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neonatal INTENSIVE CARE

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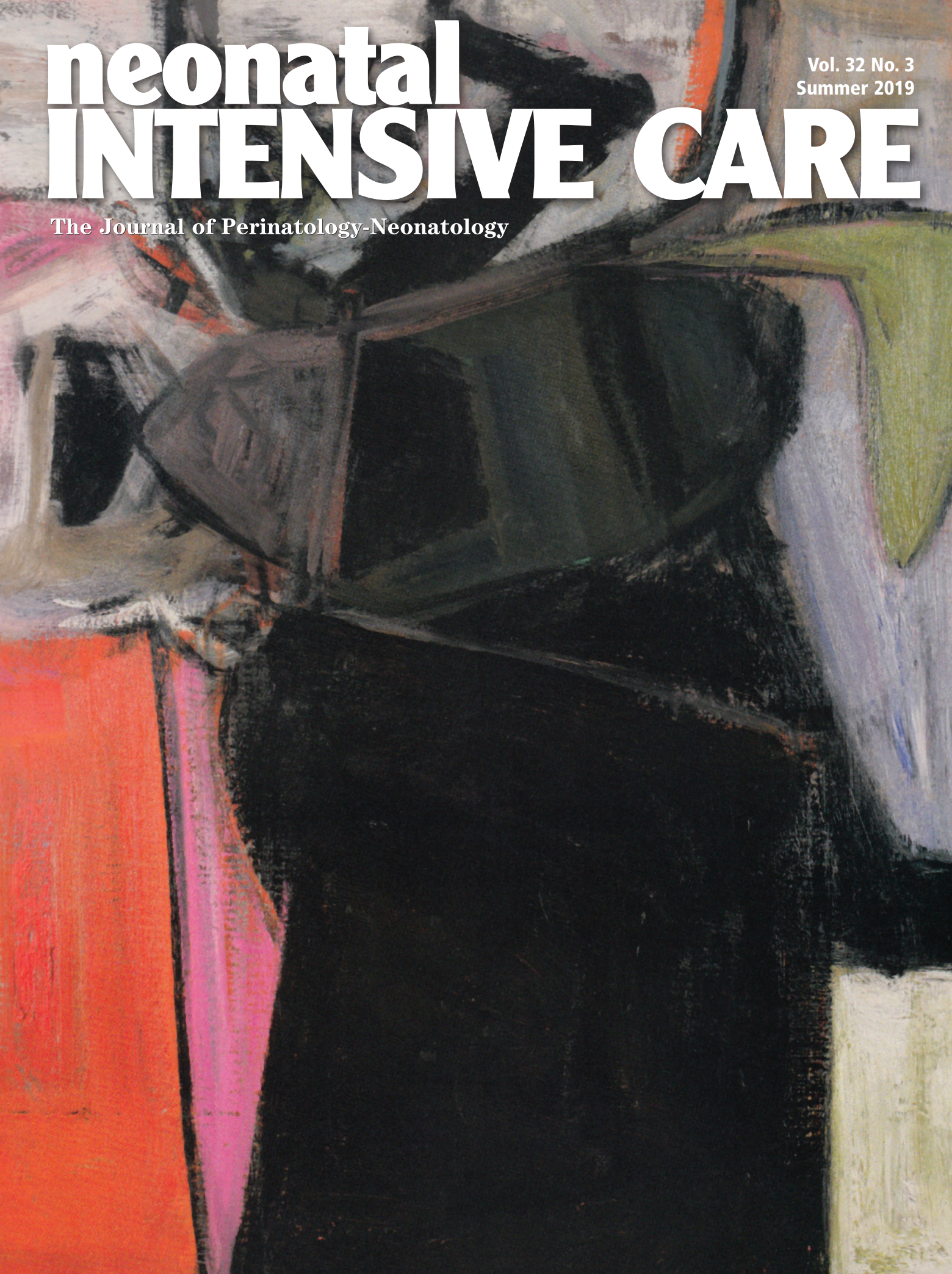

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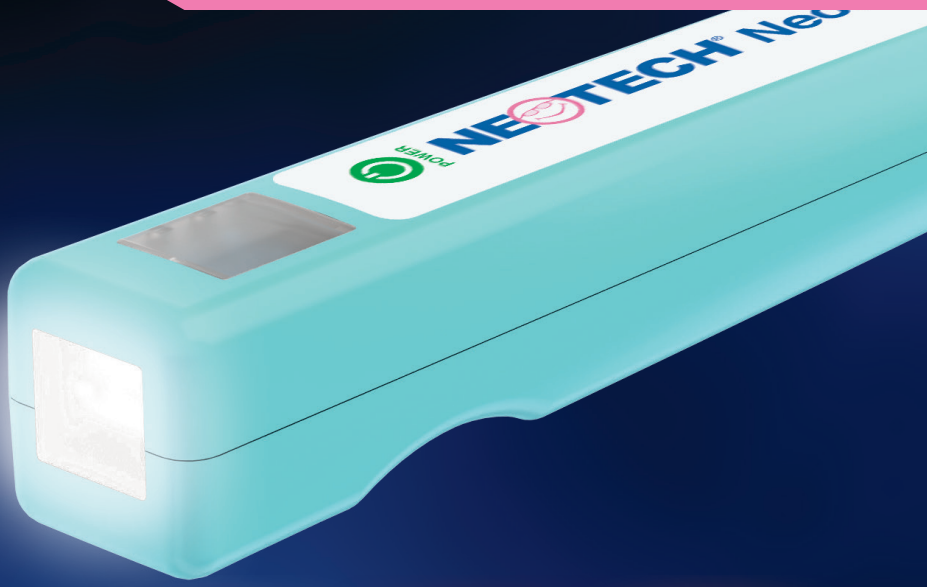

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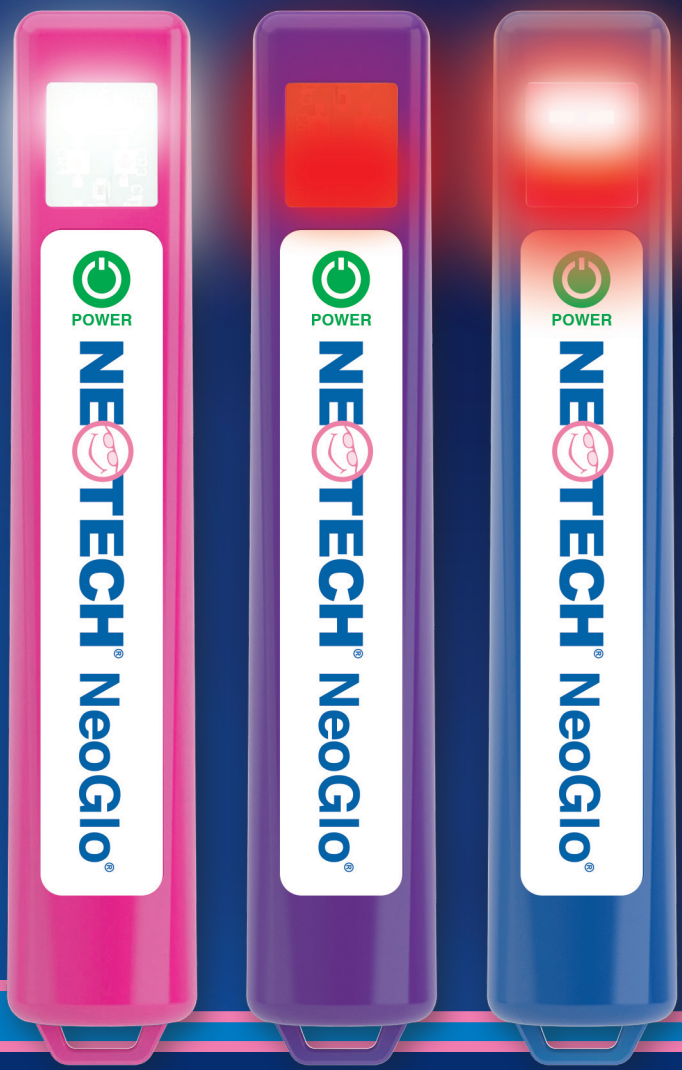

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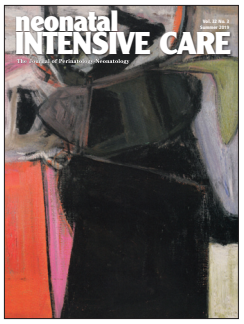

neonatal
INTENSIVE CARE

Vol. 32 No. 3
Summer 2019

Table of Contents

DEPARTMENTS

ARTICLES

Editorial Advisory Board

News

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Extreme Preterm Twins Celebrate First Birthday

Carolyn Conant of Newtown, Connecticut, had a "textbook" first pregnancy three years ago with her daughter, Teagan. That is why she was so surprised to learn about the complications she and her husband, Barton, were about to experience with the expected birth of their twins, Barton and Mabel. Although a twin pregnancy means double the excitement, it also means there is a higher risk of complications compared to a single pregnancy. One complication is the increased risk of premature birth. In the United States, about 60 percent of all twins are born prematurely (before 37 weeks gestation). As a result of this higher risk, a twin pregnancy requires more monitoring than a single pregnancy. Carolyn's obstetrician/gynecologist referred her to Dimitry Zilberman, DO, a maternal/fetal medicine specialist at Danbury Hospital, to support her throughout her pregnancy. When Carolyn was about 20 weeks pregnant, an ultrasound revealed that Mabel (Baby B at the time) had severe growth restriction. Severe growth restriction is a rare condition where a baby does not grow to a normal weight during pregnancy. The condition was most likely due to a placenta malfunction, but other factors can also lead to severe growth restriction. As the weeks progressed, Barton (Baby A at the time) was on track with appropriate growth, while Mabel continued to fall further behind. "This was a very complex case. The Conants and I had many discussions about different scenarios, and what was the best option for both babies. There was a possibility that we would have to deliver Baby B at 23 or 24 weeks to give her a chance to survive, although the odds of survival would be low. Also, the other healthy baby could have complications from being delivered too prematurely. There was also a possibility that we could wait until later in the pregnancy to deliver the babies, but then the weaker baby may not survive in utero," explained Dr Zilberman. "We decided to continue the pregnancy, with very close monitoring. Our goal was to make it to 28 weeks." Although being born at 28 weeks is still extremely preterm, Mabel would be at risk of stillbirth if they waited any longer to deliver. "We were almost certain that Mabel would have to be delivered early to give her a chance to survive. So the most heartbreaking part for my husband and me was that Barton was just along for the ride—he would have to be delivered early too, which meant he would be in for a tough fight as well," said Carolyn. "Dr Zilberman gave us safe options for extending the pregnancy. We had complete confidence in him knowing how far we could push it and when Mabel had reached her limit." Carolyn was an inpatient at Danbury Hospital the last week and a half before the babies were born. She was on continuous observation, with three monitors on her stomach—one for her, and one for each baby. During this time, Dr Zilberman worked closely with Danbury Hospital's neonatologists, Jeffrey Bartlett, DO, Director of Neonatology, Catherine Hansen, MD, and Morgan Spaight, MD. Drs. Bartlett, Hansen, and Spaight are neonatologists for the Western Connecticut Health Network (WCHN) and Connecticut Children's Medical Center (Connecticut Children's). "That week and a half in the hospital was surreal. While I tried to stay positive, I knew that something bad could be coming. Sometimes I thought, 'Is this the last day I'm going to be really happy?' because I was never sure what the next day, and toward the end, what the next hour was going to bring," recounted Carolyn. "I think because I had a rough pregnancy, I was more prepared for what was to come. I started to live life moment to moment." During their respective shifts, Drs Zilberman, Bartlett, Hansen, and Spaight kept Carolyn informed each hour about whether or not they needed to deliver the babies. Carolyn's due date was March 3, 2018. On December 13, 2017, Barton Rohde and Mabel Rose Conant were born at 28 weeks. Barton weighed 2.5 pounds. Mabel was one of the smallest babies ever born at Danbury Hospital, weighing just 1.5 pounds. Newborns who weigh less than 3.25 pounds are considered very low birth weight (VLBW).

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Only about 1.08 percent of babies born in the United States each year are VLBW. Yelena Paranyuk, MD, of Physicians for Women and Danbury Hospital, delivered the babies via Cesarean section. There were about 10 Danbury Hospital Family Birthing Center medical staff in the delivery room, including Dr Bartlett and two nurses per baby. The hospital staff stabilized both babies quickly and brought them immediately to the Neonatal Intensive Care Unit (NICU). Danbury Hospital is one of only a few in the state of Connecticut that has a Level IIIB NICU. Neonatologists, neonatal nurses, and respiratory therapists are available 24 hours a day to care for very small or very sick newborn babies. "I didn't see the babies right away because they needed immediate medical attention. I knew they were alive and had 10 fingers and 10 toes, so I felt relieved," said Carolyn. "The baby boy needed respiratory support, but his condition was mild in comparison to his sister's," said Dr Bartlett. "The baby girl had urgent breathing problems. We focused on establishing an airway and inserted a breathing tube for respiratory support via a ventilator. We also inserted central intravenous lines into her umbilical stump to expedite the delivery of nutrition to her body." After the babies were stable in the NICU, Carolyn and Barton visited their twins. "I knew they were small, but nothing could have prepared us for how heartbreakingly tiny they actually were," said Carolyn. "Despite the long road I knew we had ahead of us, I found comfort knowing my babies were in the Danbury Hospital NICU. Since Barton and I knew the babies were going to go to the NICU, we toured the space before the babies were born. We had already gotten to know the nurses and they were prepared for us, which was reassuring."Danbury Hospital's NIC-View helped Carolyn and Barton stay in close contact with Mabel when they were home with Baby Barton and their 3-year-old daughter Teagan. The bedside video camera allows parents and family members anywhere in the world to see their babies by using a secure, encrypted login. Mabel spent 99 days in the NICU. During this time, she overcame many obstacles including pneumonia and heart surgery. She underwent Patent Ductus Arteriosus (PDA) ligation at Connecticut Children's. Brendan Campbell, MD, MPH, FACS, pediatric surgeon at Connecticut Children's, surgically repaired a heart problem that was also causing Mabel lung complications. PDA is common in babies born prematurely. It was clear after medication therapy did not improve her symptoms that surgery was Mabel's best option. The surgery marked a turning point for Mabel. Her vitals—breathing and blood pressure—improved and she was much more stable. "We have been working closely with Connecticut Children's for many years before their neonatologists were officially onsite at Danbury Hospital and Norwalk Hospital starting in July 2018—part of an exciting new pediatric care alliance between WCHN and Connecticut Children's. Through the alliance, we can provide the majority of care that babies need right here at home," said Dr Bartlett. "Because of the existing relationship, babies like Mabel and their families have benefited from streamlined communication between WCHN's hospitals in Danbury and Norwalk and Connecticut Children's in Hartford." When Mabel needed surgery to repair PDA, she was back at Danbury Hospital in just three days to continue her recovery close to home. "Connecticut Children's relationship with Danbury Hospital helped a lot. When Mabel needed to go to Hartford for a special surgery, Connecticut Children's came to Danbury Hospital, stabilized her, took her in an ambulance to Hartford, and performed the surgery. She was transported back to Danbury Hospital the same way. In just three days, we were all back home and hopeful," said Carolyn. "Upon returning to Danbury Hospital, before I even got past the parking garage, I ran into Dr Hansen. Following a hug and sharing the good news about Mabel's surgery, I realized that Mabel wasn't just a patient … she was one of their babies, too." Carolyn and Barton developed very close relationships with Mabel's Danbury Hospital NICU nurses and they still keep in touch with them.

Parents Bring Newborns to ED for Many Non-Urgent Reasons

One of the hardest things about being a new parent is figuring out when babies are so sick they need to go to the emergency room and when worrisome signs or symptoms might actually be perfectly normal, doctors say. Anxious parents bring babies to the ER for all kinds of things that could go either way like goopy eyes, concerns about how the stump from the cut umbilical cord looks, vomiting, strange looking stool, irregular breathing, and jerky or unusual body movements, doctors write in the American Journal of Emergency Medicine. "Differences between potentially dangerous pathology and normal infant behavior can be subtle," said lead study author Dr Zachary Drapkin of the University of Utah in Salt Lake City. "It can be helpful if parents are counseled about what to expect over the first few days of life," Drapkin said by email. "Many of these issues could very effectively be addressed with improved access to primary care." Even for emergency department physicians, it can be challenging to distinguish normal infant signs, symptoms, and behaviors from potentially life-threatening conditions, Drapkin and colleagues write. Beyond the challenge of figuring out what infant health issues may be true emergencies, parents can also struggle to get same-day sick visits with pediatricians that could help them avoid a trip ER, said Dr Rajesh Daftary of the University of California San Francisco and Zuckerberg San

Francisco General Hospital. "It's hard to estimate what number of emergency department visits by a newborn or infant could be averted with a same day visit, but it's certainly the majority," Daftary, who wasn't involved in the paper, said by email. "The challenge is trying to obtain these same day appointments." Nurse advice phone lines may help in some cases, but it can be hard for a clinician on the phone to make an assessment without directly examining a baby, Daftary added. "Urgent care clinics can be especially helpful if they are staffed by a physician or advanced practitioner (nurse practitioner, physician assistant) specializing in pediatric care," Daftary added. "Without that level of experience, an urgent care physician may opt to transfer a child to an emergency department where a more thorough assessment can be performed."

EasyScreen Device unveiled

MAICO Diagnostics, MPLS, MN, a leading global manufacturer of hearing instruments since 1937, has unveiled the easyScreen with BERAphone. "Continuing our commitment to newborn hearing screening programs, the easyScreen unites AABR, OAE, plus the patented technology of BERAphone, our no cost disposable newborn hearing screening device," said a news release. Built on the legacy of the MAICO MB 11 BERAphone the easyScreen BERAphone allows you to perform ABR screening without the expense and waste of disposables. The reusable electrodes and ear cushion are built right into the instrument. Achieve fast test times with our technology that features the patented CE Chirp stimulus and powerful response detection algorithm. Save money; save time; help save the planet. easyScreen BERAphone®incorporates features requested by customers: Button on the BERAphone handle allows you to start, pause and stop the test right where you are, at the baby's side; Red and Blue LEDs indicate the selected test ear to assure test accuracy; LEDs provide feedback about measurement quality during the impedance test and ABR data collection; Oval, semi-transparent ear cushion helps you see the placement around the ear and provides superior fit on small heads. The power of the unique MAICO BERAphone combined with the portability and ease-of-use of the easyScreen. An unbeatable combination.

Type 1 Diabetes Tied to Increased Risk for Preterm Birth

Pregnant women with type 1 diabetes are at increased risk of delivering their baby prematurely. The risk increases as blood sugar levels rise, however women who maintain the recommended levels also risk giving birth prematurely. These are the findings from researchers at Karolinska Institutet and the Sahlgrenska Academy in Sweden, published in Annals of Internal Medicine. In a previous study published in The BMJ, the research group showed that pregnant women with type 1 diabetes were at an increased risk of having babies with heart defects. Now, a new study is published that shows how women with type 1 diabetes have an increased risk of giving birth prematurely. "High long-term blood sugar, so called HbA1c, during pregnancy is linked to an increased risk for complications, including preterm birth. The risk is highest amongst those with HbA1c levels above 8-9 per cent (approximately 60-70 mmol/mol), but even those who maintain their HbA1c (below 6.5 per cent, equivalent to <48 mmol/mol) are at an increased risk of giving birth prematurely," explains Jonas F Ludvigsson, Professor at the Department of Medical Epidemiology and Biostatistics at Karolinska Institutet and Senior Physician at the Department of Paediatrics at Örebro University Hospital. The study involved linking the

Swedish Medical Birth Register (MFR) to the Swedish National Diabetes Register (NDR) for the years 2003 to 2014. Researchers identified 2,474 infants born to women who recorded long-term glycosylated haemoglobin levels (HbA1c) during pregnancy. These were compared to 1.16 million infants born to women without diabetes. Approximately 22 per cent of infants born to women with type 1 diabetes were born prematurely, which can be compared to below five per cent of infants born to women without type 1 diabetes. 37 per cent of women with type 1 diabetes and an HbA1c level above 9 per cent gave birth prematurely. Yet even 13 per cent of those with adhering to the current recommendations for blood sugar gave birth too early. "This is the first study large enough to demonstrate a clear relationship between different HbA1c levels and preterm birth. Our study has been conducted nationally and thus provides a result that can be applied to the average woman with type 1 diabetes," says Jonas F. Ludvigsson. The study also found an increased risk of these newborns being "large for gestational age," being injured during childbirth, experiencing respiratory problems, low blood sugar and suffering from lack of oxygen ("asphyxia") in addition to higher neonatal mortality rates amongst those exposed to high blood sugar during pregnancy. Also the risk of stillbirth was linked to HbA1c levels in pregnant women with type 1 diabetes. "Now, we want to examine the long-term outcome of these children." says Jonas F Ludvigsson.

DuPont Chosen to Provide Probiotics for Sepsis Research

It is estimated that nearly 3 million newborns and 1.2 million children suffer from sepsis globally each year, with limited effective forms of prevention currently available. To help combat this,DuPont Nutrition & Biosciences (DuPont), the global leader in probiotics, will provide clinical trial probiotic and prebiotic products to the Centre for Global Child Health at The Hospital for Sick Children (SickKids) in Toronto for its research on the effects of probiotics on sepsis in infants. DuPont was selected by scientists at SickKids to provide probiotics for a new, large-scale research study in Bangladesh, which will focus on the microbiome and severe infections in infants. The research is funded by a grant from the Bill & Melinda Gates Foundation and will be conducted in collaboration with the International Centre for Diarrheal Disease Research, Bangladesh and the Child Health Research Foundation, both based in Dhaka, Bangladesh. "Sepsis continues to be a leading cause of newborn deaths, with infants in developing countries being disproportionately impacted," said Matthias Heinzel, President, DuPont Nutrition & Biosciences. "The current body of research shows that a probiotic/prebiotic blend is associated with a significant reduction in sepsis in infants, which is why we're excited to supply them for this study." DuPont will offer its scientific expertise with a comprehensive analysis of the safety and characteristics of the probiotic strain used in the clinical study. DuPont also will develop a validated molecular method for specific detection of the strain. This will support clinical research aimed at determining if a precise probiotic/prebiotic combination can effectively colonize an infant's developing microbiome, reduce the incidence of sepsis, and improve other health outcomes in early life. The study comes in the wake of a previous clinical trial in rural India, the largest infant trial to date, which showed promise in reducing the risk of neonatal sepsis using the same combination of probiotic and prebiotic. That trial, which did not involve DuPont or investigators from SickKids or its collaborators, also showed a significant reduction in lower respiratory tract infections. The findings suggested a potential beneficial effect on the development of infants' immune systems. This same probiotic strain also has been demonstrated to increase colonization of beneficial bacteria in infants. "We are honored to be able to provide our probiotic expertise for this important research," said Buffy Stahl, Global Business Development Leader at DuPont Nutrition & Biosciences, Probiotics. "This nutritional intervention holds great potential for supporting health in some of the most vulnerable people of all—babies." DuPont is committed to sustainability efforts in alignment with and support of the United Nations' Sustainable Development Goals (SDG). This latest initiative with SickKids supports SDG 3 to ensure healthy lives and promote well-being for all ages. The goal aims to end preventable deaths of newborns and children under five years of age, more specifically to reduce neonatal mortality to 12 per 1,000 live births or lower and mortality of children under five to 25 per 1,000 live births or lower by 2030.

Soft Bedding Top Cause of Suffocation Death for Sleeping Babies in US

Most sleep-related suffocation deaths among babies less than one year old happen because infants' airways got blocked by things like pillows, blankets, couch cushions or adult mattresses, a US study suggests. Unintentional suffocation is the leading cause of injury and death among infants under age one in the US, researchers note in Pediatrics. For the study, researchers examined national registry data 1,812 cases of sudden unexpected infant death (SUID) between 2011 and 2014. Overall, 250 cases, or 14 percent, involved suffocation. About 69 percent of these suffocation cases were caused by soft bedding like pillows and blankets or by infants sleeping on adult mattresses or couch cushions, which are may not be as firm as crib mattresses. "Among soft bedding deaths, more than half of infants five to 11 months old had their airways obstructed by blankets compared with less than one-third of younger infants," said lead study author Alexa Erck Lambert of the US Centers for Disease Control and Prevention in Chamberlee, Georgia. Often, the older infants in the study who were suffocated by blankets got tangled up in them, Lambert said by email. "It is likely that these older, more developed infants were mobile enough to become entangled in blankets but were not yet coordinated enough to free themselves," Lambert noted. For babies up to four months old, pillows caused suffocation almost twice as often as for older infants in the study. "Younger infants may have lacked the mobility and neck strength necessary to lift their heads to prevent an airway obstruction, especially when placed prone or on their side on a pillow," Lambert said. Almost one in five suffocation deaths in the study happened when sleeping babies got smothered by another person, which might occur when parents sleep with infants on a sofa or in an adult bed. And 12 percent of these cases were due to "wedging," when babies get trapped between two objects, such as a mattress and a wall. "Younger infants are less likely to get themselves into a wedged position because they are less mobile and cannot roll over on their own," Lambert said.

Exclusive Breastfeeding Tied to Healthier Cholesterol in Teens

Babies who consume nothing but breast milk for their first three months of life may have healthier cholesterol levels by adolescence than infants who drink formula, a new study suggests. Pediatricians recommend that mothers exclusively breastfeed infants until they're at least 6 months old. Breast milk does contain more cholesterol than formula, however, and little is known about how this might impact cholesterol

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INOMAX is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents.

Important Safety Information

- INOMAX is contraindicated in the treatment of neonates dependent on right-to-left shunting of blood.
- Abrupt discontinuation of INOMAX may lead to increasing pulmonary artery pressure and worsening oxygenation.
- Methemoglobinemia and NO_2 levels are dose dependent. Nitric oxide donor compounds may have an additive effect with INOMAX on the risk of developing methemoglobinemia. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.
- In patients with pre-existing left ventricular dysfunction, INOMAX may increase pulmonary capillary wedge pressure leading to pulmonary edema.
- Monitor for PaO_2, inspired NO_2, and methemoglobin during INOMAX administration.
- INOMAX must be administered using a calibrated INOmax DSIR® Nitric Oxide Delivery System operated by trained personnel. Only validated ventilator systems should be used in conjunction with INOMAX.
- The most common adverse reaction is hypotension.

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†Emergency deliveries of various components are often made within 4 to 6 hours but may take up to 24 hours, depending on hospital location and/or circumstances.

Reference: 1. Data on file. Hampton, NJ: Mallinckrodt Pharmaceuticals.

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Brief Summary of Prescribing Information

INDICATIONS AND USAGE

Treatment of Hypoxic Respiratory Failure

INOmax® is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilator support and other appropriate agents.

CONTRAINDICATIONS

INOmax is contraindicated in neonates dependent on right-to-left shunting of blood.

WARNINGS AND PRECAUTIONS

Rebound Pulmonary Hypertension Syndrome following Abrupt Discontinuation

Wean from INOmax. Abrupt discontinuation of INOmax may lead to worsening oxygenation and increasing pulmonary artery pressure, i.e., Rebound Pulmonary Hypertension Syndrome. Signs and symptoms of Rebound Pulmonary Hypertension Syndrome include hypoxemia, systemic hypotension, bradycardia, and decreased cardiac output. If Rebound Pulmonary Hypertension occurs, reinstate INOmax therapy immediately.

Hypoxemia from Methemoglobinemia

Nitric oxide combines with hemoglobin to form methemoglobin, which does not transport oxygen. Methemoglobin levels increase with the dose of INOmax; it can take 8 hours or more before steady-state methemoglobin levels are attained. Monitor methemoglobin and adjust the dose of INOmax to optimize oxygenation.

If methemoglobin levels do not resolve with decrease in dose or discontinuation of INOmax, additional therapy may be warranted to treat methemoglobinemia.

Airway Injury from Nitrogen Dioxide

Nitrogen dioxide (NO_2) forms in gas mixtures containing NO and O_2. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.

If there is an unexpected change in NO_2 concentration, or if the NO_2 concentration reaches 3 ppm when measured in the breathing circuit, then the delivery system should be assessed in accordance with the Nitric Oxide Delivery System O&M Manual troubleshooting section, and the NO_2 analyzer should be recalibrated. The dose of INOmax and/or FiO_2 should be adjusted as appropriate.

Worsening Heart Failure

Patients with left ventricular dysfunction treated with INOmax may experience pulmonary edema, increased pulmonary capillary wedge pressure, worsening of left ventricular dysfunction, systemic hypotension, bradycardia and cardiac arrest. Discontinue INOmax while providing symptomatic care.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from the clinical studies does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

Controlled studies have included 325 patients on INOmax doses of 5 to 80 ppm and 251 patients on placebo. Total mortality in the pooled trials was 11% on placebo and 9% on INOmax, a result adequate to exclude INOmax mortality being more than 40% worse than placebo.

In both the NINOS and CINRGI studies, the duration of hospitalization was similar in INOmax and placebo-treated groups.

From all controlled studies, at least 6 months of follow-up is available for 278 patients who received INOmax and 212 patients who received placebo. Among these patients, there was no evidence of an adverse effect of treatment on the need for rehospitalization, special medical services, pulmonary disease, or neurological sequelae.

In the NINOS study, treatment groups were similar with respect to the incidence and severity of intracranial hemorrhage, Grade IV hemorrhage, periventricular leukomalacia, cerebral infarction, seizures requiring anticonvulsant therapy, pulmonary hemorrhage, or gastrointestinal hemorrhage.

In CINRGI, the only adverse reaction (>2% higher incidence on INOmax than on placebo) was hypotension (14% vs. 11%).

Based upon post-marketing experience, accidental exposure to nitric oxide for inhalation in hospital staff has been associated with chest discomfort, dizziness, dry throat, dyspnea, and headache.

DRUG INTERACTIONS

Nitric Oxide Donor Agents

Nitric oxide donor agents such as prilocaine, sodium nitroprusside and nitroglycerine may increase the risk of developing methemoglobinemia.

OVERDOSAGE

Overdosage with INOmax is manifest by elevations in methemoglobin and pulmonary toxicities associated with inspired NO_2. Elevated NO_2 may cause acute lung injury. Elevations in methemoglobin reduce the oxygen delivery capacity of the circulation. In clinical studies, NO_2 levels >3 ppm or methemoglobin levels >7% were treated by reducing the dose of, or discontinuing, INOmax.

Methemoglobinemia that does not resolve after reduction or discontinuation of therapy can be treated with intravenous vitamin C, intravenous methylene blue, or blood transfusion, based upon the clinical situation.

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 US-1800236 August 2018

levels later in life, researchers noted. For the current study, researchers tracked 3,261 babies born in Hong Kong in 1997, until they reached an average age of 17.5 years. Overall, about 7.5% of these infants were exclusively breastfed for the first three months of life; another 40% consumed a combination of breast milk and formula and 52% drank only formula. By their late teens, compared to kids who had some formula as babies, those who didn't had lower total cholesterol levels as well as lower levels of low-density lipoprotein (LDL) cholesterol, the study found. "The differences we saw between breastfed and formula fed infants could be due to differences between the mothers who did and did not breastfeed," senior study author Mary Schooling of the University of Hong Kong said by email. "However, the adolescents in our study were born in Hong Kong in 1997 when breastfeeding was not so common and there were few differences between the mothers who did and did not breastfeed." Only about 1% of the teens in the study had high levels of LDL cholesterol. LDL levels were similar for teens who only had formula as babies and teens who were fed a combination of formula and breast milk. But exclusively breastfed babies had lower LDL and total cholesterol, and lower levels of triglycerides, or fats, compared to babies only fed formula. Overweight teens tended to have higher total and LDL cholesterol levels than adolescents at healthy weights. The study wasn't a controlled experiment designed to prove whether or how breast milk might directly impact teens' cholesterol levels, or why exclusive breastfeeding but not mixed feeding appeared to influence cholesterol levels. Even so, the results add to the evidence that early nutritional exposures—even in the first weeks or months of life—may modify so-called cardiovascular risk factors like cholesterol levels, said Christopher Owen of the Population Health Research Institute at St George's University of London. "Breast milk is high in cholesterol content and babies who are breast fed have much higher blood cholesterol compared to those formula fed," Owen, who wasn't involved in the study, said by email. "This early exposure to the high cholesterol content of breast milk may program fat metabolism, improving the body's ability to metabolize fat in later life," Owen added. "Mothers should be encouraged and supported to breast feed where possible."

Death, Severe Impairments Still Common for Tiniest Preemies

Extremely preterm infants born weighing less than 400 grams (0.9 lb) are at high risk for significant morbidity and mortality, according to data. "[Y]et with active treatment, survival to discharge and to 18 to 26 months' [corrected age (CA)] are possible," write Jane E. Brumbaugh, MD, Mayo Clinic, Rochester, Minnesota, and colleagues. "Among the 19 infants in the 2008 to 2015 birth cohort who completed follow-up evaluation (10% of liveborn infants; 21% of actively treated infants), 14 (74%) had neurodevelopmental impairment." Because low birth weight (BW) infants have a higher risk of morbidity and mortality, BW is an important predictor for survival. Indeed, BW may guide decisions to resuscitate extremely preterm infants. According to Brumbaugh and colleagues, the mortality rate for infants with a BW less than 500 grams (1.1 lb) was considered to be almost 100% in the 1980s. Although this assumption is no longer considered accurate, little is known about the outcomes of the smallest extremely preterm infants. Therefore, the researchers conducted a retrospective multicenter cohort study to determine the rate of survival to discharge among infants born weighing less than 400 grams who received active treatment, defined as any form of potentially lifesaving intervention after birth. The study included 205 (121 girls, 84 boys) extremely preterm liveborn infants born between 2008 and 2016, who had a gestational age (GA) of 22 to 26 weeks. Nearly half (101 [49.3%]) received active treatment at birth, and 26 (12.7% of all infants [95% confidence interval (CI), 8.5-18.9] of the 205 overall survived to discharge; Twenty-six (25.7%) of the 101 actively treated infants [95% CI, 17.6-35.4]) either survived to discharge home (n = 25) or were still hospitalized at 1 year (n = 1). Among infants who received active treatment, survival rate improved with increasing GA, rising from 16.7% (95% CI, 6.4-32.8) for those born at 22 to 23 weeks' GA, to 32.4% (95% CI, 18.0-49.8) for those born at 25 to 26 weeks' GA ($P < .001$). All 26 infants who survived had received active treatment at birth. In contrast, all 104 infants who did not receive active treatment died, 103 (99%) within 12 hours of birth. The main causes of death were immaturity, respiratory distress syndrome, and severe intracranial hemorrhage. For longer term outcomes, the researchers evaluated the subset of infants born between 2008 and 2015, allowing for follow-up assessments at 18 to 26 months CA. Of the 184 infants in the 2008-2015 cohort, 90 (48.9%) had received active treatment at birth, and 19 (10.3% of the cohort; 95% CI, 6.3-15.7 [21% of the actively treated infants in the cohort; 95% CI, 13-31]) survived to 18 to 26 months' CA and completed follow-up.

The Neonatal Impact of the Fukushima Nuclear Accident

Following the 2011 Fukushima nuclear accident in Japan, complex congenital heart disease (CHD) operations increased in neonates, and the number of operations remain high despite declining air levels of radiation, researchers say. Dr Kaori Murase of Nagoya City University Graduate School of Natural Sciences in Japan and colleagues studied data from 2007 to 2014 on CHD operations performed on children in Japan from birth to age 17. They separated CHDs into groups based on complexity, the time of occurrence during heart development, and age at operation. As reported online March 13 in the Journal of the American Heart Association, they found a significant 14.2% increase in the number of complex CHD operations in neonates and infants per 100,000 live births; however, no significant increase was seen in operations performed for patients ages 1 to 17. The number of CHD operations for neonates and infants has remained high, Dr Murase told Reuters Health, "in spite of the declining air dose." Therefore, it is possible that "internal exposure" and "low-dose exposure" may be having an impact by affecting the food supply and specific neighborhoods—issues that may be subjects of further study. "We also analyzed which types of CHDs were negatively influenced, so we believe this study can contribute to molecular biological research and acceleration of gene therapy and other (treatments)," he said by email. Specifically, the complex CHDs that showed significant increases were those known to occur early on, during various developmental stages of the heart, eg, single ventricle or hypoplastic left heart syndrome and very early and relatively early tetralogy of Fallot. "A nuclear accident is a problem that directly affects the lives of each of us," Dr Murase said. "We should continue to pay attention to it and not underestimate its effects." "In recent years, the number of cardiac operations has increased remarkably even in adults in Japan," he noted. The team did not analyze this trend in the current study because they would have had to consider potential confounders, such as aging. "However, we think that adults as well as neonates and infants should be monitored to enable early detection," Dr Murase said. American Heart Association expert Dr Hugh Allen of Baylor College of Medicine, Texas Children's Hospital in Houston, said. "The authors found an increase in the incidence of complex heart surgeries on infants born after the

Fukushima nuclear accident but not in older patients," he noted. "Although it is tempting to connect the dots from the accident to the increased operative volume, cause and effect cannot be determined without knowing specific patients' radiation dosages."

Reducing C-Section Rates Doesn't Harm Mother or Baby

An almost 25% reduction in cesarean deliveries for low-risk pregnancies in a California hospital quality improvement initiative did not result in worse maternal or neonatal outcomes, according to a new study. In fact, the drop in C-section rates actually occurred alongside an improvement in neonatal outcomes in those hospitals with the greatest reductions. "Some obstetricians harbor apprehensions about reducing their current high cesarean delivery rates," say Elliott K. Main, MD, and colleagues, from the California Maternal Quality Care Collaborative (CMQCC) at Stanford University School of Medicine in California. "Our findings that large reductions in cesarean delivery rates need not lead to worse neonatal or maternal outcomes is important for other hospitals and health systems embarking on this journey." "This study tells us two important things," writes Dwight J. Rouse, MD, associate editor for Obstetrics & Gynecology. "First, that a lower frequency of cesarean delivery needn't be accompanied by a higher frequency of maternal or neonatal complications and, indeed, may even be associated with fewer adverse outcomes; and second, that the success associated with implementation of the ACOG–SMFM guidelines for labor management achieved by single centers may, with a well-coordinated collaborative effort, be writ large." The study's 56 participating hospitals, which included mostly community facilities (87.5%), all had nulliparous, term, singleton, vertex (NTSV) cesarean delivery rates greater than 23.9%, the designated target rate for low-risk cesarean deliveries in the federal 2020 Healthy People goals. Their combined delivery volume over the period studied was 119,000 births, "a higher delivery volume than in all but nine US states," the authors note. Under the guidance of the CMQCC, in groups of six to eight hospitals, a physician and nurse mentor offered clinical expertise and quality improvement coaching for implementing labor management and strengthening nursing labor support as per the American College of Obstetricians and Gynecologists and Society for Maternal-Fetal Medicine (ACOG–SMFM) guidelines. Data analyzed for the study included birth certificates, routinely collected safety measures, and maternal and neonatal medical records for discharge, diagnosis, procedures, and relevant clinical data. From 2015 to 2017, rates of NTSV cesarean deliveries among participating hospitals dropped from 29.3% to 25%, resulting in a 24% lower odds of a cesarean delivery with these typically low-risk pregnancies (adjusted odds ratio [aOR], 0.76).

Prenatal Betamethasone Cost-Effective in Women at Risk for Late Preterm Delivery

Giving prenatal corticosteroids to women at high risk for delivery in the late preterm period (34 to 36 weeks' gestation) is cost-effective, according to a secondary cost analysis of the Antenatal Late Preterm Steroids (ALPS) trial. "The take-home message is that, with respect to cost, antenatal corticosteroids are both low cost and highly effective in reducing respiratory complications in pregnancies at risk for late preterm delivery from 34-36 weeks," first author Dr Cynthia Gyamfi-Bannerman from the Division of Maternal-Fetal Medicine at Columbia University in New York City said. The findings were published online today in JAMA Pediatrics. The ALPS trial showed that administration of betamethasone to women at high risk for late preterm delivery improves the rate of short-term neonatal respiratory complications. Since publication of the ALPS results in the New England Journal of Medicine in 2016, both the Society of Maternal-Fetal Medicine and American College of Obstetricians and Gynecologists (ACOG) have recommended this therapy as the standard of care, she noted. But until now, the cost implications of antenatal corticosteroid therapy were unknown. Dr Gyamfi-Bannerman and her colleagues determined costs for 1,426 mother-infant pairs treated with betamethasone and 1,395 mother-infant pairs treated with placebo in the ALPS trial. With betamethasone, the total mean woman-infant-pair cost was $4,681, which was significantly less than the mean total cost of $5,379 for women and infants in the placebo group (P=0.02). "Thus, this treatment may be an economically desirable strategy," the authors conclude. "On the basis of a 6.9% late preterm birth rate in 2015 and approximately $700 cost savings for each late preterm birth, assuming only 50% are eligible, this intervention has a potential cost saving in the United States of approximately $100 million dollars annually from the benefit in the immediate neonatal outcome alone," they point out.

New Wireless Monitors Will Let Parents Cuddle Fragile Newborns

A new wireless system for monitoring the vital signs of the most fragile newborns—those born prematurely or with debilitating diseases—could make it easier for parents to have skin to skin contact with their babies, a preliminary study suggests. Infants in the neonatal intensive care unit (NICU) typically have a large number of sensors attached to their skin, with wires emanating from them. The new system, which was tested in a study reported online March 1 in Science, accomplishes monitoring through two ultrathin wireless sensors that transmit the baby's vital signs to a base where the information can be processed in real time. The sensors—one above the baby's heart and the other on the infant's heel—"are almost like an electronic temporary tattoo," said study coauthor John Rogers, director of the Center for Bio-Integrated Electronics at Northwestern University in Evanston, Illinois. "They gently, non-invasively laminate onto the surface of the skin. They are imperceptible. You don't even know they are there." Standard sensors can damage a premature baby's skin, he added. "Premature babies, especially those at gestational ages less than 30 weeks, have skin that is highly underdeveloped, "Rogers said. "It's very common that these babies receive injury to the skin when peeling away the tapes." Another advantage of the new system is that the sensors don't need to be plugged in to a power source. They charge up in a similar way to some of the modern phones that charge wirelessly, Rogers said. The baby just needs to be within a meter from the antenna that receives vital signs information and the device that allows the sensors to keep charged, Rogers said. That means "mothers can be sitting in a chair (with the antenna mounted on the base) and have skin to skin contact and cuddling," he said. Skin to skin cuddling of low-birthweight infants has been shown to reduce mortality, severe illness, infection and length of hospital stay. Cardiorespiratory stability, sleep quality, neurodevelopment, breastfeeding and pain also appear to be improved when preemies have skin to skin contact during their hospital stay. The new system provides information on skin temperature, heart rate, respiration rate and blood oxygenation. And

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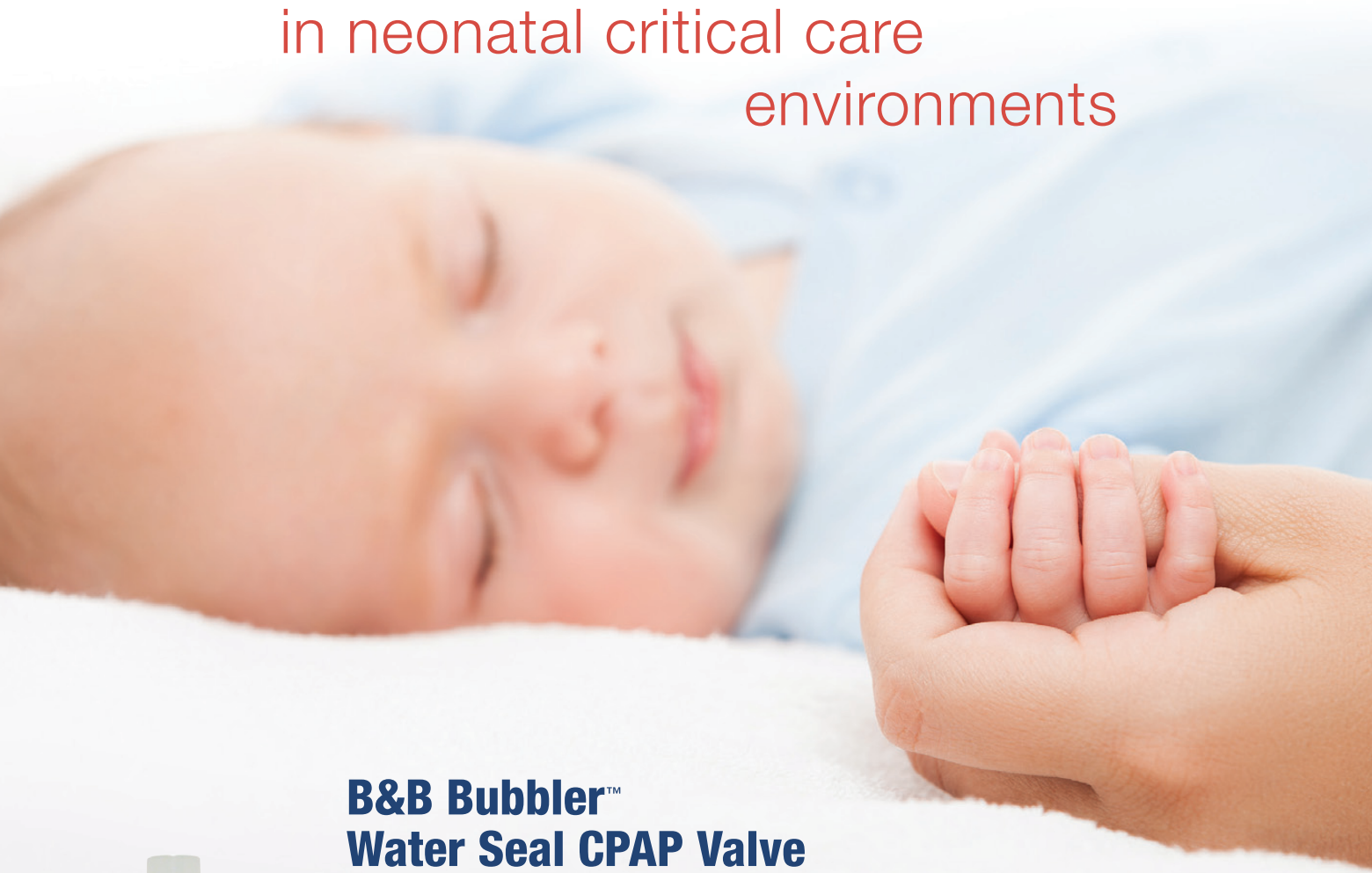

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because the two sensors are sending data in real time, it's possible to measure how quickly blood is flowing through the body, allowing doctors to calculate blood pressure, which is hard to measure in these tiny, fragile babies, Rogers said. The new study is "fascinating," said Dr Katherine Hoops, an assistant professor of pediatric critical care medicine at Johns Hopkins Medicine. "Innovations in monitoring that facilitate mobility have great potential benefit." Among the advantages of this new system is that it allows the baby "to be moved around without any worries about wires," said Dr Rakesh Sahni, a professor of pediatrics at Columbia University Irving Medical Center and medical director of the NICU at the NewYork-Presbyterian Morgan Stanley Children's Hospital. "And it allows the parents to hold their baby without worrying about whether the baby is still connected or if the wires are coming off." While calling the new system is "a really important step in improving care for our patient population," Dr Thomas Diacovo predicted that when it becomes available, not many hospitals would use it right away because of the cost. But there is one setting in which it could be implemented immediately, said Diacovo, chief of the newborn medicine program at the University of Pittsburgh Medical Center. "It would have tremendous value when you go on transport," Diacovo said. Currently "you have to take a lot of equipment to a potentially remote location and hook the baby up to various monitors. This sort of wireless system where information can be transmitted back to the home hospital could have tremendous value."

Insulin-Treated Diabetes Tied to LGA and Preterm Birth

Newborns of women with insulin-treated diabetes have the highest risk for prematurity and for being large for gestational age (LGA), according to a large study. The study also found that having type 2 diabetes before pregnancy, even when not treated with insulin, can increase the risk for LGA and prematurity. Although the effect is smaller than for insulin-treated diabetes, the risk rises among women who are overweight. The study is the largest and most comprehensive to date to evaluate the risk for LGA and prematurity in newborns of mothers with diabetes treated with insulin before pregnancy and to investigate the effect of body mass index (BMI) on these variables. "In this cohort study of 649,043 births, maternal diabetes treated with insulin was associated with a high risk for the offspring to be large and/or preterm at birth, regardless of prepregnancy body mass index, whereas type 2 diabetes not treated with insulin was associated with a mild to moderate, albeit statistically significant, risk that was stronger in mothers who were obese or severely obese," write Linghua Kong, MSc, of Karolinska Institutet, Stockholm, Sweden, and colleagues. Previous studies suggest that the babies of women who are obese and have type 1 diabetes or gestational diabetes are at increased risk for LGA and preterm birth, which can increase the risk for birth complications both to the mother and the newborn. During pregnancy, women experience an increase in insulin resistance that helps ensure that the fetus receives enough energy to grow. Prepregnancy diabetes can exacerbate the already heightened insulin resistance of pregnancy. Insulin also serves as a growth hormone to the fetus. Yet little is known about how in utero exposure to insulin treatment affects newborns. To investigate the question, researchers conducted a nationwide cohort study in Finland. They analyzed data from a national medical records database on children born from January 2004 through December 2014. They adjusted their models for maternal BMI, birth year, smoking, and other maternal factors, such as age and country of birth. The rate of LGA was highest among newborns born to mothers with insulin-treated diabetes, at 39.6%, compared with 1.5% among those born to women of normal weight who did not have diabetes (adjusted odds ratio [aOR], 43.80). The risk was also elevated among those whose mothers had type 2 diabetes (12.8%; aOR, 9.57) and among newborns of mothers with gestational diabetes (5.4%; aOR, 3.80). The likelihood of LGA did not change substantially with increasing BMI among women with insulin-treated diabetes. However, infants of insulin-treated women with moderate obesity (BMI, 30-34) still had the highest odds of LGA compared to normal weight women without diabetes (aOR, 45.04). The steepest increase in risk for LGA occurred in women with type 2 diabetes who were moderately obese. In this group, 16.4% had an LGA infant, compared to 1.5% of normal-weight women without diabetes (aOR, 12.44), which was more than three times higher than in women with type 2 diabetes who were of normal weight (aOR, 3.85).

Antenatal Steroids Tied to Reduced Birth Size

Antenatal steroid treatment to mature fetal lungs in cases of threatened premature birth may be associated with reduced birth size, even if infants go on to be born full term, according to a study. The new study is the largest on this topic to date and includes over 250,000 infants born in Finland. "Complications resulting from being born premature, especially those related to breathing problems, are the leading cause of death in infants and morbidity in survivors," first author Alina Rodriguez, PhD, Imperial College London, and University of Lincoln, UK, said in a press release issued by her institution. Steroid injections given to the mother are widely used to rapidly mature fetal lungs in countries such as the United States and in Europe, and can substantially decrease the risk of death in infants born prematurely. Guidelines recommend giving a dose of steroids to pregnant women with threatened preterm birth between 24 to 34 weeks of gestation, with a second dose repeated after 24 hours. "At present, steroid therapy is the only tool we have for maturing the lungs before premature birth. Antenatal corticosteroid therapy has been used since 1972 and attributed as a life-saving treatment for babies who would otherwise have developed severe lung disease," notes senior author Marjo-Riitta Jarvelin, MD, PhD, School of Public Health, Imperial College London. But threatened preterm birth does not always materialize, and therefore infants who go on to be born at term may be unnecessarily exposed to the potential harms of steroids. "The problem is that it is difficult to know which women will give birth prematurely and those that will go to full term when there are signs of preterm birth, so this treatment is used as a precaution," Rodriguez explained.

Inducing Labor at 41 Weeks Slightly Safer Than Waiting Longer

When pregnant women have not delivered by 41 weeks, their babies are slightly less likely to have serious complications if labor is induced, a Dutch study suggests. Researchers randomly assigned 1,801 healthy women who were 41 weeks pregnant either to labor induction or expectant management, with induction if needed by 42 weeks. Overall, 1.7% of women who were induced at 41 weeks had babies with serious complications, compared with 3.1% of mothers in the expectant management group, researchers reported. "Most pregnancies have a good outcome with both strategies, with a small difference in the risk of adverse perinatal outcomes

favoring induction of labor," said senior study author Dr Esteriek de Miranda of the University of Amsterdam. "The absolute risk of severe adverse outcome is low, which justifies women's choice for either policy," de Miranda said by email. The World Health Organization recommends labor induction at 42 weeks. But previous research on the difference in outcomes between 41 and 42 weeks' gestation has been mixed, and guidelines in many countries differ on which approach is best. There was one stillbirth in the induction group and two with expectant management, the study found. With induction at 41 weeks, three babies were admitted to the NICU, compared to eight in the expectant management group. Eleven babies in the induction group and 23 in the expectant management group had Apgar scores low enough to indicate they needed urgent medical attention. No babies induced at 41 weeks and three who arrived later had Apgar scores so low they indicated the potential for serious health impairments. Expectant management until 42 weeks is the current standard of care for women with low-risk pregnancies in the Netherlands. The goal of the study was to show whether expectant management was worse than induction at 41 weeks, and the study didn't find a big enough difference in outcomes to support this conclusion, the authors note.

Study: Climate change could lead to worse heart defects in babies

Rising temperatures associated with climate change could trigger heart defects in babies, according to a new study in Wednesday's Journal of the American Heart Association. Mothers exposed to extreme heat during the early stages of their pregnancy, approximately three to eight weeks post-conception, could lead to more babies being born with congenital heart defects (CHDs) between 2025 and 2035. The study found that higher temperatures caused by climate change could result in as many as 7,000 additional cases of CHDs in the United States during that time. Midwestern states such as Iowa will potentially have the highest increase in mothers exposed to excessively hot days during the spring and summer months, followed by the southern states such as Georgia and North Carolina. The study notes that there is a lack of research regarding heat-related CHDs, although animal studies have found that heat exposure during early pregnancy can cause fetal cell death or severe fetal malformations. CHDs are among the most common birth defects and are the leading cause of infant morbidity and mortality in the US, the American Heart Association noted. The US Census Bureau has also projected that the number of births across the nation will continue to increase through 2030, estimating that 4.2 million pregnant women could be at risk of rising temperatures. "The potential increases in both the number of pregnant women and maternal heat exposure suggest an alarming effect that climate change may have on reproductive health," the study states.

Negative Impacts of Having Babies 'Room-in'

Hospital efforts to support breastfeeding by having babies "room-in" with mothers may have a rare unintended consequence: an increased risk of newborn falls. Neonatal falls are increasingly recognized as a postpartum safety risk, with as many as 1,600 newborn falls occurring in US hospitals each year, researchers note in Pediatrics. While this represents a miniscule fraction of all births, doctors are increasingly concerned that at least some of these falls may be resulting from new mothers falling asleep while breastfeeding babies in their hospital beds. To assess the potential for breastfeeding

programs to influence the risk of newborn falls, researchers looked at three cases that happened after one hospital initiated several changes designed to support breastfeeding and mother-baby bonding. "To encourage successful breastfeeding, it is important to keep mothers and babies together in one room, as much as possible," said lead study author Dr Colleen Hughes Driscoll of the University of Maryland School of Medicine in Baltimore. "This practice is somewhat different from earlier decades when babies spent a significant part of the postpartum hospitalization in the nursery, away from their mother," Driscoll said by email. "Though this separation was likely a barrier to successful breastfeeding, it may have provided additional opportunities for mothers to rest and recover." The researchers examined data on newborn falls recorded in medical records from January 2011 to February 2018. They also looked at data on breastfeeding from medical records and from patient surveys done starting in 2015 as part of a new effort to support breastfeeding and rooming-in at the hospital. Three falls occurred within one year of starting a range of breastfeeding supports the hospital needed to implement in order to be designated as a "baby friendly hospital." Qualifying as Baby-Friendly, under the joint WHO and UNICEF program that created the designation, requires policies that include educating families to make informed decisions about infant feeding, encouraging mothers to hold babies skin-to-skin right after birth, allowing rooming-in and offering lactation support. "We found that as we improved our ability to support mothers with successful breastfeeding there was a surge in newborn falls," Driscoll said. "This suggests that we may be adding to the burden of maternal fatigue, and increasing the risk of newborn falls."

No Reason to Delay BCG Vaccine in Low Birthweight Preterm Babies

There is no reason to delay administration of bacillus Calmette-Guerin (BCG) vaccination for preterm and/or low birthweight infants, according to findings from a systematic literature review and meta-analysis. The evidence supports BCG vaccination within 7 days of birth in clinically stable infants born preterm (after <30 weeks' gestational age) and/or of low birthweight (weighing >1.5 kg), the authors say. In a report in JAMA Pediatrics, Dr Shiraz Badurdeen from the Newborn Research Center, The Royal Women's Hospital, Victoria, Australia and colleagues note that BCG vaccine, the only approved vaccine for prevention of tuberculosis (TB), is typically given soon after birth to infants born at term. However, for the 15 million infants born preterm and 20 million born with low birthweight each year, administration is commonly delayed due to uncertainty about safety and immunogenicity. To investigate further, the researchers identified 40 studies relevant studies that included infants born at 26 to 37 weeks' gestational age and/or weighing 0.69 to 2.5 kg at birth.

The BCG vaccine was administered at or before 7 days of life in 10,568 clinically stable infants who were preterm and/or had low birthweight. In 4,310 infants, vaccination was delayed and given at varying times between 8 days and 12 months after birth. Most of the studies involved healthy neonates born at more than 30 weeks' gestational age or weighing more than 1.5 kg and reported no increased risk of adverse reactions or infant death after BCG vaccination within 7 days of birth compared with BCG vaccination at later points, the authors say. There were no differences between early and delayed BCG vaccination for scar formation (relative risk, 1.01; 95% confidence interval 0.95 to 1.07) or tuberculin skin test (TST) conversion (RR, 0.97; 95% CI, 0.84 to 1.13). None of the studies evaluated protective efficacy comparing early versus late BCG.

Golimumab Detectable in Fetal Circulation

Golimumab was detected in the circulation of a fetus whose mother was being treated with the drug for ulcerative colitis, according to a case study from France. "In this report, we demonstrated that golimumab was detectable in the fetal circulation after prolonged exposure, with a significant accumulation," researchers write in a letter to the editor in the Journal of Crohn's and Colitis. "Golimumab was found in the baby's blood but there was no untoward consequence to the baby. These are not surprising findings as other monoclonal antibodies, such as infliximab and adalimumab, have similar findings and safety," Dr Miguel Regueiro, chair of the department of gastroenterology and hepatology at Cleveland Clinic in Ohio, told Reuters Health by email. He was not involved in the report. Dr Paul Berveiller of Centre Hospitalier Intercommunal de Poissy-Saint Germain and colleagues reported the case of a 28-year-old nulliparous woman with ulcerative colitis who became pregnant. Before her pregnancy, she had been treated with mesalazine and golimumab 100 mg twice a month, and she continued to be treated with golimumab throughout her pregnancy. The woman's pregnancy was normal and she delivered a healthy 2,805 g (6 lb) male infant at 37+6 weeks, three days after her last golimumab dose. Immediately after the delivery, golimumab concentrations reached 6.6 ug/mL in the mother's plasma and 8 ug/mL in the neonate's cord blood (121% of maternal concentrations). The pediatric team advised the mother that the baby should not be breastfed or receive any live vaccine during his first year. The researchers found no complications over seven months of follow-up.

Neonatal Abstinence Syndrome a Risk With Kratom Use in Pregnancy

There is a risk for neonatal abstinence syndrome (NAS) in women who use kratom during pregnancy to self-treat opioid withdrawal symptoms, doctors caution in a report. Kratom is an herbal supplement widely available on the Internet and in retail outlets as a powder, tea and capsule. Its use is increasing in the US with marketing campaigns touting it as a nonopioid remedy for opioid withdrawal. However, the US Food and Drug Administration (FDA) recently warned that compounds in kratom act like prescription-strength opioids. In their paper, Dr Whitney Eldridge and colleagues at St Joseph Women's Hospital in Tampa, Florida, describe the case of an infant with NAS born to a mother who used kratom tea daily throughout her pregnancy to help with sleep and opioid withdrawal symptoms. The mother had a seven-year history of oxycodone use but had successfully completed rehab for the addiction. Her last oxycodone use was two years before delivery and her urine was negative for drugs on admission for delivery. The infant was born at term and roomed with the mother after an uncomplicated cesarean delivery. At 33 hours of age, the baby showed signs "concerning" for opioid withdrawal including jitteriness, excessive sucking, facial excoriations and irritability. When the baby's father disclosed the mother's use of kratom daily during pregnancy, the infant was diagnosed with NAS and transferred to the neonatal ICU for further evaluation and management. In the neonatal intensive-care unit, the baby's Finnegan NAS scores

Continued on page 44…

The Benefits of Human Milk Oligosaccharides (HMOs) in Infant Nutrition

In this feature, Neonatal Intensive Care interviews clinicians and researchers about important topics in neonatal care and products that support best practices for vulnerable preterm infants. This interview is with Victoria Niklas, MD, Vice President, Innovation and Medical Communication, Prolacta Bioscience, and Professor of Pediatrics, UCLA David Geffen School of Medicine, Los Angeles; and Chloe Autran, PhD, HMO Business Development Manager, Prolacta Bioscience

Neonatal Intensive Care: HMOs and infant nutrition—these are subjects of increasing interest to researchers and to neonatologists and other healthcare professionals who care for premature infants. What, exactly, are HMOs?
Chloe Autran: Human milk oligosaccharides (HMOs)—are a family of approximately 200 structurally complex and diverse sugars that are unique to human milk.[1] HMOs are the third-most-abundant component in human milk, after lactose and lipids, and are more abundant than protein.[2] Although hundreds of structures of HMOs are found in human milk, an individual mother may have far fewer.[1,3] Indeed, the concentration and spectrum of HMOs in an individual woman's milk may vary across the stages of lactation and between women due to genetic factors. Nutritional and environmental factors may also play a role, although the precise nature of these influences is not well defined.[3]

HMOs provide many benefits to the developing infant, but unlike the nutritional components in human milk (lactose, fats, and proteins), HMOs are not metabolized by the infant as an energy source. The majority of HMOs pass through the stomach and the small intestine, arriving in the large intestine, where beneficial bacteria metabolize them and support the establishment of a healthy gut microbiome.[1] In addition to this prebiotic function (influence on the infant's gut microbiome), HMOs function as decoy receptors, blocking the action of toxins and infection by bacteria and viruses in the gut. Since a low concentration of HMOs is found in the bloodstream and the urine of breastfed infants, HMOs may also be absorbed across the gut lining, although this represents only a fraction of the HMOs consumed by the infant. The precise role of HMOs in the circulation is not fully understood and may relate to the role of HMOs in immune cell maturation, trafficking, or overall function in the gut or the systemic immune system. In this way, HMOs may play a role in the maturation of the immune system, thereby reducing the infant's susceptibility to infections.[2] Moreover, a subset of HMOs are purported to affect brain development.[4]

NIC: There are many different HMOs in breast milk. What are HMOs composed of, and what are the implications of the different types?
CA: The structures of individual HMOs are complex, but they all follow a basic blueprint. HMOs are made up of a combination of five monosaccharide "building blocks." Glucose and galactose form the lactose backbone, which is common to all HMOs. Lactose can be elongated with the addition of lacto-N-biose or N-acetyllactosamine, which are both disaccharides consisting of galactose and N-acetylglucosamine. Repeating units of these disaccharides can extend HMOs in a linear or branching fashion. The addition of the individual monosaccharides fucose or sialic acid can occur as terminal residues directly on the lactose backbone or on the extended chain of more complex structures. The addition of sialic acid introduces a negative charge, and thus all sialylated HMOs are acidic HMOs. By contrast, all other HMOs (which can be subdivided into fucosylated and non-fucosylated HMOs) have a neutral charge and are collectively referred to as neutral HMOs.[3] Although more complete data are emerging, different HMOs likely have different functions; therefore, a complete spectrum of HMOs are necessary to provide the infant with the full benefits of HMOs.[2]

NIC: What is the most well-studied function of HMOs in an infant's body?
CA: The prebiotic function of HMOs is the oldest known and most well-studied function.[3] Prebiotics are substances that induce the growth and stimulate the function of beneficial bacteria, such as the *Bifidobacterium* and *Lactobacillus* species, in the gut.[5,6] Prebiotics support the growth of beneficial bacteria and reduce the growth of harmful bacteria and pathogens, thus improving the health of the infant's gut microbiome. A healthy microbiome reduces the risk of dysbiosis-related diseases, such as necrotizing enterocolitis (NEC) and sepsis. Reduction of dysbiosis risk in preterm infants is important, as the use of broad-spectrum antibiotics, invasive procedures, and prolonged hospitalization increase this risk.[6]

NIC: What other functions do HMOs serve?
CA: HMOs function in several ways to prevent infections throughout the gut. HMOs resemble glycan receptors used by pathogens to infect epithelial cells lining the gut. Moreover, HMOs may block the binding of toxins to intestinal cells in the gut. Therefore, HMOs act as "decoy receptors," blocking infections by bacteria and viruses or the action of epithelial toxins. The binding of HMOs to other glycans on epithelial cells also influences gene expression by epithelial cells that are important for epithelial cell growth, repair, and maturation in the maintenance of barrier function in the gut. HMOs also play an essential role in the maturation of the newborn's immune system by interacting with various immune cells in the gut and in systemic circulation, thereby regulating immune cell activity and

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inflammation.[3,7] In addition, some studies indicate that sialylated HMOs may influence neurodevelopment by functioning as a supplementary source of sialic acid, which is critical for brain development. Collectively, other functions of HMOs are not as well described in infants but are supported by extensive *in vitro* and *in vivo* animal models, and the extended benefits of HMOs in newborn infants have yet to be fully defined.[4]

NIC: How do HMOs reduce disease and benefit a premature infant's health and development?
Victoria Niklas: HMOs may be the "secret ingredient" giving human milk its myriad of health advantages beyond nutrition to foster appropriate growth. Many of the health outcomes attributed to an exclusive human milk diet can be tied back to the immunity, prebiotic, and gut maturation benefits that HMOs promote.[1] These health outcomes have included significant decreases in mortality, NEC, late-onset sepsis, retinopathy of prematurity, and bronchopulmonary dysplasia in infants weighing between 500 and 1250 grams who were fed an exclusive human milk diet including a human milk-based human milk fortifier.[8,9]

There is ample evidence showing that a cow milk-based diet incites NEC by promoting the expansion of pathogenic bacteria in dysbiosis, as well as damaging the intestinal lining, thereby increasing gut permeability and permitting bacterial invasion into the gut lining. Bacterial invasion results in a proinflammatory cascade that is characteristic of NEC, resulting in further damage to the intestinal epithelium and, in severe cases, leading to the destruction of the intestine with perforation, which may lead to death. As a bloom of pathogenic bacteria may precede the onset of NEC, dysbiosis may be a primary risk factor for infants that go on to develop NEC. Because HMOs have the potential to prevent dysbiosis, their actions in the gut may be vital in reducing early steps in the pathogenesis of NEC.[10]

NIC: Some formula companies are adding one or two "HMOs" to their nutritional products for term babies. Are these HMOs "magic bullets" of some kind? Would a formula containing only a few HMOs make sense for premature infants?
VN: No cow milk-based formula contains the concentration and spectrum of oligosaccharides that are naturally found in human milk. The diversity of HMOs in human milk suggests that individual HMOs, or a group of a small number of HMOs, would not be sufficient to provide the mutual benefits of HMOs that reduce infections, support the immune system, and enhance an infant's growth and development.

To imitate the beneficial effects of mother-made HMOs, some cow milk-based infant formulas have been manufactured to contain one or two synthetically engineered oligosaccharides. These additions at best represent a mere fraction of the possible oligosaccharide content in human milk.[1] In fact, feeding infants just one or two of the up to 200 known HMOs may alter the development of the microbial community in the gut, leading to unintended short and long-term adverse health outcomes related to an altered microbiome in the preterm infant, such as NEC, sepsis, immune cell activation, and uncontrolled inflammation.[1,7,11]

NIC: Some healthcare providers are adding probiotics to the care plan of preterm and term infants. Do probiotics take the place of HMOs, or are they both critical in a premature baby's diet?
VN: Probiotics are beneficial bacteria intended to promote a healthy, balanced gut environment in an infant, in which pathogenic organisms do not outnumber "good" bacteria, such as *Bifidobacteria* and *Lactobacilli*. Prebiotics stimulate the growth and function of beneficial bacteria, while probiotics are the general term used to describe beneficial bacteria. When these bacteria are purified and isolated for consumption, they are called probiotics. HMOs are prebiotics that are naturally occurring in human milk, so infants fed human milk are receiving the prebiotic benefit of HMOs. In addition, infants fed fresh mother's milk also receive commensal bacteria comprising the milk's microbiome.[6] The microbiome of milk is significantly reduced or eliminated with pasteurization.[12] While some evidence suggests that probiotics may prevent NEC and sepsis in deficient birth weight infants, more research is needed to determine whether the addition of probiotics is of benefit to preterm infants.[13]

NIC: Prolacta's human milk fortifiers and ready-to-feed premature infant formulas—indeed, all of Prolacta's products—are 100% human milk based. Is there an HMO advantage here?
VN: There is a benefit to an exclusive human milk diet, whether based on mother's milk or donor milk, fortified with an exclusively human milk-derived human milk fortifier. The manufacture of Prolacta's donor milk, ready-to-feed products, and fortifiers uses batches of donor milk collected from 100 or more donors. Hence, all products contain a full spectrum of HMOs, thereby maximizing the various health benefits of HMOs.[14,15] The HMO advantage in an exclusive human milk diet is the full spectrum of HMOs.

NIC: Prolacta products are manufactured starting with 100% human donor milk, but that milk goes through a robust production process that includes pasteurization, ultrafiltration, and formulation. What does that mean for the final products?
VN: Prolacta's industry-leading manufacturing practices preserve the concentration and diversity of naturally occurring HMOs in its products. As demonstrated in laboratory studies, HMOs are unaffected by the proprietary pasteurization and ultrafiltration methods Prolacta uses in the manufacture of its human milk fortifiers. Additional studies demonstrate that the prebiotic activity of the HMOs is preserved as well.[15]

NIC: If a premature baby is already consuming breast milk or donor milk containing HMOs, what's the added benefit of a fortifier made from human milk?
VN: The key proven benefit of using a human milk-based fortifier is this: Fortifying human milk with a product made from human milk keeps a preterm baby on an exclusive human milk diet devoid of the deleterious effects of cow's milk. Moreover, clinical evidence has demonstrated that when used as part of an exclusive human milk diet, Prolacta's 100% human milk-based neonatal fortifiers—containing the full spectrum of mother-made HMOs—are associated with lower mortality and morbidity in extremely premature infants weighing between 500 and 1250 grams without compromising growth.[16]

NIC: With all the research currently being done on HMOs, can you comment on other areas where they may have an impact on human health?
VN: HMOs are indeed the subject of much current research, but a great deal remains to be discovered about the precise functions and potential clinical applications of HMOs. The benefits of HMOs may go beyond infancy. HMOs may even serve a purpose

as therapeutics for adults to treat diseases where dysbiosis plays an essential role, such as inflammatory bowel diseases and obesity.[17]

Currently, however, preterm infants born weighing less than 1250 grams should most certainly always receive an HMO-rich exclusive human milk diet.[8,9,16]

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The Benefits of the Smart Monitor 2 in Assessing Premature Infants

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. This interview is with Pam Stading, MPH, RN NE-BC, Patient Care Manager, Cardiopulmonary Services for Children's Minnesota about the Smart Monitor 2.

The Smart Monitor 2 family of cardiorespiratory event monitors can be used in the hospital, as well as the home, to provide caregivers with an understanding of the physical vulnerabilities of at-risk preterm infants, low birth weight infants and those infants that have tested positive for opiates. In the clinical setting, Smart Monitor 2 PS (Professional Series) can be used to measure heart rate, respiration and O2 saturation levels that can be evaluated to aid in step-down or discharge planning and follow-up care. Used as a diagnostic tool Smart Monitor 2 PS can document central apnea, bradycardia, hypopnea and other apparent life threatening events (aka BRUEs). In the home, Smart Monitor Home Care can alert anxious parents to potential BRUEs and provide clinicians with downloadable data they can access for interpretation and prescribe an appropriate course of care. In addition to monitoring preterm infants the monitors are cleared for pediatric and adult patients. The Smart Monitor 2 product line is the only FDA approved infant apnea monitor.

Apnea of prematurity is the most common problem in premature neonates. The earlier a baby is born before full term, the higher the likelihood of having apnea of prematurity. Smart Monitor 2 PS improves the bedside detection of apnea of prematurity and allows a physician to preset alarm limits for patients. These limits can be changed to accommodate the age related norms of this patient population.

Neonatal Intensive Care: The Smart Monitor 2 PS is used to assist in the bedside detection of apnea of prematurity. What has been your experience with the use of Smart Monitor 2 PS to detect apnea of prematurity?
Pam Stading: At Children's Minnesota, as a preterm infant approaches discharge, a Smart Monitor 2 PS may be placed on the infant for monitoring and recording purposes. The Smart Monitor 2 PS is interfaced with our nurse call system to alert bedside nurses of any violation in monitoring parameters. Further use of the Smart Monitor 2 PS unit is described more fully below.

Smart Monitor 2 PS has been used by some physicians to manage infants that may have subtle or intermittent problems such as cardiac conditions, seizures, parental neglect or abuse, or the onset of infections.

NIC: How has your institution used the Smart Monitor 2 PS to assist in the detection of these disorders? What other diagnosis has your institution been able to detect through the use of Smart Monitor 2 PS?
PS: The Smart Monitor 2 PS unit is the apnea monitor of choice in all of Children's Minnesota acute Medical/Surgical units when an infant is hospitalized with any apnea related diagnoses (ALTE/BRUE) or other diagnoses requiring the ability to monitor all clinical parameters (apnea, heart rate, and oxygen saturation).

The added feature of being able to record alarm conditions is invaluable for objective assessment of any alarms that occur during the hospital stay and evaluation.

The Smart Monitor 2 PS has contributed to the diagnosis of preterm infants with infections, and/or infants with seizures, cardiac conditions and Munchhausen Syndrome by Proxy.

NIC: What are some of the other ways your hospital has used the Smart Monitor 2 PS in the hospital?
PS: Children's Minnesota uses the Smart Monitor 2 PS to monitor and record apnea, heart rate and oxygen saturation when we perform diagnostic car seat evaluations.

We use the Smart Monitor 2 PS with our Smart Recorder to perform bedside 4-channel pneumogram recordings (continuous recordings).

Children's Minnesota also offers these bedside recording services to other neonatal and pediatric metro hospitals for diagnostic evaluations.

Children's Minnesota Apnea Program discharges infants requiring apnea monitoring in the home with Smart Monitor 2 Home Care.

The Smart Monitor 2 PS provides important documentation including multi-parameter recording of ECG, heart rate, respiration, SpO2 when a preset alarm parameter is violated. These monitors provide near diagnostic quality waveforms to aid in the diagnosis and treatment of cardiac arrhythmias and respiratory anomalies. Having waveforms and documented events has clinical benefits.

NIC: How has your institution benefitted clinically with the use of Smart Monitor 2 PS and the recorded waveforms?
PS: In my opinion, the use of the Smart Monitor 2 PS with associated multi-parameter event recordings is why this monitor

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is set apart from all other bedside monitoring options. The ability to record any alarm conditions to download and review actual waveforms of the alarm condition provides objective clinical information useful to determine clinical interventions that may be necessary (caffeine citrate, home monitoring, and/or other diagnostic testing).

There is no standardization as to how long to keep premature infants in the NICU. Many nurseries will put infants that are otherwise ready to be discharged (taking feedings well, able to maintain their temperature and growing) on a 5-7 day apnea-bradycardia watch. Physicians have used the Smart Monitor 2 PS to track the progress of these premature infants to determine the eligibility of discharge.

NIC: How has your facility utilized Smart Monitor 2 PS to determine if a premature infant should be discharged?
PS: In our neonatal areas, when a preterm infant has reached a stable feeding regimen and growth pattern, maintaining their body temperature and not experiencing monitor alarms resulting in the need for vigorous stimulation, we will place the Smart Monitor 2 PS for a 12-18 hour recording period at the bedside. The bedside nurse documents feeding times and any alarms that may occur during this recording period. This information is downloaded, scored and a report prepared through the Synergy-E software for the Neonatologist managing the infant's hospitalization. The waveforms from the recording are available for the Neonatologist to view as well.

This objective recording information, along with other clinical preterm infant information is used to determine the infant's readiness for discharge.

The Smart Monitor 2 PS provides important documentation including multi parameter recording of ECG, heart rate, respiration, SpO2 when an alarm or record setting is violated. The monitor provides near diagnostic quality ECG waveforms that aid in the diagnosis and treatment of cardiac arrhythmias and respiratory anomalies. The data can be downloaded into the Synergy-E software analyzed and sent to the physician for patient assessment. These summarized reports can become part of the patients MDR. The reports available in Synergy-E software are patient event report, equipment report, summaries report and monitor compliance report.

NIC: How does your facility use these reports to assess the patient?
PS: As previously mentioned, when a Smart Monitor 2 PS overnight bedside recording is completed, our Special Diagnostic Cardiopulmonary Technologist team downloads the recorded information into the Synergy-E software for alarm waveform review and scoring. Our trained staff reviews the recorded data, scores the data (deleting false alarms, saving and printing real alarm waveforms) and prepares the final printed report. The report is made available to the Neonatologist for their interpretation.

The Synergy-E report is saved directly to our electronic medical record. The Neonatologist dictates the interpretation and this is transcribed directly to the Synergy-E report.

Premature infants that are being discharged from the NICU/hospital are known to be at risk for apnea, bradycardia and oxygen desaturation while in the upright position. The Smart Monitor 2 PS is a great tool for administering the Car Seat Challenge. The test verifies the cardiac and respiratory stability of the preterm infant while in the upright position. The car seat challenge is recommended by the American Academy of Pediatrics when discharging any newborn at less than 37 weeks gestational age, or low birth weight even at full term.

NIC: What experience have you had with car seat testing using the Smart Monitor 2 PS?
PS: At Children's Minnesota, the initial car seat screening is completed at the bedside by the neonatal unit nurse. However, if the infant fails this initial screen or if the infant has other high risk problems (airway anomalies creating significant risk for airway obstruction, abnormal neurological exam resulting in abnormal muscle tone or head control, or significant anatomical CNS abnormalities) a diagnostic car seat evaluation is recommended.

This evaluation is done by a 4-day car seat certified Cardiopulmonary Technologist. The evaluation is attended by the technologist for the entire duration of the test.

The infant is placed in the car seat for a minimum of 90 to 120 minutes and monitored and recorded with the Smart Monitor 2 PS.

Following the recording period, the Smart Monitor 2 PS is downloaded and a report of the monitoring period is provided to the Neonatologist in order to objectively assess the infant's clinical status while in the car seat.

Apnea of prematurity may not resolve at term and may persist for some time after hospital discharge. These babies should be considered for home monitoring if apneas and bradycardias persist as discharge nears. Consideration for home monitoring of preterm infants is often a part of discharge planning. The reasons for considering home monitoring are:

- When apnea of prematurity is unresolved by discharge date
- Infants have experienced high risk BRUEs
- When infants have subtle or intermittent problems like cardiac conditions, seizures or the onset of infections
- Infants discharged with caffeine citrate therapy
- Enables physicians to manage discharged infants with conditions that may affect breathing, heart rate or O2 saturation

NIC: How does your hospital handle the decision to monitor discharged infants in the home? What are the benefits of monitoring in the home for the infant and their family?
PS: At Children's Minnesota, the decision to discharge an infant on a home monitor is multifaceted. The decision is made using information about the infant's current clinical status, diagnostic testing results (Smart Monitor 2 PS recording or 4-channel pneumogram recording), the need for caffeine citrate in preterm infants at the time of discharge, parental input and Neonatologist recommendation. Each infant is assessed on a case-by-case basis.

In most cases, the decision to monitor the infant in the home is comforting to the parent as they know they would be alerted to any potential life threatening situation after discharge.

Once the decision to monitor in the home is made, a referral to the Apnea Program is made.

The Apnea Program provides a benefit to the family in the home as they are able to be discharged earlier, in most cases. The family has a medical team in place for the course of the home monitoring. Apnea monitoring in the home for the infants that need it allows a safe, inexpensive transition to home from the inpatient neonatal unit.

The cost of keeping an infant in the NICU is expensive. Some facilities will put an infant on a 5-7 day apnea/bradycardia watch prior to discharging the infant.

NIC: With the ability to monitor the infant with Smart Monitor 2 Home Care in the home what are the cost savings benefits of an early discharge for the hospital?
PS: Certainly the ability to send an otherwise stable, growing preterm infant home safely on a home apnea monitor will reduce the hospital stay by several days, if not more. This saves considerable amounts of money.

Although each infant is different, we believe we save a minimum of 2-3 additional nights in the hospital.

NIC: How does home monitoring allow physicians to manage premature infants that have been discharged from the hospital?
PS: At Children's Minnesota, all infants discharged on home apnea monitor are enrolled in the Apnea Program.

The Apnea Program is medically directed by Children's Minnesota Neonatology Services providing in-home clinical management of the monitor. The same Neonatologists stay involved with the management of unresolved apnea of prematurity (or other conditions warranting home monitoring) until the infant can safely have their in-home apnea monitor discontinued. This medical management model provides consistency from the inpatient hospitalization throughout the course of home monitoring.

Prior to discharge, the Apnea Program nurses meet with individual families to train them on the use of the monitor, alarm intervention, record keeping and review of apnea protocols to be able to discontinue the home monitor. All families are trained in infant CPR and aiding the obstructed infant.

We provide 24/7 availability for families to call with questions or alarm status changed.

We download the in-home apnea monitors on a routine basis as determined by our Apnea Program protocols.

The decision to discontinue the home monitor is based on in-home monitor download results, parent reports, Apnea Program nurse input and Apnea Program Medical Director recommendations.

Physicians will discharge an infant with a prescription for home monitoring using a Smart Monitor 2 Home Care. This requires the hospital to have a relationship with a home care company that provides home monitoring services. The home care provider should set up the monitor in the NICU prior to discharge to enable the family to become familiar with the equipment and the alarms. The care givers of an infant being discharged with the Smart Monitor 2 Home Care should also be trained in CPR. Parents room in with their baby the last night in the hospital. The NICU training reduces caregiver anxiety and allows them to participate in the care of their infant.

NIC: How has having a good working relationship with your local durable medical equipment provider benefited the hospital's Apnea Program?
PS: Children's Minnesota does not have our own Durable Medical Equipment (DME) service. We rely exclusively on our local pediatric only based DME provider—Pediatric Home Service. They provide our preferred home monitor equipment for our families. We use the Smart Monitor 2 Home Care units for in the home.

Pediatric Home Services provides the technical monitor education and monitoring supplies for our families. They provide home visits, when necessary, to facilitate direct monitor downloads. This downloaded information is sent directly to the Apnea Program. This information is scored, reviewed and a report is generated for the Apnea Program Providers to interpret and direct in-home clinical management of the monitor.

Circadiance develops, manufacturers and markets remote patient monitoring and respiratory therapy products. Our clinically proven, innovative solutions address patients ranging from premature newborns to elderly. Circadiance products deliver superior patient comfort in the home care and acute care settings, ultimately resulting in reduced cost of care and improved patient outcomes.

Can Blood Drawing Technique in the NICU Be Standardized?

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. This interview is with Stacia Nickell RNC-NIC, BSN, Shift Coordinator IU Health, Riley Childrens Hospital with contributions from Bill Buss BS, Pharm D, Laura Smith RN, Shellie North RN, Jennifer Gearlds RN and the 230 Staff Nurses at Riley Childrens Hospital.

In search of the best method for Neonatal blood drawing that provides standardization, ease of use and good clinical results when used with all types of Central Line Catheters while providing a closed system in use…One level IV NICU's experience with the Hummi Micro Draw System.

Neonatal Intensive Care: In your level IV NICU what unique challenges do you have when needing to draw blood samples from premature infants, especially those who are transferred to you from other institutions and may have a need for various types of catheters to be placed?
Stacia Nickell: We receive the sickest newborns in the state of Indiana. Access can be a big issue and babies may be transferred in because of needed access. The Hummi Micro Draw System gives us the ability to draw blood easily from any line that we put in or receive from another hospital. It also allows us to draw a very small volume of blood as waste and give back that volume along with a very small volume of flush, helping us to reduce IVH risk.

NIC: Having a closed system for blood drawing has become the desired norm. What has been your experience in using closed systems commercially available for blood drawing in your level IV neonatal population?
SN: We have tried several different systems over the last few years. Some of the problems we observed were related to line clearance and flushing when running TPN with the devices we were using to draw our ABGs and Labs. Lab values were often inaccurate because the in line device was difficult to clear when used with Central venous lines. 3mL of clearance was often needed. We observed increases in infection rates possibly due to blood residual in the devices after blood drawing which was not clearing out with up to 3ml of flush. Blood exposure during use was also a problem with certain of these in line systems.

NIC: Approximately one year ago your NICU implemented the Hummi Micro Draw Closed System. What improvements vs. previous methods of drawing blood does the Hummi Micro Draw System offer to your patient population from a clinical standpoint?
SN: With the Hummi Micro Draw System we are able to standardize our clearance and flush volumes for Central Arterial and Central Venous lines. We standardized our waste/holding to 1.0 mL of blood and we do not have inaccurate labs. We run TPN through the Central Venous lines and with the Hummi Micro Draw it is very easy to flush any catheter with a standardized 0.6mL of flush after a blood draw. Actually, we do not need to draw blood into the line itself when using the Hummi Micro Draw, as the waste and sample are taken directly from the Catheter hub.

The great thing about the Hummi System is that it can be used successfully when any fluid is being administered through any type line. The draw volumes are small, and a small amount of flush completely clears the catheter. More importantly, we have had zero (0) infections with the Hummi Micro Draw system since its implementation.

NIC: Has the use of the Hummi Micro Draw improved your work flow at bedside when it comes to line setup, line maintenance and the blood drawing process?
SN: We change our fluids using an aseptic technique and the Hummi Micro Draw System fits easily into this process. The packaging is user friendly and it works nicely with our line set up with minimal components compared to other systems. The Hummi System has made our process more streamlined, and is very easy to use and easy to teach how to use.

NIC: What different types of catheters do you draw blood from using the Hummi Micro Draw system?
SN: We use the Hummi Micro Draw System for blood drawing on Central lines (subclavian. and jugular), Umbilical Arterial Lines, Umbilical Venous Lines, and IR placed PICC Catheters 2.4Fr. or larger. We also use the Hummi Micro Draw on Peripheral Arterial Lines placed in the OR and at bedside

NIC: Does drawing from different types of catheters require different equipment or techniques when using the Hummi Micro Draw?
SN: We have now standardized our blood drawing technique with the Hummi Micro Draw to 1.0mL waste and a 0.6mL flush for all type Central catheters. 95% of the time this works very well.

If needed for very low gestational age/weight babies we have the ability to reduce clearance and flush volumes with the Hummi Micro Draw as needed for different catheter sizes and still obtain accurate lab values. Also, if a slightly higher volume of clearance is appropriate for certain circumstances, we can increase our draw and flush volumes accordingly when using the Hummi Micro Draw without having to change line setup or line components.

If you would like to participate in this feature, as a company or healthcare provider, please contact Steve Goldstein at s.gold4@verizon.net.

NIC: Have you noticed an improvement in your infection rates since the adoption of the Hummi Micro Draw device? If the effect on infection rates is positive, how do you feel the Hummi Micro Draw System has contributed to lowering infection risk in your patient population?
SN: We have instituted various procedures over time to prevent infections such as our aseptic fluid change policy. And, since implementing the Hummi Micro Draw System and the improved line setup it provides, we have had **no infections** and our infection rate has decreased 58% over the previous year. Currently since implementation of the Hummi System we have a 0% infection rate.

The Hummi Micro Draw System helped us with improvements in our drawing technique and in our line setup by limiting open accesses to the line, not drawing blood into the line, elimination of blood residual in the line, reducing clearance and flush volumes and providing closed access ports for sampling, flushing and line change. These technique improvements all likely have contributed to the reduction in our observed infection rates.

NIC: What other procedures requiring blood collection have you used the Hummi Micro Draw device with successfully? What improvements do you see?
SN: We have now adopted the Hummi Micro Draw System for use in drawing Blood Cultures from our Central lines. Our procedure is to change the Hummi Micro T Connector used for access to a new one prior to the culture draw. We then access directly to the Catheter hub through the newly placed Micro T connector with the Hummi device and divert 1mL of blood prior to drawing the culture blood. After sampling we return the diverted blood to the patient. Using this technique has shown an improvement in our False Positive rates for Blood Cultures from our lines.

NIC: Has the implementation of the Hummi Micro Draw system allowed for standardization of the blood draw procedure throughout IU Health's NICU departments?
SN: Yes, we have 5 NICU's of different levels and we all use the Hummi Micro Draw for our blood sampling from all Central and Peripheral catheters. This has helped with ease of transferring babies as we are all using the same device and the same drawing technique. We have also been able to standardize our training for all NICUs for blood drawing and line setup to the Hummi Micro Draw System throughout the IU Health System.

NIC: Overall has the Hummi Micro Draw System performed to your clinical expectations for blood draw needs of a Level IV NICU?
SN: This device has performed above my expectations. We have been able to use it with all our lines and effectively draw labs without any issues. We have maintained a great low infection rate and it is easy to teach new nurses to use. Our doctors love this device and are impressed with the low draw volumes and the thinking behind how that helps reduce IVH risk. The device has allowed us to decrease the cost of repeat labs. My nursing staff was very excited to go to this device and can't believe we have ever used anything else.

Neonatal MARSI

Michael Todd Sapko, MD, PhD

Medical adhesives are a necessary part of modern medicine. Intravenous and intra-arterial lines, endotracheal tubes, and certain catheters must be tightly secured to prevent slippage, dislodgment, or even internal trauma to patients. On the other hand, medical adhesives are not without a certain amount of risk. Medical adhesives may cause mechanical problems, contact dermatitis, and other forms of local irritation and inflammation.

Premature and full-term neonates are at particular risk for problems with medical adhesives, yet securing medical devices in the neonatal intensive unit (NICU) is of the utmost importance. Thus, there is an inherent trade-off between keeping tubes and lines secure and preventing medical adhesive-related skin injury or MARSI. Fortunately, there are ways to avoid neonatal MARSI, including proper medical adhesive selection, placement, and monitoring.

What is MARSI?

MARSI is an acronym that stands for medical adhesive-related skin injury. MARSI is not a pressure injury; rather it results in trauma to the skin. Skin injuries caused by medical adhesives fall into three categories:[1]

- **Mechanical trauma**
  - Epidermal stripping – One or more layers of the stratum corneum are forcibly torn off with the removal of adhesive tape
  - Tension injury/Blistering – The epidermis separates from the dermis; may be caused by unyielding adhesive or improper tape application
  - Skin tearing – Shear, friction, or blunt force trauma resulting in partial or full thickness skin damage

- **Dermatitis**
  - Contact dermatitis – Non-allergic reaction to chemicals within the adhesive or backing
  - Allergic dermatitis – Cell-mediated allergic response to the adhesive or backing

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- **Other**
  - Skin maceration – Wrinkled, light-colored skin that is susceptible to damage
  - Folliculitis – Hair follicle inflammation that may or may not be suppurative (pus-filled)

Neonates are at risk for MARSI

The delicate tissues in the skin of premature neonates place them at increased risk of developing MARSI compared to older infants and children. At less than 30 weeks gestation, there may be as few as two or three layers of stratum corneum compared to 10 to 20 in the full term newborn or adult.[2] The dermis in even newborn infants is far thinner than it is in adult skin. Moreover, the junction between the dermis and epidermis is underdeveloped in preterm and young full-term infants, meaning there is less cohesion between the layers.[2]

The risk to immature skin is compounded by the use of medical adhesives, especially in the NICU. The more premature the infant, the longer the NICU stay generally is. Thus, the patient group with least-developed skin is exposed to the greatest amount of medical adhesives.

Epidermal stripping is the most common form of MARSI in neonates; the prevalence of skin stripping due to medical adhesives in infants is 17%.[3] Tension injury and blistering may also occur.[4] Infants in long-term intensive care may also develop skin maceration due to moisture trapped under medical tape. Contact and/or allergic dermatitis may occur; contact dermatitis resolves within 24-48 hours after the tapes is removed, while allergic dermatitis may last for up to a week.[1]

Avoiding MARSI in the NICU

One way to reduce the occurrence of MARSI is to select the proper medical adhesive for the purpose. Critical devices such as chest tubes, endotracheal tubes, and vascular access devices require relatively aggressive medical adhesives for a secure hold. The term "relatively" is important because certain adhesives can be too aggressive for NICU patients. While a medical tape should hold strongly enough to serve its intended purpose, importantly, it should also be easy to remove and cause little to no damage to the skin.

It is also advisable to choose a latex-free product to reduce the chances of priming or exacerbating a latex allergy. The adhesive should also be waterproof in that it resists rolling and curling when subjected to fluids (eg, perspiration, urine).

NICUs and nurseries often use Hy-Tape, which they commonly refer to simply as "pink tape." Hy-Tape is an excellent all-purpose tape for use in the patient population. It provides relatively aggressive adherence and is suitable for use with critical devices.[5] While it holds firm and conforms to body contours, "pink tape" can also be removed with ease. The adhesive in Hy-Tape leaves little or no residue when it is removed, and minimizes the risk of mechanical damage to the skin, specifically epidermal stripping, skin tearing, and tension injury or blistering. This especially important for devices that need to be removed frequently and re-taped. (Read about Hy-Tapes unique skin saving qualities)

"Pink tape" can reduce the risk of other forms of MARSI as well. Hy-Tape is latex-free and is not known to cause contact dermatitis or allergic dermatitis when used appropriately. Moreover, Hy-Tape contains a zinc oxide adhesive that is naturally soothing to even delicate, neonatal skin. (request a sample)

Lastly, devices can be made more secure by using particular application techniques. For example, the "chevron" technique, well known to nurses, helps provide maximal security with minimal adhesive contact with skin. The risk of MARSI can be reduced by avoiding tension on the skin at rest or leaving tape on too long. Always remember that any medical tape, including Hy-Tape, should be removed slowly, at a low angle, while supporting the skin. This is especially true in neonates and NICU patients.

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Comfort Care for Premature Conjoined Twins

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Case

It was the evening call. A woman was referred from maternal-fetal medicine clinic for cesarean section. She was 28 year old G8P6016 at 27 weeks 6 days gestation with twin pregnancy. The antenatal ultrasound was significant for conjoined twins-thoracoabdominalpagus fusion sharing heart with severe fetal ascites suggestive of cardiac failure. Due to maternal Premature prolong rupture of membrane and chorioamnionitis delivery was warranted. Urgent neonatal consultation was ordered. After reviewing maternal records and ultrasound (US) reports and a detailed discussion with the on-call obstetrics team a meeting was arranged with the mother to discuss the medical care. She was approached in the labor and delivery suite. After detailed discussion and in view of the extreme prematurity along with lethal associated anomalies a joint decision was made to provide comfort care.

A cesarean section was performed and twins were delivered. As noted in the antenatal US, the fetuses were conjoined with moderate to severe abdominal distension. Two separate heads were noted with fused chest and abdomen thoraco-abdomino-pagus type, Figure 1 and 2. Infants were wrapped in blanket-and transferred to newborn nursery for comfort care. Infants were pronounced dead in the newborn nursery at 58 minutes of life after no heart rate detected. Comfort care was provided during their stay in newborn nursery.

Discussion

Conjoined twining happens as a consequence of delayed cleavage, as depicted in Figure 3. Depending upon the area involved it could be cephalo, ischio or thoracopagus.[1] In the advent of medical and surgical advances conjoined twins—depending on the severity—are able live a decent life, in some instances separations has been possible. First pair of conjoined twins history backs to the year 1811, also known as the Siamese twins, Chang and Eng Bunker. There have been previous attempts at separating thoracopagus twins however the mortality rate is 51% and approaches 100% for those with significant cardiac fusion.[3]

As noted after birth, the decision of comfort care was in favor of the appropriate medical management. Unnecessary interventions

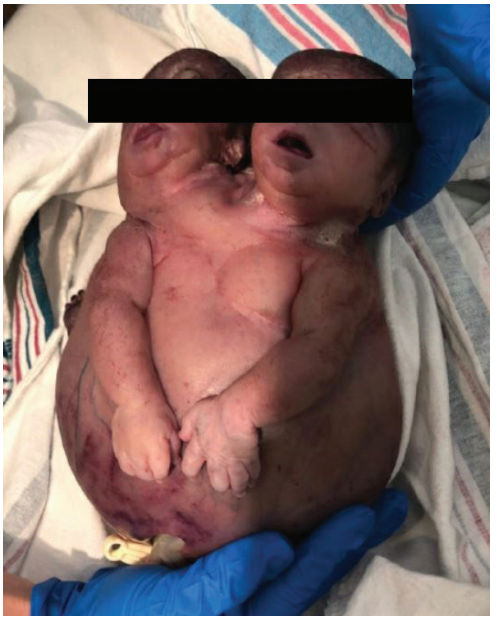

Figure 1. Visual representation of twins demonstrating thoracopagus fusion

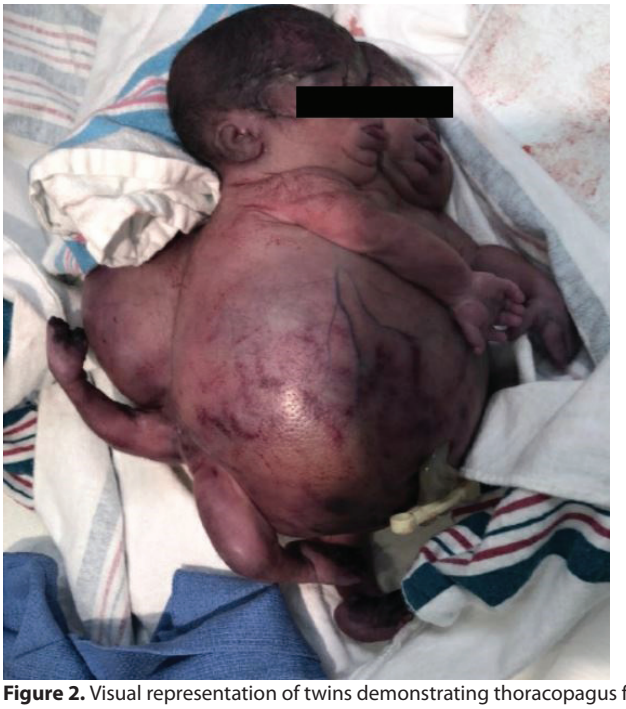

Figure 2. Visual representation of twins demonstrating thoracopagus fusion

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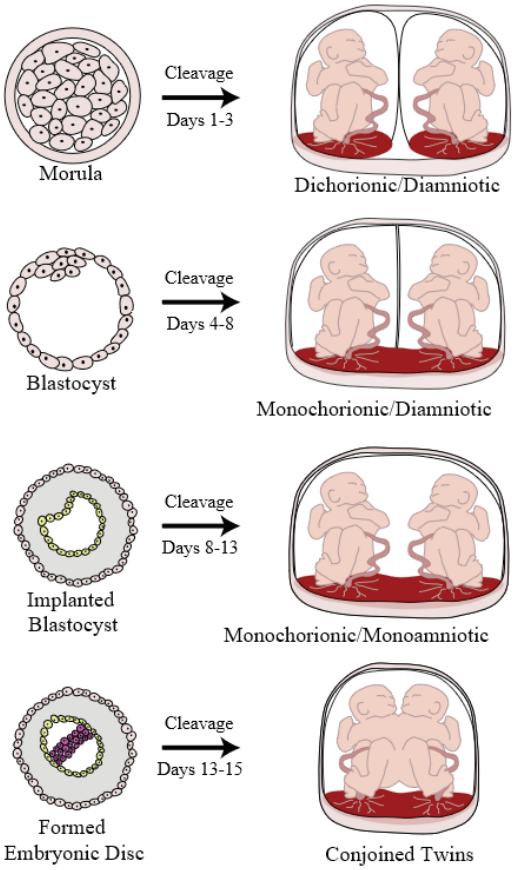

Figure 3. Timing of cleavage. Images courtesy: Kevin Dufendach – Own work, CC BY 3.0, https://commons.wikimedia.org/w/index.php?curid=5324027

would not only result in pain for the infants but also result in the emotional turmoil for the mother. By making a timely informed decision the downward spiral of medical interventions and side effects were avoided. Parents were also able to grieve properly. Bidegain and Younge[2] has recently elucidated on the topic of palliative and comfort care in neonatal intensive care unit, which is evolving day by day.

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Meeting Families Where They Are: A Global Maternal & Child Health Perspective with Andrea Goodman, MSW, MPH

Deb Discenza, PreemieWorld.com

The field of maternal-child health is one that has allowed me to meet a variety of people in the healthcare arena as well as the public policy area. I have watched Andrea Goodman, MSW, MPH from afar as she took advocacy to a whole new level with coalition building, public health programs, and now, research expansion. Andrea and I talked about the landscape from her unique perspective that blends the two fields.

Deb Discenza: How did you get into this background/ maternal-child health space?
Andrea Goodman: I have been passionate about equity and social justice for as long as I could attend protests in a stroller with my parents. M career began in social work but I quickly decided to pursue a Masters in Public Health after finding my passion for health. It just influences everything! I also realized through my graduate studies that my true love was working at the national level on domestic programs. There is so much value in international and local work, but there's something about seeing systematic processes trickle down into communities and back up that makes me tick.

I've been working in maternal and child health for almost ten years, although in health programs (including domestic violence, tobacco cessation, obesity prevention, and other topics) for another decade. For me, maternal and family health is a feminist issue. If we can't value women's lives and support their reproductive and parenting decisions throughout the lifespan, we can't effectively care for the nation.

DD: Where do you think true progress has been made in the maternal-child space?
AG: We are finally getting to a point of true patient-centricity. When the public health community used to develop solutions, we would look first to how we'd succeed. Now we want the audience at hand to succeed by their own standards and measures of success. I was trained to consider how we *change people's behaviors.* Now we ask people first *what people need* and what works *in the context of their lives* before building the solutions that will lead to healthy behaviors by virtue of value. We have shifted the culture; now, I can't imagine a project that attempts to design a project or tool or innovation without first involving the stakeholders for whom it's built.

DD: What advancements surprised you the most?
AG: Like almost everyone else, I could not have predicted the technological innovation that has exploded over the past two decades. We now have the opportunity to provide remote clinical care, connect communities using robust online social networks, support patients using devices, expand reach using geotargeting, and build precise programs using quality data and geo-mapping visualization. The opportunities are endless.

I'm excited to continue on a path of testing novel options and contributing to valuable, scalable knowledge. We do, however, have a responsibility to make sure we're using technology in thoughtful and strategic ways rather than over-saturating the public health landscape just because it's fun and sexy.

DD: Tell me about Text4baby and how that changed the landscape.
AG: Text4baby was an impactful time in my career and in the pregnancy and infant health community. It was exciting to test and scale text messages as a means of reaching all families! We have so many lessons learned from that experience and you can see the explosion of platforms now as we conceptualize all of the ways we can bridge the phones we're all so tied to with the health actions we're expected to take.

DD: How is Genetic Alliance/Expecting Health hoping to re-shape and impact this space?
AG: Genetic Alliance and our maternal and child health initiative, Expecting Health, are both strongly rooted in the idea that we need to meet people where they are. We've found the most success when we flip the problem on its head. Patients, moms, families…these people are the experts in what they need. Our models and tools start with knowledge from the people who we serve, and we supplement with strong partnerships and other experts—clinicians, industry, community and national organizations—to co-design strategies. We are committed to the cultural change away from paternalism and towards inclusion.

DD: True, meeting people where they are is key to success in solving these problems. What are some of the biggest health issues facing our country right now in this area?
AG: It's not new, but it is critical that we fully face and address the maternal mortality crisis that has recently been brought to the forefront of the media. Evidence clearly points to racism as

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a variable in fatal outcomes for black women. We cannot accept this and turn away.

Another urgent public health issue of our time is immunization-a crisis that is fully preventable. Effective solutions are being rejected because *rhetoric is powerful.* We need to use that parental influence to our advantage—adoption requires trust, community, and an understanding of the fears and barriers that families face.

DD: Very true on both of those. So what is the biggest systematic problem in maternal-child health?
AG: The biggest problem we face in providing quality, patient-centered, evidence-based maternal and child health care are the silos. Obstetric care is separate from pediatric practice is different from the research enterprise is isolated from lactation support and early intervention…and so on. This may work for the funding agencies but is totally disjointed for families. In real life, we move fluidly from reproductive health decisions to pre-pregnancy behaviors, then we need prenatal care and soon after require postpartum and pediatric services. The whole time, we are contributing critical, individualized data points that have the potential to generate important knowledge. Again, imagine if we designed the system around the people using it, rather than forcing people to navigate with their eyes closed. We would probably see an increase in utilization, healthy behaviors, self-efficacy, and activated communities. We could really improve outcomes and, most importantly, improve quality of life for families.

DD: Well put and I couldn't agree more. Thank you, Andrea.

As Ms. Goodman noted, it is definitely time to "meet people where they are" in maternal child health. Whether through technological advances shaped by the patient-family population or programs that are created with their needs in mind, we still have much to do in order to better outcomes in this space. And we need to do it as one group, together.

Improving Mother's Milk Volume and Baby's Outcomes by Understanding Technology

Lori Wood, MSN, CNS, RNC-NIC, IBCLC

Breastfeeding and breast milk is without a doubt the best nutrition for babies. Breastfeeding rates are rising and more mothers are expressing the desire to breastfeed. Among babies born in 2015, 82.3% began breastfeeding, yet only 24.9% were exclusively breastfeeding at 6 months of age. Statistics also show that 17.2% of babies in the initial breastfeeding group were supplemented with formula in the first 2 days of life. Reasons cited for supplementation include "not having enough milk".[1] Healthy People 2020 suggests that by increasing percentages of babies born in Baby Friendly facilities, the number of breastfeeding babies will be increased. Hospitals with Baby Friendly accreditation are increasing in the United States, and currently 12 states report over 40% of infants are born in such centers.[2] The early postpartum period is crucial to establishing good breastfeeding practice, infant latch, maternal and infant breastfeeding competency, and physiologic response and signaling to ensure continued milk production.[3] Many risk factors can hinder this early process of transition from Lactogenesis I (milk available in small amounts) to Lactogenesis II (milk becoming more plentiful or "coming in"). With so many factors influencing a mother's choice, decision, and ability to breastfeed, we as maternal/child healthcare providers are depended upon to provide accurate and timely advice as well as technological excellence to influence and impact breastfeeding outcomes.

Human milk provides superior outcomes for life when babies have the highest exposure possible. The American Academy of Pediatrics continues to support exclusive breastfeeding or consumption of breast milk for the first 6 months of life, continued breast milk until 1 year of life, and as long as mutually desired after.[4] Human milk improves health and reduces morbidities for term, late pre-term and prematurely born infants via many factors. Nutrition and immunology are well researched and reported. Human milk has anti-inflammatory and anti-infective properties and begins a cascade of triggers and events leading to the down-regulation of inflammation, oxidative stress, and a reduction in a multitude of life long problems.[5,6] Problems such as auto-immune and atopic disease, chronic diseases, retinopathy of prematurity, neurocognitive and developmental delays, sepsis, and gastric issues are reduced in infants born prematurely.[3] Future epigenetic changes and colonization of the infant gut and microbiome health are all positively affected when infants receive an exclusive breast milk diet.[6] Mothers who breast feed are similarly protected from postpartum depression, cardiac disease, type II diabetes, and breast and ovarian cancers.[7] The World Health Organization, National Institute for Child Health and Human Development, and many organizations unanimously support human milk feedings across the world.[8]

Education has been a major focus used to successfully increase breastfeeding rates in the United States.[1] Mothers are more determined to breast feed and greater numbers of mother/infant pairs are successfully feeding human milk until a minimum of 6 months of age and beyond. Hospitals and birthing facilities are increasingly becoming Baby Friendly, and research and evidence continues to come forward with renewed attention to such an important topic. The Joint Commission has adopted Perinatal Care Core Measures surrounding breastfeeding and the support of mothers.[9] Disparities are evident among the states.[1] With breastfeeding continuing to rise, why then do so many states, hospitals, pediatricians, obstetricians, and other mother/baby staff struggle to get more infants exclusively breast fed?

What can be done on the inpatient side of supporting moms and babies? Unifying staff through education, protocols, guidelines, competencies and in-services is a great start. Unit based councils and quality improvement projects with interdisciplinary staff are useful in an effort to review current practice, evidence-based research and information, create or update protocols, policies, guidelines, and educate staff so true change in practice can occur.[10] Evidence-based changes to practice are created when the following are in place: leadership of supportive and committed managers, a culture of support for bedside nurse involvement, and measurement and pathways allowing teams to create the change.[11,25]

Technology plays a huge part in initiating and maintaining milk supply, volume, and availability, especially in pump dependent moms. When baby is too weak to go to breast frequently, is ill or premature and taken to the Neonatal Intensive Care Unit (NICU), or unable to successfully latch due to congenital anomalies or other issues, the breast pump becomes the baby. Once baby is delivered, mom goes through three stages of milk production; initiation, building volume, and maintenance of volume. Each stage of production must be successful for the next to develop well.[12] Therefore, each person caring for mom and baby must understand the needs of mom and her pumping or breastfeeding. Staff education and practice need to begin

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the standardization of practice. A solid process of beginning pumping in labor and delivery within 1 hour of delivery, if mom is stable, is an evidence-based process that leads to early initiation of milk production.[13] Our unit began a journey in 2010 to increase milk production and have more of mom's own milk available for our NICU patients. We wanted to provide not only exclusive human milk feedings, but also provide oral colostrum administration. Considering all of the research and best practice information available, the need to obtain and provide mother's own colostrum and breast milk was not only our desire, but a necessity for all of the premature and sick babies in our NICU. New Medela© Symphony® pumps replaced our previous pumps, and new guidelines and workflows were created. Staff in Perinatal, Pediatrics, and NICU were fully educated on the evidence behind new pumping technology and the groundbreaking evidence-based work by Dr Paula Meier.[14] The change in outcomes and volumes needed to provide our human milk needs was quickly noted within 2 months' time. Our staff were convinced and practice was changed.

This initial new pump technology was originally applied to moms who had delivered prematurely, mirroring early infant suckling behavior in newly born infants. It made sense to apply this technology to any mom pumping exclusively for her infant, so we began using the Symphony® Preemie Plus™ (now called Symphony PLUS®) with Initiation Technology™ mode on all of our moms who were pumping for their baby. We followed the suggested protocol for pumping until mom had obtained 20 milliliters (mls) for 3 consecutive pumping sessions. We were seeing the same reported results of increased volume up to 250 mls more per day in our moms. We also saw a greatly reduced need for medications used to boost mom's milk supply and after 9 years of using this technology, are no longer needed.[6] Many years later, new published data demonstrating successful outcomes in pump dependent, term delivered mothers supported this practice.[16] Now this technology is evidence-based to improve milk volumes in all pump dependent mothers. Authors Post, et al noted an increase in milk production in women using Initiation Technology™, with an average achievement of lactogenesis II by 3.3 days post birth.[18] Improved neonatal outcomes due to more of mom's own milk and early colostrum feedings and oral administration can be seen when applying technology to our problematic and fragile premature population.[11,17]

Overall initiation of breastfeeding rates are the highest seen in decades, but the problem of exclusivity and the duration of breastfeeding are apparent. Many moms begin their pregnancy with a goal to breastfeed, but stop due to reported low milk volumes.[19] In addition to lack of support or knowledge, multiple risk factors can contribute to suppressed or delayed lactation. First time mothers are at an increased risk for delayed lactation. Obesity and overweight, Caesarean Section deliveries, maternal illness such as hypertension, postpartum hemorrhage, and maternal age over 30 years are also contributors.[20,6,7] Diabetes causes considerable problems with mother's ability to produce milk and increase volumes to the levels need for a growing baby due to insulin resistance and overweight/obesity issues.[24] Maternal/child staff must be aware of these factors impacting breastfeeding rates and include increased awareness and screening for these mom/baby pairs. The astute care giver will monitor milk production, pumping logs, ask mom daily about her pumping and output, working with lactation support to intervene quickly. NICU staff are the most frequently seen people involved in mother's care once she is discharged home. Continued surveillance by these staff people can ensure quick identification of milk volume or pumping problems. Evidence has existed for nearly a decade now demonstrating volume goals for exclusively pumping mothers. Mothers who have delivered prematurely need to be pumping 500 milliliters/day by day 10-14 post birth and 750 milliliters/day for term delivered moms.[15] By incorporating knowledge with practical bedside application, outcomes can be improved. At-risk mothers can receive additional stimulation through advanced Initiation Technology resulting in more milk volume. Pump technology mimicking the early sucking patterns of newborns provides interventions successful in treating moms at risk for lactation issues. When this Initiation Technology is used in the days following delivery, moms attain more milk. Initiation Technology is a completely different pattern from our usual bi-phasic pumps used solely to express milk which is already present. Early stimulation is needed to set the pace for the amounts of milk needed by 10-14 days post-delivery. Initiation Technology incorporates many phases and speeds of stimulation, expression phases, and pause phases. This pattern was designed by watching newborns breastfeed. Newly born infants suckle at the breast differently when mom has small amounts of colostrum available; this way of feeding, which is observed in every newborn baby, was thought to be integral to the next phase of lactation, "milk coming in". Application of this design, in an evidence-based research study, proved that Initiation Technology improved milk volumes and moved moms into the next step of milk attainment which is building supply, also known as Lactogenesis II.[15,21] The right technology at the right time is a crucial piece of helping mom achieve her goals, enabling mom to provide and baby to receive life giving and health building human milk.

Perinatal nurses, especially labor and delivery nurses can impact milk volumes of both breastfeeding and pumping moms early in the post delivery period. Early skin to skin care and breastfeeding in the first hour after birth result in a longer breastfeeding relationship. If mom and baby are separated, pumping in this first hour will provide the stimulation needed to activate breast tissue and promote the change from lactogenesis I to lactogenesis II.[14,22] Delays in pumping or breastfeeding can lead to delayed lactation or lactation suppression. Elevated prolactin levels secreted during breastfeeding or pump expression, can improve long term milk production in mothers of term and preterm infants.[23] Labor and delivery nurses caring for patients immediately after delivery are in the unique position to drive this practice. Education and support for nurses and staff is important to support the adoption of early skin to skin care, breastfeeding, and pump expression. Initiation Technology plays a significant role in providing this needed stimulation. Paired with hand expression to compliment Initiation Technology, volumes are significantly increased.[13]

Technology paired with technique, tracking and follow up can help to greatly improve volume issues for mothers [15]. Nurses and lactation staff can influence human milk goals of mothers in Perinatal, Mother/Baby units, NICU and Pediatrics. By checking in with mom each shift, each day, to ensure that initiation, build, and maintain modes of breast pumping are being used correctly and consistently is the first step. Helping moms to quantify their milk volumes by tracking with pumping logs, will help to ensure that she is on the right path. Lag in volumes attained can be identified, leading to solutions applied in a timely manner. Many nurses may feel that following pumping and feeding is not the most important facet of their job, but the opposite is true. With

so much research and evidence pointing to improved outcomes for all human milk fed infants, not doing everything in our power to support and obtain high volumes of milk reduces our exclusive breast feeding rates. As nurses, we are often involved in life saving work for moms and babies. Intervening quickly and skillfully in a hemorrhaging mother or titrating life-saving medications in the NICU are obvious critical skills necessitating thought and expertise. If we know that NICU infants exposed to high levels of human milk discharge with improved outcomes and fewer morbidities, then applying knowledge and technology to breastfeeding and pumping is a critical skill as well. Nurses, lactation, and other mother baby staff including Pediatricians and Neonatologist can influence milk volumes, ensure that infants receive the highest amount of human milk, and improve outcomes setting the course for our children of the future.

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The Fight Against Antimicrobial Resistance Begins at Birth

Tracy Shafizadeh, PhD

Antimicrobial Resistance is a Major Health Concern

Antimicrobial resistance is a growing health concern in the US, and now considered one of the biggest threats to global health, food security, and development today by the World Health Organization. According to the Centers for Disease Control and Prevention, at least two million people develop antibiotic-resistant infections in the United States every year[1] and 200,000 infants die globally each year as a result.[2] Antibiotic resistant pathogens harbor genes that confer drug resistance, and these antibiotic resistance genes (ARG) can be transferred to otherwise non-resistant bacteria. The gut microbiome is now known to be one of the largest reservoirs of bacteria that harbor ARG, thus providing a novel opportunity to address antimicrobial resistance through microbiome modulation.

The Infant Gut Microbiome Harbors Antibiotic Resistance Genes

The development of the infant gut microbiome is initiated at birth and its composition is largely determined by delivery mode and diet.[3,4] Gut microbes are passed from mother to infant during vaginal delivery, and human milk selectively promotes the growth of beneficial gut bacteria specifically adapted to the infant gut. Among them, *Bifidobacterium longum* subsp. *infantis* (*B. infantis*) is a key species that can create a highly functional and protective gut microbiome in the newborn. However, multi-generational antibiotic use and Cesarean section delivery has disrupted this mom-to-baby transfer of beneficial microbes, leaving the infant gut microbiome vulnerable to colonization by potentially pathogenic bacteria present on surrounding surfaces of a hospital environment.[5]

> Today, antibiotic resistant genes can be found in infant stool as early as the first days of life.

Interestingly, a recent study by Brooks et al. demonstrates that the NICU room environment can serve as a significant source of bacteria for the early colonization of the newborn gut microbiome.[6] Analysis of fecal samples from preterm infants in the NICU, along with sinks and surfaces from the same room, showed that the infants were commonly colonized by nosocomial antibiotic-resistant pathogens found on surfaces of the hospital. This provides a possible explanation of how infants in the same NICU are often colonized by the same strains, even if their stay in the NICU is separated by a year or more. Antibiotic use in NICUs is associated with an increased abundance of multidrug-resistant pathogens found in the gut microbiome of infants, and is associated with increased morbidity, mortality, cost, and length of stay.[7,8] Today, antibiotic resistant genes can be found in infant stool as early as the first days of life.[9]

B. infantis plus Breastmilk Protects the Infant Gut

Recently, researchers established a protective effect of *Bifidobacterium* in the infant gut microbiome, showing that high abundance of this organism was associated with reduced levels of ARG in early life.[10] In clinical studies, probiotic use of *B. infantis* EVC001 in breastfed infants was shown to increase short chain fatty acid production in the stool and, consequently, reduce the infant fecal pH to historically normal levels.[11] This reduction in fecal pH was accompanied by a dominance of *B. infantis* in the infant microbiome, along with a 93% reduction in the abundance of potentially pathogenic bacteria, including *E. coli*, *C. difficile*, *Klebsiella pneumoniae*, and *Streptococcus pneumoniae*, often shown to harbor antibiotic resistance genes.[12] These bacteria fail to thrive under the acidic conditions found among infants colonized by *B. infantis*.

> Feeding *B. infantis* EVC001 to human milk-fed infants is a safe and effective method for rapidly stabilizing the newborn gut microbiome, reducing potentially pathogenic bacteria that often harbor antibiotic resistance genes.

In summary, antimicrobial resistance is a major health concern in both healthy term and hospitalized infants, and *Bifidobacterium* has now been correlated with reduced antimicrobial resistance in infants. Furthermore, feeding *B. infantis* EVC001 to human milk-fed infants is a safe and effective method for rapidly stabilizing the newborn gut microbiome, reducing potentially pathogenic bacteria that often harbor antibiotic resistance genes.

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BCV for Tiny Lungs

Gary W. Mefford RRT

I was asked recently to provide some articles for a Neonatologist on Biphasic Cuirass Ventilation (BCV). There are several that document the benefits for infants, so I thought I would pull some of them together and provide a review. In this paper I hope to show how BCV can make a huge difference for patients with tiny lungs needing support. We will look at a group of articles documenting some of the benefits obtained via the use of BCV or other similar means of extrathoracic negative pressure applications. Upon rereading these papers, I find the authors express the benefits and reasons for utilizing this intervention in quite compelling terms. If you have seen the damage to an infant's lungs that can be wrought by the efforts required to support their breathing with positive pressure, and feel there's got to be a better way, then you need to learn about BCV. Biphasic Cuirass Ventilation (BCV) is a clinical intervention that can be applied to smaller patients than most realize and applied as a lung tool that offers many new strategic approaches to seriously improving clinical outcomes for tiny lungs. Join me for a few minutes as I share information from these papers and discuss the potential for improving outcomes with infants in the NICU and PICU through the therapies and support functions offered with BCV.

For those unfamiliar with BCV's modes and applications I will review. BCV is the brainchild of the late Dr. Zamir Hayek. Dr. Hayek was a brilliant British Pediatric Pulmonologist and world-renowned expert on Cuirass Ventilation. BCV is a group of cuirass applied cardiopulmonary interventions available only with the Hayek RTX ventilator. The Hayek RTX combines a cuirass or chest shell and flexible foam seal that covers the chest and upper abdomen with a power unit that connects with the cuirass via a pressure delivery hose and a pressure sensing tube. The cuirass creates an air chamber over the chest and abdomen and the RTX power unit controls the pressure within the cuirass to affect the dimensions of the thoracic cavity and thus inflation and deflation of the lungs. Inhalation occurs due to the power unit creating a negative pressure within the cuirass, which in turn gently pulls the chest wall and abdomen outward. The ribs expand and the diaphragm is moved to a lower position creating greater thoracic volume. From this a negative intra-thoracic pressure relative to ambient is created and air is pulled into the lungs just like natural inspiration. Inflation can be static or cyclical. In modes that provide ventilation, the power unit will switch the pressure in the cuirass from negative to positive providing the opposite effect on the thorax causing the lungs to deflate.

The patented technology used in the Hayek RTX noninvasively provides a very safe means of lung recruitment, offers a method for greatly increasing minute ventilation, and can function as a secretion clearance device with assisted cough even for infants. These capabilities enable the RTX to benefit many patients with cardio pulmonary compromise and respiratory distress. It produces effective ventilation in both normal and injured lungs, in clinical conditions marked by increases in pulmonary shunt and/or increased dead space ventilation. Additional benefits of BCV include improved perfusion of pulmonary capillary bed and improvements in cardiac output during ventilation without many of the side effects of other support techniques. BCV can be used as a highly effective means of standalone non-invasive support of lung inflation and/or ventilation. BCV can also be used adjunctively with all modes of intermittent positive pressure ventilation (IPPV) as a means to decrease side effects, and to shorten the duration that IPPV. The Hayek RTX provides either continuous negative, controlled, triggered or synchronized inspiration and expiration. BCV requires no mask or invasive interface. BCV can positively influence alveolar ventilation, oxygenation, lung volume and cardiac output. An inspiratory pressure of -15 cmH2O with an expiratory pressure of +5 cmH2O gives a pressure swing, span or deltaP of 20 cmH2O. Although there is an active expiration, lung capacity does not go below FRC. Cardiac output is not compromised with BCV as mean intrathoracic pressure is never positive thus no negative effect on venous return. The RTX is FDA cleared for all patient groups. BCV is used in hospitals from ICU to discharge as well as at home. BCV is applied via a cuirass sized to the patient. Patients from 1.5 up to 180 kg can Be fitted with one of the 12 sizes of cuirass.

We will begin our look at BCV for tiny lungs with some excerpts from Pediatrics. 1996 Dec;98(6 Pt 1):1154-60.

Continuous Negative Extrathoracic Pressure in Neonatal Respiratory Failure

Samuels MP(1), Raine J, Wright T, Alexander JA, Lockyer K, Spencer SA, Brookfield DS, Modi N, Harvey D, Bose C, Southall DP.

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Objective: In uncontrolled clinical trials, negative extrathoracic pressure has been shown to be an effective respiratory support. We aimed to assess its role in the context of current neonatal intensive care. *Design:* A randomized controlled trial, with sequential analysis of matched pairs of infants. Matching was undertaken by stratified randomization from 15 groups divided according to gestational age, oxygen requirement, and whether patients were intubated at 4 hours of age.

Setting: Two neonatal intensive care units.

Patients: Two hundred forty-four patients (birth weight 1.53 ±0.69 kg (mean ±SD); gestational age 30.4 ±3.5 weeks) with respiratory failure.

Interventions: Patients were randomized at 4 hours of age to receive either standard neonatal intensive care, or standard care plus continuous negative extrathoracic pressure (CNEP, -4 to -6 cmH2O) applied within a purpose-designed neonatal incubator. *Outcome Scores:* Clinical scores were calculated for each infant at 56 days of age, or death if earlier. Scores included measures for mortality, respiratory outcome, the presence of cerebral ultrasound abnormalities, patent arterial duct, necrotizing enterocolitis, and retinopathy. The treatment given for the higher score for each pair was recorded and the cumulative net number of pairs favoring CNEP plotted in the sequential analysis to provide an ethical early termination strategy. Individual components of the outcome score and other secondary measurements were analyzed on completion of the trial.

Results: The sequential analysis reached a decision boundary after 122 out of a possible maximum of 124 pairs were completed. The overall outcome score showed an overall significant benefit for CNEP.
- 5% fewer patients were intubated
- The total duration of oxygen therapy among surviving infants at 56 days was lower
  - CNEP 20.5 days, compared with 38.9 in controls; difference 18.4 days.
- Among all infants, the mean total duration of oxygen therapy was
  - 18.3 days among CNEP-treated infants compared with 33.6 days among the controls difference -15.3 days.

This reduction in mean levels is entirely attributable to substantially fewer patients requiring prolonged oxygen therapy, the median duration of treatment being very similar in the two groups.
- As a result, commensurately fewer surviving infants showed chronic lung disease of prematurity.

Conclusions: The use of continuous negative pressure improves the respiratory outcome for neonates with respiratory failure.

The positives on continuous negative pointed out in this paper:
- The overall outcome score showed an overall significant benefit for CNEP
- 5% fewer patients were intubated
- 18.4 days difference in duration of O2 therapy for infants surviving to 56 days
- 15.3 days difference in duration of O2 therapy for all infants
- Commensurately fewer surviving infants showed chronic lung disease of prematurity.
- The use of continuous negative pressure improves the respiratory outcome for neonates with respiratory failure

Broncho Pulmonary Dysplasia or Chronic Lung Disease of Prematurity places heavy challenges on the patients, caregivers and the system. This paper shows that use of CNEP in these patients can decrease duration of oxygen use and offer potential of improving lives or or even lessening the number of infants with chronic lung disease.

Let's look at another paper:

Efficacy of Noninvasive Biphasic Cuirass Ventilation in Neonates: Comparison with Invasive Positive Pressure Ventilation

Fabien G. et al

The abstract of this paper:

Purpose: In spite of surfactant therapy, bronchopulmonary dysplasia (BPD) remains frequent. A major contributor to this complication is the persistent need, notwithstanding normalized lung mechanics, for respiratory support by invasive positive pressure ventilation(IPPV). Biphasic Cuirass Ventilation (BCV), a non invasive form of respiratory support could thus be an advantageous alternative. Our purpose was to compare efficacy of BCV to IPPV in terms of gas exchange, stability of pulmonary mechanics and hemodynamic status.

This was an animal model study with neonatal piglets. The authors' conclusion was "Hemodynamic status and gas exchange were similar for both modes of ventilation." In considering the clinical implications of their findings the authors state "The use of non invasive biphasic cuirass ventilation may be feasible in preterm infants. Its use may become an alternative for invasive positive pressure ventilation and thus enable a reduction of the frequency of chronic lung disease in preterm infants."

So what we gain from this look into comparing PPV with BCV is:
- Similar effects measured as to gas exchange and hemodynamics in normal neonatal lungs
- Use of BCV in this population could well have a beneficial effect on the development of chronic lung disease
- BCV offers the potential to "enable a reduction of the frequency of chronic lung disease in preterm infants"

In another look at treating tiny lungs with negative lung inflation we have:

Negative Extrathoracic Pressure in Treatment of Respiratory Failure in Infants and Young Children

M P Samuels, D P Southall
Br Medj 1989;299:1253-7

This paper looks at 88 infants and young children aged 1 day to 2 years with respiratory failure due to bronchopulmonary dysplasia, neonatal respiratory distress syndrome, bronchiolitis, myopathy, congenital hypoventilation syndrome, pneumonitis, and postoperative phrenic nerve palsy. Their conclusion:

"Negative pressure respiratory support is a non-invasive yet effective treatment for respiratory failure. It may avoid the need for intubation, reduce the pathophysiological consequences of positive airway pressure ventilation and aid extubation."

From these authors' discussion segment:

"Continuous negative extrathoracic pressure and continuous positive airway pressure both increase transpleural pressure, thereby helping to splint open small airways and alveoli and re-expand atelectatic regions. Systemic oxygenation depends, however, not only on alveolar expansion and diffusing capacity but also on adequate pulmonary capillary perfusion with matching of perfusion to ventilation. Positive airway pressure reduces cardiac output, probably by impairing venous return to the right atrium and by increasing pulmonary vascular resistance. Thus at a certain unpredictable point increases in positive airway pressure may cause a fall in effective pulmonary blood flow with a resulting increase in ventilation-perfusion mismatch and worsening of hypoxaemia. Negative extrathoracic pressure, however, increases thoracic volume with less compression of vascular structures and consistently reduces pulmonary vascular resistance, particularly at the pressures used in our patients. In addition, it may dilate pulmonary capillaries and improve ventilation-perfusion matching. This may explain its recently reported value in persistent pulmonary hypertension of the newborn." Bancalari et al reported the physiological effects of negative extrathoracic pressure in infants with the neonatal respiratory distress syndrome. They showed a rise in arterial oxygen pressure, a fall in minute ventilation, and no change in arterial carbon dioxide pressure. Our results confirm the effects on gas exchange, and work in progress supports the idea that negative extrathoracic pressure has predominant effects on ventilation-perfusion matching. The changes in carbon dioxide concentrations, however, suggest that an increase in alveolar ventilation does occur in some patients. In addition, our observations that some patients maintain good respiratory function during the day when treated with negative pressure at night suggests that other mechanisms may also be operating. An increase in the patient's functional residual capacity, an increase in lung compliance, support of a compliant chest wall, or a reduction in diaphragmatic fatigue may all occur as a result of inflation of the lung under negative pressure. In hyaline membrane disease constant negative extrathoracic pressure has been compared with nasal positive airway pressure. Both were effective, although negative pressure produced a more rapid improvement in oxygenation. This may have arisen partly because negative pressure produced a more definitive change in transpleural pressure than a technique relying on the transmission of positive pressure through the nose. In addition, ventilation to perfusion matching may have been enhanced by negative pressure support as discussed above. The presence of an endotracheal tube is associated with increased bronchial secretions, impairment of ciliary clearance, mucus plugging, and upper airway trauma. It also increases the risk of airway and parenchymal infections. All of these factors may contribute to a continuing need for respiratory support after the acute condition has resolved. Both our experience and that of Mokrin and Bancalari has supported the idea that early initiation of treatment for respiratory failure will reduce the need for intubation. Non-invasive means of respiratory support will reduce the incidence of factors that contribute to chronic lung disease, particularly in preterm infants. Fanaroff et al reported that infants with the respiratory distress syndrome treated with negative extrathoracic pressure had less need for positive airway pressure ventilation and a shorter need for supplemental oxygen than infants treated with oxygen alone. Monin et al compared intermittent negative and positive airway pressure ventilation in 115 infants with the respiratory distress syndrome. There was equal oxygen exposure and no difference in the incidence of patent ductus arteriosus, intracranial haemorrhage, or mortality but a significant reduction in the incidence of pneumo-thorax and bronchopulmonary dysplasia in those treated with negative pressure.

Okay, so…This group looked at use of CNEP in NICU and PICU and confirmed previous findings showing "that early initiation of treatment for respiratory failure will reduce the need for intubation. Non-invasive (negative pressure) means of respiratory support will reduce the incidence of factors that contribute to chronic lung disease, particularly in preterm infants."

Are we seeing a trend here?

Notwithstanding the many potentials discussed in this article let's boil down some of the key positives pointed out from their experience and those cited from various other sources in their conclusion:

- Negative pressure produced a more rapid improvement in oxygenation
- Negative pressure respiratory support is a non-invasive yet effective treatment for respiratory failure
- May avoid the need for intubation, reduce the pathophysiological consequences of positive airway pressure ventilation, and aid extubation."
- Negative extrathoracic pressure increases thoracic volume with less compression of vascular structures and consistently reduces pulmonary vascular resistance
- (Negative extrathoracic pressure) may dilate pulmonary capillaries and improve ventilation-perfusion matching
- Some patients maintain good respiratory function during the day when treated with negative pressure at night
- An increase in the patient's functional residual capacity, an increase in lung compliance, support of a compliant chest wall, or a reduction in diaphragmatic fatigue may all occur as a result of inflation of the lung under negative pressure
- Infants with respiratory distress syndrome treated with negative extrathoracic pressure had less need for positive airway pressure ventilation and a shorter need for supplemental oxygen than infants treated with oxygen alone

It is hard to say it any better. This paper clearly delineates many of the benefits of negative pressure lung inflation.

The next paper documents the use of BCV in a medically very challenging infant with history of prematurity and low birth weight:

Biphasic Cuirass Ventilation in an Infant with Severe Respiratory Failure

Keiko Nishiyama, Makiko Komori, et al
Journal of Anesthesia (2009) 23:166-167

Figure 1

Few studies have reported the effect of biphasic cuirass ventilation [BCV] in infants. BCV is a noninvasive, ideal technique for mechanical ventilation that overcomes the shortcomings of conventional mechanical ventilation. Moreover, BCV prevents complications associated with endotracheal intubation, and patients can have conversations and eat meals while receiving BCV. When used in infants, BCV permits attachment between children and their mothers. We describe our experience with a male infant with chronic pulmonary disease associated with severe respiratory failure who responded well to BCV. Mechanical ventilation was performed for 3 days after birth in a 1367-g-weight infant, who was born with transient tachypnea at 29 weeks of gestation. Supplemental oxygen was given until 34 days after birth. The infant was in the neonatal intensive care unit until 39 weeks of age corrected for gestation. At discharge from the neonatal intensive care unit, chest radiography showed that atelectasis of the upper right lobe persisted, in association with emphysema-like changes. Wilson-Mikity syndrome was thus diagnosed. Bronchiolitis caused by rhinovirus developed 4 months after birth, and mechanical ventilation was needed. Airway pressure release ventilation (APRV)[4,5] was therefore performed for about 2 weeks. At the introduction of APRV, the patent's airway pressure was maintained at 28 cmH2O to prevent retraction of the chest wall. The lung collapse and hypoxemia were attenuated. The trachea was therefore extubated. Nasal noninvasive positive-pressure ventilation was first performed to treat the persisting atelectasis. Stable positive pressure was not achieved because of a poorly fitting nasal mask. A skin ulcer developed at the site of attachment, interfering the infant's feeding. Two weeks after the extubation, BCV was started, with the use of a Respiratory Therapy External (RTX; Medivent, London, UK) device. Airway pressure was maintained by the intermittent use of continuous negative pressure. Four weeks after extubation, however, bronchiolitis due to respiratory syncytial virus developed. The infant again required mechanical ventilation and received APRV for 8 weeks. Then, BCV continuous negative pressure was again intermittently applied. Because of the chronic respiratory disorder, continuous negative pressure was used while the infant was nursing. Sputum removal was promoted by performing BCV in the clearance mode. Then a continuous negative pressure of –7 cmH2O was applied for 24 h to expand the thorax. Respiratory muscle retraction subsided, and the atelectasis showed marked attenuation on chest X-ray films.

The infant was able to become attached to his mother and drink milk from a bottle while wearing the appliance; his nutritional status was good (Fig. 1). Six weeks after the reintroduction of BCV, mechanical ventilation was no longer needed, even while the infant was nursing. As compared with other types of noninvasive mechanical ventilation, BCV is easily fitted to the patient and does not require sedation. BCV can also be used intermittently as physical therapy and is easily accepted by the hospital staff, as well as by patients' families. We are now assessing the possibility of performing BCV at home in infants who have acute respiratory infections.

In this letter to the editor this group describes what for them was a clear demonstration of the therapeutic application of BCV on a very challenging infant.

This case provides a typical example of the effects of BCV use in children with respiratory related support needs. Here we see the failure of NIPPV to achieve the clinical goals for the patient. The all too common mask fit with facial skin issues and the fact that the patient couldn't feed naturally during mask support prevented the patient from improving. During use of Continuous Negative he was able to bottle feed in his mother's arms. Natural nutritional intake, mother child bonding while the baby receives breathing support. Revolutionary! One line in this that stands out for me is "Respiratory muscle retraction subsided, and the atelectasis showed marked attenuation on chest X-ray films." Here is described the effect seen so often. That is relatively rapid relief of respiratory distress, often accompanied by onset of a series of good naps, then frequently followed by general improvement of respiratory status. Offering the potential of this type of dramatic turnaround makes BCV a very exciting intervention to apply.

In this case BCV kept reoccurring atelectasis at bay, provided support of breathing and facilitated the ultimate weaning from PPV. These are typical results with BCV. The next paper we draw from documents BCV use in a group of respiratory failure infants.

Negative Pressure Ventilation via Chest Cuirass to Decrease Ventilator-Associated Complications in Infants with Acute Respiratory Failure: A Case Series

Klonin H., Cheifetz I.M. et al
Respiratory Care, May 2000,Vol 45 No. 5: 486 – 490
http://www.rcjournal.com/contents/05.00/05.00.pdf

Abstract: Pulmonary and nonpulmonary complications of invasive positive pressure ventilation are well documented in the medical literature. Many of these complications may be minimized by the use of noninvasive ventilation. During various periods of medical history, negative pressure ventilation, a form of noninvasive ventilation, has been used successfully. We report the use of negative pressure ventilation with a chest cuirass to avoid or decrease the complications of invasive positive pressure ventilation in three critically ill infants at two institutions. In each of these cases, chest cuirass ventilation improved the patient's clinical condition and decreased the requirement for more invasive therapy. These cases illustrate the need for further clinical evaluation of the use of negative pressure ventilation utilizing a chest cuirass.

In this paper three cases in which the Hayek Oscillator, the predecessor to the RTX, was used to dramatically improve the course of illness with BCV.

Case 1 describes a 6-month-old male infant worsening respiratory failure with peripheral oxygenation saturations of 80% on a fraction of inspired oxygen (FIO2) of 0.60. Chest radiograph revealed a lingular infiltrate. Bronchoscopy confirmed the diagnosis of Pneumocystis carinii pneumonia. Presented to PICU with a respiratory rate of 60 breaths per minute, severe intercostal retractions, grunting, and nasal flaring. Arterial oxygen saturation 96% on face mask with FIO2 of 1.0. The patient was initiated on continuous negative airway pressure (–6 to –8 cm H2O) using a Hayek Oscillator. Shortly after initiating continuous negative pressure via chest cuirass, the patient's respiratory rate decreased to 40 breaths per minute. The FIO2 was weaned from 1.0 to 0.80 while maintaining oxygen saturation above 95%. Over the next several hours the patient's oxygen saturation again decreased to, 90% with the FIO2 remaining at 0.80. The infant's ventilatory support was, therefore, changed to intermittent NPV with a ventilatory rate of 40 breaths per minute and peak inspiratory and expiratory pressures of –18 cm H2O and –2 cm H2O, respectively. On these settings, the patient had decreased work of breathing, as evidenced by decreased retractions, grunting, and nasal flaring. The FIO2 delivered via face mask was weaned to 0.60 while maintaining oxygen saturation 95%. Subsequently, the patient improved with routine supportive care. The infant had progressive normalization of respiratory effort, respiratory rate, and oxygenation. He did not require further admission to the intensive care unit during his hospital course.

Case 2 describes a 4-month-old former 26-week premature male infant with history of Chronic Lung Disease of Prematurity with increasing respiratory distress. He intubated and ventilated. Post extubation this patient developed atelectasis, tachypnea and grunting. BCV was started at -30 to in an attempt to decrease his work of breathing and to improve the atelectasis. In addition, routine use of the Secretion Clearance mode was utilized. After two days the left lung re-expanded, the next day the right lung expanded. His lungs subsequently remained expanded and he was able to be discharged in another two days.

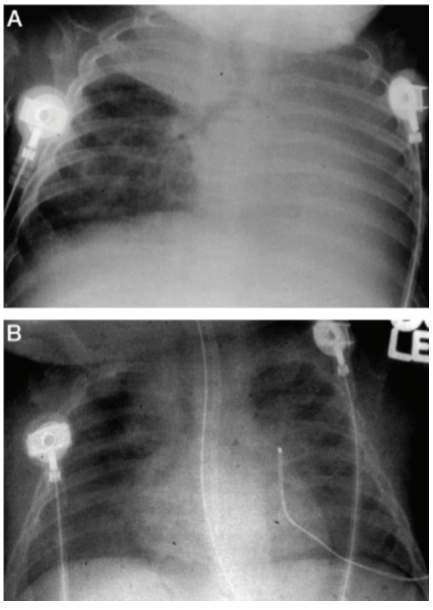

Figure 2

Case 3 describes a 16 month infant with respiratory failure and bronchiolitis obliterans. Severe atelectasis and airway plugging, and was requiring daily bonchoscopic clearance. This patient failed conventional mechanical ventilation, was advanced to positive pressure high frequency oscillatory ventilator. Development of arrhythmias and hemodynamic instability resulted in placing the patient on ECMO. Poor oxygenation with a pulmonary compliance of 0.35 mL/cm H2O/kg observed.

Following day 18 of the ECMO course BCV was initiated in Control Mode at -25/5 at 30 cycles per minute with I:E 1:1 along with PPV CPAP 5 PS 10. The patient was also provided two cycles of secretion clearance q2h. Good chest movement was observed and hemodynamic stability was maintained. Large volumes of secretions resulted and were cleared with routine suctioning. After 24 hours on BCV dynamic compliance doubled to 0.72 mL/cm H2O/kg. After the next 24 hours oxygenation improved adequately for the patient to be decannulated from ECMO. This infant was able to be extubated from PPV after three more days weaned to nasal O2 and returned to referring hospital.

In the author's discussion of these cases they provide the following considerations:

- Chest cuirass NPV may be used to avoid the potentially deleterious effects of invasive PPV
- The potential beneficial effects of NPV can be divided into several categories,
  - □ reduced airway complications
  - □ improved pulmonary parenchymal inflation at reduced airway pressures
  - □ reduced cardiovascular compromise
  - □ decreased sedation requirements
  - □ improved enteral nutrition
- By eliminating the need for intubation, the potential airway complications associated with invasive PPV can be completely avoided
- Barotrauma, also associated with PPV, can be avoided by the use of NPV
- Not only does NPV avoid the detrimental effects that PPV can have on hemodynamics, NPV may actually improve the patient's hemodynamic status
- NPV may minimize sedation requirements, as it is generally well tolerated by most patients
- Additionally, enteral feeding is usually well tolerated in patients treated with NPV alone

"Chest cuirass NPV may provide a partial solution that avoids many of the pitfalls of previous ventilation strategies."

The next article documents BCV use helping overcome the challenges presented in infants with acute symptoms of Cystic Fibrosis (CF).

Negative extrathoracic pressure in infants with cystic fibrosis and respiratory failure.

Klonin H, Campbell C, Hawthorne J, Southall D.P., Samuels M.P
Paediatric Pulmonology 30: 260-264 (2000)

This paper describes results of the application of Continuous Negative on 3 patients with infant onset of some of the severe pulmonary system challenges of Cystic Fibrosis. The

presentation and treatment of the respiratory failure symptoms described in this group provide additional clear examples of how BCV can offer significant improvement, even in infants with severe compromise.

From the opening of this paper:

> A small proportion of infants with cystic fibrosis and bronchiolitis suffer prolonged and severe courses, with up to a 60% mortality when mechanical ventilation is required. Hospital admission may be prolonged, with significant morbidity and sequelae. However, the outlook for infants who require ventilation may be better than previously thought. Nevertheless, the Cystic Fibrosis Foundation consensus report (1993) states that "because clearance of secretions from small airways by endotracheal suctioning is less effective than coughing, all possible measures should be instituted to limit the duration of intubation."
>
> We report on 3 infants who had cystic fibrosis diagnosed by sweat tests in early infancy, 2 with genotype confirmation. All developed severe and prolonged wheezing illnesses and deteriorated clinically despite maximal medical therapy, including bronchodilators, steroids, antibiotics, and, when indicated, antireflux therapy. In order to avoid endotracheal intubation or tracheostomy, we applied trials of continuous negative extrathoracic pressure (CNEP)…(usually –4 to –8 cm H2O).

The authors go on to describe in detail the clinical course of these 3 very sick CF patients and how they benefitted from Continuous Negative use.

From their discussion:

> The placement of an artificial airway and the administration of intermittent positive pressure ventilation (IPPV) are both associated with complications. These include high rates of infection, and barotrauma may be a problem for patients with underlying bronchiectasis.
>
> Continuous supervision is required by skilled personnel within the PICU to maintain an airway free from secretions. In contrast, negative pressure ventilation may be safely applied outside the PICU and indeed within the patient's home, as in case 2. The patient can communicate, cry, cough, and swallow while undergoing negative pressure ventilation. The use of noninvasive respiratory support has not previously been described for severe wheezing in infants with cystic fibrosis. Face or nasal mask IPPV has been used for severe respiratory failure or in end-stage respiratory disease as a bridge to transplantation in older patients. Our 3 patients all had severe, acute, and chronic respiratory symptoms that appeared to contribute to their failure to thrive and warranted further respiratory support. Nasal mask IPPV or CPAP is more difficult to apply to infants and young children, usually because they are less tolerant of any facial appliance. As we knew that CNEP was well-tolerated at this age, we considered this to be worthy of a treatment trial for these patients. In Case 3, the infant subsequently needed intubation for more severe clinical deterioration, although it was our impression that using CNEP/ECWO reduced the duration of intubation. These techniques provide effective respiratory support on extubation and enabled us to wean ventilation earlier than would otherwise have been possible. Case 1 was considered for a tracheostomy, which is a procedure with its own morbidity and mortality in infants. This was avoided by the use of negative pressure ventilation. Case 2 clearly thrived in negative pressure ventilation when all else had failed. Achieving adequate growth and weight gain are important indicators of successful treatment in chronic respiratory failure. We consider using CNEP in any patient with moderately severe respiratory distress where intubation might be indicated. Our largest experience is in patients with acute bronchiolitis. Assessment of improvement is based on clinical parameters, including respiratory and heart rates, chest wall retractions, oxygen requirement, and transcutaneous PCO2. Patients receive negative pressure ventilation outside the PICU and do not necessarily have indwelling arterial lines. Capillary or arterial blood gas analysis may be used in assessing the patient's course when noninvasive blood gas monitoring shows unfavorable trends. We aim to start treatment before hypercapnia develops, as a rising level of carbon dioxide implies exhaustion which may limit the effectiveness of CNEP. We do not offer CNEP to patients in an impending arrest situation or where the disease process is thought to be progressing too rapidly to warrant a trial of negative pressure ventilation. This is in line with current trials of noninvasive positive pressure ventilation. CNEP works by recruitment of alveoli and improvement in ventilation/perfusion matching. Negative extra-thoracic pressure of any sort provides a distending pressure on both airways and alveoli by increasing the transpulmonary pressure gradient. It may differ from positive airway pressure by avoiding compression of the pulmonary vascular bed. In the infant, it may also stabilize the easily collapsible chest wall, overcoming small airway closure and reducing air trapping. Two of our patients showed an increase in respiratory system compliance in CNEP, which may have resulted from improved airway conductance or lung compliance. This was associated with a decrease in WOB and gave the clinical impression that they were more comfortable. In patients with chronic obstructive airways disease, intermittent negative pressure ventilation has been thought to increase muscle strength and endurance, decrease hypercapnia, improve functional reserve of the respiratory muscles, and decrease inspiratory muscle fatigue. In patients with cystic fibrosis and acute or chronic respiratory failure, the same mechanisms may operate. ECWO has decreased muscle fatigue and improved blood gases in adult patients with chronic obstructive airways disease. Like CNEP, it also operates around a negative baseline, but may provide more control of functional residual capacity by maneuvers such as changing the end expiratory chamber pressure; this may prevent or decrease hyperinflation. Furthermore, ECWO has a physiotherapy mode that may be particularly useful in cystic fibrosis. High-frequency chest compression is associated with increased mucus clearance and a long term improvement in lung function in patients with cystic fibrosis. A 29-year-old woman with cystic fibrosis also had improved weight gain with high-frequency chest compression, similar to our case 2. We feel this may be associated with decreased WOB, due to the extra support provided by noninvasive respiratory support. Noninvasive positive pressure ventilation using BiPAP was prospectively studied in a pediatric population with acute respiratory failure, but the average age of children was 11 years, and the youngest was 6 months. Although we are experienced with face mask ventilation in our unit, we have found that infants with copious secretions tolerate poorly the presence of the face mask and high gas flows. Thus we feel that nasal CPAP would not have been as effective in our patients because it was harder to apply and maintain, particularly with longer periods of treatment or respiratory support used at home. In conclusion, negative pressure ventilation provided useful support to 3 infants with acute respiratory failure associated with severe chronic wheezing symptoms in cystic fibrosis. It was not associated with any apparent adverse effects. Further experience

with these techniques of respiratory support is warranted, as well as research into the role of ECWO as a physiotherapeutic aid in CF.

The mentioned improvement in compliance along with immediate patient response warrants a closer look in the 2 patients on whom pulmonary compliance was collected. The following is that information:

Patient 1

- Respiratory rate decreased from 40 to 24 breaths per minute
- Pulmonary function tests were performed using the PEDS Pulmonary Function Evaluation System (Mas, Inc., Hatfield, PA). This involved an esophageal balloon, face mask, and pneumotachograph to calculate tidal volume, minute volume, inspiratory and expiratory resistance, dynamic compliance, and pulmonary energetics at 0, –4, –8, and –12 cm H2O over a 1-hr period and then 24 hr later (in –8 cm H2O).
- These showed a rise in pulmonary compliance
  - 0.37 mL/cm H2O /kg baseline,
  - 0.82 at –4 and –12 cm H2O
  - 0.92 at 24 hr
- decrease in pulmonary resistance
  - 91.8 cm/L/sec baseline
  - 69.5 at –4 cm H2O
  - 55.3 at –12 cm H2O
  - 29.7 at 24 hr
- In work of breathing (WOB)
  - 0.24 kg.cm/kg at baseline
  - 0.11 at –4 cm H2O
  - 0.10 at –12 cm H2O
  - 0.08 at 24 hr

Patient 2

CNEP at –6 cm H2O

- Obviously more comfortable, with decreased nasal flaring and rib retractions
- Produced more secretions in CNEP
- Respiratory rate dropped from 60 to 30 breaths per minute
- Heart rate decreased from 150 to 130 beats per minute
- Transcutaneous PCO2 readings remained at the upper limit of normal
- Pulmonary function testing using a face mask and pneumotachograph revealed that his dynamic compliance in natural quiet sleep rose
- Pulmonary Compliance rose from 72.6 to 91.8 ml/cm H2O in CNEP

BCV has been well demonstrated to lower pulmonary artery pressure in respiratory failure in a group of adults. The following article shows that same effect of CNEP in infants with Persistent Pulmonary Hypertension of Newborn (PPHN).

Continuous negative pressure in the treatment of infants with pulmonary hypertension and respiratory failure.

J Perinatol. 1989 Mar;9(1):43-8.
Sills JH, Cvetnic WG, Pietz J.

Abstract: We report the successful use of continuous negative pressure (CNP) with standard intermittent mandatory ventilation (IMV) in five patients suffering from respiratory failure and persistent pulmonary hypertension of the newborn (PPHN). These infants all fulfilled criteria for use of extracorporeal membrane oxygenation (ECMO) with PaO2 less than 40 torr, alveolar-arterial oxygen difference (AaDO2) greater than 620 mm Hg, and oxygenation index (OI) greater than 50. Despite a considerable amount of conventional ventilation with mean airway pressures (PAW) between 14 and 26 cm water, none of these patients were able to improve oxygenation. All infants demonstrated significant improvement in ventilation requirements after initiation of CNP as reflected by a decrease in PAW, proximal inspiratory pressure (PIP), and IMV. Oxygenation dramatically improved in all infants. All five patients survived without any pulmonary or neurological complications at discharge. Availability of CNP may circumvent the need for ECMO in infants with severe lung disease and PPHN.

As the lung is recruited with negative pressure so is the pulmonary vasculature. There is zero potential of this beneficial natural effect of spontaneous inspiration that is enhanced by negative pressure support of the lungs when positive pressure is used in support of breathing. Frequent dramatic improvements in gas exchange and markers of respiratory distress are experienced by patients following close on application of BCV. Increased rates of recovery from respiratory compromise occur routinely with BCV application. Using BCV for tiny lungs opens new strategic intervention options that as seen in the papers reviewed here can and often does change the course of infant cardio-pulmonary illness for the better.

You can follow Gary on LinkedIn or reach him by email at gary.mefford@HayekMedical.com. Learn more by visiting HayekMedical.com.

Mr. Mefford's list of publications on BCV can be downloaded at https://app.box.com/s/7f810fe3ef3ca6b06dc3

Investigation or Litigation

Shabih Manzar, MD

Case

A female infant, born at 38 weeks 6 day with birth weight of 2755 grams to 31 year old G3P3003, by C-Section secondary to repeat c-section. Level II prenatal ultrasound (US) at 34 weeks showed the possibility of Dandy-Walker variant (a notch in the cerebellar vermis seen with no evidence of hydrocephalus or ventriculomegaly), fetal spine was normal. Post-natal US (Figure 1) showed unremarkable ventricles and sulci, no evidence of intracranial hemorrhage or hydrocephalus. The echo texture of the brain parenchyma is within normal limits. The corpus callosum, choroid plexus, and visualized posterior fossa appear unremarkable.

A complete physical examination including a detail neurological exam was normal. Infant had transitioned well and was tolerating feeding well. Mother was counseled and she understood the situation and did not request any further investigation. The on-call neonatologist was consulted and basing on normal head US (HUS) and physical examination (PE), a plan was made to discharge the infant with close follow with the pediatrician. However, a second opinion was sorted from the other neonatologist and decision was made to obtain a brain MRI. The explanation and rationale given was that posterior structures are difficult to see on HUS. The other reason was the possibility of legal implication if a diagnosis is missed. The MRI (Figure 2) was unremarkable and showed no mass, mass effect or no areas of restricted diffusion. Myelination pattern was according to the patient's age.

Discussion

Day by day our health system is becoming the most costly health system in the world. Strategies have been taken to decrease the health cost. The introduction and concept of high-value care is one example.[1,2] However, it is easier said than done. We have a high litigation society and that has a profound impact on the medical practice. Due to scare of law suit, physicians over investigate, as seen in the case. In resource limited centers, a normal post natal HUS and normal PE with good follow should be suffice. However, with the fear of legal implication and availability of high technological resources, physicians are pushed to maximize the investigations to avoid the risk of medical malpractice law suit. MRI is not only costly but requires sedation. Also antenatal US, in cases of Dandy-Walker variant, is not very reliable if performed before 18 weeks of gestation[3] thus obtaining a follow-up head US is not justifiable. The case presented clearly highlights on the need for a discussion of a standardized balance approach and a management pathway in making sure that high-value care is provided with minimal fear of litigation.

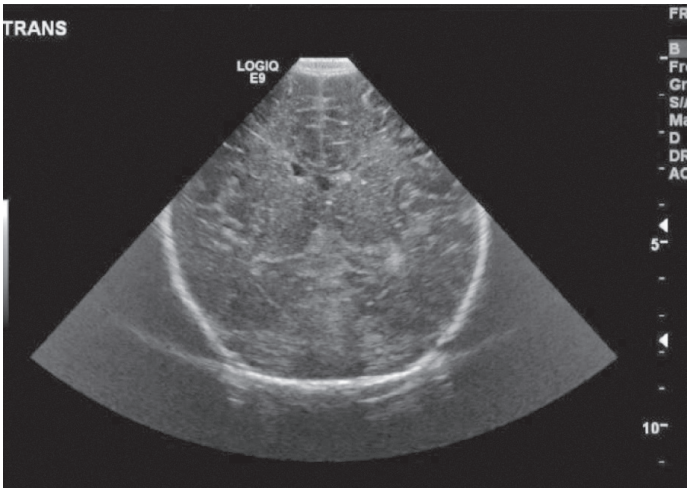

Figure 1. Head ultrasound showing normal posterior fossa ruling out Dandy Walker Malformation

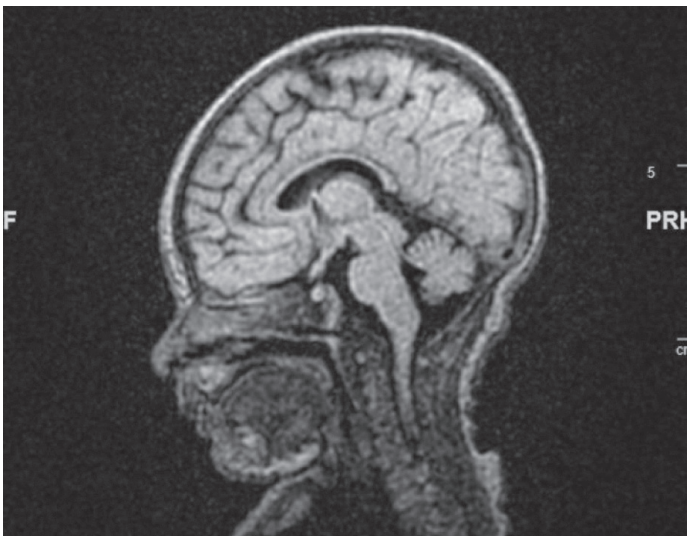

Figure 2. MRI brain showing normal posterior fossa ruling out Dandy Walker Malformation

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3 Alam A, Chander BN, Bhatia M. Dandy-Walker Variant: Prenatal Diagnosis by Ultrasonography. Med J Armed Forces India. 2011; 60(3):287–289. doi:10.1016/S0377-1237(04)80066-2

News…continued from page 16

were elevated, ranging from 9 to 14. The baby was started on morphine (0.03 mg/kg every three hours per protocol) and his Finnegan scores dropped significantly (range, 2 to 3). However, the infant appeared to be overly sedated without respiratory depression but with sinus bradycardia. The infant remained sedated despite rapid weaning from morphine. Other etiologies of bradycardia and lethargy were ruled out. Completely off morphine (on day 3 of life), the infant again developed signs of withdrawal and his Finnegan scores climbed. He was then trialed on clonidine (1 mcg/kg every three hours). His Finnegan scores improved, but he again developed sinus bradycardia. Clonidine was discontinued on the fifth day of life. The infant improved over the next few days and was discharged.

Dr Eldridge and colleagues note in their paper that kratom use in pregnancy and its effects on the developing fetus and newborn are "largely unknown. Only a few case reports of NAS due to maternal Kratom use are reported internationally. There is a lack of literature to help guide the pediatrician in management of NAS in the kratom-exposed infant." With the current opioid epidemic and increasing incidence of opioid use among pregnant women, cases of NAS due to maternal kratom use are likely to increase "as mothers look to what they believe to be nonopioid alternatives for opioid dependence," they point out. "As highlighted by our case, it is important for pediatricians to be aware of nonprescription self-treatments for opioid withdrawal. Because Kratom is not reported on urine drug screens, pediatricians need to ask specifically about nonprescription uses during pregnancy when taking histories from mothers with opioid dependence to better care for their newborns," they conclude.

Newborn-Specific Antibiotic-Stewardship Programs Falling Short

Few newborn-specific antibiotic-stewardship programs (ASPs) fully adhere to the Centers for Disease Control and Prevention (CDC) Core Elements of Hospital ASPs, according to an audit. "The most striking finding was that out of 412 infants on antibiotics for greater than 48 hours (meaning they were supposedly being treated for some sort of infection), only a quarter of them had positive blood cultures," said Dr Timmy Ho from Beth Israel Deaconess Medical Center, Boston, Massachusetts. "This signal of antibiotic overuse represents a huge potential for improvement in treating the right patient with the right medication for the right amount of time," he said.

The widespread inappropriate use of antibiotics has led several organizations to endorse the use of ASPs. Recently, the American Academy of Pediatrics Section on Neonatal Perinatal Medicine joined the Choosing Wisely campaign, whose type top-5 list of potentially overused tests and treatments includes "routine continuation of antibiotic therapy beyond 48 hours for initially asymptomatic infants without evidence of bacterial infection."

As part of the Vermont Oxford Network's recent initiative to decrease antibiotic overuse in the newborn period, Ho's team evaluated neonatal antibiotic usage among 143 centers and 725 infants who were on antibiotics to establish a baseline. Their cross-sectional examination looked at seven CDC core elements: capacity for leadership commitment, accountability, drug expertise, action, tracking, reporting and education. None of the 143 participating centers addressed all seven CDC core elements, the researchers report. Of the 725 infants receiving antibiotics, 87% had blood cultures, 15% had urine cultures and 8% had cerebrospinal fluid cultures before initiating antibiotics. Ultimately, 85% of the blood cultures did not reveal an organism. Of the 412 infants >48 hours of age and on >48 hours of antibiotics, only 26% had positive culture results, 17% had no culture obtained and 69% had at least one negative culture result. More than one-third of patients received antibiotics because of maternal risk factors, and 44% received antibiotics because of suspected early-onset sepsis.

Phototherapy Bed Surface to Support Neonatal Skin Preservation

Deepakshyam Krishnaraju, MSc, ME and Sivakumar Palaniswamy, MSc, BME

Background

Skin is the largest organ of the human body. It plays a crucial role in protecting the transition for a newborn from the womb into the postpartum world. Skin is the first line of defense against a dry, harsh, and pathogen-loaded environment. It plays an important role in thermoregulation and in maintaining fluid balance; perturbations may require intervention. The skin of a term newborn baby is not considered to be mature until 3 weeks of age and a preterm baby's skin takes even longer to mature.[1] During the first few weeks of life, a neonate's skin is more susceptible to pressure ulcers (PU), also known as bed sores. The baby's skin is also affected due to implications requiring interventions such as thermoregulation, eg, hypothermia, and excessive dehydration.

Until relatively recently, when compared to adults, pediatric and neonatal populations were not considered at risk of developing PU due to the relative ease of repositioning lightweight patients by caregivers. If a newborn developed a PU, the cause was attributed to being hospitalized.[2]

Most prevention and treatment protocols for PU in pediatric populations are extrapolated from adult practice. Several recommendations have been adopted such as high-specification foam mattresses, air mattresses, sheepskin, gel mattresses and other alternatives[4] to mitigate the incidence and prevalence of PU. This article will explore more closely the positioning of neonates and the use of the NeoLight GelMat, a cost-effective product designed to support healthy skin in the newborn population.

Neonatal Pressure

Ulcers Definition: In 2014, the National Pressure Ulcer Advisory Panel (NPUAP), the European Pressure Ulcer Advisory Panel (EPUAP), and the Pan Pacific Pressure Injury Alliance (PPPIA) defined a pressure ulcer as "a localized injury to the skin and/or underlying tissue usually over a bony prominence, because of pressure, or pressure in combination with shear. A number of contributing or confounding factors are also associated with pressure ulcers; the significance of these factors is yet to be elucidated".[5]

The authors are with NeoLight LLC.

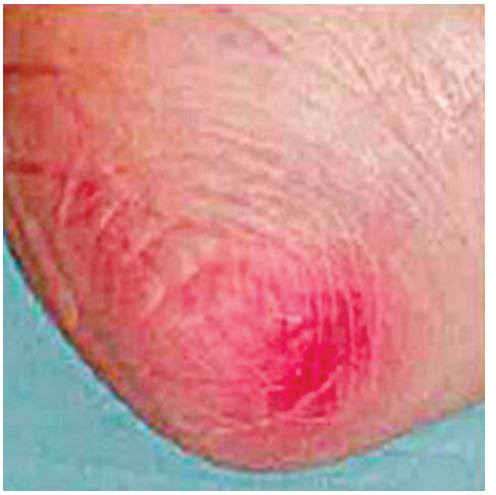

Figure 1. Example of PU in the Heel region of a Neonate – Non-blanchable redness over bony prominence

Causation and Categories of PU: The developmental mechanism of PU is based on prolonged occlusion of the blood capillaries obstructing blood supply to the tissue. The magnitude and duration of the applied pressure determine the severity of injury.[6,7] As stated above, four (4) Stages have been described and agreed upon and drawings of each Stage are shown in Figure 2. However, despite risk factors for adult PU, a consensus has not been achieved for neonatal PU risk factors.

NPUAP describes 4 Stages of PU:

Stage 1: a non-blanching erythema is produced on intact skin;
Stage 2: partial loss of skin thickness or blisters may appear;
Stage 3: total loss of skin thickness;
Stage 4: total loss of tissue thickness, with exposed muscle or bone.

There are 2 additional Stages:
Unstageable: Bottom of the sore is not visible, therefore the depth is unknown. The physician will stage it once it's cleaned out.
Suspected Deep Tissue Injury (SDTI): Surface of the skin has the appearance of Stage 1 or 2, but underneath the surface, it's Stage 3 or 4.

Pervasiveness of PU: Some of the risk factors for PU in neonates reported in the United Kingdom National Institute for Health and Care Excellence (NICE) guidelines include reduced mobility, acute/chronic illness, extremes of age,

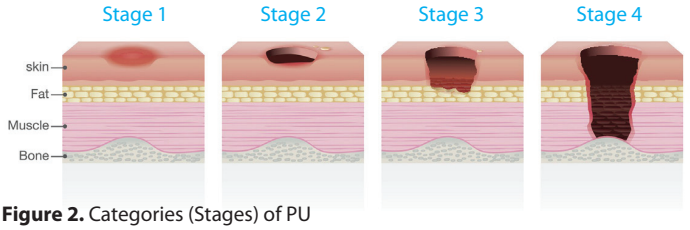

Figure 2. Categories (Stages) of PU

duration of pressure, amount of pressure, shear on the skin, moisture, diminished perfusion, infection, and malnutrition.[4] Therefore PU prevention in neonates focuses on skin care (hygiene and hydration), pressure management, and adequate nutrition. However, a fundamental part is the assessment of PU by a valuation scale. Neonatal dermatology experts agree that prevention lies in early risk identification, and risk assessment scales for PU are an excellent tool for this purpose. There are 14 validated, published, pediatric, risk assessment scales[5] which were originally derived from scales designed for pediatric populations. Amongst them, 4 are used for the neonatal population that includes Braden Q, Glamorgan Scale, Starkid, and Neonatal Skin Risk Assessment Scale (NSRAS).[26-30] These scales have good sensitivity and specificity values, perform well in identifying a patient at risk of PU and propose prevention strategies. However, these scales are adapted from adult scales. More comprehensive scales suitable for neonates of different gestational ages and corrected ages are needed.

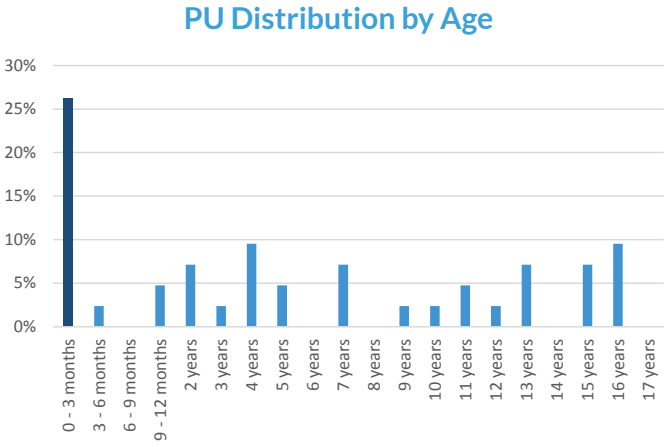

Figure 3. Pervasiveness of PU distributed by age group[9]

The pervasiveness of PU in a population — neonates in this case — is usually reported using incidence and prevalence rates. Incidence is defined as the number of new cases of PU commencing during a specified period in a given population; Prevalence is the number of cases with PU at a given time. A delimited literature review has revealed that NICU incidence rates vary from 3.70% to 21.60% with a prevalence of 23%.[12-17]

The metrics for PU reported in the survey[18] conducted by the Minnesota Department of Health and in the national pediatric survey[9] conducted by Texas Children's Hospital offer insights into the seriousness of PU in the neonatal population. Children less than 3 months of age have the highest prevalence (~ 25%), eclipsing the second highest by a significant margin (Figure 3). Wherein, Stage I PU were reported as the most common Stage and were observed within the first 2 days of admission. Please see Figure 4 for the complete distribution of PU in the pediatric population by Stages. Additionally, nearly 66% of pediatric

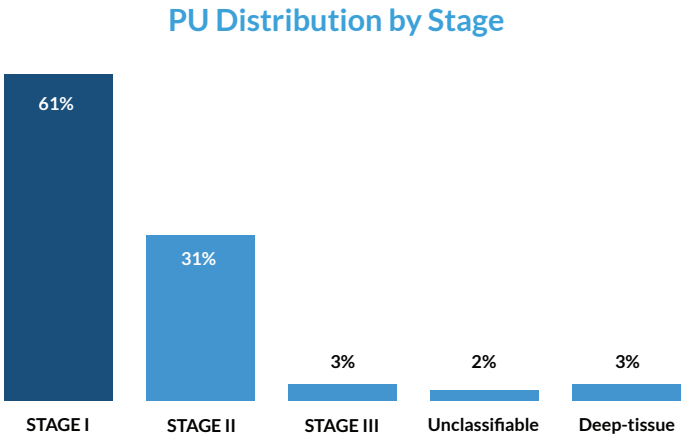

Figure 4. Pervasiveness of PU distributed by the stages[9]

patients were reported acquiring Stage 3 and Stage 4 PU in the hospital facility (see Figure 7).

Impact of PU on a Hospital

In the 21st century, a hospital-acquired Stage 3 or Stage 4 PU is classified as a "Never Event" by the Center of Medicare and Medicaid Services (CMS). Never Events are serious and costly errors that occur in the provision of health care services that can be avoided by using evidence-based care.[3] Medicare, Medicaid, and some private insurers will not reimburse physicians or facilities when one of their patients suffers a Never Event. When the Minnesota Department of Health reported on 312 Never Events, PU had the highest incidence (39%)[18] (Refer to Figure 6). The cost to heal the mildest PU can be as high as $900.[4]

To better understand the monetary burden, several studies have quantified the direct impact of PU on a hospital by studying the increased hospital costs and lengths of stay (LOS). One study estimated that a hospital spends an additional baseline amount of $900 for a Stage 1 PU. This figure rises to $17,500 in the case of Stage 4 PU.[4] In another study conducted by the Agency for Healthcare Research and Quality (AHRQ), 431,524 discharges from 38 different pediatric hospitals were investigated. The study reports a statistically significant increase in the average LOS of 8.07 days (Standard Deviation – 1.73 days) and an increase in the average treatment cost of $59,225 (Standard Deviation – $17,581) for patients with severe PU. Even though these numbers are indicative of the entire pediatric population and not just the neonatal subset (12%), conservative estimates from the reported figures indicate that the increase in LOS and hospital costs would be approximately 4.63 days and $24,063, respectively. It is evident that hospital PU can benefit from utilizing cost-effective solutions like pressure relieving devices.[30]

Pressure Relieving Devices for Neonates

In addition to causing pain and dermal damage, PU can cause life-threating infections,[19] disfigurement, and impact overall body image.[20] PU are most commonly near bony prominences with neonatal PU are focused near the occiput, heels, elbows, ears, and coccyx — areas that touch the bed surface (Figure 8). This survey was conducted in 2003 gives an insight into the distribution of PU frequency in a neonate, and a more recent survey in 2017 confirms those numbers.[10] The best-known method to prevent and lessen the impact of PU is by using pressure-relieving devices. These devices work by spreading the weight of the body over a larger area. For example, if a neonate

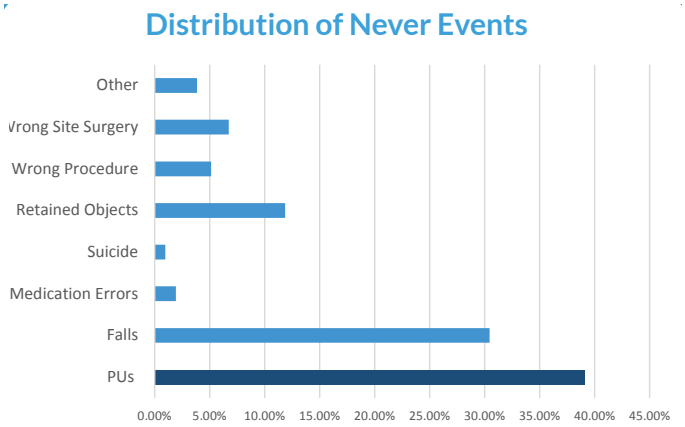

Figure 6. Distribution of Never Events[18]

laid on a firm mattress, approximately two square centimeters area under the head would rest on the mattress, whereas if the mattress was softer, it would conform to the shape of the head offering a larger contact area to relieve localized pressure. These pressure-relieving devices can be broadly classified as low-tech devices or high-tech devices.[25] Low-tech devices provide a conforming surface to distribute weight over a larger area. Examples include standard foam mattresses and air- filled mattresses. High-tech devices are like low-tech devices, but they are more dynamic in nature. Some examples of high-tech devices include alternating- pressure mattresses, which periodically inflate and deflate at various anatomical sites to relieve pressure and turning beds that aid manual repositioning of the patient by motor-driven turning and tilting.

Guidance by NICE[4] and The Association of Women's Health, Obstetric and Neonatal Nurses (AWOHNN)[21] recommends the use of high specification foam mattresses, water/air/gel mattresses, and sheepskins to relieve pressure on areas susceptible to PU. Studies validated usage and relative advantages of their recommendations over standard hospital mattresses. In one study that surveyed 215 NICUs, 67% of the NICUs used sheepskins for preventive neonatal skin protection

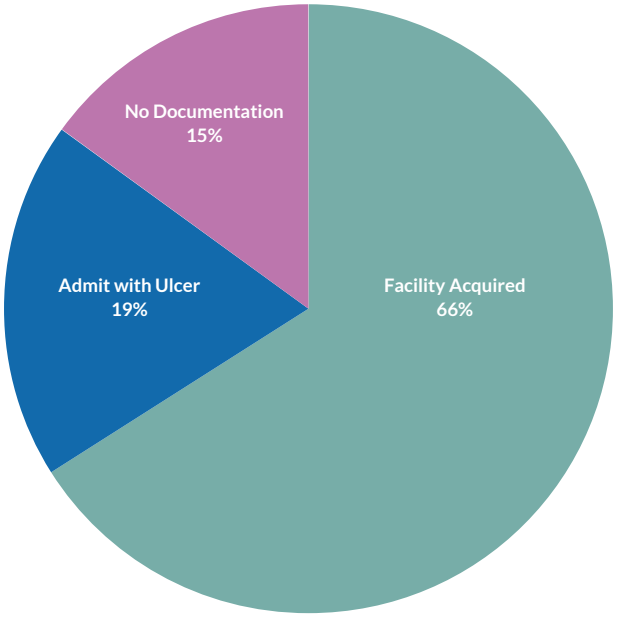

Figure 7. Pervasiveness of PU distributed by the source[9]

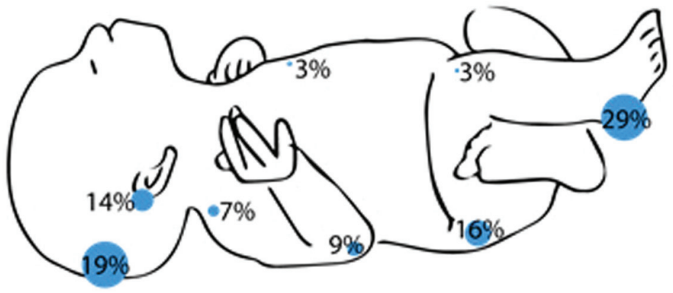

Figure 8. Regions of Most Common Occurrences of PUs in a neonate[8]

from PU and 77% use the same to treat once skin breakdown has occurred.[22] Another study reported that gel mattresses were effective in relieving occipital pressure and concomitantly reduced PU and scarring in neonates.[23] Evidence suggests that gel surfaces are equally effective as sheepskin in preventing PU[11] and might reduce head-molding over time for smaller infants who are hospitalized longer.[24] The fact that gel solutions can be customized and have a price point comparative with sheepskins make them an effective solution to prevent PU in newborns.

GelMat: A Solution for PU in Neonates

The NeoLight GelMat addresses one of the recommended methods to prevent PU,[4,5,25] ie, gel mattresses. Unlike solutions currently available, such as foam mattresses which have been designed for adults and do not cater to the requirements of a neonate, the GelMat has been designed by working closely with NICUs.

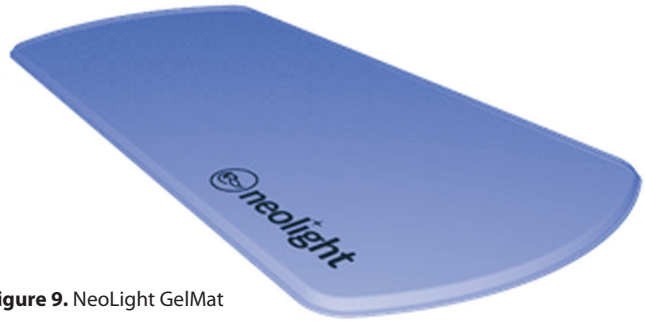

Figure 9. NeoLight GelMat

The GelMat is filled with a unique polymer material that is extremely soft. Its softness can be vicariously imagined as a material that is 3 times softer than a gummy bear. At this softness, the material almost flows like a gel under a load and returns to its original shape after the load is removed. As a result, unlike any other type of mattress that undergoes global deformation, the GelMat is softer and can locally form to the shape of the baby's bony prominences, eg, elbows, occiput, and heels. This helps to distribute the pressure uniformly by increasing the area of the GelMat contact around the bony prominences and as a result, reducing the incidence of PU. Additionally, since the GelMat is made up of a polymeric material, it does not alter its temperature rapidly when exposed to a change in environmental temperature during patient transport or other patient management activities.

Cleaning and disinfection are routine activities in hospitals and especially in a NICU. Over a short time, mattresses and sheepskins, because of their texture, trap dead skin cells. The only way to clean them is to machine wash them. GelMat is

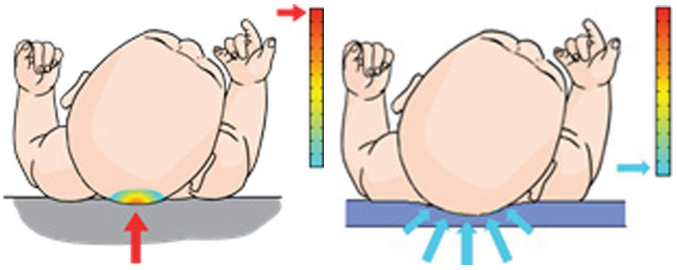

Figure 10. The GelMat changes form locally for more uniform pressure redistribution (see right) vs standard hospital mattress (see left)

designed to be nurse friendly, biocompatible, and allow cleaning with common disinfectants such as CaviWipes™. Also, the GelMat surface is smooth and designed to offer less shearing for the patient's skin. A mattress can be cleaned within 5 minutes, potentially allowing the hospital to maintain fewer mattresses in inventory.

In addition to patient comfort and skin preservation, teaching families about Safe to Sleep® practices and demonstrating acceptable positioning is done while the newborn is hospitalized. Following these recommendations, the GelMat is designed to be thick enough to redistribute pressure over bony prominences, while being thin enough to completely conform to the surface of the body ie, prevent a sinking effect. This allows the GelMat to hold a firm shape while alleviating pressure points.

Only a small number of products are appropriate to consider for use in the prevention/treatment of PU. Unfortunately, many of the solutions available are designed for adults, exposing neonates to the risk of systemic absorption, toxicity, hypersensitivity, and possible adverse reactions. The NeoLight GelMat is a unique solution that is designed specifically for neonates that meets both the safety and comfort requirements of the patient and the caregiver to potentially reduce the incidence and prevalence of PU. Currently, GelMat is being used in NeoLight Skylife™ neonatal phototherapy system to relieve pressure developed during the treatment of hyperbilirubinemia.

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Reduction of Analgesia Duration after Tracheostomy during Neonatal Intensive Care: A Quality Initiative

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Abstract

Introduction: As survival has improved in the Neonatal Intensive Care Unit (NICU), there has been a 10-fold increase in the proportion of infants requiring a tracheostomy. At our institution, we observed a wide variation in the duration of opioid use posttracheostomy from 6 to 148 days. We aimed to decrease the duration of opioid exposure in postoperative tracheostomy patients in the NICU from a baseline average of 24 days to 7 days by December 31, 2017.

Methods: We established a multidisciplinary team to develop change ideas to implement in 3 Plan-Do-Study-Act cycles that focused on enhanced care plan standardization and communication in patient care rounds with subsequent documentation in the medical record and the timely addition of dexmedetomidine to the postoperative care plan.

Results: Baseline population was from October 2014 to December 2016. The mean posttracheostomy opioid duration was 24.6 days (range, 6-148 days); neuromuscular blockade was 2.89 days (range, 0-9 days), and benzodiazepine exposure was 20.9 days (range, 1-114 days). Following our interventions, the mean duration of posttracheostomy opioid duration was 5.4 days (range, 4-21 days); neuromuscular blockade was 3.14 days (range, 1-5 days), benzodiazepine duration was 8.88 days (range, 4-25 days), and dexmedetomidine was 4.6 days (range, 0-32 days).

Conclusions: We utilized quality improvement methodology to standardize posttracheostomy management and demonstrate that we could significantly reduce the duration of opioid and benzodiazepine use after tracheostomy with the timely addition of dexmedetomidine, a structured written daily care plan, and clarification of roles and responsibilities.

Introduction

As neonatal practices and survival have improved, the proportion of infants requiring a tracheostomy has increased 10-fold from 1997 to 2005.[1] Infants in the Neonatal Intensive Care Unit (NICU) that require a tracheostomy tube placement have a myriad of airway and pulmonary conditions.[2]

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Following tracheostomy, the most common complications during the immediate postoperative period include accidental decannulation, tube obstruction, and wound problems.[3,4] To limit these complications, some organizations and institutions have created guidelines and protocols that address postoperative care including the initial tracheostomy tube change, wound care, and management of emergencies and complications.[3,5] Several national and international organizations have emphasized the importance of effective postoperative pain management in neonates.[6-8]

Emerging reports of adverse effects of opiates and GABA agonists such as benzodiazepines in patients during a time of rapid brain growth generates a sense of urgency to minimize drug exposure when possible to this vulnerable patient population.[9] In animal studies, morphine use has resulted in microglial apoptosis, decreased myelination, decreased motor activity, and impaired learning ability.[10] Patients require sedation during the first few days posttracheostomy to avoid large motor movements of the head, neck, and trunk. They may also require neuromuscular blockade in addition to adequate sedation to prevent movements that may impair wound healing of the ostomy site. Dexmedetomidine is a potent alpha-2 agonist that has hypnotic, anxiolytic, sedative, sympatholytic, and analgesic properties and provides a rapid onset of action.[11,12] In animal models, dexmedetomidine has demonstrated neuroprotection via antiapoptotic effects, reduced N-methyl-D-aspartate receptor activation, and reduction of calcium influx and glutamate scavenger abilities. These protective drug properties are effective against the neurotoxic effects of anesthetics.[13-15]

Although dexmedetomidine is less studied in infants than opiates and GABA agonists, its pharmacologic properties make it promising for use as a bridge to provide sedation and allow weaning of opioids to minimize or eliminate the risk of opioid withdrawal.[12,16] In pediatric surgical populations, intraoperative administration of dexmedetomidine reduced postoperative pain intensity, reduced use of opioids, and reduced agitation or delirium.[17] It would seem appropriate to optimize the use of analgesics and sedatives to achieve an intended sedation goal with the least amount of drug necessary for the shortest period.

Nationwide Children's Hospital NICU, a Level IV referral nursery in Columbus, Ohio consisting of 114 beds within a free-standing children's hospital, is capable of caring for the most medically complex infants. The pain assessment scale used in our NICU is the Neonatal Pain, Agitation and Sedation Scale.[18] From our

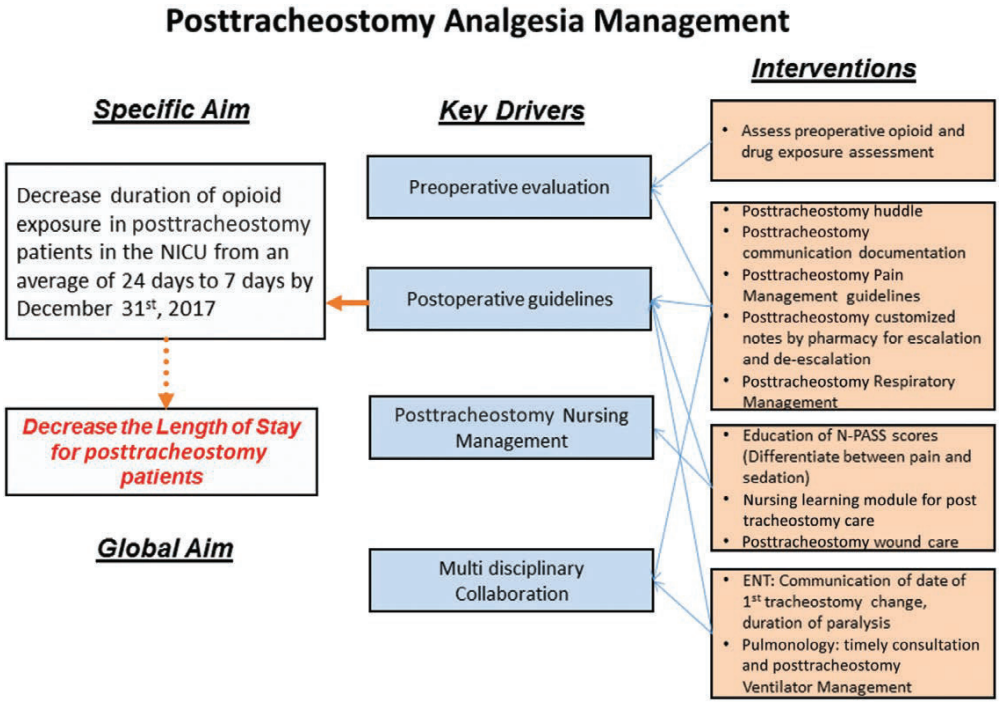

Figure 1. Key Driver Diagram: depicts the specific aim, global aim, the key drivers, and the interventions that impact posttracheostomy management.

local experience, patients who require tracheostomy have the potential for severe pain postoperatively. Our center has utilized consensus guidelines for 10 years to assist with optimizing postoperative analgesia and minimizing the incidence of abstinence.

Problem

In our NICU, the duration of postoperative opioid use in infants that required tracheostomy tube placement varied from 6 to 148 days.

Irrespective of the etiology for tracheostomy, these infants have complex medical needs, thereby providing opportunities to optimize care, including standardization of postoperative care. This variability in sedative duration, and the recent Food and Drug Administration warning to minimize the duration of exposure to sedatives when possible suggested there was a potential opportunity for improvement.

Aim

We aimed to decrease the duration of opioid exposure in postoperative tracheostomy patients in the NICU from a baseline average of 24 days to 7 days by December 31, 2017.

Design

Methods

We established a multidisciplinary quality improvement (QI) team, consisting of neonatologists, ear, nose, and throat (ENT) surgeons, an advanced practice nurse, a respiratory therapist, a wound team representative, a parent advisor, and a clinical pharmacist. The study was classified as QI and thus did not require full review by the Institutional Review Board at Nationwide Children's Hospital.

Figure 1 shows the key driver diagram with the identified key drivers and our planned interventions. Our team utilized brainstorming, process mapping, careful dive into patient charts and discussions with the frontline clinical team members to identify our drivers. Patients who undergo tracheostomy tube placement in our NICU receive a continuous infusion of morphine and midazolam after tube placement that is titrated to effect until the date of the first tracheostomy tube change. After the tracheostomy tube change both drugs are weaned as tolerated. In the pre-QI phase, baseline data collected included the duration of therapy in days, of opioids, benzodiazepines, and neuromuscular blockers after the tracheostomy placement. We also reviewed medical progress notes to determine if the patient care team documented the plan for the duration of paralysis and date of first tracheostomy tube change. These data indicated opportunities for improvement in communication and documentation among medical professionals regarding the patient care plan. Postoperative wound care protocol was not changed during this process.[19]

The ENT surgeon in collaboration with the neonatologist determined the duration of postoperative paralysis and the date of tracheostomy tube change. This QI team developed change ideas to improve communication with ENT.

The patient's preoperative opioid and drug history exposure were also evaluated. The primary medical team collaborated with pharmacy both pre- and postoperatively to develop individualized posttracheostomy analgesia and sedation care plans along with guidelines for daily escalation or de-escalation of medications on each post-operative day as determined by patient need. This care plan was documented in the medical progress notes. We progressed through 3 Plan-Do-Study-Act (PDSA) cycles.

PDSA Cycle 1

The first step in our process change to improve care plan was to optimize communication. We called a team "Huddle" when the patient returned to the NICU from surgery. The huddle intended to facilitate handoff from the ENT service to the

neonatology service. It was not uncommon for patients to return to the unit after hours, which resulted in an incomplete team available for the handoff. Collaboration with the ENT surgeons allowed subsequent tracheostomy procedures to be scheduled earlier in the day when more personnel were available. In addition, the ENT surgeon documented the minimum duration of paralysis and the anticipated date of tracheostomy tube change in the postoperative note. The ENT surgeon would evaluate the tracheostomy wound site each morning and write a note that typically occurred before the neonatology rounds, which allowed the medical team to make adjustments to the analgesia and sedation. The series of interventions, allowed the daily patient care team rounds to become the venue for care plan coordination and implementation. Postoperative analgesia and sedation plans were documented in the patient care chart the day before surgery. Medications were ordered from the pharmacy before the patient returning to the NICU from the operating room to prevent any delays in initiating postoperative medication plans.

PDSA Cycle 2

We identified that some patients required additional sedation following the discontinuation of the neuromuscular blocker. Before the intervention, our standard practice to maintain the desired level of sedation and prevent large motor movements was to increase the dosage of both morphine and midazolam. This dose increase would often impact our ability to wean these medications following the first tracheostomy tube change. When we could not attain the desired level of sedation to prevent large muscle movement, wound healing was adversely affected. The addition of dexmedetomidine (rationale for use available as **Supplemental Digital Content 1 http://links.lww.com/PQ9/A38**) to the sedation regimen allowed rapid attainment of the desired level of sedation, appeared to avoid wound breakdown, and allowed reduction of the morphine dose before the first tracheostomy change and subsequent discontinuation on the day of tracheostomy tube change if the tracheostomy wound was healed. We implemented a structured postoperative daily analgesia and sedation guideline (available as **Supplemental Digital Content 2** at **http://links.lww.com/PQ9/A39**) that included escalation and de-escalation options for the evening hours. The guideline included the addition of dexmedetomidine either the day before tracheostomy change or when the desired level of sedation could not be not easily attained with an opioid and benzodiazepine without paralysis. The sedation guideline was discussed in patient care rounds and individualized for each patient as needed. The team clinical pharmacist recorded the agreed upon detailed plan in the daily pharmacist note.

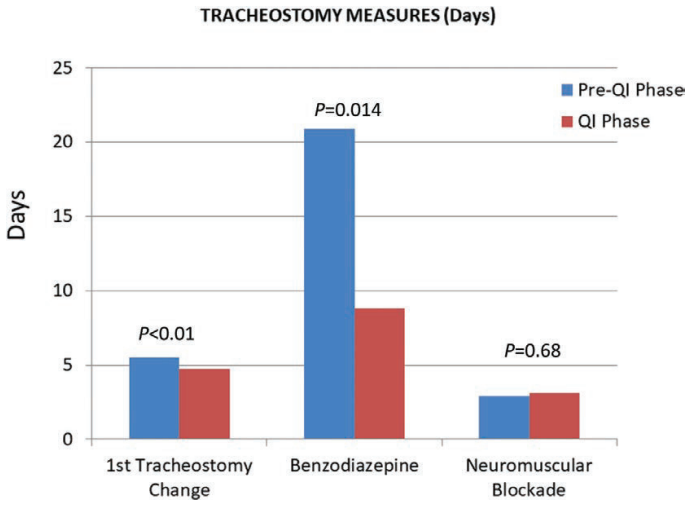

Figure 2. Bar graph displaying the comparison of the mean number of posttracheostomy days for the first tracheostomy change, benzodiazepine use, and neuromuscular blockade.

PDSA Cycle 3

Determination and documentation of the date of tracheostomy tube change by the ENT surgeons initially varied from 5 days to 9 days. Communication of the date and standardization of the time for first tracheostomy change post-operatively is important for determining the duration of sedation and the general care of the patient. This communication also determines the duration and weaning of opioids and thereby minimizes opioid withdrawal.

The ENT surgeon recorded the planned date of tracheostomy change and minimum duration of paralysis in the postoperative day 1 note. This documentation allowed effective and proactive individualized management of analgesia and sedation. Tracheostomy tube change was typically changed on postoperative day 5 if the wound healing was adequate and would not be delayed even on the weekend.

We also developed posttracheostomy nursing care learning modules and bedside tracheostomy cards to improve interdisciplinary communication. These cards specified the date of anticipated first tracheostomy change and the duration of neuromuscular blockade.

Analysis

We evaluated the impact of the interventions over time by statistical process control charts. Statistical process control uses statistical methods to differentiate common cause and special cause variations in a process, to assess the process capability, and to identify statistically significant variability due to special causes.[20] Centerline represents the mean values; the upper control limit and lower control limit are set at 3 SDs from the mean. We used the unpaired 2-sample t test for means and Mann-Whitney test for the medians as applicable. $P < 0.05$ was considered significant.

Results

Our baseline population was from October 2014 to December 2016. We included all patients who received tracheostomy tube placement in our NICU. We excluded patients with a tracheostomy tube at admission. The average corrected gestational age for our population at the time of tracheostomy was 51 weeks.

At baseline, the mean posttracheostomy opioid duration was 24.6 days (range, 6-148 days), and the neuro-muscular blockade was 2.89 days (Range 0-9 days). The duration of benzodiazepine was 20.9 days (range, 0-114 days) (This measure includes the duration of midazolam infusion plus the time to wean off with enteral lorazepam/ diazepam or the time to return to pretracheostomy lorazepam/diazepam dosing if the patient had been receiving before surgery) and dexmedetomidine was 4.6 days (range, 0-32 days).

Outcome Measure

Figure 2 shows the comparison of means of first tracheostomy change, benzodiazepine duration, and posttracheostomy neuromuscular blockade duration of the pre-QI phase in comparison to the QI phase. Following our interventions, the

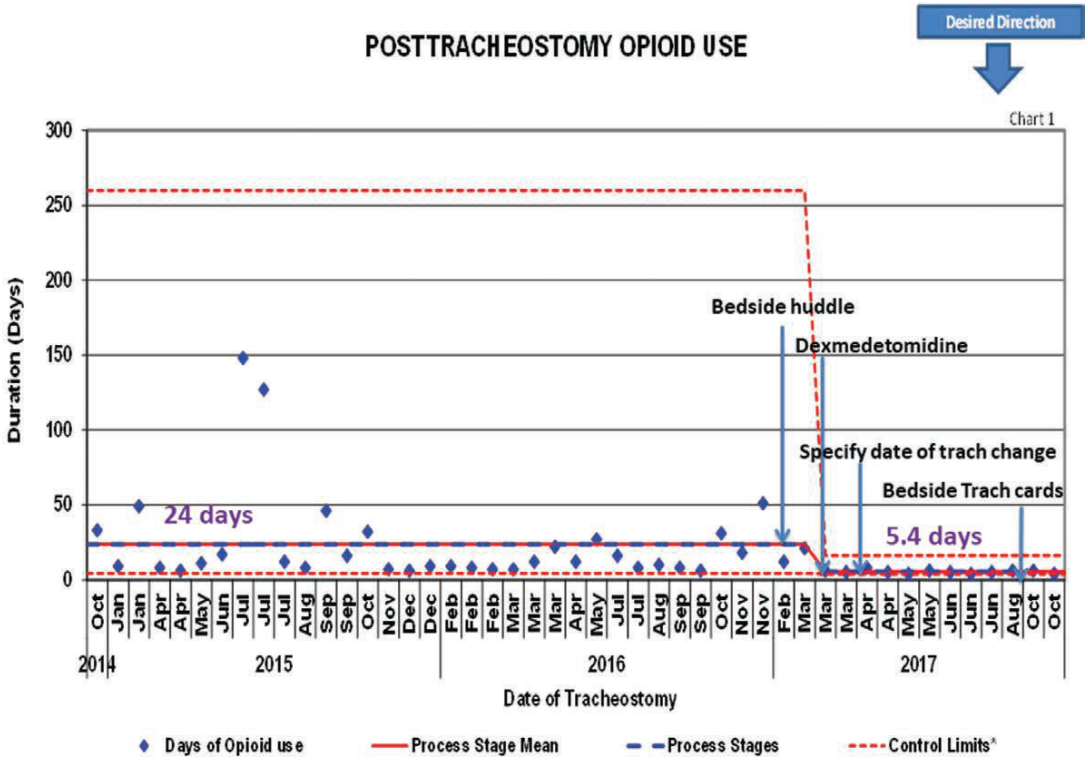

Figure 3. Annotated i-chart demonstrating the opioid usage posttracheostomy over time. The dotted lines represent the upper and lower control limits, and the center line is the mean.

mean duration of first tracheostomy change decreased from 5.55 to 4.71 days ($P < 0.01$), the mean duration of benzodiazepine decreased to 8.88 days (range, 4-25 days) ($P = 0.014$) and mean neuromuscular blockade was 3.14 days (range, 1-5 days). Figure 3 shows the Individual control chart (i-Chart) with the date of tracheostomy on the x axis, the duration of opioid exposure on the y axis, and each diamond is an individual patient. There were a total of 14 patients in the QI phase. The mean number of days of exposure decreased significantly from 24 days before the onset of the project to 5.4 days after implementation of the interventions (P value = 0.0487; 2-tailed t test).

Process Measure

The pharmacy and the primary team evaluated and documented preoperative opioid exposure for all patients. Pharmacy compliance in completing electronic notes to the team specifying an escalation and de-escalation plan was 100%. There was 1 patient in the QI period where the protocol was not followed. There was an escalation of the opioid rather than the sedative after tracheostomy change, which may have been due to multiple issues that included a breakdown of communication and the unavailability of a pharmacist to round with the primary team.

Balancing Measure

The revised analgesic guidelines were developed to ensure adequate sedation and pain control. As a balancing measure, we followed the wound site for pressure injury or skin breakdown that might increase if sedation and agitation control were not adequate. There have been no reports of wound site compromise following the revised guidelines. In our population, patients did not display hypotension after starting dexmedetomidine. Hence, dexmedetomidine was not discontinued in any patients secondary to hypotension.[21]

Discussion

Improved communication between ENT and neonatology services expedited the change process. This change included moving surgery times from afternoon to morning to allow initiation of postoperative sedation during the daytime. Early determination of the date of first tracheostomy change, with the provision of adequate wound healing, and duration of paralysis not only minimized variation but also impacted our ability to wean morphine and midazolam in a window of opportunity that prevented abstinence in most cases. Implementation of a postoperative analgesia order set in the electronic medical records in addition to a written postoperative pain plan by the pharmacist facilitated the medications to be ordered and available at the bedside with lines primed before the patient returned from the operating room. Addition of dexmedetomidine, detailed daily progress notes by the pharmacist regarding the analgesia and sedation plans, including escalation and de-escalation options, permitted maintenance of the care plan throughout all patient care shifts. Development of the bedside posttracheostomy cards enhanced communication among all caregivers. Learning modules were developed for the nurses to improve the posttracheostomy care.

There is limited literature regarding the pharmacological management of infants in the immediate posttracheostomy period. Multiple factors determine the success of postoperative opioid wean strategies. There is also significant heterogeneity in the etiology that necessitates tracheostomy placement. Several additional factors such as gestational age at the time of tracheostomy, duration of preoperative exposure to opioids and other sedatives, and steroid exposure before tracheostomy significantly influences the response to paralysis, the duration and success of postoperative opioid wean and wound healing.

Although we have not addressed these factors yet, in this single-center QI initiative, we have highlighted that despite these limitations, multiple other factors that could still be addressed to effectively minimize the duration of opioid exposure and thereby decrease its neurotoxic effects.

The rapid onset of action of dexmedetomidine allowed the rapid attainment of sedative needs and allowed opioid to be weaned quickly in patients who had a stable and well-healed tracheostomy site. We do not recommend it's routine use as further safety and efficacy studies in infants need to be done (see **Supplemental Digital Content 2** available at **http://links.lww.com/PQ9/A39**). Daily rounds in the postoperative period with the pharmacist helped to improve compliance with the sedation and analgesia plan. Nonpharmacologic management options for comfort care need to be maximized whenever possible, and ventilation management strategies for this subpopulation of infants that may allow less use of sedation in general.

In this project, we did not intervene in patient selection for tracheostomy or evaluate the effects based on gestational age at the time of tracheostomy. There might also be further opportunities to focus on patients with intrinsic lung disease as compared with those with airway or neurological disorders as a unique population. Challenges of ventilator management on and off of paralysis and managing inflammatory response in patients with lung disease also affect the sedation needs, and, have not been addressed in this project.

Conclusions

We demonstrated that we could significantly reduce the duration of opioid use after tracheostomy from an average of 24 days to less than 7 days and benzodiazepine use from an average of 21 days to 8.9 days. Successful interventions in the postoperative period included improved communication between ENT and neonatology, standardizing the posttracheostomy care with regard to the first tracheostomy change, early identification of the duration of paralysis, standardizing nursing care, a structured written daily sedation plan by the pharmacist, and the timely addition of dexmedetomidine. Physician leadership was crucial in expediting the change cycles and coordinating physician roles and responsibilities for postoperative care plans. Quick identification of barriers and subsequent discussion of potential solutions on a regular basis allowed the process to continue as a fluid improvement project with positive forward momentum.

Acknowledgments

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Disclosure

The authors have no financial interest to declare in relation to the content of this article.

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When used as part of an exclusive human milk diet, Prolact+6 H²MF fortifier (15 mL) can:

- Solve the challenge of providing small-volume fortified feeds for smaller premature infants
- Help fulfill nutritional needs while total parenteral nutrition (TPN) volumes are decreasing
- Support infant growth that meets or exceeds targeted standards[1]
- Increase survival[2] and decrease costly complications associated with the intake of cow milk-based products[3,4,*]

Adds 6 kcal/fl oz when mixed; delivers 90 kcal and 2.9 g of protein per 100 mL of nutrition.[†,5]

Available frozen in 125 mL bottles containing 15 mL of fortifier, which must be mixed with 35 mL of human milk (ratio 3:7) to achieve a total volume of 50 mL. Also available in 30 mL volume.

*For babies weighing between 500 and 1250 g. Outcome measures were statistically based on mean weight data.

†Based on the assumption that preterm mother's own milk provides 67 kcal and 1.6 g of protein per 100 mL.

References: **1.** Hair AB, Hawthorne KM, Chetta KE, et al. Human milk feeding supports adequate growth in infants <1250 grams birth weight. *BMC Research Notes*. 2013;459(6):1-8. **2.** Abrams SA, Schanler RJ, Lee ML, Rechtman DJ. Greater mortality and morbidity in extremely preterm infants fed a diet containing cow milk protein products. *Breastfeed Med*. 2014;9(6):281-285. **3.** Hair AB, Peluso AM, Hawthorne KM, et al. Beyond necrotizing enterocolitis prevention: improving outcomes with an exclusive human milk-based diet. *Breastfeed Med*. 2016;11(2):70-74. **4.** Ganapathy V, Hay JW, Kim JH. Costs of necrotizing enterocolitis and cost-effectiveness of exclusively human milk-based products in feeding extremely premature infants. *Breastfeed Med*. 2012;7(1):29-37. **5.** Koletzko B, Poindexter B, Uauy R, eds. Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines. *World Review of Nutrition and Dietetics*; vol 110. Basel: Karger; 2014:300-305.

For complete information on Prolacta's human milk-based human milk fortifiers, call 1-888-PROLACT (1-888-776-5228).

www.Prolacta.com/Human-Milk-Fortifier

Prolacta® BIOSCIENCE
Advancing the Science of Human Milk

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