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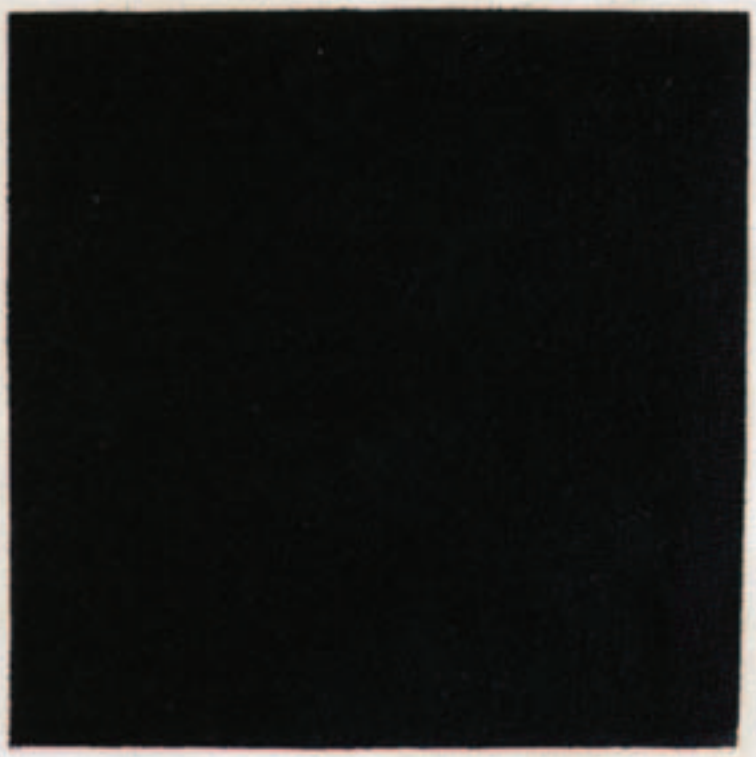
neonatal INTENSIVE CARE

The Journal of Perinatology-Neonatology



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Editorial

Your Death and Theirs

Are neonatalogists' decisions about life sustaining/end of life decisions affected by their take on their own mortality? An interesting question. Medical News Today reports that doctors who fear their own death say they are more prepared than other doctors to hasten death in sick newborns for whom further medical treatment is considered futile. The findings are based on a survey of 138 neonatologists across Australia and New Zealand, to be published in an upcoming issue of Archives of Disease in Childhood Fetal & Neonatal Edition. The doctors were asked questions about their ethical practice and to complete the Multidimensional Fear of Death Scale (MFODS), which measures different facets of personal fear of death. According to Medical News Today, "Of the 138 doctors contacted, 78 (56%) completed the questionnaire. Virtually all of them said they sometimes withheld or withdrew life-sustaining treatment in newborns with severe mental and/or physical disability and those for whom further medical treatment was considered to be overly burdensome or futile." The respondents said they used painkillers or sedatives in both situations to alleviate pain and suffering, but without intending to hasten death. However, one in three specialists was prepared to use painkillers or sedatives to relieve pain and suffering by intentionally hastening death in newborns with severe disability, and more than three out of four were prepared to hasten death for this purpose in babies for whom further treatment was considered futile. According to Medical News Today, "In this situation, they preferred to use painkillers or sedatives to hasten death rather than withhold minimal treatment, such as tube feeds or oxygen, in a bid to prevent unnecessary pain and suffering. One in five neonatologists said that hastening death in this context was unacceptable by either means. The study also reported a link between the neonatologists' personal fear of death and their ethical practice. Doctors who said they were not prepared to hasten death had significantly less fear of the dying process and of premature death than those prepared to hasten death with painkillers or sedatives. But they had significantly more 'fear of being destroyed.' The author suggests that doctors' fear of the dying process or of premature death may unconsciously motivate them to hasten a newborn's death in order to relieve their own death anxiety. Similarly, those who fear being 'destroyed' may not be prepared to hasten death, because of their own fears, even though this may be the most humane way to relieve a newborn's suffering." Of course, the study doesn't really suggest that neonatal physicians are condoning euthanasia, or that it's even happening in neonatal intensive care units. Still, it demonstrates how personal views definitely impact treatment modalities and options. It's certainly something to think about.

Les Plesko, Editor

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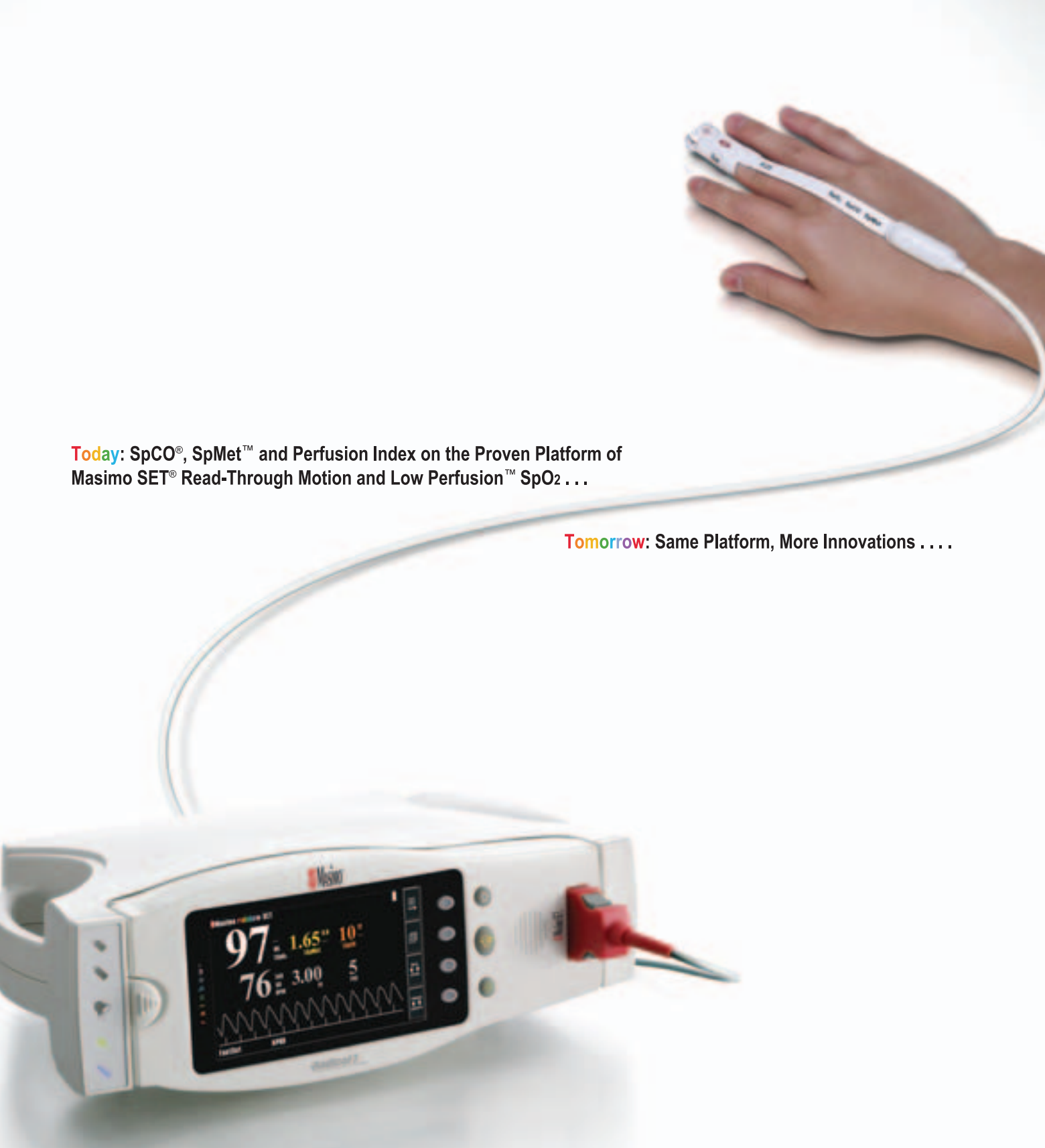

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HELP PROTECT HIGH-RISK INFANTS FROM SEVERE RSV* DISEASE...

Premature infants born near the start of or during the RSV season may be at especially high risk for RSV[1]

...TAKE PREVENTATIVE MEASURES IN THE NICU

* Respiratory syncytial virus.

Reference: 1. Law BJ, Langley JM, Allen U, et al. The Pediatric Investigators Collaborative Network on Infections in Canada study of predictors of hospitalization for respiratory syncytial virus infection for infants born at 33 through 35 completed weeks of gestation. *Pediatr Infect Dis J.* 2004;23:806–814.

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News

☐ May-June 2007

RENT-A-UTERUS

Rob Stein, writing in the Washington Post, reports on plans for the first US uterus transplant. Researchers in Manhattan have begun screening women left barren by cancer, injuries or other problems who want a chance to bear their own children. The planned operation, Stein reports, is stirring objections among some transplant experts, fertility specialists and medical ethicists, who question whether the procedure has been tested sufficiently and whether the benefit of being able to carry a pregnancy outweighs the risks for the woman and fetus. Others said having a childbearing experience had little to do with actual parenting and shouldn't be so important. But defenders of the transplant effort said that thousands of women cannot bear children because they were born with a malfunctioning uterus or their wombs were damaged, and said women should make the choice to have the transplant, not doctors or ethicists. Doctors in Saudi Arabia reported the first human uterus transplant, in 2002, on a 26-year-old woman whose womb had been removed six years earlier because of hemorrhaging after the birth of her first child. The donor was a 46-year-old woman with an ovarian condition that required removal of her ovaries and uterus. Although blood clots forced surgeons to remove the organ after 99 days, doctors called the procedure a technical success.

US researchers have practiced on rats, pigs, rabbits and a monkey, and said problems that occurred in Saudi Arabia could be avoided. To perform the transplant, doctors would wait to make sure the organ was working properly. An embryo created through in vitro fertilization would then be placed in the womb. If the pregnancy went well, the baby would be delivered by Caesarean section, and the doctors would remove the uterus.

BIG BABY

A huge baby has been born in Cancun, Mexico. He's been nicknamed Super Tonio and weighs in at 6.6 kilograms. Cancun residents crowded the nursery ward's window to see Antonio Vasconcelos, who was born early on Monday by a C-section at Jesus Kumate Rodriguez Hospital. The baby drank 5 ounces of milk every three hours, and measured 55 centimeters in length. "We haven't found any abnormality in the child, there are some signs of high blood sugar, and a slight blood infection," said the hospital's director.

In Brazil, a baby born in January 2005 in the city of Salvador weighed 7.6 kilograms at birth. According to Guinness World Records, the heaviest baby born to a healthy mother was a boy weighing 10.2 kilograms, born in Aversa, Italy in September 1955. Antonio's mother, Teresa Alejandra Cruz, 23, and father, Luis Vasconcelos, 38, said they were proud of the boy, and noted that Cruz had given birth to a baby girl seven years ago who weighed 5.2 kilograms. "It's good, because now with this one, we'll have a pair" of big babies, said Vasconcelos.

LITTLE BABY

Agence France Press reports that the world's most premature living baby, born at 21 weeks and six days, has headed home after spending four months in a neonatal intensive care unit at Baptist Children's Hospital in Miami. No baby born at less than 23 weeks was previously known to have survived, according to the University of Iowa, which keeps a record. When she was released from the NICU, the girl was four pounds. At birth, she weighted only 280 grams and measured 9.5 inches. Doctors said that at the time of her release, the baby girl was thriving and well enough to be cared for by her parents at home. The baby was delivered via C-section after attempts to delay a premature delivery failed. She was breathing without assistance at birth and even made several attempts to cry.

KICKING IT

Paediatric Anaesthesia presented a paper on severe withdrawal syndrome in three newborns subjected to continuous opioid infusion and seizure activity dependent on brain hypoxia-ischemia. Authors Bachiocco, et al with the Department of Anesthesia-Analgesia and ICU at S. Ortola Hospital, Bologna, Italy, investigated whether brain hypoxia represented a risk factor for the occurrence and severity of opioid abstinence syndrome. Three newborns who manifested seizure activity as a result of hypoxia, focal brain ischemia, and hypoxia and sepsis, respectively, were compared with 17 neonates who suffered from hypoxia without developing seizure activity. The first three neonates suffered a severe withdrawal syndrome (a rating on the neonatal abstinence score>17), the others did not. The authors hypothesized that brain hypoxia facilitated the occurrence and severity of the withdrawal syndrome because some key neurochemical processes (such as N-methyl-D-aspartate activation, protein kinase C activation and nitric oxide production) are common to both phenomena. For the full article see Paediatr Anaesth. 2006 Oct;16(10):1057-62.

BRAIN GROWTH

Medical News Today reports that the regions of the brain that control vision and other sensory information grow dramatically in the first few months following birth, while the area that controls abstract thought experiences very little growth during the same period. University of North Carolina at Chapel Hill researchers have found that the back regions of the brain, which control vision and sensory integration, grew significantly faster than the prefrontal region, which controls abstract reasoning. In addition, the type of brain tissue called gray matter, which contains most of the neurons or nerve cells, grew much more robustly than another type of tissue called white matter, which contains the connecting fibers between neurons in different brain regions. Gray matter size grew by roughly 40 percent in the first months after birth, while white matter grew very little. The study was the first to systematically obtain very high resolution magnetic resonance imaging (MRI) scans on a large group of newborns. The results appear in the Journal of Neuroscience. Another key finding by the UNC team is that boys, on average, are born with brains about 10 percent larger than the brains of girls. This is consistent with the pattern seen in adults, Gilmore said in so far as men typically have a brain about 10 percent larger than that seen in women. However, the scans revealed that brain asymmetry was opposite in newborns and adults. In adults, the right side of the brain is usually slightly larger than the left side. Gilmore and his collaborators found the left side was slightly larger in the newborns who were included in the study. For the study, 74 newborns at the University of

North Carolina Hospitals were given high-resolution magnetic resonance imaging (MRI) scans in the first few weeks after birth. In terms of brain volume, the researchers found newborn male brains were 7.8 percent larger than females. In addition, males had 10.2 percent more gray matter and 6.4 percent more white matter than females. No significant difference in brain asymmetry was observed between males and females; the left side of the brain was on average 4.3 percent larger than the right side. The researchers noted that the dramatic growth in gray matter, the part of the brain that contains most of the neurons, or nerve cells, may have implications for autism research. Children with autism have larger brains and more gray matter than average. The study suggests that in autistic children, something may go awry during gray matter growth in the first year of life.

GIVE IT A SHOT

A group of Portuguese researchers at the Institut Pasteur and the Institute for Biomedical Sciences - Abel Salazar - in Porto have identified a protein in a micro-organism which allows it to colonize a host by modulating its immune system. According to these scientists, who have published this study in the Journal of Immunology, the protein thus identified is a possible candidate for the development of a vaccine against Group B Streptococci. Some 800 cases of invasive infections in newborn infants caused by group B streptococci are recorded each year in France; they mainly result from transmission from the mother to the infant. Mortality linked to these infections remains high (50 to 100 deaths each year), and despite antibiotic therapy, 25 to 50% of the infants who survive suffer from neurological after-effects. The scientists demonstrated that a protein secreted by group B streptococci, called GAPDH, was capable of raising the level of one of the messengers in the immune system, the cytokine IL-10. Such an increase in IL-10 diminishes the immune defenses, so that invasive bacterial infection is facilitated. The researchers also showed that IL-10-deficient mice were much more resistant to infection by group B streptococci. The team concluded that GAPDH could be used to ensure immune protection. The researchers are now working on the development of a vaccination strategy.

HEAD 'EM OFF

Researchers at the University of Virginia Health System have developed a way to monitor babies in neonatal intensive care units and predict sepsis before there is any indication of illness. Results of this research appear in the February issue of the journal Pediatric Research. Researchers were instrumental in developing a novel bedside monitoring system to predict the likelihood that sepsis will occur in a baby in the next 24 hours. The system analyzes heartbeat signals obtained from a standard bedside heart rate monitor and looks for patterns that give an early indication that the baby is getting sick. Characteristics such as decreased variability of the heart rate along with brief episodes of slowing of the heart rate indicate that the infant may be getting an infection. These characteristic patterns can serve as an early warning to the physicians and nurses caring for the infants. After years of testing and clearance from the Food and Drug Administration, academic research hospitals are participating in a multicenter National Institutes of Health-sponsored study to further test if heart rate characteristic monitoring improves outcomes for NICU babies. The patented monitoring technology was developed by Griffin and Moorman at the University of Virginia Health System. The rights are licensed by the University of Virginia Health System Patent Foundation to Medical Predictive Sciences Corporation in Charlottesville, VA.

HEARTACHE

There is an increased risk of fetal heart problems when mothers carry particular antibodies associated with rheumatic diseases, according to an abstract presented by Yale School of Medicine researchers at the recent Society for Maternal-Fetal Medicine Conference. CHB carries a 20 percent death rate and nearly all survivors require pacemakers. Researchers at Yale's Department of Obstetrics, Gynecology & Reproductive Sciences helped conduct the PR Interval and Dexamethasone Evaluation (PRIDE) study with a team of other researchers to evaluate an early marker of cardiac injury before there is permanent scarring.

The PRIDE group conducted a longitudinal (observational) study following over 100 women with the anti-Ro and anti-La antibodies to determine if there were early signs of fetal heart problems. They also explored whether early treatment would reverse the problems. The team found that while first-degree fetal heart block may be reversible with the steroid drug dexamethasone, the condition could advance within as little as one week to a third-degree block, which is irreversible even with further intervention.

UP THE DOSAGE

Researchers at the 27th Annual Society for Maternal-Fetal Medicine (SMFM) meeting announced that high-dose progesterone treatment helped at-risk pregnant women avoid premature delivery. In the study, 45 hospitalized women who already had experienced premature labor were randomly divided into a treatment group and an observation group. The 23 members of the treatment group received twice-weekly 341-mg doses of progesterone until week 36. The progesterone injections appeared to prevent continued shortening of the cervix, a factor in premature labor. The study's purpose was to determine if a higher dose of alpha hydroxy-progesterone caproate (17P), commonly used now to prevent preterm birth among women with that history, can affect cervical changes and thus increase preventive effectiveness in women during their first pregnancy. Findings revealed that 22 percent of the women in the high-dose treatment group had a preterm delivery, compared to 54 percent of those in the observation group, and the researchers believe this was the result of reduced cervical shortening and inhibited local inflammation. In an unrelated study, similar 17P treatment reduced the risk of preterm delivery by 85 percent. The study, Alpha Hydroxy-Progesterone Caproate (17P) Treatment Reduces Cervical Shortening Inhibiting Cervical Interleukin-1 Secretion, was the first to address the relationship between progesterone, cervical changes, and preterm deliveries.

BORN TO LOSE

A recent study by Mount Sinai School of Medicine (MSSM) found that children born with low birth weight who suffered child abuse are substantially more likely to develop psychological problems such as depression and social dysfunction in adolescence and adulthood. The study, appearing in The Archives of Pediatric & Adolescent Medicine, was the first to investigate the possible interaction between LBW and later adversity. To examine the possible conjoined effects of LBW and child abuse on adaptation and on the development of psychiatric and medical problems, researchers looked at data from the

John Hopkins Collaborative Perinatal Study, an epidemiologic study that followed a random sample of mothers and their children from pregnancy for more than 30 years. They compared outcomes in the transition to adulthood among four groups of children: those with LBW and childhood abuse, those with LBW alone, those with childhood abuse alone and those with neither. The researchers found that participants with both LBW and subsequent child abuse, relative to those with neither risk, were at a substantially elevated risk of psychological problems: a 10-fold for depression; a nearly 9-fold for social dysfunction and an over 4-fold for somatization. However, they were not at an elevated risk for medical problems in adulthood. Those exposed to child abuse were more likely to report delinquency, school suspension, repeating grades during adolescence and impaired well-being in adulthood, regardless of LBW status. For those with LBW alone, the prevalence of those problems was comparable to that of those without either risk factor.

SPRINGTIME ROMANCE

Women who become pregnant in spring are more vulnerable to preterm birth than those who conceive in other seasons, according to researchers at the University of Pittsburgh. Researchers analyzed data from 75,399 deliveries over a 10-year period at the university-affiliated Magee-Womens Hospital of UPMC, grouping each by season of last menstrual period, a date physicians historically have used to estimate conception. Women conceiving in summer had the lowest rate of preterm birth at 8.4 percent, with steadily increased rates for the fall (8.8 percent), winter (9.1 percent) and spring (9.2 percent). Preterm birth also took place less often with conceptions in summer and fall than for those in winter or spring, the researchers noted. In fact, those conceiving in summer or fall had a 25 percent reduction in risk over those who conceived in winter or spring.

EXPLOSIVE RESULTS

A recent Canadian study showed that giving nitroglycerin to women who enter labor early results in significant improvement to their babies' health. The improvement is most marked in babies who are born very prematurely. The five-year, randomized controlled trial involved 153 women who were recruited at the time they went into preterm labor. The study was organized by the Queen's Perinatal Research Unit at Kingston General Hospital, with data management by the Ottawa Maternal Neonatal Investigators at the Ottawa Health Research Institute. It revealed that using nitroglycerin patches for pregnant women helps to prolong pregnancy and most importantly improves babies' outcome, with fewer side effects than experienced through the use of other drugs.

SEXY BABY

Doctors at Newcastle's Royal Victoria Infirmary used Sildenafil (Viagra) to open up tiny blood vessels in the lungs of an infant weighing 24 ounces whose lung had failed. According to a neonatologist at the hospital where the drug was employed, the problem with preemies is that doctors could blow oxygen into the lungs, but there isn't enough blood to carry oxygen to the rest of the body. Sildenafil opened the blood vessels so they could capture the oxygen and take it around the body. Reported by the BBC.

THE BREAST OF THEM

Babies who are breastfed are more likely to move up the social ladder as adults, a study has suggested. A University of Bristol team looked at 1,400 babies born from 1937-1939 and followed their progress for 60 years. Those who were breastfed were 41% more likely to move up in class than those who were bottle-fed.

Experts said the Archives of Disease in Childhood study supported the idea that breastfeeding led to better long-term outcomes for children. The people studied had all originally taken part in the Boyd Orr Study of Diet and Health in Pre-War Britain carried out in 1937-1939. They were followed up until an average age of 73. The study found there was no difference in breastfeeding rates when the researchers looked at household income or social class. Those who had been breastfed had a 58% chance of moving up the social ladder compared to 50% of those who were bottle-fed, a relative difference of 41% when the statistics were adjusted to take into account other factors which might influence the outcome. The longer a child was breastfed, the greater were the chances of upward mobility. In families where one child was breastfed while a sibling was bottle-fed, there was still a difference in their chances of social mobility, with the breastfed child 16% more likely to move up in class. The researchers opined that breastfeeding may affect brain development, or that breastfeeding typically took place in a better environment, or that it indicated better bonding with the mother.

OLDER ISN'T BETTER

Women who have a baby past age 40 are at an increased risk of stillbirth. Researchers at Yale University wanted to see if age alone, rather than a health problem in a previous pregnancy, affected the risk of both stillbirth and the death of a child in the womb for older mothers. They looked at six million babies born to women aged 15 to 44 between 1995 and 1997 and correlated their information with data from the US Centers for Disease Control, which registered the deaths of babies. They calculated that women aged 40 to 44 had three times the risk of stillbirth than women aged 25 to 29. The researchers also found that fetal checks at 38 weeks of pregnancy had the greatest impact on reducing stillbirth rates in older women.

These checks include listening to the baby's heartbeat and testing the amniotic fluid to pick up any signs of distress. The researchers suggested that 1,700 such checks would be needed to prevent one stillbirth in women aged 35 to 39, compared with just under 500 tests to prevent a baby born to women aged 40 to 44 dying, and concluded that women expecting babies over 40 should be monitored from 38 weeks onwards.

DO NOT DISTURB

Researchers believe that a new noninvasive blood test could be developed to detect genetic abnormalities such as Down's syndrome in the womb. Current non-invasive tests such as ultrasound are limited, and invasive tests pose a risk to the pregnancy. The new technique works by examining samples of fetal DNA present in the mother's blood for tiny variations in the sequence of the genetic material. Analyzing fetal DNA from a mother's blood sample has been possible for some time, but its effectiveness has been limited because only a small amount of the DNA makes its way into the mother's blood. A team at the company Ravgen, Inc, has been able to maximize the amount of DNA that can be recovered by treating the blood samples with formaldehyde. The researchers took blood samples from 60 pregnant women and searched the genetic material for variations of single nucleotide polymorphisms (SNPs). As each chromosome has a characteristic pattern of SNPs, the researchers were able to distinguish between DNA from the

mother and the fetus. They were also able to determine whether the fetus was carrying extra copies of key chromosomes which cause genetic disease. For example, carrying an extra copy of chromosome 21 causes Down's syndrome. Of the 60 samples tested, the technique identified the number of chromosomes correctly in 58, including two cases of trisomy 21. The researchers noted that there were still problems to be overcome.

RELAX!

Researchers at Imperial College London found that children whose mothers were stressed out during pregnancy were vulnerable to mental and behavioral problems like ADHD. Stress caused by parental fighting or violence was found to be particularly damaging. Experts blame high levels of the stress hormone cortisol crossing the placenta. The researchers found that high cortisol in the amniotic fluid bathing the baby in the womb tallied with the damage. The babies exposed to the highest levels of cortisol during their development had lower IQs at 18 months. The same infants were also more likely to be anxious and fearful. The work suggested that maternal stress is a true risk factor in its own right, although the researchers acknowledged that genetic factors and home environment after birth would also have an impact on a child's development.

PRODUCTS

WHAT'S IN A NAME

Tyco Healthcare today announced that Covidien will be its new name once the global healthcare leader separates from parent company Tyco International this spring and becomes an independent, publicly traded company. Tyco Healthcare is a leading global manufacturer and distributor of medical products, with annual sales of nearly $10 billion. Its product portfolio includes disposable medical supplies, monitoring equipment, medical instruments and bulk analgesic pharmaceuticals. The Covidien brand will be the master identifier that unites Tyco Healthcare's brand names, including Autosuture, Kendall, Mallinckrodt, Nellcor, Puritan Bennett, Syneture, and Valleylab. Its upcoming separation from Tyco International will introduce a new era for the diversified healthcare products organization, which employs more than 43,000 people worldwide. As Covidien, the newly independent company will embark on a distinct new direction that focuses exclusively on healthcare and benefits from increased flexibility to invest in innovation and organic growth. Covidien is an original name, inspired by themes of collaboration and life. It was selected for its global meaning and appeal from among some 6,000 possible names in a rigorous process that began more than nine months ago.

PARTNERSHIP

Draeger Medical, Inc was recently awarded membership into the American Association for Respiratory Care (AARC) Corporate Partner Program. Draeger Medical has earned elite Corporate Partner status because of its exceptional support of AARC and the respiratory care profession. "Without the level of support and commitment exhibited by Corporate Partners such as Draeger Medical, AARC would not be able to advance its mission to promote optimum respiratory care for patients with lung diseases," said AARC Executive Director Sam Giordano, MBA, RRT, FAARC. As a corporate partner, Draeger Medical provides support to the largest professional association for respiratory therapists and other professionals. Draeger Medical's support is used to provide much needed educational and research efforts aimed at ensuring that respiratory therapists have the information and tools they need to deliver top quality care to patients with asthma, chronic obstructive pulmonary disease, cystic fibrosis, and other respiratory problems. The Corporate Partner Program is comprised of best-in-class organizations interested in supporting the goals and work of the Association. The program aims to give respiratory care providers information, insights, and innovative approaches to improve performance and advance the health of their patients. Contact draeger.com.

ON ITS WAY

Discover Laboratories, Inc announced that it has received guidance from the FDA in a recent meeting regarding the key remaining steps necessary for potential approval of Surfaxin (lucinactant) for the prevention of RDS in premature infants. The guidance provides the clarity and defined pathway that Discovery believes is necessary to address key remaining issues identified by the FDA Approval Letter, followed by a six-month review cycle by the FDA for potential approval of its New Drug Application for Surfaxin. Surfaxin is a precision-engineered, peptide-containing, synthetic surfactant that is designed to closely mimic the function of natural human lung surfactant and represents a potential alternative to animal-derived surfactants. Contact discoverylabs.com.

ALL IN ONE

Nova Biomedical announced the incorporation of total bilirubin (tBil) to the comprehensive test menu on its Stat Profile Critical Care Xpress (CCX) "All-in-One" Analyzer. Bilirubin is an important indicator of liver function particularly in neonatal applications. With the addition of total bilirubin, the CCX analyzer now offers 20 measured tests, including pH, PCO_2, PO_2, SO_2%, hematocrit and hemoglobin, sodium, potassium, chloride, ionized calcium, ionized magnesium, glucose, BUN, creatinine, lactate, deoxyhemoglobin, oxyhemoglobin, methemoglobin, and carboxyhemoglobin, in a single, compact instrument. While incorporating more on-board tests than any competitive analyzer, the Critical Care Xpress is 20 to 40% smaller and easily transported on its mobile cart. Key CCX features include a color touch screen interface for intuitive, on-screen prompted operation; a single, snap-in reagent pack that eliminates bulky gas tanks, regulators and humidifiers, and the waste containers needed in other analyzers; a fully automated, on-board Auto-Cartridge QC system that eliminates the manual quality control, dramatically reducing labor time and costs; and a unique automated maintenance system that allows the operator to initiate maintenance and then walk away from the analyzer. Contact novabio.com.

STRIP TEASE

The new StatStrip Glucose Monitor from Nova Biomedical has received clearance from the US Food and Drug Administration for use in neonatal testing. While every other glucose monitor may report an error if the hematocrit value is abnormal, StatStrip accurately measures glucose and hematocrit on a single strip, automatically correcting for an abnormal hematocrit value. In addition, its small 1.2 microliter sample volume is attractive for the NICU environment where blood conservation is essential. Introduced in May 2006, StatStrip has rapidly become the gold standard in hospital glucose testing.

Incorporating a patented new Multi-Well strip technology, StatStrip elevates bedside glucose monitoring to a level of speed, accuracy, quality, and patient safety on a par with central laboratory testing. In addition to hematocrit, StatStrip measures and corrects for interferences from acetaminophen (Tylenol), uric acid, ascorbic acid (Vitamin C), maltose, galactose, xylose, and lactose. StatStrip also eliminates oxygen interference to provide accurate glucose results regardless of the sample's oxygen status. StatStrip's 6-second analysis time, color touch screen operation, and simple operating steps make bedside glucose testing fast and easy for point of care staff. Unlike competitive glucose analyzers, StatStrip requires no calibration codes thereby eliminating an operator step and preventing a potential input error. Contact novabio.com.

FIFTH TIME'S THE CHARM

Viasys Respiratory Care, a subsidiary of Viasys Healthcare Inc has again won the American Association for Respiratory Care (AARC) Zenith Award. It's the fifth time the company has won the award, which is the industry's top recognition award for respiratory care product and service providers, and was presented at AARC's 52nd Annual International Respiratory Congress in Las Vegas. "We are extremely honored to be recognized by the AARC with the Zenith Award for the fifth time," stated Randy Thurman, Chairman, President and Chief Executive Officer of Viasys Healthcare Inc. During the awards ceremony Thurman pledged the company's continued support for the AARC and the dedicated respiratory therapists throughout the world. The AARC established the Zenith Award program in 1989 to honor respiratory care product and service providers for exemplary service. All 35,000-plus members of the AARC choose the Zenith recipients in a special election. Candidates are judged on the quality of delivered goods, the accessibility and clinical helpfulness of the sales force, the responsiveness and service record of the service group, and the overall support provided by the company to respiratory care professionals. Contact viasys.com.

TAKING THE PULSE

Nonin Medical, Inc announced that it has entered into an agreement with MedAssets Supply Chain Systems, a leading US healthcare group purchasing organization (GPO), to make its comprehensive line of pulse oximeters and sensors, including the only wireless oximeter based on Bluetooth technology, available to MedAssets customers. Under the multi-year agreement with Nonin, MedAssets customers, numbering more than 1,500 acute care hospitals and 25,000 alternate-site facilities nationwide, will have access to these pulse oximeters and sensors. Minneapolis-based Nonin Medical, Inc designs, manufactures and distributes a broad spectrum of physiological monitoring devices, currently used by health and medical professionals in more than 125 countries. The company draws upon its industry-leading capabilities in signal processing and sensor design to develop innovative pulse oximeters, sensors, accessories and software with features not available in competing products. MedAssets partners with healthcare providers to improve operating margins and cash flow while supporting quality of care goals. MedAssets implements integrated solutions to address the greatest opportunities for financial and process improvement and drives performance in revenue cycle, supply chain and clinical service line management. MedAssets is a business partner to more than 2,400 hospitals and 25,000 non-acute care healthcare providers. For more information, go to medassets.com.

GET SMART

Children's Medical Ventures (ChMV), a subsidiary of Respironics, Inc, announced the release of a new patient monitoring system for health care professionals called SmartMonitor 2 Professional Series Light (PS Light). The PS Light is the latest in a series of monitors from ChMV designed to track a patient's cardiorespiratory activity. SmartMonitor 2 PS Light is specifically intended for hospital use to measure and record a patient's pulse and respiration, and sounds an alarm if levels fall below defined limits. The "Light" designation refers to the PS Light's ability to provide high-quality, cost-effective heart and respiration monitoring parameters without integrated pulse oximetry. ChMV currently offers the SmartMonitor 2 PS for healthcare settings requiring patient monitoring with integrated pulse oximetry. SmartMonitor 2 PS Light is cleared for use with infant, pediatric, and adult patients making it ideal for documenting patient response to conscious sedation, post-anesthesia recovery, patient controlled analgesia, and general floor monitoring. The PS Light offers many of the same features found in ChMV's other cardiorespiratory monitors including separate digital readouts for pulse and respiratory rates, device and patient alarms, internal modem, lightweight design and battery backup. SmartMonitor 2 PS Light also incorporates universally recognized symbols that help simplify operation while reducing potential language barriers, utilizes Synergy-E Event Software to review patient event data and is compatible with ChMV's SmartRecorder. Contact childmed.com or respironics.com.

CASTING A WIDER WEB

Dräger Medical introduces a comprehensive, web-based information management solution that integrates vital OR, PACU and ICU patient information from medical devices and systems across the Acute Point of Care (APOC). Innovian Solution Suite streamlines access to patient information by providing one platform for the critical and perioperative care environments. It strengthens Dräger Medical's suite of information management solutions, which also includes a distributed, client-based anesthesia information management solution for the OR. The new web-based components of the suite include solutions for the perioperative and critical care environments. In the perioperative environment, Dräger Medical's OR/Anesthesia information management system covers scheduling, pre-op, holding, intra-op and PACU. For critical care there is an ICU documentation system that provides full electronic patient charting, flowsheet, scoring and printed reports. Working together, these solutions continually capture vital patient information from perioperative and critical care medical devices and clinical information systems. That data is integrated into one, easy-to-navigate interface for direct access by clinicians. A more accurate patient record is possible when patient data is automatically placed into the record. With electronic charting clinicians can spend less time writing and have more time for patient care. Dräger Medical's web-based information management solutions support Pick and Go technology. This enables information collected by Infinity monitors during patient transfer to be automatically backfilled into the database. Moreover, because it is built on open standards, it fully supports HL7 interfaces to the hospital information system. Contact draeger.com.

KID STUFF

WeeSpecs Supreme from Children's Medical Ventures combines innovative materials and superior light-blocking

capabilities to produce a cutting-edge phototherapy mask designed to fit even the smallest babies. The anatomically contoured goggle design and new ultra-soft, slip-resistant fabric keep the baby's eyes protected under any conditions. Three different sizes, preemie, small and medium, ensure appropriate fit of premature through full-term infants… **Prone Plus**, the newest addition to the Children's Medical Ventures line of positioning products, is designed to meet the prone positioning needs of hospitalized infants. The unique hourglass shape facilitates natural rounding of the shoulders, hand-to-mouth coordination and head and trunk alignment. Prone Plus provides consistent, appropriate positioning for premature and critically ill infants. Contact respironics.com.

NEW TEAM

Tyco International Ltd announced the executive team that will lead Tyco Healthcare as it becomes a separate, independently traded company. Richard J. Meelia continues as the head of the team. Jose (Joe) Almeida, president of the medical devices business, is responsible for managing the advanced medical, respiratory, surgical and Valleylab global business units. James C. Clemmer, president of the medical supplies business, is responsible for day-to-day operations of the Ludlow, Curity and OEM business units, and for directing new product development and ongoing operations. Douglas E. Strohmeier, president of Tyco Healthcare's retail business, is responsible for managing the development, manufacturing and marketing of a wide variety of retail brand, private label products for retail markets in the US, Canada and Mexico. Tyco Healthcare includes Mallinckrodt, Nellcor, Puritan Bennett, and other units. Contact tycohealthcare.com.

EXEC-CELLENCE

Viasys Healthcare Inc announced several executive appointments including the naming of Ed Pulwer as Executive Vice President, Chief Operating Officer. He has also been named Group President, Viasys NeuroCare. Additional appointments included Greg Martin to Group President, Viasys International Operations and Arie Cohen as Group President, Viasys Respiratory Care. Randy Thurman, Chairman, President and Chief Executive Officer, said, "We are celebrating our fifth anniversary as a public company this year. During these five years, we have achieved significant and consistent growth throughout our organization. These achievements are the result of the leadership and commitment that has been the foundation of the Viasys success. Today's promotions recognize the outstanding professionals that have made Viasys what it is today. In just five years, we have experienced significant revenue growth across the entire spectrum of our business, and we are now the market leader in several of our product categories. With a best in class management team, we look forward to continued achievement across our businesses." Viasys also announced that Rebecca W. Rimel, President and CEO of The Pew Charitable Trusts has joined the Board of Directors of Viasys Healthcare Inc. She became President and CEO of the Trust in 1994. Contact viasys.com.

NEWS FEATURE

Mechanical Ventilation in the Neonatal/Pediatric Population

Justin Tse, RRT, NPS
Justin Tse is with Hamilton Medical. This feature is reprinted from the company's Ventilation Newsletter.

A low tidal volume strategy for mechanical ventilation has been shown to improve morbidity and mortality in adults with acute respiratory distress syndrome (ARDS) or acute lung injury (ALI). There have been numerous studies supporting this strategy in adults but very few have been done in pediatrics. Does utilizing a low tidal volume strategy work for children? Do protocols in mechanical ventilation for pediatrics work? This newsletter will discuss some of the differences between adults and pediatrics and discuss protocols in children.

Lung development is different in neonates and pediatrics than adults. Lung development starts in utero and "continues to grow and mature over the first 8 years of life." Due to this difference alone, it would be predictable that ARDS and ALI would effect the neonatal/pediatric lung differently than adults. Newborn infants also have only 1/6th the number of alveoli than adults. Other than physical differences, the causes of ARDS are different in neonatal/pediatric population. I have listed some common causes of ARDS below.

- Neonatal
- Pediatric
- Adults
- Meconium Aspiration
- Acute upper airway obstruction
- Multiple transfusions
- Congenital Diaphragmatic Hernia
- Pneumonia
- Overdose of narcotics
- Prematurity
- Bronchiolitis/Asthma
- Smoke inhalation
- Persistent Pulmonary Hypertension of the Newborn
- Chest trauma
- Near Drown
- Congenital Cyanotic Heart Disease
- Cardiac Arrest
- Sepsis
- Seizures
- Gastrointestinal or hepatic disorder

As we can see, there are some similarities within each group, but there are more differences. Another major difference between adults and children is ventilator length of stay. Pediatrics patients generally have shorter time on the ventilator than adults.

Even with the differences with pediatrics and adults, many pediatric intensivists agree with the opinion of Mehta and

Arnold, that "optimal alveolar recruitment with judicious use of positive end-expiratory pressure (PEEP) and low tidal volumes will remain the mainstay for managing respiratory failure in children."

Ventilator management protocols that have been developed for adults are supported by numerous studies. There are far fewer studies in pediatrics. Graham et al discusses the many potential difficulties in creating a protocol for pediatrics from initiation to extubation. One key point made by Graham et al is that "no single ventilator management protocol is applicable to all children who require mechanical ventilation." They go on to state "the clinician must contemplate the reason why each individual patient is intubated… then must consider whether the patient is within the group for which a specific protocol was intended."

The article also states that most protocols are designed to address a certain phase during the course of illness and we must be aware of the patient's treatment course at all times. The phases of mechanical ventilation as defined by Graham et al are initiation, maintenance, weaning, and discontinuation of mechanical ventilation.

Because mechanical ventilation in neonates and pediatrics are so individualized, closed loop ventilation protocols may benefit this population. Optimal Closed Loop Ventilation systems that adapt to a particular patient's pulmonary mechanics and drive are now available and being employed in several pediatric centers. (vs standard written protocols or knowledge based systems which apply a set of rules to all patients). Closed loop ventilation helps set up a safe "flight plan" in which the clinician can individualize the care for each patient while taking the patient thru all phases of mechanical ventilation. Closed loop ventilation incorporated as part of a multi-disciplinary team approach can result in giving the best possible outcome for our critically ill patients who require mechanical ventilation.

SOURCES

1 Moore K, Persaud T. The developing human-clinically oriented embryology. 6th edition. Philadelphia: WB Saunders; 1998.
2 Hanson JH, et al. Application of the acute respiratory distress syndrome network low-tidal volume strategy to pediatric acute lung injury. Respir Care Clin N Am, 2006 Sep; 12(3):349-57.
3 Grahams AS, et al. Ventilator management protocols in pediatrics. Respir Care Clin N Am, 2006 Sep; 12(3):389-402.

SPOTLIGHT ON PHOTOTHERAPY

TAKE A SHOT

Using light instead of a needle, **BiliChek** from Children's Medical Ventures allows health care professionals to test bilirubin levels regardless of gender, gestational age, or body weight – without needing a blood sample. Only the individual calibration tip touches the baby, so BiliChek greatly reduces the risk of infection or cross contamination. BiliCheck is approved for use before, during and post phototherapy making it ideal for the newborn nursery and NICU… Ideal for hospital and home use, the **Wallaby 3 Phototherapy System** allows a mother to hold and even nurse her baby without interrupting therapy. At 7.2 pounds, the Wallaby 3 is light enough to be easily transported with the baby. There is no infrared or ultraviolet light to harm the baby… The **Joey Dosimeter** is specifically designed to measure fiber-optic irradiance and validate the performance of the Wallaby 3 Phototherapy System between patients. The sensor head measures 20 square centimeters and calculates an average irradiance across the entire therapeutic spectral range of 425nm to 475nm when it is placed on the Wallaby fiber-optic panel. Results appear on a digital display… Children's Medical Venture's **Jaundice Management Program**, Ensuring Optimal Outcomes, helps caregivers identify infants at increased risk for hyperbilirubinemia, implement effective screening criteria, develop unit-based protocols consistent with the most recent literature, and establish a parent teaching forum to promote awareness for parents after early discharge to home. Contact respironics.com.

EXECUTIVE PROFILES

Instrumentation Laboratory

Ramon E. Benet-Ferran

Ramon E. Benet-Ferran is Vice President, Worldwide Marketing and US Sales and Service, Instrumentation Laboratory.

Who is Instrumentation Labs?

For almost half a century, Instrumentation Laboratory (IL) has set the gold standard in the development, manufacturing, marketing and service of diagnostic instruments for clinical laboratories and point-of-care settings. Singular in our focus, we are the acknowledged world leader in critical care and hemostasis diagnostics. IL's history shines with innovation. In 1959, we were the first to introduce a bloodgas analyzer into routine clinical use; and today, we continue that leadership tradition with the new GEM Premier 4000, the most comprehensive, flexible and user-friendly analyzer on the market. In between is a long history of industry innovation.

Over the years, IL has brought breakthrough clinical functionalities as well as automation, computerization and system integration into the marketplace and continues to pioneer new technologies. In 1967, we introduced CO-Oximetry testing, followed by chemistry and coagulation centrifugal analysis. In 1984, we debuted the first blood gas analyzer with built-in data management and video display. Introducing new levels of efficiency to the market, several years later IL offered a device with disposable cartridge technology. By 2000, IL touched off a revolution in the industry with its standardized critical care testing platform across all hospital locations.

Complementing this innovation has been an ongoing commitment to meeting the full range of needs of our customers and the patients they serve. Our research and development efforts have always been a high priority and driven by the demands of the marketplace to make available the functionality and features our purchasers want and need. Similarly, unwavering dedication to product support and service is an integral part of our corporate philosophy.

How do you provide technical service and support and of what nature?
IL has always been committed to providing a strong group of technical service representatives in the field who are highly skilled and dedicated to supporting our customers. We focus heavily on recruiting professionals with clinical experience so that they know firsthand the needs, goals and workplace of our customers. Our representatives are given extensive product training and are taught to cater to the needs of clients and to provide comprehensive education about the use of IL products. Additionally, we offer onsite product-specific training.

Finally, IL has a highly trained technical support staff accessible on the telephone 24/7 to answer all questions relating to applications, quality control and performance of its equipment. Recently, an independent research group found that IL outranked every other major manufacturer of critical care analyzers in a full range of measures of customer satisfaction. The study of U.S. hospitals at the point-of-care found that IL achieved the highest ratings in overall satisfaction as well as product satisfaction, ease of use, accuracy, ease of maintenance and much more.

How do you support customer's needs through product development?
At IL, the customer's needs are a major driver, and customer satisfaction is key. Even more important than our support and training is our commitment to addressing the needs of our product purchasers through the design of our products themselves. As part of this philosophy, we are dedicated to offering the most technically advanced, yet user- friendly analyzers on the market.

Our newest technology has been created with several key goals in mind. In addition to cutting-edge, comprehensive clinical functionality, these goals are ease-of-use, reliable operation and results, automated QC procedures, as well as remote connectivity. In some clinical settings, standardization of results in decenteralized testing scenarios also is crucial.

Perhaps the most important of these goals is automated quality control, which we address through our Intelligent Quality Management (iQM) system that brings new efficiency and reliability to the traditional, time-consuming blood gas quality control (QC) process. After all, no one chooses a career in healthcare to spend time with machines. With iQM, IL liberates therapists from traditionally time-consuming tasks. iQM provides a more efficient and accurate alternative to manual QC by automatically and continually checking the IL analyzer to deliver real-time system diagnostics. Time to error detection and correction is just minutes. iQM checks extend beyond analyzer electronics to include sensors and the chemical measurement process, which typically requires manual intervention, even on other advanced analyzers. The process automates all corrective actions, freeing up therapists from labor-intensive manual trouble-shooting, as well as eliminating lengthy equipment training and possible human error that might compromise test results. Also, all regulatory compliance documentation is automated. With this system, routine analyzer maintenance is eliminated through the use of a single cartridge that contains everything needed for whole blood testing. Every three weeks, a new cartridge is simply snapped into place and the analyzer is ready to function. A closed system, the PAK maintains the complete integrity of the testing process throughout the cartridge life. Another benefit of iQM is significant cost-savings realized through elimination of staff time spent with QC, which can amount to 48 hours monthly.

Also key to our product line is leveraging digital technologies to deliver advanced connectivity among our products to maximize efficiency and deliver a higher standard of care. A good example is our GEMweb technology and newest GEMweb Plus system for the GEM Premier 4000 analyzer. This unique suite of information management software enables clinicians, wherever located—across the hallway or the globe— to access and control multiple IL analyzers as if they were in the same room. This means that wherever and whenever needed, therapists and other clinicians can access and track test results, reports and current patient status as well as download and process orders and more. They can manage administrative tasks when convenient by remotely validating samples, accessing compliance documents and troubleshooting testing locations. The most advanced technologies in the world mean nothing if busy clinicians cannot take advantage of them. That's why user-friendly, easily accessible technology is one of our goals. Certainly, our advanced automated iQM and cartridge systems go a long way towards accomplishing that goal. But on a more micro-level, all our technology is designed to facilitate easy learning and operation. For example, our hardware controls are designed with clear, concise, intuitive menus and large touch-screen displays. Software screens are similarly intuitive and designed with an understanding of department workflow. Because critical care and hemostasis technology is our core business, we dedicate our full resources to the product category and make reliability a top priority across our entire product line.

Where do you see the future of your products in relation to end-user requirements?
Again, end-user needs and customer satisfaction drive our product development to a large extent. Our new GEM Premier 4000, ushers critical care analyzer technology into a new era of high performance and ease-of-use and clearly demonstrates our commitment. The GEM Premier 4000 is a state-of-the art device that is the most complete on the market and is extremely sophisticated, yet simple to use. It standardizes, centralizes and controls patient testing throughout the institution—and beyond. A major benefit of the GEM Premier 4000 is the complete integration of CO-Oximetry testing for truly consolidated measurements with the efficiency of a single sample. This, combined with iQM and GEMweb Plus, adds up to another first in blood-gas monitoring. As technology continues to advance, IL is committed to serving the needs of our customers by staying in the forefront of critical care and hemostasis diagnostics.

BD Medical

Vicki Harder
Vicki Harder is Product Manager/Marketing, BD Medical.

AFTER SALE & SERVICE

Who is responsible within your company, by title or name or job description, for training and education of your staff and your customers?
The sales representatives are responsible for the initial product introduction to the customer. Once the customer converts to

our product line, they work with our Internal Clinical Marketing team for actual clinical education of the use of our product with our customers.

What types of education do you provide?
We provide a full range of training to specialty areas including formal educator led classes at the facility and self learning modules, both written and CD ROM based. CE credit is provided through AACN.

How do you manage "off-hours" assistance for clinical questions?
BD has a toll-free 800 number: (800) 227-2918.

Do you provide technical service support, and of what nature?
We provide a full staff of engineers, clinicians, marketing and sales representatives for support of our product line. Facility visits are available upon request.

What do you feel is important to support the customer/end-user of your products?
With our end-users being clinicians we place an importance on clinical support. We implement a Conversion Management Process for each institution, which allows for an effortless conversion, and reduction of anxiety for the account when converting to a new product.

What activities does your company undertake to promote the products?
We advertise in applicable journals as well as support and attend the major trade shows for our customer base. We have local sales representatives for rapid response to customer needs.

How does your company reach out to its customers regarding product performance and R&D?
We conduct annual market research, surveys and Voice of the Customer for current products as well as product improvements.

What mechanisms are in place to assist hospitals in their educational requirements and ongoing education?
We provide a full range of training to specialty areas including formal educator led classes at the facility and self learning modules, both written and CD ROM based. CE credit is provided through AACN. Educators are actively working in the clinical setting that they teach in their classes.

Where do you see the future of your product in relation to end-user requirements?
We strive for continuous improvement and product diversity in order to meet the needs of our growing customer base.

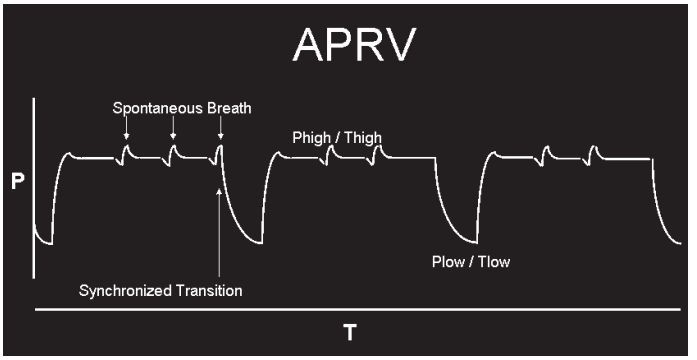
APRV Making Waves in the Neonatal Population

Melissa Turner BA, RRT

Mechanical ventilation in the neonatal population is a very delicate science to say the least. Pressure control has been the mode of choice for some time with volume targeted ventilation rearing its head recently as another possibility. Once the neonate's condition has advanced beyond the point where these more conventional modes are adequate, clinicians often turn toward high frequency oscillatory ventilation (HFOV). In some facilities HFOV is used from the start of ventilation in critically ill neonates. Another mode, not commonly employed, but gaining traction in some centers is airway pressure release ventilation (APRV). APRV may hold many advantages for neonates, but is not widely explored as an option because of lack of knowledge about the mode as well as a lack of availability until recently in neonatal ventilators.

APRV was first introduced in 1987. It is a time cycled, pressure limited mode of ventilation. Habashi helps to describe it as a mode using "CPAP to maintain adequate lung volume and promote alveolar recruitment"[1] with the addition of timed releases to a lower pressure. Spontaneous breathing is allowed anytime independent of the ventilation cycle. APRV can essentially be viewed as two levels of CPAP termed Phigh and Plow. The patient remains at the higher CPAP level, Phigh, the majority of the time. Timed releases from Phigh to the lower CPAP or baseline, Plow, for only a brief fraction of a second helps facilitate CO_2 clearance and in effect allows a periodic mandatory tidal volume delivery. As spontaneous breathing can occur at anytime during the ventilatory cycle, the patient is able to contribute smaller tidal volumes which add to the mandatory minute ventilation derived from the releases. Ventilators with the APRV mode incorporate an "active exhalation" valve that allows this to occur. In effect, APRV allows application of extreme inverse ratios without the need to paralyze patients to avoid asynchrony.

The time at the high CPAP level is termed "T_{high}" and the time at the lower CPAP level is termed "T_{low}" or "release time." T_{high} + T_{low} defines the respiratory cycle time : $60/(T_{high} + T_{low})$ = mandatory rate ("releases" per minute).



APRV contrasts to conventional ventilation as we are creating a driving pressure by transitioning from the peak pressure (P_{high}) down to a lower pressure (P_{low}) in order to deliver a mandatory tidal volume. The Phigh essentially is the "recruiting" PEEP level to maintain an open lung. Rather than apply a tidal volume (pressure) above the high PEEP level, the PEEP is cyclically decreased to provide periodic bulk tidal volume delivery.

The P_{high} defines the maximum plateau pressure applied. (assuming pressure support and/or significant patient efforts do not in effect increase the transpulmonary pressure gradient). Compared with volume ventilation peak pressures have been shown to be lower for a given volume in APRV.[4] Other advantages reported are less adverse hemodynamic effects, decreased sedation requirements, and a near elimination of the need for neuromuscular blocking agents (NMBAs) required despite the high mean airway pressures and "inverse ratios" achieved with this modality. When compared with conventional ventilation, studies have shown a 30-40% reduction in sedation use and a 70% reduction in NMBAs. (These studies were in adults and may not be applicable as NMBA's are not commonly utilized during neonatal ventilation.)

By setting a Phigh, APRV is consistent with lung protective strategies by limiting pressures to avoid alveolar overdistention.

Melissa Turner is with Hamilton Medical, Inc.

Spending the majority of time at Phigh allows facilitation and sustainment of alveolar recruitment. APRV proponents suggest collateral ventilation is a mechanism that promotes recruitment in addition to a high mean airway pressure. Being able to recruit the lung and keep it open is advantageous because it increases surface area available for gas exchange and improves V/Q mismatching. This would be highly beneficial in the neonate with a restrictive lung disease, such as respiratory distress syndrome (RDS) where a decrease in surface area for gas exchange results from surfactant deficiency. These neonates present with progressive atelectasis and V/Q mismatch.

As previously described, spontaneous breathing is facilitated throughout the ventilatory cycle which may improve patient-ventilator synchrony. In conventional modes such as pressure control IMV, spontaneous breathing can only occur during the expiratory phase and the inspiratory time needs to be matched to the patient's desired inspiratory time.

Allowing spontaneous breathing additionally has the advantage of improving gas distribution or V/Q matching vs mechanically controlled breaths. During mechanical breaths volume displacement is passive and non-dependent regions are the ones that primarily receive ventilation. In order for ventilation to reach the dependent areas which may be atelectatic, airway pressures are increased in order to overcome the threshold opening pressures (TOP) of those portions of the lungs which can result in overdistention in the non-dependent areas. Studies have shown that spontaneous breathing patients that are transitioned to mechanical ventilation during anesthesia show worsening gas exchange and dependent atelectasis within minutes. During a spontaneous breath, dependent ventilation is improved through negative pleural pressure changes, not by additional applied airway pressure. With spontaneous efforts, the pleural pressure changes cause redistribution of gas flow to more dependent zones while potentially limiting overdistension in non-dependent zones. Gas distribution is not the only positive effect of spontaneous breathing. As the diaphragm contracts and descends into the abdomen, pleural pressure decreases and abdominal pressure increases. This causes right atrial pressure to decrease while abdominal pressure increases and helps force more blood into the inferior vena cava. Hence, there is an increase in venous return which enhances cardiac output (or at least helps maintain cardiac output despite high mean airway pressures). This may also decrease deadspace ventilation. Another reported benefit is an increase in systemic perfusion which also leads to better renal and splanchnic perfusion (adult studies).

Spontaneous breathing also has the advantage of facilitation of secretion clearance since the patient's cough reflex is not restricted due to sedation and NMBAs. Proponents of APRV also suggest that secretion clearance during APRV is safer since it can be done without an increase in intrathoracic pressures that can occur against a closed exhalation valve. Proponents of APRV also suggest that spontaneous breathing during APRV facilitates recruitment without adverse effects. Conventional recruitment maneuvers with a passive respiratory system distend non-dependent regions first. Then continued application of high pressures is required to exceed threshold opening pressures in dependent lung regions which may cause overdistention in non-dependent zones.

Many times when conventional ventilation modalities have been exhausted, clinicians turn to HFOV. HFOV and APRV have similar goals in that both utilize a high mean airway pressure to recruit and maintain lung volume, eg an "open lung approach," while limiting peak airway pressures. In addition, both modes are intended to optimize V/Q matching, improve gas exchange, decrease shear forces, and reduce stress and shear forces applied to the lung.

During HFOV, spontaneous breathing may result in an increased work of breathing, especially in neonatal/pediatric patients as spontaneous breathing can cause large airway pressure fluctuations, complicate safe alarm settings and has even caused some HFOV ventilators to shut off. Heavy sedation must frequently be used with HFOV. Sedation used also depresses the cough reflex which increases the risk of VAP. During APRV, spontaneous breathing is actively promoted. APRV does not require a dedicated single purpose ventilator as does HFOV.

APRV is also used to transition from HFOV. Phigh is initially matched to the HOV mean airway pressure and then a continued gradual reduction in Phigh setting is attempted.

As the patient's condition improves, patients may be weaned directly from APRV. Once FIO_2 has been decreased to less than or equal to .40, the Phigh is dropped 1-2 cmH_2O at a time to ensure the patient condition remains stable. Thigh is progressively lengthened to in effect reduce the mandatory rate. Once P_{high} is at a minimum and there are relatively few releases, for example, a P_{high} of 8 cmH_2O with one release every 30 seconds (Thigh set at 30 seconds), the patient is essentially on CPAP. The patient can then be extubated once clinician specific criteria have been met. Many neonates have been extubated from APRV to nasal CPAP. Studies are lacking in the use of APRV in the neonate although what little information we have does show promise. Below is an example of one case study reported in the November 2004 Journal of Respiratory Care.[2]

Introduction: *The critically ill neonate at times requires mechanical ventilation directed towards multi-system support versus conventional mechanical ventilation. The use of APRV allows for alveolar recruitment while minimizing circulatory compromise.*

Case Study: *A 32 week neonate presents with tracheoesophageal fistula and ventricle septal defect. The neonate had an infarct in the right upper and right middle lobes of the lung which were removed on day of life (DOL) 38. On DOL 76, the ventilator settings increased to peak Inspiratory pressure (PIP) 28 with positive end expiratory pressure (PEEP) 7, with no improvement in ventilation and oxygenation. Mean airway pressure (MAP) in SIMV was 15-16 mmHG. APRV was initiated using MAP of 25 mmHg. Additional settings included: pressure high 26, pressure low 2, time high 2.7 with a time low 0.2. The neonate's capillary blood gas showed improvement in the carbon dioxide (CO2) level and improvement in the SpO2 on lower level on fraction of inspired oxygen (FiO2). As shown in the table, the patient required less sedation as ventilatory status improved.*

Discussion: *APRV uses continuous positive airway pressure levels to maintain oxygenation and time releases for CO2 removal. APRV allows for unrestricted, spontaneous breathing throughout the entire ventilatory cycle. Spontaneous breathing results in better ventilation-perfusion (V_A/V_Q) matching which in turn decreases intrapulmonary shunting. Within hours of*

MODE	FIO[2]	TI/TE	END PRESSURE	PEAK	MAP	SPO2
SIMV	.83	.50/.70	7	28	16	.94
	pH=7.32	PaCO2=87	PO2=46	HCO2=43.8		
APRV	.52	2.7/0.2	2	26	25	.94
	pH=7.43	pCO2=71	PO2=47	HCO2=46.1		
APRV	.50	2.2/0.2	2	25	23	.94
	pH=7.48	pCO2=39	PO2=108	HCO2=28.4		

	NEO Newly intubated	NEO Transfer from conventional	NEO Transfer from HFOV	PED Newly intubated	PED Transfer from conventional	PED Transfer from HFOV
Phigh*	10-25cmH2O (desired Pplat)	Pplat in conventional mode	mPaw on HFOV + 0-2cmH2O	20-30 cmH2O (desired Pplat)	Pplat in conventional mode	mPaw on HFOV+ 2-4cmH2O
Plow	0cmH2O	0cmH2O	0cmH2O	0cmH2O	0cmH2O	0cmH2O
Thigh	2-3 s.	2-3 s.	2-3 s.	3-5 s.	3-5 s.	3-5 s.
Tlow	0.2-0.4s	0.2-0.4s	0.2-0.4s	0.2-0.8s	0.2-0.8s	0.2-0.8s

initiating APRV the neonate showed marked improvement in ventilation and oxygenation at lower peak pressures.

***Conclusion:** This particular case demonstrates that APRV may have alternative uses for the neonatal population with poor ventilatory status due to restrictive lung disease."*[2]

When applying APRV, it is important to note that a greater time spent at P_{high} (T_{high}) is advantageous. It increases the potential for recruitment while limiting or preventing derecruitment. Also, lung volumes will be maintained while helping to induce spontaneous breathing for which we have already discussed potential advantages. In table 1 are guidelines to use when setting up APRV in both the neonatal and pediatric populations.[1] It includes guidelines used for a newly intubated patient, for a patient transitioning to APRV from conventional mechanical ventilation and for patients transitioning to APRV from HFOV.

*NEO- P_{high} greater than 25 cm H2O may be necessary if decreased thoracic/abdominal compliance.

*PED- P_{high} greater than 30 cm H2O may be necessary if decreased thoracic/abdominal compliance.

APRV is certainly another worthy tool for consideration in the bag of tricks for neonatal and pediatric critical care clinicians. More case studies and research as well as education about APRV are certainly needed in order to apply this mode in its most advantageous manner. This mode is commercially available today on some ventilators infant ventilation "packages." APRV should be explored as an option for clinicians serving the critically ill neonatal and pediatric populations.

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How Can Neonatologists Help Deal With Increasingly Large NICU Drug Budgets?

An interview with Ken Abreu, MBA, CMR

Expensive drugs such as INOmax® (nitric oxide) for inhalation can increase the NICU drug budget to the point that Administration expresses concern. Neonatologists may even be pressured to make changes in order to deal with financial issues. One way of dealing with large drug budgets – and justifying them to your administration - is to improve inpatient drug reimbursement. We interviewed Ken Abreu, MRA, CMR, Director of National Accounts and Managed Markets at INO Therapeutics on the subject.

Is it true that inpatient drugs are reimbursable outside of current payment systems?
Yes, that can be true, although that is not always the case. The more expensive the drug, the more likely it is that private payers will have some kind of special provision to pay for it.

Normally, all drugs used in an inpatient setting are covered by some kind of lump sum payment like a DRG or a *per diem* payment. However, payers understand that some drug costs are too high to be covered by the normal payment, so they make special provisions. Many private payers, including private Medicaid programs, which represent the majority of Medicaid patients, may have special payment plans for patients whose costs are outside the norm.

Is it true that reimbursements do not change based on length of stay or patient acuity?
That is not always true. A lot depends on how the hospital is paid and what kinds of contracts the hospital makes with payers. That being said, there are a few common ways that hospitals can get extra reimbursement for drugs.

What separate reimbursement options may be available? Do I have to know all the details?
There are a number of reimbursement options. Neonatologists need not fully understand them because the hospital has experts who make it their business. However, it helps to know a little about them.

First, many payer contracts contain outlier clauses. An outlier clause essentially pays extra for patients whose costs or charges far exceed the normal payment.

Another way contracts can be structured is to have the payer "carve out" costs or charges for a certain drug. When a drug is carved out there are two calculations for payment. The first is the typical payment for the diagnosis. The higher-cost items, such as expensive drugs, can be carved out; in other words, they are paid for separately from the regular payment.

A third common approach to covering high-cost items is the stop-loss. A stop-loss clause in a contract allows for the standard payment up to the point a hospital has spent a certain amount of money. If the hospital gets to the point that they are losing a specified amount on a given case, the payer increases reimbursement to stop the hospital from losing too much money.

Some managed care contracts have special clauses that essentially obligate the payer to cover new technologies. Sometimes a drug is considered to be a new technology for a hospital, especially if it is new to the hospital.

While there are a few other ways for hospitals to get extra reimbursement for high-cost patients, these are the most common.

Do neonatologists have to do a lot of work to get reimbursement for high budget items?
No, not at all. In fact, neonatologists can contact a number of internal and external resources that can do the majority of the work.

What resources can help with drug reimbursement?
Within the hospital are a number of people and departments who can work together to improve reimbursement. These include the hospital's finance department, managed care contracting department, and the chargemaster. The Pharmacy and Respiratory departments may also be able to help. Neonatologists can contact any or all of these internal resources for help.

Outside of the hospital, the drug's manufacturer may be able to help. Many companies, including INO Therapeutics, offer reimbursement information that may be very useful. Another good source is professional organizations; the American Association for Respiratory Care (AARC) offers reimbursement information tailored for Respiratory issues.

What specific actions should neonatologists take to help with reimbursement?
The first thing neonatologists should do is contact the resources mentioned above. While Neonatology can take the lead on reimbursement, it is often a good idea for other departments, such as Respiratory, to be the coordinator of the various hospital departments and external resources like the drug company. It is not uncommon that, because Respiratory is not always known as a department that pays for drugs, the hospital's administration does not even know that there is a lack of reimbursement there. Often just bringing everyone to the table starts a process that leads to a good outcome for the department.

For more information, please contact Ken Abreu at ken.abreu@inotherapy.com.

Ken Abreu is Director of National Accounts at INO Therapeutics.

An Experience of Rapid HIV Testing During Labor and Delivery at an Inner City Hospital

Muhammad Aslam, MD; Ben K. Rajegowda, MD; Yekaterina Sitnitskaya, MD

Abstract

The HIV serostatus of all women who delivered at Lincoln Medical and Mental Health Center (LMMHC) from 01/01/05 to 12/31/05 was reviewed. We compared OraQuick results to the results of confirmatory Western Blot, compared the compliance with HIV testing in women who had prenatal care (PNC) at our institution vs. those who had PNC elsewhere or none, and lastly compared our data to the data from New York State Department of Health (NYSDOH). 2496 women were admitted at LMMHC for labor and delivery during the study period. HIV sero-status was documented prior to admission in 2260 (90.54%) women; 1635 of 1659 (98.55%) women with PNC at our institution vs. 625 of 837 (74.67%) women with PNC elsewhere or none. The remaining 236 women had rapid HIV testing by OraQuick at the time of admission. None of them was HIV-infected, including one patient who had false-positive result, as confirmed by Western Blot. Thus, in our small cohort specificity of OraQuick was 99.5%, and negative predictive value was 100%. On conclusion rapid HIV tests are very reliable in predicting HIV serostatus of women during labor and delivery and are an important tool in decreasing perinatal HIV transmission.

Introduction

According to the Centers for Disease Control and Prevention (CDC), approximately 6,000 to 7,000 HIV infected women gave birth in the United States in 2000, and approximately 280 to 370 HIV infected infants were born.[1] An estimated 40 percent of the mothers of these HIV infected infants had not been diagnosed with HIV before labor and delivery.[2] When the recommended antiretroviral and obstetric interventions are used, a woman with known HIV infection early in pregnancy has a less than 2% chance of delivering an HIV infected infant. Without intervention, this risk is approximately 25% in the United States. CDC recommends routine rapid HIV testing using an opt-out approach for women in labor whose HIV status is unknown. The rapid HIV test kits licensed in the United States allow test results to be available in 20 minutes or less.

Lincoln Medical and Mental Health Center, a level III perinatal center located in South Bronx, serves a high-risk urban population that seldom seeks consistent prenatal care. Approximately 75% of the population is Hispanic, 20% African-American; 77% are on public assistance, 10% abuse drugs, 20% have no prenatal care and 20% have some medical or obstetric complication. It is, therefore, vital to review the perinatal HIV status of this socioeconomically disadvantaged population. Such data obtained from the rapid HIV tests can lead to a timely intervention and a marked decrease in perinatal HIV transmission rate.

Methods

We performed a retrospective review of HIV sero-status of all women who delivered at Lincoln Medical and Mental Health Center (LMMHC) from 01/01/05 to 12/31/05. We have analyzed the Maternal - Pediatric HIV Prevention and Care Program - Test History and Assessment Form New York DOH - 4068 (02/05), and Hospital Medical Records of the mother - infant pairs. We compared OraQuick results to the results of confirmatory Western Blot. We also compared the compliance with HIV testing in women who had prenatal care (PNC) at our institution vs. those who had PNC elsewhere or none at all. Lastly, we compared our data to the data from New York State Department of Health (NYSDOH).

Results

LMMHC reports an average delivery rate of approximately 2500 per year. During the study period (year 2005) 2496 women were

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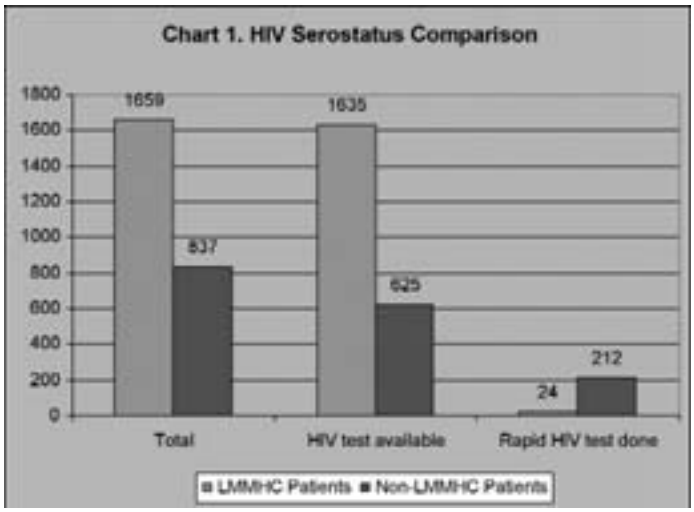
admitted for labor and delivery. Of these, HIV sero-status was documented prior to admission in 2260 (90.54%) women. Of these, 1659 women had PNC at LMMHC and 837 women had PNC outside LMMHC. 1635 of 1659 (98.55%) women with PNC at LMMHC had a documented HIV test as compared to 625 of 837 (74.67%) women with PNC elsewhere or none. The remaining 236 women had rapid HIV testing by OraQuick at the time of admission. None of them was HIV-infected, including one patient who had false-positive result, as confirmed by Western Blot. Thus, in our small cohort specificity of OraQuick was 99.5%, and negative predictive value was 100% (Table 1 and Chart 1).



Discussion

The year 2007 marks the 26th anniversary of the first documented case of Acquired Immune Deficiency Syndrome (AIDS) in the United States. Today, almost 40,000 new HIV infections occur in the United States each year; 11,000 of which are women and 200 are babies.[3] Almost all new cases of infant HIV infections are caused by mother to child transmission. An estimated 6,000 to 7,000 HIV infected women give birth each year.[4] As of year 2003, there were approximately 5000 cumulative deaths from perinatally acquired HIV and AIDS in the United States.[4] Perinatal transmission of HIV can occur during pregnancy, labor and delivery, or through breastfeeding; however in the United States, infants most commonly acquire the virus during labor and delivery.[5] Research from the past fifteen years indicates that proper preventions and interventions during pregnancy, labor, and delivery can reduce the rate of infants born with HIV to less than 2%.[6]

ACTG 076 (AIDS Clinical Trials Group protocol number 76) trial of 1994 confirmed that administering Zidovudine (ZDV) to HIV infected mothers could reduce the transmission of HIV from infected mothers to their babies by two thirds.[7, 8] In 2003, the CDC recommended a shift from an "opt-in" to an "opt-out" approach. This implemented universal HIV testing as part of the routine battery of pregnancy tests. Several studies revealed that testing rates of pregnant women increased from 33% - 74% to 81% - 88% using the opt-out method.[6] From 2001 to 2004, nearly 7% of HIV infected pregnant women were still undiagnosed by the time of delivery.[9] This prompted the CDC to recommend rapid HIV testing at the time of delivery for all pregnant women whose HIV status was unknown. American College of Obstetricians and Gynecologists (ACOG) and CDC also recommended that medical care givers provide a routine second HIV test during the third trimester to women known to have elevated risk for HIV infection.[9]

In 2004, the CDC conducted the Mother-Infant Rapid Intervention at Delivery (MIRIAD) study, which included more than 14 hospitals in six cities: Atlanta, Baton Rouge, Chicago, Miami, New Orleans, and New York City. The primary goal of the MIRIAD study was to identify optimal ways to use rapid HIV tests and initiate therapy for women who do not know their HIV status late in pregnancy or at the time of delivery. A rapid HIV-1 antibody test (OraQuick) for whole blood was used. Sensitivity and specificity of the rapid test were 100% and 99.9%, respectively; positive predictive value was 90% compared with 76% for enzyme immunoassay (EIA). Median time from blood collection to patient notification of result was 66 minutes compared with 28 hours for EIA (P<.001).[10] The conclusion of the MIRIAD study demonstrated that rapid testing was acceptable and feasible in the delivery setting, and that women were less likely to refuse testing. Following this report, ACOG expanded its recommendations to include rapid testing for women in labor with unknown HIV status.[9] Although the best way to reduce the risk of mother-to-child transmission of HIV is through early diagnosis and treatment, rapid testing now provided physicians an additional opportunity to treat both the mother and child with appropriate antiretroviral therapy.[3]

In November, 2005, ACOG released a legislative stressing that, "in light of the increased risk of infection to women and their unborn children and with the availability of effective treatment for HIV positive women during pregnancy and for exposed infants, states should re-examine their HIV/AIDS testing requirements for pregnant women and make the necessary

Table 1. HIV Serostatus Comparison

Data	Total patients	HIV test available prenatally		HIV test not available Expedited test done	
		No.	%	No.	%
LMMHC registered patients	1659	1635	98.55	24	1.44
Non-LMMHC patients	837	625	74.67	212	25.32

changes now."[3] ACOG and the CDC now recommend an HIV test in the 3rd trimester for women who were not tested earlier in pregnancy; a repeat HIV test in the 3rd trimester, preferably before 36 weeks of gestation, to each pregnant patient who is at high risk for acquiring HIV; routine repeat HIV test in the 3rd trimester to all pregnant women at health care facilities in areas with high rates of HIV prevalence among women of childbearing age (5 per 1,000 or 0.5% or greater); a rapid HIV test in labor to pregnant women with unknown or undocumented HIV status; and antiretroviral prophylaxis without waiting for the results of the confirmatory test if a rapid HIV test in labor is positive.[11]

After reviewing the policies New York (NY) State recommended routine testing of all pregnant women during labor and delivery. As part of the New York City Health and Hospitals Corporation, LMMHC launched the rapid HIV testing by OraQuick in 2005. We took an initiative to determine the efficacy of rapid testing and found comparable results to conventional tests. The advantages of rapid testing include high specificity and short turnaround time. Different studies have demonstrated that rapid HIV testing is reliable and there is a very high specificity. In our study all women with negative test results were confirmed negative by Western blot. There was only one HIV positive woman by rapid test who confirmed negative with Western blot. Our study demonstrated that the negative predictive value of OraQuick was 100%. Average time to get results was 80 minutes for rapid test (OraQuick) as compared to 30 hours for EIA. We also compared our data with the NYSDOH and our average HIV testing rate of 98.55% was far higher than recommended 95% in NY State.

Conclusions

Rapid HIV testing is an effective and time saving method to determine perinatal HIV status of women presenting in labor and delivery whose HIV status is unknown. It has even higher value in inner city hospitals who serve a socioeconomically disadvantaged population. Patients undergoing rapid testing should be advised that in case of a positive test result the mother and the infant will receive prophylaxis with antiretrovirals until confirmatory test result is available. Although the rapid test has the advantage of early treatment, it can also lead to considerable anxiety among patients who test positive because they need to be treated until the confirmatory results are available. This requires proper counseling and support. At present all rapid test results are confirmed by definitive tests, but once reasonable data on the efficacy of rapid tests become available these guidelines may change. Our results of 100% negative predictive value were very promising. In conclusion rapid tests are reliable, fast and provide an opportunity for a timely antiretroviral prophylaxis during labor and delivery settings and are an important tool in decreasing perinatal HIV transmission rate.

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Bradycardias Following Cordocenteses: Are They Always Ominous?

O. Langer Most, B.M. Petrikovsky, D. Roshan

Introduction

The consequences of fetal bradycardias, which may occur during, or following cordocentesis remain controversial. Ghidini[1] considered cordocentesis induced bradycardia to be mostly self-limited and of no particular significance. Tongsong reported a 3.2% fetal loss rate and a 1% procedure-related loss rate.[2] In contrast, Ulm[3] reported a 61.5% incidence of fetal or neonatal loss in cases with bradycardia following cordocentesis. Our objective is to report the outcomes associated with bradycardias following cordocentesis at two institutions.

Materials and Methods

A six-year follow-up study was performed to assess possible long-term sequelae for fetuses that had cordocentesis-induced bradycardias. 229 diagnostic cordocenteses were performed at two institutions (Stony Brook University and North Shore University Hospital) from 1991 to 2000. The technique for cordocentesis was the same at both institutions.[4] The technique involved a needle guide attached to a high-resolution curvilinear transducer with an attached needle guide and a 22-guage disposable spiral needle directed to the cordocentesis site under ultrasound guidance (Acuson XP-128, Mountainview, CA). Freehand technique was used for aspiration of the target vessel. Cordocentesis vessel selection was based on sonographic appearance and flow direction using color Doppler. Sites of insertion included the placental insertion of the cord, free-floating loop or cord entry into the fetal abdomen. Patients were monitored after the procedure for signs of fetal bradycardia. Bradycardia was defined as a drop in the fetal heart rate (FHR) to less than 100 (bpm) lasting more than 60 seconds.[5] Neonatal and pediatric outcomes were monitored and recorded following the delivery.

Results

The gestational age at the time of cordocentesis ranged from 24 to 37 weeks. The mean gestational age at the time of cordocentesis was 31.45 weeks. Clinical indications for cordocentesis are presented in tables 2 and 3. Indications for cordocentesis included fetal hemolytic disease, immune thrombocytopenic purpura (ITP), advanced maternal age (AMA), 2- vessel cord (2VC), and intra-uterine growth restriction (FGR). The most common indication for cordocentesis in our sample was rapid fetal karyotyping (55%) and within this designation, a diagnosis of FGR was the most frequent justification to perform a cordocentesis (66%). Of the 229 procedures performed, cordocentesis was done using the placental insertion of the cord in 146 cases (64%). Free-floating loop was sampled in 69 cases (30%). Cord entry into the fetal abdomen was sampled in 14 cases (6%). Fetal bradycardia was observed in 11 of the 229 cordocentesis procedures performed (4.8%). Mean duration of bradycardia was 7.5 minutes. Based on our findings, the incidence of fetal bradycardia was 2.7% when sampling was performed at the placental insertion, 7% in sampling a free loop, and 14% in sampling fetal cord insertion. Both neonatal deaths occurred after sampling a free loop of the umbilical cord. Mean gestational age at delivery was 33.8 weeks. Clinical information on the 11 cases is presented in table 1. Pediatric records were available on 6 children experiencing post cordocentesis bradycardia. Of these cases 2 children expired (cases 8, 9) and the others were lost to follow up. Physical characteristics (height, weight, head circumference) and child development were normal in all cases.

Discussion

Fetal bradycardia is a known complication of umbilical cord sampling,[1,5-7] although the literature has been limited to case reports. Benacerraf[5] reported a case of acute fetal distress associated with percutaneous umbilical cord sampling in which the infant was born 12 minutes after the procedure by cesarean section with Apgar scores 0 and 5 at 1 and 5 minutes, respectively. The newborn suffered from severe anemia and acidosis. The authors concluded that cordocentesis should be performed in a setting where access to labor and delivery is readily available. Ulm[3] reported a 61.5% fetal/neonatal loss rate in 13 cases of fetal bradycardia occurring after cordocentesis. The gestational age and the presence of fetal hydrops correlated significantly with the appearance of bradycardia in their study.

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The puncture site and number of puncture attempts did not correlate with the incidence of fetal bradycardias. The duration of post-procedure bradycardia in Ulm's series was between 1 and 40 minutes. The fetus that had a 40 minute bradycardia was born with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. Alternatively, 6 of 9 fetuses expired, although their post procedure bradycardia was <3 minutes. Han et al evaluated 117 cordocenteses and reported an incidence of 10.3% post-cordocentesis bradycardia. In their study fetal heart rate returned to normal in ≤5 minutes post-procedure.[8]

In our study, 3 of 11 fetuses with post cordocentesis bradycardia (33%) were delivered by cesarean section due to persistent bradycardia. However, only one poor neonatal outcome was noted in those who underwent cesarean section. Four (37%) fetuses recovered from the bradycardia prior to the onset of emergency cesarean section and an additional four fetuses (37%) with ominous fetal tracings recovered from the bradycardia prior to the decision to perform a cesarean section. One fetal demise was attributed to severe cytomegalovirus infection. Ulm's data observed more ominous outcomes for post-cordocentesis bradycardia than the current study. Liao et al reported a 2.7% total fetal loss rate and a 1% cordocentesis-related loss rate.[9] Our data indicates that the given indications for performing the procedure may be associated with fetal outcomes after the procedure. Seven of 13 fetuses in Ulm's series were hydropic, and three were prone to hydrops (two with Rhesus iso-immunization and one with polyhydramnios). The fetal mortality for hydrops fetalis ranges from 50-100% even in the absence of invasive procedures. In our series, 6 of 11 fetuses did not exhibit signs of hydrops fetalis. Rather, these fetuses underwent cordocentesis for rapid karyotyping.

Similarly, Antsaklis[6] concluded that fetal loss is not solely due to post cordocentesis bradycardias. In his study, 1981 cordocentesis procedures were reviewed. Of these, 177 were performed for detection of congenital infection, 1437 for detection of hemoglobinopathy, 233 for prenatal diagnosis, and 73 for severe growth restriction. Pregnancy loss within two weeks of the procedure was considered procedure-related loss. The difference of procedure-related loss between the groups was significant.

These results suggest that cordocentesis entails a higher risk when the fetus is structurally abnormal or severely growth restricted. In contrast, late karyotyping for advanced maternal age, abnormal triple test, or failed amniocentesis culture, carries an approximated risk of 1%, which is comparable to that of chorionic villus sampling or amniocentesis (CVS).[6] No control group was used in Antsaklis' study. For this reason a precise procedure related risk was not defined. Nanal et al observed a procedure-related pregnancy loss rate of 0.7% for amniocentesis, 0.23% for CVS and a 1.19% procedure-related loss rate for fetal blood sampling.[10] The total pregnancy loss rate reported was 4.1%.[10] The mechanisms for fetal bradycardia following cordocentesis are poorly understood. The leading hypothesis is that the needle insertion causes vasospasm with reflex bradycardia. Bradycardias are more common following puncture of the artery than that of the umbilical vein, which is more prone to vasospasm. An alternative theory is that the needle causes mechanical trauma to the vessel resulting in hematoma formation and cord compression. This theory is less likely since most studies have failed to demonstrate the presence of umbilical cord hematoma at histopathological examination of the presumed puncture site.

Table 1: Summary of clinical data

	Indication for Cordocentesis	GA at Cordocentesis	Site of Sample	Duration of Bradycardia	GA at Delivery	Indication For Delivery	Delivery Mode	APGARs	Cord pH	Comments
1	Rapid Fetal Karyotype (AMA)	24	Placental Insertion	6 min				9,10		
2	Rapid Fetal Karyotype (2VC)	29	Placental Insertion	4 min	35			7,9		
3	Rapid Fetal Karyotype (FGR)	34	Placental Insertion	2 min	34 (48 hr after cordo-centesis)				7.21	Neonatal exchange transfusion
4	Fetal hemolytic Disease	28	Placental Insertion	3 min	33					No sequelae (age)
5	Rapid Fetal Karyotype (FGR)	34	Free Loop	14 min	34	Persistent Brady	C/S	3,7	7.18	
6	ITP	37	Free Loop	9 min	40	Spont Labor	NSVD	9,10		? Sequelae
7	ITP	37	Free Loop	11 min	37	Persistent Brady Fetal thrombo-cytopenia	C/S	4,9	7.18	CMV at Autopsy
8	Rapid fetal Karyotype (FGR Liver Calcification)	28	Free Loop	6 min	28	Recurrent Brady (6 hrs)		Neonatal death		Severe anemia expired 6 hrs of life
9	Rapid Fetal Karyotype (Fetal Hemolytic Disease)	26	Free Loop	11 min	26	Persistent Brady	C/S	0,1		
10	FGR (Cleft Lip Otodactyly)	32	Fetal umb cord Insertion	8 min	38	Spont labor or induction	NSVD	8,10		
11	ITP	37	Fetal umb cord Insertion	9 min		Fetal thrombo-cytopenia	C/S	7,9		

Table 2: Indications for cordocentesis

Indications	Number of cases	Percent
Immune thrombocytopenic purpura	3	27
Fetal hemolytic disease	2	18
Rapid Fetal Karyotyping	6	55

Table 3: Rapid Fetal Karyotyping

Indications	Number of cases	Percent
Advanced maternal age	1	17
2 vessel cord	1	17
Intrauterine growth restriction	4	66

We conclude that the outcome of fetal bradycardia occurring after cordocentesis may be attributable to the initial fetal status. A moribund fetus (hydrops fetalis) prior to cordocentesis is more prone to lethal post-procedure complications. Alternatively, if the fetus is without complications prior to cordocentesis, a post-procedure bradycardia will often be self-limited and rarely life threatening. If the fetus is not compromised, any post-cordocentesis bradycardia is unlikely to be associated with long term consequences. Alternatively, if the fetus is compromised, the outcome depends on the initial fetal status. In these cases of fetal compromise, post-cordocentesis bradycardia does not worsen the outcome.

This knowledge is important clinically because a trend has been noted in the decline of cordocentesis procedures performed at tertiary care centers over the past decade. The database at our institution was reviewed on cordocentesis procedures that were performed between 1992-1995 versus the ones performed between 1996-1999.[11] A significant decline was observed in the number of cordocentesis performed from two hospitals. If this noted decline is sustained on a nationwide basis, the level of training and proficiency in this procedure will decrease even further. Procedures related to fetal loss rate has been shown to be associated with the level of proficiency in the cordocentesis technique.[2] The fetal loss rate has also been shown to be related to factors that are more difficult to control, such as maternal age, gestational age and the indication for the procedure.[10] There are several indications for performing cordocentesis which include fetal thalassemia, fetal infection, fetal hemolytic disease and rapid fetal karyotyping for advanced maternal age or history of chromosomal abnormalities.[2] Therefore, the need for cordocentesis and training for proficiency in this technique needs to be encouraged. Research to enhance knowledge and management of post procedure bradycardia should be pursued for the clinically pertinent indications.

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Fetal Growth Restriction: Be Aware of Genetic Syndromes

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Introduction

Fetal intrauterine growth restriction (IUGR), formerly termed intrauterine growth retardation, refers to a process that causes a reduction in an expected pattern of fetal growth. It is a relatively common condition that affects as many as 5% to 10% of all pregnancies.[1] The incidence varies depending on the population. About one third of all infants weighing less than 2500 grams at birth have IUGR. Four to eight percent of infants born in developed countries and six to thirty percent born in developing countries are classified as growth restricted.[2]

Fetal IUGR is a confusing problem during the pregnancy, based on non-consistent definitions and overall modest predictive capability of current diagnostic tests. Therefore clinicians are often unclear as to the overall significance of the prenatal diagnosis of the IUGR, since many diagnosed fetuses do not result in severely compromised neonates. Nonetheless, it is important to make definitive diagnosis based on the best available criteria and to exclude important etiologies, such as chromosomal abnormalities, congenital anomalies, and genetic syndromes, that may have long-term neonatal sequalae. This process will inevitably include significant numbers of falsely identified fetuses. The goal is to capture all those truly at risk.

Significance

IUGR is the second leading contributor to the perinatal mortality, which is 6-10 times greater for IUGR infants than that for appropriate-for-gestational-age infants.[3] Fifty-three percent of preterm and twenty-six percent of term stillbirths are growth restricted.[18] Growing evidence indicates that effects of decreased fetal growth are not limited to the immediate newborn period, but extend into adulthood and likely into future generations of offspring. Fifteen to twenty percent of children born with IUGR are at risk of being short as adults. Previously IUGR infants have higher rates of neurodevelopmental delay and physical handicap.[8,26]

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Definition

Estimated birth weight below the population 10th percentile, corrected for gestational age, has been the most widely used criterion for defining growth restriction at birth. The definition of IUGR is imprecise. The true definition implies a pathologic process that affects normal fetal growth. Genetic factors may influence growth, and thus different populations have different growth curves.[9] Compared with population-based birth weight curves, customized disease-specific growth curves should increase the identification of fetuses at risk for adverse outcomes such as stillbirth, neonatal death, low Apgar score, and improve the association with neonatal anthropometric features of growth restriction. Disease- specific growth curves are not readily available for the diagnosis of the IUGR.[10,11,12,13]

Diagnosis

It is difficult to make an accurate diagnosis of IUGR.[30] Maternal weight gain and fundal height are not sensitive and have a low positive predictive value.[4] Clinical estimates of fetal weight are notoriously inaccurate especially in the lower fetal weight ranges. Weight prediction has a wide 95% confidence range of ±15%, even when based on multiple fetal part measurements.

Abdominal circumference (AC) in combination with head circumference (HC) has been widely adopted for the identification of growth restriction by many clinicians, where the AC seems to be the best predictor of IUGR. When the AC measurement falls below the 2.5th percentile for gestational age, IUGR may be suspected and correctly identified in approximately 95% of the cases. Approximately 70% of these fetuses are constitutionally small, or small for gestational age (SGA), rather than true IUGR. 46% of the variation in liability to giving birth to a SGA offspring can be explained by genetic factors, of which fetal genes constitute 37% and maternal genes 9%. Several studies have reported a 5% to 27% incidence of chromosomal abnormalities associated with IUGR, as compared to a 0.1% to 4% rate in control groups of appropriately grown neonates. For example, a recently described disorder comprising IUGR, metaphyseal dysplasia, adrenal hypoplasia, and genital anomalies (IMAGe) has been shown to be inherited

Table 1: Syndromic Short Stature Associated with IUGR

- Bloom syndrome
- Cockayne syndrome
- Down syndrome
- Noonan syndrome
- Prader-Willi syndrome
- Progeria
- Rubinstein-Taybi syndrome
- Seckel syndrome
- Silver-Russell syndrome
- Turner syndrome

via the maternal line.[14] The association between low birth weight and risk of type 2 diabetes mellitus in some studies could theoretically be explained by a genetically determined reduced fetal growth rate.[15]

Etiology

The causes of morbidity and mortality for IUGR infants are primarily hypoxia and congenital anomalies.[5] Some of the causes of hypoxia can be avoided if growth-restricted fetuses are appropriately identified and managed. Approximately 10% of cases of IUGR are associated with chromosomal abnormalities, congenital malformations, and genetic syndromes, such as Silver-Russell syndrome, Noonan syndrome, and Prader-Willi syndrome.[31,16] Many less common syndromes also have IUGR component as part of their clinical description.

Neonatal prognosis in these cases is determined by the specific abnormality identified. Appropriate patient counseling and infant surveillance is important. Although these infants benefit from careful monitoring and timely delivery, they will often carry the permanent stigmata of the original disease process.

Classification

IUGR is further described as symmetric or asymmetric. In asymmetric, or head-sparing IUGR, length and weight are decreased for gestational age but head circumference is appropriate for gestational age. This pattern of altered head growth ("late flattening") represents approximately two thirds of all cases of IUGR.[27]

Chromosomal abnormalities, congenital malformations, and genetic syndromes have been mostly associated with cases of symmetric ("low profile") IUGR.[17] Symmetric IUGR generally occurs early in gestation, and there is a proportionate decrease in length, weight, and head size for gestational age. Abnormalities in cell replication and reduced cell number produce a pattern of impaired growth that is symmetric and early in onset. This growth abnormality may manifest as early as the first trimester. The prognosis seems to be particularly poor in the setting of early IUGR. When growth restriction, associated with severe congenital anomalies, occurs in first and second trimester, fetal morbidity cannot always be avoided. (Table 1 summarizes examples of genetic disorders characterized by prenatal growth deficiency.)

Management

Once a small fetus is identified, an extensive attempt should be made to determine the etiology of the IUGR. A careful sonographic examination should be performed to search for associated structural anomalies. Ultimate usefulness of ultrasound is highly reliant on the person interpreting the images being obtained and acting on that information.[24,25]

If a chromosomal abnormality is suspected, an amniocentesis or percutaneous umbilical blood sampling should be suggested to the patient and then performed to confirm the diagnosis. Fetal karyotyping should be recommended, especially in cases of early symmetric severe IUGR.[19,20]

Once a fetus is recognized as growth-restricted, a heightened level of surveillance is necessary. The best interval for serial growth scanning is every 2-3 weeks.[21,22] The most common testing modalities include the biophysical profile and Doppler velocimetry.

Biophysical profile (BPP)

The biophysical profile evaluates fetal well-being using amniotic fluid volume and three dynamic ultrasound variables: fetal breathing, fetal movement, and fetal tone. Nonstress tests (NST) is used as a fifth, nonsonographic parameter.[23] Observational studies have shown that growth-restricted pregnancies complicated by oligohydramnios have a markedly increased risk of perinatal mortality. Abnormal findings in any of the individual components of the biophysical profile require further investigation or follow-up (28,29). Often management is based on gestational age and the degree of abnormality of the biophysical profile in conjunction with the severity of the IUGR. Unfortunately, in cases of symmetric early severe IUGR, NST and BPP are not reliable.

Doppler Velocimetry

Doppler velocimetry evaluates the impedance of flow through selected fetal vessels in an effort to assess the fetal condition. Surveillance with Doppler is based on the premise that the fetal condition is reflected by circulatory changes. The redistribution of blood flow is the principle mechanism by which the IUGR fetus preserves adequate oxygenation in the central nervous system, known as the "brain sparing" effect.[39] The two most common vessels studied in the fetal circulation are the umbilical artery and the middle cerebral artery.[32] Angle-independent parameters are used and primarily consist of systolic-diastolic ratio, pulsatility index, and resistance index.[33,37] Doppler studies of the umbilical artery searching for decreasing diastolic flow and reverse flow along with worsening pulsatility index of the middle cerebral arteries are part of the fetal surveillance undertaken once IUGR is identified. Reversed diastolic flow is an ominous finding and is associated with high mortality rate.[36] Normal amniotic fluid volume, normal middle cerebral artery Doppler waveforms, and normal umbilical artery parameters in a small fetus are reassuring and essentially exclude immediate adverse perinatal outcome.[38]

More recent studies have looked at the fetal venous system and have found that the IUGR fetus seems to be at even greater risk of hypoxia or mortality when Doppler abnormalities are observed in the ductus venosus and the umbilical vein.[6,7]

Doppler velocimetry has been used to differentiate the truly growth-restricted fetus from the fetus that is constitutionally

Table 1 summarizes examples of genetic disorders characterized by prenatal growth deficiency

Disorder	Some of the characteristics
Trisomy 18	Fetal activity, polyhydramnios, small placenta, single umbilical artery
Trisomy 13	Holoprosencephaly type defect, microphthalmia, colobomata of iris, cleft lip or cleft palate, localized scalp defects
Trisomy 21	Hypotonia, flat facies, tendency to protrude tongue, upslanting palpebral fissures, speckling of iris, wide gap between first and second toes, loose folds in posterior neck
Trisomy 9 mosaic syndrome	Long, narrow face, broad, bulbous nose, cutis marmorata
Triploidy syndrome	Complete extra set of chromosomes, severe IUGR, large placenta with hydatidiform changes
Deletion 3p syndrome	Hypotonia, microcephaly with flat occiput, micrognathia, long philtrum
Deletion 4p syndrome	Microcephaly, hypotonia, cleft lip or palate, midline scalp defects, simian creases, talipes equinovarus
Duplication 4p syndrome	Hypertonia in infancy followed by hypotonia, macroglossia, microcephaly, micropenis, hypospadias, cryptorchidism
Deletion 5p syndrome	Cri du chat (cat-like cry) syndrome, hypotonia, microcephaly, low-set ears, simian crease, congenital heart disease
Duplication 10q syndrome	Microcephaly, microphthalmia, cleft palate, syndactyly of second and third toes
Deletion 11q syndrome	Ocular hypertelorism, malformed ears, low-set or malformed ears
XO (Turner) syndrome	Congenital lymphedema of dorsum of fingers and toes, broad chest, low posterior hairline
Brachmann-De Lange syndrome	Cornelia De Lange syndrome, synophrys, micromelia, thin downturning upper lip
Russell-Silver syndrome	Short or incurved fifth finger, small triangular facies, micrognathia, café au lait spots
Mulibrey nanism syndrome	Muscle, liver, brain, and eye involvement, triangular facies, small tongue
Dubowitz syndrome	High-pitched hoarse cry, microcephaly, micrognathia
Bloom syndrome	Malar hypoplasia, facial telangiectatic erythema
Seckel syndrome	Microcephaly, prominent nose, cryptorchidism

small but otherwise normal.[34,35] However, it is less clear how to correlate data for expected blood flow with birth weight and neonatal complications in cases of congenital anomalies. The overall value of second-trimester maternal uterine artery Doppler waveforms in screening of pregnancies at risk for growth restriction is unclear as well.

Timing of delivery

The most appropriate timing for delivery depends on the gestational age and assessment of the severity of the fetal condition. For fetuses at term or near term, delivery may be indicated when there is little interval growth over a short period of time, or if fetal lung maturity has been determined. For fetuses at earlier gestational ages, more remote from term, management requires close surveillance and the use of multiple testing modalities. The timing of the delivery of IUGR fetuses with genetic syndromes is not always clear due to poor reliability of the present testing modalities.

Future implications and counseling

It is important to identify the etiology of fetal growth restriction whenever possible because there are often additional benefits to the patient from having that information. For instance, knowing that there may be a chromosomal or genetic etiology may enable better counseling for the patient in terms of pregnancy termination or delivery preparations and future pregnancy planning, particularly when genetic syndromes are encountered.

Patients with an IUGR fetus should be counseled that their neonates might have some immediate complications at birth but also some long-term complications including impaired cognitive function such as learning disabilities and cerebral palsy. More recently, concerns have been raised that abnormal fetal growth is responsible for adult diseases including diabetes, hypertension and cardiovascular disease.

The most important aspects of IUGR are the intellectual or other neurological developmental outcomes, including learning disabilities. These issues point out the importance of further research in attempt to better diagnose, differentiate and manage pregnancies, complicated by IUGR, so that the appropriate plan of therapy is developed for the specific child.

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The Effect of Changing Ventilator Settings on Indices of Ventilation Inhomogeneity in Small Ventilated Lungs

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Abstract

Background: In ventilated newborns the use of multiple breath washout (MBW) techniques for measuring both lung volume and ventilation inhomogeneity (VI) is hampered by the comparatively high dead space fraction. We studied how changes in ventilator settings affected VI indices in this particular population.

Methods: Using a computer simulation of a uniformly ventilated volume the interaction between VI indices (lung clearance index (LCI), moment ratios (M_1/M_0, M_2/M_0, $AMDN_1$, $AMDN_2$) of the washout curve) and tidal volume (V_T), dead space (V_D) and functional residual capacity (FRC) were calculated. The theoretical results were compared with measurements in 15 ventilated piglets (age <12 h, median weight 1135 g) by increasing the peak inspiratory pressure (PIP). FRC and VI indices were measured by MBW using 0.8% heptafluoropropane as tracer gas.

Results: The computer simulation showed that the sensitivity of most VI indices to changes in V_D/V_T and V_T/FRC increase, in particular for $V_D/V_T > 0.5$. In piglets, the raised PIP caused a significant increase of V_T from 15.4 ± 9.5 to 21.9 ± 14.7 (p = 0.003) and of the FRC from 31.6 ± 14.7 mL to 35.0 ± 15.9 mL (p = 0.006), whereas LCI (9.15 ± 0.75 to 8.55 ± 0.74, p = 0.019) and the moment ratios M_1/M_0, M_2/M_0 ($p < 0.02$) decreased significantly. No significant changes were seen in $AMDN_1$ and $AMDN_2$. The within-subject variability of the VI indices (coefficient of variation in brackets) was distinctly higher (LCI (9.8%), M_1/M_0 (6.6%), M_2/M_0 (14.6%), $AMDN_1$ (9.1%), $AMDN_2$ (16.3%)) compared to FRC measurements (5.6%). Computer simulations showed that significant changes in VI indices were exclusively caused by changes in V_T and FRC and not by an improvement of the homogeneity of alveolar ventilation.

Conclusion: In small ventilated lungs with a high dead space fraction, indices of VI may be misinterpreted if the changes in ventilator settings are not considered. Computer simulations can help to prevent this misinterpretation.

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Background

In ventilated newborns respiratory problems are often caused by impaired lung development and uneven alveolar ventilation. Surfactant deficiency or dysfunction may increase the ventilatory inhomogeneity by collapse or over distention of the alveoli. Thus, there is an increasing clinical interest in multiple breath washout techniques (MBW) to measure both the functional residual capacity (FRC) and ventilatory inhomogeneity (VI) indices.[1-4] Lung clearance index (LCI) and moment ratios of the wash out curve are the most frequently used indices in infancy.[5] Commonly, the first and the second moment related to the zeroth moment (M_1/M_0, M_2/M_0) are calculated.

Most VI indices are easily calculated, however, a key disadvantage is their dependency on the breathing pattern.[6] In 1975, Saidel et al.[7] suggested that this dependency can be reduced by performing a moment analysis of the washout curve plotted as a function of the cumulative exhaled volume related to the FRC. However, the dependency of the moment ratios on the ventilatory dead space (V_D) remained. Therefore, Habib and Lutchen[8] replaced the cumulative exhaled volume by the cumulative alveolar volume to reduce the influence of V_D. They referred to the first two moment ratios of the wash out curve as alveolar-based mean dilution numbers $AMDN_1$ and $AMDN_2$.

Dead space fractions (V_D related to the tidal volume V_T) in adults commonly lie between 0.05 to 0.2.[8] In ventilated newborns the dead space fraction V_D/V_T is often markedly higher[9] depending on the ventilator settings. Typical values lie between 0.4 and 0.6[10] and in preterm or surfactant-depleted lungs V_D/V_T can rise up to 0.7.[11] Such small lungs are ventilated with a relative low

tidal volume to prevent volu-trauma. Mainstream flow sensors and gas analyzers considerably increase the apparatus dead space so that high dead space fractions are not uncommon. The effect of an increased V_D/V_T on the sensitivity of VI indices to parameter changes is not well known. Therefore, the aim of this study was to investigate how changing ventilator settings affect the different VI indices in this particular population by mathematical modeling and by measurements in newborn piglets using the MBW technique with heptafluoropropane (HFP) as tracer gas.

Methods

In patients ventilated with a constant V_T the LCI is given by

$$LCI = \frac{N_{LCI} \cdot V_T}{FRC} \qquad (1)$$

where N_{LCI} is the number of breaths required to lower the end tidal tracer gas concentration to 1/40th of the starting concentration.[12] The ideal washout curve of an inert gas from a uniformly ventilated volume can be expressed as

$$c^n = c_0 \left[\frac{1}{1 + \frac{V_T}{FRC}\left(1 - \frac{V_D}{V_T}\right)} \right]^n, \quad n = 0,1,2.....N. \qquad (2)$$

where c^n is the end-expiratory gas concentration of the nth breathing cycle and c_0 is the initial gas concentration. Using computer simulations of the washout curve LCI can be calculated as a function of V_T/FRC and V_D/V_T.

The moments M_0, M_1, M_2 of the washout curve were calculated up to N_{LCI}. For a constant V_T the moment ratios are given by

$$M_1/M_0 = \left(\frac{V_T}{FRC}\right) \frac{\sum_{i=0}^{N_{LCI}} i \cdot c^i}{\sum_{i=0}^{N_{LCI}} c^i} \quad \text{and} \quad M_2/M_0 = \left(\frac{V_T}{FRC}\right)^2 \frac{\sum_{i=0}^{N_{LCI}} i^2 \cdot c^i}{\sum_{i=0}^{N_{LCI}} c^i}, \qquad (3)$$

where "i" is the number of the breathing cycle. For an infinite number of cycles M_1/M_0 has a fixed limit given by

$$M_1/M_0 = \frac{V_T}{V_T - V_D}. \qquad (4)$$

Following Habib and Lutchen,[8] the replacement of V_T by the alveolar ventilation V_T-V_D yield the alveolar-based mean dilution numbers

$$AMDN_1 = \left(\frac{V_T - V_D}{FRC}\right) \frac{\sum_{i=0}^{N_{LCI}} i \cdot c^i}{\sum_{i=0}^{N_{LCI}} c^i} \quad AMDN_2 = \left(\frac{V_T - V_D}{FRC}\right)^2 \frac{\sum_{i=0}^{N_{LCI}} i^2 \cdot c^i}{\sum_{i=0}^{N_{LCI}} c^i} \qquad (5)$$

For a well-mixed volume and an infinite number of breathing cycles, $AMDN_1$ is equal one regardless of V_D/V_T or V_T/FRC

$$AMDN_1 = \frac{V_T - V_D}{V_T - V_D} = 1 \qquad (6)$$

and an $AMDN_1 > 1$ implies inhomogeneity purely at alveolar level.[8] For very low dead spaces ($V_D/V_T \approx 0$) the alveolar-based mean dilution numbers are equal the moment ratios ($AMDN_1 = M_1/M_0$, $AMDN_2 = M_2/M_0$). An important feature of all VI indices is that they rise with increasing inhomogeneity of the alveolar ventilation which can be shown easily by computer simulations of multi-compartment models.

Animal experiments

Fifteen newborn piglets (age <12 h, median weight 1135 g) placed in supine position within a heated incubator were anesthetized (azaperon 8 mg·kg^{-1} and ketamin 10 mg·kg^{-1}), intubated (shortened neonatal endotracheal tube (ETT) with 3.5 mm outer diameter, Vygon, Ecouen, France), paralyzed (pancuronium-bromide 0.2 mg·kg^{-1}·hour^{-1}) and mechanically ventilated with a neonatal ventilator (Babylog 8000, Draeger, Lübeck, Germany). During the study period, air flow (6 L/min), respiratory rate of 40/min and fraction of inspired oxygen (FiO_2) of 1.0 were kept constant. Positive end-expiratory pressure (PEEP) was set to zero, peak inflation pressure (PIP) was set initially to 8.3 ± 3.1 cmH_2O and elevated to 12.1 ± 5.0 cmH_2O. Ventilatory parameters were taken from the Babylog 8000 and recorded continuously. Lung volume and VI indices were measured by heptafluoropropane (HFP) wash in and wash out as previously described.[13] Briefly, a new infrared HFP sensor was sited between the flow sensor of the Babylog 8000 and the ETT. The total apparatus dead space of HFP sensor, flow sensor and ETT was 4.5 mL determined by water displacement. The constant flow of the ventilator was 8 L/min in all measurements. Using a mechanical valve to start wash in or wash out, a HFP flow from a gas cylinder (medical grade HFP, Solvay, Hannover, Germany) was fed into the inspiratory limb of the ventilatory circuit to achieve a constant HFP concentration of 0.8%. The flow signal of the Babylog 8000 and the concentration signal from the HFP sensor were used to calculate FRC and the VI indices from the wash-in or wash-out curve up to 1/40th of the starting concentration by an external computer. The Fowler dead space V_D was determined from the first 5 cycles. The calculation was stopped automatically after N cycles when the total amount of alveolar turnovers exceed the tenfold of the calculated FRC (minimum number 40 cycles).

After instrumentation and onset of mechanical ventilation a stabilization period of 15 minutes was allowed before the measurements were started with a HFP wash-in procedure ($FRC_{wash\text{-}in}$) and a consecutive wash-out procedure ($FRC_{wash\text{-}out}$). Such a cycle was accepted for evaluation if the deviation between $FRC_{wash\text{-}in}$ and $FRC_{wash\text{-}out}$ was lower than 20% and the V_T was higher than 4.5 mL (V_{Dapp}). In order to investigate the effect of ventilator settings on VI indices PIP was increased by 4 cm H_2O. After a stabilization period of 15 minutes the MBW was repeated in the same manner.

Computer program

A computer program written in Visual Basic as a macro of a EXCEL worksheet (Microsoft Corp,) was developed to compare the VI indices measured in the piglets with the VI indices of a uniformly ventilated volume using the same ventilator settings. The program calculates the washout curve according equation 2 and the corresponding VI indices according equations 1, 3 and 5. For each measurement in the piglets at least 5 wash-in and wash-out cycles were performed and averaged. Data are presented as mean ± SD and mean individual differences with 95% CI as appropriate. Differences in the animals were compared by the paired t-test. To assess the within-subject variability of repeated measurements the coefficient of variation (CV) was calculated for all parameters and compared by a rank test. A level of statistical significance of $p < 0.05$ was accepted.

Results

Computer simulation: The computer simulation of a uniformly ventilated volume showed that the LCI increased with

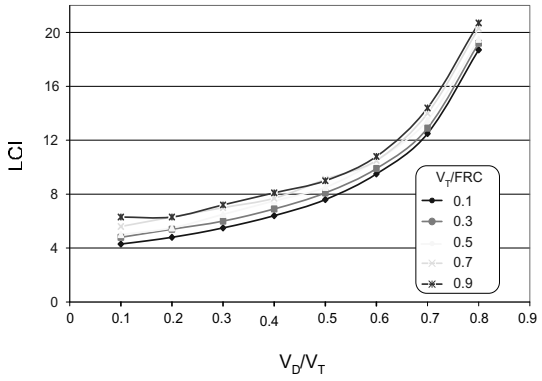

Figure 1
Numerical calculation of the lung clearance index (LCI) of a uniformly ventilated space as function of V_D/V_T and V_T/FRC.

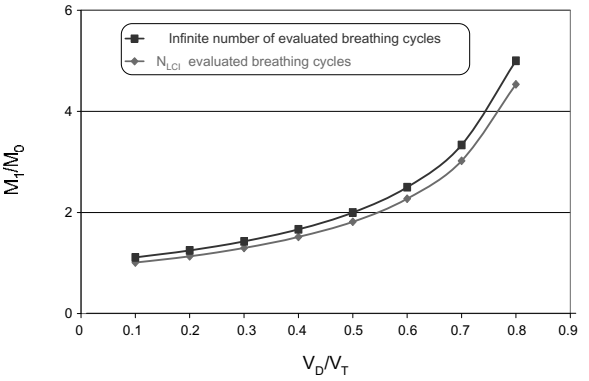

Figure 2
Effect of V_D/V_T on the moment ratio M_1/M_0 using an infinite number and N_{LCI} breathing cycle (The influence of V_T/FRC on M_1/M_0 was negligible).

increasing V_D/V_T and V_T/FRC (Fig 1). However, the influence of V_D/V_T on the LCI is distinctly stronger than that of V_T/FRC. In particular for $V_D/V_T > 0.5$ the LCI increased dramatically.

The moment ratio M_1/M_0 was independent of V_T/FRC but the dependency on V_D/V_T remained. As shown in Fig.1, the calculated values were about 10% lower than predicted by equation 4 because only N_{LCI} breathing cycles were evaluated. The second moment ratio M_2/M_0 showed a similar dependency on V_D/V_T and V_T/FRC like the LCI.

The alveolar-based mean dilution number $AMDN_1$ ranged between 0.91 and 0.94 independent of V_T/FRC and V_D/V_T. Due to the finite number of evaluated cycles $AMDN_1$ was <1 as given by equation 6. In contrast to M_2/M_0 the dependencies of $AMDN_2$ differed considerably and were distinctly lower (Fig. 2). $AMDN_2$ decreased with increasing V_D/V_T and increased only slightly with increasing V_T/FRC (Fig. 4).

Animal study: The results of the FRC and VI measurements in the piglets are shown in Table 1. An increase in PIP of about 4 cmH_2O caused a significant increase in V_T of 39% ($p = 0.003$) and of the FRC of 11% ($p = 0.006$). Because the increase in V_T was much higher compared with the increase in the FRC the ratio V_T/FRC increased significantly ($p = 0.003$). Due to the increase in V_T there was a significant decrease of V_D/V_T ($p = 0.006$). A significant decrease was also seen in the LCI ($p = 0.019$) and the moment ratios M_1/M_0 ($p = 0.006$) and M_2/M_0 ($p = 0.017$). No significant changes were seen in $AMDN_1$ and $AMDN_2$.

There was a strong correlation between LCI and the moment ratios (M_1/M_0, M_2/M_0) with $r = 0.885$ and $r = 0.907$, respectively, and independent of which PIP was used. Thus, it was not surprising that there was a similar effect of the increased PIP on LCI and the moment ratios (M_1/M_0, M_2/M_0). No statistically significant correlations were found between the alveolar-based mean dilution numbers ($AMDN_1$, $AMDN_2$) and LCI, M_1/M_0 and M_2/M_0. The within-subject variability of the measured parameters showed considerable variations but it was not affected by the increase of the PIP. The median CV of all FRC measurements was 5.6%. The median CV of the LCI was significantly greater (9.8%, $p = 0.0004$). Compared with the LCI the CV of M_1/M_0 was significantly smaller (6.6%, $p = 0.003$), whereas the CV of M_2/M_0 was distinctly greater (14.6%, $p = 0.004$). The CVs of $AMDN_1$ (9.1%) and $AMDN_2$ (16.3%) were always greater than the CVs of the other moment ratios.

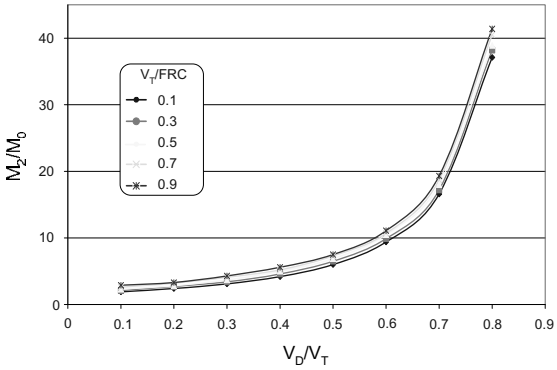

Figure 3
The moment ratio M_2/M_0 of an uniformly ventilated space as function of V_D/V_T and V_T/FRC using N_{LCI} breathing cycles.

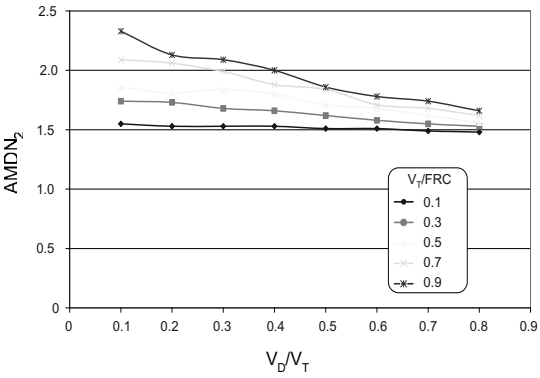

Figure 4
Numerical calculation of the alveolar-based mean dilution numbers $AMDN_2$, using N_{LCI} breathing cycles.

Using the same ratios V_T/FRC and V_D/V_T as measured in the animals the VI indices of a uniformly ventilated volume were only slightly lower (Table 2) than in the animals measured. The relative changes of the VI indices were in well agreement with the relative changes measured in the animals (Fig 5). All VI indices calculated for a uniformly ventilated space were within the confidences range of the animal measurements (Fig 5). This means that the significant changes in the VI indices of Table 1 were exclusively caused by the changes in V_T/FRC and V_D/V_T due to an increase in PIP and not by a more even alveolar ventilation.

Table 1: Effect of increased peak inspiratory pressure on ventilation, FRC and ventilatory inhomogeneity indices in 15 ventilated piglets (Presented are groups means ± SD and the mean individual changes with 95%CI compared to the baseline)

	Baseline	Increased peak inspiratory pressure	Mean individual difference in % with 95%CI	P value
V_T (mL)	15.4 ± 9.5	21.9 ± 14.7	38.9 (20.4 to 57.45)	**p = 0.003**
FRC (mL)	31.6 ± 14.7	35.0 ± 15.9	11.1 (4.5 to 17.8)	**p = 0.006**
V_T/FRC	0.48 ± 0.17	0.59 ± 0.20	25.0 (10.7 to 39.4)	**p = 0.003**
V_D/V_T	0.49 ± 0.15	0.43 ± 0.13	-10.2 (-21.0 to 0.5)	**p = 0.006**
LCI	9.17 ± 0.75	8.55 ± 0.74	-6.4 (-11.8 to -1.0)	**p = 0.019**
M_1/M_0	2.03 ± 0.16	1.84 ± 0.16	-9.4 (-14.0 to -4.9)	**p = 0.006**
M_2M_0	8.41 ± 1.60	7.22 ± 4.80	-12.1 (-23.1 to -1.4)	**p = 0.017**
$AMDN_1$	1.034 ± 0.30	1.028 ± 0.19	-0.6 (-9.1 to 7.9)	p = 0.886
$AMDN_2$	2.88 ± 1.56	3.01 ± 1.06	4.5 (-9.9 to 18.1)	p = 0.515

Discussion

The measurement of lung volume and ventilation inhomogeneity by MBW is a fascinating, non-invasive technique. It is relatively easily performed, even in ventilated patients. In a previous study,[13] we have shown that by this technique the effect of surfactant-depletion by lung lavage on the FRC and the VI indices is reliably measured: before and after lavage V_D/V_T was not significantly different, therefore, the significant increase of the VI indices has to be predominantly attributed to the effect of lung lavage. In the present study the measurements were performed in healthy lungs and V_D/V_T was distinctly changed by an increase of the PIP. As shown in Fig. 5 the changes of the VI indices are mainly caused by physical laws of gas mixing.

The interpretation of significant changes in VI indices may be misleading if their dependency on the ventilator settings is not considered. This is a particular problem in small lungs where the relatively high dead space fraction increases the sensitivity of VI indices to parameter changes. Any changes in V_D (e.g. by applying of a new mainstream sensor) or changes in V_T and FRC (eg by changing of ventilator settings or by surfactant substitution) will affect the VI indices and therefore hamper their comparability.

As shown by the computer simulation, most VI indices increase with increasing V_D/V_T. This may explain why in newborns much higher VI indices values were measured[4,13,14] than in spontaneously breathing children.[15,16] These higher values in newborns are more likely an expression of functional dependencies than the result of impaired alveolar ventilation. The relatively good agreement between the VI indices measured in healthy piglets (Table 1) and the calculated VI indices of a uniformly ventilated volume (Table 2) was surprising. There was only a small difference in the VI indices between the animal measurements and the modeling which can be attributed to the more complex ventilation distribution in the lungs of the piglets.

In infancy the LCI is one of most frequently used VI index[16-19] and easy to comprehend. It describes the number of turnovers to lower the end tidal tracer gas concentration to 1/40th of the starting concentration. Theoretically, the LCI is a static value of the flat tail of the washout curve and may vary if the signal is noisy. This explains its relatively high within-subject variability. The limitation on N_{LCI} breathing cycle seems to be useful to reduce the influence of the signal noise on the measured LCI. Its main disadvantage is its high dependency on V_T/V_D as shown in Fig 1.

Moment ratios are more abstract mathematical measures considering the whole washout curve. Only for M_1/M_0 a theoretical value for a well ventilated volume exists (equation 4). M_1/M_0 reflect more the first part of the washout curve, whereas M_2/M_0 better describe the tail of the curve. Therefore the within-subject variability of M_2/M_0 is distinctly higher compared to M_1/M_0 and similar to the within-subject variability of the LCI. A moment analysis makes higher demands on the wash out curve compared to LCI measurements. It requires a rapid rise of the tracer gas after the switch-on so that the full tracer gas concentration is reached during the first inspiratory cycle. This is sometimes difficult to achieve, in particular if the tracer gas is fed into the inspiratory limb of the ventilator circuit, far from the ETT, which may delay such a swift rise. Such a delay is tolerable for FRC measurements but will affect the calculation of the moment ratios.

In contrast to LCI and the ratios M_1/M_0 and M_2/M_0, no significant effect of the increased PIP on $AMDN_1$ and $AMDN_2$ was seen, as predicted by the computer simulation. These parameters suggested by Habbib and Lutchen[8] seem indeed to be less sensitive to the changes in the breathing pattern than the other ones. This dos not necessarily mean that they have a higher predictive value: with the exception of the above authors,[8] a higher diagnostic value of these corrected moments could not

Table 2: Modelling of ventilatory inhomogeneity indices of a uniformly ventilated volume using the measured V_D/V_T and V_T/FRC of table 4

	Modelling 1	Modelling 2	Difference in %
Model parameters			
V_D/V_T	0.49	0.43	
V_T/FRC	0.48	0.59	
Inhomogeneity indices			
LCI	8.16	7.67	**-6.00%**
M_1/M_0	1.79	1.61	**-10.08%**
M_2/M_0	6.48	5.48	**-15.41%**
$AMDN_1$	0.91	0.92	**0.49%**
$AMDN_2$	1.69	1.78	**5.66%**

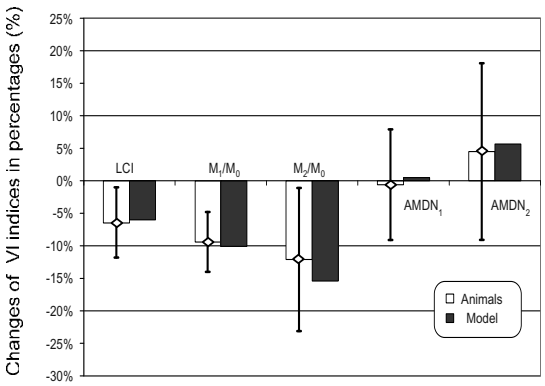

Figure 5
Comparison on the changed VI indices due to increased PIP in the piglets (mean with 95% CI) with the numerically calculated VI indices of a uniformly mixed volume (blue bars) using the same ratios V_D/V_T and V_T/FRC as shown in table 1.

be demonstrated until now.[20] The main problem with these parameters is that they need an exact determination of the Fowler dead space. This is often difficult to evaluate in small lungs because the three phases of the gas concentration-volume diagram of the exhaled air are often not well defined.[11] This may explain why in animals $AMDN_1$ and $AMDN_2$ often showed a very high within-subject variability (>20%). This high variability may limit their diagnostic value.

A central problem of all moment ratios is their dependency on the number of evaluated breathing cycles.[14] The computer simulation has already shown that the theoretical values for M_1/M_0 and $AMDN_1$ were not reached due to the finite number of evaluated cycles (Fig 2). This hampers the comparability of the data between different laboratories if the start and the end of the evaluated breathing cycles are not specified.

The within-subject variability of LCI, M_1/M_0 and M_2/M_0 in our study was similar to those measured by Shao et al.[14] in preterm infants. In both studies the variability of the VI indices was distinctly higher compared with the CV of the FRC. Thus, in small ventilated lungs the determination of VI indices needs a higher number of wash-in and washout cycles than for FRC measurements to obtain reproducible results.

Conclusion

With the availability of dead space-minimized mainstream gas analyzers there is an increasing interest to measure ventilation inhomogeneity by MBW techniques. However, the use of VI indices in small lungs needs particular attention. Especially in small ventilated lungs with a relatively high dead space fraction most indices are significantly affected by ventilator settings. Changes in tidal volume and lung volume, or changes in the apparatus dead space hamper their comparison. Model simulations of a uniformly ventilated volume can help to decide if the changes in the VI indices are caused by changing ventilator settings or whether they indicate any changes in the homogeneity of alveolar ventilation.

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A Survey of Transcutaneous Blood Gas Monitoring Among European Neonatal Intensive Care Units

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Abstract

Background: PCO_2 and PO_2 are important monitoring parameters in neonatal intensive care units (NICU). Compared to conventional blood gas measurements that cause significant blood loss in preterms, transcutaneous (tc) measurements allow continuous, non-invasive monitoring of blood gas levels. The aim of the study was to survey the usage and opinions among German speaking NICUs concerning tc blood gas monitoring.

Methods: A questionnaire was developed and sent to 56 head nurses of different NICUs in Germany, Switzerland and Austria.

Results: A completely answered questionnaire was obtained from 41 NICUs. In two of these units tc measurements are not performed. In most NICUs (77%), both $P_{tc}O_2$ and $P_{tc}CO_2$ are measured simultaneously. Most units change the sensors every 3 hours; however, the recommended temperature of 44°C is used in only 15% of units. In only 8% of units are arterial blood gases obtained to validate tc values. Large variations were found concerning the targeted level of oxygen saturation [median upper limit: 95% (range 80–100%); median lower limit: 86% (range 75–93%)] and PO_2 [median upper limit: 70 mmHg (range 45–90 mmHg); median lower limit: 44 mmHg (range 30–60 mmHg)].

Conclusion: Our survey shows that the use of tc monitors remains widespread among German speaking NICUs, despite earlier data suggesting that their use had been abandoned in many NICUs worldwide. In addition, we suggest that the current method of monitoring oxygenation may not prevent hyperoxemia in preterm infants.

Background

Preterm infants are vulnerable to alterations in arterial oxygen or carbon dioxide tension.[1] Changes in oxygen supply contribute to the subsequent development of retinopathy of prematurity or bronchopulmonary dysplasia.[2] Hypocarbia has been associated with the subsequent development of periventricular leucomalacia[3] and cerebral palsy,[4] and while hypercarbia may protect the perinatal brain from hypoxemic-ischemic damage,[5,6] it could also cause retardation of retinal vascularization.[7]

Despite an ongoing discussion concerning the optimal values of blood gas levels, there is consensus that the partial pressures of arterial oxygen and carbon dioxide (P_aO_2 and P_aCO_2) should be kept within a narrow range. Thus, intermittent or continuous determination of blood gases is required. However, the repeated arterial blood sampling that is required for the correct measurement of P_aO_2 and P_aCO_2 is difficult to perform in preterm infants because the usage of indwelling catheters is associated with complications and significant blood loss. Capillary blood samples, which are painful but easier to obtain, provide satisfactory values for P_aCO_2 but tend to underestimate P_aO_2.[8]

Transcutaneous (tc) measurement of oxygen ($P_{tc}O_2$) and carbon dioxide ($P_{tc}CO_2$) tension is a non-invasive method that has recently offered some promise.[1] Several studies have shown a good correlation between tc and arterial values.[9-11] However, during routine clinical treatment, several problems – such as burns – appear.[1] Furthermore, a poor correlation between P_aO_2 and $P_{tc}O_2$ was found under routine clinical conditions.[12] On the basis of these reports, alert letters on the subject of tc PO_2 measurements were published by Canadian and British health authorities,[13,14] and after clinical introduction of pulse oximetry, the interest in tc oxygen monitoring decreased and was abandoned altogether in many neonatal intensive care units (NICUs) around the world.[15] However, the actual status of tc blood gas monitoring in German speaking NICUs remains unknown.

The present observational study was performed to answer the following questions:

1) To what extent is tc blood gas monitoring performed in

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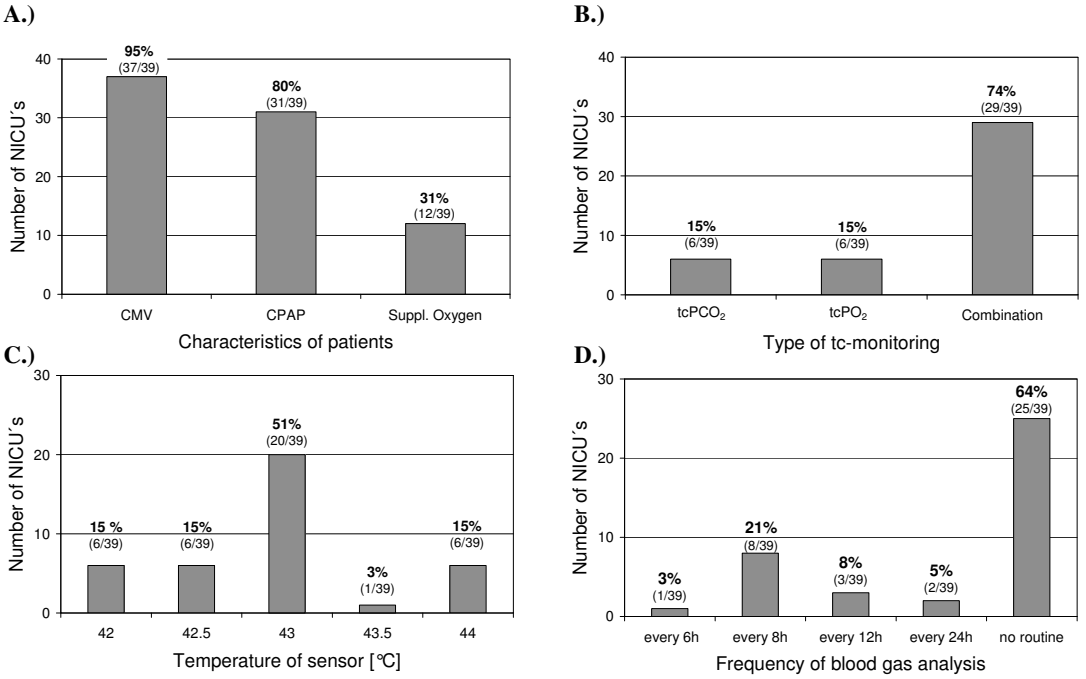

Figure 1
Shown are the number of NICUs. (A) that use tc monitoring on patients on conventional mechanical ventilation (CMV), continuous positive airway pressure support (CPAP) or supplemental oxygen (suppl. oxygen) [multiple answers were possible]; (B) that use a combination of tc PO_2 and tc PCO_2 sensors (Combination), or a single sensor; (C) that use a sensor temperature of 42°, 42.5°, 43°, 43.5° or 44°C; (D) that compare tc values with blood gases routinely every 6, 8, 12 or 24 h or do not have a specified routine.

German speaking NICUs?
2) Given reports that nurses are reluctant to perform tc monitoring because they question its reliability,[15] what are the opinions of nurses concerning the reliability of tc values?
3) Are there any differences between NICUs concerning technical aspects of tc sensor application?
4) What methods are used to detect hypo- or hyperoxia and what are the upper and lower limits for oxygen saturation and partial pressure in different NICUs?

Methods

The questionnaire consisted of four main parts and is described below. A pre-test of the questionnaire was performed at the authors' institution. Twenty nurses were asked to answer the questions. Four of the questions in the original version were found to be misleading and were reworded for the final version of the questionnaire.

The final questionnaire was sent to NICUs by ordinary mail. To avoid any bias due to differences in national medical regulations, the questionnaire was distributed only in German speaking countries. From a list of 168 university hospitals in Germany, Austria and Switzerland every third unit was chosen (n = 56 units). Because nurses are mainly responsible for the usage of tc equipment, head nurses were asked to answer the questionnaire according to their institutional guidelines.

Usage of tc measurements

The first part of the questionnaire was designed to obtain information concerning the usage of tc measurements. The following questions were included:

1. What aged patients do you mainly care for (only preterm infants / preterms and neonates / neonates and older infants)?
2. On which patients do you perform tc measurements (conventional mechanically ventilated patients / CPAP patients / only supplemental oxygen patients / every patient)?
3. Which parameters do you measure (tc PO_2 / tc PCO_2 / both)?
4. What manufacturer does the monitoring system come from?

Nursing practice

The second part of the questionnaire consisted of questions concerning nursing practice during tc measurements:

1. How often do you change the site of the sensor (every 1 / 2 / 3 hours / more / less frequently)?
2. Do you think the changes violate "minimal handling" practices?
3. Do you use a special treatment for erythematous skin areas?

Technical details of tc monitoring

The third section investigated technical details of tc usage and included the following questions:

1. How often do you change the sensor site?
2. What is the temperature of the sensor?

Accuracy of transcutaneous measurements

The final part of the questionnaire was dedicated to the correlation of tc and invasive blood gas measurements. The following questions were asked:

1. What is your impression concerning the accuracy of tc measurements (good / moderate / poor)?
2. On average, how often do you compare tc values with blood gases (routinely / depending on the values)?
3. What source of blood do you use for validation (capillary / arterial / venous)?

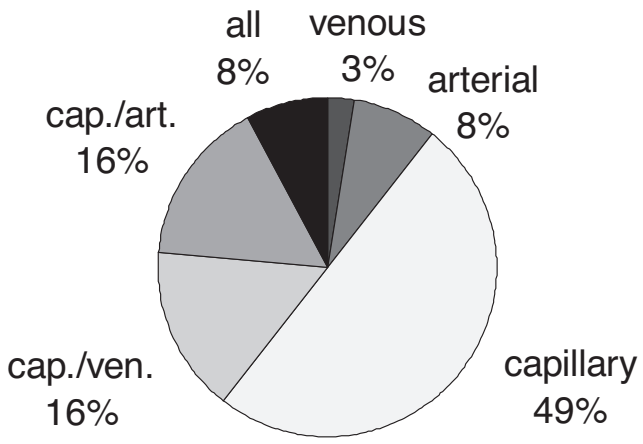

Figure 2
Distribution of blood sample type used to compare tc values.

4. Concerning monitoring of oxygenation in preterm infants, which value is more important when estimating hypoxia (saturation / tc PO_2) and hyperoxia (saturation / tc PO_2)? What are the lower and upper limit values?

Statistics: Data were analyzed with descriptive statistics using Excel (Microsoft) software. Data are presented as median and range or as relative percentages where appropriate.

Results

The questionnaire was completed by 41 of the 56 NICUs (73%). Among the 41 units with completed questionnaires, 2 did not perform tc measurements and hence were excluded from the subsequent analysis.

The head nurses of the 15 non-responding units were contacted by telephone by which it was confirmed that no tc measurements were performed in 8 units, tc measurements were performed but no further information was voluntarily offered in 4 units, and no information at all was offered in 3 units.

Usage of tc measurements

Most of the evaluated NICUs (28/39) mainly care for preterm and term new-borns. In the remaining 11 NICUs, both new-borns and infants are treated. Most of the units perform tc measurements on mechanically ventilated infants or on infants on continuous positive pressure (CPAP) support (Fig 1A). About 30% of units also use tc monitoring for infants on supplemental oxygen.

The majority of the answering units use a combination of tc PO_2 and tc PCO_2 sensors. Some units use either tc PO_2 or tc PCO_2 and two units use both sensors separately (Fig 1B).

Devices for tc blood gas measurements were from multiple suppliers; however, Radiometer was the most commonly used manufacturer, followed by Hewlett Packard and Hellige.

Nursing practice

Analysis of handling showed that most units change the site of the sensor every 3 hours or even more frequently, 6 of 39 units change the sensor every 4 hours, and 3 of 39 less often than every 4 hours. There was no correlation between frequency of changes and manufacturer.

In 60% of the participating units, nurses considered the changing of the sensor as a discomfort for the patient and a violation of the minimal handling policy.

About one third of the units do not have a special treatment of erythematous sensor areas, whereas the remaining units use various ointment therapies.

Technical details of tc measurements

Large differences were found concerning the technical aspects of tc blood gas monitoring. In 17 of 39 units, sensors are calibrated after each change of sensor site. A routine calibration of the sensor is performed every 4 hours in 8 units and once daily in 11 units.

Sensor temperature mainly depends on the age of the patient; however, in most units the sensor works at a temperature of 43°C. In some units temperatures between 42 and 44°C are used (Fig. 1C).

Individual opinion concerning the accuracy of transcutaneous values

Invasive blood gas measurements are routinely performed for comparison with tc values in 14 of 39 units (Fig 1D). Blood gases are mainly obtained from capillary blood, with only 8% of units obtaining arterial samples (Fig 2).

The majority of respondent nurses considered the tc measurements as a good (29/39) or intermediate (9/39) estimate of arterial blood gases, while only one NICU nurse stated that tc measurements lead to poor estimates.

The question concerning hyperoxia and hypoxia detection was answered by only 35 units, but these provided some interesting data. To detect hyperoxia in preterm infants, 16 of the 35 NICUs use only oxygen saturation, 10 use only $P_{tc}O_2$, 8 use both and 1 uses neither method. The median upper limit for saturation was 95% (range 80–100%) and the median upper limit for $P_{tc}O_2$ was 70 mmHg (range 45–90 mmHg).

To detect hypoxia, the majority (24/35) of units use only saturation, whereas 9/35 units use both methods ($P_{tc}O_2$ and saturation) and two units use only invasive blood gas methods. The median lower limit for saturation was 86% (range 75–93%) and the median lower limit for $P_{tc}O_2$ was 44 mmHg (range 30–60 mmHg).

Discussion

To prevent acute or chronic damage, blood gases must be monitored in preterm infants.[1] Transcutaneous (tc) measurement of blood gases represents a valuable tool for continuous, non-invasive monitoring.

Tc monitoring is associated with several problems and it has been reported that this type of monitoring has been abandoned in many NICUs around the world.[15,16] Up until now, no data were available concerning the usage of tc monitors in German speaking neonatal units. In our observational study, we received answers from 41 of 56 NICUs approached. Of these, 39 responded that they currently use tc monitoring. Four of the 15 non-responding units also performed tc measurements but did not provide any further information. Thus, our representative survey suggests that at least 43 of 56 NICUs (77%) use tc blood gas monitoring. In six units tc monitoring had been completely abandoned. In contrast to data that suggest a reluctance of nurses to use tc monitoring,[15]

our study shows wide acceptance of the technique among NICU nurses. The majority of surveyed nurses stated that the accuracy of the tc readings is mostly reliable. However, the need for frequent changes in sensor sites was considered a violation of the minimal handling policy.

Tc monitoring and pulse oximetry are useful techniques for the non-invasive monitoring of oxygenation in new-borns that require supplemental oxygen. Whereas capillary blood gases and pulse oximetry are sufficient to detect hypoxia, it is not sufficient to use either method to prevent hyperoxia. Nevertheless, in the present survey 16 of 35 NICUs used only saturation to detect hyperoxia. Since pulse oximetry values cannot be used to detect hyperoxia, arterial PO_2 should also be measured intermittently. About half of all answering units stated that they perform blood gas analysis exclusively from capillary blood samples, but capillary PO_2 estimations can only exclude hypoxia and are insufficient for detecting hyperoxia.[17] Thus, it could be speculated that the current oxygen-monitoring policy of some units exposes infants requiring supplemental oxygen to a higher risk of subsequent development of oxygen associated damage, such as retinopathy.[18]

Large variations were found among the different NICUs with regard to the definition of hypoxia and hyperoxia. The upper limit for oxygen saturation ranged between 80% and 100%, and if tc measurements were used, the upper limit ranged between 45 and 90 mmHg (median 70 mmHg). A similarly wide range was found for the detection of hypoxia with a lower saturation border between 75% and 93% (mean 86%). These differences are substantial and could explain some of the described differences in outcomes of preterm infants.[19] These differences require further investigation and specification. The present data do not allow a differentiation between the target values for infants with supplemental oxygen or those with respiratory support.

The present study included some limitations that are partially associated with the chosen method of obtaining information. First, the study sample is based on the return of completed questionnaires. We achieved a return rate of 73%, which is considered a good result and allows reliable interpretation. Secondly, the questionnaire was not designed to identify an association between the monitoring policy at the institution and the clinical outcome parameters; however, the present study does provide sufficient data to plan an appropriate study protocol to address that question. Finally, the questionnaire was only designed to receive information consistent with institutional guidelines. In some cases, the unique situation of an individual patient could lead to deviations from the general policy. A follow-up study could further specify the use of tc monitoring under different clinical conditions (ventilation, oxygen supply, CPAP) and in different populations (preterm, term infants), and could also include the primary reason for the use of tc monitoring. However, surveys of these factors should be mainly performed among the attending neonatologists.

Conclusion

The present survey provides valuable data concerning the current situation of routine clinical blood gas monitoring in German speaking NICUs and has produced the following conclusions: 1) Transcutaneous blood gas monitoring is frequently used in neonatal intensive care units; 2) large variations exist concerning the targeted range of oxygen saturation or PO_2; and 3) in infants requiring supplemental oxygen, the current method of monitoring oxygen may not be sufficient to prevent hyperoxia.

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Evaluation of Pulse-Oximetry Oxygen Saturation Taken Through Skin Protective Covering

Jyotsna James, Lokesh Tiwari, Pramod Upadhyay, Vishnubhatla Sreenivas, Vikas Bhambhani and Jacob M Puliyel

Abstract

Background: The hard edges of adult finger clip probes of the pulse oximetry oxygen saturation (POOS) monitor can cause skin damage if used for prolonged periods in a neonate. Covering the skin under the probe with Micropore surgical tape or a gauze piece might prevent such injury. The study was done to see if the protective covering would affect the accuracy of the readings.

Methods: POOS was studied in 50 full-term neonates in the first week of life. After obtaining consent from their parents the neonates had POOS readings taken directly (standard technique) and through the protective covering. Bland-Altman plots were used to compare the new method with the standard technique. A test of repeatability for each method was also performed.

Results: The Bland-Altman plots suggest that there is no significant loss of accuracy when readings are taken through the protective covering. The mean difference was 0.06 (SD of 1.39) and 0.04 (SD 1.3) with Micropore and gauze respectively compared to the standard method. The mean difference was 0.22 (SD 0.23) on testing repeatability with the standard method.

Conclusion: Interposing Micropore or gauze does not significantly affect the accuracy of the POOS reading. The difference between the standard method and the new method was less than the difference seen on testing repeatability of the standard method.

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Background: Pulse oximetry oxygen saturation (POOS) monitors are now commonplace in paediatric intensive care areas and in neonatal units. A variety of probes are available for use with saturation monitors. Adult finger-clips have a longer useful life than neonatal clip probes and disposable wrap-around probes. In the long run, adult finger clips are cheaper to use and we have been using them across the neonate's palm or feet for obtaining saturation readings. Sensor placement over the palm or foot of the neonate has been described previously.[1] However the rigid edges of these probes when used for long periods can cause injury and skin necrosis as shown in figure 1. Injuries may be prevented if the palm or sole is first covered with a layer of 3 M Micropore surgical tape or 2 layers of gauze. This study was done to test the degree of inaccuracy introduced in the POOS by the use of Micropore or gauze in this manner.

Methods: A convenience sample of fifty neonates was enrolled in the study after obtaining verbal consent from their parents. The neonates were all born in the hospital, less than a week old, and admitted on the post-natal ward. No effort was made to select babies – so as to get a wide range of readings. Babies

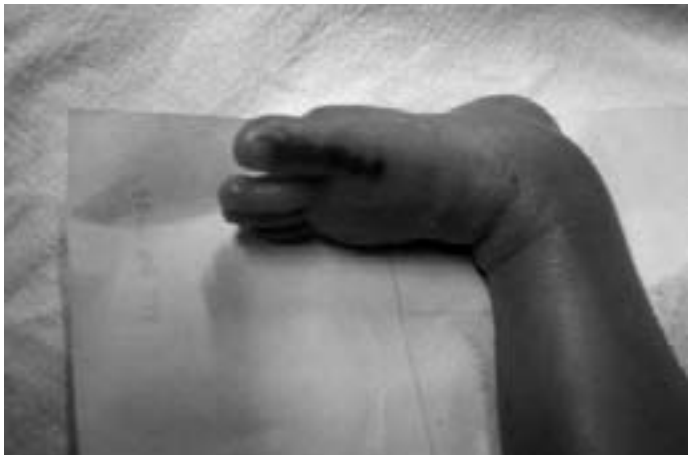


Figure 1. Showing pressure injury to the foot of a neonate through application of a adult clip probe for saturation monitoring.

Figure 2a

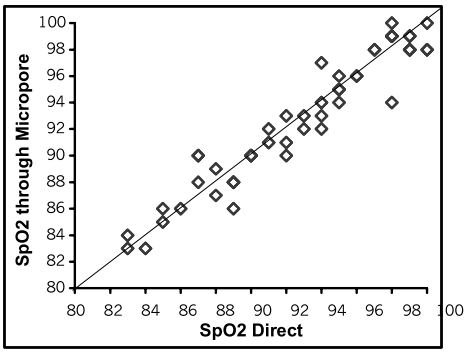
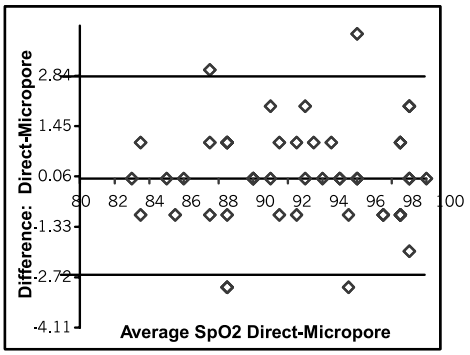


Figure 2b



	Mean	Std. Dev.
	0.0588	1.39

Figure 2
SpO_2 Direct and through Micropore

with low saturations were treated as per hospital protocol. Each neonate had readings taken thrice, at intervals of 5 minutes, using a Larsen & Tourbo Stellar pulse oximeter (Hebbal, Mysore India). The POOS monitor readings were taken in random order with the right foot covered with 3 M Micropore surgical tape (1530-1 hypoallergenic. St Paul USA) or covered with two layers of gauze (weight 27 gm/sq m ± 5%: Government of India specification) or directly without any covering. Readings were noted after the saturation display had steadied. The investigator noting the readings was seated so that he could read the saturation monitor but he was blinded as to how the probe was applied. The readings with Micropore and gauze were each compared with the readings taken with the probe applied directly (standard method). Five minutes later the procedure was repeated on the opposite limb. Only the first measurements were used to illustrate comparison of methods. The second measurement was used in the study of repeatability – a technique described by Bland and Altman.[2]

Statistical methods: A 0.05 two-sided Fisher's z test of the null hypothesis suggests that the Pearson correlation coefficient r = 0.50 will have 90% power to detect an r of 0.0 when the sample size is 38. We used a sample size of 50 for greater confidence in the findings.

Bland-Altman plots were used to study agreement between methods and to test the repeatability of the methods.[2] As a first step, the data was plotted and the line of equality was drawn (a line on which all points would lie if the two methods gave exactly the same reading every time). Then a plot of the difference between methods against their mean was made. The estimated mean difference d and standard deviation s of the difference were calculated. We would expect most of the differences to lie between d -2s and d +2s. Bland and Altman suggest that provided the differences within d ± 2s are not clinically important, we could use the two measurements interchangeably.

Results: Figure 2a and 2b shows the SpO_2 readings taken directly and through Micropore. The mean difference was 0.06 with SD of 1.39. Figure 3 (a&b) shows the SpO_2 readings taken directly and through gauze. The mean difference was 0.04 SD 1.3. Figure 4 (a&b) shows the plots testing repeatability with the direct method. The mean difference was 0.22 SD 0.23. Figure 5

Figure 3a

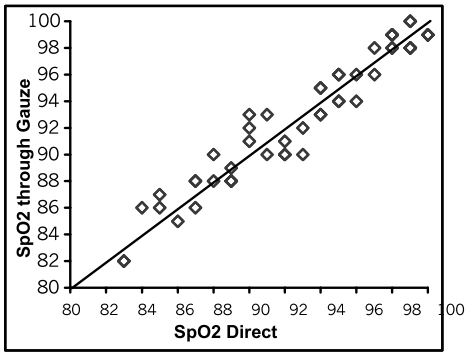
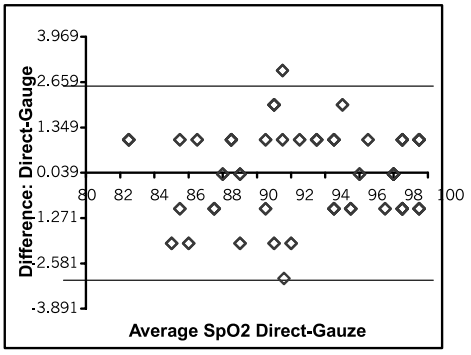


Figure 3b



Mean	Std. Dev
0.039	1.31

Figure 3
SpO_2 Direct and through Gauze

Figure 4a

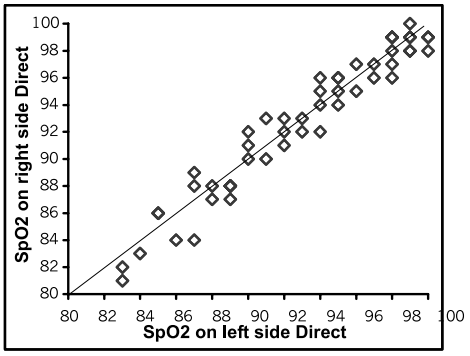
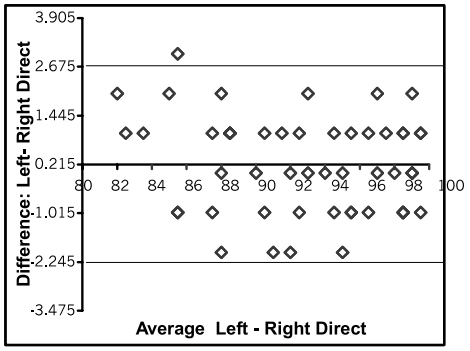


Figure 4b



Mean	Std. Dev
0.215	1.23

Figure 4
Reapeated meausures of SpO_2 with direct method

(a&b) shows mean difference on repeatability of readings through Micropore. The mean difference was 0.23 SD 1.69. Figure 6 (a&b) shows repeatability of readings through gauze. The mean difference was 0.02 SD 1.50.

Discussion

Theoretically, if the translucent material (interposed between the light emitting diode and the photo detector sensor in a POOS) is more transparent to one of the two wavelengths used by the POOS diode, it will induce an error and the machine will give a false reading. We employed the Bland-Altman plots to look at the comparability of methods. It is seen that difference between readings taken through the skin protecting coverings (Micropore and gauze) and the readings taken directly are not very different from the differences seen on testing repeatability of the direct method. These differences can therefore be considered clinically insignificant. Our findings suggest that interposing Micropore or gauze does not affect the accuracy of the readings to a clinically significant level in the range of saturations we studied.

Bland and Altman have compared the oxygen saturation meter and pulsed saturation oxymeter. They found a mean difference of 0.42 percentage points with 95% CI 0.13 to 0.70. They concluded that the limits of agreement (-2.0 and 2.8) were small enough for confidence that the new method can be used in place of the old, for clinical purposes.[22] Hess and colleagues have found that the standard error on using the probe directly was 2% (95% confidence interval was about ± 4%).[3] Alexander et al found that the 95% prediction limit of a single pulse oximeter reading was ± 6% throughout the 70–100% range of saturation, such that there is a 95% probability that an oximeter reading of 90% corresponds to an arterial saturation between 84 and 96%.[4] We found that the agreement between the direct method and readings taken through Micropore (and through gauze) was less than the variations taken as acceptable by previous authors.

We also found on examining repeatability of the direct method that the mean difference was 0.22 with SD of 1.23.

This test of repeatability of the direct method defines what must be considered acceptable because such variability is inherent in using the standard method. The differences we found between methods (and the differences that were shown on repeatability testing through Micropore and through gauze) were less or only marginally more than the variability seen on testing

Figure 5a

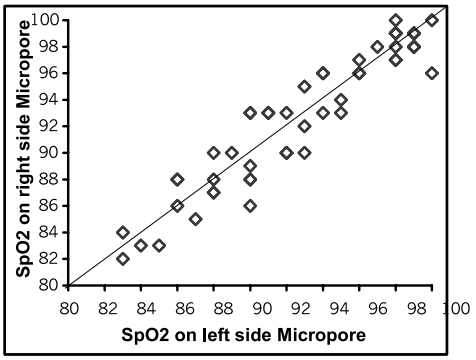
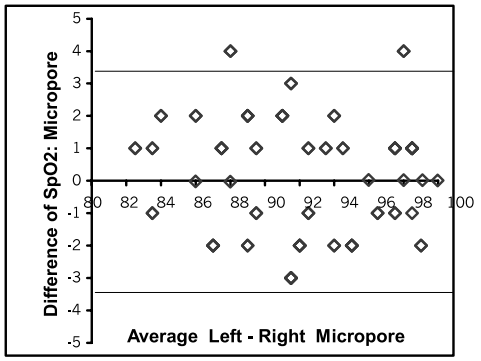


Figure 5b



	Mean	Std. Dev
	0.215	1.23

Figure 5
Repeated measures of SpO_2 through Micropore

Figure 6a

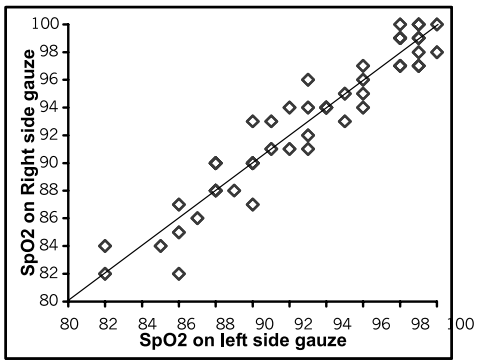
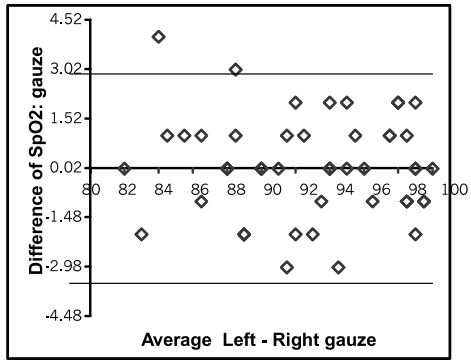


Figure 6b



Mean	Std. Dev
0.0196	1.5

Figure 6
Repeated measures of SpO_2 through Gauze

reproducibility of the direct method. This is a novel use of the Bland-Altman test of repeatability of the standard method to define the range of what must clearly be "acceptable differences" between methods.

We have not used blood gas readings as the gold standard for comparison. This was not considered necessary as Bland-Altman plots were employed. According to Bland and Altman, a 'gold standard' is needed for comparison only for calibration.[2] They suggest that "new methods" can be compared to an "established technique" rather than with the true quantity. If the new method agrees sufficiently well with the old the old may be replaced.

The practice of using adult probes in neonates is not confined to resource scarce countries. Recent Advances in Pediatrics 18 describes how to use adult probes if infant probes are not readily available.[5] In India, adult clip probes (Oximax Durasensor DS 100A Nellcor USA) cost US $175 and lasts for 6 – 9 months in our nursery. The neonatal clip probe (Dura Y sensor Nellcor USA) costs US $188 and lasts for a month. The disposable neonatal sensor costs about US $16 and is for single use only.

Conclusion

In conclusion, considerable saving can be achieved with the reusable adult probe by using 3 M Micropore or a gauze piece to wrap around the skin below the clip, and this practice does not compromise accuracy of readings taken by POOS monitors.

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Palatal Development of Preterm and Low Birthweight Infants Compared to Term Infants – What Do We Know?

Ariane Hohoff, Heike Rabe, Ulrike Ehmer, Erik Harms

Abstract

Background: It has been hypothesized that prematurity and adjunctive neonatal care is 'a priori' a risk for disturbances of palatal and orofacial development which increases the need for later orthodontic or orthognathic treatment. As results on late consequences of prematurity are consistently contradictory, the necessity exists for a fundamental analysis of existing methodologies, confounding factors, and outcomes of studies on palatal development in preterm and low birthweight infants.

Method: A search of the literature was conducted based on Cochrane search strategies including sources in English, German, and French. Original data were recalculated from studies which primarily dealt with both preterm and term infants. The extracted data, especially those from non-English paper sources, were provided unfiltered in tables for comparison (Parts 1 and 2).

Results: Morphology assessment of the infant palate is subject to non-standardized visual and metrical measurements. Most methodologies are inadequate for measuring a three-dimensional shape. Several confounding factors were identified as causes contributing to disturbances of palatal and orofacial development.

Conclusion: Taking into account the abovementioned shortcomings, the following conclusions may be drawn for practitioners and prospective investigators of clinical studies. 1) The lack of uniformity in the anatomical nomenclature of the infant's palate underlines the need for a uniform definition. 2) Metrically, non-intubated preterm infants do not exhibit different palatal width or height compared to matched term infants up to the corrected age of three months. Beyond that age, no data on the subject are currently available. 3) Oral intubation does not invariably alter palatal morphology of preterm and low birthweight infants. 4) The findings on palatal grooving, height, and asymmetry as a consequence of orotracheal intubation up to the age of 11 years are inconsistent. 5) Metrically, the palates of orally intubated infants remain narrower posteriorly, beginning at the second deciduous molar, until the age of 11 years. Beyond that age, no data on the subject are currently available. 6) There is a definite need for further, especially metrical, longitudinal and controlled trials on palatal morphology of preterm and low birthweight infants with reliable measuring techniques. 7) None of the raised confounding factors for developmental disturbances may be excluded until evident results are presented. Thus, early orthodontic and logopedic control of formerly premature infants is recommended up to the late mixed dentition stage.

Background

The research on palatal development dates back to the beginning of the last century. Unfortunately, the results of many studies are conflicting in some respects and may be difficult to interpret. Compared to the significant improvements in the survival rate of preterm infants, the knowledge on late consequences of orofacial development in these small patients is still unsatisfactory. A recently published systematic review concluded that further well-designed studies are needed. Therefore, a fundamental analysis of existing methodologies, confounding factors, and outcomes seems motivated.

Traditional reviews are characterized by less stringent inclusion criteria than systematic reviews. Thus, studies from the pre-'evidence based medicine' (EBM) era were included. This has revealed important information about the research on development of the term infant's palate. It could be shown (Part 1) that the newborn's palate can vary considerably and is subject to various influences. Therefore, palatal growth may occur undetected or appear excessive or inadequate.

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The general methodologies used for morphometry are comparable between studies from the pre-EBM and EBM eras, whereas the quality of study designs improves over the years. The assessment of palatal alterations is only as accurate as the measurements that are taken from the palate and therefore independent of the general study type. Two-dimensional measurements – however reliable – are of limited value for the description of three-dimensional shape changes, and this measurement technique may contribute conflicting results.

Discussion

Clinical relevance of visual inspection of the newborn palate

Palatal height is often employed as a diagnostic criterion of craniofacial syndromes, as is an abnormal number of frenula. Thickening of the alveolar ridges may be congenital or acquired, for example following prolonged anticonvulsant therapy. There is the risk that thickened (lateral) palatine and alveolar ridges producing narrowness of the palate may give a false impression of increased palatal height. The latter is a less common anomaly, but may be a manifestation of a number of syndromes. The distinction is important clinically, since prominent lateral palatine ridges most commonly imply a long-term deficit of neuromuscular function and thus may be an important diagnostic clue to alterations dating back to early prenatal development. Prominent lateral palatine ridges are, for example, a characteristic feature of Smith-Lemli-Opitz syndrome. They are also a feature in Apert's syndrome and in disorders in which the tongue is small, displaced or immobilized, including a narrow palate, as well as in mucopolysaccharidosis and other storage diseases with an abnormal accumulation of various metabolic substances within the connective tissue.

Clinical relevance of a metric description of the palatal configuration

'Growth is the essence of the developing system. Growth of different parts of the body follows a predictable schedule during normal development and maturation. This timetable of development is influenced and controlled by many genetic and environmental factors. Any disturbance in the normal schedule of development and growth may lead to disproportion of physical features. These imbalances may be transient and can sometimes be compensated for by later catch up growth.

In order to establish whether a palate is normal, it is necessary to have reliable information on the extent of variation of the normal gum pad. 'There is a definite need for standards of oral-facial dimensions in children within ... this age range' (6 weeks to 36 months of age). The information would be extremely valuable for the health care professional treating posttrauma patients or patients with craniofacial anomalies. Manufacturers also would benefit from metrical information for example for designing appropriate pacifiers. Data for height and weight are available up to 36 months of age, but there is lack of information on oral dimensions. Palatal height is often employed as a diagnostic criterion of craniofacial syndromes. It was suggested, as a rough guide, that 'when maximum palatal height is greater than twice the height of the teeth, it should be considered abnormally high'.

Consequences of intubation on the maxillofacial region

PT and LBW infants often require short or long-term neonatal intubation for resuscitation and to relieve respiratory distress. Complications resulting from intubation, however it is performed, are always to be expected: in cases of nasal intubation, potential problems are nasal deformation and subsequent choanal stenosis. Airway obstruction, possible hypoxia or respiratory problems may occur in cases of nasogastric tubes. Neonates and small infants are nasal breathers due to immature coordination of respiratory and oral function; only 6% of PT infants (gestational age 31 – 32 weeks) are able to breathe orally. Because PT neonates are nose breathers orotracheal intubation is often preferred to nasal intubation, but also reported to be associated with a higher rate of unplanned extubation.

As the palatal bones of fetuses are spongy and connective tissue interspersed at the midline forms a weakened palatal configuration, oral defects can easily result from the trauma of oral intubation. This may result in the inability of the tongue to meet the palate correctly and may give rise to considerable functional impairment like sucking problems and impaired middle ear function or articulation disturbances, e.g. in the form of a significantly higher incidence of fair or poor speech intelligibility in contrast to non-orally intubated infants.

The following dental complications are described as potential consequences of oral intubation and can be either caused by lack of oxygen, by the larynoscope blade or by the tube itself: enamel hypoplasia in 18 – 70% of preterm neonates, severe disruption of the developing enamel organ and deviation of the crown/root angulation, dilaceration of primary teeth, retarded eruption of primary teeth, impaired amelogenesis, effects on the position of the central incisors.

Palatal complications reported in connection with oral intubation are erosion and indentation of the alveolar ridge, notching, a high, and narrow palatal shape, asymmetry of the palate and cleft palate. It was recommended not to use the term clefting, since no oral nasal communication has been demonstrated.

Alveolar grooving, and 'palatal grooving' have also been described, never occurring in combination. The majority of articles dealing with the phenomenon fail to give a definition of palatal grooving. However, there are three exceptions:

1. Two authors defined a palatal groove as follows: "Narrow channel of variable depth located near the midline of the palate as identified by visual inspection of the maxillary cast." (Comment: Consider the variability of the term 'narrow').
2. Two other authors, performing intraoral measurement with a micrometer "from its floor to the surface of the palate at the midpoint of the hard palate," selected a palatal groove of ≥0.5 cm arbitrarily as significant. (Comment: Consider how difficult it is to make precise intraoral measurements in a tiny infant).
3. A further group stated: "By definition, a palatal groove is an architectural deformity of the palate caused by external pressure from the orotracheal tube."

There are various hypotheses on the cause of grooving:

1. It is an oral manifestation of head flattening commonly seen in very premature infants. The same compressive interplay of forces that contribute to craniofacial narrowing is transferred from the zygomatic structures through the lateral aspects of the hard palate and causes the palatal grooving.
2. The deformation results from continuous pressure of the endotracheal tube against the median palatine suture. This

might be aggravated by the direction of pressure applied to the front of the tube in order to hold it in its desired position and also by sucking and result in a pressure necrosis.
3. The groove is caused by constriction of the palate adjacent to the tube. This broadening of the alveolar ridges creates the false impression that the palate has been eroded as a groove; in fact, the palate is intact but partially obscured. This finding is confirmed metrically: "Palatal grooving did not always correspond with relative palatal depth, but did usually occur in intubated infants. We therefore consider that palatal grooving is not caused by the direct pressure of the orotracheal tube. It is more likely that it is due to overgrowth of the lateral palatine ridges." However, the term "palatal groove" might be misleading. Groove does not necessarily imply a palatal defect or cleft but rather a transient mechanical obstruction to normal ingrowth of the lateral palatine ridges.
4. Several authors regard an impeded tongue function as the cause of the palatal deformation. Grooving was observed even when the tube did not have a midline location, as there was also an absence of tongue thrust against the palatal shelves, which allowed the shelves to grow together.

Unusually prominent lateral palatine ridges have been regarded as a nonspecific feature of a variety of disorders in which there is either a neuromotor dysfunction or a malformation which prevents tongue thrust into the palatal vault, suggesting that a long-standing deficit of tongue thrust is the common pathogenetic mechanism. This is frequently associated with reports of a poor sucking reflex in early childhood. In most of these conditions the ridges ultimately appear to attain a normal adult configuration. These authors believe, however, that truly narrow, highly arched palates are a very infrequent occurrence and are confused with primarily structural aberrations of the maxilla or the palate, or with prominent lateral palatine ridges.

At age 3–5 a characteristic high palatal vault on the dental casts of formerly intubated children was still observed, and 21% of the intubated infants with high palatal vaults also had palatal grooves; nearly 1/4 of the children suffered from crossbites; neither birthweight nor intubation was related to palatal symmetry. No data was given in the abstract concerning the method nor if preterm or term children were examined.

Quality of studies

Firstly the authors[of previous studies] were already strongly involved in the matter and thus not blinded to its subject. Secondly, in only four of the "metrical control studies" did the authors state explicitly that fullterm infants had been investigated. In an additional two studies, data for term infants could be extracted by the authors of the review because all single figures concerning weight or maturity were given by the authors of these dissertations. In most of the metrical studies with term infants, the reliability of the method was not given. We have to comment that the data included in the study are the best evidence we have for the moment concerning a control group of term infants.

Thirdly, non metrical studies and studies without dental casts should be interpreted with caution due to several shortcomings: they suffered from a lack of definition or a non-uniform definition of the term "palatal grooving," from low case numbers in some studies, from the difficulty of intraoral assessments in very small babies and from subjective assessment of palatal shape. In some studies, the intra-examiner reliability was not given or statistically significant inter-examiner differences existed, whereas in one paper the subjective assessment of relative palatal height turned out to be fairly reliable (approximately 80% inter-and intraexaminer agreement).

Visual descriptions alone cannot always give rise to valid decisions on whether the alterations described in the palatal configuration are in fact palatal grooves respectively deepened palatales or only thickened lateral palatine ridges: putting the visual assessment of the palatal configuration into perspective by means of metric assessments revealed that, although oral intubation may lead to palatal grooving, palatal grooving was not necessarily associated with an increase in palatal depth, whereas in another study the subjective assessment of palatal height correlated reasonably well with the palatal index.

The above mentioned shortcomings affected the comparability of the non-metrical data and gave rise to vastly varying data on the incidence of grooving (7–90%). Subjective assessments have not the kind of discriminatory power which is nowadays desirable for identifying potential genetic, environmental or developmental associations of deformities. However, a visual inspection of the infant palate may give the pediatrician some important diagnostic clues with respect to syndromes and changed functional patterns. This is why intraoral examinations should be an integral part of postnatal pediatric routine examinations and why non-metric diagnoses were included in this review.

Fourthly, only twelve metrical studies concerning PT infant's palates were found, with the methodological quality varying widely. One had the exactness of different measuring methods as the primary interest of outcome, three examined the effect of protective appliances, four included preschool or school children of a wide age range (one study showed the mean difference in palatal width from 9 – 12 years in girls was 0.9 mm in the molar region), one measured palatal depths intraorally, entailing the risk of being imprecise, one study included term and preterm infants. In the majority of studies a problem with the reliability of the measuring method was present: Either the reliability was not given, or a significant measuring error for palatal depth was recorded, or the coefficient of variation for repeated palatal height measurements ran up to 11.73%.

Fifthly, the confounding of prematurity, ie birthweight and gestational age vs intubation in most cases cannot be resolved, as many preterm infants need the latter.

Sixthly, there is the risk of some papers being "double publications" referring to the same group of infants. This entails the risk of bias and impact on the conclusions of the review.

Seventhly, the following problems are worth to be mentioned:

The calcium phosphate metabolism has so far been taken into account in only one study, the type of milk intake in only one other. As two-thirds of the newborn's stores of calcium and phosphorus are accumulated during the third trimester of pregnancy, and a premature infant born prior to about 28 or 30 weeks gestation would have missed much of his mineral accretion, it cannot be excluded that bias came over the metrical studies on PT infants palates due to missing data on nutrition.

The development of the palate is linked to that of the mandible

and can thus not be seen in isolation: the dimensions for the maxillary gum pad do vary considerably beginning with an overjet, i.e. a sagittal distance of upper and lower jaw of >6 mm.

The development of the maxilla is linked to that of the cranial base and cranium. Only two of the metric studies in PT infants took this mutual relationship into account.

The development of the palate is subject to various functions: in comparison with the closed mouth of the term-born infant, the mouth of the PT infant is commonly open, which might have a significant implication for orofacial development and was not considered in any of the studies. Attention to the influence of oral feeding was made in only one study.

Conclusion

Considering the shortcomings of the currently available articles on palatal development (lack of uniform definitions of palatal morphology, lack of control studies with term infants, lack of studies with determination of the reliability of the measuring method), the following conclusions may be carefully drawn:

The palate of the term newborn

1. The distinctive feature of the infantile palate is the groove system. The lack of uniformity in the nomenclature of the groove system and of the frenula of the infant jaw underlines the need for a uniform definition in the anatomic terminology.
2. The shape of the palate of the term infant can considerably vary, both, visually and metrically.
3. Contradictory information is given with regard to gender differences in palatal shape of term infants.
4. With the exception of one study, in which Indian and Latino children were included, all studies reported more palatal cysts in term white children compared to black babies. Alveolar notches and alveolar lymphangioma occur more often in black neonates. In term infants, no gender differences were found with respect to alveolar notches, palatal cysts, alveolar cysts or lymphangioma.
5. Contradictory statements were given for term infants with respect to a correlation of birthweight or gender and palatal size at birth.
6. No significant differences between spontaneously and forceps delivered term infants have been described with respect to palatal size.
7. Contradictory statements were given concerning a correlation between nasal deformity and palatal symmetry, thus no conclusions concerning that subject can be drawn in this review.

The palate of the preterm/low birthweight infant

1. Orotracheal intubation has been reported to be harmful for teeth, tooth eruption, palatal shape and speech as early as 12 hours after intubation.
2. Due to a non-uniform definition and a subjective, non-metric evaluation in the majority of the studies there is a marked difference in the percentage data on the incidence of palatal grooving in PT infants (7 – 90%).
3. The following facts have been accused for provoking grooving: head flattening, pressure of an oral tube, pathologic or impeded tongue function and broadening of the alveolar ridges adjacent to the tube. Thickened palatine ridges may give a false impression of palatal height.
4. Metrically, the palates of intubated PT babies remain narrower, what has been examined up to the age of 11 years. Thus, an earlier orthodontic control of formerly orally intubated PT infants compared to non-intubated infants is advisable. From the orthodontic point of view, nasal intubation should be favored.
5. Contradictory information is given in the literature on PT infants concerning the correlation of length of intubation time and amount of grooving, the duration of 'grooving' (which was examined up to the age of ten years), the incidence of crossbites compared to non-intubated babies, a possible difference in palatal asymmetry compared to non-intubated babies, palatal depth compared to non-intubated babies. Thus, no conclusions are possible concerning those subjects on the base of this review.
6. It remained unclear, if gestation or birthweight of preterm infants were related to palatal height, due to confounding with intubation time.
7. Palatal plates have proven to protect palates with inserted tubes from deepening. Pressure dispersing pads for the head, however, did not have a significant impact on palatal height. It remained unclear, if changes in palatal width occurred due to pressure dispersing pads or due to oral feeding. There is a need of prospective studies to assess the infection rate and development of the tooth buds in children with protective plates.
8. PT children seem to have significantly less palatal cysts than term babies (be aware of different examination times for PT and term children and of the difficulty of an oral examination in a tiny infant!).
9. Up to the corrected age of 13.8 weeks, the palatal morphology of non-orally intubated PT infants does not differ from that of (probably) term infants. Beyond that time, no controlled long term studies comparing palatal dimensions of non-intubated PT children with those of non intubated term children are available. Thus, it cannot be excluded, that (e.g. as a consequence of functional impairment) PT infants do have a priori an altered palatal shape, which has been wrongly attributed to oral intubation.
10. No statement can be made on the development of biometric palatal data of term infants in the period from 1930 to present on the basis of the reviewed studies, as age groups were formed over several non-comparable months and data on the body height and weight of the probands were unfortunately lacking in most studies.
11. Further investigations in which the parents are also examined are needed to clarify the implication of genetic factors in the palatal configuration.
12. Parameters such as diet (breast milk versus PT formula), mode of feeding (bottle- versus breast-versus orogastric vs. nasogastric feeding), positioning, habits as well as biometric data and the influence of the mandible must be included more consistently in future studies than they have been to date.
13. Future studies should quote the product of palatal height and width in order to give a numerical expression of relative palatal height. As two palates with apparently different shapes may have an identical palatal index, the palatal length should also be included for a better three-dimensional understanding of palatal shape, as well.

Challenges in Critical Care: Scripps Mercy Hospital

Providing excellent patient care is a top priority for Scripps Mercy Hospital, the longest-operating hospital in San Diego, CA. To ensure state-of-the-art care in its respiratory services, the hospital recently replaced its entire fleet of ventilators with the SERVO-i ventilators equipped with BiVent.

BiVent is an effective mode of mechanical ventilation similar to Airway Pressure Release Ventilation (APRV), but with additional features. BiVent applies CPAP to maintain adequate lung volume and promote alveolar recruitment. BiVent also adds a time-cycled release phase to lower set pressure (P-low). In addition, spontaneous breathing can be integrated and is independent of the ventilator cycle.

Current research shows that APRV improves respiratory care in critically ill patients, especially patients with low compliance. In a study in Critical Care Medicine in 2005 (Vol 33 No 3, S228-240), Nader M. Habashi, MD, FCCP, an assistant professor at the University of Maryland in Baltimore, found that APRV has distinct clinical advantages for ventilator management of patients with ALI or ARDS. Among them are improvement in cardiac and renal function, decreased use of sedation, and near elimination of neuromuscular blockages. In his study, Habashi noted that some recent research suggests using APRV results in fewer ventilator days and shorter ICU stays for many patients. Although randomized controlled trials are still needed, Habashi expects APRV to become the gold standard for patients with ALI or ARDS.

BiVent is an improvement on APRV because it allows pressure support to be set independently. Also, it allows the practitioner to set auto PEEP when recruiting the lung. “Spontaneous breaths at the P-high improve dependent ventilation through pleural applied pressure changes, rather than the application of additional applied airway pressure,” explains Jodi Brewer, RCP, RRT, an educator and clinical respiratory specialist in the Respiratory Therapy Department at Scripps. “The advantage is that the recruited lung requires less pressure than the recruiting lung.”

BiVent allows Scripps’ busy trauma unit to offer leading-edge respiratory care. “Since the arrival of these ventilators,” says Stephen Kaminski, MD, FACS, a leading trauma service physician at Scripps, “we have been able to advance our ventilator care and our lung management to match state-of-the-art information.”

Scripps Mercy demands such technology because it has one of the busiest emergency departments and trauma centers in San Diego and Chula Vista, the two communities that it has served for 113 years. Last year, the hospital treated more than 50,000 ER patients and 2,200 trauma patients.

Kaminski, who was trained on APRV during his fellowship, has noticed that his trauma patients are more comfortable on BiVent. Because they are able to breathe on their own, they are not bucking the respirator, as often happens with conventional ventilation, he explains.

It is widely recognized that the use of sedation makes it more difficult to wean a patient from a ventilator. Because patients on BiVent breathe spontaneously throughout the ventilatory cycle, the mode requires much less sedation and nearly eliminates paralytics.

Thus, Kaminski has found that patients who are on the mode are often easier to wean and may be able to be weaned sooner, lowering the risk of serious complications that are commonly associated with long-term mechanical ventilation.

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Anecdotally, physicians at Scripps have found that BiVent reduces patient stays in the ICU. The department plans to confirm its anecdotal findings with a retrospective study looking at patients with the same diagnoses before and after it acquired the SERVO-i ventilators.

Kaminski believes so strongly in the benefits of BiVent that he uses it prophylactically on all his trauma patients. The earlier the intervention with BiVent, the better the outcome, he says. The only exception is for those with severe head injuries. "Patients with head injuries might require control of carbon dioxide and therefore might be better managed by automode," he notes.

BiVent, Kaminski says, works well not only as lung protection strategy but also as a salvage method. "It's good for patients at risk of ARDS and for patients who are difficult to oxygenate."

When Kaminski introduced BiVent to the five other physicians in his trauma practice, they were eager to incorporate it as well. "They all adapted it with open arms, from our senior docs to our more junior partners," he says.

George Silva, RCP, a lead respiratory therapist, says that as a Level I Trauma Center, Scripps Mercy has always been dedicated to the highest level in trauma care. "So it is the perfect place to use the BiVent mode," he says.

BiVent is proving to be the best mode for acute-care patients at Scripps as well. At Scripps Mercy, BiVent is now not only the mode of choice for trauma patients, but is also becoming so for its critically ill medical/surgical patients.

"It gives us an extra dimension in being able to ventilate our patients, especially the very sick cases," says Julian Lichter, MD, who has been Medical Director of Respiratory Care Services at Scripps Mercy since 2002. The hospital has a total of 32 intensive care beds and is among the top hospitals for cancer and cardiac care as well as bariatric surgery.

Lichter says that on several occasions, BiVent has proven to be a lifesaving mode for some patients who are more difficult to ventilate because of their size or other pre-existing health conditions. "Before we had the BiVent capability, we probably had 20% who we were not able to oxygenate or who oxygenated very poorly," Lichter says. "Now we can oxygenate upwards of 95% of patients.

While BiVent requires a change in thinking, it has become standard protocol in difficult cases, Lichter says. "In circumstances where we have patients who are difficult to ventilate, we will always use that mode to see if it helps them."

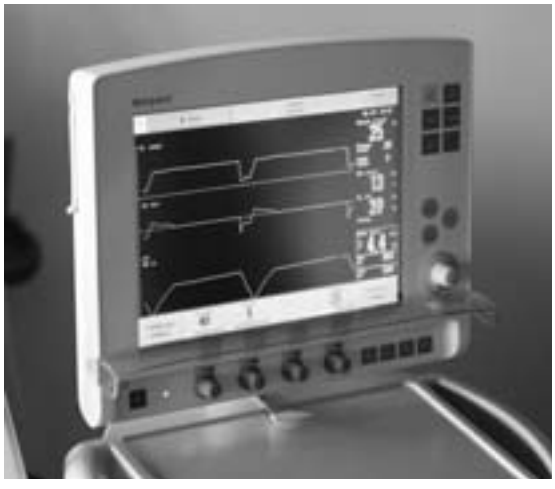
One advantage to BiVent, Lichter says, is that it can be used in conjunction with proning, which one small study suggests can improve gas exchange and survival rates among critical care patients. BiVent is easier to employ than proning because it is a matter of changing settings, whereas proning is more nurse-and-technician intense because it requires placing the patient on a special bed to be turned. Once the patients are on the bed and prone, it becomes more difficult to examine them, Lichter says. Also, he says, proning requires special care so tubes and other equipment are not displaced when the patient is turned. Still, he says, proning and BiVent can work well together when assisting difficult patients.

Another positive feature of BiVent is that it can be used in conjunction with pressure support, says Glenn Tanaka, RRT, RCP, Manager of Respiratory Care Services at Scripps Mercy. The SERVO-i allows the judicious addition of pressure support due to its floating exhalation valve, he explains.

"The idea is to use the tools so you don't have change to an oscillatory ventilation strategy," Tanaka says. "Thanks to BiVent, we reduced the need for oscillation."

Some researchers report success with BiVent in neonatal and pediatric populations as well as adults. For that reason, Scripps is looking at employing BiVent in its Neonatal Intensive Care Unit.

Physicians and staff are anxious to incorporate BiVent and help patients. As an educator, Brewer was pleasantly surprised at how well the staff embraced the new mode and other SERVO-i open-lung capabilities. "To be honest," she says, "I didn't expect people to be as enthusiastic as they were because when there is a new theory out there, it is often hard to get everyone thinking



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it is advantageous." However, Brewer says, the respiratory therapists were eager to learn BiVent and to assist the physicians in using it in appropriate cases. Brewer is helping the hospital to write protocols for BiVent.

With the support of Maquet's clinical applications specialists, a select group of specialists and RTS were trained first and they, in turn, trained others, including the nurses, on the use of BiVent. Maquet provides continued support as needed. Scripps Mercy believes in collaborative healthcare and thus cross-trains its staff, which was easy to do in this case because the ventilators and BiVent operate with a touch screen, Tanaka notes. "BiVent is very user-friendly," he says.

The respiratory therapists favored the SERVO-I when the hospital was looking to provide new and more effective ventilation strategies. A committee had narrowed the choices on the recommendations of physicians and staff, Tanaka says.

"It is very important that the therapists appreciate the ventilator and are comfortable with all its modes because they are very closely involved with the equipment," Lichter says. The hospital has 70 respiratory therapists and staff.

Tanaka says that like with everything new, the physicians and staff had to be convinced that BiVent works, but it did not take long once they saw how easily it could be employed, and how beneficial it could be for their trauma and medical patients. "Going forward," Tanaka says, "we want to be able to provide the best care possible for our patients, and we believe that with BiVent, we can do that."

The views, opinions and assertions stated by Scripps Mercy staff are those of the clinicians and administrators, and don't necessarily reflect the views of Maquet. This article was provided to Respiratory Therapy by Maquet.

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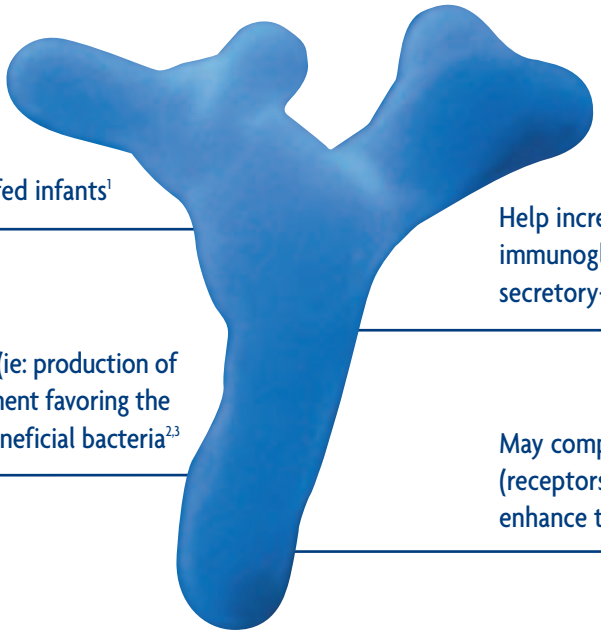

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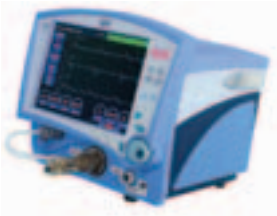

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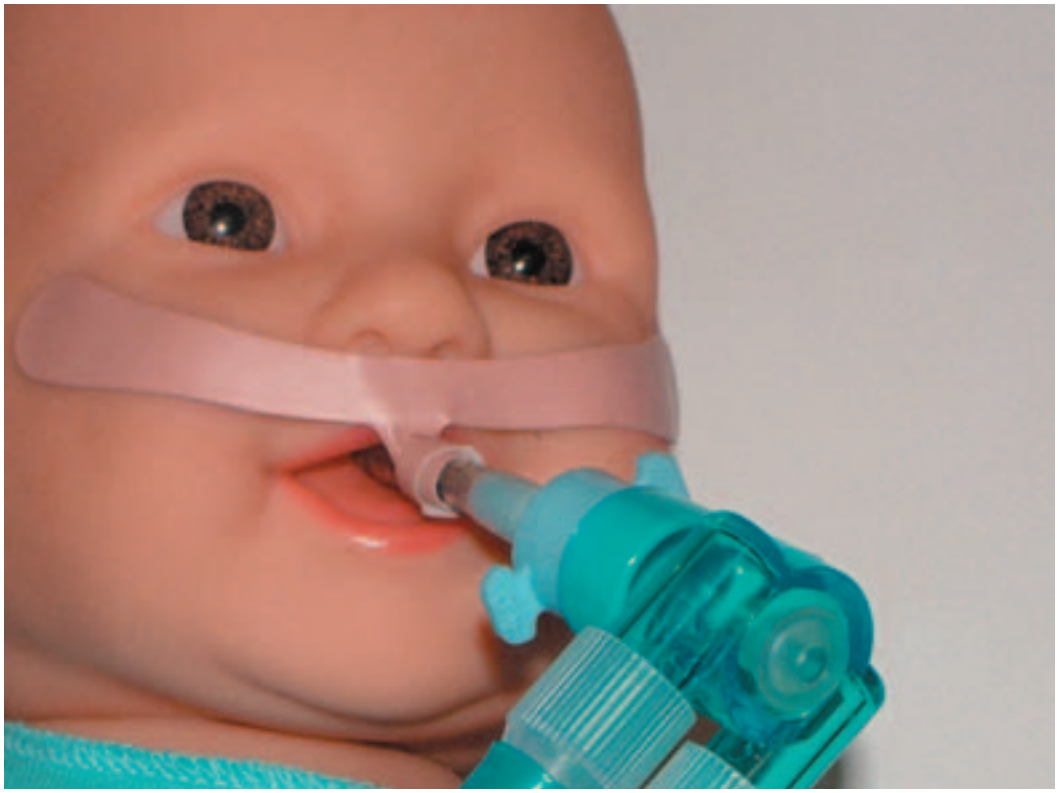

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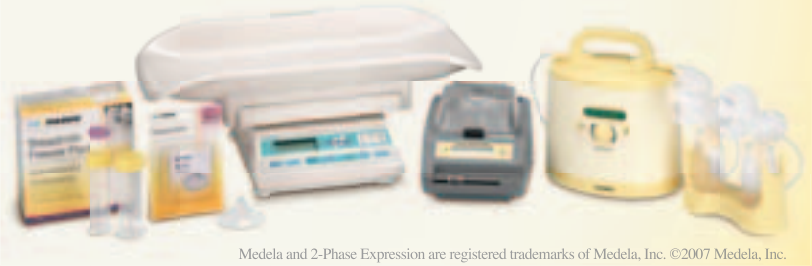

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