnancies, maternal anti-HPA-1a antibody titration has been recently shown to provide indications for the risk of severely affected fetuses (if measured in standardized conditions, before any therapy, and determined before 28 weeks of gestation).[40] The optimal antenatal therapy to reverse fetal thrombocytopenia is still a matter of debate.[41-44] As the results obtained by different teams in Europe[42] and in the USA[41] do not rely on randomized studies, conclusive recommendations cannot be provided. There is a consensus that women with high-risk pregnancies should be followed-up in referral centers (where they could receive antenatal therapy), with minimal use of invasive procedures. Maternal therapy including weekly maternal injection of high doses of immunoglobulins, with or without corticosteroids, is currently recommended as the first-line approach. Therapy can be stratified on the basis of the sibling history of NAIT.[42-44] Weekly intrauterine platelet transfusions with antigen negative platelets may be used as salvage therapy when maternal therapy has failed. Elective cesarean section is preferred when the fetus is

thought to be severely affected.

Unresolved questions are: mechanism of maternal sensitization; modulation of the maternal immunization; real incidence of ICH; best antenatal management; and setting up of the routine antenatal screening.

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Moving the Womb

Arthur L. Caplan, Constance Perry, Lauren A. Plante, Joseph Saloma, Frances R. Batzer

Recently, a team of physicians at the New York Downtown Hospital announced they had received approval from their institutional review board to attempt the first uterus transplant in the world from a cadaver donor.[1] Teams in the United Kingdom and Sweden have also publicly stated their interest in trying uterus transplantation in women.

Transplantation always involves serious risks for recipients, stemming both from the solid organ transplant surgery itself and from the immunosuppressive drugs that transplant recipients will have to take for the rest of their lives. These risks, however, have been generally viewed as acceptable by surgeons, third-party payers, government regulators, and patients because the success rate is high and the benefit of receiving a heart, kidney, lung, or liver—continued life—is self-evident.

The point of a uterus transplant would not be to save a life, however. Uterus transplants would be attempted only to improve the recipient's quality of life: they would allow her to give birth. This very different risk-benefit calculation raises many ethical questions that should be thoroughly aired and understood before the procedure is attempted.

The Need

Thousands of women in the United States cannot bear children. Disease, accidents, complications from earlier pregnancies, and congenital malformations can impair a woman's uterine function, and some women simply do not have a uterus at all. But not all women who cannot bear children are flatly barred from parenthood. In some states in the United States and in other nations, there has been for many years an active market in surrogate mothers—women who will "rent" their wombs for a fee to other women so they may bear children. Gestational surrogacy is not an option for all women who do not have a functioning uterus, however. It is illegal in some states and in some countries, and, even in states where it is legal, many ethical and legal uncertainties surround the practice. Some religions, including Islam, have specific prohibitions against surrogacy. It can also be very expensive, yet it may not even satisfy a woman's need to have her own baby. Many women wish to bear their children themselves as part of the parenting experience. Various cases of older woman who have utilized donor embryos or donor sperm and egg to be become pregnant, despite great risks to themselves and their potential children, show how strong this desire can be.[2]

Women who want to experience pregnancy and those for whom gestational surrogacy is out of reach (whether for religious or financial reasons) form a group who are willing, even eager, to subject themselves to experimental uterine surgery. Their eagerness puts these women—and those seeking to recruit them—at risk of the "therapeutic misconception": they need to be frequently and emphatically reminded that the women who first receive uterus transplants are subjects in a research study, not patients getting a new treatment. It is unlikely that they will benefit by delivering a baby. Their motivation for participating ought to be that they will shed light on the safety and practicality of uterus transplants.

The Experience So Far

Only one known uterus transplant using a living donor has been attempted in humans. Physicians at the King Fahd Hospital in Saudi Arabia performed the operation in 2002. The donor was a forty-six-year-old woman, and the recipient was a twenty-six-year-old who had undergone a hysterectomy. Doctors had to remove the transplanted uterus after three months due to circulatory problems.[3]

A number of attempts have also been made with different kinds of animals. The team of transplant researchers at New York Downtown Hospital has been experimenting with uterus transplants in pigs and rats for five years. The transplanted uteri reportedly survived and functioned for several months in the pigs, producing normal menstrual cycles.[4] However, none of the animals were able to become pregnant, and the researchers do not know why. A few attempts have been made to transplant uteri in sheep and monkeys, but no pregnancies have resulted. A

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Swedish team that has been working with mice for many years has achieved one pregnancy that produced a birth.[5]

This work is not enough. There are significant differences between the reproductive anatomy of humans and that of rodents, pigs, and sheep. The fact that so few experiments—much less successful ones—have been carried out in primates should generate considerable concern about the wisdom of moving to human trials any time soon.

Donor Issues

The New York team wants to obtain a uterus for transplant from a deceased donor, yet it makes more sense biologically to use a donor uterus from a tissue-matched sibling or relative. Such a donor would be able to consent to the donation knowing the risks and benefits. Living donation might also improve the quality of the organ to be transplanted, and close tissue matching might prolong its lifespan in the recipient, thereby decreasing the dose of immunosuppressive medications necessary to prevent rejection.

Obtaining the uterus from a deceased donor raises some unique ethical issues. The doctors in New York say they will use someone who has signed a donor card and whose family has no objection to uterus donation. But is this really enough? Few, if any, American women ever thought that the uterus might be one of the organs considered for donation when they signed a donor card. A woman might not prove as willing to donate her uterus as she would be to donate her heart or liver. The transplant team would be on firmer moral ground if they used a donated uterus from a woman who had explicitly consented to donate that organ prior to her death, and who made it very clear that she and her family renounced any and all claims to a relationship with any child that might result.

However, while using a close relative or sibling may seem to be the better choice, it also increases the risk of coercion. There could also be potential problems if a family member initially consents to being a uterus donor and then changes her mind—a possibility that a transplant team considering living donors must be prepared to manage.

Risks

Surgeons proposing uterus transplant have tended to dismiss concerns about risk to the prospective recipient by noting that, since the uterus is not a life-preserving organ, it can simply be removed if complications arise. But what if that uterus contains a fetus? What if the mother decides she is willing to die to try to give birth? What if the father or the mother decides they want the uterus removed even if it contains a fetus or an embryo? The surgical team has not said as much as they need to about their "exit" strategy if the experiment does not go as planned.

The New York surgical team says that risks to fetuses are not at issue because women who have had other types of transplants have given birth. This is not exactly true. Women have given birth following solid organ and bone marrow transplantation, which require the use of immunosuppressive agents during pregnancy. A national transplantation pregnancy registry provides some data as to the effects of immunosuppressive drugs on offspring.[6] The power of that data is limited, however, by the relatively small number of pregnancies tracked to date. There is no reliable data yet on the long-term health of children born post-transplant. When a woman has received a solid organ transplant, doctors usually recommend postponing pregnancy for two years to ensure that the graft survives. No one knows what guidelines to recommend concerning pregnancy after uterus transplantation.

A woman who has a transplanted liver and later undertakes a pregnancy presents a very different case from a woman who subjects both herself and her potential offspring to these drugs purely for the purpose of carrying a pregnancy. Also, the potential risk to a fetus or fetuses from the procedure is not solely that of exposure to immunosuppressive drugs. There is a risk of structural failure caused by clotting and thrombosis of major arteries supplying oxygen to the transplanted uterus. This could have a negative effect on fetal development, increasing the possibility not only of fetal death, but of preterm delivery and developmental problems associated with poor circulation, infection, and loss of fluid.

For uterus transplantation, the risks seem to be justifiable only if clinical equipoise exists—that is, if the risk-benefit ratio of the experimental procedure can reasonably be assumed to be equal to existing alternatives. Uterus transplants fail the clinical equipoise test. We lack solid animal data on the impact of uterus transplant on maternal health and fetal well-being, so we don't really know the risks. In addition, most women have the safe alternatives of gestational surrogacy, adoption, and foster care to allow them to experience parenthood. The desire to experience a pregnancy, while certainly legitimate, cannot be considered separately from the ultimate goal of pregnancy—namely, a healthy child. The available evidence cannot yet assure that outcome.

Finally, aside from the physical risks, a child born from a uterus transplant could also face some unique psychological issues. The child or adult might seek contact with the survivors of the woman who had donated the uterus. Children born after sperm donation, adoption, or surrogacy sometimes go to great lengths to find information about their conception; surely children gestated in a dead woman's uterus would wonder about their origins. Provisions must be made for handing these issues prior to undertaking the first cadaver uterus transplants.

Subject Selection

Many women who want a uterus transplant might not be candidates for one, but the selection process for identifying subjects has received very little discussion. Women born without a uterus or with certain congenital anomalies will not have the appropriate vascular connections for attachment. Women who had their uteri removed because of cancer—particularly cervical or childhood cancer—may not be candidates if the original cancer treatment involved radiation that led to scarring, which makes vascular reattachment difficult. And there are obvious questions that must be asked about the psychological stability and social support necessary to undergo an experimental transplant fraught with unknown risks.

The prospect of uterus transplant has also led to some discussion about the possibility of a male pregnancy.[7] While this idea may seem appealing to some, the physiological requirements for nourishing a uterus and maintaining a pregnancy make it exceedingly unlikely that a uterus transplant would work in a man. During a pregnancy, up to one-fifth of a woman's cardiac output goes to the pregnant uterus. Since the

vascular connections for a uterus do not exist in males, they would have to be created. Hormonal supplementation would also be required, along with the immunosuppression. Obviously, the bodily incompatibilities are so daunting that to even try for a male pregnancy seems inappropriate. While it makes for some fascinating science fiction scenarios, the risks involved make the selection of a male subject for this experiment ethically dubious.

The Glory of Being First

There are transplant teams willing to undertake uterus transplants and women willing to undergo them. But this is an experiment that requires more than willingness. Multiple studies demonstrate the difficulty of achieving informed consent with desperate patients. The transplant team must manage conflicting roles and interests in order to ensure truly informed and voluntary consent from potential donors, donor families, and recipients. In the midst of all this, the prospect of being the first to successfully transplant a uterus—and win acclaim and publicity for the programs, doctors, and institutions involved in the effort—raises deep concerns about conflict of interest. The desire to be first could make it very difficult for the team to seriously consider whether sufficient evidence exists to support a favorable risk-benefit ratio for initiating a clinical trial. Society must be reassured that donation involving a cadaver donor will be done according to the highest standards of informed consent. The transplant team must be clear about how it will manage a pregnancy if the transplant goes wrong. And the risk to the fetus of being conceived and carried in a transplanted uterus must be carefully weighted against the woman's desire to have the experience of the gestational component of motherhood. Is that worth a lifetime of risk to a child? Until these questions are answered, it is not time to initiate experiments with uterus transplantation.

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What Motivates British Parents to Consent for Research? A Questionnaire Study

Helen M. Sammons, Maria Atkinson, Imti Choonara, Terence Stephenson

Abstract

Background: Informed consent is the backbone of a clinical trial. In children this is given by their parents. There have been many studies in the neonatal population but little is known about the views of the parents of infants and young children from within the United Kingdom. The objectives of this study were to assess what motivates parents to consent to a randomized clinical trial (RCT), their feelings on consent and participation and the factors that would influence their decision to take part in a future study.

Methods: The setting was a multi-center randomized but non-blinded equivalence trial of oral versus intravenous (IV) treatment for community acquired pneumonia in previously well children aged 6 months to 16 years in the UK (PIVOT Study). Parents were sent a postal questionnaire at the end of the study which included open and closed-ended questions. Fishers Exact Test was used to analyse associations in non parametric categorical data.

Results: 243 children were recruited into the PIVOT study. Of a possible 235, 136 questionnaires were returned (response rate 59%). Of those questionnaires returned; 98% of parents remembered consenting, 95% felt they were given enough time to make their decision and 96% felt they received enough information. Major reasons for participation were benefit to other children in the future 31%, contribution to science 27%, benefit to their own child 18%. Most parents (85%) did not feel obliged to participate. 62% felt there was an advantage to taking part and 18% felt there was a disadvantage. 91% of parents said they would take part in a similar study in the future, stating influences on their decision being benefit to their own child (91%) and benefit to all children (89%).

Conclusion: The major motivation in parents consenting for their previously well child to participate in an RCT of therapy for an acute medical illness was to increase medical knowledge in the future. Most saw an advantage in taking part in the trial and did not feel obliged to participate.

Background

Research in a child is different to that in adults. Informed consent is essential for recruitment into a randomized controlled trial. The informed consent process is undertaken in the majority of pediatric trials by the child's parent. It has been found that a child's ability to assent or consent to research under the age of 9 years is limited.[1] Recruitment is said to be difficult within pediatric trials and quoted as being the single most difficult problem to overcome; leading to delays, increased costs and failure to complete drug trials.[2-4] Therefore understanding why a parent allows their child to participate in research is essential in taking forward pediatric research in the future.

There have been several studies on the consent process and the information retained by parents following this process. The majority of work within the United Kingdom has centered on neonatal research.[5,6] A study in the Netherlands[7] of a randomized placebo controlled trial of ibuprofen syrup to prevent febrile convulsions found that, within the infant age group, the major factors in parents granting approval were contribution to clinical science (51%) and benefit to the child (32%). A quarter of parents felt obliged to participate and over half (60%) said they would be willing to participate in a similar study in the future.

Based on the information provided by the clinician, parents decide whether or not to permit their child to participate in that

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1. AHA Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, Part 6, p. 1-87.

Dear Parents,

Many thanks for allowing your child to participate in the PIVOT study of children with pneumonia. We are looking at the reasons why parents participate in studies and would appreciate if you could complete this short questionnaire.
Thank you for your time.

1. What was your major reason for taking part in the study?

.....

.....

2. In deciding to take part in the study, which for the following influenced your decision? (please tick)

	Agree	Disagree
- Contribution to science		
- Benefit for your child		
- Benefit for other children in the future		
- Give something in return for the care of our child		
- Doctor asked us		
- No reason		

3. Did you feel obliged to participate? (please circle) YES NO

. Did you feel there were any advantages to taking part? YES NO

Please give any reasons:

.....

.....

5. Did you feel there were any disadvantages to taking part? YES NO

Please give any reasons.

.....

.....

6. Would you take part in a similar study again? (please circle) YES NO

7. Which of the following would influence your decision to take part in future studies:(please tick)

	Agree	Disagree
- Contribution to clinical science		
- Benefit for your child		
- Benefit for other children in the future		
- Received extra medical care and support		
- No benefit for your child		
- The extra time and work involved		
- The uncertainty of which treatment will be received		
- Involved more blood tests		
- It would depend on the study		
- No reason		

8. Do you remember consenting for your child to take part? YES NO (please circle)

9. Did you feel you had enough time to make your decision? YES NO

10. Did you feel you received sufficient information? YES NO

Thank you for taking the time to complete this short questionnaire. Please return in the stamped addressed envelope provided

Figure 1: Original Questionnaire.

study. Understanding the parent's major thoughts and motivations at this time may help improve this process and increase the numbers participating in future studies. This present study aims to look at a group of parents approached for consent in a multi-center randomized controlled trial of previously well infants and children presenting with pneumonia, within the United Kingdom.[8] The aim was to see if the motives of British parents are similar to those seen in Europe, to assess parental views on the informed consent process, the information provided and their reasons for taking part in the study. Their willingness to participate in future research was also examined.

Methods

The Trial

A multicenter randomized controlled equivalence trial compared oral amoxicillin and IV benzylpenicillin for community acquired pneumonia in children in hospital (PIVOT).[8] It was undertaken at eight hospitals in England. Children aged 6 months to 16 years with fever, respiratory symptoms or signs and radiologically confirmed pneumonia were eligible. 245 children were randomized to either oral amoxicillin or IV benzylpenicillin. The primary outcome measure was time for the temperature to be less than 38°C for 24 continuous hours and oxygen requirement to cease.

Informed consent procedure: Once the diagnosis had been made the parents were approached regarding the trial. Written parent information was provided at the child's diagnosis and the parent was then asked to reach a decision on participation prior to the start of treatment. Information sheets were provided for children aged 7 years and over. Older children and teenagers were asked for their assent and could complete the consent form as well as their parents. Unlike studies of children's cancer, for example, when parents may have 24 hrs to reflect, consent had to be decided rapidly as treatment could not be deferred. All children had blood tests performed and those in the intravenous group had a cannula left in situ for antibiotics. If the parents declined consent and volunteered a reason, this was recorded on a separate data collection form anonymously.

The Questionnaire

Ethical approval was obtained from the Southern Derbyshire Local Research Ethics Committee. A parental questionnaire was designed to try and elicit parental views on consent and participation in research. The questionnaire included both structured and semi-structured questions as detailed below (Figure 1). This was kept to two sides of A4 paper to try and encourage return. Because of this the questionnaire was limited to include the primary question on reason for participation. Demographic details on the person completing the questionnaire were not collected.

The themes for reasons for participation were taken from a previous questionnaire based study conducted with parents in the Netherlands[7] as these had already been validated in a European population. Parents were asked to agree or disagree with a list of reasons that might have influenced their decision to enrol their child in the study, such as benefit to all children in the future (Figure 1- Questionnaire). Open free text questions were posed for the main reason for participation and any advantages or disadvantages they experienced from the study. The questionnaire was not piloted as there were no parents available in hospital who had taken part in research studies at the time of its development.

The anonymous questionnaire was mailed to all parents in July 2004 after the two-year recruitment period had finished. A stamped addressed envelope was included. It was felt not to be appropriate to send questionnaires to the two parents who withdrew during the study. The questionnaire was re-mailed in September 2004. A returned completed questionnaire was taken as consent by the parent. Completed questionnaires were coded and analysed using the SPSS statistical package. Fishers Exact Test was used to analyse association in non parametric categorical data.

Results

Demographics: 243 parents were identified from the PIVOT study after the two year recruitment had finished. Eight addresses were incorrect and therefore questionnaires were

unable to be delivered. 136 questionnaires were returned (30 after the re mailing), a response rate of 59%. The response rate was not affected by time, with a constant response rate across the whole duration of the study. The median age of the child for which parents responded to the questionnaire was 2.0 years (range 6 months to 12 years and 4 months) compared to a median age of 2.4 years in the overall study. The questionnaire did not specify which parent was filling in the questionnaire. The PIVOT study had a 69% consent rate and details on the socioeconomic status of the families within the study or the questionnaire were not collected.

Reasons for participation: The major reason given by parents for taking part in the study was benefit to all children in the future and a contribution to science in 57% (Figure 2). Only 18% said that the major reason they took part was benefit to their own child. Parents answered this question in their own words. The remainder stated that they participated because they were asked by a doctor or that there was no reason not to. When questioned directly on each theme, 96% agreed that benefit to all children and 72% benefit to their own child had influenced their decision to participate. 67% said that they consented in order to give something in return for care for their child and 63% because the doctors asking had influenced their decision. This was not statistically influenced by the child's age.

Advantages and disadvantages of participation: Just under two thirds (62%) felt that there had been an advantage to taking part in the study. Of those that expressed an advantage, for over half (57.5%) this was theoretical in giving knowledge for treatment of all children in the future. The remainder felt the benefit was to their own child including oral medication, quicker recovery, more information given and closer monitoring.

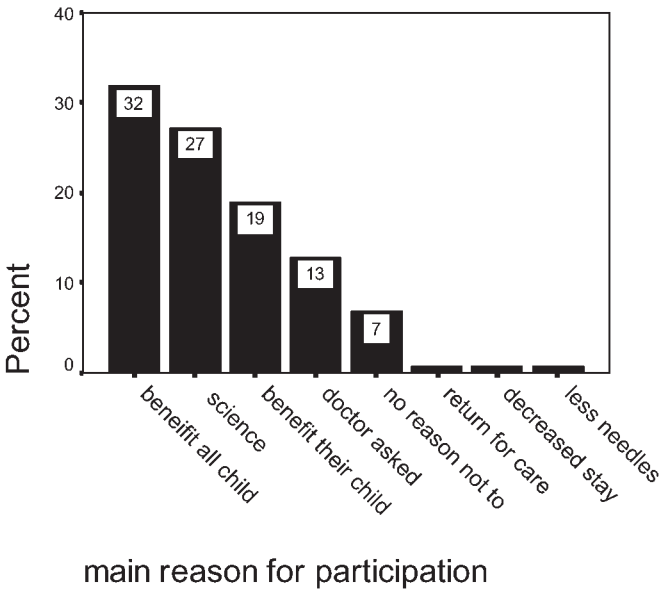

Figure 2: Main reason given by parents for their participation.

24 parents (18%) felt that there had been a disadvantage in participating. The disadvantages stated were the use of needles (although it had been explained that both groups would have blood tests as standard), delay in starting treatment due to randomisation, anxiety that randomized treatment would be less effective and having no choice over treatment. Four parents felt their child had a poorer recovery due to oral treatment (though this was not born out in the overall results which showed equivalence of the two treatments).[8] 18 parents (13%) said that they felt obliged to take part and 9 (7%) felt that they would not take part in a similar study in the future. 98% of parents remembered consenting, 95% felt that they had enough time to make their decision. 96% felt that they had received enough information. These answers were not statistically influenced by the child's age or the time since recruitment had taken place.

Future studies: Parents were asked which factors would influence their decision to take part in a future study with their child. The major factors were benefit to their own child (91%), benefit to all children (89%) and contribution to medical science (83%). Interestingly only 14% said they would not take part if there was no benefit to their own child and 23% if it involved blood tests. The uncertainty of treatment would influence just under a third of parents' decisions but the majority (80%) said that it would depend on the design of the trial.

If a parent expressed an advantage, 62% (p = 0.002), or did not express a disadvantage, 81% (p = 0.05), then they were statistically more likely to say that they would take part in a similar study in the future. However 42 (84%) of those parents who did not feel there was an advantage would still take part in a similar future study. This was not statistically influenced by the child's age.

The relationship between wanting to take part in a similar study in the future was examined in relation to the views expressed on motivations for future studies. Parents who did not feel that 'benefit for other children in the future' influenced their decision to participate were less likely to participate again in the future (p = 0.045). If a parent felt that they did not receive enough information (p = 0.053), or have enough time to make their decisions (p = 0.004) then they were statistically more likely to express a wish not to participate in future studies. Randomisation to oral or IV treatment did not make a difference to this decision (p = 0.28).

Declined to participate: 43 parents approached to participate in the PIVOT trial declined for their child to take part. Of these 30 expressed a reason to the clinician and these were collected anonymously. The majority (25) stated that they wanted a specific treatment for their child, either IV (20) or oral (5). Many parents expressed a view that IV treatment was superior and therefore were unwilling to undergo randomisation. Of the remaining parents, two declined consent because they did not want to participate in a trial, two expressed that they were too distressed by their child's admission to consider consenting and one declined consent because of the paragraph on the consent form saying that the ethics committee would have access to their child's notes.

Discussion

In this study, of a general pediatric condition in the childhood population in the UK, the major motivator for the participation in clinical trials is for the good of all children and the furthering of clinical science. This is a positive finding and good for future trial recruitment. It means that if a trial is designed well with a clear clinical question with which parents can identify, then they are likely to consider taking part. As an important predictor of consent this had previously been recognised in work carried out on clinical anaesthesia and surgical studies in children.[9] This is reinforced in our results in that parents who felt that they did not receive enough time to consider their decision or receive enough information were statistically less likely to wish to take part in future studies. The main reason expressed by those parents who declined to consent was the perception that one treatment was superior to another. This may show a lack of understanding of the information presented and this has been found to be another important predictor of consent.[9] The PIVOT study recruitment rate was 82% which was high compared to that quoted in previous studies of 68% and 43%.[10] This may be related to the pragmatic nature of the trial and the fact that it did not ask for any extra blood taking or immunisation, which have been quoted as reasons for non-enrolment in other studies.[10]

The attitudes of our British parents were very similar to those seen in the previous Dutch study[7] with contribution to clinical science being the biggest motivator in both groups. A more recent study[11] in France showed that the possibility of receiving the most advanced treatments and the confidence placed in the medical team were their highest motivations for participation. Their population were children treated for either a cancer or HIV infection. The relatively high risk nature of these diseases is most likely the reason for the difference between their results and those seen in our own population. In a study conducted in the United States[12] the importance of receiving the newest drugs, financial benefit, and free office visits were highlighted. A statistical correlation was noted between the importance of free medication and lower family income. Financial incentives can be offered within the USA; in the study above the mean compensation was $570 per child recruited. This reflects the differences in the health care systems between the USA and the UK, where there is free access to health care. In our study, over two thirds of our parents responded that giving something in return for their care had influenced their decision to participate.

One of the limitations of the present study, and the questionnaire method, is the response rate (59% in our current study). This was lower than the previous Dutch study of 79%.[7] Of those who did not respond we do not know if their views would be similar to those who were willing to fill in the questionnaire. This may mean that we overestimate the positive attitudes to this and future studies. There would also have been a recall bias associated with mailing the questionnaire to all parents at the end of the study. Some parents may have been recruited to the trial up to two years prior to the questionnaire being completed and therefore their recall would have been different to those recruited in the last few months. There was however an equal spread of responses over the recruitment period and the time since recruitment did not statistically alter the responses to the questions of information, time and remembering consent. Our results are based on the responses to a single study, in a general pediatric condition, and thus the results may not be generalizable to other studies that have different risk/benefit profiles.

Conclusion

This study has highlighted that the reasons that parents consent for clinical trials in the United Kingdom is similar to that seen in other European countries. Future work, ideally within a multinational trial of the same disease profile, to compare parental attitudes within different health care systems would be interesting. The majority of parents consent because they see the clinical need of the trials to answer questions for the treatment of future children. When financial incentives and cost of health care are introduced this may change motives. It is important that we understand the motivation of parents, within our own populations and different disease profiles, with the introduction of European legislation to ensure that all medicines are studied in children and the challenges that it will bring.

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Pre-publication history

The pre-publication history for this paper can be accessed here: http://www.biomedcentral.com/1471-2431/7/12/prepub

A Conservative Call for Universal Access to Health Care

Donald W. Light

The United States remains the only industrialized or second-tier country in the world that fails to guarantee its citizens access to medical services. This is a curious omission for a country based on rights and liberty. It is equally strange from an economic and business point of view. For while foreign competitors get full medical benefits at one-third less the cost, American employers are weighed down by ever-growing expense for health care. For Nokia, Volkswagen, and Siemens, this is an advantage worth billions over their American competitors, Motorola, Ford, and GE.

Despite these consequences, US fiscal conservatives continue to belittle universal access. They argue that healthcare should be private, with a public safety net only as a last resort. In so doing they diminish some of their most cherished principles. For universal access to needed medical services enhances individual freedoms, liberties, opportunities and the ability to be productive. Illness and disability hobble them.

Conservatives in every other industrialize country support universal access to health services in one form or another. Only American conservatives hold the mistaken view that their values do not support it. Other countries provide universal access in a variety of ways. Many countries use insurance, even private insurance, coupled with firm rules that require everyone to contribute in equitable ways. Many rely on tax-based systems, which studies show are the most efficient means and holds down costs best. Often, medical services in these countries are private.[1]

A conservative argument for universal access to healthcare can be put quite simply: When people are ill, in pain, or disabled, they are less able to take care of themselves or others. In such circumstances, individual liberty and personal responsibility are quickly compromised. Even small disorders can turn liberty and responsibility into dependency. Needed medical care can be a great financial burden on the seriously and chronically ill. Losses in wages and earned income make matters even worse, particularly when able-bodied citizens can no longer care for themselves and their dependents.

Medical bankruptcy is quite common in the United States but unknown in the rest of the modern world where there is universal access. Costs totaling 10 percent of household income are not uncommon, and rise to 15 percent among the working class.[2] Forty percent of all personal bankruptcies in the United States are attributed to medical bills people are unable to pay.[3]

Voluntary Insurance Does Not Work

In the United States, voluntary private health insurance has traditionally been seen as the answer for covering medical expenses. Elsewhere, it was abandoned long ago as incapable of protecting individual liberty, fostering personal responsibility, and promoting economic opportunity. One problem is that nearly half of all employers choose not to offer health insurance to their employees. As a result, most of the 40 million Americans who lack health insurance are workers or their dependents. These Americans have attempted to act responsibly and to better themselves. But when illness compromises their liberties and abilities, healthcare is often not there to get them back on their feet.

Among the employers who continue to offer private voluntary insurance, most are thinning it out rapidly. Headlines appear weekly announcing forms of "disinsurance," of less coverage and high co-payments. Today we have what Uwe Reinhardt calls unsurance, because we are unsure what it covers and unsure what it will cover next month. The feature film John Q was about unsurance: Denzel Washington finds that his policy has been switched without notice and his coverage in the fine print greatly reduced. The goal of private insurers is to minimize coverage for those most in need of it, while the goal of a free society is to treat those who need medical assistance the most, to get them back on their feet, restore their liberties, and enable them to be productive.

The philosopher Paul Menzel has written that the anti-free-riding principle "is itself fundamentally a pro-individualist principle with libertarian senses of justice. In holding people

Donald W. Light is a Senior Fellow at the Center for Bioethics. Reprinted from PennBioethics, University of Pennsylvania Volume 9, No. 4 Center for Bioethics Email Newsletter, Adapted from Light DW. Health care for all: a conservative case. Commonweal, Feb. 22, 2002:14-16.

responsible, not just for the effects of their voluntary actions on others, but also for the costs of the collective enterprises from which they benefit, the anti-free-riding principle keeps collective solutions to human needs in tow, tying them tightly to people's ability and willingness to pay their costs."[4] This principle is closely linked to another conservative tenet, the primacy of personal integrity: People ought to hold to the implications of their beliefs, values, and actions, for themselves and for others. Yet thousands of employers and insurers are free riders. They dump their medical problems on the public system and force overloaded physicians and hospitals into deciding how hard they want to work without pay.

The nightmare conservative is the motorcycle gang rider: Live for the moment with free abandon and let others pay for the consequences. But there are many more nightmare conservative capitalists who do the same on a larger scale. Why are these enterprises and individuals not held responsible by their fellow conservatives?

Universal access to needed medical services is essential to achieve four traditional conservative moral principles: the anti-free-riding principle, the principle of personal integrity, the principle of equal opportunity, and the principle of just sharing. The question then becomes: How can conservatives refuse universal access to health care and remain consistent with their conservative values? Here are some guidelines:

1. Everyone is covered, and everyone contributes in proportion to his or her income.
2. Decisions about all matters are open and publicly debated. Accountability for costs, quality, and value of providers, suppliers, and administrators is public.
3. Contributions do not discriminate by type of illness or ability to pay.
4. Coverage does not discriminate by type of illness or ability to pay.
5. Coverage responds first to medical need and suffering.
6. Nonfinancial barriers by class, language, education, and geography are to be minimized.
7. Providers are paid fairly and equitably, taking into account their local circumstances.
8. Clinical waste is minimized through public health, self-care, prevention, strong primary care, and identification of unnecessary procedures.
9. Financial waste is minimized through simplified administrative arrangements and strong bargaining for good value.
10. Choice is maximized in a common playing field where 90-95 percent of payments go toward necessary and efficient health services and only 5-10 percent to administration. The $350 billion, or 24 percent of healthcare expenditures paid for managing, marketing and profiting from our fragmenting system could be cut in half and go to paying doctors and nurses for uncovered services.[5] But too many profit from the waste and inequities. Unfortunately, most of the "real remedies for the uninsured"[6] lock in these wasted billions and lock out any efficient solution.

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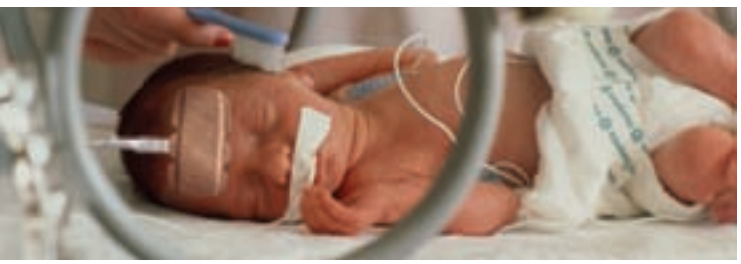

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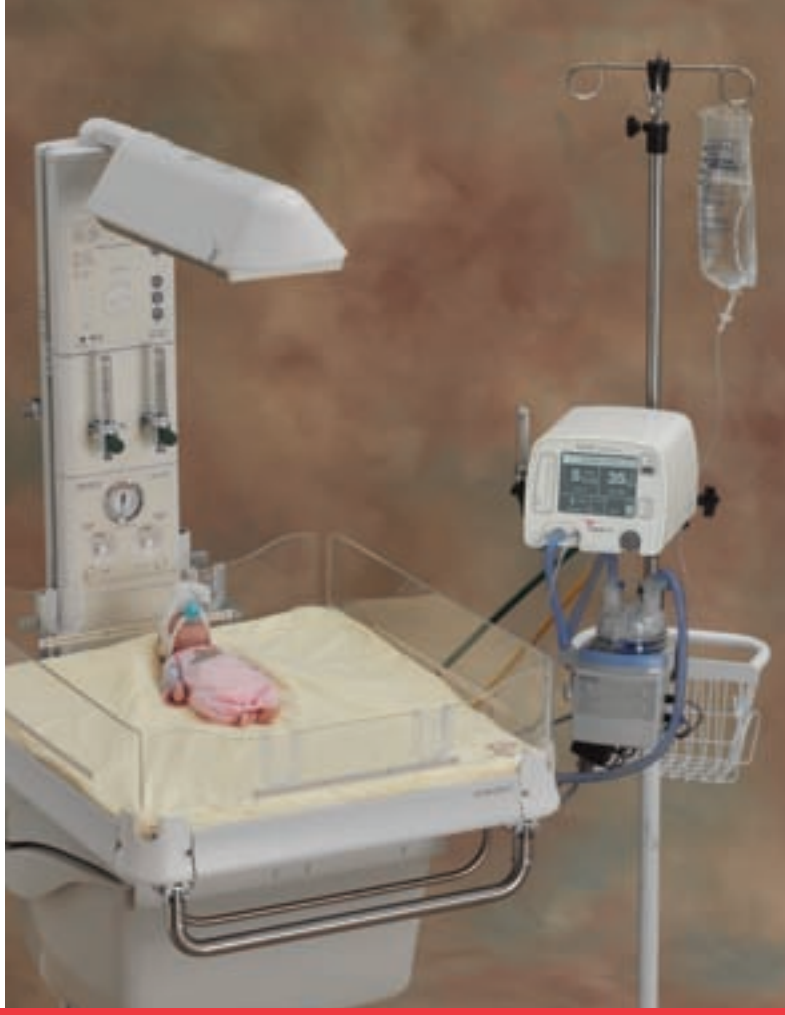

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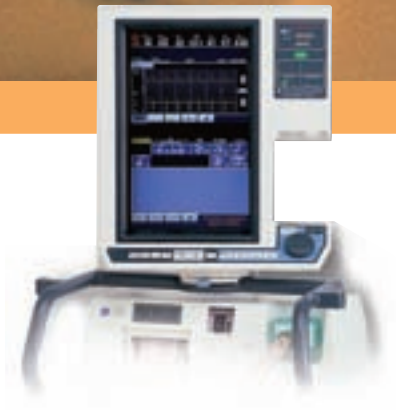

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