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neonatal INTENSIVE CARE

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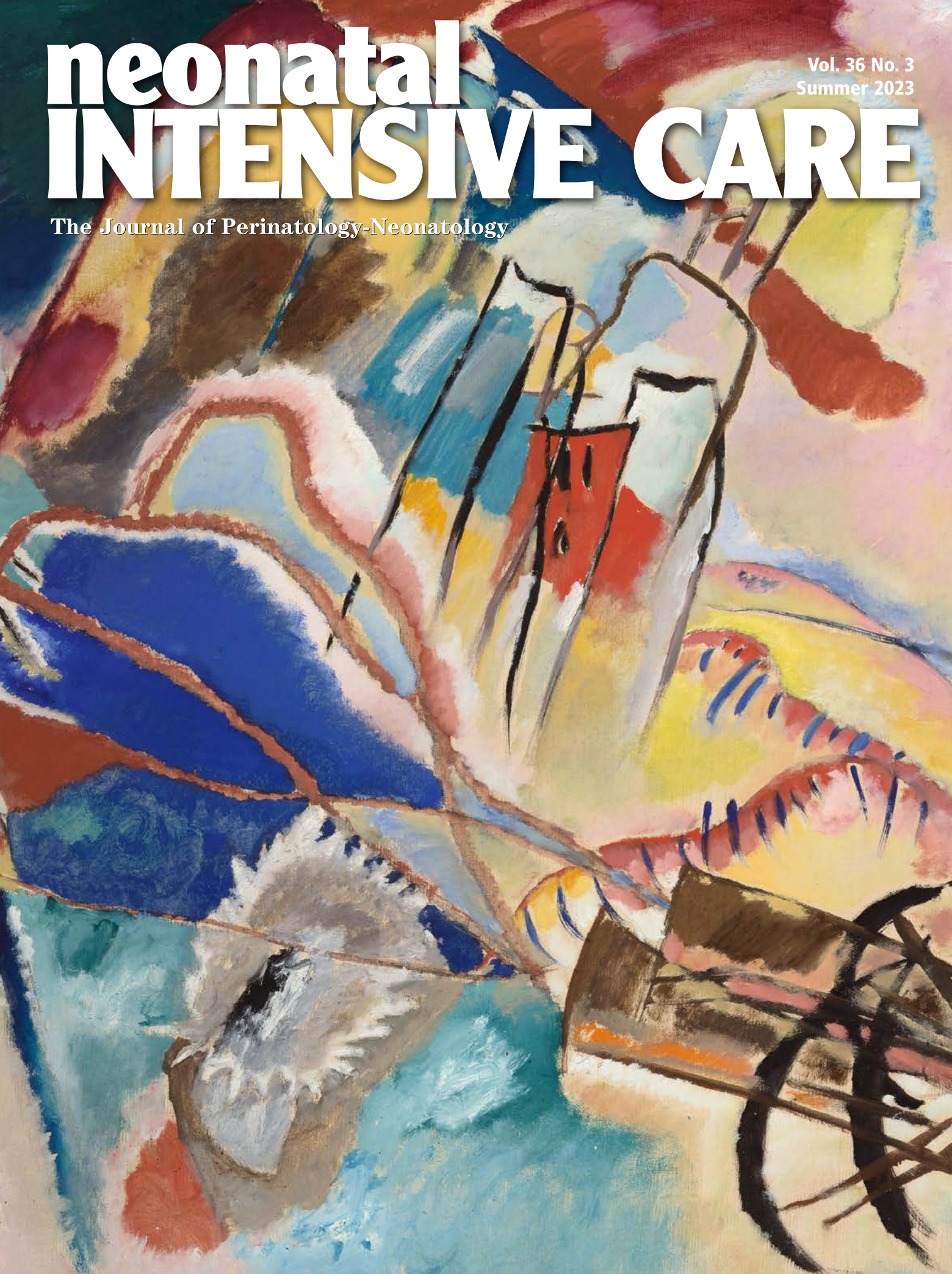

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News

☐ Summer 2023

New Device Launched to Monitor Oxygen Concentration

Maxtec, a global leading manufacturer of respiratory care products, is excited to announce the launch of its newest device, the MaxO2ME+p. This device is designed to monitor both oxygen concentration and pressure during bubble CPAP therapy, a care method for infants to treat respiratory distress syndrome (RDS) or other respiratory conditions. This device will help provide clinicians with the critical data they need to deliver effective care to their patients. The MaxO2 ME+p is a state-of-the-art device that helps healthcare providers monitor the oxygen concentration and pressure of the air delivered to neonatal patients during bubble CPAP therapy. By providing real-time, accurate data on oxygen concentration and pressure, the MaxO2 ME+p helps healthcare providers ensure that their patients are receiving the correct therapy. "We are thrilled to introduce the MaxO2 ME+p to the market," said Kathy Ouellette, President and CEO of Perma Pure Group (consisting of Maxtec and Perma Pure). "This device is the result of our ongoing commitment to developing innovative medical devices that make a real difference in the lives of patients and healthcare providers. We believe that the MaxO2ME+p is a game-changer in the field, and we are excited to see the impact it will have on patient care." Maxtec is dedicated to providing clinicians with the tools they need to deliver effective care to their patients. The MaxO2 ME+p is the latest example of this commitment, and Maxtec is proud to bring this product to market as they continue to pursue a mission of helping the world to Breathe Easier and Be Healthier.

Noisy Incubators Could Stunt Infant Hearing

Incubators save the lives of many babies, but new data suggest that the ambient noise associated with the incubator experience could put babies' hearing and language development skills at risk. Previous studies have shown that the neonatal intensive care unit (NICU) is a noisy environment, but specific data on levels of sound inside and outside incubators are limited, wrote Christoph Reuter, MA, a musicology professor at the University of Vienna, Austria, and colleagues. "By the age of 3 years, deficits in language acquisition are detectable in nearly 50% of very preterm infants," and high levels of NICU noise have been cited as possible contributors to this increased risk, the researchers say. In a study published in Frontiers in Pediatrics, the researchers aimed to compare real-life NICU noise with previously reported levels, to describe the sound characteristics, and to identify resonance characteristics inside an incubator. The study was conducted at the Pediatric Simulation Center at the Medical University of Vienna. The researchers placed a simulation mannikin with an ear microphone inside an incubator. They also placed microphones outside the incubator to collect measures of outside noise and activity involved in NICU care. Data regarding sound were collected for 11 environmental noises and 12 incubator handlings using weighted and unweighted decibel levels. Specific environmental noises included starting the incubator engine; environmental noise with incubator off; environmental noise with incubator on; normal conversation; light conversation; laughter; telephone sounds; the infusion pump alarm; the monitor alarm (anomaly); the monitor alarm (emergency)l; and blood pressure measurement. The 12 incubator handling noises included those associated with water flap, water pouring into the incubator, incubator doors opening properly, incubators doors closing properly, incubator doors closing improperly, hatch closing, hatch opening, incubator drawer, neighbor incubator doors closing (1.82 m distance), taking a stethoscope from the incubator wall, putting a stethoscope on the incubator, and suctioning tube. Noise from six levels of respiratory support was also measured.

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Cover: Improvisation No. 30 (Cannons), 1913. Vasily Kandinsky. French, born Russia, 1866-1944. Arthur Jerome Eddy Memorial Collection.

SARS-CoV-2 Crosses Placenta and Infects Brains of Two Infants: 'This Is a First'

Researchers have found for the first time that COVID infection has crossed the placenta and caused brain damage in two newborns, according to a study published online today in Pediatrics. One of the infants died at 13 months and the other remained in hospice care at time of manuscript submission. Lead author Merline Benny, MD, with the division of neonatology, department of pediatrics at University of Miami, and colleagues briefed reporters ahead of the release. "This is a first," said senior author Shahnaz Duara, MD, medical director of the Neonatal Intensive Care Unit at Holtz Children's Hospital, Miami, explaining it is the first study to confirm cross-placental SARS-CoV-2 transmission leading to brain injury in a newborn. The two infants were admitted in the early days of the pandemic in the Delta wave to the neonatal ICU at Holtz Children's Hospital at University of Miami/Jackson Memorial Medical Center. Both infants tested negative for the virus at birth, but had significantly elevated SARS-CoV-2 antibodies in their blood, indicating that either antibodies crossed the placenta, or the virus crossed and the immune response was the baby's. Dr Benny explained that the researchers have seen, to this point, more than 700 mother/infant pairs in whom the mother tested positive for COVID in Jackson hospital. Most who tested positive for COVID were asymptomatic and most of the mothers and infants left the hospital without complications. "However, (these) two babies had a very unusual clinical picture," Dr Benny said. Those infants were born to mothers who became COVID positive in the second trimester and delivered a few weeks later.

Can Asthma Be Prevented in Children Before Birth?

Controlling asthma in mothers-to-be, removing dust mites, taking probiotics and vitamin supplements - is there evidence showing that women's behavior during pregnancy could reduce the risk for asthma in their unborn children? At the 27th French-language convention on respiratory medicine, Cécile Chenivesse, MD, of the department of respiratory medicine, immunology, and allergies at Lille Regional University Hospital in France, answered this question. The risk factors of developing asthma differ with age. "During the fetal period, the first risk factor for asthma in unborn children is having asthmatic parents, especially an asthmatic mother," said Chenivesse. "A second important factor is smoking: first, having a mother who smokes during pregnancy, but this also refers to the environment surrounding the pregnant woman, including, but not exclusive to, the father."

Parental asthma, prenatal environmental tobacco smoke, and prematurity (especially in very premature births) are well-established risk factors of childhood asthma. What's more, current results suggest mild-to-moderate causal effects of certain behaviors or modifiable exposure during pregnancy (such as maternal weight gain or obesity, maternal use of antibiotics or paracetamol, and maternal stress); during the perinatal period (such as cesarean birth); or during the postnatal period (such as serious infection with respiratory syncytial virus, excess weight or obesity, exposure to moisture or mold in the home environment and to air pollution outside of it) on childhood asthma. These findings need to be confirmed via interventional studies or at least well-designed prospective studies.

Inhaled Corticosteroids Can controlling a mother's asthma during pregnancy prevent asthma in her baby? "Yes," said Chenivesse. Taking inhaled corticosteroids (ICS) early on and making sure asthma is well controlled during pregnancy (this includes medication other than ICS too) reduces the risk for asthma in the child. "It is logical to assume that exposure to Th2 inflammation during the fetal period could contribute to the risk of developing asthma," Chenivesse added. "A single center, double-blind, randomized, controlled Australian study carried out in 179 women recruited before 22 weeks' gestation confirms that FeNO-guided (fractional exhaled nitric oxide, an eosinophil inflammation marker) asthma treatment during pregnancy reduces the rate of asthma in children between 4 and 6 years of age (140 children; 36% asthmatic). This study already shows the protective effect of inhaled corticosteroids for everyone. They reduce the risk of asthma in the child."

Neonatal Bilirubin Meters Need Better Accuracy

Despite their convenience and low cost, handheld point-of-care (POC) devices lack precision for measuring neonatal bilirubin and need refinement in order to tailor jaundice management in newborns, a systematic review and meta-analysis reports in JAMA Pediatrics. Lauren E.H. Westenberg, MD, of the division of neonatology at Erasmus MC Sophia Children's Hospital in Rotterdam, the Netherlands, and colleagues reported that POC meters tended to underestimate neonatal bilirubin levels, compared with conventional laboratory-based quantification. Furthermore, pooled estimates from 10 studies found these devices to be too imprecise overall, with substantial outer-confidence bounds. On the plus side, Dr. Westenberg's group said POC bilirubin testing was as much as 60 times faster than lab measurement, and used 40-60 times less blood. "Conventional laboratory-based bilirubin quantification usually requires up to 500 mcL, but sometimes even 1,500 mcL, while POC tests require up to 50 mcL, which means less stress for the baby," Dr Westenberg said. "Especially when infants are cared for at home, it usually takes a few hours between deciding to quantify bilirubin and obtaining the test result. Meanwhile, bilirubin levels may rise unnoticed." On the positive side, POC devices are useful where laboratories in low-resource areas may be remote, poorly equipped, and not always able to provide an accurate bilirubin level. "As a result, the diagnosis of jaundice relies mainly on visual inspection, which is known to be unreliable," she said. POC devices, however, need near-perfect conditions for optimal use, and results can be affected by humidity, preanalytic conditions such as test strip saturation, and hematocrit. Yet results from these devices have recently proven to have acceptable accuracy, resulting, for example, in the same clinical decisions as the reference standard in 90.7% of times according to a 2022 study in a hospital in Malawi. Nevertheless, the authors concluded that the devices' imprecision limits their widespread use in neonatal jaundice management, especially when accurate lab-based bilirubin quantification is available. Results from these POC tests should be interpreted with caution, Dr Westenberg said. In terms of clinical decision-making, POC devices entail a risk of missing neonates with jaundice who need phototherapy or, in the case of overestimation, of starting phototherapy too early.

Beyond Air Appoints New Chief Medical Officer

Beyond Air, Inc., a commercial stage medical device and biopharmaceutical company focused on developing inhaled nitric oxide (NO) for the treatment of patients with respiratory conditions, including serious lung infections and pulmonary hypertension, and, through its affiliate Beyond Cancer, Ltd., ultra-high concentration nitric oxide (UNO) for the treatment of solid tumors, announced the appointment of Dr Jeff Myers as Chief Medical Officer of the Company, effective March 27, 2023. Dr Andrew Colin, the Company's incumbent Chief Medical Officer, has transitioned to the role of Senior Medical

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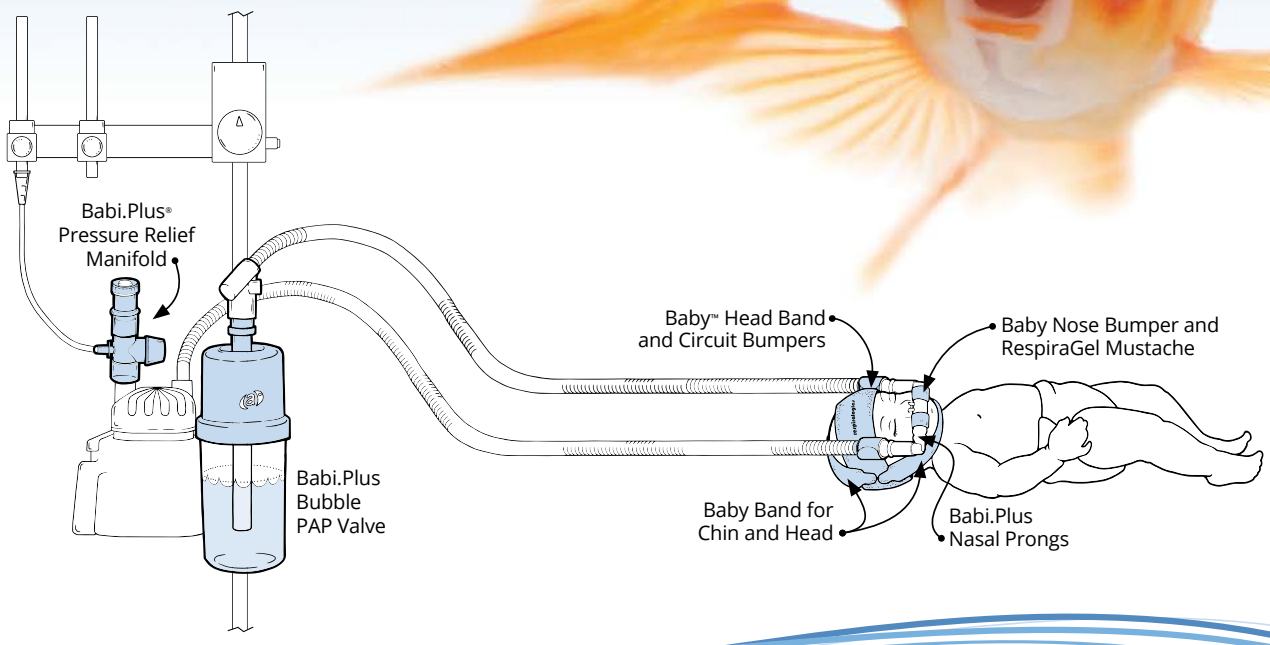

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Director Global Clinical Leadership and will remain an integral part of the Beyond Air team. Dr Colin will be working closely with Dr. Myers to ensure a seamless transition. Dr Myers joins Beyond Air with nearly 15 years of leadership experience as a biopharmaceutical executive overseeing clinical development, clinical operations, and regulatory affairs. Prior to industry, Dr Myers was a cardiothoracic surgeon for nine years, most recently at Massachusetts General Hospital. "We are excited to appoint Dr Myers as our Chief Medical Officer. Being an accomplished cardiothoracic surgeon with success at several healthcare companies in medical capacities provides Dr Myers with the attributes Beyond Air needs as we move forward with developing the pipeline for our revolutionary LungFit platform," stated Steve Lisi, Chairman and Chief Executive Officer of Beyond Air. "I want to thank Dr Colin for his commitment to Beyond Air and look forward to working with him in his new role." "I am excited to join Beyond Air's highly accomplished team of scientists, engineers, and investigators. This team has successfully advanced development of the Company's pipeline, including announcing the first FDA-approved product for the LungFit platform in mid-2022. I look forward to building upon this momentum as we continue to harness the power of nitric oxide to treat a broad variety of indications," commented Dr Myers. Dr Myers' previous leadership responsibilities include overseeing clinical development, clinical operations, business development, medical affairs, and implementing regulatory strategies in the US and abroad. Previously, he was the Chief Medical Officer for Revolo Biotherapeutics, initiating clinical trials in the US and Europe before leaving to become the CEO of Bioceptive where he continues to serve as a member of the Board of Directors. Dr Myers also served as the Chief Medical Officer for Portola Pharmaceuticals where he was instrumental in the acquisition by Alexion Pharmaceuticals, and Vice President, Medical and Regulatory Affairs, at SteadyMed Therapeutics. Prior to beginning his career in biotechnology, he was a practicing congenital cardiac surgeon and served as the Chief of Pediatric Cardiac Surgery at Tulane University and Massachusetts General Hospital with appointments to Tulane and Harvard Medical Schools. He is passionate about developing novel, first-in-class therapies that significantly improve the lives of patients. Dr Myers began his work with inhaled nitric oxide in pursuit of his PhD at Georgetown University and is thrilled to join Beyond Air and its pursuit of the potential of these therapies across multiple indications in critically ill patients. In connection with the appointment of Dr Myers, the Company granted Dr Myers an inducement stock option award and restricted stock unit award as inducements material to Dr Myers' entering into employment with the Company in accordance with Nasdaq Stock Market Listing Rule 5635(c)(4). The Inducement Option is being granted effective as of March 27, 2023 and is exercisable for the purchase of 50,000 shares of the Company's common stock, at an exercise price equal to the last reported sale price on Nasdaq on March 27, 2023. The Inducement RSU for 50,000 shares of the Company's common stock is being granted effective as of March 27, 2023. The Inducement Awards were approved by the independent compensation committee of the Board in accordance with Nasdaq Stock Market Listing Rule 5635(c)(4). The Inducement Option has a ten-year term and will vest over a four-year period, with 25% of the shares underlying the stock option award vesting on the first anniversary of the date of grant and annually thereafter in three equal installments, subject to Dr Myers' continued service with the Company through the applicable vesting dates. The Inducement RSU will vest over a five-year period, with 20% vesting in December 2023 and 20% annually thereafter. The Inducement Awards are subject to the terms and conditions of the Company's 2013 Equity Incentive Plan.

Etiometry Announces CE Mark and Health Canada Authorization for Adult Use of AI-Based Algorithm that Detects Risk of Hypercapnia

Etiometry, the leader in clinical decision-support software for critical care, today announced CE Mark and Health Canada authorization of its IVCO2 Index for adult populations, which allows clinicians to visualize inadequate ventilation of carbon dioxide with other contextual data from the Etiometry Platform to help inform intervention decisions and get ahead of patient deterioration. The IVCO2 Index was first FDA-cleared for pediatric use in 2019 and now carries CE Mark and Health Canada licenses for both pediatric and adult use. On the heels of January's FDA clearance of its IDO2 Index for adults—which was previously licensed for adult use by Health Canada and CE Marked in 2022—Etiometry continues to seek authorizations for all of its risk algorithms to be used for both pediatrics and adults in the U.S., Canada and Europe. "We are serious in our pursuit to expand authorizations of all four of our current risk indices," said Shane Cooke, CEO of Etiometry. "What drives us forward is knowing how our precision analytics bring situational awareness to strained care teams to help mitigate risk and enhance patient outcomes." Using mathematical models of human physiology to determine the likelihood a patient is experiencing inadequate carbon dioxide (CO2) ventilation or hypercapnia, Etiometry's IVCO2 Index continuously tracks the probability that a patient's arterial blood gas sample has a partial pressure of CO2 (PaCO2)

Continued on page 52…

Benefits of Implementing an Airway Monitoring System at Children's Hospital of Illinois

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. this interview is with Dr Jawad Javed and Dr Ashley Fischer at OSF Healthcare Children's Hospital of Illinois.

For Dr Jawad Javed, Medical Director and Division Head of Neonatology at OSF Healthcare Children's Hospital of Illinois and Professor of Clinical Neonatology, improving monitoring of endotracheal tube (ETT) movement while implementing kangaroo care and improving unplanned extubation (UE) rates was a priority to ensure the safety of his facilities' patients. Located in Peoria, Illinois, the 60-bed neonatal intensive care unit (NICU) is a level four with the American Academy of Pediatrics' designation system. The comprehensive facility is set up with private rooms divided into neighborhoods, with each having between seven to ten rooms. Patients commonly range from 22 to 30 weeks' gestation, and while Javed and his team belonged to the Vermont Oxford Network of data-driven quality improvement, the global burden of UEs still impacts his facility.

I sat down with Javed and his colleagues — Dr Ashley Fischer, Quality Improvement Director and Associate Professor of Pediatrics, and John Sanford, Respiratory Therapist of Neonatology — to learn what it meant to integrate SonarMed™ airway monitoring system into their hospital for improving ETT monitoring, enhancing their kangaroo care offerings, and improving UE rates overall.

What were your team goals regarding unplanned extubations in your hospital?

Jawad Javed: The patients — it's why it's so important to for us to get a handle on our unplanned extubation rate and to ensure that we are doing more neuro-developmentally appropriate care.

Patient satisfaction for our parents was important — wanting to do kangaroo care and be involved. Having the confidence of holding their babies is a big thing. It didn't matter if they were preemies from 24 weeks up to term infants, whenever we used the device it worked efficiently for us. It gave parents confidence.

We presume that the ETT tended to move during critical moments, but there was no great way to measure and monitor if drifts occurred. There was no good way to determine if you're too high or too low, because the chest X -ray isn't always the most effective way to diagnose. We wanted to monitor these ETT movements in real time and that's what the SonarMed™ system was able to do for us — give us real-time information as to where that (ETT) tip is.

We pride ourselves on getting that mom-baby connection to start off quickly, so we get into kangaroo care positions early in life. We encourage families to hold their children; however, this does come with increased risk of potential of an unplanned extubations.

We want to provide safer care to improve our unplanned extubation rate and take that metric to the next level. These major interventions* we participated in brought our unplanned extubation rate down from 2.1 to roughly around 1.3 and 1.4 events per 100 ventilator days. We made great headway with our team and a team-based approach, but had a hard time breaking that threshold of below 1.0. **multiple UE bundle practices*

Were there any obstacles in launching this technology with your staff?

Jawad Javed: Medtronic did a nice job with our onboarding process, and this was a big challenge with COVID-19 and difficulties trying to bring personnel into the hospital.

We went through a champions course initially with our respiratory therapist and our clinical nurse educators to go through the device in a more meticulous fashion, and this education was conveyed to the staff. Medtronic spent time with our group to help the onboarding of all of our staff — a lot of the staff concerns would have been there otherwise.

Because of the great planning and education that was done by John (Lead RT and educator) and his group, our nurse educators, and the Medtronic support working with our staff one-on-one, it removed a lot of obstacles.

Did you do an evaluation of this device or how did you get this device adopted into your institution?

Jawad Javed: When I learned about the device, we started with the situation-background-assessment-recommendation (SBAR) process of understanding why we needed it and then spoke extensively about what this device had to offer. We sent it to our products committee, and it was really a matter of where the foundational funding would come from — the capital budget that exists within our unit and the device fit within that process.

I presented to our products committee and executive board. We spoke highly about what this could do for us and strongly

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Abigail Scaggs is a Global Marketing Manager with Medtronic. If you would like to participate in this feature, as a company or healthcare provider, please contact Steve Goldstein at s.gold4@verizon.net

SonarMed™ Airway Monitoring System.

believed in the science that existed within the device — it could be a game changer.

The actual purchasing part of it wasn't too bad once we got the approvals. But from a value-based approach, looking at the cost of an unplanned extubation in a premature infant, it becomes cost effective to invest. Additionally, our patient experiences of babies being able to bond quickly with kangaroo care — we try to get these small preemies into the parents' arms and support skin-to-skin bonding.

How does the SonarMed™ airway monitoring system support kangaroo care in your hospital?

Ashley Fischer: For me, it's families having skin-to-skin contact and performing kangaroo care confidently. But for the mothers — to feel more comfortable holding their child — is valuable. Over the last six to ten months, we still have been doing our kangaroo care and have been able to optimize that a little bit more for patients.

John Sanford: We've embraced the thought of having parents participate in kangaroo care or skin-to-skin care. We encourage this on daily rounds. We always do a patient assessment to see how the patient's doing and if they are able to tolerate getting the baby into the parents' arms. We facilitate that as much as we can. We don't have too many limitations to keep the baby in the isolette, and even if they're on high-frequency ventilation, that doesn't automatically disqualify them from kangaroo care. But it is a little intimidating when getting the baby out. Making sure we keep the ETT in the proper place can be tense, stressful. Parents pick up on that, and they know when the caregivers are watching more closely.

When we're using the SonarMed™ device during those movements, it reassures us quite a bit and eases that tension while it's in place. While the parents are holding the baby, we tend to turn the monitor towards the parent, and they, too, can watch as that ETT migrates up and down.

It helps parents relax a bit more if the baby moves a little. For parents that have seen an unplanned extubation, it's terrifying for them, so it's really heartbreaking to hear parents not wanting to participate in kangaroo care after they've had one of those episodes. It's nice to have this monitor to help reassure them that the tube is where it should be and we're watching.

They can feel that sense of security now with that monitor in line. Parents are more apt to participate in kangaroo care if they can keep an eye on that airway.

How has using the SonarMed™ airway monitoring device impacted the number of X-rays and your suctioning practice?

John Sanford: Actually, having the device has cut down on repeated ETT movement orders as it's this dance that we sometimes do with the X-rays. Hopefully we're cutting down on the number of X-rays that we're getting because we can look at the monitor and see where the tube is then decide whether we need to adjust tape position or not. †

You're adding those encounters more every time you tape and re-tape, either with something slipping out or the tape failing, so you decrease the number of times you're moving those in and out.

Ashley Fischer: We're not doing routine monitoring with X-rays for ETT placement — it's just really needed if there's a clinical change.

John Sanford: Our suctioning procedures have changed with the device. We use safe suction distance measurements for every baby that's intubated, so we've got to add more length to get down to the tip of the airway (with the inline sensor). We do that calculation and post it for the nurses, which also gets passed into a report for the RTs. The device displays a percent of occlusion in the airway, so we have a frequency that we go in and assess for our patients if they need to be suctioned. In between, if we notice the monitor is alarming and showing a percent of occlusion as well as if it was to the point where we can see if our baby was desaturating or having a bradycardic component, we go in and do additional suctioning.

Sometimes we may pass on deep suctioning of our patient because it isn't necessary. A nice feature on the monitor is listening to breath sounds without putting a stethoscope on the baby's chest. If we turn that feature on and the breath sounds are clear, heart rate, and stats we're doing fine with everything else stable, we may differ away from the invasive suctioning to another point of care.

What sets off the alarm and how do you adjust it to avoid it becoming a nuisance alarm?

Ashley Fischer: When we were learning about the SonarMed™ device as we trialed it for a day on a patient in a private room, the nurse was asking me what the alarm sounded like, right then the alarm went off and the patient was experiencing occlusion. The patient then started coughing with hacking noises, and we realized we should try suctioning.

Abigail Scaggs: There are three main alarms that you can set specific to a patient, and we provide some guidance around those levels:

- Movement of the tip of the ETT
- Specific severity of obstructions
- Circumference around the tip of the tube

How did you tackle your unplanned extubation goals?

Jawad Javed: We trialed different things, and a lot of collaborative efforts in our quality work with our respiratory therapist (RT) and nursing colleagues. We did a full audit of the bundled measures for a root cause analysis of all UE events.

Ashley Fischer: Before implementing SonarMed™, we've been able to reduce our unplanned extubation rate to 1.5 per 100 ventilator days for the last six months and we've noticed the bedside staff realizes how much movement has occurred with the ETT.

This allows more focus on watching the ETT tip during movement when we're conducting X-rays during transport. By ensuring everybody in the unit had a uniform way of doing their X-rays, ensuring heads were midline and straight, but that it is held in a proper position. Then working with our peripherally inserted central catheter (PICC) line positioning during that same time. We are able to work with our radiologists to annotate the X-ray exactly where that ETT tip was.

We did more education with our fittings and ensuring they had optimal fit during X-ray. All those things made some difference, and we dropped it to about 1.4, but you can see in

SonarMed System in use at Children's of IL on neonate during kangaroo care.

April to June of 2020, we had three outliers as the result of a couple of really big feisty babies that were difficult to control and monitor.

How do you do choose which patient goes on the SonarMed™ device? Is there a certain patient population or patient criteria to help you choose which babies go on the device?

John Sanford: We have five monitors, and we've quickly outpaced those five monitors. We're in the process of getting additional monitors. But a tough decision. We don't have a priority to the patients; if there's a monitor that's available, it goes to an intubated patient. We have five monitors right now on our unit. We try to push the monitors towards a patient that has already had an unplanned extubation or a patient that has a tenuous airway. We don't want any repeat offenders.

Even some of the bigger neonates that we noticed have strong and purposeful movements with their hands — something that has worried us or caught our attention — we may try to steer the monitor towards that patient.

What would your message be to those considering this type of airway monitoring technology?

Jawad Javed: For the NICU, we did what we could do with our team-based quality approach. We tried different modalities to bring that unplanned extubation rate down as best as we could. We made headway — going from 2.1 to 1.4 and 1.3 — but it was a tremendous amount of work from our amazing staff and crew. Taking it to the next level was a game changer for us to get below the 1.0 mark.

My message is that the technology is a potential game changer for the area of unplanned extubations — if you really want to make a significant dent. Now we're looking at other populations in the PICU as there's a lot of interest to try to get a handle on these because of the cost burden that exists there.

What are your team goals for the future with this airway monitoring device?

Jawad Javed: For me, honestly, the patient care is always first and foremost. To see what the families are doing around kangaroo care is incredible. When you work so hard to move a metric number even a few points, it's so much effort. To provide this kind of device moves that bar to a different level to support the team's efforts while watching that cultural transformation — it's astounding.

It's great to be able to utilize this. We started a neonatal fellowship program in our institution, so getting our fellows to work on the research aspects of this device is going be very fascinating over the coming months and years — to see how much we can push the folds of the metrics and what we can get off of this device while pushing towards a zero unplanned extubation rate.

Footnotes

†The SonarMed™ Airway Monitoring System should not be used as the sole basis for diagnosis or therapy and is intended only as an adjunct in patient assessment.

††This testimonial is based on one facility's experience. Experiences vary.

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Application of Noticing Lexicon Using Neonatal Opiate Withdrawal Syndrome (NOWS) as an Example

Shabih Manzar, MD, MPH

In a recent article, Clement et al.[1] address a crucial issue in the healthcare profession. In clinical medicine, we are witnessing a slow decline in 'noticing.' Clement et al[1] commented that the young doctors being less expert in performing physical examinations than their contemporaries of 50 years ago are valid, and the reasons are plausible. There is more reliance on technology and clinical tests, which are on top of shorter attention spans, declining interpersonal empathy, and worsening communication skills. The same is true for younger nurses. Clement et al[1] proposed a noticing lexicon template. They called it the 'conceptual forest.'

Using this template, let's apply the concept to a clinical bedside scenario. A neonate was admitted to the newborn nursery with a possible diagnosis of neonatal opiate withdrawal syndrome (NOWS). He had evident jitteriness on clinical examination and was crying inconsolably. The mother looks anxious and worried. Regarding noticing, there are four possibilities: not noticing, ordinary noticing, intentional noticing, and professional noticing. By filtering them through the model proposed by Clement et al,[1] we could come up with a reasonable response (Figure 1). The medical staff, knowing that the mother's urine toxicology was positive for opiates, could consider the diagnosis of NOWS, not noticing any maternal concerns. They could tell the mother that the infant should stay in the hospital and might have to be started on morphine or process the case with a sensemaking solution (Figure 1).

As seen in the example, applying the idea of noticing could apply to neonatal-maternal care. These ideas could make the practitioners rethink their practice by sharpening their noticing abilities so that they can become better at teaching medical students and nurses and would be able to apply these to their day-to-day clinical practice.

Abbreviations

NOWS: neonatal opiate withdrawal syndrome

Reference

1 Clement T, Bolton J, Griffiths L, Cracknell C, Molloy E. 'Noticing' in health professions education: Time to pay attention?. *Med Educ.* 2023;57(4):305-314. doi:10.1111/medu.14978

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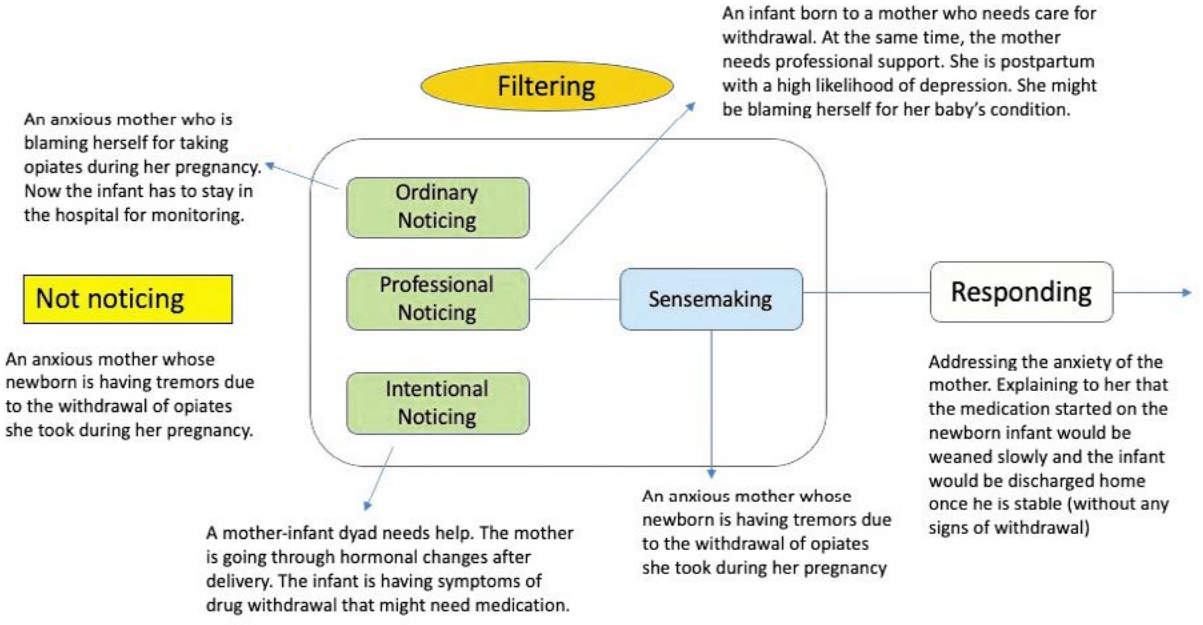

Figure 1. Clinical application of the 'noticing lexicon' Adapted from Figure 1, Clement et al. 1

Neonatal Game Changers: The NeoMagic EPIV and MST for Vascular Access

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. This interview is with Kimberlee Chenoweth, DNP, APRN, NNP-BC, Intermountain Healthcare, Primary Children's Hospital, Neonatology discussing vascular access for patients in the NICU.

Tell us about your background.
In 2000 I began working as a NICU nurse in a Level 3 NICU delivery hospital. I always wanted to be an advocate, a voice, for newborns that are unable to speak for themselves and it didn't take long for me to realize that one of the most common challenges a newborn faces while hospitalized is vascular access.

I committed to improving my IV skills with the hope of decreasing the number of IV sticks thereby providing my patients with a more comfortable hospitalization experience. In 2013 I joined the Central Line Management Team which increased my skills by placing PICC lines and extended dwell catheters (EPIVs). In 2014, I started working toward my doctoral degree which focused on vascular access in the newborn population; this included compiling data that compared PIVs, EPIVs and PICCs. When I graduated in 2017, I continued to work on the project until publication in 2018.

In 2020, I began working as a Neonatal Vascular Access Consultant and had the opportunity to team up with NeoMagic. Together, we began developing education and learning modules for vascular access to train NICU staff during COVID restrictions using a virtual format. I continue to work in Level 2, 3, and 4 NICUs, which allows me to combine hands-on clinical experience to enhance the training and education I provide as a consultant.

What is the most difficult part of deciding what product to use to save such fragile little patients?
When assessing a patient you must consider not only their current needs, but how their needs may change. It would be an easy decision to just look at the infant's present needs, but vascular access is a moving target and the infant's situation may frequently change. To help make this decision easier, there are three things I consider. First, I look at what will be running through the line today and then what is anticipated in the future. For example, it may be nutritional fluids, hydration, medications, or a combination of any of those therapies. Additionally, I consider what type of access is needed based on the osmolarity, vesicant properties, pH, etc. There are more limitations with PIVs and EPIVs than with PICC lines.

The second consideration is the anticipated length of time that the vascular access will be needed. PIVs generally don't last long in infants (1-2 days), while EPIVs can be in place for up to 29 days, and PICCs can be in place for months.

The third issue I consider is the condition of the infant's veins. I look at what veins are currently available, how many options are available, and whether there are previous vascular access experiences with that patient that could help us make a more informed decision.

What is an EPIV and MST?
An EPIV is an Extended-dwell Peripheral Intravenous catheter inserted into veins of the upper and lower extremities and is threaded into the proximal portion of the extremity. It can also be inserted into veins on the scalp that thread directly into a jugular vein. The tip of the catheter rests in the area of greatest blood flow, thereby avoiding the smaller, more delicate, peripheral veins.

The Modified Seldinger technique (MST) is a method to insert tubes or catheters over a guide wire to the final tip location. This method adds steps to the insertion process but has many advantages. The NeoMagic MST kit comes with a small introducer needle, but it also allows the clinician flexibility in utilizing introducers they are already comfortable with, and allows for smaller insertion devices in general, compared to any other devices available.

How long have you been using NeoMagic products?
I have been using NeoMagic products since 2012 after we trialed them in our Level 3 NICU. Because of the success rate, and the positive experience we had, we are now using them throughout our entire healthcare corporation.

How does the NeoMagic EPIV and MST change the game for your patients?
NeoMagic EPIVs have allowed an improved hospitalization experience for our NICU patients, and their families, on so many levels. We have been able to decrease the number of needle sticks a baby has while hospitalized, thereby decreasing the number of painful procedures, cost, and the risk of infection. The use of these EPIVs have also decreased the number of complications when compared to PIVs; this includes fewer infiltrations requiring hyaluronidase. Also, level criteria prevents some NICUs from using PICC lines which often makes vascular access a challenge for smaller, sicker infants. Previously, if PIVs didn't last long, or if peripheral veins were tenuous, these infants would often need to be transferred to a Level 3 or Level 4 NICU

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for something as simple as antibiotics or IV nutrition. With the introduction of EPIVs in our Level 2 NICUs we rarely have such issues; this allows infants to stay close to their families which is crucial, especially if the mother is hospitalized and unable to travel.

The MST offers many advantages for the NICU population. Generally, when a clinician is allowed to place PICC lines or EPIVs it is because they have demonstrated exceptional skill at placing PIVs. One of the challenges when training with PICCs and EPIVs is using a new insertion device. One advantage of the MST is that it allows the clinician to continue to use the device they are already comfortable with. Also, the MST can utilize introducers as small as a 27 G, which is the size of the introducer needle included in the NeoMagic kit. Many other products are larger and bulkier, which can be problematic with our small patients.

How often do you need to exchange the product to complete therapy?
PIVs notoriously don't last long and generally require replacement multiple times before the IV therapy is complete. However, EPIVs tend to last much longer. Data we collected found that 72% of our EPIVs stayed in place until the end of treatment as compared to 84% of our PICC lines. EPIVs can remain in place for up to 29 days before requiring replacement.

What are the therapies you can deliver with EPIVs?
EPIVs are categorized as peripheral vascular access devices, putting them in the same category as PIVs. IV therapies are restricted to osmolarity < 900 mOsm/L, a pH > 5 and < 9, and non-vesicant/non-irritant solutions and medications. If any of the therapies the infant requires are outside these parameters, a central line is indicated.

Have you tried competitor's products and if so, why do you prefer NeoMagic products?
I haven't tried competitor's products, but I have worked with many clinicians who have, and the biggest difference reported is the bulkiness of other products as compared to the NeoMagic EPIVs and MSTs. When working with small patients, larger products can be cumbersome.

PIVs are notorious for leakage, but do you see this with EPIVs? If not, why?
We do see leakage from EPIVs, but at a much lower rate. An EPIV tip should be well nested in the upper portion of the extremities, or the jugular veins, where the vasculature is larger and less fragile. If leakage occurs, it is often due to user error. For example, inadvertently puncturing the catheter during placement may cause leakage at the insertion site. Another reason the EPIV may leak is from failure to advance the catheter the full 6-8 cm. The less the catheter is advanced into the vein, the more it mimics a PIV, including the associated problems. If the EPIV is only advanced 3-4 cm, there is a higher likelihood that problems such as leakage will occur. This is one of many reasons why an ideal insertion site and tip position is key. Proper securement is also an important factor.

NeoMagic products were created by Tim Duvall at Neo Medical, and he was the pioneer in creating the EPIV. Do you know if Neo Medical has any other game-changing products planned for release in the future?
I recently had the opportunity to speak with Tim about new products that will be available this year. Neo Medical is planning to release a new catheter product designed specifically for the NICU's smallest patients, which is so exciting since they are often the most overlooked patients when it comes to medical advancements. It will be the NeoMagic 1.2Fr Reduced Trauma Micro-Preemie Catheter System. It currently is a patent-pending design registered throughout the world. This catheter is a game changer for our smallest patients who struggle with vascular access. I'm looking forward to using it and any other new NeoMagic products.

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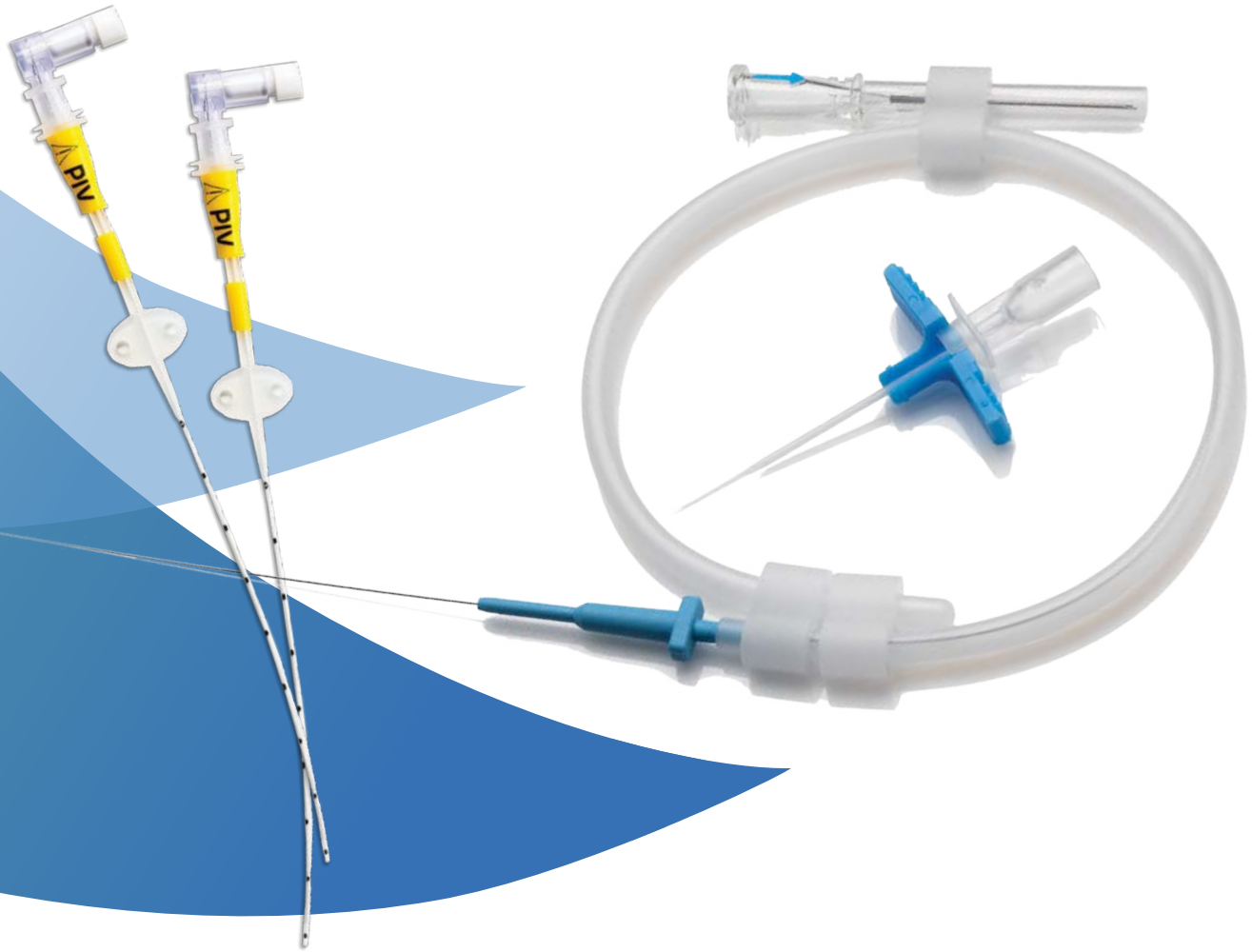

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Benefits of LungFit PH System Compared to Cylinder-based Systems

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. This interview is with Jeff Griebel, Director, Clinical Services, Beyond Air.

Tell us about your background.

Jeff Griebel, Director, Clinical Services, Beyond Air. Jeff Griebel has more than 30 years of experience working with iNO delivery systems. Prior to joining Beyond Air, he served as Clinical Program Director at medical device company, Spinal Stabilization Technologies and was Senior Manager of Clinical Device Innovation at Mallinckrodt Pharmaceuticals, a large specialized pharmaceutical manufacturer of generic pharmaceuticals and agents. Prior to Mallinckrodt, he held the positions of Field Manager of Medical Affairs and Country Manager on the US Clinical Specialist Team at IKARIA, Inc., a company acquired by Mallinckrodt. Mr. Griebel also spent 16 years as a Clinical Specialist on a research team at Children's Hospital Colorado working within the NICU/PICU and neonatal and adult transport teams.

Can you tell us about your career in respiratory care within the NICU and PICU and how this experience ties into your work focusing on clinical device innovation related to inhaled nitric oxide (iNO) delivery?

I worked as a clinician and clinical educator in the NICU/PICU, as well as working on neonatal and adult transport teams. I started working with iNO delivery systems before any commercial systems were available. As part of a research team at Children's Hospital Colorado we created very basic iNO delivery and monitoring systems. We used iNO in multiple clinical settings, including NICU, PICU, OR, transport, CAT scan, and MRI. I was involved in treating hundreds of patients receiving iNO therapy and gained experience in not only how to administer and monitor the therapy, but also valuable insights into how patients responded to the therapy. I also gained valuable insights from speaking to clinicians across the country and participating in clinical trials. I was often involved in discussions about what the ideal nitric oxide system should be while I was working in the hospital and later working in the medical device industry.

What drew you to Beyond Air?

I have known, been friends with, and worked alongside the inventors of Beyond Air's LungFit® systems for more than 20 years. They are also the inventors of the first commercialized iNO system in the US. Once I understood how the LungFit's Ionizer™ technology accurately controls and delivers iNO to patients using only room air and small pulses of electricity, combined with a very similar platform that clinicians already understand, I was intrigued. Combining the ability to produce an unlimited amount of iNO at the bedside with the simplicity of not having to deal with large, compressed gas cylinders—it made perfect sense to me. The sum of these factors made joining Beyond Air a natural fit.

What are the advantages of the LungFit PH System compared to cylinder-based systems?

I think you must look beyond just the obvious advantages of not having to manage cylinders. The weight, the storage requirements, and the constant movement of materials add to the labor cost. We estimate that each cylinder can take up to 1 hour of time: receiving them, moving them to the clinical area, attaching them to a delivery system, and returning the cylinders when the contents have been depleted. The advantage the LungFit system brings is familiarity and simplicity. Familiarity in that the LungFit is a universal delivery system, has the same basic connections clinicians have been using for more than 20 years, and also includes improved technology for flow sensing and monitoring. Simplicity in that there are really no other connections to make, no regulators to connect, and gas purges are never necessary. You basically turn on the device, make the few connections on the front of the device, and set a dose. The pre-use procedure is also very easy and only takes a few minutes. Once the device has been checked out (about 5 minutes) you can literally have the patients on therapy in less than 1 minute. We use a 12-hour filter to remove the NO_2 that is created in the iNO generation process; each filter weighs 2.5 oz and fits in the palm of your hand. The best part about the system is that you never run out of iNO since it is made at the bedside, on demand, from room air.

LungFit PH generates iNO from room air. How does this impact iNO supply and predictability of that supply compared to other iNO delivery systems?

Cylinder consumption can vary based on patient dose and ventilator flow. Clinicians need to keep track of inventory and plan ahead since shipping and delivery of high-pressure cylinders generally requires special handling, and it can be difficult if an emergency supply is needed for a surge in therapy. Being able to generate iNO from room air eliminates the concern regarding iNO supply. The NO_2 filter is a required accessory, but it is a lot easier to ship a box of filters (you can send weeks or months of supply in one shipment vs the space and handling characteristics of high-pressure cylinders). The filters require seconds to change

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Jeff Griebel, Director, Clinical Services, Beyond Air and the LungFit PH.

and last 12 hours, even at the maximum dose using high gas flows. You can basically set your watch to know how long a filter will last vs constantly checking the cylinder pressure and knowing what the pressure/volume relationship is for a specific cylinder size.

How does it improve NICU workflow and potentially improve patient care?

With a cylinder-based system, a clinician needs to maneuver the delivery system to gain access to the cylinders, often times in tight spaces. During therapy, there is nothing to access on the back of the LungFit PH since the small NO_2 filter is easily accessible on the front of the device.

Removing and replacing a large compressed gas cylinder on a delivery system can create a lot of stress on the body (especially the back muscles). There is a risk of injury any time you are moving a heavy cylinder.

You can keep several days' supply of NO_2 filters in a small drawer and, of course, you never have to worry about the iNO supply.

Once the cylinder is near empty, the clinician has to remove the cylinder from the delivery system and take the necessary steps to have it returned to the manufacturer for refilling. When the 12 hour NO_2 filter is depleted, a clinician can quickly replace the filter during the course of therapy and discard the old filter without using any special precautions.

LungFit PH employs a dual channel system, why was it designed this way?

From the earliest days of delivery system development, I felt a dual channel system was the safest and most accurate way to deliver iNO therapy.

A dual channel system basically means you have two separate systems, one to deliver and one to monitor the delivered gases (eg, iNO). One channel controls delivery and the second channel monitors the gases delivered to the patient (ie, iNO, NO_2 and O_2). The delivery is controlled by a mass flow sensor and a microprocessor that delivers a precise, proportional amount of iNO to the ventilator circuit to achieve the desired set dose. The whole delivery process is monitored and updated several times per second. The flow sensor is also on the dry side of the ventilator circuit, so no contamination from humidity or medications can affect the iNO delivery. The LungFit PH can accurately deliver the desired dose, even if the monitoring system completely fails.

Systems that rely on a monitoring system to adjust the iNO delivery are, in my opinion, far from ideal. All currently available systems use electrochemical cells to monitor the iNO dose delivered to a patient (including the LungFit PH). Electrochemical cells and sampling systems can be affected by humidity in the ventilator circuit (from condensation in the sampling circuit) and other contaminants such as medication. Also, in single channel systems, the response time of the sample system is measured in seconds which limits the response time of iNO delivery, and is slower than the response time of dual channel, gas flow sensor based systems. In both single and dual channel systems, the gas is sampled from the ventilator circuit, then the electrochemical cells need to respond, which takes a few more seconds. The cells can also become saturated with iNO causing them to respond less efficiently. There are a number of compensations that can be done with software to make the monitored values look better to the observer, but the bottom line is the sampling system is the weakest point of any delivery system. If you base your iNO delivery solely on a monitored value, you can have a single point of failure and the device is only as accurate as the previous iNO sensor calibration. A dual channel system can deliver an accurate dose even if the iNO calibration is inaccurate or the sample system fails.

What is the level of NICU team training required for LungFit PH compared to cylinder or cassette-based systems?

This is one of the strengths of the LungFit PH. Again, clinicians are making the same basic connections to the ventilator circuit they have been making for more than 20 years. After that, you just set the dose; there are no regulators to connect, and no purging needs to be done. There is also no need to calculate how long a cylinder or cassette will last, you just change a filter every 12 hours. You also do not have to check to see the remaining cylinder pressure when initiating iNO therapy, because the time remaining on an installed filter is always displayed on the LungFit PH screen and alarms at 30, 10, and 2 minutes, reminding you exactly how long you can use that filter. If you want to install a new one, you just remove the currently installed filter and pop in a new one. It is that easy. A frequent comment I hear following an in-service for the LungFit PH is that clinicians sometimes think they missed a step in the set up when they are first introduced to the device. I often have to say, I know it feels that way, but it really is so easy to set up it feels like you missed a step, especially if you are used to connecting cylinders and regulators and going through a leak test and purge routine. You will soon forget all about purging an iNO delivery system after spending a short time working with the LungFit PH. The device completely purges all iNO out of the system up to the point of delivery (ventilator circuit) within 6 seconds of stopping

therapy. The iNO is purged with the same room air that was used to generate iNO. Once the dose is set to zero, the Ionizer stops producing iNO and the room air passes though at the same flow rate into the ventilator circuit. The device will also purge the delivery lines if you turn it off without setting the dose to zero.

What has been the initial feedback from NICU teams and RTs who have used or evaluated LungFit PH?

Common comments I receive are: "the device is so easy to use, it does not require hours of training and retraining"; and "set up is so easy, I don't think we need a software wizard to assist with the setup." Staff love the fact that they don't have to manage cylinder logistics anymore.

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The nitric oxide from the LungFit PH System 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. Refer to the full Prescribing Information within the LungFit PH System Operator's Manual before use.

Visit **www.LungFitPH.com** for full Important Safety Information.

References: 1. LungFit PH System Operator's Manual. Garden City, NY: Beyond Air Inc. 2022. **2.** Data on file. Beyond Air Inc. 2021.

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New Technologies to Help Monitor Patients in Bedside Environments

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. This interview is with Danny Wade MSN, BSN, RN with the company Medtronic to support products on the market and assist in the development of new devices.

Can you talk a little bit about what you do at Medtronic and your history in healthcare?
Prior to joining Medtronic I spent 15 years as a bedside nurse working in a variety of clinical arenas. My experience moved from telemetry, general ICU, cardiac catheterization lab, Cardiac ICU and then on to healthcare leadership. In August of 2022, I decided to go back to the bedside as a PRN staff member in a community hospital, general ICU.

For the past 5 years at Medtronic, I have worked with both the Respiratory Interventions (RI) and Patient Monitoring (PM) groups to ensure their product offerings are supported and ready for the regulatory transition from MDD to EU MDR. I can actually feel the eyes of readers glazing over as they read this, and I get it! I didn't even know what this meant, but the bottom line is: I help assess the clinical evidence that supports our products to make sure it is up to date and state of the art. This means, if we see gaps that need to be addressed, we come up with testing or studies to address those gaps. In addition, I bring my experience so that the engineers and other functions can gain perspective on how our products are used in practice.

I realize this is an incredibly broad question, but how have you seen the integration of technology at the bedside go from being a considerable hinderance to helping to improve the care being delivered?
This is a fantastic question, and I'm so glad you asked! While working at the bedside, it can be challenging to see how things are working together as every small change does impact workflow. Being away from the bedside for a few years has provided me with a perspective that I can now see these changes that I may have seen as a workflow challenge, to be a benefit. A case and point would be how the integration of smart pumps has helped my workflow. Even as recent as 5 or 6 years ago, nurses would receive an order in the electronic medical record (EMR), ensure that it was appropriate, await pharmacy to review, obtain medication, conduct all the rights at the bedside and then hang the medication, program the pump and make sure the rates were appropriate. Now, the order is placed in the EMR and once all the reviews are complete, the EMR will communicate with the pumps and sync medication, rate and even the intake of the medication. This kind of integration is extremely helpful when the patient is on multiple medications with multiple pumps to ensure each channel is assigned and tracked in the EMR. The integration and automatic uploading of the intake is also extremely helpful when working on patients requiring Continuous Renal Replacement Therapy (CRRT) or other closely monitored intake and output therapies.

Are there experiences that you've had at Medtronic that impact your work at the bedside?
Having uninterrupted opportunities to look at literature and consider how devices are used has really and begin to see how the medical device industry can address gaps in their knowledge along side the gaps found in the available products has been extremely impactful. Gaining a much more in depth understanding of specific patient monitoring technologies such as pulse oximetry, regional oximetry, end tidal CO2 monitoring and bispectral index monitoring (in pediatric patients and adults) has influenced conversations with providers and other bedside staff almost every time I work.

I'm sure there are ample experiences you've had at the bedside that impact your work at Medtronic. Can you give an example of one or two experiences that have been a lightbulb moments for you?
If we stay in the lane of integration of technology with workflows, I see how medical device companies need to maintain dual focus on innovation for patients and on how the provider interacts with the device. If new or more steps are required to place or use the device, this workflow impact is a big deal. Seeing firsthand how the providers I work with have moved from using direct laryngoscopy for intubation in the ICU to their almost universal adoption of video laryngoscopy has been staggering. This availability of technology is amazing and has allowed the rest of the clinical team to be more aware of what is going on during the intubation process. Watching how many steps are involved in a clinically uncomplicated intubation is something that has been on my mind as of late. The proliferation of smaller and smaller optical hardware and other technologies has made video laryngoscopy accessible and has likely led to improved education.

The facility I work in is extremely well connected from a technology standpoint. Having a virtual ICU provider able to see what's going on in the room at any given time, especially on the night shift has been a real eye opener for me. Having someone reach out from a virtual ICU to the bedside staff was something I had heard about, but until I came back to the bedside, I hadn't seen this in action. Having an extra set of eyes on the patients

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we deal with is really important and it is made possible through technology.

Are there any projects you can talk about that would impact the NICU?
The one project that I've been extremely close too has recently been submitted to the FDA for approval, so unfortunately, I'll have to wait to discuss that in detail.

However, there are 2 recent developments that the respiratory interventions and patient monitoring groups have recently launched. The first would be the updated Nellcor™ Pulse Oximetry Neonatal Sensors. These devices have improved adhesives that were designed for the delicate skin of the neonate. The sensors are industry leading in SpO_2 accuracy during low saturation conditions.

An extremely exciting addition to the Respiratory Interventions portfolio has been the SonarMed™ Airway Monitoring System. This product provides the NICU clinician with a visual way to monitor endotracheal tube position in the trachea. It measures the location of the endotracheal tube tip and thus may assist in the detection of movement within the trachea, provides a measurement of the circumference of the trachea to help the clinician identify if the ETT has migrated and it also provides information related to obstruction within the ETT to help optimize the removal of secretions during suctioning.

What keeps you going back to the bedside?
Knowing that there will always be gaps between what appears in the literature and how care is actually being delivered is something that keeps me going back. Seeing the way technology CAN assist and be integrated in such a way that it is almost seamless, is encouraging and that's something I want to continue to be a part of: development of products that improve the health of the patient and do so in a way that feels seamless to the provider.

What technologies have you seen come into the NICU over the last 10 years?
A few of the new technologies that I've seen come into the NICU space would of course include the aforementioned SonarMed™ and Nellcor™ products but would also expand to devices outside of my direct business groups and even outside of Medtronic. A few years ago, the newly released Carpediem™ Cardio-Renal Pediatric Dialysis Emergency Machine made it to the market and has seen some good results. I've also seen the miniaturization of other devices such as the Embrace® Aspect Imaging Neonatal MRI system that are of great interest to me as this will impact patient safety by providing an appropriately sized device within reach of the patient's it was designed for.

As I've already said, the integration of all of these existing technologies into the electronic medical record has been a big deal over the last 10 years. I can't imagine what we'll see in the next 10 years, but I want to be a part of helping to develop and implement the next generation of medical technology in the NICU.

Danny Wade has been an RN in Colorado for the last 19 years. Danny gained a passion for healthcare while obtaining his EMT-B, and then enrolled in nursing school. He has worked in a variety of critical care environments, is now working at the bedside and at Medtronic to support products on the market and assist in the development of new devices.

First-person Accounts of Implementing an Exclusive Human Milk Diet (EHMD) in the NICU

Kim Mack, MS, RD, LDN, CNSC and Stacia Pegram, MA, RD, LD

One of the biggest challenges facing clinicians in the NICU is the need to continually optimize management of very low birth weight (VLBW) and extremely low birth weight (ELBW) infants to improve outcomes in light of ongoing advancements in knowledge and technology in this arena. This is not just about keeping up with the medical literature. These infants are so vulnerable that even the tiniest alterations in feeding protocols can have life-or-death consequences. Here, two NICU dietitians offer first-person accounts of how they have improved outcomes over the past decade by making incremental improvements in their NICU feeding protocols that include adopting an exclusive human milk diet (EHMD).

Kim Mack, MS, RD, LDN, CNSC
Ascension St. Alexius Medical Center

I always say that we are a small community hospital that does great things. I started thinking beyond our standard fortification protocols in 2014 when I had a 33-week little girl who really challenged me. She needed total parenteral nutrition (TPN) to provide calcium, phosphorous, and protein because she did not tolerate enteral fortification in the form of standard human milk fortifier (HMF) or elemental formula as HMF. I found an HMF made from donor human milk by Prolacta Bioscience through a web search and brought it first to the NICU team, then to administration. We ordered it for this patient on a trial basis and … well … the rest is history.

We have been using a variety of human milk-derived nutritional products for more than 9 years. We started combining them with mother's own milk (MOM). Our first guidelines were to use human milk-derived fortifiers in infants who were < 1500 g or < 33 weeks at birth and continue it until 34 weeks, at which time we weaned to standard fortifier or formula. We started with Prolact+4 fortifier at 80 mL/kg/day, advancing to Prolact+6 at 100 mL/kg/day when TPN was discontinued. After a few years using this protocol, we noted that patients required fewer TPN days. In fact, our team presented at a poster session for the Illinois Perinatal Quality Collaborative and the American Academy of Pediatrics (AAP) Conference in 2015 that showed a decrease from 14 to 7 TPN days after implementing human milk-derived nutritional fortifiers. At the time, our focus was on the cost savings associated with decreased TPN days, but in hindsight I realize the benefits of an EHMD for our patients were far more meaningful.

Kim Mack is with Ascension St. Alexius Medical Center.
Stacia Pegram is with Prisma Health Richland.

As our unit's maternal breastfeeding rates have historically been higher than most, we did not begin with donor milk at the same time we started using human milk-derived nutritional fortifiers. Initially, when an adequate supply of MOM was not available, the infants received preterm formula alone. We shifted toward adopting donor milk following AAP recommendations for use of an EHMD in our smallest and youngest patients and after a 6-month quality improvement project revealed we had many patients who were receiving formula early on because there was not enough MOM available. Usually, there was adequate MOM after only 5-7 days, so we decided to bring on donor milk as a bridge to MOM, to provide an EHMD consistently until 34 weeks before transitioning.

In our NICU, we all carefully followed the latest research on early fortification. This led us to discontinue Prolact+4 and begin fortification with Prolact+6 at 60 mL/kg/day. Once again, this modification decreased days on TPN to an average of 6 days without increasing intolerance or feeding complications. A human milk-derived cream was added to our guidelines for infants who were not meeting their growth goals for approximately 3 days. Our protocol consisted of 4 mL of cream for every 100 mL fortified feeds. This was soon updated to start cream proactively for any infants on continuous feeds. We also started to automatically initiate increasing Prolact+6 or +8 when an order for enteral fluid restriction occurred. We continued with this for about another year with good results.

As much as we try to put our patients into our guidelines, some just do not fit in. Considering their needs individually helps me to successfully attain the best growth. We start with a standard approach, but at times we must explore other ways to support growth velocity in order to meet growth goals. We have had babies who have not grown as we have wanted, and we have been challenged with hypoglycemia during the transition from parenteral to enteral nutrition. This is what led us to move from reactive use of cream to proactive use. We currently add cream at 4 mL for every 100 mL fortified feeds when TPN and lipids are discontinued for our infants < 1250 g at birth on every 2-hour feeds.

I see myself not only as a dietitian but also a growth expert. I challenge myself to fit my guidelines to my patients and not my patient to my guidelines. We strive to look at the latest research and adjust our guidelines according to evidence-based research and our own human milk unit's workflows. We have a duty to do everything we can to help our patients not only in the NICU

but also for the future. Evidence demonstrates that an EHMD improves growth and development in the NICU and beyond. Through our evidence-based modifications to our protocols, both our clinical and financial teams have seen the benefit of an EHMD, while we remain financially responsible by charging for these products.

Stacia Pegram, MA, RD, LD
Prisma Health Richland

I work in a 69-bed Level III NICU. Although the systems in place for a larger unit may be different from those in a smaller one, the goals of promoting the best possible patient outcomes and quality care are consistent among NICUs of all sizes. As a dietitian working in our unit for over 20 years, I have seen numerous changes and advancements in the field of neonatal nutrition that have been largely driven by a greater focus on quality improvement through data collection. Some of the major improvements include involving a full-time dietitian as part of the medical team, developing feeding guidelines to improve consistency in nutritional practices amongst the various neonatologists and nurse practitioners, implementing pasteurized donor breast milk, and implementing human milk-based HMF in the VLBW and ELBW population.

I was hired as the first full-time dietitian in our unit in 2002, and feeding guidelines were created and implemented about a year later. Those guidelines have been updated numerous times throughout the past 20 years. As long as I have worked in the unit, breast milk has been promoted as the gold standard in feeding, and we have initiated multiple initiatives over the years regarding best practices in achieving high rates of MOM provision. I have also had the pleasure of witnessing the switch to pasteurized donor breast milk in place of formula in my unit as well as its subsequent benefits for patients.

The shift toward an EHMD was prompted by quality improvement initiatives. Given the evidence-based research supporting the use of breast milk, particularly the reduction in the risk of necrotizing enterocolitis (NEC), our unit implemented donor breast milk in place of formula when MOM was unavailable for all VLBW infants in the latter part of 2009. We also moved to human milk-based HMF in place of cow milk-based HMF (in other words, an EHMD) for the highest-risk infants as part of our NEC reduction initiative. The qualifying birth weight for use of human milk-based HMF changed a few times over the initial year of usage but always included ELBW infants. Once we found the right fit for our unit, we continued the same general guidelines over the following 13 years. Although we review and adjust feeding guidelines often based on clinical outcomes as well as new research and/or published standards of care, use of donor breast milk and human milk-based HMF has remained constant in our guidelines due to our own positive outcomes.

Since NEC was our initial focus, we collected data for medical as well as surgical NEC. There was a notable decrease in both. Nevertheless, since medical NEC was not as well-defined 13 years ago as it is today, the numbers for that first year may be skewed. Our medical NEC rate decreased from 11.5% to 7%, and our surgical NEC rates decreased from 4.5% to 1.5% for our ELBW population after the first year of implementation of an EHMD. The average rates of medical and surgical NEC during the period between initial implementation of an EHMD and the most recent year of data collection also dropped significantly. We noted no change in medical NEC with a slight increase in surgical NEC over the past year, but the numbers remain lower than prior to implementation of an EHMD.

As quality improvement remains an ongoing goal, we continue to evaluate our clinical outcomes. Since evidence now demonstrates an association with improved outcomes in areas beyond NEC with use of an EHMD, we began monitoring other clinical outcomes such as late-onset sepsis, bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), and length of stay. We have noted improvement in all these measures associated with the switch to an EHMD.

As in Kim's unit, our unit has adapted guidelines specific to an EHMD to better meet nutritional needs based on improved tolerance, which include advancement from initiation of fortification with Prolact+4 to a +6 concentration. Over the years, we reduced the timing of fortification from initiating at an enteral volume of 100 mL/kg/day to initiating at 80 mL/kg/day. We further reduced enteral volume needed to implement fortification to 60 mL/kg/day in the most recent revision of our feeding guidelines. We also use human milk-derived cream to replace fat losses that naturally occur when the fat from MOM/donor breast milk feeds adheres to plastic bottles, syringes, and tubing. We strive to proactively provide cream in an effort to support growth before a deficit can occur. Growth and development in this population has always been and will continue to be a challenge. Thus, it is crucial to adapt feeding guidelines and practices based on clinical outcomes and new research.

As a neonatal dietitian, I believe nutrition will remain an evolving component in the care of preterm infants. One shoe will never fit all patients, but feeding guidelines give us a good place to start. Continued focus on quality improvement and advances in neonatal nutrition allows us to adapt our care and reassess based on results. I am honored to be part of a field in which positive outcomes drive changes in practice. I am proud of the changes adopted in our unit over the past 21 years that have improved clinical outcomes for our patients. I appreciate the team members I work with, and I feel appreciated by the medical team because we are all striving to provide the best care we can to the most vulnerable of patients.

Bridging the Experience-Complexity Gap: How AI is Empowering NICU Nursing Staff

Chelsea Adams, MHA, BSN, RN, CCRN

I was observing in a NICU two weeks prior to my team implementing our critical care clinical decision-support platform. A patient slated to be discharged that day experienced a bradycardic episode. Because there was not sufficient documentation to support that this was an isolated event, the baby needed to remain in the unit for an additional three days for observation.

With my background in critical care nursing, this scenario is all too familiar to me. Patients in the intensive care setting are increasingly complex, and with that, clinical workflows do not always provide meaningful clinical data at your fingertips to spot subtle deterioration or an impending adverse event.

With our platform, this care team will soon be able to leverage the power of relevant and timely clinical insights via an intuitive display of trended patient data. This allows nurses to bring attention to the patient and inform clinical decisions. Simply put, Etiometry augments a nurse's ability to provide safe care, identify clinically relevant changes in patient condition, and provides a mechanism to avoid similar events in the future.

We know these types of situations are not unique – especially when we consider current rates of high clinician turnover and, in turn, the need to rely on newer nurses to care for increasingly complex patients. This situation is what the healthcare industry has coined the Experience-Complexity Gap.

Nurses, in general, carry the immense responsibility of monitoring and managing patients clinically, coordinating with multi-disciplinary teams, and providing continuous communication to caregivers and loved ones. This–in the setting of a novice caregiver with high acuity patients–can lead to burnout over time.

However, if an inexperienced nurse were armed with the right contextual information in the right place at the right time, they would have the tools to paint a clinical picture and communicate their findings with the care team, potentially improving upon an otherwise stressful situation. Furthermore, a shared mental model surrounding a patient's clinical condition and plan of care benefits many facets of care, such as: driving efficient ventilator weaning, reduction in readmissions, and offsetting the burden of data collection. These are just a few examples of what is possible with Etiometry.

Chelsea Adams is Etiometry's Vice President of Customer Success.

Etiometry's AI-powered software helps nurses and other clinicians better understand patient status, communicate more effectively, and deliver more consistent care. The Etiometry platform's capabilities include data aggregation and visualization, clinical pathway automation, and a powerful quality improvement tool.

Data aggregation and visualization enable a holistic view of patient data from monitoring systems, peripheral devices, EHR data and others.

Often during rounds and shift change, nurses provide a summary of vital signs, significant events and pertinent changes to the plan of care during the last 12 hours. Collecting the data can be time-consuming, and the result is likely a handwritten account of the prior shift. Reporting vital signs ranges and shift anecdotes may under-represent or completely miss significant findings. Etiometry's data aggregation and visualization solution allows clinicians to paint a picture of the patient's recent state directly from a bedside display and aligns the care team with the same insight into abnormal trends or significant events to identify a potential needed change in treatment.

According to a Medical Director of Cardiac Critical Care and Clinical Informatics at a large east coast children's hospital, "Etiometry is automated with no user bias of the data. And it is dynamic - visualizing granular events that lead to a physiological change."

He queried his team of nurses regarding their thoughts on using Etiometry and found that 88% said it was easy to use, makes tasks easier and helps them accomplish tasks in the fewest steps possible; 79% said Etiometry saved them time.

Embedded hospital protocols can be automated to track hospital-specific guidelines to standardize workflows and drive consistent, timely adherence to guidelines to improve outcomes.

Etiometry's clinical pathway automation can be used to guide clinical decision-making based on hospital-specific criteria and alert clinicians when a patient is ready for a particular intervention or procedure, helping to reduce variability in care and improve patient outcomes. One example is the ability to alert clinicians when the patient is eligible for an extubation readiness test (ERT). Reduction in ventilator time can reduce length of stay, drives bottom-line savings and could result in an open bed for another patient, thus increasing throughput and revenue.

According to a CVICU Medical Director and avid user of Etiometry, "Getting the information for an ERT takes only one click. You get all the data you need on one screen so you can look at everything – Easy."

Clinical pathway automation eases the burden of complying with clinical guidance, allows clinicians to practice at the top of the licenses, and provides an easy mechanism to evaluate quality improvement initiative effectiveness while providing insight into patient outcomes.

Drive quality initiatives and research with accessible long-term storage and reporting of clinical data.
Interactive reporting of embedded automated pathways in the Etiometry Platform revolutionizes the ability to evaluate performance and ensure the implemented care guidelines are having the desired impact of improving quality. Without a tool like Etiometry, measuring the success and outcomes of clinical guidance is a labor-intensive process, and lacks the supporting data to evaluate the effectiveness to reach the best possible outcomes.

What most critical care leaders appreciate about the Etiometry Quality Improvement database is the ability to quickly retrieve large volumes of normalized patient data with APIs to complete research or develop and deploy your algorithms and eliminate gaps in the EHR when data archives represent activities charted hourly.

As a leader in clinical decision-support software, Etiometry is utilized in several NICUs in the top children's hospitals nationwide. We believe that the widespread utilization of the Etiometry platform will yield relief for nurses and other clinicians in the NICU and will contribute to closing the experience-complexity gap affecting our nation's high-acuity care teams. In doing so, we give nurses time back in their day to provide high-quality care and allow patients and their families to be discharged with peace of mind.

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Modulating the Newborn Microbiome and its Implications in the NICU: It's So Much More than NEC

Jennifer Bragg, MD and Payal Adhikari, MD

What is the Newborn Microbiome and why is it important?

The microbiome is increasingly being recognized as an important modulator of long-term health outcomes. In adults, dysbiosis (microbiome patterns are associated with disease states). has been hypothesized to play a role in allergy, autoimmune, cognitive, and metabolic disorders including obesity, dyslipidemia, hyperglycemia.[1-3]

In the newborn, development of the microbiome begins at birth when the initially sterile newborn gut is quickly colonized by bacteria, both healthy and potentially pathogenic.[4] The first three years of life are a critical time of physical growth, as well as immune and cognitive development,[5-8] and are influenced by many external and host factors, including how infants are fed, maternal microbiota, mode of delivery, and home environment, among others. Infants hospitalized in the NICU are at particularly high risk of dysbiosis, the imbalance of organisms within the gut microbiome that can contribute to disease state.[9]

Bifidobacterium in the Newborn Microbiome and its relationship with human milk

Bifidobacteria is an anaerobic bacterium historically ubiquitous to the newborn intestinal microbiome but also present elsewhere in the body such as the vagina and mouth, the prevalence of which varies significantly amongst countries.[10,11] In countries with a low historical rate of breastfeeding such as the United States, levels of B*ifidobacteria* are alarmingly decreased compared to countries such as Bangladesh or Gambia where historical breastfeeding rates are high.[11] The prevalence of babies in the United States who are naturally colonized with *Bifidobacterium infantis* is estimated to be less than 10%, while prevalence in Bangladesh and Gambia, countries with high historical rates of breastfeeding is up to 84% and 92%, respectively.[11]

Jennifer Bragg, MD, Vice President of Clinical Implementation at Infinant Health and a neonatologist with a passion for optimizing pediatric outcomes, she has spent over a decade building multidisciplinary neurodevelopmental programs that support families as they navigate healthcare systems and challenges.
Payal Adhikari, MD, Clinical Implementation Director at Infinant Health and a board-certified, practicing pediatrician for over a decade, she is passionate about supporting new families and encouraging peaceful parenting.

An important partner to bifidobacteria are Human milk oligosaccharides (HMOs), the third most abundant component of breastmilk.[12] While HMOs are non-digestible to the infant, their role is to provide an energy source for beneficial intestinal bacteria, mainly *Bifidobacterium.*[13]

What makes bifidobacteria beneficial compared to other bacterial strains is its ability to colonize the infant intestinal tract, and one of its subspecies, *B. infantis*, contains a large gene cluster devoted specifically to the uptake and metabolism of HMOs.[14] *B. infantis* is particularly well adapted to the infant gut, and metabolites produced by *B. infantis* from HMOs can positively impact the lungs, brain, and liver, along with overall beneficial metabolic effects.[15]

Higher prevalence of adverse health outcomes with lower levels of *Bifidobacteria*

Research shows that early dysbiosis is associated with long-term adverse health outcomes, and in Estonia and Finland, lower levels of bifidobacteria early in life were associated with an increased susceptibility to autoimmunity and allergies in later years.[16] Infants in the NICU, especially those born via caesarean section (as many high risk NICU infants are), have been found to lack this important bacterium.[9]

Use of *B. infantis* EVC001 for Immunomodulation in the NICU-the Role of Inflammation in Modulating Disease

An article published in Cell in 2021[17] showed that term infants fed exogenous *B. infantis* EVC001 subsequently had higher levels of *B. infantis* colonizing their GI tracts. Interestingly, babies fed *B. infantis* EVC001 from days 7-28 of life continued to be colonized with the bacterium up to one year of life.[18] Other studies have shown a similar immunomodulatory effect, and infants in the NICU who were fed *B. infantis* EVC001 received fewer courses of antibiotics.[19]

In addition, infants fed *B. infantis* EVC001 exhibited diminished enteric inflammation. Amongst those preterm infants fed *B. infantis* EVC001, colonization by *B. infantis* also resulted in the displacement of bacteria associated with increased risk of preterm morbidities including *Escherichia* and *Staphylococcus*, pathogens that are known for causing NEC, late onset sepsis, amongst other complications in the NICU.[19] This and others


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studies have concluded that the use of *B. infantis* EVC001 in conjunction with human milk in premature infants provides a meaningful and low-risk approach to alter the gut microbiome composition and increase the abundance of a well-established infant gut symbiont that: (1) increases human milk utilization; (2) diminishes enteric inflammation; and (3) decreases the abundance of taxa associated with antibiotic-resistance and poor health outcomes.[19,20]

Hypothesized relationship between growth and inflammation

Preterm infants often have a decreased growth trajectory compared to their term counterparts. Historically, efforts have focused on standardizing feeding protocols, maximizing balancing micronutrients such as protein, fat and dextrose.[21] Studies have started to examine the role of the microbiome in metabolism and growth, and several have demonstrated dysbiosis in infants with malnutrition.[22] Studies also have shown that there are improved anthropometric scores in infants supplemented with *B. infantis* EVC001. Most recently, a single blind randomized clinical trial was performed to examine the effects of supplementation with *B. infantis* EVC001 in infants with severe acute malnutrition in Bangladesh. The study found that the mean rate of weight gain was highest in babies supplemented with *B. infantis* EVC001 (5.90 g/kg/day), which is considered moderate weight gain by WHO standard. A significant increase in weight gain of 2.03 units was observed with the probiotic group compared to the placebo group.[23]

While this group of infants varies from infants in the NICU, it does raise the question of how variations in the microbiome and subsequent inflammation affects weight gain. As demonstrated here, infants with malnutrition and a chronic inflammatory state had improved weight gain with administration of *B. infantis* EVC001 and it warrants further investigation into the effects of modulating inflammation in hospitalized infants as a strategy to improve weight gain.

Conclusion

Emerging research about the newborn microbiome suggests the critical importance of reducing inflammation in the intestinal microbiome for improved outcomes. *B. infantis* is identified as one of the few strains that is hypothesized to play a role in mediating inflammation and improving growth. Providing newborns with *B. infantis* EVC001 at the earliest stages of development may play a role in long-term health outcomes.

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Breaking Down the Milk Expression and Breastfeeding Barriers Common to NICU Mothers

Nicole Nyberg, MSN, APRN, NNP-BC, Grace Dwyer, MS, MA, RD, LDN, IBCLC and Jaylee Hilliard, MSN, RN, NEA-BC, CPXP

NICU families and their care teams experience a challenging mismatch; while preterm and critically ill neonates need the unique properties and benefits from their Mother's Own Milk (MOM), they also face more significant breastfeeding barriers than other families. Common barriers may include: mother-infant separation, stress, competing demands, dependence on pumping to maintain milk production rather than direct breastfeeding, and delayed lactogenesis.

This paper reviews the lactation barriers that NICU parents face, followed by what we, as NICU clinicians, can do to help families succeed in their feeding goals and provide optimal care.

Why MOM is Critical

Healthcare professionals recognize MOM as the gold standard for infant feeding — especially for preterm infants. In addition to serving as an easily digestible nutrition source, MOM also contains beneficial immunologic, antimicrobial, anti-inflammatory, epigenetic, growth-promoting, and gut-colonizing properties.[1]

The benefits of specifically MOM for NICU patients are well documented:

- Improved feeding tolerance,[1,2] which may translate to earlier NICU discharge
- Decreased incidence of sepsis and necrotizing enterocolitis (NEC).[2,3-5]
- Reduced incidence of retinopathy of prematurity (ROP).[4-7]
- Reduced risk of bronchopulmonary dysplasia (BPD).[5,8]
- Decreased length of stay related to reduced comorbidities.[4]
- Improved neurodevelopmental outcomes.[9,10]

It is the standard of care in many NICUs to utilize Donor Human Milk (DHM) as an alternative or to help bridge the gap for infants, especially preterm infants when the mother's breast milk is either unavailable or there is insufficient volume. However, MOM remains superior in its antimicrobial and protective mechanisms against prematurity-related complications.[5,7,11-14] The pasteurization process for DHM diminishes certain protective elements and macronutrient content.[15-19]

The Barriers to Milk Expression among NICU Parents

Given the clinical benefits, it is clear why MOM is indicated as the ideal food for hospitalized infants. Yet, preterm and low birth weight infants in the U.S. receive MOM at consistently lower rates compared to term infants: 63.8%-71.3% for preterm infants versus 76.5%-84.6% for term infants.[20] In addition, at the 6-month mark, NICU graduates who were preterm or critically ill received less than 20% of their own mother's milk.[16,21]

Insufficient MOM production is the main proposed reason for low MOM provision in the NICU.[16,21,22,23] NICU parents face several challenges with the initiation of lactation and their ability to maintain an adequate milk supply, ranging from physiological to emotional.

Additionally, racial disparities exist within the NICU populations: fewer African American and Hispanic Very Low Birth Weight (VLBW) patients continue to receive their mother's milk at discharge compared with non-Hispanic White infants,[16,23-25] which may partially explain why these groups also have 2- to 4-fold increased risk for developing NEC, BPD, ROP, and intraventricular hemorrhage.[11]

Mother-Infant Separation

When an infant, mother, or both are hospitalized, this separation cascades into several different breastfeeding barriers. Without a vigorous infant to stimulate the hormones of breastfeeding every one-three hours, parents must proactively pump to mimic this same pattern and build up a supply in the absence of latching. Around-the-clock pumping is no easy feat; one study found that only 4% of NICU parents who knew the benefits of human milk and felt well-supported by hospital lactation staff were meeting the recommended eight pumping sessions per 24 hours, with the majority pumping four or five times daily instead.[26]

Consistent parental presence in the NICU with skin-to-skin care and holding leads to improved parent-child attachment and neurodevelopmental outcomes.[27] While some families can visit the NICU more frequently, increasing their ability to perform skin-to-skin care and pump at the bedside, many families cannot due to the competing demands of returning to work, caring for additional children at home, and transportation issues.

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Even if there is minimal separation, mothers of preterm infants, especially very low birthweight (VLBW) infants, must rely on pumps since their infant is not physiologically stable or developed enough to breastfeed directly.

Maternal Comorbidities & Delayed Lactogenesis

Often mothers experience medical challenges of their own, which may be exacerbated when their infant is born critically ill or premature. These comorbidities may delay lactogenesis II - the onset of copious milk production. Conditions that hinder lactogenesis include but are not limited to:[24,28]

- Traumatic/complicated birth
- Postpartum hemorrhage
- Unplanned C-section
- Preeclampsia
- Diabetes
- Obesity
- Hypertension
- Infections
- Abruption
- Inadequate Weight Gain

Additionally, parents of extremely preterm infants may experience incomplete mammary gland development and have delayed milk letdown.[11]

Stress & Altered Parental Role

The uncertainties and trauma surrounding the experience of having a child in the hospital present stress, which can impair lactation at the physiological level. Mental stress can inhibit the milk ejection reflex,[29] serving as an additional potential lactation barrier. In addition, the NICU environment itself can impede milk expression since the lack of privacy and structured routines often lead to exhaustion and anxiety. Yet a mother's presence in the NICU is crucial for them and increases their ability to provide frequent skin-to-skin care, facilitate adequate milk production, and breastfeed.[22]

Additionally, research has shown that mothers who display decreased confidence in their maternal role (which is common for NICU mothers) will experience parental role alteration.[22,30] An alteration in parental role negatively impacts their feelings toward motherhood and disempowers them to express their milk.

The Role of Donor Milk

Studies have suggested that the availability of DHM in NICUs may reduce MOM consumption in preterm infants.[16,31] However, hospitals need to ensure that the availability of DHM does not prevent the proper education and, ultimately, the decision for mothers to provide breast milk for their infants. If mothers and their support partners are given another option, especially after delivering a preterm or critically ill infant, they may decide not to provide their own milk.

Interventions

NICU care team members are in a position to have a significant impact on MOM production, whether positive or negative. Given their proximity to the patient and their family, nurses have a particularly impactful role in educating, supporting, and encouraging lactation. The following interventions are evidence-based strategies NICUs can implement for optimal provision of MOM.

Intervene Early

Setting parents up for success as early as possible is an effective strategy for supporting lactation, as a mother's preconception attitude toward MOM expression is integral to successful lactation.[22] Ideally, the benefits of breastfeeding or expressing MOM are reviewed with mothers during pregnancy or after birth—particularly if the infant is born prematurely or with anticipated medical concerns.

Parents should initiate milk expression as soon as possible after delivery, with a goal of no later than 6 hours after birth.[16] Appropriately trained staff should provide expression assistance, and all mothers, especially NICU mothers, should have access to hospital-grade pumps.

The first 3-5 postpartum days are a critical window for lactogenesis, as research has shown that a decrease in expression frequency is associated with decreased long-term milk volume.[16]

Educate & Bring Awareness

Nurses and NICU clinicians play a vital role in the parents' decision to provide MOM and the ongoing coaching and support necessary to achieve their goals.

It has been reported that NICU mothers felt that the support and knowledge they received regarding lactation and breastfeeding varied widely among all the healthcare professionals they interacted with.[22] Therefore, bedside staff must be adequately trained and maintain competency in the importance of MOM and its benefits to both mom and baby. Additionally, staff should maintain competency in skills to support MOM initiation and maintenance, including pumping and breastfeeding.

It is also essential to include fathers and care partners in lactation education. Social support is a significant determinant among African American women for initiating and continuing milk expression.[25] In addition, once fathers or care partners gain knowledge of lactation and the benefits for the infant, they begin to show more readiness to support their partner in their lactation goals and efforts.[25]

DHM usage should be explained to parents and framed as a bridge until the mother's milk supply is established to support maternal lactation efforts, not as an alternative solution.

To mitigate the racial disparities, women and their care partners from all backgrounds should be provided with evidence-based and culturally relevant information on providing MOM in a timely manner.

Encourage & Monitor

A supportive environment coupled with education has the potential to positively impact the mother's milk production in the NICU and beyond. Therefore, NICU nurses must be empathetic and try to build trusting partnerships with NICU mothers to promote milk expression, establish breastfeeding, and nurture the feelings of motherhood.

NICU care team members must empower and encourage all NICU mothers to actively participate in caring for their infants so they become confident in their parental role. However, NICU mothers may have some difficulty transitioning into their role as

a mother once their infant is admitted to the NICU due to their feelings of fear, worry, anxiety, and intimidation.

Staff who proactively monitor parents' pumping behaviors and output trends can provide informed, timely support. In addition, several studies have encouraged proactive monitoring of parents' pumping logs and daily milk output.[32-34]

Using software that enables lactation professionals and nurses to monitor pumping trends securely and in real time is ideal. Comprehensive feeding management systems like AngelEye Health's MilkTracker, which offers a suite of parent-facing tools including pumping statistics and two-way chat with lactation staff, enable care teams to have greater insight into lactation behaviors.

Promote Bonding & Minimize Separation

A zero separation goal must be encouraged between the infant and mother when possible to minimize toxic stress and promote maternal confidence, bonding, and, ultimately milk supply.

Zero separation also promotes skin-to-skin contact. Skin-to-skin care should be done early and as long as possible, depending on the infant's clinical condition.[17] Non-nutritive sucking and direct nursing, when physiologically appropriate, are both beneficial and will enhance the mother's supply and promote continued breastfeeding post-discharge.[35] Mothers should be encouraged to begin oral feeding at the breast once the infant is clinically stable and shows physiologic readiness.

When able, NICU mothers should be encouraged to pump at their infant's bedside because greater milk volumes have been reported when mothers pump in close contact with their infants.[17]

Several qualitative studies have demonstrated that virtual NICU webcams are beneficial for pumping mothers when in-person visits are not possible. For example, in one study, Weber et al., 2021 found that using 'video visitation" throughout the NICU stay helped improve breastfeeding rates at discharge. Similarly, both Kerr et al. (2017) and Reimer et al. (2021) found that parents who viewed their baby via webcam while pumping reported that they were better able to "physically respond" to pumping and pumped larger volumes of milk.

Conclusion

Recognition of the common inhibiting circumstances NICU mothers face in their attempt to establish adequate milk volumes aids NICU clinicians in finding adaptable ways to support each family better. NICU clinicians are key influencers and can facilitate individualized support and targeted lactation education specific to each mother's circumstances. NICU clinicians must educate families with evidence-based information on the superior quality and benefits of MOM. Encouraging mothers to set lactation goals has been shown to increase lactation success, especially in minority groups (11, 33). By providing parents and their support system with the basic facts along with empathy, support, resources, and a hospital-grade pump, we can make a significant impact and change the outcomes for this high-risk population.

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Impact of a Tracheostomy on Pressure and Function: Neonatal and Pediatric Considerations

Kristin A King, PhD, CCC-SLP

The number of neonatal and pediatric patients with tracheostomies is growing each year secondary to advancements in medical care and interventions to sustain life. Watters (2017) reported that tracheostomies are less commonly performed in pediatrics as compared to the adult patient population, with tracheostomies occurring in < 3 % of pediatric patients.[1] While the number is lower than in adults, the number of tracheostomies in children is increasing secondary to the chronic nature of the complex conditions seen in pediatrics, such as abnormal ventilatory drive and irreversible neuromuscular conditions. This change in the needs for pediatric patients has led to more than 50% of the patients being under the age of 1 year at the time of tracheostomy placement.[2]

Aerodigestive changes following tracheostomy

With tracheostomies, changes in the aerodigestive system become evident through impacts on voice, swallowing, cough, and other functions. The prevalence for these aerodigestive challenges, which may lead to feeding and swallowing difficulties, is high.

The placement of a tracheostomy tube and prolonged mechanical ventilation with an inflated cuff causes a disconnect between the upper and lower airway. The lack of airflow through the upper airway often leads to multiple negative changes affecting speech and swallowing: reduced subglottic pressure;[3] decreased sensation to the pharynx and glottis;[3] reduced laryngopharyngeal reflex;[4] decreased ability to manage secretions, requiring more frequent suctioning;[5] decreased sense of taste and smell;[6] inability to vocalize; increased aspiration risk; and muscle disuse and atrophy.[7] A disconnect between respiration and swallowing also may negatively impact the ability to coordinate breathing and swallowing. Another consideration for pediatrics with long term tracheostomy placement is that it also has been associated with delayed acquisition of language, delayed social development, and risk of impaired parent-child bonding.[8,9]

With 25 years of experience in medical, academic, and industry settings, Dr King brings a unique perspective of medical speech pathology. Her research, publications, and teachings focus on traumatic brain injury, swallowing disorders, and critical care (tracheostomy and mechanical ventilation) for both pediatric and adult patient populations. She has been an invited speaker both domestically and internationally and has published in peer-reviewed journals. Currently, Dr King is the Vice President of Clinical Education and Research for Passy-Muir, Inc.

A primary means for closing the system to restore more normal physiology and pressures for patients with tracheostomies is the use of a bias-closed position, no-leak valve. When a patient has a tracheostomy, airflow is directed in and out through the tracheostomy tube and bypasses the upper airway. The Passy-Muir® Valve works by closing at the end of inspiration, which redirects 100% of airflow upwards through the vocal cords and upper airway. Research has shown that this redirection of airflow assists with improving secretion management, increasing sensory awareness, improving swallowing, and restoring natural physiologic PEEP (positive end- expiratory pressure), among other benefits.[10]

Normalizing function

Assessment and usage of a Valve also is important for the normalization of functions for all patients and for development in children. The primary consideration during assessment is that the patient has a patent airway, meaning the patient can exhale around the tracheostomy tube. Having a qualified team, familiar with airway management, is a key component of successful Valve use. The participation of infants, toddlers, and young children in the assessment process often requires both a team and play-based approach because of their limited ability to follow commands and volitionally vocalize. To ascertain airway patency in young children and infants, additional methods, such as transtracheal pressure (TTP) measurements, may be used to assess airway patency.[11] TTP is an objective method for measuring airway patency with tracheostomy tubes. It is a process involving the use of a manometer to measure the pressure that is occurring within the airway. Research has shown that when the TTP measurement is at 6-10 cmH_2O, then the airway is patent and airflow past the tracheostomy tube occurs.[12] TTP is a method for measuring the pressure in the airway with the tracheostomy tube in place. It can be used with finger occlusion or a speaking valve to determine airway patency. TTP has been found to be a predictor associated with successful use of the Passy-Muir Valve (PMV). [13] Brooks et al. (2019) found that TTP, age, weight, and ventilator rate were predictors of success with a Valve.

Pullens and Streppel (2021) discussed the importance of restoring normal airway physiology to assist with feeding and swallowing, which would include restored pressure, by using a speaking valve in the pediatric population.[14] The adult population has several studies which indicate the need to restore subglottic pressure to assist with improved laryngeal function, swallowing, cough, and secretion management.[15]

Infant with placement of the PMV 007 Valve in-line with mechanical ventilation.

The negative impact on pressures and the diminished stimulation of sensory receptors may affect feeding and swallowing in the pediatric population, to include oral-motor sensation. Henningfeld, Lang, and Goday (2019) reported that g-tube feeding and delayed feeding skills were associated with tracheostomy. They also hypothesized that children with tracheostomies would have more feeding issues than their age-matched peers without tracheostomies.[16] During review, they found that a history of ventilator-dependence, cuffed tracheostomy tube, and speaking valve use during inpatient care were inconsistently associated with later feeding and nutrition evaluations. However, the authors suggested that their findings also indicated that earlier speaking valve use has the potential to decrease later issues with feeding.

Early assessment for speaking valve use either in-line with mechanical ventilation or with a spontaneous breather leads to early intervention—in this case, establishing treatment plans, accommodations, and interventions earlier during their care. Early intervention and use of the PMV has been shown to have benefits with restoring the physiology of the upper airway to its more "normal" state by returning airflow through the upper airway during exhalation.[7] This restoration of airflow to the upper airway allows evaluation of airway patency, vocal cord function, secretion management, swallowing, and communication skills.[7] Research has shown that the use of a Passy-Muir Valve can provide benefit during swallowing by increasing laryngeal excursion, returning cough and throat clear, and providing overall improved protection of the airway.[7] Whitmore et al. (2020) also reported that the use of speaking valves for patients with and without mechanical ventilation was highly supported among the reviewed literature to promote speech and communication, which had an additional impact on patient satisfaction, and has been shown also to contribute to alveolar recruitment, weaning, and quality of life.[17]

Intrathoracic and intra-abdominal pressures

Additional primary areas of pressure to consider when addressing the needs of patients with tracheostomies are the effects on the respiratory system and intrathoracic and intra-abdominal pressures, which also are diminished by having an open system.[18] With the redirection of airflow, the patient is no longer using the upper respiratory airway—airflow does not go through the upper airway and glottis (vocal cords). Use of the upper airway and glottis typically allows for control of exhalation and assists with controlling expiratory lung volumes.[19] This loss of pressure may impact gross motor function for mobility and postural stability.

With an open tracheostomy tube and therefore, an open system, thoracic pressures cannot be increased or sustained as airflow passes through the tracheostomy tube and bypasses the upper airway. This difficulty would be observed when a patient needs to crawl, sit, push, or stand up. The typical means of gross motor movement for mobility is to engage the glottis (vocal cords) to restrict the expiratory lung volume to stabilize the chest and upper body.[7,8] Placing a Passy-Muir Valve on the tracheostomy tube closes the system and restores a patient's ability to use the upper airway to control expiratory flow and improve ITP and IAP.

Consider that with infants and young children, a tracheostomy also could limit or diminish gross motor development. During infancy and early development, children are progressing through the stages of head control, trunk control, sitting, reaching, standing, and walking. Without good ITP and ITA, these functions could be significantly impacted and even delayed. A vicious cycle may begin as fine motor skills related to feeding, self-feeding, and other levels of function are directly linked to gross motor development. These delays and limitations can be mitigated by using a Passy-Muir Valve to return the young child to a more normalized use of the upper airway with control of volumes and improved trunk control and postural stability.

Conclusion

Taking into consideration the impacts disease processes and intubation or tracheostomies have on communication and swallowing, early assessments may be a key component to restoring patients' abilities to communicate, eat, and return to more normal function, no matter the age.

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Management Dilemma of Neonatal Opiate Withdrawal Syndrome

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The exposure of drugs to the developing fetal brain and the use of post-birth withdrawal medications in neonatal opiate withdrawal syndrome (NOWS) may have a long-term impact on affected infants.[1] The associated short-term problems on NOWS are shown in Figure 1.

As seen in figure 1, NOWS management is associated with the three following sequelae:

A. NICU admission

Infants are often admitted to the neonatal intensive care unit (NICU) if the admitting hospital does not have the facilities to room both the mother and infant. This leads to decreased mother-infant bonding and changes to the infant's gut flora.[2,3] Infant admission to NICU influences the case mix index (CMI), a health quality and reimbursement benchmark. The CMI is the average relative diagnosis-related group (DRG) weight of a hospital's inpatient discharge, which is calculated by adding the Medicare Severity-Diagnosis Related Group (MS-DRG) weight for each discharge and dividing the total by the number of discharges. Hence CMI reflects the diversity, clinical complexity, and resource needs of the hospital's patients. For administration, a higher CMI indicates a greater complexity and resource-intensive caseload.[4] As NOWS is neither a clinically complex nor high resource requiring DRG, it has a low CMI and subsequently impacts billing.

B. Length of stay

With the strategy of eat-sleep-console (ESC), the length of stay (LOS) for NOWS has decreased.[5] When infants are started on medications, the LOS increases. Hann et al.[6] showed that the cost is more dependent on the LOS than the admission to NICU in NOWS. In their adjusted association model, Hann et al.[6] studied four dyads (maternal treatment-infant pharmacotherapy, maternal treatment-no infant pharmacotherapy, no maternal treatment-infant pharmacotherapy, and no maternal treatment-no infant pharmacotherapy). They found that the dyad with no maternal-assisted therapy (MAT) and no infant pharmacotherapy had the lowest NICU use, while the maternal treatment-no infant pharmacotherapy dyad had the lowest LOS and cost. This highlights the complex relationship between maternal and infant treatment of NOWS, LOS, and associated costs.

C. Medications

The commonly used medications for NOWS are methadone, morphine, and buprenorphine, all with variable pharmacokinetics, pharmacodynamics, and results.[7,8] Performing a placebo trial is complicated by the placebo use, as shown in a recent study where high oral sucrose was used as a placebo that may have affected the Finnegan scoring.[9]

The team taking care of the infants with NOWS has to be aware of these ramifications. We suggest using Appendix A, B, and C for parents, which explain drug dosing and the need for treatment. Appendix B provides them with a timeline and roadmap, while Appendix C explains the components of NAS scoring. Active involvement of parents may alleviate anxiety and stress.

As noted above, NOWS management is multifactorial. More research is needed to find the best approach and guidelines for managing infants with NOWS.

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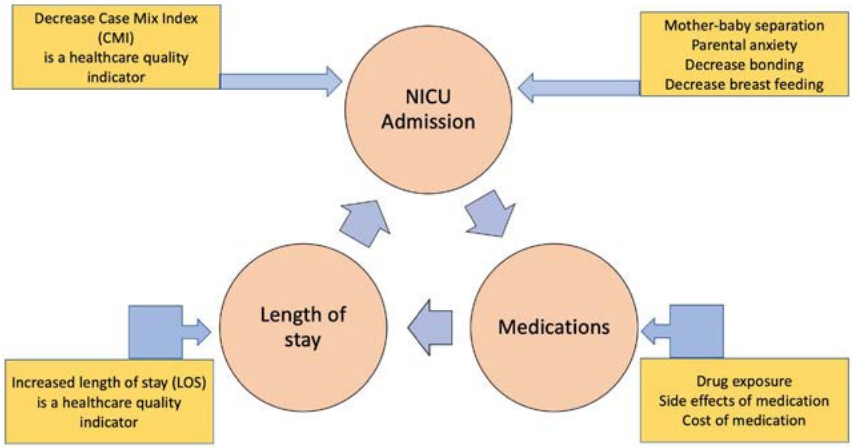
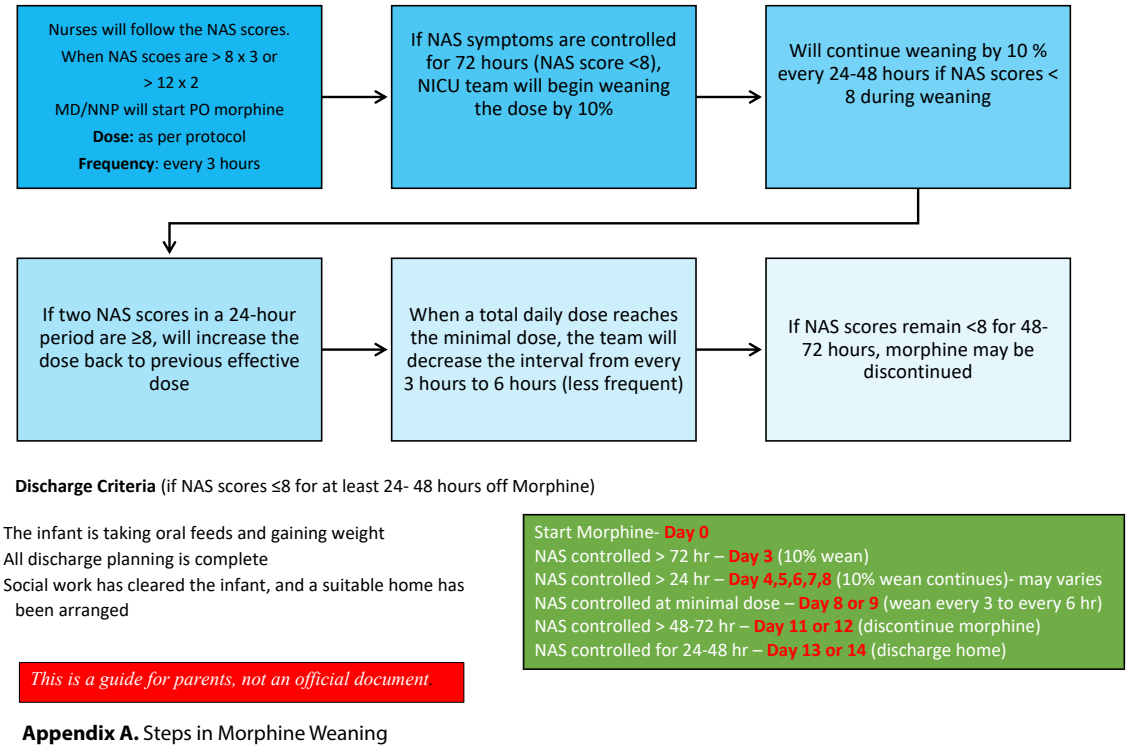


Figure 1



Discharge Criteria (if NAS scores ≤8 for at least 24- 48 hours off Morphine)

- The infant is taking oral feeds and gaining weight
- All discharge planning is complete
- Social work has cleared the infant, and a suitable home has been arranged

Start Morphine- **Day 0**
NAS controlled > 72 hr – **Day 3** (10% wean)
NAS controlled > 24 hr – **Day 4,5,6,7,8** (10% wean continues)- may varies
NAS controlled at minimal dose – **Day 8 or 9** (wean every 3 to every 6 hr)
NAS controlled > 48-72 hr – **Day 11 or 12** (discontinue morphine)
NAS controlled for 24-48 hr – **Day 13 or 14** (discharge home)

This is a guide for parents, not an official document.

Appendix A. Steps in Morphine Weaning

References continued

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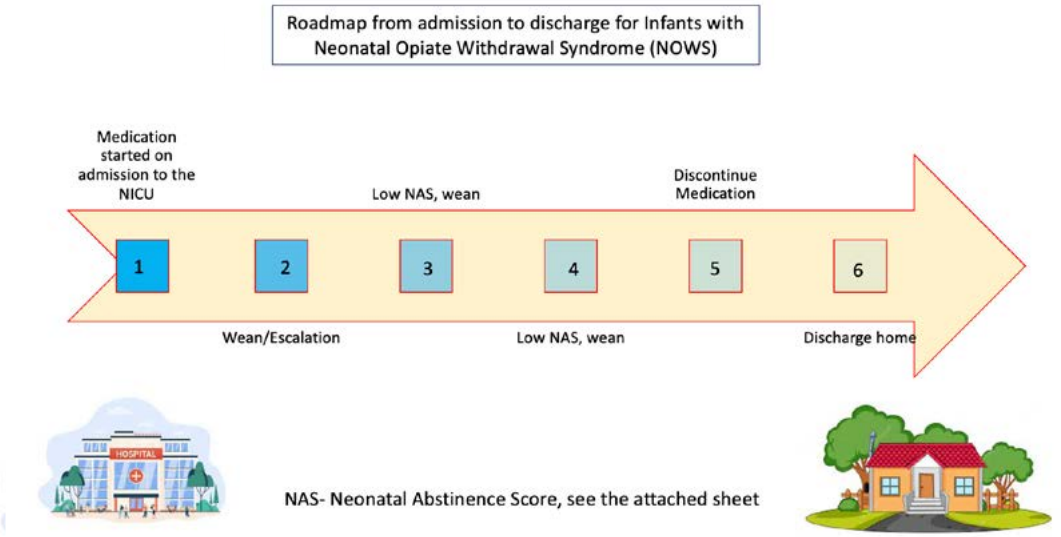

Appendix B

NAS (Neonatal Abstinence Score)

Finnegan Neonatal Abstinence Score			
CNS: Cry			
CNS: Sleep			
CNS: Moro Reflex			
CNS: Tremors Disturbed			
CNS: Tremors Undisturbed			
CNS: Muscle Tone			
CNS: Excoriation			
CNS: Myoclonic Jerks			
CNS: Convulsions			
Sweating			
Fever			
Yawning			
Mottling			
Nasal Stuffiness			
Sneezing			
Nasal Flaring			
Respiratory Rate			
GI Disturbances: Excessive Sucking			
GI Disturbances: Poor Feeding			
GI Disturbances: Regurgitation/Vomit...			
GI Disturbances: Stools			
Finnegan Neonatal Abstinence Score			

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Appendix C

Patent Ductus Arteriosus and Rebound Hyperbilirubinemia in Preterm Infants

Shabih Manzar, MD, MPH

Abstract

Rebound hyperbilirubinemia (RHB) is common in neonates treated with phototherapy (PT). About 11-20% of the neonates were reported to have RHB after being treated with PT. We have noticed that RBH is more common in preterm (PT) infants, possibly due to the immaturity of the liver and kidneys to excrete excess bilirubin. However, some PT infants get a higher RBH than others. Recently, we noticed an interesting observation that might explain why some PT infants get an exaggerated RBH. We observed a different magnitude of RBH among twins with respect to patent ductus arteriosus (PDA). Both infants were born at a gestational age of 26-5/7 weeks. Twin A (no PDA) weighed 545 grams, while twin B (with PDA) weighed 755 grams at birth. Both infants were treated with phototherapy. Both infants had no ABO incompatibility (maternal and infants' blood groups were O-positive). In comparison to their response to phototherapy, we noted that the infant with persistent PDA continues to have high RHB. We postulated that PDA with a left-to-right shunt exposes the lungs to more blood flow and excess bilirubin. Although one case is insufficient to build a cause-and-effect relationship, the observation is novel and needs further confirmation.

Introduction

Rebound hyperbilirubinemia (RHB) is common in neonates treated with phototherapy (PT). So and Khurshid,[1] in a cohort of 305 neonates who received PT, found 20.3% of treated cases with RHB. In another study on late preterm and term infants, 11% of RHB was reported.[2] We have noticed that RBH is more common in preterm (PT) infants, possibly due to the immaturity of the liver and kidneys to excrete excess bilirubin. However, some PT infants get a higher RBH than others. Recently, we noticed an interesting observation that might explain why some PT infants get an exaggerated RBH.

Cases

The twins were born at a gestational age of 26-5/7 weeks. Twin A weighed 545 grams, while twin B weighed 755 grams at birth. Twin A had no patent ductus arteriosus (PDA), while twin B had a moderate PDA. Both infants had high serum bilirubin requiring phototherapy. There was no history of ABO incompatibility (maternal and infants' blood groups were O-positive). We observed a different magnitude of RBH among twins.

In comparison to their response to phototherapy, we noted that the infant with persistent PDA continues to have high RHB. Figure 1 shows the difference. As noted, the bilirubin continued to trend down in the infant with no PDA, while we observed a rebound in serum bilirubin in the infant with persistent PDA.

Discussion

Patent ductus arteriosus (PDA), with a left of a right shunt, steals the blood from the aorta and divert it into the pulmonary system. For premature infants suffering from hyperbilirubinemia, this diversion not only increases the pulmonary blood flow but also provides excess bilirubin exposure to the lung tissues. At the same time, due to the diastolic steal, relatively less blood enters the descending aorta decreasing the renal clearance of bilirubin. Theoretically, these factors could predispose premature infants to a relatively higher serum bilirubin level. Fluctuations in unbound bilirubin levels in PT infants have been reported during ibuprofen therapy for PDA.[3,4] However, the RBH in Twin B was before the use of ibuprofen. No other risk factor for the rebound was noted. It was important to note that soon after the treatment of PDA, the bilirubin trended down in Twin B, supporting the hypothesis as stated earlier.

The postulated mechanism for RHB in PDA with the left to right shunt could be explained by the shunt diverting blood from the aorta to the pulmonary artery. The blood delivering excess bilirubin to the pulmonary vasculature could be deposited in the lung tissue and then released later, causing rebound hyperbilirubinemia (Figure 2). Lung deposition of bilirubin has been shown in postmortem analysis.[5]

In conclusion, we noted a higher magnitude of RHB in the twin infant with PDA, possibly due to the release of deposited bilirubin from the lung tissue. Although one case is insufficient to build a cause-and-effect relationship, the observation is novel and needs further confirmation.

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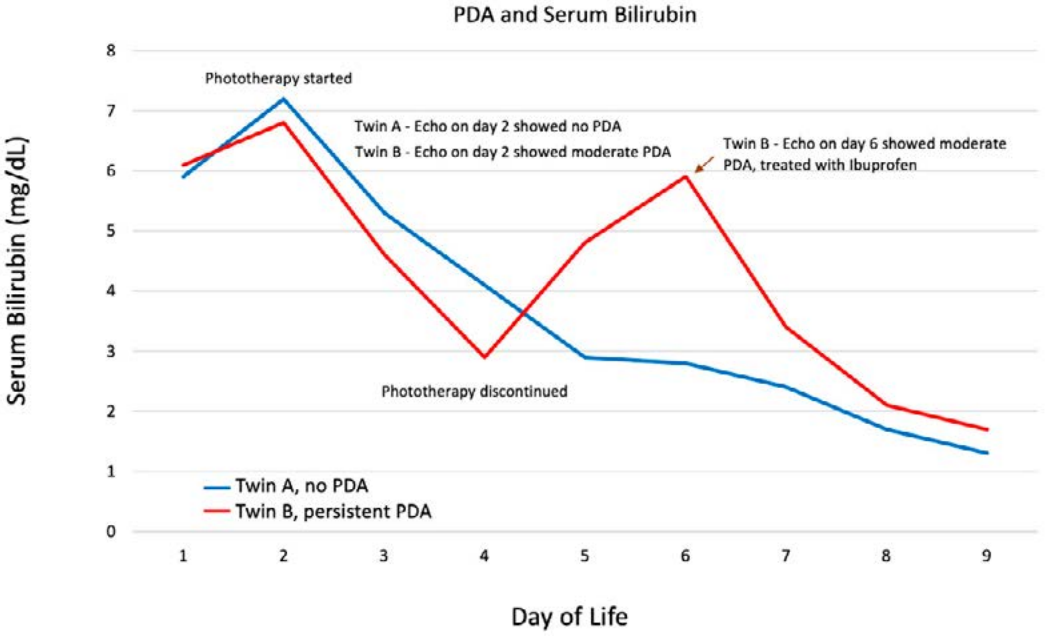

Figure 1. Graph showing the effect of PDA on serum bilirubin. The blue line represents Twin A, who had no PDA on the day two echocardiogram. The red line represents Twin B, who had persistent PDA on day two and day six echocardiograms. The brown arrow indicates starting of the Ibuprofen treatment. PDA–Patent ductus arteriosus, Echo- echocardiogram. Use the 17.1 conversion factor to covert bilirubin in SI units from mg/dL.

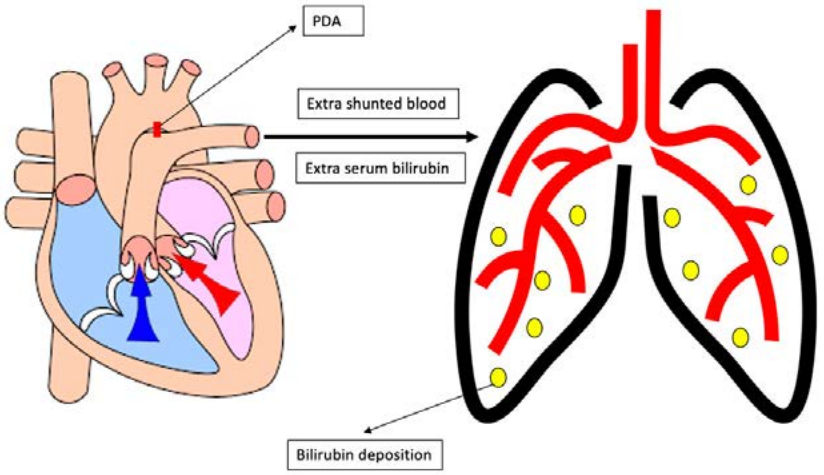

Figure 2. Cartoon showing how a left-to-right shunt through the patent ductus arteriosus (PDA) shunts extra blood into the pulmonary circulation. The blood reaching the lungs deposits bilirubin in the lung tissue (small yellow circles). PDA–thin black arrow. The direction of pulmonary circulation–thick black arrow. The animation is obtained online under creative commons license for free sharing.

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Safeguarding the Health of Vulnerable Patients: The Importance of Donor Human Milk Safety Standards

Sandra E Sullivan, MD, FAAP, IBCLC and Susan Neumann, MBA

Medically fragile infants in the neonatal intensive care unit (NICU) require a safe and reliable donor milk supply. Not all new mothers are able to provide their preterm infants with the volume of breast milk they require. Moreover, to optimize growth, breast milk often requires the addition of a nutritional fortifier. Preterm infants born very low birth weight (VLBW) or extremely low birth weight (ELBW) have been shown to have better outcomes when fed an exclusive human milk diet (EHMD), consisting of breast milk from mom or donors combined with human milk fortifier that is made from 100% donor breast milk.[1,2,3,4,5] The American Academy of Pediatrics (AAP), World Health Organization, and US Department of Health and Human Services all recommend that preterm infants receive donor milk when mother's own milk is not available in sufficient quantities. Thus, achieving optimal outcomes for the most vulnerable patients requires a human milk supply that is reliable and safe enough to be used as food as well as to be processed into fortifier.

Like all human tissue, human milk has the potential to harbor pathogens that can be harmful to vulnerable preterm infants. Without stringent safety protocols, there is always the risk that tainted milk will make it into the NICU. In 2016, an infant born at 29 estimated gestational weeks and with a birth weight of 1405 g died of sepsis following infection with *Cronobacter sakazakii* (*C. sakazakii)* that was likely contracted via the breast pump.[6] This same pathogen was responsible for the death of another preterm infant this year, with the origin of infection again traced to a breast pump.[7] Notably, *C. sakazakii* also is the same bacteria that led to the recent recall of infant formula.[8]

Ensuring a Safe and Reliable Source of Human Milk

To ensure that vulnerable NICU infants receive a safe supply of human milk, donor milk programs need to introduce more stringent safety protocols that include comprehensive screening of donors; thorough protocols for safely collecting, storing, and shipping milk; as well as direct testing of milk (DTOM). While donor milk banks in the United States generally screen donors and pasteurize their milk to reduce the risk of pathogens, there are no universal, national standards for ensuring that donor milk is safe when it reaches the NICU. Given that NICU infants have died from improperly handled human milk in the past, this lack of standardization is another avoidable tragedy waiting to happen.

Prolacta Bioscience makes nutritional fortifiers exclusively from human milk that are designed specifically for fragile NICU infants. Given the known vulnerability of these patients, Prolacta pioneered a model of collection, shipping, processing, and distribution of donor milk and nutritional products made from donor breast milk that is not only safe for donor milk recipients but also for donors and their own infants.

Prolacta donors are screened extensively for health and lifestyle factors, including prescription medication use, that could impact the quality of their milk. They undergo a multitude of tests for infections such as HIV and hepatitis, and they all receive a DNA ID, so that their donated milk can be tracked throughout the collection, processing, and distribution process should a potential problem arise. Prolacta directly tests the milk it receives using a nucleic acid amplification test (NAAT) for multiple pathogens, and adulterants. To ensure a safe milk supply for vulnerable infants, all milk banks should adopt a similar screening and testing protocol.

Ethical Compensation for Donor Milk

In addition to being safe, the supply of donor milk must be consistent and reliable to ensure it meets the needs of infants in NICUs throughout the world. In this light, it is important to recognize the time and effort that donors dedicate to providing safe milk. This includes undergoing a series of screening tests; following explicit and detailed instructions for pumping, storing, and shipping their milk; as well as being open and upfront about life circumstances (such as short-term medications use or getting a tattoo) that may temporarily make milk unsafe to use. Donors must follow milk bank guidelines regarding alcohol consumption. Donors must refrain from smoking, or using marijuana in any form, and from traveling to locations where certain communicable diseases are endemic. Guidelines for pumping and handling human milk earmarked for NICU infants must be more stringent than current Centers for Disease Control and Prevention guidelines designed for term infants who are not as medically fragile.

A survey that Prolacta conducted of its donors revealed that they spend 2-8 hours per day pumping, storing, and shipping milk as well as cleaning their breast pumps. These numbers help explain why Prolacta opts to offer donors compensation

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of $1.10 per ounce. Donors are also given the option to redirect the compensation to charity (Susan G. Komen) if they prefer.

Non-exploitative donor milk compensation can be mutually beneficial for donors and recipients. Ethical milk donor practices must ensure the safety and well-being not only of recipients but also of donors and their infants. Donor compensation can be part of such practice by focusing applicant outreach efforts on moms who have excess milk with documented confirmation from the physicians of each donor and their infant confirming that donation is safe for both.

Giving donors the option of compensation for their time and effort has important benefits, including offering donors the opportunity to make supplementary income at home while caring for and in many cases providing breast milk for their own infants rather than rushing back into the workforce. This is particularly important in the United States, where few mothers have extended paid maternity leave. More than 85% of Prolacta applicants, all of whom are based in the United States, indicate that they plan to provide breast milk to their own infants for 12 or more months, suggesting that compensation allows them to provide breast milk for their own infants longer. In comparison, 35.9% of U.S. children were fed breast milk for 12 months.[9] Compensation also encourages donors to donate for a longer time, which is important because qualifying and educating new donors on extensive safety precautions is expensive and time-consuming.

Donor compensation not only acknowledges donors' time and lifestyle changes required to be a donor, it also helps to offset the considerable costs of being a milk donor. Yale researchers recently estimated that breastfeeding a child in the United States costs more than $11,000 per year if one takes into account pumping supplies, increased nutritional intake for the donor, AAP-recommended vitamin D supplementation, and opportunity cost.[10]

Prolacta donor applicants are educated (72% graduated from a technical school, have a college degree, or an advanced degree) and well-informed on how their breast milk is being used to help infants in need. These moms make the decision to donate their breast milk because they want to, not out of dire need. Many have infants who received Prolacta's nutritional products in the NICU, and about 35% requalify to donate for longer than the initial 6 month qualification period. Donors are educated about safe pumping, storage, and shipping. Prolacta also provides donors with access to a dedicated team of certified lactation education counselors for support.

If we fail to secure a reliable human milk supply for vulnerable infants, NICUs will have to default to non-human milk-based nutrition, which is associated with life-threatening complications such as necrotizing enterocolitis.[11] If we fail to ensure that the donor milk supply is safe, these same infants risk serious harm from pathogens, drug metabolites, or adulterants. The time to protect these fragile infants is now, not after another tragedy occurs. Ensuring a safe and reliable human milk supply includes an extensive screening of donors, safe milk handling practices, and DTOM that goes far beyond the current national standard. Given the time and effort required for donors to meet these high safety standards, offering compensation is a reasonable and ethical way to recognize their contribution to the well-being of their own infants and fragile infants in NICUs throughout the world.

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The Effect of Inhaling Mother's Breast Milk Odor on the Behavioral Responses to Pain Caused by Hepatitis B Vaccine in Preterm Infants: a Randomized Clinical Trial

Zahra Akbarian Rad, Parvin Aziznejadroshan, Adeleh Saebi Amiri, Hemmat Gholinia Ahangar and Zahra Valizadehchari

Abstract

Background: Nowadays, it is generally assumed that non-pharmacologic pain relief in preterm infants is an important measure to consider. Research findings suggest that familiar odors have soothing effects for neonates. The aim of this study was to compare the effect of maternal breast milk odor (MBMO) with that of another mother's breast milk odor (BMO) on the behavioral responses to pain caused by hepatitis B (HB) vaccine injection in preterm infants.

Methods: This single-blind randomized clinical trial was performed over the period between February 2019 and March 2020 in the neonatal intensive care unit of Babol Rouhani Hospital, Iran. Ninety preterm infants, who were supposed to receive their HB vaccine, were randomly assigned into three groups: MBMO (A), another mother's BMO (B), and control with distilled water(C). Oxygen saturation (SaO2), blood pressure (BP) and heart rate (HR) were recorded for all participants through electronic monitoring. In addition, premature infant pain profiles (PIPP) were determined through video recording for all three groups during intervention. The chi-square, ANOVA and ANCOVA were used for analyzing the data, and $P < 0.05$ was considered significant in this study.

Results: No significant differences were found between the three groups in mean ± SD of HR, BP, and Sao2 before the intervention ($P > 0.05$). After the intervention, however, the means for heart rate in groups A, B, and C were 146 ± 14.3, 153 ± 17.5 and 155 ± 17.7, respectively ($P = 0.012$). Moreover, the means for PIPP scores in groups A, B and C were 6.6 ± 1.3, 10 ± 2, and 11.4 ± 1.9, respectively ($P < 0.001$). There was no significant difference found between groups in their means of SaO2, systolic and diastolic blood pressure after the intervention ($P > 0.05$).

Conclusions: The results indicate that stimulation with MBMO is effective in reducing pain in preterm infants; therefore, it can be postulated that this technique can be considered in less invasive procedures such as needling.

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Background

Many innovative measures to relieve pain in preterm infants are considered by various neonatal intensive care units (NICU) worldwide.[1,2] It is assumed that neonatal pain in preterm infants can adversely affect their development in such multiple domains as nociceptive changes, altered brain development, stress systems, and functional abilities. Prolonged exposure to pain has also been associated with impaired brain development while preterm infants are in the NICU.[3] Pain assessment methods are currently performed through physiological (heart rate and respiratory rate) and behavioral criteria (crying time, changes in facial expression and limb movements).[4]

The premature infant pain profile (PIPP) is a set of measurable behavioral and physiological responses such as facial expression changes (squeezing eyes, raising eyebrows, wrinkling nasolabial groove) as well as changes in heart rate, SaO2, intrauterine age, and behavioral status of the infants, which are all definite reasons demonstrating pain in premature infants.[5]

There is a strong tendency to use nonpharmacological interventions, as simple and secure techniques, for relieving pains in infants. Several methods have already been applied to relieve pain based on five senses.[5] Among them, the sense of smell is fully developed at birth[6] which can affect the neonate's emotional relationship with his/her mother.[7] Familiar odors, maternal odor for instance, supposedly have soothing effects on newborn infants. It is widely known that infants have the ability to detect their mother's breast odor even without experiencing breastfeeding at birth.[8] The breast milk odor (BMO) can enhance infants' sucking through the facial and trigeminal motor nerves in the brain, which, in turn, stabilizes the physiological state in infants.[9] In some cases, research findings has demonstrated that breastfeeding in human newborn infants can completely eliminates pain responses, and animal models have also depicted that the pain modulating effect of breastfeeding is likely mediated by opioid and non-opioid mechanisms.[10] Some studies have shown that Some other studies have also shown that fetal-maternal odors (mother's breast milk, body and amniotic fluid odors) can decrease stress responses including crying and motor activities in infants, especially those separated from breast milk or the ones under painful interventions.[11] In a relevant study, it was suggested that the maternal breast milk odor (MBMO) had a soothing effect on preterm infants, and that their pain score was

lower than that of those exposed to formula odor.[12] Nevertheless, the results of Küçük Alemdar et al. (2017) demonstrated that the BMO made no statistically significant difference in the physiological and behavioral responses of MBMO group compared to other groups (amniotic fluid odor, maternal body odor and control groups).[13]

Given all the contradictory results on the effect of MBMO and another mother's BMO on preterm infants and the importance of pain relief for preterm infants, this study strove to investigate the effect of inhaling human milk on the behavioral responses of pain caused by HB vaccine in preterm infants.

Methods

Study design and setting

This single-blind randomized clinical trial was done from February 2019 to March 2020 in a NICU of academic center (Rouhani Hospital, Babol, Iran).

Participant

Preterm infants 28-37 weeks of gestation, who have to be vaccinated for hepatitis B — zero turn the vaccine — were randomly assigned to three groups. The inclusion criteria were infants with no painful procedure and no feeding for up to 1 h before the intervention, stability in vital signs, no head and skull abnormalities as well as no receiving painkillers, sedatives and anticonvulsants. The exclusion criteria were maternal withdrawal from the study and infant sever disease or death.

Groups characteristic

After obtaining written consent from the parents, each of the eligible subjects was assigned a number. The numbers were written on paper and tossed into the box, and the desired number was taken out of the box by drawing lots based on the assigned rank. Statistics specialist generated the random allocation sequence, one of the researchers enrolled participants, and assigned infants to three groups: MBMO (A), another mother's BMO (B) and control with distilled water (C). This study followed the CONSORT guidelines for reporting randomized controlled trials (Fig. 1).

Sample size

Considering 80% power and 0.05 error probability in this study, the number of cases was determined to be at least 30 neonates in each group.[2]

Data collection and processing

According to the ward's schedule during the first 4 days of life, injection of HB vaccine was done. Preterm neonate was placed on a warmer by servo control and skin temperature 36.5-37 °C in quiet room. All conditions including room temperature (25 °C), light, injection device were the same for all three groups as well as the vaccine administration was done by one person. The researcher and nurse did not use any aromatic substances in vaccination room during the study. The probe of monitoring was placed on the right wrist of baby without applying additional pressure. Heart rate, blood pressure and SaO2 of all preterm infants were recorded before starting the intervention as the initial time and immediately after completing vaccination (using the standard pulse oximeter and ECG monitoring of Saadat Company, Iran).

In both groups of A and B, the breast milk samples taken in the early morning before eating breakfast were used to stimulate the smell sense of neonates. Pouring 2 ml of maternal breast milk and another mother's breast milk on a cotton swab was done as an intervention, and 2 ml of distilled water as control group (group C). Next, these swabs were placed three centimeters away from the baby's nose. This process started 3 min before vaccination and continued until the vaccination was completed.[2]

Pain measurement

The Premature Infant Pain Profile (PIPP) was used as the primary outcome variable. PIPP scores were recorded immediately before and after the vaccination for each infant. The PIPP is a behavioral measure of pain for premature infants. It includes seven indicators: 1) gestational age, 2) the behavioral state, 3) change in heart rate, 4) change in oxygen saturation, 5) brow bulge; 6) eyes squeeze and 7) nasolabial furrow. The total score is the summation of all seven indicators, with a minimum of 0 and maximum of 21; the higher the score, the greater the

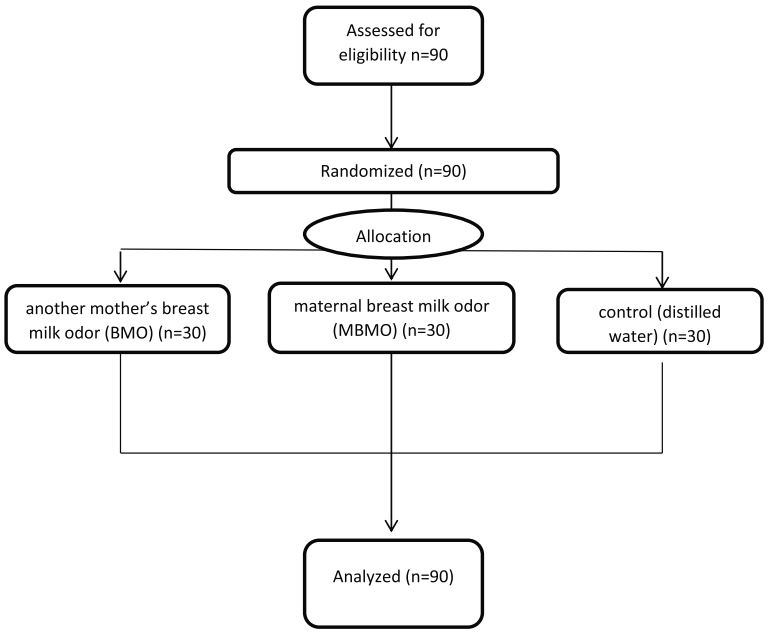

Fig. 1 study flowchart: allocation to study groups

pain behavior.[14] If the overall PIPP score is between 0 and 6 points, the pain level is mild; if between 7 and 12 points, it is moderate; and if between 13 and 21 points, it is severe.[15]

The PIPP tool was revised and validated for use with preterm babies born at 26-37 weeks of gestation by Gibbins et al. in 2014.[16]

Video recording of behavioral responses was taken from the beginning to the end of the process by a trained nurse, and then PIPP scoring was performed through watching video by the first author. The scoring was done while the video viewer was unaware of the test group. Throughout the intervention, any actions on the neonates such as contact, movement and so on were avoided.

Data were collected by using the demographic questionnaire including: birth weight, current disease (respiratory distress syndrome, transient tachypnea of newborn, sepsis and very low birth weight), sex, gestational age, postnatal age, Apgar score and PIPP score.

Data analysis

Statistics advisor performed the data analysis blindly by using SPSS Version 18. Descriptive information was shown as frequency, percentage, mean and standard deviation. Chi-square test for the relationship between two qualitative variables (demographic and PIPP qualitative variables with group variable), ANOVA test for comparing quantitative variables at the levels of more than two variables (quantitative demographic variables with group variable) and ANCOVA test for comparing research outcomes (SBP, DBP, SaO2 and heart rate) were used to remove the pretest effect and a P value< 0.05 were considered significant.

Ethical consideration

The study protocol was approved by the Ethics Committees of Babol University of Medical Sciences (IR.MUBABOL.REC.1397.253). The trial is registered in the IRCT20190220042771N1 Before participation in the study, written informed consent was obtained from each child's primary guardian.

Results

Study subjects

ALL 90 preterm infants, who included, were completed the study. The infants of the three groups were not significantly different in terms of sex, age, infant's current disease (Spsis, Respiratory Distress Syndrome (RDS), Transient Tachypnea of Newborn (TTN), very low birth weight (VLBW), gestational age, weight and APGAR score ($p > 0.05$) (Table 1).

Table 2 shows variables including SBP, DBP, SaO2 and heart rate before and after the intervention by using ANCOVA test.

As shown in Table 2, by eliminating the effect of the pretest variable and use of ANCOVA test, there is no significant difference between the means± SD of SBP ($p = 0.482$), DBP ($p = 0.341$) and SaO2 ($p = 0.193$) in terms of group membership. ANCOVA test showed that change in heart rate was significantly lower in group A ($p = 0.012$) (Table 2).

PIPP score

The mean ± SD of pain score in group A was 6.6 ± 1.3, and 10 ± 2 and 11.4 ± 1.9 in groups B and C, respectively. The ANOVA test showed that there is a significant difference between groups ($P < 0.001$), and the results of post-hoc Tukey's test determined that this difference was between group A with groups B and C (Fig. 2).

Discussion

This study showed that MBMO greatly affected heart rate as well as behavioral responses to pain scoring in preterm infants compared with another mother's BMO and the control groups, but there were no significant differences found between the three groups in terms of SBP, DBP and SaO2.

Zhang et al. (2018) conducted a systematic review study to investigate the analgesic effects of BMO on infants. Their results demonstrated that there was a change in the heart rate of infants

Table 1 Comparison of demographic variables of preterm infants in three groups

Groups Variable	MBMO(A)	Another mother BMO(B)	Control(C)	*P* value
Sex n(%)				0.562[a]
Male	15 (50)	16 (53.3)	12 (40)	
Female	15 (50)	14 (46.7)	18 (60)	
Infant's age (hour) n(%)				0.112[a]
24–48	16 (53.3)	12 (40)	20 (66.7)	
48–96	14(46.7)	18 (60)	10 (33.3)	
Infant's disease n(%)				0.943[a]
RDS, Sepsis	3 (10)	4 (13.3)	3 (10)	
VLBW	22 (73.3)	23 (67.7)	23 (67.7)	
TTN	5 (16.7)	3 (10)	4 (13.4)	
Infant's gestational age (WK) (Mean ± SD)	32.9 ± 2.4	31.5 ± 2.1	32.5 ± 2.4	0.074[b]
Infant's weight (g) (Mean ± SD)	1806 ± 553	1620 ± 425	1688 ± 404	0.294[b]
Infant'sApgar score(Mean ± SD)	7.8 ± 1	7.6 ± 1.3	8.3 ± 0.9	0.071[b]

[a]chi^2, [b]ANOVA

Table 2 Mean and standard deviation scores of SBP, DBP, SaO2 and heart rate in the studied groups pre and post intervention

Groups	MBMO(A)		Another mother's BMO(B)		Control(C)		*P* value[a]
Variables	Pre intervention	Post intervention	Pre intervention	Post intervention	Pre intervention	Post intervention	
SBP (mm Hg)	69.3 ± 9.4	70.9 ± 8.2	69.5 ± 7.6	70.2 ± 6	69.7 ± 9	71.7 ± 9	0.482
DBP (mm Hg)	40.6 ± 9.8	43.6 ± 0.5	40.8 ± 9.9	41.7 ± 7.1	40.9 ± 7.9	44 ± 10.7	0.341
SaO2 (%)	97 ± 2.7	95.2 ± 5.2	97.1 ± 3.7	94 ± 6.2	96.4 ± 3.2	91.1 ± 11.7	0.193
Heart rate	139 ± 16.1	146 ± 14.3	141 ± 15.6	153 ± 15.5	139 ± 17.8	155 ± 17.7	0.012

[a]ANCOVA test

and that SaO2 pain scores were lower in MBMO group during and after blood sampling compared with those of the control group.[17] It is worth noting that their result is consistent with the findings of the current study, except for SaO2. The stimulation with MBMO had a soothing effect on the behavioral responses to pain and reduced infant's pain in our study.

In another relevant study, Sajjadi et al. (2016) reported that the mean scores of PIPP had a significant effect on MBMO group compared to control group.[2] Nonetheless, a significant difference was found in the heart rate as well as SaO2 after the intervention. Their results are in line with those of the present study, except for change in SaO2. Likewise, Küçük Alemdar et al. (2017) conducted a study through which they investigated the effect of mother's BMO, amniotic fluid odor, and body odor on the physiological and behavioral responses to heel stick pain in preterm infants and found no statistically significant difference between groups in terms of physiological and behavioral responses to pain such as heart rate, duration of crying and pain scale. Although the SaO2 was slightly different in the amniotic fluid odor group,[13] as it can be seen, this finding is vividly inconsistent with the results of the present study. One possible reason for this discrepancy is the difference between both studies in terms of methodology and intervention process. In their study, 5 cc of the mother's breast milk was poured on a sponge and placed five centimeters away from the neonate's nose for fifteen minutes before and after the intervention, while the cotton swab had been placed three centimeters away from the infant's nose in our study. This process started 3 min before vaccination in the current study and continued until the vaccination was completed. Attempts were also made to minimize the effect of accustoming to the sense of smell in our study. Aziznejad et al. (2013) evaluated the physiological indicators and concluded that there was a statistically significant difference in the respiratory rate only between the intervention group with sucrose and the other groups immediately after the intervention, but there was no significant difference between the four groups in other variables (duration of crying, heart rate and SaO2).[18]

In three above-mentioned studies (Zhang, Sajjadi and Küçük Alemdar) which were different with our study in terms of methodology, there were no significant changes found in SaO2 between the intervention group and the control group. Moreover, in a similar study by Aziznejad et al. (2013), which was performed under the same condition, there were no differences in SaO2, either. One possible reason could be the difference in the equipment used.

Conclusion

On the basis of this research, the MBMO can be used as a familiar smell to manage the preterm infant's pain before performing any needling procedures such as vaccination.

Limitations

Due to the limited amount of equipment, the use of special probes for infants during the study was provided by several companies. The differences in the sensitivity of these probes may have caused the SaO2 changes not to be accurately determined.

Abbreviations

ANOVA: Analysis of Variance; MBMO: Maternal Breast Milk

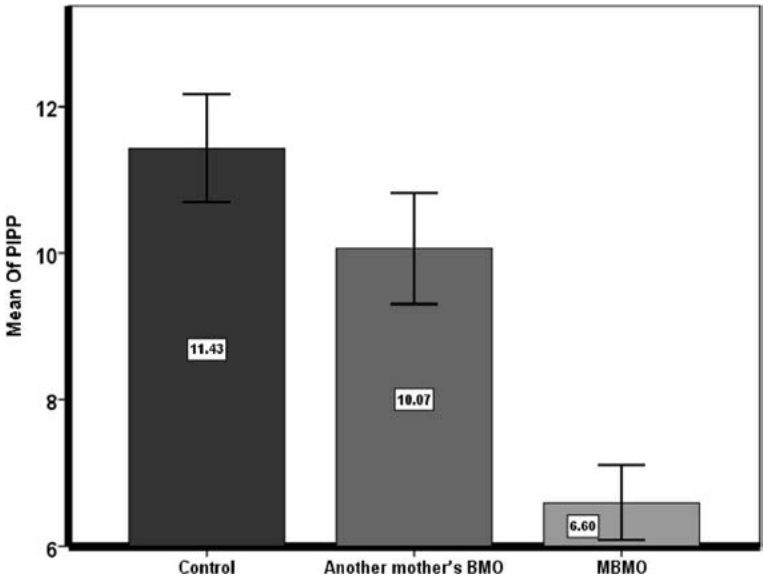

Fig. 2 The PIPP score's changes in three groups (Note: the same letters indicate no significant difference at level 5%)

Odor; BMO: Another Mother's Breast Milk Odor; HBV: Hepatitis B Vaccine; HR: Heart Rate; NICU: Neonatal Intensive Care Unit; PIPP: Premature Infant Pain Profile; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; SaO2: Arterial Oxygen Saturation; RDS: Respiratory Distress Syndrome; VLBW: Very low birth weight; TTN: Transient Tachypnea of Newborn; ANCOVA: Analysis of Covariance; chi^2: Chi-square; APGAR: Appearance, Pulse, Grimace, Activity, Respiration

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Authors' contributions

ASA studied the conception/design, carried out the analysis, interpreted the data, and helped drafting the manuscript. PA, the first supervisor of the study, studied the conception/design, analyzed the data, helped drafting the manuscript, did the critical revisions for important intellectual content, provided administrative/ technical/ material support, and did the final revision. ZAR critically revised the proposal, did the analysis, interpreted the data, and designed the article. The shares of the first and the third authors was equal. HGA performed the data analysis, and ZV contributed in the data collection. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets analyzed in the current study are not publicly available due to an agreement with the participants upon the confidentiality of the data, but they are available from the corresponding author upon request.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committees of the Babol University of Medical Sciences (IR.MUBABOL.REC.1397.253). The trial is registered in the Iranian Registry of Clinical Trial (IRCT20190220042771N1). Before participation in the study, written informed consent was obtained from each child's primary guardian.

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less than 50 mmHg—with the ability to select patient-specific thresholds at the bedside. The IVCO2 Index provides care teams an additional safety net to detect deterioration in patients with conditions that require tight control of PaCO2 or when V/Q mismatch can hamper the management of PaCO2. The IVCO2 Index, along with Etiometry's other risk indices, indicate the probability a patient will experience a harmful physiologic state and can also be embedded into the Etiometry Platform's growing list of automated clinical pathways to improve length of stay and decrease ventilation time.

Neonatal Bilirubin Meters Need Better Accuracy

Despite their convenience and low cost, handheld point-of-care (POC) devices lack precision for measuring neonatal bilirubin and need refinement in order to tailor jaundice management in newborns, a systematic review and meta-analysis reports in JAMA Pediatrics. Lauren E.H. Westenberg, MD, of the division of neonatology at Erasmus MC Sophia Children's Hospital in Rotterdam, the Netherlands, and colleagues reported that POC meters tended to underestimate neonatal bilirubin levels, compared with conventional laboratory-based quantification. Furthermore, pooled estimates from 10 studies found these devices to be too imprecise overall, with substantial outer-confidence bounds. On the plus side, Dr Westenberg's group said POC bilirubin testing was as much as 60 times faster than lab measurement, and used 40-60 times less blood. "Conventional laboratory-based bilirubin quantification usually requires up to 500 mcL, but sometimes even 1,500 mcL, while POC tests require up to 50 mcL, which means less stress for the baby," Dr Westenberg said in an interview. "Especially when infants are cared for at home, it usually takes a few hours between deciding to quantify bilirubin and obtaining the test result. Meanwhile, bilirubin levels may rise unnoticed." On the positive side, POC devices are useful where laboratories in low-resource areas may be remote, poorly equipped, and not always able to provide an accurate bilirubin level. "As a result, the diagnosis of jaundice relies mainly on visual inspection, which is known to be unreliable," she said. POC devices, however, need near-perfect conditions for optimal use, and results can be affected by humidity, preanalytic conditions such as test strip saturation, and hematocrit. Yet results from these devices have recently proven to have acceptable accuracy, resulting, for example, in the same clinical decisions as the reference standard in 90.7% of times according to a 2022 study in a hospital in Malawi. Nevertheless, the authors concluded that the devices' imprecision limits their widespread use in neonatal jaundice management, especially when accurate lab-based bilirubin quantification is available. Results from these POC tests should be interpreted with caution, Dr Westenberg said. In terms of clinical decision-making, POC devices entail a risk of missing neonates with jaundice who need phototherapy or, in the case of overestimation, of starting phototherapy too early.

Human and Nonhuman Milk Products Have Similar Effect on Preemies' Gut Microbiota

No significant differences emerged in gut microbial diversity in preterm infants who exclusively received human milk products, compared with those receiving bovine milk formula or fortifiers, a randomized controlled trial found. Nor were any differences noted in the secondary endpoint of clinical outcomes in the UK study, published online in JAMA Network Open. The finding was unanticipated, according to lead author Nicholas D. Embleton, MBBS, MD, a professor of neonatal medicine at Newcastle University in England. "Over the last 10 years we've focused particularly on the role of the microbiome to better understand causal mechanisms of necrotizing enterocolitis, or NEC," he said in an interview. "We anticipated that an exclusive human milk diet would have measurable impacts on microbiome diversity as a potential mechanism [in] disease modulation as part of the mechanism by which exclusive human milk diets benefit preterm infants." Shortfalls in a mother's own milk supply often necessitate the use of bovine formula or pasteurized human milk from donor milk banks or commercial suppliers. The effect of an exclusive human milk diet versus one containing bovine products on vulnerable preterm infants is unclear, but some studies have shown lower rates of key neonatal morbidities, possibly mediated by the gut microbiome. In two randomized controlled trials, for example, one showed a lower rate of NEC with donated human milk while the other showed no difference. Neither, however, was powered to detect a clinically important difference in surgical NEC.

Infinant Health, Inc Announces "Clean Label Project" and "First 1,000 Day Promise" Certifications for Evivo

Infinant Health, Inc, a company focused on improving infant health through the gut microbiome, announced that it received the "Clean Label Project" and "First 1,000 Day Promise" certifications from the Clean Label Project on its flagship product, Evivo, an infant probiotic. Infinant's Evivo is used by parents at home as well as in healthcare environments, including with the most vulnerable infant populations in the NICU. The Clean Label Project is a national non-profit committed to transparent food and consumer product labeling. Their awards are given to products that emphasize purity and surpass FDA regulations. Product awards are designated based on safety and require rigorous product sampling and testing. The Clean Label Project's First 1,000 Day Promise standard uses elements of European food regulations to set thresholds products for pregnant women, infants, lactating mothers, and children. Infinant Health's mission is to change the trajectory of human health, one baby at a time, through a deep understanding of infant nutrition and the gut microbiome. The company offers Evivo, an infant probiotic containing B. infantis EVC001, a proprietary strain that helps infants develop a healthy microbiome. B. infantis EVC001 has unique features that work with human milk to reduce potential harmful bacteria and support healthy immune system function. Potentially harmful bacteria are linked to inflammation and this inflammation may be associated with prevalent childhood issues such as allergies and type 1 diabetes. Evivo is a food for special dietary use, meeting all FDA regulations for food products, and has been used by hospitals, providers and parents for five years with over 4 million feedings to date in over 60,000 babies. "Infinant Health is committed to creating high-quality nutritional products," said Anthony Franco, Chief Operating Officer for Infinant Health. "We maintain best-in-class standards for product testing, manufacturing, packaging and distribution. These certifications are a testament to our commitment to quality and leadership in infant health. At Infinant Health, we focus on a continuous improvement process to perfect our product – that starts by creating and following the highest standards in quality. The Clean Label certifications reflect this commitment." Infinant Health uses third-party testing to ensure viability and purity. Each manufacturing batch of Evivo includes a Certificate of Conformance, and all packaging is BPA free and protects Evivo from moisture, light and oxygen. "Much of the narrative we've been hearing lately about baby food safety is limited to cereals,

fruits, and veggies. In addition to the food marketed towards children and toddlers, the focus should include pregnant women, newborns, infants, and lactating mothers," said Jaclyn Bowen, executive director at Clean Label Project. "As a mother and public health practitioner, it's exciting to see brands like Infinant Health, voluntarily choosing to think of food safety differently and setting even stricter specifications than regulations require when it comes to ingredient quality and safety." These efforts are in line with the FDA Closer to Zero initiative aimed to make food safer for babies and young children. Infinant Health supports the FDA's commitment to setting regulations to minimize chemical contaminants.

Babies' Movement in the Womb Means Something

The random movements that babies make while in the womb help boost their sensorimotor movement that will aid them after birth, according to researchers at the University of Tokyo.

What to know: The hundreds of neurons that control each muscle are synchronized in a fetus to create strong contractions that stimulate its activity. Random movements of babies in the womb help their development and boost the growth of their sensorimotor system, which supports everything from language development, cognitive growth, and hand– eye coordination to problem solving skills and social interaction. Infants develop their own sensorimotor system based on explorational behavior or curiosity, so they are not just repeating the same action but a variety of actions implying a linkage between early spontaneous movements and spontaneous neuronal activity.

Newborns and infants can acquire coordination skills through spontaneous whole-body movements without an explicit purpose or task, showing more common patterns and sequential movements, with an increase in coordinated whole-body and anticipatory movements as they grow older.
Understanding how the sensorimotor system develops starting in vitro could lead to understanding and treating a wide range of neurodegenerative disorders such as multiple sclerosis, spinal cord injuries, motor neuron disease, and even cerebral palsy.

Moms' and Babies' Medical Data Predicts Prematurity Complications, Stanford Medicine-led Study Shows

By sifting through electronic health records of moms and babies using a machine-learning algorithm, scientists can predict how at-risk newborns will fare in their first two months of life. The new method allows physicians to classify, at or before birth, which infants are likely to develop complications of prematurity. A study describing the method, developed at the Stanford School of Medicine, was published online in Science Translational Medicine. "This is a new way of thinking about preterm birth, placing the focus on individual health factors of the newborns rather than looking only at how early they are born," said senior study author Nima Aghaeepour, PhD, an associate professor of anesthesiology, perioperative and pain medicine and of pediatrics. The study's lead authors are postdoctoral scholar Davide De Francesco, PhD, and Jonathan Reiss, MD, an instructor in pediatrics. Traditionally defined as birth occurring at least three weeks early, premature birth is linked to complications in babies' lungs, brains, vision, hearing and digestive system. Although earlier births generally carry higher risks, the timing of birth predicts only approximately how a specific infant will fare. Some infants who are born quite early develop no complications, while others born at the same stage of pregnancy become very ill or die. "Preterm birth is the single largest cause of death in children under age 5 worldwide, and we haven't had good solutions," Aghaeepour said. "By focusing our research on predicting the health of these babies, we can optimize their care." Many complications of prematurity take days or weeks after birth to emerge, causing substantial damage to newborns' health in the meantime. Knowing which infants are at risk could enable preventive measures. "We look mainly at the baby to make treatment decisions in neonatology, but we are finding that we can get valuable information from the maternal health record, really homing in on how individual babies' trajectories have been shaped by exposure to their specific maternal environment," said study coauthor David Stevenson, MD, a neonatologist at Lucile Packard Children's Hospital Stanford, professor of pediatrics and director of the March of Dimes Prematurity Research Center at the Stanford School of Medicine. "This is a move toward precision medicine for babies," he added.

Maternal COVID-19 Vaccine Curbs Infant Infection from Delta Variant

Maternal vaccination with two doses of the mRNA COVID-19 vaccine was 95% effective against infant infection from the delta variant, and 45% effective against infant infection from the omicron variant, a new study shows. Previous research has confirmed that COVID-19 neutralizing antibodies following maternal vaccination or maternal COVID-19 infection are present in umbilical cord blood, breast milk, and infant serum specimens, wrote Sarah C.J. Jorgensen, MD, of the University of Toronto, and colleagues in their article published in The BMJ. In the study, the researchers identified maternal and newborn pairs using administrative databases from Canada. The study population included 8,809 infants aged younger than 6 months who were born between May 7, 2021, and March 31, 2022, and who underwent testing for COVID-19 between May 7, 2021, and September 5, 2022. Maternal vaccination with the primary COVID-19 mRNA monovalent vaccine series was defined as two vaccine doses administered up to 14 days before delivery, with at least one of the doses after the conception date. Maternal vaccination with the primary series plus one booster was defined as three doses administered up to 14 days before delivery, with at least one of these doses after the conception date. The primary outcome was the presence of delta or omicron COVID-19 infection or hospital admission of the infants. The study population included 99 COVID-19 cases with the delta variant (with 4,365 controls) and 1,501 cases with the omicron variant (with 4,847 controls). Overall, the vaccine effectiveness of maternal doses was 95% against delta infection and 45% against omicron. The effectiveness against hospital admission in cases of delta and omicron variants were 97% and 53%, respectively. The effectiveness of three doses was 73% against omicron infant infection and 80% against omicron-related infant hospitalization. Data were not available for the effectiveness of three doses against the delta variant. The effectiveness of two doses of vaccine against infant omicron infection was highest when mothers received the second dose during the third trimester of pregnancy, compared with during the first trimester or second trimester (53% vs. 47% and 53% vs. 37%, respectively). Vaccine effectiveness with two doses against infant infection from omicron was highest in the first 8 weeks of life (57%), then decreased to 40% among infants after 16 weeks of age.

Hope for Catching Infants with CP Early

A new prognostic tool may help identify infants with cerebral palsy (CP) earlier, allowing them to receive therapies to improve later outcomes. Researchers from Canada used 12 clinical

variables to predict the condition. The tool accurately predicted 75% of CP cases. The study was published January 17 in JAMA Pediatrics. The prevalence of CP in the US is two to three children per 1000, a rate that has been relatively unchanged for decades. Although recent innovations in diagnosis using motor scores and MRI scans have aided in diagnosis, these techniques have historically been reserved only for infants who were cared for in neonatal intensive care units, were born prematurely, or who had other neurologic risk factors, such as birth defects. The tool identified 2.4 times more children with CP than would have been detected using current diagnostic methods, according to the researchers. "We developed the prediction tool to try to make these findings accessible to any healthcare provider, which will hopefully help break down the long-held perception that CP is usually related to prematurity or a difficult delivery," said Mary Dunbar, MD, an author of the study. "We know that about half of children with CP aren't premature and didn't have a particularly difficult birth."

The bedside tool weighs factors such as the use by mothers of illicit drugs and tobacco; the presence of diabetes and preeclampsia during pregnancy; whether the infant is male; birth weight; and the number of miscarriages the mother had prior to the birth. The tool also factors in results from a test that measures how well the infant is adjusting to life outside the womb. Dunbar and her colleagues compared 1265 infants with CP from the Canadian Cerebral Palsy Registry from 2003 to 2019 to a control group of 1985 children without CP from the Alberta Pregnancy Outcomes and Nutrition longitudinal study. The study authors hope that the prognostic tool can be integrated into existing newborn screenings and completed by nurses or physicians as part of routine care. "Its cost is low especially in comparison to MRI and specialized neurological assessments," said Sarah Taylor, MD, section chief of neonatal-perinatal medicine at Yale New Haven Children's Hospital in Connecticut. Health systems and doctors may be more apt to adopt the tool, since it does not require specialized equipment or training, Taylor added.

State Quality Initiative Can Reduce Postpartum Hemorrhage and Maternal Morbidity

A statewide quality initiative can improve severe maternal morbidity (SMM) and reduce the incidence of maternal morbidity and mortality from postpartum hemorrhage (PPH), a modeling analysis found. Such measures could potentially provide savings to birthing hospitals, according to the California cost-effectiveness study, published in Obstetrics & Gynecology. A team led by Eric C. Wiesehan, MHA, MBA, a PhD candidate in health policy at Stanford (Calif.) University, examined the effects of the safety initiative of the California Maternal Quality Care Collaborative (CMQCC) in a theoretical cohort of 480,000 births across a mix of hospital settings and sizes. The CMQCC developed a PPH toolkit and quality-improvement protocol to increase recognition, measurement, and timely response to PPH. Drawing retrospectively on a large 2017 California implementation study, the simulation estimated that collaborative implementation of the CMQCC added 182 quality-adjusted life-years (0.000379 per birth) by averting 913 cases of SMM, 28 emergency hysterectomies, and one maternal mortality. Additionally, it saved $9 million ($17.78 per birth) owing to avoided SMM costs. According to the Centers for Disease Control and Prevention, pregnancy-related maternal deaths in the United States have increased from 7.2 per 100,000 live births to 16.9 per 100,000 live births over the past 20 years, making it the only country in the Organization for Economic Cooperation and Development with rising rates of maternal mortality. PPH accounts for 11% of maternal deaths. As to the study's broader applicability, Dr. Wiesehan said in an interview, "findings of effectiveness in terms of reducing PPH-related SMM are well known outside of California. In terms of costs, however, it is more of an unknown how much is generalizable. It would go a long way if another state quality care collaborative implementing such a project recorded costs prospectively. Prospective costing, particularly microcosting, would be optimal to precisely place where the most, or least, value of this quality improvement project is achieved."

NICU Use Up, Birth Weights Down in Babies of Mothers with HCV

Infants born to women infected with the hepatitis C virus (HCV) faced twice the risk of stays in the neonatal ICU (NICU) and 2.7 times the risk of low birth weight, a new analysis finds, even when researchers adjusted their data to control for injectable drug use and maternal medical comorbidity. Clinicians should be "aware that the infants of pregnant people with HCV may have a high rate of need for higher-level pediatric care," said Brenna L. Hughes, MD, MSc, chief of maternal fetal medicine at Duke University Medical Center, Durham, N.C. She spoke in an interview about the findings, which were presented at the meeting sponsored by the Society for Maternal-Fetal Medicine. As Dr Hughes noted, "HCV remains a serious problem in pregnancy because it often goes undiagnosed and/or untreated prior to pregnancy. It can be passed to infants, and this can cause significant health-related outcomes for children as they age." For the multicenter US study, researchers identified 249 pregnant mothers with HCV from a 2012-2018 cohort and matched them by gestational age to controls (n = 486). The average age was 28; 71.1% of the cases were non-Hispanic White versus 41.6% of the controls; 8.4% of cases were non-Hispanic Black versus 32.1% of controls ($P < .001$ for race/ethnicity analysis); and 73% of cases were smokers versus 18% of controls ($P < .001$). More than 19% of cases reported injectable drug use during pregnancy versus 0.2% of controls ($P < .001$). The researchers adjusted their findings for maternal age, body mass index, injectable drug use, and maternal comorbidity. An earlier analysis of the study data found that 6% of pregnant women with HCV passed it on to their infants, especially those with high levels of virus in their systems. For the new study, researchers focused on various outcomes to test the assumption that "adverse pregnancy outcomes associated with HCV are related to prematurity or to ongoing use of injection drugs," Hughes said. There was no increase in rates of preterm birth or adverse maternal outcomes in the HCV cases. However, infants born to women with HCV were more likely than the controls to require a stay in the NICU (45% vs. 19%; adjusted relative risk, 1.99; 95% confidence interval, 1.54-2.58). They were also more likely to have lower birth weights (small for gestational age < 5th percentile) (10.6% vs. 3.1%; ARR, 2.72; 95% CI, 1.38-5.34). No difference in outcomes was seen when HCV cases with viremia (33%) were excluded. "The most surprising finding was that the need for higher-level pediatric care was so high even though there wasn't an increased risk of prematurity," Hughes said.

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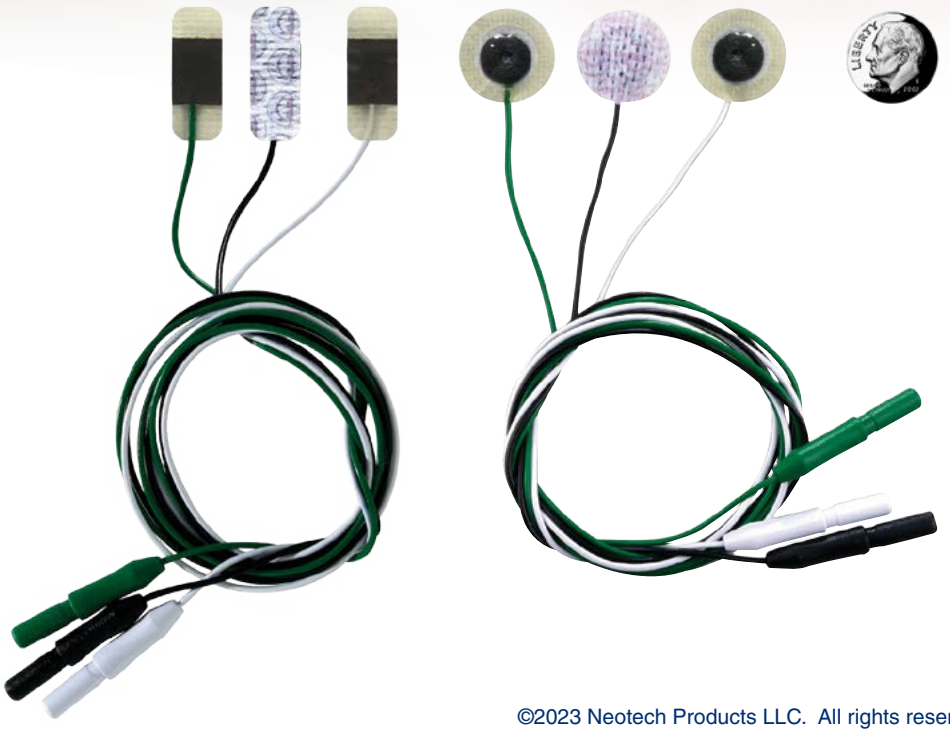

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