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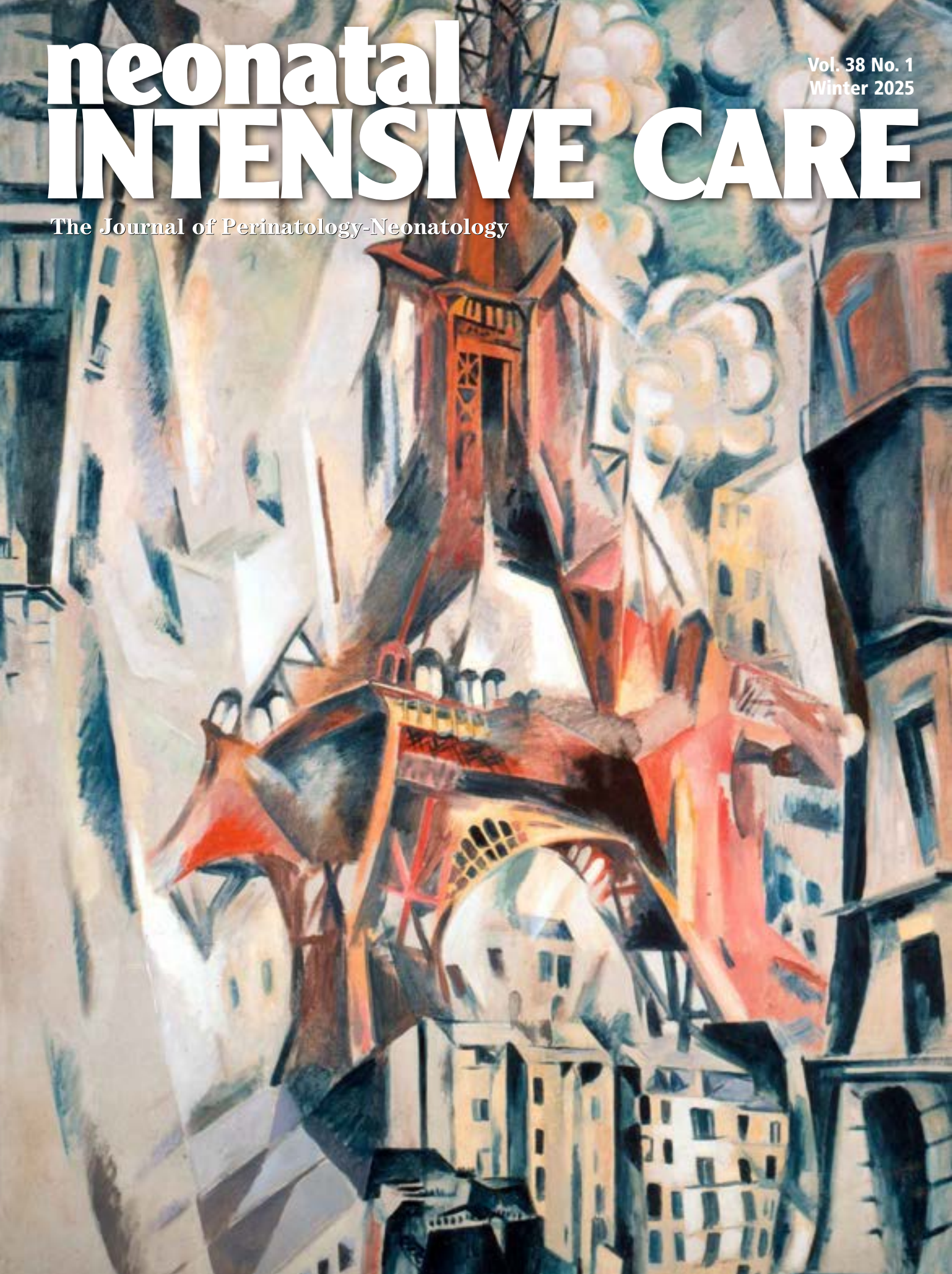

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Vol. 38 No. 1
Winter 2025

Table of Contents

DEPARTMENTS

Editorial Advisory Board

News

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RSV Vaccine Research in Infants May Proceed With Caution

Research and development of a respiratory syncytial virus (RSV) vaccine for infants should continue, but with awareness of documented safety concerns, according to the Vaccines and Related Biological Products Advisory Committee (VRBPAC) of the US Food and Drug Administration (FDA). The VRBPAC met on December 12 to review and discuss safety findings for mRNA-1365 and mRNA-1365, which have been in development for infant immunization against RSV. No vaccines for RSV are currently approved in the United States for individuals aged ≤ 17 years, but RSV disease is associated with approximately 100-300 deaths, 58,000-80,000 hospitalizations, approximately 520,000 emergency department visits, and approximately 2,100,000 outpatient visits each year, according to the FDA briefing document for the meeting. The monoclonal antibody nirsevimab, though not a vaccine, is approved by the FDA for the prevention of RSV lower respiratory tract disease in newborns and infants born during or entering their first RSV season and in children aged ≤ 24 months who are at risk for severe RSV disease in their second RSV season, according to the document. Safety and immunogenicity data from ongoing studies in adults and RSV-seropositive children aged 12 months through 59 months supported vaccine studies in younger children. However, in July 2024, manufacturer Moderna halted its study because of concerns about severe side effects in a subset of infants aged 5-8 months. In this population, 12.5% of infants who received an mRNA vaccine developed clinically significant/severe RSV compared with 5% of placebo patients. Matthew Snape, MBBS, MD, a pediatrician and vice-president of pediatric and maternal vaccines for Moderna, presented clinical data from the study. As of October 2024, a total of five cases of severe RSV had been reported in the subset of infants aged 5-7 months vs one case in the placebo group. Although the company has no current plan to continue an RSV vaccine program in children aged ≤ 2 years, "safety and immunogenicity surveillance will continue in this study," Snape said in his presentation. The company's understanding of the clinical and immunological picture will evolve with the collection of more data, he said.

Preterm Birth Shows Complex Pattern of Cardiovascular Outcomes

Adults aged 50 years who were born preterm have a higher risk for hypertension but lower risk for cardiovascular events than those born at term, with similar risks for diabetes, prediabetes, and dyslipidemia between groups. The researchers conducted a prospective cohort study of the Auckland Steroid Trial — the first randomized trial of antenatal corticosteroids (betamethasone) for women who were at risk for preterm birth, conducted in Auckland, New Zealand, between December 1969 and February 1974. They analyzed 470 participants, including 424 survivors recruited between January 2020 and May 2022 and 46 participants who died after infancy. The outcomes for 326 participants born preterm (mean age, 49.4 years) and 144 participants born at term (mean age, 49.2 years) were assessed using either a questionnaire, administrative datasets, or both. The primary outcome was a composite of cardiovascular events or risk factors, defined as a history of a major adverse cardiovascular event or the presence of at least one cardiovascular risk factor, including diabetes mellitus, prediabetes, treated dyslipidemia, and treated hypertension. The secondary outcomes included respiratory, mental health, educational, and other health outcomes, as well as components of the primary outcomes. The composite

Continued on page 7…

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Draeger

Revolutionizing Neonatal Care with the Dräger Babyroo® TN300 AutoBreath Resuscitator

In Support of the Latest NRP Guidelines

With approximately 10% of newborns requiring some assistance to begin breathing at birth,[1] labor & delivery (L&D) teams are faced with resuscitating babies in hectic situations where they risk under- or overinflation of fragile lungs.

Access to a user-friendly and precise respiratory support tool at the moment of birth and beyond is critical to reducing the number of respiratory complications that impact poor long-term outcomes and preventable deaths.

The Dräger Babyroo® TN300 configurable open care warmer, featuring AutoBreath, automatically delivers the desired levels of fractional concentration of inspired oxygen (FiO2), flow, peak inspiratory pressure (PIP), and positive end-expiratory pressure (PEEP) in precise intervals at an I:E ratio of 1:2. Think T-Piece with an automated rate!

Focus on your patient while AutoBreath delivers set pressures at your set rate

AutoBreath keeps a consistent respiratory rate and shows the applied inflation pressure on the Dräger Babyroo® TN300 Resuscitation Module. This optional feature frees the clinicians' hands to seal and secure the face mask and thus helps to stabilize ventilation. This is especially helpful in high-stress situations or during intra-hospital transfers when babies need further respiratory support after initial stabilization.

Versatile AutoBreath resuscitation circuit

The AutoBreath breathing circuit can be used to provide both automatic and non-automatic (T-piece) resuscitation. This capability allows for a seamless transition to automatic resuscitation without having to change the circuit.

How AutoBreath works

AutoBreath, a gas-powered resuscitator for operator-attended airway management of neonates and infants, consists of a pneumatic oscillator and an adjustable PEEP feature, which allows the operator to control the baseline.

The ventilation cycle of the AutoBreath infant resuscitator consists of an inspiratory and expiratory phase:

Inspiratory phase

- The exhaust port of the expiratory valve is blocked by the operation of the circuit and fresh gas from the Resuscitation Module is forced into the patient's lungs. As the lungs fill, the pressure in the patient airway and fresh gas supply line increases.
- Once this pressure reaches the pressure setting of the adjustable pressure relief valve in the Resuscitation Module, the additional fresh gas flow is relieved by the pressure relief valve and the flow of fresh gas into the baby's lungs ceases.

Expiratory phase

- Expiration begins when the expiratory valve pressure drops to the set PEEP, which is set by the user on the AutoBreath module. During the expiratory phase, gas from the baby's lungs — as well as any gas flow from the resuscitator — vents to the atmosphere.

Conclusion

The Dräger Babyroo® TN300 with AutoBreath provides clinical teams with a user-friendly, reliable, and efficient respiratory support tool for neonatal resuscitation. By automating precise delivery of key respiratory parameters, AutoBreath helps clinicians adhere to resuscitation guidelines, supporting effective respiratory care for babies from the moment of birth and through critical transitions.

1 Wyllie J, Perlman JM, et al. , Neonatal Resuscitation Chapter Collaborators Part 11: neonatal resuscitation: 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Resuscitation. 2010;81 Suppl 1:e260–e287.

News…continued from page 5

of cardiovascular events or risk factors occurred in 34.5% of participants born preterm and 29.9% of participants born at term, with no differences in the risk factor components. The risk for cardiovascular events was lower in participants born preterm than in those born at term (adjusted relative risk [aRR], 0.33; $P = .013$). The participants born preterm had a higher risk for high blood pressure (aRR, 1.74; $P = .007$) and the composite of treated hypertension or self-reported diagnosis of high blood pressure (aRR, 1.63; $P = .010$) than those born at term. From randomization to the 50-year follow-up, death from any cause was more common in those born preterm than in those born at term (aRR, 2.29; $P < .0001$), whereas the diagnosis or treatment of a mental health disorder was less common ($P = .007$); no differences were observed between the groups for other outcomes. "Those aware of being born preterm also may be more likely to seek preventive treatments, potentially resulting in a reduced risk of cardiovascular disease but a greater prevalence of risk factors if defined by a treatment such as treated dyslipidemia or treated hypertension," the authors wrote. "In this cohort, the survival advantage of the term-born control group abated after infancy, with a higher all-cause mortality rate compared with that of the group born preterm," wrote Jonathan S. Litt, MD, MPH, ScD, and Henning Tiemeier, MD, PhD, in a related commentary.

Nirsevimab Resistance Mutations Rare in RSV, Study Shows

Nirsevimab (Beyfortus), an antibody targeting respiratory syncytial virus (RSV), is indicated for newborns and infants to prevent bronchiolitis. Available since September 2023, its widespread use may lead to resistance mutations. However, according to the French POLYRES study on prospective monitoring of nirsevimab, published recently in *The Lancet Infectious Diseases*, these mutations are very rare at this stage. "The low prevalence of nirsevimab resistance mutations in treated patients is reassuring. However, escape mutations have been observed in a few RSV-Bs from treated patients, prompting caution and highlighting the importance of active molecular surveillance in the context of future wider global use of nirsevimab," commented Slim Fourati, MD, PhD, head of the Virology Unit at Henri Mondor Hospital, Paris-Est University and INSERM U955, Paris, France, and lead author, in a press release. The 2023-2024 season marked the first preventive immunization campaign against RSV with nirsevimab, which has shown a positive impact on preventing bronchiolitis in infants. Nirsevimab targets a specific epitope on the F fusion protein located on the surface of RSV that is involved in viral replication, thereby blocking the virus. Because RSV is a variable virus, there is a theoretical risk of emerging variants with resistance mutations to nirsevimab, even without antibody-driven selection pressure. During phase 2b/3 clinical trials, only 48 RSV cases of infected children treated with nirsevimab were analyzed, with escape mutations identified in two cases. Nirsevimab is now available to all infants, and the risk for resistance mutations could increase with the generalized preventive use of the drug. This concern led to the POLYRES study, which aimed to evaluate the risk for virological resistance to nirsevimab on a larger sample via a large-scale, real-world observational multicenter study conducted during the 2023-2024 winter season. "This study is the largest surveillance study of nirsevimab virological failures to date. It was made possible thanks to collaborative synergy

Continued on page 16…

Surfactant Combined With Budesonide: A Review of the Evidence

Chris Russian, PhD, RRT, RRT-NPS and Joshua Gonzales, DHSc, RRT-NPS, RRT-SDS

Historical Context of Surfactant

Surfactant treatment has been a major advancement in neonatal care, particularly for infants suffering from respiratory distress syndrome (RDS), a condition that results from immature lungs that lack sufficient natural surfactant.[1] The understanding of pulmonary surfactant grew over time, even before it was identified as a crucial part of lung structure. Early observations included the concepts of surface tension and the behavior of insoluble films on water surfaces.[2] Surface tension, which played a crucial role in the development of pulmonary physiology, evolved over centuries.[2] The scientific investigation began with foundational work on capillary action by scientists such as Boyle, Jurin, Young, and Laplace, whose studies laid the groundwork for later insights into how surface tension operates in the alveoli of the lungs.[2] These early investigations were mathematical and physical explorations but were necessary to our understanding of pulmonary surfactant.[2] More recent research has expanded our knowledge on various aspects such as the functions, morphology, chemical composition, metabolism, regulation, fetal development, and therapeutic applications of surfactant.[2] A breakthrough came in 1957 when Dr. Clements published a key paper on lung extracts, showing that surfactant could reduce surface tension to extremely low levels. Although initially overlooked, this discovery later gained recognition, especially when Mary Ellen Avery and Jere Mead linked surfactant deficiency to RDS in premature infants, marking a pivotal moment in neonatology.[2]

In the 1960s, experiments to treat RDS with synthetic or animal-derived surfactants often failed due to insufficient knowledge about surfactant composition and the technical challenges of delivering the therapy.[2] However, by the 1970s and 1980s, researchers such as Enhorning and Robertson showed that instilling surfactant into the lungs of premature animals significantly improved lung function.[2] This success culminated in clinical breakthroughs, such as Fujiwara's 1980 study, which demonstrated the benefits of surfactant replacement therapy in human infants with RDS.[3] By 1990, surfactant therapy was approved by the FDA and became standard practice for treating preterm infants with RDS.[1]

Surfactant Mechanism

Surfactant treatment works by lowering the opening pressure required to inflate the lungs, which is especially high in surfactant-deficient preterm infants. By decreasing surface tension, surfactant increases lung volume and improves gas exchange. This effect is demonstrated by a shift in the pressure-volume curve, with surfactant-treated lungs showing better inflation and deflation stability.[1] Surfactant also stabilizes alveoli of varying sizes, preventing the collapse of smaller alveoli due to high surface tension (as predicted by Laplace's law).[1] The surfactant used in clinical settings has been developed to mimic the properties of natural surfactant, which reduces surface tension in the alveoli, preventing collapse and aiding in lung expansion.[1] Surfactant is primarily composed of phospholipids (80-85%), neutral lipids (5-10%), and surfactant proteins (5-10%).[4] The main phospholipid, dipalmitoylphosphatidylcholine (DPPC), is crucial for lowering surface tension. Surfactant proteins (SP-A, SP-B, SP-C, SP-D) are vital to enhancing the surface-active properties of surfactant, surfactant homeostasis, and host defense.[4] Genetic disorders affecting surfactant metabolism, such as deficiencies in SP-B and SP-C, can result in serious respiratory issues in infants.[3]

The dynamic effects of surfactant treatment on lung function are profound. It quickly increases functional residual capacity (FRC) and lung compliance, which reduces the need for high ventilator pressures.[1] Combining surfactant with positive end-expiratory pressure (PEEP) further improves lung volume and compliance, especially in animal models.[1] Surfactant also improves oxygenation rapidly, with significant effects visible within minutes of administration. However, proper ventilator management is crucial to avoid lung overdistension and other complications.

Surfactant Administration

There are two main strategies: early prophylactic surfactant administration and later rescue treatment after a diagnosis of RDS. Both strategies reduced death and improved outcomes. However, the timing of surfactant treatment is an important consideration.[1] Early administration, ideally within the first minutes to hours after birth, has been shown to prevent severe RDS and reduce complications. However, waiting until RDS is fully diagnosed before administering surfactant may delay its benefits.[5] Some infants require multiple doses, especially in cases where surfactant function is inhibited by proteins or other factors within the lung. Re-treatment is common and necessary in about 20% of infants.[1]

Surfactant is typically administered via endotracheal intubation or through a thin catheter, and various techniques have been

The authors are with the Texas State University, Department of Respiratory Care.

developed to ensure optimal distribution in the lungs.[1] While most infants respond well to treatment, some complications, such as bradycardia, cyanosis, and, more seriously, pulmonary hemorrhage, have been noted.[1] Pulmonary hemorrhage, though rare, is the most significant complication and is associated with elevated pulmonary vascular pressures.[1]

Surfactant treatment has also been integrated with noninvasive ventilation techniques, such as continuous positive airway pressure (CPAP), to reduce the need for mechanical ventilation and further protect preterm infants' lungs from injury. Today there is widespread use of surfactant replacement in preterm infants and new developments of synthetic surfactants that mimic natural lung proteins. Despite the advancements, challenges remain, particularly in reducing the incidence of chronic lung diseases like bronchopulmonary dysplasia in RDS survivors.[2]

Neonatal Lung Disease and Steroid Use

Prematurity is the leading cause of neonatal mortality and morbidity worldwide, with infants born extremely preterm (before 28 weeks' gestation) being at the highest risk.[6] Thanks to modern intensive care, most premature infants survive into infancy, but a large number will develop bronchopulmonary dysplasia (BPD), a chronic lung disease.[6] BPD, first described by Northway in 1967, is associated with increased infant mortality, frequent hospitalizations due to respiratory illnesses, and adverse neurodevelopmental outcomes.[7] BPD is clinically diagnosed if an infant requires supplemental oxygen and/or respiratory support at either 28 days postnatal age or 36 weeks postmenstrual age (PMA) in a preterm neonate (<32 weeks gestational age [GA]) with radiographic evidence of parenchymal lung disease.[7] Over time, there is evidence of worsening lung function in children with BPD, and they are at risk of developing early chronic obstructive pulmonary disease as adults.[6] It is most common in extremely preterm infants who need prolonged mechanical ventilation and oxygen therapy for respiratory distress syndrome (RDS), a condition linked to surfactant deficiency.[6] Despite advances such as surfactant therapy, which has been available since the 1990s and is effective for treating RDS, BPD rates have remained static. Consequently, preventing BPD remains a major research priority.[6]

Budesonide, a glucocorticoid known for its anti-inflammatory properties, has gained recognition for its effectiveness in preventing and treating bronchopulmonary dysplasia (BPD) in premature infants.[8] By targeting inflammation, budesonide helps facilitate better lung function and reduces the risk of complications associated with RDS.[8] Systemic corticosteroids are effective in treating BPD by reducing inflammation, which is a key factor in the disease's development.[6] However, their use in preterm infants, especially at higher doses in the first week after birth, is associated with significant risks.[6] Short-term adverse effects include hyperglycemia, sepsis, hypertension, cardiomyopathy, gastrointestinal hemorrhage, intestinal perforation, and reduced growth.[6] Long-term effects can include additional neurodevelopmental delays.[6] Prenatal corticosteroids, which are commonly administered to mothers at risk of premature delivery, have a synergistic effect with postnatal surfactant treatment.[1] Corticosteroids accelerate lung maturation and improve the infant's response to surfactant therapy.[1] Together, these treatments significantly improve lung compliance, reduce pulmonary edema, and enhance survival outcomes for preterm infants.[1]

Inhaled corticosteroids have not proven to be an effective solution for reducing BPD in extremely preterm infants.[6] Early trials failed to show significant benefits, likely due to challenges in delivering the medication effectively to the distal airways.[6] The NEUROSIS trial indicated that administering inhaled budesonide from the first day of life to infants born before 28 weeks of gestation would decrease the incidence of BPD at 36 weeks postmenstrual age (27.8% vs 38.0%, p=0.004).[9] However, this potential benefit was overshadowed by a nonsignificant increase in mortality (16.9% vs. 13.6%, p=0.17).[9] Although the reduced incidence in BDS is encouraging, the increased mortality in the BPD group is likely to give some clinicians pause when considering inhaled budesonide to preterm infants.

Intratracheal budesonide combined with surfactant shows promise as a treatment for respiratory distress syndrome (RDS) and for preventing bronchopulmonary dysplasia (BPD) in preterm infants.[6] Budesonide, a long-acting anti-inflammatory agent, binds strongly to glucocorticoid receptors and is more effective than other corticosteroids at reducing inflammation with fewer systemic side effects.[6] When administered intratracheally, budesonide forms lipophilic esters in lung tissue that release slowly, extending its anti-inflammatory effects for up to a week.[6] This method minimizes systemic absorption, with less than 10% entering the bloodstream, and it is rapidly metabolized, limiting side effects.[6] Importantly, studies have shown no detection of budesonide in the brain, ensuring its safety.[6]

Surfactant-Vehicled Budesonide Use

Surfactant-vehicled budesonide is an innovative approach used primarily in neonatal care, particularly for preterm infants at risk of developing BPD. This method involves mixing budesonide with surfactant for simultaneous administration. Budesonide helps reduce lung inflammation and the surfactant reduces surface tension and improves lung function. Surfactant helps deliver budesonide to the deeper parts of the lungs, enhancing its distribution and anti-inflammatory effects without compromising the surfactant's performance.

Below we discuss the available clinical trials and the encouraging results from these studies, such as increased survival rates, reduced incidence of BPD, and improved respiratory function in preterm infants. Much of the research has been conducted outside the US. While these studies are promising, more research is needed to confirm the long-term benefits and to influence clinical practice, as current trials have not definitively proven the therapy's effectiveness for routine use.[6]

Kuo et al[10] reported on a follow-up study of preterm infants who received budesonide combined with surfactant as a treatment to prevent chronic lung disease (CLD) in preterm infants. The original study, conducted from 2004 to 2006, involved infants with severe respiratory distress syndrome (RDS) requiring mechanical ventilation, where the treated group received budesonide with surfactant, while the control group received only surfactant. The follow-up study, conducted 2 to 3 years after the original intervention, found that infants who received the combination treatment had better pulmonary outcomes, with no significant long-term adverse effects compared to the control group. The authors concluded that early intratracheal instillation of budesonide using surfactant as a vehicle improves pulmonary outcomes without causing long-term adverse effects, making it

a potentially valuable treatment for preventing CLD in preterm infants.[10]

Yi et al[11] conducted a meta-analysis that included 10 studies, ranging from 2016 to 2021, and involving 1177 infants, 580 in the treatment group and 597 in the control group. Eight of the studies followed an instillation strategy while the other two studies used an atomizer to aerosolize the therapy. All studies compared surfactant combined with budesonide versus surfactant alone. The authors reported that surfactant combined with budesonide demonstrated a reduction in mechanical ventilation time (OR = −1.72, 95% CI: −2.44 to −1.01, p<0.00001), a reduction in hospital length of stay (OR = −5.17, 95% CI: −9.35 to −0.99, p=0.02), and a reduction in the incidence of BPD (OR = 0.52, 95% CI: 0.39–0.68, p<0.00001). The authors stated there were no significant differences in mortality, retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), or sepsis between the experimental and control groups. The authors also discussed the differences in administration methods, noting that intratracheal instillation was more effective than aerosol inhalation for reducing mechanical ventilation duration but not for reducing the length of stay.[11]

Following the systematic review by Yi et al in 2022, there have been additional investigations into the use of surfactant combined with budesonide for premature infants. McEvoy et al[12] investigated the optimal dose for budesonide (0.025, 0.05, 0.10 mg/kg) combined with surfactant. Although the primary outcome (predefined clinical respiratory criteria and a 50% suppression of IL-8) was not met, a reduction in respiratory severity score by 50% was achieved using the lowest budesonide dose. The authors hypothesized that a lower dose of budesonide, below the previously used 0.25 mg/kg, would be equally effective in reducing the need for respiratory support and decreasing the inflammatory response associated with BPD in extremely low gestational age neonates (ELGANs).[12]

Safa et al[13] investigated the effectiveness of combined surfactant and budesonide, versus surfactant alone, in treating RDS in preterm neonates. The authors sought to assess the ability of this combination therapy to reduce the incidence of bronchopulmonary dysplasia (BPD), apnea, and other complications in preterm infants born between 800 and 1500 grams. The study included 70 preterm neonates, randomly divided into two groups: one receiving surfactant alone, and the other receiving combination therapy. The risk of developing BPD was seven times higher in the monotherapy control group compared to the combination therapy experimental group (p=0.004). The experimental group also experienced a significant reduction in the hospitalization period and the incidence of ROP (p=0.02). While no statistically significant difference was observed in the occurrence of intraventricular hemorrhage (IVH) or the need for reintubation, the experimental group had fewer instances of repeat surfactant administration and required shorter durations of continuous positive airway pressure (CPAP) (p=0.02). The authors concluded that the surfactant/budesonide combination was more effective in preventing BPD and reducing the need for respiratory support than surfactant alone, with minimal additional complications.[13]

Gharehbaghi et al[14] evaluated the efficacy of combining budesonide with surfactant, administered intratracheally, in preventing BPD in preterm infants with RDS. The study investigated combination therapy to the administration of surfactant alone, aiming to determine whether the addition of budesonide could reduce the incidence of BPD and other complications in preterm neonates. The study included 128 preterm neonates (gestational age < 30 weeks, birth weight < 1500 g), randomly assigned to two groups: one receiving surfactant alone and the other receiving a combination of surfactant and budesonide. The authors reported the incidence of BPD was significantly lower in the group receiving the surfactant-budesonide combination (37.5%) compared to the surfactant-only group (59.4%) (p=0.040). The duration of mechanical ventilation days (2.8 vs 0.8, p=0.006), continuous positive airway pressure (CPAP) days (5.21 vs 4.0, p=0.04), and high-flow nasal cannula (HFNC) days (7.7 vs 4.1, p=0.001) were significantly shorter in the combination therapy group. Infants in the combination group had shorter hospital stays (median of 20 days) compared to the surfactant-only group (median of 30 days) (p=0.050). There were no significant differences between the two groups in terms of complications such as sepsis, patent ductus arteriosus (PDA), ROP, or necrotizing enterocolitis (NEC). The authors concluded that combining budesonide with surfactant reduced the incidence of BPD and shortened the need for respiratory support without adding significant complications.[14]

Most recently, Marzban et al[15] compared the effects of combining intratracheal budesonide with surfactant versus using surfactant alone in reducing BPD and mortality rates among preterm infants with respiratory distress syndrome RDS. The researchers used a single-blind, randomized controlled trial to determine whether this combination therapy could improve outcomes in premature infants at high risk of BPD. The overall analysis did not show a statistically significant difference between the groups in terms of BPD and mortality rates. However, the group receiving surfactant and budesonide had a lower number of cases of BPD (9 vs. 10) and mortality (10 vs. 19) compared to the surfactant-only group. Although both previous metrics were not statistically significant, the authors conducted subgroup analysis on birth weight and gestational age to assess how these factors influenced the primary and secondary outcomes of the study. Birth weight categories were under 1500 grams, 1500–2000 grams, and 2000–2500 grams, while gestational age was categorized as under 30 weeks, 30–34 weeks, and 34–37 weeks. Gestational age had a greater influence on mortality than birth weight. Infants under 30 weeks who received surfactant and budesonide had significantly fewer deaths (5 vs.17; p=0.014) compared to those who received surfactant alone. The combined therapy also reduced the occurrence of pulmonary hemorrhage (3 vs. 16; p=0.003). Weight less than 1500 g (9 vs. 35; p=0.001), gestational age less than 30 weeks (5 vs. 23; p=0.001), and 30-34 weeks (5 vs. 23; p=0.001) all demonstrated a less frequent need for a second dose of surfactant. There was no significant difference in the incidence of bronchopulmonary dysplasia (BPD) across subgroups. Infants under 30 weeks and weighing less than 1500 grams showed better outcomes with the combination therapy, particularly in terms of oxygen index, mean blood pressure, and mean arterial pressure (p<0.05). However, no significant differences were observed in other complications, such as intraventricular hemorrhage (IVH) or pneumothorax.[15]

Conclusion

In conclusion, the combination of surfactant and budesonide represents a promising therapeutic approach for treating respiratory distress syndrome (RDS) in preterm infants. The available clinical trials, while not universally definitive, suggest significant potential in reducing both the incidence of

bronchopulmonary dysplasia (BPD) and mortality, particularly among extremely preterm infants born before 30 weeks gestation. The ability of budesonide to target lung inflammation, combined with the surface tension-reducing properties of surfactant, offers a synergistic effect that enhances respiratory outcomes without substantially increasing complications. However, further research is needed to solidify the long-term benefits and to fine-tune dosage and administration methods to ensure both efficacy and safety. This evolving treatment strategy has the potential to become a standard intervention in neonatal care for high-risk preterm infants, but ongoing studies are crucial to confirm its role in broader clinical practice.

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Practical Use of Transcutaneous CO_2 Monitoring in the NICU

This article is based on the content of a webinar hosted by Anne M. Geistkemper, MSc, RRT, RRT-NPS, neonatal-pediatric section manager of respiratory care services at Rush University Medical Center and instructor in the Department of Cardiopulmonary Sciences at Rush University.

Summary
Anne M. Geistkemper, MSc, RRT, RRT-NPS discusses the practical applications of transcutaneous CO_2 monitoring in the NICU, its integration into neonatal care practices, and the evolution of this technology's adoption in the Rush University Children's Hospital NICU.

The following has been adapted from its original presentation for clarity and brevity.

Why Use Transcutaneous CO_2 Monitoring in the NICU?

The NICU admission process is fairly invasive for infants; lights, sounds and sticking for lab tests. So, the less invasive we can be within the NICU, the better. If we can introduce something that minimizes invasiveness, especially in those first 72 hours of a neonate's life, it's a valuable addition to our care regimen. Transcutaneous CO_2 monitoring, because it's noninvasive, is one such addition.

Transcutaneous monitoring provides continuous, real-time measurements of CO_2, allowing us to closely observe changes and trends. This becomes crucial when considering hypercapnia (elevated CO_2 levels) and hypocapnia (low CO_2 levels). Research has demonstrated that both hypercapnia and hypocapnia heighten the likelihood of injury to the brain, including intraventricular hemorrhage (IVH).[1] Because of this risk, we want to make sure that we're closely monitoring CO_2 to maintain levels within a safe range. Transcutaneous monitoring facilitates continuous monitoring of CO_2, providing greater visibility to support its effective management.

Clinical Applications of Transcutaneous Monitoring for Neonates

Reducing Iatrogenic Blood Loss

The most common reason for blood sampling is arterial blood gases (ABGs), which account for about 47% of neonatal blood samples.[2] One study found that neonates lost approximately a third of their blood volume within the first month of life, which is significant especially if you consider micro-preemies.[3] This blood loss can have implications for things like anemia and infection.[4]

At Rush, we're frequently getting labs, especially in the first 36 to 72 hours of life, as we strive to stabilize neonates and adjust ventilator settings in a timely fashion. If we can reduce the frequency of these blood gases, while also improving the monitoring of ventilation, that's ideal—something that transcutaneous monitoring can help us accomplish by providing continuous visibility into CO_2.

Rush University Children's Hospital NICU: An Overview

- Part of a large teaching hospital
- 60-bed level III NICU
- 700 admissions per year
  17% are very low birth weight (VLBW) infants
- Unit comprised of neonatologists, fellows, advanced practice providers (physician assistants and nurse practitioners), nurses, respiratory therapists, and ancillary staff

Continuous Monitoring on Mechanical Ventilation

Titrating mechanical ventilation is important for neonates due to their immature respiratory system. This is especially vital during the "honeymoon period," a well-known concept in the NICU, particularly for micro-preemies. It refers to the period following their birth, often after they've been given a surfactant, where settings are titrated down to minimize support. However, they can abruptly exit this honeymoon phase due to a large cytokine release, requiring prompt adjustment of settings to ensure adequate ventilation.

Because a neonate's status can constantly change, frequent adjustments are often needed. In these cases, having the option to continuously monitor CO_2 can be extremely beneficial. Instead of depending on scheduled blood gas draws to drive care decisions, continuous transcutaneous monitoring can offer greater visibility for enhanced titration support. The goal is to decrease our use of the ventilator while ensuring proper gas exchange; transcutaneous technology can give us continuous visibility into ventilatory status to help support this goal.

Continuous Monitoring on High-Frequency Oscillatory Ventilation

High-frequency oscillatory ventilation is highly effective in removing CO_2, but consequently, there's the potential for rapid fluctuations. We want to prevent these fluctuations as they can impact an infant's cerebral blood flow, which can put their brain at risk for injury, including IVH.[1] The use of transcutaneous monitoring is helpful because we can closely monitor CO_2 and catch these fluctuations, allowing for proactive management of levels in real time.

Anne M. Geistkemper, MSc, RRT, RRT-NPS, neonatal-pediatric section manager of respiratory care services at Rush University Medical Center and instructor in the Department of Cardiopulmonary Sciences at Rush University.

Reducing Neonatal Pain

Research has shown that in newborn infants, a high number of early-life skin breaks correlate with worse mental development when examined at both 8 and 18 months.[5] Furthermore, more frequent invasive procedures early in life have been associated with decreased white matter at 7 years old.[6]

We're drawing labs, we're getting gases, and maybe even placing lines. What can we do to help reduce the frequency of painful stimuli?

To minimize pain, we can employ noninvasive methods like transcutaneous CO_2 monitoring. This approach offers continuous CO_2-level visibility, helping to reduce the need for frequent heel sticks. There are also some developmentally appropriate strategies that can help reduce pain and stimuli. This includes swaddling, prone positioning, kangaroo care, or utilizing anesthetic cream or short-acting systemic analgesia for skin-breaking procedures.

Managing Specific Disease Processes

Table 1 outlines recommended CO_2 targets for neonates based on their specific disease process, as well as recommended interventions for neonates experiencing severe hypocapnia or severe hypercapnia. The use of transcutaneous CO_2 monitoring is valuable as we address the unique needs of each patient, providing enhanced titration support to maintain CO_2 levels within the targeted range.

When effectively managing CO_2, observing a reduction in CO_2 levels throughout making adjustments to ventilator settings is important. Transcutaneous monitoring provides instant visualization of the impact of our titrations. We can see the changes happening, and that can help guide effective titrations and drive care.

Special Considerations

Edema

Edema can lead to altered capillary hemodynamics and cause an increase in the blood-skin barrier due to excess fluid. As a result, transcutaneous readings can be inaccurate, making it important to avoid edematous areas when monitoring. Avoiding areas of edema can be challenging, particularly for infants who are fluid-overloaded. In these cases, however, we can still leverage transcutaneous monitoring to track the trend of CO_2 over time rather than using it for precise values.

Premature Skin

For neonates, especially in 22-23-weekers, the skin is thin and fragile, something we want to make sure we consider when using our transcutaneous monitor. To prioritize skin integrity, we should ensure the sensor is at the appropriate temperature (41°C) and that we're not leaving it on for too long (no more than 8 hours at a time). While the transcutaneous monitor will automatically apply appropriate settings, it is crucial to be aware of this consideration, so you can promptly identify deviations and take action if needed.

Note	It is recommended that the site time be evaluated and adjusted more frequently on premature skin to reduce the risk of skin injury.

Shunting and Low Perfusion

Correct sensor placement is crucial for patients with a shunt. As per AARC Clinical Practice Guidelines, it is recommended to place the transcutaneous sensor on the same side as a shunt.[7] In these cases, arterial sampling should also be done on the same side, as having these two monitoring methods aligned will allow for an accurate correlation.

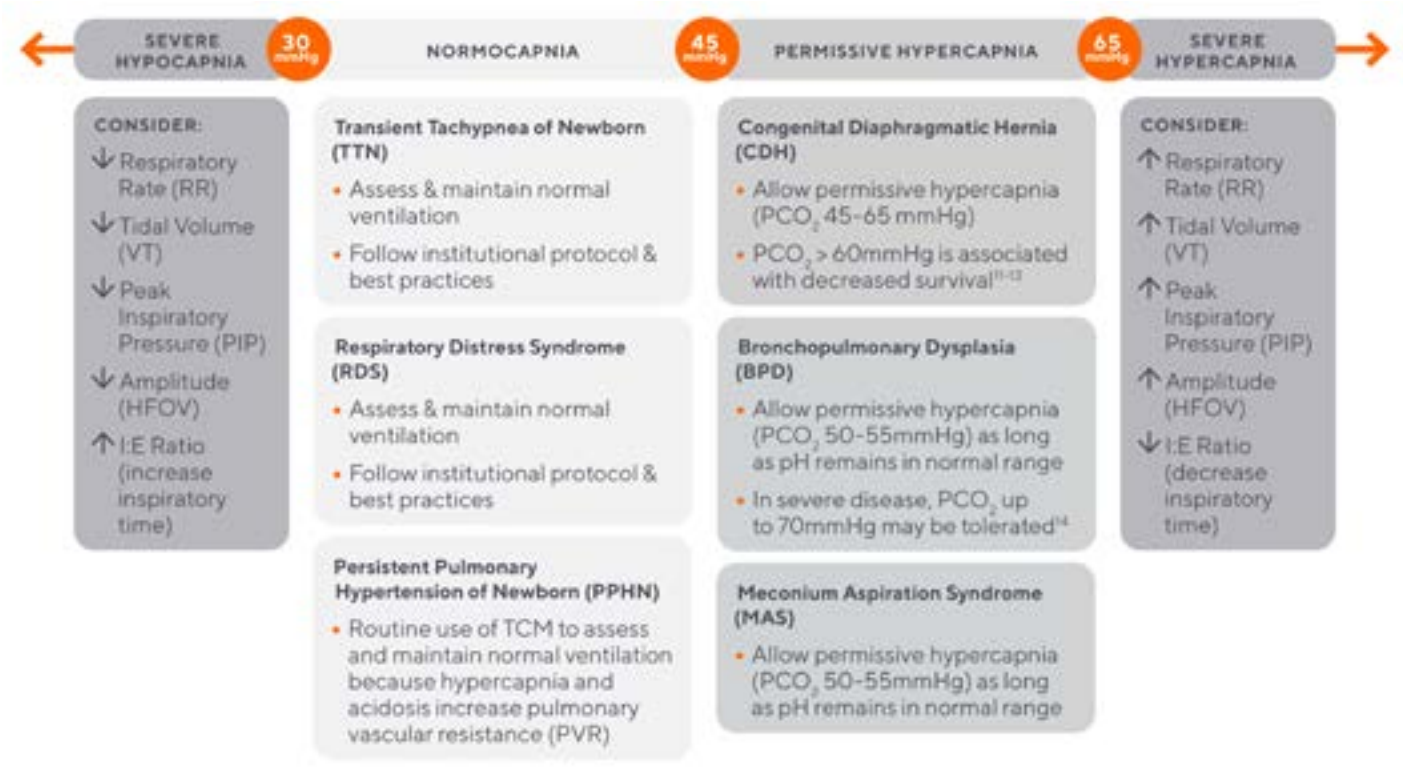


Table 1. Recommended CO_2 targets for neonates based on disease process and recommended titrations of ventilatory settings for severe hypocapnic and severe hypercapnic infants

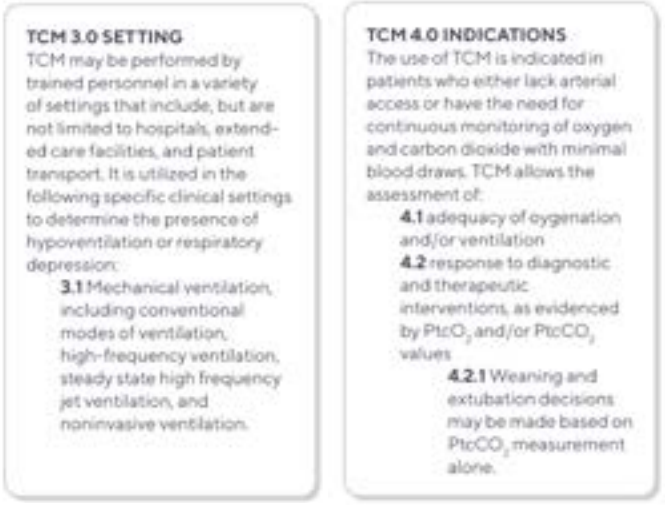
Low perfusion may cause transcutaneous CO_2 values to be falsely high. In this situation, similar to the case of edema, it may be more helpful to utilize the monitor to trend CO_2 in order to observe patterns and track progress during care.

Hypothermia

Hypothermia is something we see often in NICUs, especially with hypoxic-ischemic encephalopathy (HIE) or post-cardiac arrest patients undergoing cooling therapy. HIE, hypovolemia, reduced myocardial contractility, and bradycardia can all lead to decreased cardiac output. Consequently, if the region experiences hypoperfusion, it is important to note that the correlation between the transcutaneous and arterial CO_2 may be poor. In this situation, prioritizing establishing a correlation between the two values, rather than focusing on the exact values, becomes more clinically valuable. Again, this can be used for tracking the trend in CO_2 throughout care.

AARC Clinical Practice Guidelines

The AARC Clinical Practice Guidelines (shown in part in Figure 1) provides recommendations for the effective use of transcutaneous CO_2 monitoring in clinical care.[7] If you're not fully utilizing your transcutaneous monitors, haven't developed guidelines or implemented it into any protocols, or don't have devices at all, the AARC clinical practice guidelines can guide you. I encourage you to develop a process for your NICU. It can be difficult to get started, but aligning with the AARC guidelines is going to create a standard practice. By adopting this approach, you can foster growth within your team, encouraging increased utilization of the technology. We have a great opportunity especially as respiratory therapists, to help drive care in an efficient, noninvasive manner.



TCM 3.0 SETTING

TCM may be performed by trained personnel in a variety of settings that include, but are not limited to hospitals, extended care facilities, and patient transport. It is utilized in the following specific clinical settings to determine the presence of hypoventilation or respiratory depression:

3.1 Mechanical ventilation, including conventional modes of ventilation, high-frequency ventilation, steady state high frequency jet ventilation, and noninvasive ventilation.

TCM 4.0 INDICATIONS

The use of TCM is indicated in patients who either lack arterial access or have the need for continuous monitoring of oxygen and carbon dioxide with minimal blood draws. TCM allows the assessment of:

4.1 adequacy of oxygenation and/or ventilation

4.2 response to diagnostic and therapeutic interventions, as evidenced by $PtcO_2$ and/or $PtcCO_2$ values

4.2.1 Weaning and extubation decisions may be made based on $PtcCO_2$ measurement alone.

Figure 1. 2012 AARC Clinical Practice Guidelines for Transcutaneous Monitoring of Carbon Dioxide and Oxygen[7]

Benefits of Transcutaneous CO_2 Monitoring in the NICU

Transcutaneous CO_2 monitoring offers a noninvasive method to continuously analyze CO_2 levels in all modes of ventilation. With continuous monitoring, we're able to get real-time values for instant visualization of a patient's response to care strategies. This newer technology preserves skin integrity for delicate patients and helps reduce the need for frequent blood draws.

Additional benefits of transcutaneous CO_2 monitoring in the NICU:

- Provides accurate measurements
- Compatible with any ventilation strategy
- Supported by AARC guidelines
- Supports cost reductions
- Supports neuroprotective care
- Simplifies workflows
- Enables lung-protective ventilation strategies

Tips for Selecting a Monitoring Site

Choosing the ideal site for transcutaneous monitoring depends on your patient. The main determinant for location is perfusion, so the sensor is often placed on the thighs. This is a particularly good choice when swaddling, as there's less of a risk of the sensor falling off. However, in a 22-, 23-, 24-weeker, you might not have the real estate available in these areas, given the presence of a peripheral intravenous line (PIV) and/or other lines they may have.

In the past, we utilized the upper chest and thigh areas at our institution, but encountered challenges in achieving good correlation with these sites. In discussion with the manufacturer, we were advised to try the forehead. While some caregivers initially had concerns, once everyone embraced the idea, we saw remarkable improvements.

In most scenarios, the forehead is well-perfused, making it a great location for monitoring. For us, we keep our preemies midline for 72 hours, which also means there's typically nothing obstructing this area. And when they are being repositioned, we don't have to worry about the sensor as much, and whether there will be pressure placed on it. It's an easy-access area where we found much better correlation, and for my staff, it was less stressful to manage the sensor and troubleshoot appropriately. If you're not using the forehead yet, I challenge you to try it.

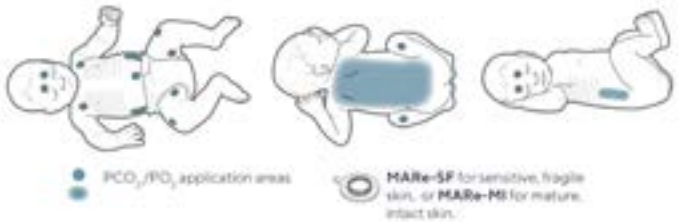


Figure 2. Recommended sensor sites for transcutaneous monitoring include the thorax, the abdomen, the back, the area low on the forehead, the temples, and the inner or anterior aspect of the thigh

Using Contact Gel: How Transcutaneous Monitoring Use Transformed at Rush

Our facility got by without using contact gel with our transcutaneous sensors for a long time. However, we were having correlation issues. We were experiencing frequent sensor errors and doing a lot of troubleshooting.

We learned from our clinical specialist that by using normal saline in place of contact gel, it meant that we were putting salt on an electrode—no wonder our membranes were struggling. When we replaced the saline with contact gel, we found our sensors were providing much better correlation. In addition, it was more cost-effective because our machines required less maintenance and troubleshooting, and we didn't have to replace membranes as frequently.

Present day, our correlation has improved significantly, and I attribute that to using contact gel, as well as using the forehead as a monitoring site. Before, we owned 6 devices and had an average of about 3-4 in use. Now, while we still own 6, we are renting additional units because our usage has increased after gaining the trust of not only the RTs, but also complete medical teams. If you are struggling with usage, I encourage you to reach out to your vendor's support team to see if there is any education to help you along the way.

The Five S's: Troubleshooting Tips for Your Transcutaneous Monitoring System

When it comes to troubleshooting your transcutaneous monitoring device, I like to refer to the "Five S's": sample, site, seal, sensor, and status. When you're trying to figure out why your transcutaneous readings aren't correlating as well as you'd like, figuring out which issue you're dealing with can help you troubleshoot appropriately.

Sample	Site	Seal	Sensor	Status
Record the tcPCO2 value when you draw the sample, not when results are read. Verify proper lab draw technique and operation of blood gas analyzer.	Check for external pressure on the sensor. Check perfusion at measurement site. Sampling site and sensor should be on same side of shunt.	Verify attachment ring is secure on the skin. Use 1–2 drops of Contact Gel during application. Ensure sensor is clipped into the ring.	Verify correct sensor temperature. Check the quality of the sensor membrane. Check when the sensor was last calibrated.	Shock, sepsis, and edema can impact the local perfusion. Consider the effect of vasoactive medications. Increased perfusion may cause falsely high tcPCO2.

Table 2. "Five S's" of troubleshooting a transcutaneous monitoring device: sample, site, seal, sensor, and status

Integrating Transcutaneous Monitoring Into NICU Protocols

At Rush, we implemented transcutaneous monitoring within our unit protocols, not only to increase the usage of the devices that we bought, but also to showcase its value and get everybody on the unit more comfortable with the technology.

If you don't have protocols in your unit yet, that's okay. You can use the AARC Clinical Practice Guidelines to start utilizing the technology and building trust. If you do have protocols, there are simple ways to implement the usage of transcutaneous monitoring in your unit, just by adding it to your existing processes.

NICU Conventional Ventilation Protocol

As part of our NICU conventional ventilation protocol, patients who are born at less than 35 weeks get a transcutaneous sensor placed on them for the first 72 hours of life, which allows us to start trending our gases with our $tcPCO_2$. Because there is a high volume of gases and labs being drawn in the first 24 to 36 hours, we're able to lay a good foundation for our correlation. This protocol also gets everybody more comfortable with transcutaneous monitoring in the NICU.

High-Frequency Jet Ventilator Protocol

As part of our care goals for our high-frequency jet ventilator protocol, any patient who goes on a jet ventilator must have a transcutaneous monitor.

Other Cases to Integrate Transcutaneous CO_2 Monitoring

Other cases where we use transcutaneous monitoring are BPD and noninvasive ventilation (NIV). While we don't necessarily have these protocolized yet, we still utilize transcutaneous monitoring to continuously monitor ventilation in these patients.

- **BPD |** Although gases are not frequently obtained from patients with BPD, their status can change quickly. These patients are often sweaty, which can make finding the proper transcutaneous sensor placement difficult. However, transcutaneous monitoring is a useful tool for this population, providing continuous CO_2 visualization when gas sampling is infrequent.
- **NIV |** Patients on noninvasive mechanical ventilation are often teetering on the verge of needing an escalation of care, perhaps requiring intubation. Or, they may have just been extubated, and there is uncertainty about their ability to thrive. To be able to have constant CO_2 monitoring in these cases is helpful in guiding our management strategies.

Summary

Transcutaneous monitoring provides clinicians with a noninvasive method to monitor CO_2. This isn't just beneficial for patients in terms of lessening pain; it has the potential to yield benefits for your hospital in terms of cost-effectiveness by supporting the reduction of blood draws. And importantly, as a respiratory therapist, it offers valuable insights into the efficacy of ventilation strategies, which helps guide care.

The more you use transcutaneous monitoring, the more comfortable you're going to be and hopefully the better you'll become at it. In the Rush University Children's Hospital NICU, we already had active protocols, so we took the opportunity to integrate transcutaneous monitoring. This not only got our staff more comfortable using it, but also allowed our bedside caregivers to begin to trust the technology and rely on it during care.

As we continue utilizing transcutaneous CO_2 monitoring, keeping up with current research remains valuable. However, actively engaging with other facilities, who are utilizing devices even more than we are, has also proven significant for our hospital. If you're looking to embrace this technology, or increase its usage, consider reaching out to your colleagues at other hospitals to gain valuable insights on successful implementation. This has played a vital role in our adoption of transcutaneous monitoring in the NICU, and our progress towards utilizing its fullest potential for our patients.

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https://www.sentec.com/neonatal-pediatric-intensive-care/

News…continued from page 7
with the consortium of virologists at the ANRS MIE [Emerging Infectious Diseases]. It is a nationwide project that will help identify the resistance phenomenon associated with the widespread use of the drug. This type of study is essential for analyzing the evolutionary dynamics of viruses, in the light of existing medical solutions," explained the study's corresponding author Marie-Anne Rameix-Welti, MD, PhD, head of the National Reference Center for Respiratory Viruses at the Pasteur Institute and of the Molecular Mechanisms of Multiplication of Pneumoviruses (M3P) Unit, Paris-Saclay-Versailles St. Quentin University, INSERM U1173, Paris, France. The study included 695 infants with RSV infection, of whom 349 had received nirsevimab prophylaxis. RSV-A was predominant this season, found in 86.6% of infected children. The study teams analyzed the characteristics of RSV-A and RSV-B strains present in nasopharyngeal samples collected as part of routine care. The complete viral genome sequence was determined, specifically to identify mutations in the nirsevimab binding site (genotypic analysis). They also studied nirsevimab's ability to inhibit viral replication in cell cultures (phenotypic analysis).

Company Earns Mark in Europe

Beyond Air, Inc., a commercial stage medical device and biopharmaceutical company focused on harnessing the power of nitric oxide (NO) to improve the lives of patients, announced European CE mark approval of the LungFit PH system. This CE mark approval allows Beyond Air to market LungFit PH in the European Union and all other countries that recognize this certification. LungFit PH, the first device in the LungFit therapeutic platform of nitric oxide generators, leverages the company's patented Ionizer technology and has already received FDA approval in the United States. "We are thrilled to announce CE mark for LungFit PH, paving the way for commercial sales in Europe and other global regions. In anticipation of this approval, we partnered with Business Asia Consultants to leverage their extensive international distribution network," stated Steve Lisi, Chairman and Chief Executive Officer of Beyond Air. "I am incredibly proud of the team that made this happen over the past 30 months and look forward to initiating shipments to our Asia-Pacific partner, Getz Healthcare, and other international partners in 2025." Under the terms of Beyond Air's existing commercialization agreement with Getz Healthcare for LungFit PH, Getz will make a $1 million milestone payment to Beyond Air upon CE mark certification. In addition, Beyond Air will receive ongoing royalty payments based on LungFit PH net sales. The partnership provides access to hospitals in Australia, New Zealand, Thailand, Philippines, Taiwan, Hong Kong, Malaysia, Pakistan, Singapore and Vietnam. The specific indications for LungFit PH under CE Mark certification include: the treatment of infants ≥34 weeks gestation with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension, in order to improve oxygenation and to reduce the need for extracorporeal membrane oxygenation; the treatment of peri- and post-operative pulmonary hypertension in adults and newborn infants, infants and toddlers, children and adolescents, ages 0-17 years in conjunction to heart surgery, in order to selectively decrease pulmonary arterial pressure and improve right ventricular function. LungFit PH uses Ionizer technology to generate unlimited on-demand NO from ambient air and deliver it to a ventilator circuit, regardless of dose or flow. The device uses a compressor to drive room air through a plasma chamber where pulses of electrical discharge are created
Continued on page 18…

California Excels at Screening Babies for Main Cause of Childhood Blindness

Erin Digitale, PhD, Stanford Medicine Children's Health

Rates of retinopathy of prematurity, a top complication of premature birth, have nearly doubled across the United States in the last 20 years. But, thanks to meticulous efforts to care for premature newborns at hospitals throughout California, neonates there are less likely to develop the condition.

The findings were reported in October in *JAMA Ophthalmology*.

"Because California has been going in a different direction, there is potential to learn lessons here that can be used in the rest of the country," said the study's lead author, MK Quinn, PhD, a postdoctoral scholar in neonatal and developmental medicine at Stanford Medicine.

Retinopathy of prematurity, which is the leading cause of childhood blindness, happens mostly in the earliest-born preemies. The study focused on rates of the condition in newborns who arrived at least eight weeks early.

Not only have California's retinopathy rates held steady, but the gap in disease rates between babies of different racial and ethnic backgrounds in California has shrunk, with the biggest declines in retinopathy among Hispanic and Asian infants, the study found.

"We're decreasing racial disparities," said study co-author Jochen Profit, MD, co-chair of the California Perinatal Quality Care Collaborative and a professor of neonatal medicine at Stanford Medicine. Quinn and Profit collaborated with scientists at the University of California, San Diego and UCLA on the research.

Although doctors can't stop every case of retinopathy, which happens when abnormal blood vessel growth in preemies' eyes damages their vision, better medical care prevents some cases, he noted. And by checking preemies' eyes at the right time, physicians can find cases early, when there is an opportunity to keep the disease from worsening.

"Screening for this disease requires its own system in neonatal intensive care units, where people are really dedicated to making sure that no baby is missed," Profit said. In the past, preemies from minority groups were less likely to get their eyes checked at the right time. Making sure all of them receive an eye exam has helped close the disparities, he explained.

"There are a lot of ways you can approach health equity," Profit said. "But quality improvement and limiting variability in care lift all boats."

The blood vessel challenge

Because they're born early, preemies' eyes aren't fully developed. They still need to grow blood vessels throughout the retina, the light-sensing layer at the back of the eye. The retina receives light through the pupil and sends signals to the brain that get turned into the images we see.

"For blood vessel growth to happen normally, you must limit noxious stimulants which can derail the process," Profit said. Abnormal blood vessels can bleed into the eye and cause the retina to detach from the back of the eye, which causes blindness.

The challenge is that blood vessel growth can be derailed by something else preemies need: oxygen. Preemies have immature lungs and may require a ventilator to help them breathe. But on a ventilator, they sometimes get too much oxygen, or experience big swings in oxygen levels. Both situations can stimulate abnormal blood vessel growth in the eyes.

Experts across California have been learning how to support preemies' breathing with less risk to their eyes. They have instituted oxygen management practices statewide, such as figuring out soon after birth which babies can receive breathing assistance from a device known as continuous positive airway pressure (CPAP) instead of a ventilator. With CPAP, it can be easier to prevent fluctuations in oxygen levels. For tiny patients who do require a ventilator, medical teams are also working hard to provide just the right amount of oxygen, not too little and not too much, following what they call the "Goldilocks rule of neonatology."

In addition, doctors are checking infants for early signs of retinopathy. Every baby at risk needs to be screened, usually around four weeks of age, depending on how early they were born. In severe cases, doctors can sometimes surgically reattach a detached retina, but at that stage, most infants will not recover vision, so the aim is to find cases before detachment occurs.

If they find problems early on, doctors can give a drug that slows blood vessel growth. The drug hinders a natural growth factor in the blood vessel walls. If a baby has early signs of retinopathy, the drug can be given directly into the eye to moderate blood

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vessel growth there without affecting other parts of the body. In some cases, if that is not successful, they can use laser therapy or cryotherapy, although these options risk damaging babies' peripheral vision.

Steady screening, better outcomes

The study included more than 48,000 infants born in California between 2012 and 2021 who arrived at least eight weeks premature or were very small, weighing less than 3.3 pounds at birth. The babies were hospitalized in neonatal intensive care units.

The researchers found that hospitals were doing a good job of looking for retinopathy: 95% to 98% of babies who needed screening had their eyes checked throughout the period studied. Screening rates were equally high in California newborns of all races.

The overall rate of retinopathy declined slightly throughout the study period. The change was driven by reductions in retinopathy in Hispanic and Asian babies, who had the highest retinopathy rates at the beginning of the study. Rates in other groups remained steady.

"We weren't expecting the decreasing racial and ethnic disparities," Quinn said. "That's what we were most surprised by."

The researchers also investigated the treatments used to address retinopathy and found that doctors increasingly utilized the growth factor-inhibiting drug, with a 14% average increase in its use per year—a good sign as it preserves more vision than other treatment options.

"As they grow up, it's common for preemies to have nearsightedness or astigmatism, mild to moderate vision problems," Profit said. They can usually be helped with glasses, and those kids can lead normal lives, he noted, adding, "What we're really trying to prevent is blindness or near blindness. Hopefully in the future, we will learn how to prevent the other visual impairments."

"Many people across the state have been trying to improve this," Quinn said. "All those little steps took years before the payoff, but now we're seeing some great results."

News…continued from page 16

between two electrodes. The LungFit PH system ionizes the nitrogen and oxygen molecules, forming NO with low levels of nitrogen dioxide (NO_2) created as a byproduct. The gas is then passed through a Smart Filter, which removes toxic NO_2 from the internal circuit. LungFit PH represents a significant step forward in sustainable healthcare solutions. Since the device generates NO conveniently and cleanly from ambient air, without the need for tanks or chemicals, it is highly energy-efficient, using only the power equivalent to a 60-watt light bulb. By eliminating the emissions associated with truck transport and cylinder refills, LungFit PH supports hospital sustainability initiatives, helping facilities reduce their carbon footprint while delivering critical care to patients. For the approved indications, the novel LungFit PH system is designed to deliver a dosage of NO to the lungs that is consistent with the current standard of care for delivery of 20 ppm NO, with a range of 0.5 ppm – 80 ppm (low concentration NO) for ventilated patients. Each Smart Filter will last 12 hours regardless of ventilator demands, and replacing a filter only takes seconds. Potential customers can visit the LungFit PH website, www.lungfitph.com, for additional information, including the product label, and to sign up for updates.

Whooping Cough and Newborns: How to Set Boundaries

Whooping cough is making a dangerous comeback across the US, with cases soaring to 4.5 times more this year than last, according to the CDC. For parents of newborns, this highly contagious respiratory illness poses a serious threat — and protecting your baby starts with setting clear boundaries. That might mean asking grandparents, friends, and other loved ones to follow precautions before meeting your little one. If the pandemic taught us anything, asking people to take medical precautions doesn't always go over well. Still, it's necessary. "Babies are very vulnerable in the first 6 months of life," said Rachel C. Orscheln, MD, medical director of ambulatory pediatric infectious diseases at St. Louis Children's Hospital. "So, we try to have multiple layers of protection around them." The stakes are high: *Bordetella pertussis*, the bacteria behind whooping cough, spreads easily through airborne droplets, often hiding behind symptoms that look like a common cold. But with the right strategies, parents and caregivers can work together to keep infants safe. The CDC and American Academy of Pediatrics recommend that parents, relatives (including kids and teens), and caregivers who will be in close contact with a new baby get the pertussis vaccine shots and boosters. Immunity to pertussis develops over about 2 weeks after the shot. "Since pertussis is most serious in those less than 1 year of age, anyone who has close contact with infants should be up to date with their vaccine," said Dean Blumberg, MD, chief of the Division of Pediatric Infectious Diseases at the University of California, Davis, and a spokesperson for the American Academy of Pediatrics. "This protects the infant by decreasing the risk that a contact will potentially infect them. About one third of babies with pertussis need to be hospitalized. And almost all deaths due to pertussis occur in those less than 1 year of age." Asking visitors with cold-like symptoms to postpone their visit is critical. "Pertussis is generally transmitted by close contact, being within 6 feet of an infant," Blumberg said. "Symptom screening — excluding visitors who have symptoms such as fever, cough, sneezing — is always a good strategy to protect infants against pertussis and other respiratory infections." Ultimately, it is up to the parents to decide what measures they would like in place to protect their baby, the experts said. But in

Continued on page 27…

Enhancing Pediatric Tracheostomy Care with a Multidisciplinary Airway Management Team

Rebecca L Brooks, MSN, APRN, PCNS-BC and Carmin Bartow, MS, CCC-SLP

Pediatric tracheostomy teams are essential in improving patient outcomes by delivering specialized, coordinated care for infants and children with tracheostomies. These multidisciplinary teams, comprising healthcare professionals such as physicians, advanced practice providers, speech-language pathologists, respiratory therapists, and nurses, work together to meet the complex needs of these patients. Through comprehensive management, these teams help shorten hospital stays, reduce tracheostomy-related complications, and enhance overall patient safety and quality of life (Chorney et al. 2021).

A prime example of a successful team is the Dallas Children's Health Airway Management Program (CHAMP). In this interview, Rebecca ("Becky") Brooks, MSN, APRN, PCNS-BC, Pediatric Clinical Nurse Specialist for CHAMP, shares insights into the team's development, its members, caregiver training, and the overall success of their program.

Becky, can you tell me about how the CHAMP team was formed and how it has evolved?

We began in 2015 with an idea shared between Dr Eric Gantwerker, Dr Romaine Johnson, and myself. When I began as the Clinical Nurse Specialist covering pulmonology, I found many patients with tracheostomies who had lack of follow-up, missing items, and gaps in care. I approached the Ear Nose and Throat (ENT) surgeons at Children's Medical Center – Dallas (CMC) to discuss the possibility of creating an airway management team. Many large hospitals, like ours, had dedicated tracheostomy teams and at that time we did not. We invited all provider disciplines as well as administration and had a meeting to discuss tracheostomy practice at our institution. We had 46 providers come and everyone agreed we needed to make some changes.

We began by reviewing our current data on tracheostomy. Next, we created teams to investigate the problems with tracheostomy management such as staff and caregiver education, length of stay, and tracheostomy tube sizing. We spent a lot of time conducting chart reviews and gathering data on our patients. One of the biggest problems we discovered was the time from tracheotomy to delivering patient and caregiver education.

Rebecca Brooks is a Pediatric Clinical Nurse Specialist with the Children's Health Airway Management Program (CHAMP).
Carmin Bartow is a speech pathologist and tracheostomy clinical educator with Atos Medical.

Our trach team was built from this need. We started with two educators and myself. We rounded every Thursday and began providing education for all trach patients, regardless of where they were in the hospital. Two of the biggest accomplishments of our team were reducing the time from trach placement to the first day of caregiver education from 18 days to 2-4 days and cutting the length of stay (LOS) by nearly half. In 2018 the organization made us an official program titled CHAMP.

Who are the CHAMP team members and what are their roles and responsibilities?

Our team includes the following members:

- Four Otolaryngologists who provide care in our clinics and perform surgeries
- One Advanced Practice Provider who provides inpatient management of patients with tracheostomies, including pre-tracheostomy assessment with families, performing endoscopies, changing tracheostomy tubes, and providing tracheostomy management of wound or stoma issues
- Three Tracheostomy Educators
  - Two are Respiratory Therapists (RT), and one is a Registered Nurse (RN) who provide inpatient education and simulation prior to first discharge
- Two outpatient Clinic Nurses who manage all Durable Medical Equipment (DME) orders, assist physicians in clinic, and manage all airway phone calls
- One Case Coordinator who provides outpatient follow ups on new and existing patients with tracheostomies to ensure families are well-equipped with necessary tracheostomy supplies
- Two Speech-Language Pathologists who provide communication and swallowing intervention
- Two Surgery Schedulers
- One Program Manager
- One ENT Manager
- One Medical Assistant

What would you like other healthcare professionals to know about pediatric tracheostomy teams?

A tracheostomy team will add a huge value to your organization by increasing patient and family satisfaction, enhancing education, reducing length of stay, and improving the safety and quality of care for all trach patients from pre-placement to discharge and beyond. It is well worth the investment.

Can you provide an overview of the caregiver education and training that your Trach Educators provide?
Please see our Journey Maps, which cover everything we do as it is a quite lengthy process. (See Figures 1 & 2).

Can you share the decision-making process that led your team to transition to Tracoe Silcosoft tracheostomy tubes?
The quality of the tube, the decrease in granulation tissue we have noticed when using the tube, the ease of ordering and obtaining the stock, and the ease of insertion led us to this decision.

Have you made other significant changes in practices or products since you started your team?
We have developed a standard dressing algorithm for fresh tracheostomies and to treat granulation tissue. We have also incorporated dressings that have become available to improve stoma care. Additionally, we have added one way valve use and developed a policy for eligibility. One way valve use begins prior to leaving the hospital and as soon as patients meet criteria.

What are you most proud of as a member of the CHAMP team?
We are most proud of the improved quality of care our families receive. Developing a tracheostomy emergency simulation program using a high fidelity mannikin has also been a huge achievement. All families practice five emergency trach scenarios before discharge. Our CMC Healthcare Professionals (HCPs) and community providers such as new graduate nurses, medical students, and residents also participate in our simulation program. Because of our success, we have a lot of requests to provide this simulation education to outside organizations. So we are excited that we are reaching other HCPs for this education and training.

We are also proud of the patients themselves! And, lastly, I'm very proud of our team. Every member is really dedicated to improving the care and outcomes for our patients. Our team has also conducted research, published several articles, and presented at numerous meetings and conferences all related to pediatric tracheostomy. (See "CHAMP Papers" and "CHAMP Presentations" below).

What are some of the biggest challenges in tracheostomy care for families?
The number of tracheostomies placed in children is increasing due to the extensive technology now available to keep children alive. This is not just locally but across the country. Many research articles also discuss the increasing number of children with tracheostomies and the impact on family life. Parenting children with tracheostomies and complex medical conditions can put a strain on the family and negatively impact quality of life (QOL).

Our team investigated the quality of life among families with children with tracheostomies and found that QOL scores were similar to QOL scores with families with children with chronic illnesses. Problems with worry and daily activities were impacted the most, and results indicated that tracheostomy does have a dampening effect on the family's QOL. However,

Figure 1

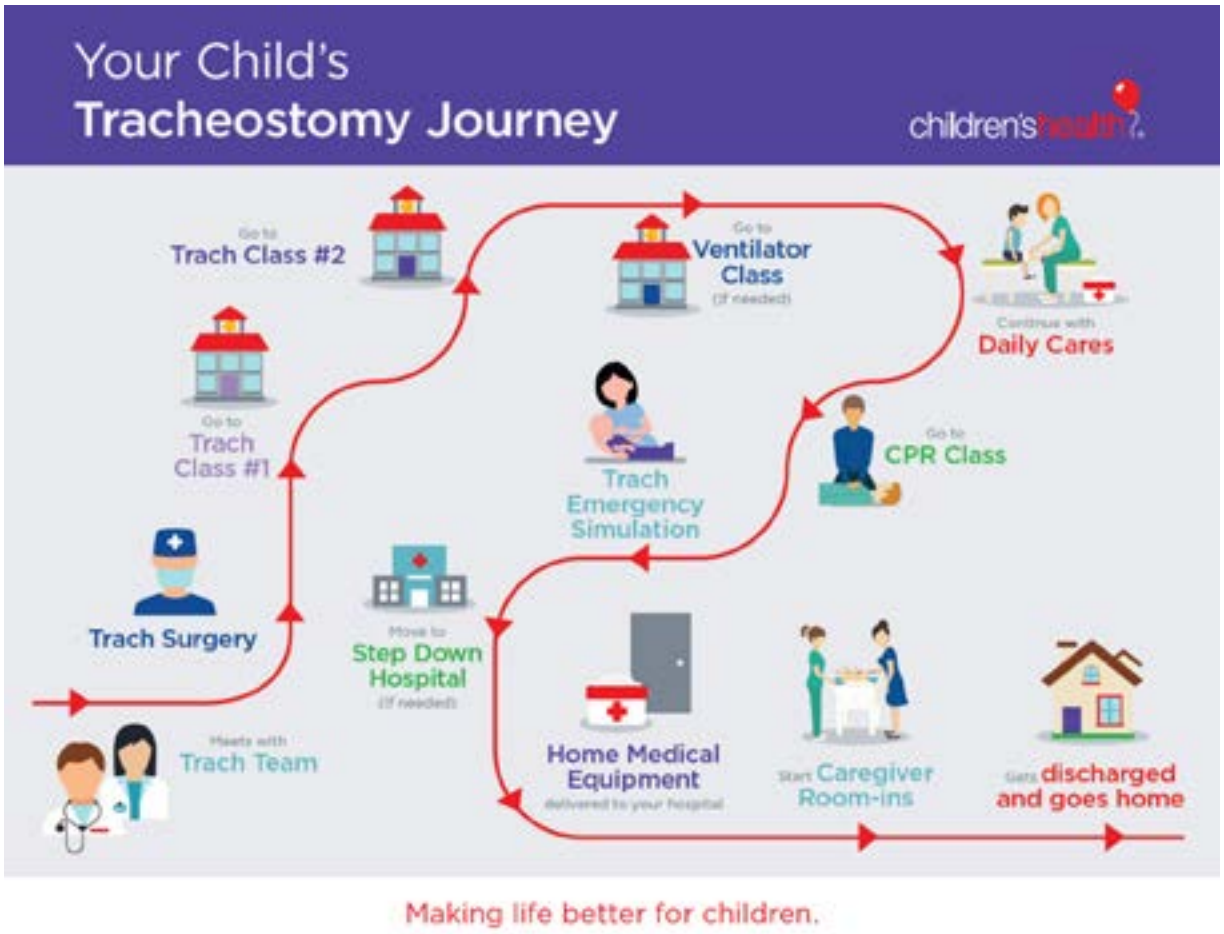
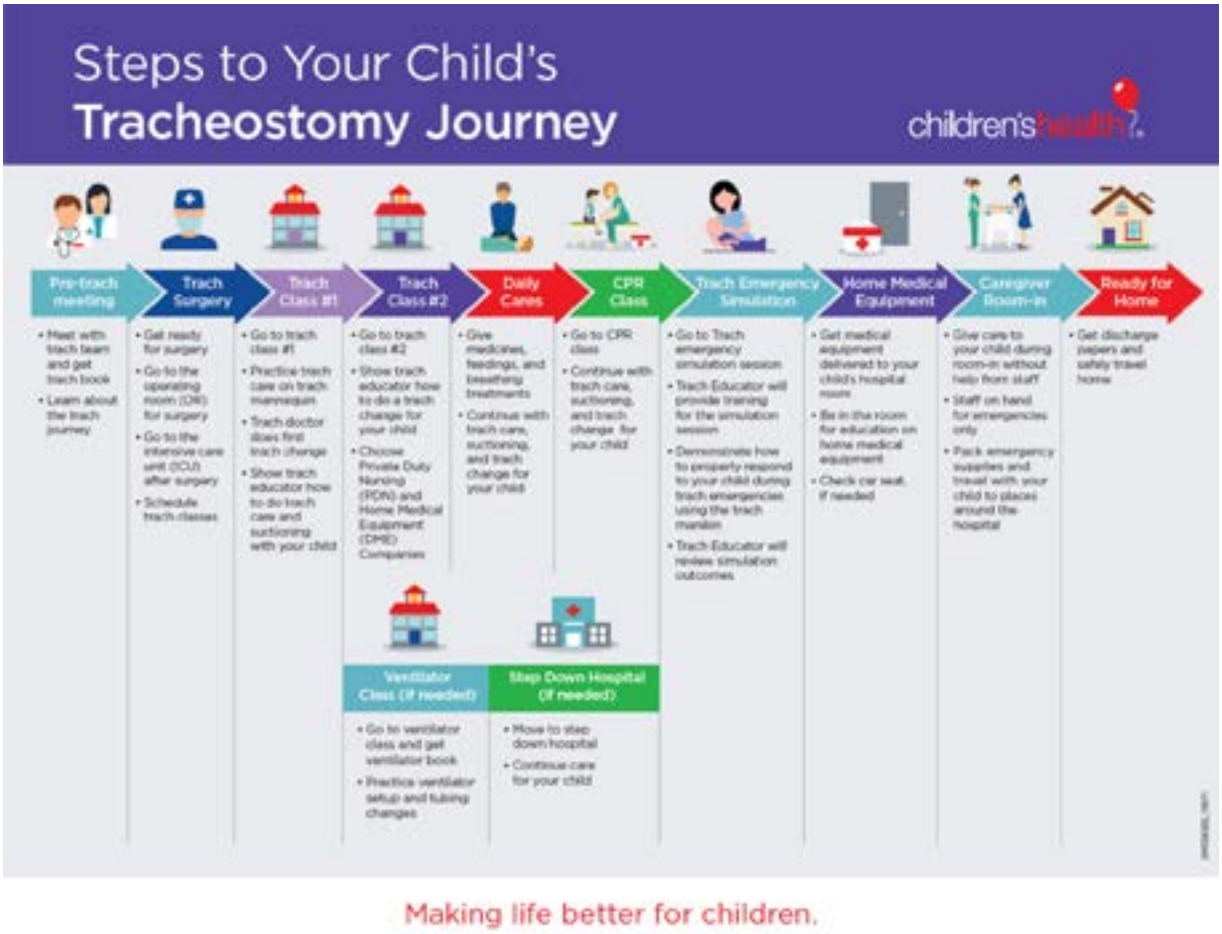


Figure 2



the results also showed a remarkable resiliency for many domains such as physical, emotional, and cognitive functioning.

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Where do you feel the future of pediatric tracheostomy care is headed?

The future of pediatric tracheostomy care is undoubtedly expanding, with an increasing number of pediatric patients in the community requiring tracheostomy tubes. It is imperative for the medical team to meet these demands to ensure patient safety and provide support for families. Numerous research articles focus on the lived experiences of patients and families post-tracheostomy, highlighting their needs and the impact on the community. As more patients are discharged with tracheostomy tubes, it is crucial for providers to educate community members, including school systems, primary care physicians, first responders, DME companies, and home health nurses. Ensuring the community is well-informed about caring for these patients will enable safe management at home, ultimately improving patient outcomes.

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- Chorney S, Brown AL, Jaffal H, Johnson RF. Swallowing Assessment of Children using a Tracheostomy Speaking Valve. Otolaryngology-Head and Neck Surgery Foundation. Annual Meeting. October 2021, Los Angeles, California.
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- Salley J, Kou YF, Shah GB, Johnson RF. A Longitudinal Analysis of Pediatric Tracheostomy Patients. The American Broncho-Esophagological Association Annual Meeting Abstracts. May 2019.
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Passy-Muir Valve Use in the NICU: Considerations with Mechanical Ventilation

Gabriela Ortiz, BSRT, RCP

Using the Passy Muir Valve (PMV) allows patients to speak, breathe, and swallow more easily while on mechanical ventilation. It can be particularly beneficial for neonates who are mechanically ventilated, but its use requires careful consideration and monitoring. In the Neonatal Intensive Care Unit (NICU), its use is becoming increasingly common, offering both immediate and long-term benefits for neonates with complex respiratory needs. The Valve works by redirecting exhaled air through the vocal cords, providing the infant with the opportunity to vocalize and even engage in oral feeding with a more normal physiologic process utilizing a closed system and restored pressures.

Understanding the Passy Muir Valve

The Passy-Muir Valve is a one-way valve that attaches to the tracheostomy tube of a patient or directly within the ventilator circuit of mechanical ventilation. When a patient has a tracheostomy tube and mechanical ventilation, typically the cuff is inflated to seal the airway during mechanical ventilation so that airflow goes in and out through the tracheostomy tube. The Passy-Muir Valve is designed to allow the patient to breathe in through the tracheostomy tube but air flows out through the upper airway during exhalation. This redirection of airflow helps facilitate vocalization, swallowing, and cough; improves lung recruitment; and supports normal respiratory patterns.

In the context of the NICU, the PMV can serve a range of purposes:

- **Vocalization:** enabling them to vocalize, a key developmental milestone.
- **Swallowing and Feeding:** assisting in the transition to oral feeding, as the Valve helps maintain appropriate airflow, allowing the infant to breathe more easily while sucking or swallowing (Da Cunha de Lima, 2021).
- **Airway Clearance:** supporting better airway clearance by promoting more effective exhalation and cough, reducing the risk of secretion retention (Zabih, 2017).

In cases where the infant is mechanically ventilated, the PMV can be placed directly within the ventilator circuit. This helps the infant breathe more naturally by allowing air to flow out through the trachea and vocal cords during exhalation, which can help restore more normal respiratory patterns and prevent the buildup of carbon dioxide.

Facilitating Communication and Vocalization

For neonates, the PMV facilitates vocalization by redirecting airflow upwards, through the vocal cords. For infants who cannot breathe independently, vocalization is often suppressed, as the air required for speech cannot pass up to the upper airway. The PMV addresses this issue by allowing air to pass through the vocal cords, permitting the infant to make sounds, which can aid in social bonding and early communication, important milestones in early infant development.

Support for Feeding and Swallowing

The transition from tube feeding to oral feeding is another major developmental milestone for infants in the NICU. The PMV plays a crucial role in facilitating this transition by improving respiratory control during feeding. When the Valve is used, it helps to maintain a steady airway pressure during sucking, reducing the risk of aspiration and making it easier for infants to coordinate breathing with swallowing. Da Cunha de Lima et al. (2021) addressed how infants resumed breastfeeding with use of the Valve. The authors reported that patients were able to feed more safely and managed secretions much easier when using the Valve.

Improved Respiratory Function

One of the most significant advantages of the PMV is its ability to improve respiratory function. When infants are placed on mechanical ventilation or have a tracheostomy, it alters the respiratory process. The one-way Valve restores airflow in a more natural, physiological manner. This reduces the risk of atelectasis (collapse of the lung tissue), supports more efficient gas exchange, and can lead to improved oxygenation. As a result, it may decrease the need for prolonged ventilation and enhance

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Gabriela Ortiz earned her Respiratory Care Practitioner license in 2006. She has extensive experience managing patients at different stages of care, including acute, sub-acute, sleep therapy, and homecare. As the Respiratory Clinical Director and General Manager at a respiratory care provider, Gabriela managed all company operations, including patient assessment and case management for pediatric and adult patient populations. With her clinical knowledge, Gabriela advanced into clinical training and sales for critical care ventilation products for the ICU and PICU within acute and subacute hospitals. Gabriela has combined her clinical experiences to support others through education and is a regularly invited speaker for university programs, Better Breather's Club, and ALS support groups. She has authored and co-authored multiple peer-reviewed papers on respiratory topics such as the progression of ALS, the effects of a tracheostomy in neonates, and respiratory care plans for patients in homecare. Gabriela is currently a full-time Clinical Specialist with Passy-Muir, Inc.

Using a PMV 007 Valve in-line with mechanical ventilation allows for more patient interaction.

the chances of successful weaning and decannulation. This may lead to shorter hospital stays and decreased risk of ventilator-associated complications, such as ventilator-associated pneumonia (VAP).

Ventilator Settings & Parameters: If a neonate is still dependent on mechanical ventilation, the PMV can change the airflow dynamics, which may require adjusting ventilator settings to ensure proper oxygenation and ventilation. Therefore, meeting patient selection guidelines and ventilator parameters that maintain medical stability is beneficial.

Traditional ventilation modes, whether pressure-controlled or volume-controlled, are compatible with the PMV. In neonates and pediatrics, pressure control (PC) ventilation is common, as it regulates the peak inspiratory pressure (PIP), which helps minimize the risk of lung injury. It is important to ensure that the chosen ventilation mode can provide adequate respiratory support, even in the presence of system leaks, such as those caused by a deflated cuff on a pediatric tracheostomy (PED) tube or with the use of the Valve in-line.

When managing patients on mechanical ventilation, particularly in critical care settings, it is essential to adhere to guidelines that ensure both patient safety and ventilator effectiveness. For example, the PMV helps restore physiologic PEEP, so if the neonate has high extrinsic positive end-expiratory pressure (PEEP) or peak inspiratory pressures, you may need to adjust these settings to ensure that the patient's ventilation remains adequate.

Here are more detailed suggestions to justify and support ventilator management using these parameters:

1. **$FiO_2 \leq 50\%$**
   - **Rationale:** The goal is to use the lowest FiO_2 that can maintain adequate oxygenation (usually targeting an SpO_2 within normal range for the patient). Patients receiving low levels of oxygen would be considered in a stable state. Prolonged exposure to high concentrations of oxygen can lead to oxygen toxicity, so FiO_2 should be minimized whenever possible.
2. **PEEP ≤ 10 cmH_2O**
   - **Rationale:** Positive End-Expiratory Pressure (PEEP) is critical in managing oxygenation, where it helps to maintain alveolar recruitment and prevent atelectasis. However, having a higher PEEP may indicate the patient is too sick for Valve use.
3. **Peak Inspiratory Pressure (PIP) within the normal range for the patient**
   - **Rationale:** PIP is an important indicator of airway resistance and lung compliance. Elevated PIP values often suggest that the ventilator settings might be too aggressive, and the patient's lungs may be at risk for barotrauma.

Adjustments should always be individualized based on the patient's response, underlying pathology, and clinical goals.

The clinician must ensure that the patient is a good candidate for Valve placement. The following are suggested patient selection guidelines:

1. **Awake and alert:** The patient should be conscious and able to engage in the assessment process to ensure cooperation with the procedure and appropriate responses.
2. **Medical stability:** The patient must be in a stable condition, without significant fluctuations in blood pressure, heart rate, or respiratory function, as these can complicate the procedure and make it unsafe.
3. **Cuffed tracheostomy tube deflation:** If the patient has a cuffed tracheostomy tube, the cuff must be fully deflated before placing a speaking Valve.
4. **Thin, manageable secretions:** The patient should have secretions that are easy to clear, as thick, copious secretions may obstruct the airway.
5. **Patent airway:** Most importantly, the patient must have a clear, unobstructed airway to ensure that air can flow freely to the upper airway, allowing for safe and effective use of the speaking Valve.

These factors should be assessed thoroughly by the clinician before proceeding and are critical to ensure the safe and successful placement of the PMV.

Transtracheal Pressure (TTP) Measurement: Assessing airway patency is more commonly done by transtracheal pressure manometry. This involves measuring the pressure within the airway at the end of exhalation. This measurement is considered a reliable predictor of little to no obstructions in the airway. A lower TTP generally indicates a more patent airway, which is associated with a higher likelihood of success when using the PMV. A study by Brooks et al. (2019) highlighted that a TTP between 0 and 14 cmH_2O was highly predictive of PMV success in pediatric patients with complex medical conditions. Transtracheal pressures and guidelines may vary, and clinicians should adhere to the protocols established by their facility.

In addition to TTP measurements, the study identified other factors that could influence the successful use of the PMV:

- **Higher weight (correlated with age):** Larger, older patients tended to have a better chance of successful PMV use.
- **Tracheostomy tube size:** A properly sized tracheostomy tube increases the likelihood of a patent airway.

Assessing Airway Patency Using Ventilator Parameters:

- **Cuff deflation and ventilator changes:** When the cuff is deflated, the change in ventilator readings can provide insight into airway patency.
  - Volume-Controlled Ventilation (VCV):
    - A 40%-50% drop in exhaled tidal volume after cuff deflation indicates that a sufficient leak is present, which suggests a patent upper airway. With less resistance, seeing a decrease in peak inspiratory pressure (PIP) is

likely as well.

- Pressure-Controlled Ventilation (PCV):
  - In PCV, a drop in exhaled tidal volume would be expected with cuff deflation, but a significant drop in PIP would not be as pronounced.

These methods, particularly TTP measurements and changes in ventilator readings, are crucial in determining if the patient has a patent airway and can safely use the PMV. The factors identified by Brooks et al. (2019) further contribute to a comprehensive understanding of the variables involved in predicting PMV success.

Factors Affecting Airway Patency in Tracheostomy Patients

Airway patency is crucial for the proper and safe use of the Passy-Muir Valve. Maintaining airway patency in patients with tracheostomies requires close monitoring and an understanding of the dynamic factors that can affect airflow. In neonatal and pediatric populations, changes in growth, tube size, and anatomical structures require careful management.[3] Additionally, monitoring for obstructions and ensuring proper tube positioning are critical for maintaining optimal airway function. Any signs of decreased patency should prompt a thorough evaluation to identify and address potential causes, thereby facilitating effective respiratory support.

- **Developmental changes:** As infants grow, their tracheal lumen enlarges, which can improve patency and may allow for better clearance of secretions and easier use of the PMV.
- **Tube position:** The position of the tracheostomy tube in relation to the airway is critical for maintaining patency. If the tube shifts or becomes displaced due to external factors, like changes in patient positioning, it can obstruct the movement of airflow to the upper airway.
- **Ventilator circuit support:** The weight of the ventilator circuit should be appropriately supported to prevent any stress on the tracheostomy tube. An improperly supported circuit can pull on the tube, potentially dislodging it or causing the distal part of the tube to rest against the tracheal wall.
- **Patient position:** Certain positions, such as lying flat or turning on one side, can also affect airway patency. Ensuring the patient is positioned to maintain an open airway is essential.
- **Other obstructions:** Measuring the presence and degree of other obstructions, like tracheomalacia, granulomas, stenosis, and edema.
- **Anatomical differences:** Some patients may have inherent anatomical differences, such as congenital malformations, that affect the structure and function of the upper airway.
- **Foam cuff tracheostomy tube:** A foam cuff tracheostomy tube is contraindicated with PMV. The design of the cuff may not allow airflow to move freely, creating an obstruction, therefore considering it unsafe.

Recent Research and Findings

Recent studies have provided valuable insights into the benefits of using the PMV with pediatric patients. Brooks et al. (2019) reported the use of the no-leak PMV is underutilized with infants and children who are medically fragile whether on mechanical ventilation or tracheostomy collar. Most patients who were medically stable met their inclusion criteria and were considered candidates for PMV trial. They defined a successful Valve trial in children without any signs and symptoms of distress during use for at least 5 minutes and with increased tolerance wearing the Valve longer. The goal of the study by Da Cunha de Lima (2017) was to understand the experience of mothers of babies with tracheostomy tubes who resumed breastfeeding with the use of the Passy Muir Valve. Eleven children aged 0-24 months were monitored and assessed by a multidisciplinary team and structured interviews were conducted with the mothers. Mothers reported that the PMV minimized the difficulties in breastfeeding and additional benefits were also realized. The authors concluded that with the Valve on, patients were able to feed safely, manage secretions, experience reduced aspiration, improve coordination of sucking and breathing patterns, vocalize, and experience improved sleep quality.

Enhanced Family-Centered Care

The ability to vocalize is an essential element of communication for infants. The PMV allows for improved family-centered care by allowing families to interact with their infants more meaningfully. Vocalization, even if it's just simple sounds, can have a profound emotional impact on parents and caregivers, helping to promote bonding. Additionally, the PMV helps caregivers feel more confident in managing the infant's respiratory needs and progressing toward oral feeding.

Conclusion

The Passy Muir Tracheostomy & Ventilator Swallowing and Speaking Valves have been adopted as a vital tool in the NICU for improving respiratory function, promoting vocalization, and facilitating the transition to oral feeding in neonates. While the benefits are clear - ranging from improved lung function and oxygenation to enhanced family interactions - careful patient selection, training, and monitoring are crucial for its successful implementation.[4-5] As research continues to explore the full potential of PMV use in neonatal care, it is evident that it holds significant promise in improving both short-term outcomes and long-term developmental progress for critically ill infants.

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Environmental Benefits of Bedside Ionic Nitric Oxide Generation

David Webster and Mark Rimkus RRT, P.Eng

Abstract

Nitric oxide (NO) has been recognized for its therapeutic potential, particularly in respiratory care for conditions such as pulmonary hypertension and neonatal asphyxia. Traditionally, NO is generated industrially, stored in high-pressure cylinders, and transported to healthcare settings. This process, while effective, poses environmental challenges related to production, transportation, and storage hazards. Recent advancements in technology have enabled the bedside generation of inhaled NO using ionic chambers, which extract nitrogen from room air. This paper explores the environmental benefits associated with bedside generation of inhaled nitric oxide over traditional methods.

Introduction

Nitric oxide plays a critical role in various physiological processes, and its inhalation has emerged as a crucial therapeutic intervention in clinical settings. However, the methods of NO generation and delivery can significantly influence environmental sustainability. This paper aims to highlight the environmental impact of traditional high-pressure storage systems compared to bedside generation technologies utilizing ionic chambers.

Traditional Nitric Oxide Generation

Industrial Generation

Nitrous oxide is produced commercially by heating ammonium nitrate to a temperature of 245-270°C. This process creates several compounds, including nitric oxide, ammonia nitrogen, nitrogen and nitric acid which contribute to the Earth's greenhouse gas burden. Additionally, the transport of high-pressure cylinders requires extensive energy, resulting in a carbon footprint associated with logistics and transportation. Finally, the disposal of high-pressure tanks can have significant environmental impacts, including gas emissions, safety hazards, material waste, and chemical contamination.

High-Pressure Cylinder Storage

Storing NO in high-pressure cylinders presents environmental risks such as potential leaks or explosions, which can lead to air pollution and other hazardous situations. The disposal of these cylinders also poses challenges, where improper handling can introduce toxic materials into the environment.

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Bedside Generation of Nitric Oxide With Ionic Chambers

Process Overview

Ionic chambers generate NO by extracting nitrogen from ambient air and utilizing electrochemical processes. This innovative technology not only produces nitric oxide on-demand at the bedside but also eliminates the need for bulky storage tanks.

Environmental Advantages

- **Reduction in Carbon Footprint:** By generating nitric oxide from ambient air, bedside systems significantly reduce the reliance on fossil fuels for both production and transportation purposes, thereby lowering CO2 emissions associated with traditional methods.
- **Elimination of High-Pressure Tank Manufacturing:** The environmental impact of manufacturing high-pressure cylinders, typically used for storing gases like oxygen and nitrogen, involves various stages, from raw material extraction to production processes, and end-of-life disposal. While high-pressure cylinder manufacturing is essential for various industries, its environmental impact can be substantial, efforts towards eliminating tanks where possible are crucial for mitigating its effects.
- **Minimized Transportation Needs:** The implementation of bedside ionic generation alleviates the need for frequent transportation of high-pressure cylinders, reducing logistics emissions and fostering a more efficient use of healthcare resources.
- **Lower Risk of Environmental Hazard:** The elimination of high-pressure storage reduces risks associated with leaks and bursts, minimizing potential contamination of hospital environments and surrounding areas. In cases of fire, high pressure cylinders become very dangerous to hospital staff and firefighters, irrespective of cylinder contents.
- **Sustainability:** Utilizing room air for NO generation aligns with sustainability principles, as it leverages readily available resources, leading to a reduction in resource depletion associated with traditional manufacturing processes.

Conclusion

The shift from traditional industrial generation of nitric oxide to bedside generation using ionic chambers offer significant environmental benefits. The reduction in fossil fuel dependence, lower transportation emissions, decreased risk of hazards, and enhanced sustainability underscore the potential of this technology to promote a greener healthcare paradigm. As the medical community continues to prioritize environmentally friendly practices, the adoption of bedside nitric oxide generation could play a pivotal role in advancing public health while respecting ecological health.

News…continued from page 18
general, stricter measures are often better for younger babies, as that's when pertussis is most serious, Blumberg said.

Preterm Birth Associated With Increased Mortality Risk Through Early Adulthood

Individuals born preterm face an increased risk for death from all causes even into their third and fourth decades of life. Researchers conducted a population-based study in Canada, analyzing data from 4.99 million births that occurred between January 1983 and December 1996, with follow-up through December 2019. The researchers compared preterm births (24-37 weeks gestation) with term births (37-41 weeks), breaking down preterm births into subcategories of 24-27 weeks, 28-31 weeks, 32-33 weeks, and 34-36 weeks. The analysis attempted to account for factors including sex of the child, multiple births, birth province, birth year, parents' ages, maternal marital status, maternal parity, and parental birth origins. Over a median follow-up of 29 years, 72,662 people in the study died, including 14,312 who had been born preterm and 58,350 born at term. The highest risk difference in the rate of death (2.29%; 95% CI, 2.23%-2.35%) and risk ratio ([RR], 11.61; 95% CI, 11.09-12.15) were observed in birth through infancy. Mortality in early childhood (ages 1-5 years) was elevated among preemies (risk difference, 0.34%; 95% CI, 0.31%-0.36% and RR, 2.79; 95% CI, 2.61-2.98). Increased mortality was associated with respiratory, circulatory, and digestive system disorders. The highest risk was found in conditions that start during the perinatal period (hazard ratio, 37.50). Compared with individuals born at term, prematurity was associated with elevated risk differences for death linked to several health conditions, including respiratory problems (2.4), digestive issues (1.7), and nervous system diseases (4.1). The increased mortality risk associated with prematurity declined over the study period but appeared to tick higher in the last decade (RR, 1.30 for all-cause mortality among people aged 29-36 years). "The findings of this cohort study suggest that individuals born preterm were at increased risk of death from birth to their third and fourth decades of life, and the risks were higher with decreasing GA at birth," the study authors wrote. "Some of these associations may have been partly due to underlying health determinants that affected both PTB and mortality. These findings suggest that [preterm birth] should be recognized as a risk factor for mortality and could inform preventive strategies. Additionally, they highlight the need for further follow-up studies to assess possible adverse consequences of [preterm birth] into adulthood. The study was led by Asma M. Ahmed, PhD, MD, MPH, of the Department of Epidemiology and Prevention at Wake Forest University School of Medicine in Winston-Salem, North Carolina. It was published online on November 20, 2024, in *JAMA Network Open*.

Fine Particulate Matter Exposure During Pregnancy Linked to Increased Risk for Spontaneous Preterm Birth

Exposure to fine particulate matter ($PM_{2.5}$) during pregnancy is associated with an increased risk for spontaneous preterm birth, with peak vulnerability in the second trimester. Lower socioeconomic status, limited green space exposure, and extreme heat amplify this risk, whereas living around more trees provides protective effects. The researchers conducted a population-based retrospective cohort study to examine the associations of exposures to total $PM_{2.5}$ and five constituents

Continued on page 35…

Revolutionizing NICU Care With Ultrarapid Whole Genome Sequencing and CNGnome® NGS Array

Christin Collins, PhD, FACMG

Introduction

The neonatal intensive care unit (NICU) is a high-stakes environment where every minute counts. For critically ill newborns, rapid and accurate diagnosis can be the difference between life and death. Many of these infants present with complex, rare, or undiagnosed genetic conditions, leaving healthcare providers struggling to determine the best course of treatment. This is where Revvity Omics ultra-rapid whole genome sequencing (urWGS) and the CNGnome® NGS array are proving to be game-changers.

The Challenge in the NICU

Newborns in the NICU often present with severe symptoms that could be caused by a wide range of genetic conditions. Traditional diagnostic methods, including targeted genetic testing or biochemical assays, can take weeks or even months to provide answers, leaving families in a dilemma and delaying critical interventions. In some cases, conventional tests fail to yield a diagnosis , prolonging the uncertainty and adding to the emotional toll and financial burden on families.

How Revvity Omics' ultrarapid WGS and CNGnome® NGS Array Work

Whole genome sequencing involves decoding nearly all of an individual's DNA, providing a comprehensive picture of their genetic information. Ultra-rapid WGS goes a step further by optimizing the sequencing process for speed while maintaining accuracy. Through advances in technology, streamlined workflows, and analysis by scientific experts, results can be delivered in a fraction of the time of traditional methods.

The ultrarapid Whole Genome Sequencing offers genome analysis, detection of chromosomal and intragenic copy number events, short tandem repeat screening and *SMN1* copy number characterization while the CNGnome® NGS array offers high- resolution detection of copy number variations (CNVs). This array is designed to provide a detailed view of the genome, identifying even smaller chromosomal variations that might be missed by traditional CNV detection methods. Together, ultrarapid WGS and the CNGnome® NGS array provide a powerful combination for comprehensive genetic analysis in the NICU.

Photo submitted.

Impact on NICU Care

The benefits of integrating ultrarapid whole genome sequencing and CNGnome® NGS array in the NICU can be profound:

1. **Faster Diagnosis:** Ultra-rapid WGS can deliver results in as fast as 5 days, helping healthcare providers to determine diagnosis and initiate targeted treatments sooner. This is especially critical in conditions where early intervention can significantly improve outcomes.
2. **Precision Medicine:** With a clear genetic diagnosis, treatment plans can be tailored to the specific needs of the infant. For instance, identifying a treatable metabolic disorder can lead to life-saving dietary modifications or enzyme replacement therapies.
3. **Avoiding Unnecessary Interventions:** In the absence of a definitive diagnosis, infants may undergo a battery of tests and procedures, some of which may be invasive or risky. A rapid genetic diagnosis can prevent unnecessary interventions, reducing the burden on the baby and the family.
4. **Ending the Diagnostic Odyssey:** Ultra-rapid WGS may bring closure to families who have been searching for answers. Even when the diagnosis is a severe or untreatable genetic disorder, knowing the cause allows families to make informed decisions about care and helps in planning for the future.

Christin Collins, PhD, FACMGG is an ABMGG-board certified clinical molecular geneticist. Dr. Collins is currently a senior laboratory director at Revvity Omics, leading the global clinical reporting team. Previously, she was an Assistant Professor at Emory Medical School and a director of the molecular laboratory at Emory Genetics Laboratory. She received her Ph.D. from the University of Florida, did her post-doctoral fellowship at the Children's Hospital Boston, and completed her clinical molecular genetics training at Harvard Medical School.

5. **Cost-Effective Care:** Although sequencing technology itself is costly, the early diagnosis and precise treatment it may enable can reduce overall healthcare expenses by shortening hospital stays, preventing complications, and minimizing the need for additional testing.

Real-Life Success Stories

Several hospitals and research institutions have already implemented ultra-rapid WGS and the CNGnome® NGS array in their NICUs with remarkable success. In some cases, infants whose health was deteriorating rapidly were diagnosed and treated by healthcare providers within days, leading to improved outcomes.

For example, ultra-rapid WGS in conjunction with biochemical screening reported elevated levels of Propionylcarinitine (C3) and a pathogenic variant in the *PDHA1* gene in a 3-day-old male who presented with hypotonia, significant birth defects, and metabolic acidosis. Healthcare providers were able to determine a diagnosis with the assistance of these results in just 53 hours, allowing for early intervention and significantly improving the child's outcome.

In another case, an 8-year-old male presented with symptoms typical of Kleefstra Syndrome (KS), alongside growth hormone deficiency and unexplained muscular dystrophy. Initial genetic testing through chromosomal microarray (CMA) identified a 9q34.3 microdeletion in the *EHMT1* gene, confirming KS. However, the muscular dystrophy required further investigation. The CNGnome® NGS Array was performed, which allowed healthcare providers not only to confirm the *EHMT1* deletion but also to identify a 119 kb pathogenic deletion in the *DMD* gene, allowing those healthcare providers to diagnose the child with Duchenne/Becker Muscular Dystrophy (DMD).

Key Insights

1. **Missed Diagnosis with CMA**: While CMA detected the EHMT1 deletion, it failed to identify the smaller DMD gene deletion due to limited probe coverage.
2. **Comprehensive Detection with CNGnome® NGS Array**: The CNGnome® NGS Array, with its uniform genome-wide coverage, successfully detected both deletions, illustrating its superiority.
3. **Improved Patient Care**: This comprehensive diagnosis enabled personalized medical management and precise genetic counseling for the family.

These cases highlight the clear advantage of the CNGnome® NGS Array over chromosomal microarray, especially in detecting clinically significant CNVs that might be missed due to the probe design of CMA platforms. Whole genome-based CNGnome® NGS Array offers a non-biased, comprehensive approach to genetic testing, allowing for better diagnostic outcomes and more personalized patient care.

The Future of Neonatal Care

As technology advances and the cost of sequencing continues to decline, ultra-rapid WGS and the CNGnome® NGS array are poised to become standard tools in NICUs worldwide. Efforts are also underway to integrate these technologies into broader healthcare systems, enabling healthcare providers to provide faster diagnoses and better outcomes across various patient populations.

Conclusion

Revvity Omics's comprehensive ultra-rapid Whole Genome Sequencing (urWGS) and the CNGnome® NGS array offer a range of features, including mitochondrial genome sequencing, biochemical testing, cCMV analysis, CNV detection, and more. With a turnaround time of 5-8 days and flexible sample types, including dried blood spots, our services provide a convenient and efficient option for your needs. By helping to reduce the diagnostic timeline for complex genetic conditions in newborns from months to days, these technologies are helping to end the diagnostic odyssey for countless families, offering hope when needed most. As they become more widely available, urWGS and the CNGnome® NGS array have the potential to transform neonatal care and set a new standard for precision medicine in pediatrics.

Disclaimer

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A summary of the prescribing information, including indication and other important safety information, is on the adjacent page. For the full prescribing information, visit www.noxiventus.com.

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NOXIVENT® Indication and Important Safety Information

Indication

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

Important Safety Information

Contraindications

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

Warnings and Precautions

Rebound: Abrupt discontinuation of NOXIVENT may lead to worsening oxygenation and increasing pulmonary artery pressure.

Methemoglobinemia: Methemoglobin levels increase with the dose of NOXIVENT; it can take 8 hours or more before steadystate methemoglobin levels are attained. If methemoglobin levels do not resolve with decrease in dose or discontinuation of NOXIVENT, additional therapy may be warranted to treat methemoglobinemia.

Airway Injury from Nitrogen Dioxide: Monitor nitrogen dioxide (NO_2) levels. Nitrogen dioxide may cause airway inflammation and damage to lung tissue.

Heart Failure: In patients with pre-existing left ventricular dysfunction, Noxivent may increase pulmonary capillary wedge pressure leading to pulmonary edema.

Adverse Reactions

The most common adverse reaction of NOXIVENT is hypotension.

Drug Interactions

Nitric Oxide donor compounds may increase the risk of developing methemoglobinemia.

Administration

Use only with a calibrated, FDA-cleared NOxBOX®$_i$ Nitric Oxide Delivery System (NODS). Refer to the NODS labeling for needed information on training and technical support for users of this drug product with the NODS.

Please see the full Prescribing Information for additional important NOXIVENT® safety and risk information.

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AdventHealth for Children Study Finds 90% Relative Humidity in Dräger Babyleo Significantly Reduces Insensible Water Loss (IWL) in Extremely Preterm Infants (EPTI)

Anduin Anderle, RN

First-of-its-kind study led by Narendra Dereddy, MD offers evidence to support benefits of high relative humidity levels when caring for the youngest and smallest NICU babies.

Executive Summary

Extremely preterm infants (EPTI) are at considerable risk for complications, including those associated with insensible water loss (IWL) given their body mass is primarily constituted of water.

While most neonatal intensive care unit (NICU) teams routinely use a high relative humidity in their incubators to decrease trans-epidermal IWL, there has been little research documenting optimal relative humidity level for the care of EPTI in the first week of life — until now.

This first-of-its-kind study conducted by Narendra Dereddy, MD and his team of researchers at AdventHealth for Children offers evidence supporting the use of very high relative humidity (90%) in the care of extremely preterm babies to reduce IWL.

NICU teams can leverage the study's physiology-based formula to calculate IWL and optimize initial fluid prescription for the babies in their care.

Key Takeaways for NICU Teams

- Researchers at AdventHealth for Children conducted a study to determine impact of humidity levels on insensible water loss (IWL) in extremely preterm infants (EPTI).
- IWL can be significant in EPTI babies, increasing preterm morbidities, such as PDA, BPD and mortality.
- Babies in the study were cared for in Dräger Babyleo IncuWarmers set to 70% or 90% relative humidity.
- IWL was significantly lower in the 90% relative humidity group compared with those in the 70% relative humidity (p=0.009).
- The results of this research provide NICU teams a physiology-based formula they can use to optimize initial fluid prescription based on relative humidity levels in their incubators.

Challenge: Preventing insensible water loss (IWL) in extremely preterm babies

A preterm baby's body is primarily constituted of water, and extremely preterm infants (EPTI) have considerably higher water content and lower lean body mass compared to term infants.[1]

For instance, approximately 90% of the body mass in a 24-week gestation preterm infant is composed of water when compared to 75% in a term neonate and 50% in an adult.[2]

Extremely low birth weight (ELBW) babies experience large trans epidermal water losses immediately following birth.[3] Furthermore, insensible water loss (IWL) may be as high as 60-70 mL/kg/24 hours among EPTI with gestational age of 24-26 weeks.[4]

There is an abundance of published research citing complications that arise from IWL in EPTI/ELBW babies. Such complications include:

- Hypernatremia, which can lead to severe and permanent neurological damage[5]
- Fluid replacement therapy to address IWL can increase the risk for fluid overload and acute kidney injury[6]
- Administration of high amounts of fluid for high IWL may result in a higher incidence of hemodynamically significant patent ductus arteriosus (PDA), and if this persists beyond the first week of life is associated with higher incidence of bronchopulmonary dysplasia (BPD)[7,8]

Therefore, it is critical to proactively address IWL.

Solution: Groundbreaking research finds high relative humidity (70-90%) can reduce IWL

Current clinical practice is to use high relative humidity (70-90%) for EPTI to decrease trans epidermal IWL. The principle behind this practice is fluid replacement for IWL is likely to be:

- Much lower at higher relative humidity levels (70-90%)
- Much higher at lower relative humidity levels (40%)

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*This study was supported by an unrestricted grant from Draeger Inc. Draeger Inc. did not influence the design, conduct, analysis or manuscript preparation of this study.

With no published data on the IWL in EPTI in high relative humidity, Narendra Dereddy, MD and a team of researchers conducted a study to assess how humidity levels of 70% and 90% impacted IWL in preterm infants.*

Study Design

The single center retrospective cohort study included a patient population of 144 infants born between 23-28 weeks of gestation and admitted to the level IV NICU at AdventHealth for Children from October 1, 2016, to December 31, 2022. The babies were cared for in Dräger Babyleo incubators with:

- 83 infants in the 70% humidity group
- 61 in the 90% humidity group

Dr Dereddy and team calculated IWL of study infants between days four and five of life using a formula that utilized each baby's actual fluid intake, urine output and body weight changes over a 24-hour period. The formula is as follows:

IWL (mL/kg/24 hours) = Total fluid intake (mL) – Urine output (mL) – (body weight difference on D4-and D5) ÷ initial body weight (gm).

As noted by the researchers, they calculated IWL between days four and five of life "because we do not weigh the infant during the first three days of life to minimize infant handling and decrease the risk of intraventricular hemorrhage."

If the time interval for fluid data collection between day four and day five weights was not exactly 24 hours, IWL per 24h was obtained by calculating the IWL per hour and multiplied by 24.

The researchers compared IWL between the two groups using an independent t-test. They used multivariate linear regression to assess the effects of humidity on IWL after adjusting for confounding variables.

About the Dräger Babyleo TN500

Humidification System The Babyleo® TN500 IncuWarmer by Dräger features a closed-loop humidification system designed to provide precise and consistent humidity levels for neonatal care. Here are some key points about this system:

- Compartment relative humidity is continually displayed when bed is in closed mode.
- Closed System: The humidification system is completely closed, which helps to prevent germs from entering the humidity reservoir, ensuring a safer environment for the baby.
- Auto Mode: The system can automatically adjust humidity levels based on the temperature settings.
- Manual Mode: For more control, the system also allows manual setting in 1% increments of humidity levels up to 99% relative humidity (RH).
- Ease of Cleaning: Between patients the humidification system can be sterilized when using Auto Clean Mode.

> "The strength of our study is that, although labor intensive, the IWL can be calculated using this physiology-based formula."
>
> – Narendra Dereddy, MD and team

Results

IWL was significantly lower in extremely preterm infants in the 90% relative humidity group compared with those in the 70% relative humidity (p=0.009).

The researchers found that 90% humidity resulted on an average 18 ml/kg/day of decreased IWL compared to 70% humidity.

They adjusted for race, maternal diabetes, gestational age and birth weight and found only humidity levels showed a significant correlation with IWL.

Table 1. Maternal and neonataldemographics and clinical characteristics

	70% Humidity n =83	90% Humidity n =61	p-Value
Maternal Characteristics			
Race			0.033
White	41 (49.4%)	28 (45.9%)	
Black	38 (45.8%)	22 (36.1%)	
Other	4 (4.8%)	11 (18.0%)	
Hypertension	33 (39.8%)	12 (19.7%)	0.010
Diabetes	10 (12.0%)	9 (14.8%)	NS
Antenatal Steroids	56 (67.5%)	45 (73.8%)	NS
Cesarean Birth	62 (74.7%)	46 (75.4%)	NS
Singleton pregnancy	68 (81.9%)	61 (91.8%)	NS
Infant Characteristics			
Gestational age (wk) (mean±SD)	26.7±1.4	25.2±1.9	<0.001
Birth Weight (gm) (mean±SD)	969±230	775±237	<0.001
Male sex	49 (59.0%)	31 (50.8%)	NS
APGAR at 5 min <7	18 (21.7%)	28 (45.9%)	0.002
SGA	5 (6.0%)	6 (9.8%)	NS
Phototherapy	72 (86.7%)	50 (82.0%)	NS

Table 2. Comparison of Insensible water losses and secondary outcomes

	70% Humidity n =83	90% Humidity n =61	p-value
Insensible Water Loss (ml/kg/24h}	46.9±31.7	28.4±39.8	0.002
Late-onset Sepsis	27 (32.5%)	37 (60.6%)	0.001
BPD	25 (30.1%)	20 (32.7%)	NS
PDA requiring treatment	23 (27.7)	21 (34.4%)	NS
Severe IVH	10 (12%)	5 (8.2%)	NS
Mortality	2 (2.4%)	8 (13.1%}	0.03
Severe ROP	2 (2.4%)	4 (6.5%)	NS

Table 3. Univariate analysis of General Linear Model between IWL and each independent variable (n=144)

Variable	Coeff	Std. Error	t	p-value	95% CI	
					LB	UB
Group						
70% Humidity	18.5	4.5	3.11	0.002	6.8	30.3
90% Humidity	Ref					
Race				0.056		
Black	-15.4	6.3	-2.43	0.016	-27.9	-2.9
Other	-8.1	10.2	-0.79	0.430	-28.3	12.1
White	Ref					
Gestational Age	2.9	1.7	1.72	0.087	-0.4	6.3
Birth Weight	0.02	0.01	1.73	0.087	-0.003	0.04
Hypertension	3.8	6.6	-0.58	0.570	-9.2	16.7
Diabetes	-16.7	8.8	-1.88	0.062	-34.2	0.9
SGA	-1.9	11.5	-0.17	0.870	-24.6	20.7
Phototherapy	-4.73	8.5	-0.56	0.577	-21.4	11.9

Coeff - Coefficients
Std. Error - Standard Error
CI - Confidence Interval
LB - Lower Bound
UB - Upper Bound
Ref - Reference

What this means for NICU teams

Given optimal relative humidity level for the care of EPTI in the first week of life has not been well studied, these research findings offer valuable evidence of the benefits of high humidity in decreasing trans epidermal IWL in this patient population.

Most NICUs routinely use a high relative humidity in the incubators to decrease trans-epidermal IWL with the aim of minimizing the total fluids given and decrease the risk of preterm morbidities, such as PDA, BPD and mortality.

The results of this research provide NICU teams a proven formula they can use to optimize initial fluid prescription based on relative humidity levels in the incubator.

Pro Tips for Managing High Humidity

In their published research findings, Narendra Dereddy, MD and his team noted how the risks of very high humidity levels need to be weighed against the benefits of decreasing the IWL.

One risk in using very high relative humidity (90%) is water condensation in the incubators and the potential increased risk of bacterial infections, such as Staphylococcus aureus and Pseudomonas aeruginosa.

The following are Pro Tips from Dräger for managing a high humidity care environment:

- Ensure ambient temperature in the room is at least 72-74 degrees Fahrenheit.
- Make sure the bed is positioned away from any drafts or air conditioning vents.
- When indicated, utilize a bed hood cover. This can help reduce the impact of ambient temperature changes and provide an additional buffer to minimize excessive condensation.
- To warm your Babyleo hood and help reduce condensation, turn on the ClearView Feature. This provides a low output of heat from the radiant warmer to facilitate a "clearer view" of the baby when in a high humidity environment.
- Regularly replace moist linens and positioning aids with warm dry linens. This can help mitigate microbial growth, which can occur in warm moist environments.

Microbiological Investigation Finds Babyleo Auto Clean Function Eliminates Tested Germs

Study conducted by the German Commission for Hospital Hygiene and Infectious Disease Prevention (KRINKO)

The Babyleo's integrated humidification system features an automatic humidifier cleaning (Auto Clean) function. To test the effectiveness of this function, researchers inoculated the Babyleo's water reserve with test germs that have predominantly high resistance to chemical and/or thermal disinfection processes (e.g., Staphylococcus aureus, Pseudomonas aeruginosa).

They ran the Babyleo at 99% humidification for 5-hour test intervals over a period of 5 days with the inoculated water in the reserve. Upon completion of each test series, Babyleo's Auto Clean function performed automatic thermal disinfection of the water boiler.

The germ inoculated water was replaced with clean water and Babyleo was again run at 99% humidification for 5-hour test intervals.

When the condensate was re-examined for test germ residues, the researchers found a complete elimination of the tested germs in all test series.

Conclusion

This study by Narendra Dereddy, MD and his team highlights the importance of optimizing relative humidity levels in neonatal incubators to reduce insensible water loss (IWL) in extremely preterm infants (EPTI).

Their findings support the use of very high humidity (90%) to help NICU teams effectively manage IWL during the critical first week of life, providing a physiology-based formula for calculating and adjusting initial fluid prescriptions.

Their work fills a gap in neonatal care research by offering evidence-backed guidance on the optimal humidity level for reducing IWL and minimizing associated complications in this vulnerable patient population.

However, the study also emphasizes the need for careful consideration of the potential risks associated with maintaining very high humidity levels in incubators, including the increased likelihood of bacterial infections due to water condensation.

NICU teams must balance the benefits of reducing IWL with the potential for infection, implementing appropriate measures to minimize condensation, as outlined in this paper's section, The "Dos" and "Don'ts" of High Humidity.

Incubator features and design play a role in risk reduction as well. For example, the auto clean function of the Dräger Babyleo IncuWarmer had proven effective in eliminating germs of high

risk (e.g., Staphylococcus aureus, Pseudomonas aeruginosa) in a test scenario, as evidenced by the research conducted by the German Commission for Hospital Hygiene and Infectious Disease Prevention (KRINKO).

Furthermore, Babyleo's design helps support effective hygiene practices, including fewer contact surface areas and parts to clean, a flat, even surface that minimizes places for germs to grow, and the ability to raise and lower the mattress for access and visibility to help facilitate cleaning under the mattress.

About AdventHealth for Children

With more than 250 pediatric specialists practicing over 35 pediatric specialties, AdventHealth for Children is a leader in care throughout Central and West Florida. An award-winning destination for pediatric health care, AdventHealth for Children provides a statewide care network with innovative specialty programs, pioneering technologies and unmatched compassion. The health system is consistently recognized as one of the best and safest children's hospitals in the country by *US News & World Report* and the Leapfrog Group.

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News…continued from page 27

(black carbon, nitrate, organic matter, and sulfate) during pregnancy with spontaneous preterm birth. They included 409,037 singleton live births from the Kaiser Permanente Southern California health care system between 2008 and 2018, with mothers having a mean age of 30.3 years at delivery (51% Hispanic). Daily total $PM_{2.5}$ concentrations and monthly data on the constituents in California were obtained; mean exposures during the entire pregnancy and in each trimester were calculated. Spontaneous preterm births were identified through the evaluation of preterm labor visits and were defined as a delivery occurring before 37 weeks following the onset of spontaneous labor, without pregnancy complications, and within 7 days of the last preterm labor visit. The analysis also examined the effect of factors such as race and ethnicity, education, median household income, exposure to green spaces, wildfire smoke, and temperature. Each 2.76 $\mu g/m^3$ increase in total $PM_{2.5}$ exposure during pregnancy raised the risk for spontaneous preterm birth by 15% ($P < .001$), with black carbon showing the highest risk (adjusted odds ratio [aOR], 1.15; 95% CI, 1.12-1.18; $P < .001$). Exposure to $PM_{2.5}$ during the second trimester showed the highest association with spontaneous preterm birth (aOR, 1.10; $P < .001$), followed by that during the third (aOR, 1.09; $P < .001$) and first (aOR, 1.07; $P < .001$) trimesters. Individuals with lower education levels showed a higher risk for spontaneous preterm birth than those with more than 4 years of college education ($P = .003$). Exposure to extreme heat ($P < .001$) and lower exposure to total green space ($P = .003$) increased the risk for spontaneous preterm abortion. "Targeted and preventive public health interventions among these subpopulations with high risk may be critical for minimizing the burden of spontaneous preterm birth," the authors wrote.

Early Bilirubin Screening Identifies Neonates Needing Phototherapy

Approximately 1% of neonates born to O+, antibody-negative mothers qualified for phototherapy within 24 hours of birth, with most identified through routine bilirubin screening. The visual detection of jaundice was not a common trigger for starting phototherapy. Researchers reviewed the birth records of 6098 neonates (≥ 35 weeks' gestation) born to O+, antibody-negative mothers to identify those qualifying for phototherapy within 24 hours of birth. Neonates were screened to determine if they needed phototherapy on the basis of visual jaundice detection and 24-hour bilirubin screening (transcutaneous bilirubin or total serum bilirubin measurements). Phototherapy was initiated based on total serum bilirubin, according to the 2004 guidelines from the American Academy of Pediatrics. ABO hemolytic disease was defined by a positive direct antiglobulin test in offspring with blood type A or B born to O+, antibody-negative mothers. Neonates with total serum bilirubin within 3 mg/dL of exchange transfusion thresholds were identified as those with severe hyperbilirubinemia requiring potential intravenous immune globulin treatment. From the entire cohort, 1% qualified for phototherapy within 24 hours of birth. Early bilirubin screening identified 83% of neonates needing phototherapy at a median postnatal age of 24 hours, whereas 17% were identified using visual detection of jaundice at a median postnatal age of 13 hours. A majority of newborns (81%) who required phototherapy within 24 hours of birth were ABO incompatible and had a positive result on a direct antiglobulin test, highlighting ABO hemolytic disease as a key cause of early neonatal hyperbilirubinemia. Seventeen neonates had total serum

Continued on page 41…

Study Results Suggest Near-Infrared Device Improves Success For Staff With Less Experience

Chris Campbell

Anyone who dreads going for a blood test will recall the pain of a healthcare professional trying to find their vein to insert the needle.

Not fun.

Now imagine how that experience must be for a hospitalized newborn — and their anxiety-filled parents — when a venipuncture is required.

This painful and invasive procedure is a tough job for healthcare professionals in neonatal intensive care units, resulting in far-from-optimal success rates and discomfort for babies.

A 2022 cross-sectional study out of Italy, however, has results that suggest a certain device can improve those success rates, especially for healthcare professionals with less experience, as well as reduce the pain involved in the procedure.

The study by Silvio Ferrario et al was entitled "Near-infrared (NIR) system's efficiency for peripheral intravenous cannulation in a level III neonatal intensive care unit: a cross-sectional study."

Venipuncture is a procedure that delivers nutrients or medication by placing a peripheral venous catheter. It is considered very painful and invasive, and difficult to administer in a NICU setting.

"NIR devices facilitates the visualization of veins to help improve the performance of cannulation in the neonatal population," according to the study authors.

As the study authors wrote, the idea was to test the results using two arms of the neonatal patients, as well as nurses with varying levels of experience. A goal was to see if the nurses with less experience would have improved success with the cannulation.

The other goal is to find a way to reduce the pain for the most vulnerable patients.

"We hypothesised that device use could increase the proportion of success at the first attempt in newborns, independent of the nurse's experience," the author wrote. "Consequently, it could decrease the pain measured using a standard neonatal pain scale during the procedure."

This observational study published results that suggest that using the NIR device did indeed boost the success rate with nurses with less than five years of experience, while reducing pain levels.

Addressing Difficulties

The study authors detailed the difficulties and challenges of peripheral intravenous cannulation for newborns due to the limits of their venous patrimony.

"The veins are thin and deep, and visualisation and tactile sense might be reduced," The authors wrote. "Furthermore, other factors such as the physical status, condition of the skin, weight of the patient, site of the procedure, and the healthcare professionals' abilities can affect cannulation. Nevertheless, peripheral venous cannulation is one of the most commonly used invasive and painful procedures performed for drug administration or obtaining venous blood samples in newborns admitted to the neonatal intensive care unit (NICU).[1] As this procedure is not risk-free, healthcare professionals should

Chris Campbell is the Senior Editor of Neonatal Intensive Care.

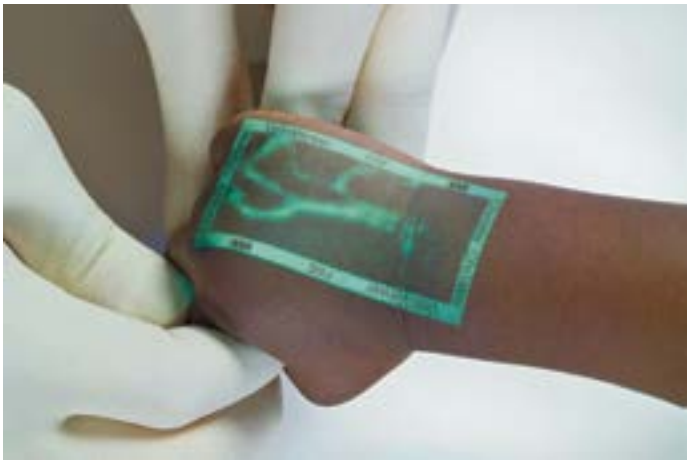


Photo of Christie Medical VeinViewer submitted.

perform it with specific knowledge and abilities.[2,3] On the other hand, cannulation success could also depend on the attempts and ability to visualise veins."[3-5]

Other studies have detailed the kind of pain connected to venipuncture, the study authors wrote, but that stress and pain can be reduced in procedures that are conducted by staff with expert experience.[6-12]

"In recent years, technological development in healthcare settings has led to the use of certain devices such as a transilluminator, ultrasound, and near-infrared light (NIR) device, to aid healthcare professionals in venous cannulation by facilitating the visualisation of veins, thereby decreasing the failure rate and potential complications,"[5,13-16] the study authors wrote. "NIR allows veins to be highlighted because it is absorbed by hemoglobin, facilitating vein visualisation without heating, radiation emission, and contact with the skin."[5,17]

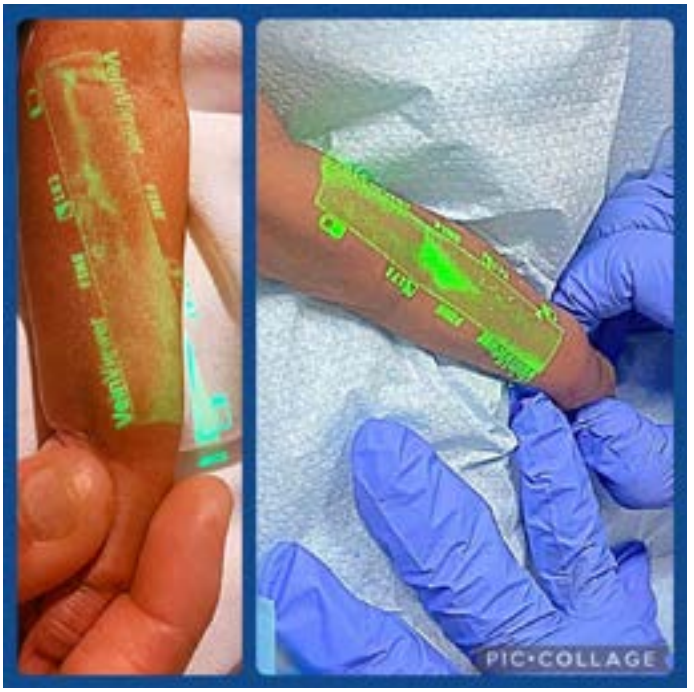
The Study

The observational study was conducted in a NICU of a tertiary-care university hospital in Italy. The study was performed at the NICU of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, which has 23 neonatal intensive care beds and 33 special care beds.

The study only included nurses who worked in the specific NICU. All were experienced in peripheral venous cannulation and trained to use the NIR device, which has been in use a year prior to the beginning of the study.

For the first arm, only nurses with five years of experience in the NICU were involved. For the second arm, all nurses in the NICU were eligible, but only newborns with a minimum body weight of 2,500g. Some nurses had less than one year of experience. A pain response was considered a secondary outcome.

"In the first arm of the study, no statistically significant differences between the NIR and control groups were found in terms of proportion of successful at the first attempt 60.6% (confidence interval [CI] 95%: 48.8; 72.4) vs 56.1% (CI 95%: 44.1; 68.0) and the mean premature infant pain profile score 6.3 (CI 95%: 5.4–7.1) vs 5.8 (CI 95%: 5.0–6.6)," the study authors wrote. "In the second arm, only among less experienced nurses (<1 year), we observed a significant increase in the proportion of success in the NIR group



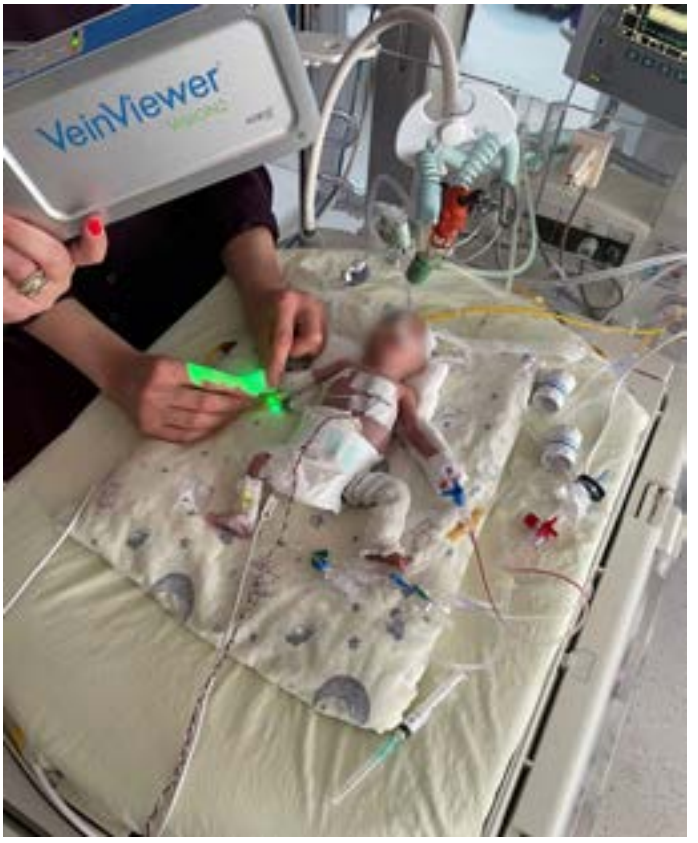
compared with the control group, nearly tripling the success rate (72.7% [54.1; 91.3] vs 23.1% [0.2; 46.0]).”

If more than three attempts were required then that newborn was withdrawn by randomization, and cannulation was performed using the standard method. Venipuncture was performed with a peripheral venous catheter (24 G, BD Neoflon™) if the newborn needed peripheral venous access to administer drugs or parenteral nutrition.

Results

The study authors detailed the results that they found. “Our study demonstrated no difference in the proportion of success at the first attempt and pain response between NIR device use and the standard method for placing a peripheral venous catheter in term and premature newborns admitted to the NICU,” they wrote.

“NIR improved the number of attempts, procedure time, and pain response compared with a transilluminator and the standard method in preterm newborns.[13] In contrast, our data demonstrated that the number of attempts in both groups was similar and inconsistent with those of previous studies. The differences may be related to the fact that the procedures were performed only by a nurse with 10 years of experience and were achieved in newborns without previous venipuncture, while in our study, nurses with varying professional experience and newborns that underwent previous venipuncture were included.”



The authors highlighted the results found with the second arm testing, which included nurses with less experience than those involved with the first arm.

“Our results highlighted that the NIR device helped nurses with lesser than 1 year of professional experience than nurses with more than 1 year of work experience. Thus, it is reasonable to argue that these nurses have less confidence in their ability to place a peripheral venous catheter than experienced nurses.[19] Indeed, Rothbart et al. demonstrated that its use might facilitate cannulation performed by nurses with less experience.”[18]

Conclusions

The study authors did write that their results do have some limitations, saying they can’t necessarily generalize all newborns because healthy newborns weren’t included.

But the results do suggest success in two main areas: helping nurses with less experience and reducing pain in newborns.

“In each case, the pain due to cannulation was low. The results also suggest that using a NIR device may be advantageous for nurses with lesser experience performing cannulation for the first time. Indeed, nurses with less experience were more likely to perform peripheral venous catheterisation with a NIR device than those with >5 years of experience, who had almost the same probability of cannulation success with or without a NIR device. However, these results must be clarified, particularly for the role of body weight, in further studies.”

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Harnessing the Power of Algorithms and AI in the NICU Space

Christopher Rand, CEO

The transformative potential of artificial intelligence (AI) and machine learning (ML) has begun to ripple across industries, and healthcare is no exception. In the highly specialized and emotionally charged environment of the Neonatal Intensive Care Unit (NICU), these technologies are poised to revolutionize both the education of healthcare professionals and the care of the tiniest and most vulnerable patients. From reshaping medical school education to enhancing clinical practice and improving outcomes, AI and ML are becoming indispensable tools in neonatal care.

Medical School Education: Laying the Foundation

Medical students are the future of healthcare, and their training needs to keep pace with advancements in technology. AI and ML offer unique opportunities to deepen understanding, streamline learning, and prepare students for the realities of modern medicine.

1. Personalized Learning: AI-driven platforms can assess individual learning styles and adapt content to suit specific needs. For example, an aspiring neonatologist might use AI tools to simulate complex neonatal cases, honing diagnostic and critical thinking skills in a risk-free environment.

2. Enhancing Diagnostics Training: Medical students can use AI to study neonatal imaging, such as X-rays or MRIs, with algorithms identifying patterns and abnormalities. This exposure helps students develop a sharper eye for diagnostics before encountering real-world cases.

3. Summarizing Research: Keeping up with the rapid advancements in neonatology is challenging, even for seasoned professionals. AI tools like natural language processing (NLP) systems can sift through vast amounts of medical literature, extracting key findings and trends to keep students informed. As highlighted in a recent review on AI in neonatal care,[1] NLP applications have already demonstrated the ability to streamline access to critical knowledge.

By integrating AI into their education, medical students gain not only technical proficiency but also the ability to critically evaluate and apply these tools in practice.

Christopher Rand is the CEO of AngelEye Health. AngelEye Health is advancing NICU care by equipping care teams with tools that optimize workflow while empowering families through a comprehensive suite of engagement technologies.

Photo submitted.

Practical Applications in the NICU

For practicing neonatologists, nurses, and other care team members, AI and ML present game-changing opportunities to enhance patient care. Here are several key applications:

1. Streamlining Research Insights: Healthcare professionals often face the daunting task of staying current with medical advancements. AI-powered systems can summarize recent research findings, highlighting actionable insights for the care team. For instance, algorithms can identify emerging treatments or interventions for preterm infants and present them in a digestible format. This aligns with findings that AI can efficiently synthesize complex datasets to improve clinical decision-making.[1]

2. Enhancing Patient Monitoring: AI can process and analyze vast amounts of data from neonatal monitors, detecting subtle changes that might indicate potential complications. Predictive analytics can alert clinicians to conditions such as sepsis or respiratory distress before they become critical. The aforementioned review also underscores the role of AI in early detection, emphasizing its potential to reduce mortality and morbidity rates in neonates.[1]

3. Reviewing Medical Records: Patient records in the NICU are often dense and complex. AI algorithms can comb through electronic medical records (EMRs), flagging potential issues such as medication interactions, abnormal lab results, or overlooked trends. While human oversight remains essential, AI serves as a powerful second set of eyes.

4. Supporting Decision-Making: Decision support systems powered by AI can help clinicians evaluate treatment options based on patient-specific data. These systems offer evidence-based recommendations, empowering the care team to make more informed choices.

The careful integration of AI into daily practice ensures that these tools augment, rather than replace, the expertise and empathy of healthcare professionals.

AngelEye Health: Pioneering AI in the NICU

At AngelEye Health, we are committed to transforming neonatal care through the strategic application of algorithms, AI, machine learning, and camera vision. Building on our core mission to support NICU care teams and families, we are leveraging these technologies to create smarter, more effective solutions.

1. Neuromotor Screening with EDNA: With the recent acquisition of EDNA (Early Detection of Neuromotor Impairments), AngelEye is advancing the use of AI in assessing infant movement. By analyzing video footage of babies on a specialized mat, EDNA's algorithms identify subtle movement patterns that may indicate neuromotor risks. This innovative approach has the potential to detect issues earlier, enabling timely interventions and improving long-term outcomes.

2. Camera Vision Applications: AngelEye's existing NICU CameraSystem — which allows families to view their babies remotely — is being enhanced with AI capabilities. For instance, computer vision algorithms could analyze video streams to monitor infant activity and detect changes that may warrant clinical attention.

3. Integration with EHR Data: Through our NICU2Home application, AngelEye provides families and care teams access to extensive EHR data. By combining this data with insights from AI-powered video analytics, we can deliver a more holistic view of an infant's health. This integration paves the way for new applications, such as tracking feeding patterns, identifying pain indicators, and monitoring hyperbilirubinemia levels.

4. Partnership with Researchers: AngelEye recognizes the value of collaboration. We are actively engaging with researchers to explore new applications for AI and computer vision in neonatology. By partnering with academic and clinical institutions, we aim to commercialize cutting-edge technologies and bring them to the bedside.

Looking Ahead

The future of AI in the NICU is bright and full of promise. By empowering medical students with AI tools, enhancing the capabilities of care teams, and pioneering innovative applications, we can ensure better outcomes for neonates and their families. AngelEye Health is proud to be at the forefront of this transformation, harnessing the power of algorithms and AI to create a brighter, healthier future for the most vulnerable among us.

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1 PMC Article: https://pmc.ncbi.nlm.nih.gov/articles/pmid/38097685/

News…continued from page 35

bilirubin levels within the exchange transfusion thresholds; 14 of these cases were identified using 24-hour bilirubin screening, and three were identified using early jaundice detection. The total serum bilirubin levels in six of the 17 neonates exceeded the exchange transfusion thresholds, with four cases identified using bilirubin screening. "These data suggest that visual assessment of jaundice is of limited value as a surveillance tool to consistently detect hyperbilirubinemia meriting treatment at ≤ 24 hours after birth," the authors of the study wrote. "Our findings support routine birth hospitalization bilirubin screening and suggest screening no later than 24 hours may be beneficial," they added.

Live Rotavirus Vaccine Safe for Newborns of Biologic-Treated Moms With IBD

More evidence suggests there is little risk in administering the live rotavirus vaccine to the babies of mothers on biologics during pregnancy for inflammatory bowel disease (IBD). No adverse events or impairment of the immune system emerged in babies at 7 days, 1 month, and 9 months postvaccination, in findings from a small Canadian study published in *Clinical Gastroenterology and Hepatology*. The study found normal extended immune function testing in infants despite third-trimester maternal biologic therapy and regardless of circulating drug levels. The data provide reassurance about live rotavirus vaccination in this population and may also offer insights into the safety of other live vaccines in biologic-exposed individuals, wrote investigators led by gastroenterologist Cynthia H. Seow, MD, a professor in the Cumming School of Medicine at the University of Calgary in Calgary, Alberta, Canada. "Despite the well-established safety and effectiveness of non-live vaccination in individuals with IBD, including those on immunomodulators and biologic therapy, vaccine uptake in pregnant women with IBD and their infants remains suboptimal," Seow said in an interview. This largely arises from maternal and physician concerns regarding transplacental transfer of IBD therapies and their impact on the safety of vaccination. "These concerns were heightened after reports emerged of five fatal outcomes following the administration of the live Bacille Calmette-Guérin [BCG] vaccine in biologic-exposed infants. However, it had already been reported that inadvertent administration of the live oral rotavirus vaccine, a very different vaccine in terms of target and mechanism of action, in biologic-exposed individuals had not been associated with significant adverse effects," she said.

Infant's Rash Defies Most Likely Diagnoses

Clinicians should consider zinc deficiency in premature infants having an erythematous, scaly, sharply demarcated rash that does not respond to treatments for the most likely diagnoses. Investigators report the case of a 5-month-old infant born prematurely, at 26 weeks of gestation, brought to the emergency department with a rash. The rash consisted of erythematous, scaly, crusted skin lesions of the head, neck, and perineal and genital areas; other symptoms included irritability and diarrhoea. The initial differential diagnosis included eczema, allergy, and infection. The infant's history was noteworthy for exclusive breastfeeding, chronic lung disease of prematurity, recent bronchiolitis, and psoriasis in a paternal aunt. The rash was non-responsive to systemic antibiotics (for suspected superinfected eczema), exclusion of dairy from the mother's diet (cow's milk protein allergy), topical emollients and steroids (eczema), topical miconazole and oral nystatin (fungal infection), oral aciclovir (viral infection), and repeated oral co-

Continued on page 57…

Shared Decision-Making in the NICU Should Include Nutrition

Medicine is at its best when it listens — not just with a stethoscope, but with the heart

Cristal Grogan, Cristina Harrison, Dr Erin Hamilton Spence, Dr Sandra Sullivan, Dr Melinda Elliott

Introduction

There is nothing quite as disorienting for new parents as sitting by their infant's isolette surrounded by a sea of wires and numbers while conversations swirl around them that they barely understand. In the neonatal intensive care unit (NICU) — a space where parents feel like so much is out of their control — shared decision-making (SDM) is a lifeline. When SDM becomes part of the NICU culture, it promotes a partnership where families and the care team work together toward the same goal. In this kind of trusting relationship, parents can feel confident in the recommendations being made, ask questions without fear or hesitation, and lean on their care team's expertise. The care team gains a valuable resource in the form of an engaged and educated partner, and the parents gain the connection and trust that makes the unimaginable feel just a little more bearable.

Cristal Grogan is a preemie parent who has worked with the NICU and Special Needs community for over a decade. She has advanced education and awareness through prominent organizations, including NICU Parent Network, National Perinatal Association, Hand to Hold, NICU Helping Hands, and now serves as the Parent Outreach and Event Associate at Prolacta.

Cristina Harrison is a passionate neonatal intensive care nurse with more than 21 years in the field. She holds a Master's in Nursing Leadership and Administration, is board certified in Nursing Professional Development, and certified in Neonatal Intensive Care. She is a consultant for Prolacta.

Erin Hamilton Spence, MD, NABBLM-C, IBCLC, FAAP, FABM is Director of Clinical Education and Professional Development at Prolacta. As a NICU parent and experienced neonatologist, she has a proven track record of clinical leadership in some of the nation's leading NICUs and a strong background in community-based milk banking.

Sandra Sullivan, MD, IBCLC, FAAP, was recently appointed as Director of Clinical Education and Professional Development at Prolacta. She continues to practice neonatology and breastfeeding medicine part time with Envision Healthcare. Dr. Sullivan is a dedicated advocate for trauma-informed and family-centered care, working to improve outcomes for patients and families through education and compassionate care.

Melinda Elliott, MD, FAAP, is Chief Medical Officer at Prolacta. She serves as the voice of the patient, working to ensure that the needs of premature infants are being articulated and that relevant treatment and product opportunities are identified. She also continues to serve as a clinical neonatologist with the Pediatrix Medical Group.

In some contexts, the need for SDM is obvious, such as initiating a new medication or considering surgery. But it is important to remember that food is as important as medicine in the NICU. Thus, the nutrition strategy must absolutely be discussed in collaboration with parents to fully embrace SDM in the NICU.

The Importance of Shared Decision-Making in the NICU

In the highly medicalized environment of a NICU, decisions are complex and the stakes are high. Interventions that are routine for the NICU care team may be extremely stressful, even traumatic, for parents.[1] When parents feel excluded, decisions can often feel like they're happening to them, not with them. When the NICU care team takes the time to sit with parents, not only to explain the current situation and potential outcomes but also to listen to their concerns and perspectives, parents feel truly seen, heard, and valued. It conveys much-needed empathy as well as the message that the parents' voice matters and that everyone is in this together. In this context, parents' role is magnified instead of diminished. Instead of feeling like an outsider in their infant's care, they feel like an empowered and informed partner.

Parents are an often untapped resource in the NICU. They are present day in and day out, watching, worrying, and hoping. They notice when their infant's breathing changes ever so slightly or when a particular position seems to bring comfort. They observe minute changes that may not be picked up by monitors or test results. SDM promotes a cooperative relationship between parents and the NICU care team, which offers the opportunity to take advantage of a very dedicated and tuned-in extra set of eyes, ears, and hands.

Ultimately, it is parents who hold the final responsibility for their infant's care and well-being. They cannot be fully informed unless they understand the benefits and risks, are aware of alternative options, and know the reasoning behind key decisions. When parents are well-informed and fully understand all factors and considerations, they are better equipped to make decisions that align with their values and priorities while supporting the NICU team. This preparation empowers them to make difficult choices during a crisis. Thus, SDM recognizes that NICU decisions must be clinically sound while acknowledging they are also deeply personal.

NICU parents often have strong feelings about the care their infant receives. By working with them on the care plan and sharing decisions with them every step of the way, hospitals

Baby Aria born at 27 weeks, weighing 630 g.

Baby Aria post-NICU, 6 weeks adjusted weighing 2778 g.

can help to ensure they support the care plan. SDM helps even the playing field for overwhelmed or intimidated parents. It reinforces the reality that while the care team provides medical expertise, parents bring the invaluable expertise of knowing their infant best. This empowers them to show up informed, engaged, and ready to advocate.

The difficult truth is that when parents don't feel well-informed by their NICU care team, they often seek information elsewhere — on the internet, social media, or online forums. Though well-intentioned, this can lead to misinformation, confusion, and mistrust in the care team. When parents feel excluded, they are more likely to make requests or demands that may not align with evidence-based care. Adopting SDM helps prevent this by keeping families informed, engaged, and aligned with the care team, reducing frustration for everyone involved.

The Role of SDM in Decisions About Nutrition

Within the NICU setting, the right nutritional protocol is vital. An optimal feeding protocol has been shown to have a profound impact on growth,[2] short-term morbidity and mortality,[3] as well as long-term outcomes[4-7] among premature infants born very low birth weight (VLBW). SDM in the NICU means that parents understand that feeding in the NICU isn't just about calories; it's about survival, growth, and setting the stage for a healthier future. Yet feeding protocols are treated like a checklist instead of a conversation. Parents need to be part of that discussion because feeding, like so many other decisions made in the NICU, is personal. These decisions carry weight, and families deserve to understand their options, share their goals, and feel confident that they are making the best possible decisions for their infant.

SDM means that NICU parents are informed that human milk, in the form of mother's own milk (MOM) or donor milk (DM), represents the nutritional standard of care.[8,9] For VLBW infants, however, fortifier must be added for them to grow and develop in a healthy way.[10-12] For parents in the NICU, understanding why fortification is necessary can feel overwhelming at first. They are often told that breast milk is the gold standard for feeding and provides unmatched protection and nutrients, but what isn't always discussed is why breast milk is not always enough on its own for these fragile babies to grow and develop in a healthy way. Being educated and understanding the "why" behind fortification helps parents feel more confident in these decisions and reinforces the importance of balancing nutrition and safety.

SDM in the NICU also means that parents understand the real risks associated with fortification and how the type of fortifier used can help mitigate those risks.[13,14] This is particularly important for the most fragile infants, born weighing 1250g or less. Among these infants, for instance, using fortifier made exclusively from human milk, when combined with MOM or DM, has been shown to reduce mortality, necrotizing enterocolitis (NEC), as well as other complications.[3,13-19] In addition, VLBW infants fed an exclusive human milk diet (EHMD) using human milk-based fortification have been shown to have better growth metrics,[20,21] particularly when fortification is started early,[22] as well as improved long-term neurodevelopmental outcomes.[4]

Human milk-based fortifiers can be pasteurized in a manner that preserves human milk bioactivity (eg, via vat pasteurization). When this type of fortifier is added to DM, it replenishes bioactive factors that are sometimes lost in processing of the DM.[23] These bioactive factors promote absorption of key nutrients[24] protect against infection,[24-27] and promote healthy development of the gut and the immune system.[28-30]

Despite this evidence, not all NICUs offer human milk-based fortifiers for VLBW NICU infants. Parents cannot advocate for something they don't know exists. In those early days of the NICU stay, when every decision feels impossibly heavy, and they are trying to hold onto hope, what they don't know can leave them feeling helpless. By understanding the differences in

fortifiers, parents can ask the right questions, have meaningful conversations with the care team or hospital administration, and participate in the decisions that impact their infant's care. It's not about questioning the expertise of the NICU team; it's about being informed partners in this journey.

A clear, detailed discussion about nutrition and the use of fortifiers or macronutrient additives helps prevent unnecessary panic by offering insight into why a specific nutritional plan was chosen. Human milk is the gold standard, but there is a time and a place for fortifier made from either cow milk or human milk. These are decisions that should be individualized to each patient.

Equipped with knowledge about nutrition in the NICU, parents are empowered to ask, "What type of fortifier are you using? Why was that choice made? Is an EHMD an option for my baby?" These questions aren't confrontational—they're collaborative. Parents demonstrate to the care team that they are not only loving caregivers but also informed advocates, fully engaged and invested in their infant's future.

Providing the best available nutritional care for VLBW NICU infants is not just about offering human milk-based fortifiers. The specific feeding protocol used can also affect outcomes.[20,31] In the NICU, every detail counts, and the smallest decisions, the ones parents don't even know they can question, may be the ones that make the biggest difference. Understanding different feeding protocols doesn't mean parents need to become nutrition experts overnight—just as they're not expected to master the complexities of respiratory care and ventilatory support. Instead, it's about recognizing that, just as the choice of a ventilator and its settings are carefully tailored to a baby's specific needs, not all fortifiers are the same—and how they're used can make a critical difference. Every NICU has its own approach to feeding and nutrition. For parents, understanding why the NICU has chosen a specific protocol can help build trust and reduce uncertainty. Whether the NICU uses human milk-based or cow milk-based fortifiers, offers an EHMD, or manages feeding intolerance in a particular way, it's crucial for parents to know how these decisions are made and how evidence informs those choices.

Overcoming Barriers to SDM in the NICU

Within the NICU, adoption of SDM can often be hampered by the highly technical and medicalized environment, combined with the fact that parents are under extreme stress. Parents recognize that the NICU staff has the most knowledge and may feel too intimidated to ask questions or challenge decisions. If, for any reason, the relationship between parents and the care team breaks down, efforts at collaboration can quickly become fraught.[32]

NICU staff can promote SDM by integrating a psychologist into the team, who can provide the emotional support and empathetic ear that parents need. Skills training for the NICU staff also can be helpful, so that they understand the importance of educating parents about their infant's care and feel empowered to initiate difficult conversations in a way that is collaborative rather than prescriptive.[32] NICUs should consider reaching out to advocacy organizations, such as the Family-Centered Care Taskforce, a collaborative initiative dedicated to quality improvement in NICU family-centered care that offers education free of charge. Training in trauma-informed care can be obtained from organizations such as Caring Essentials.

Conclusions

NICU parents do not get to choose the journey, but they do get to choose how they show up for their infants. More often than not, they are scared but strong, overwhelmed but determined, and feel powerless in a very unfamiliar setting. In this whirlwind, one thing remains true: they are responsible for their infants. When the alarms quiet, the doors close, and the care team steps away, their infants belong to them alone. That responsibility comes with a fierce love and a deep need to understand—to be informed, to participate, and to have a voice in decisions that will shape their child's future. That's why SDM isn't optional—it's essential.

SDM means educating parents about all decisions that could impact their infant's outcomes, including nutrition protocols. By including parents in critical conversations about fortifiers, protocols, and feeding strategies, the care team isn't just providing exceptional medical care. They are building trust, empowering families, and nourishing partnerships that ripple far beyond the hospital walls.

When parents understand the options, they step out of the shadows of helplessness and into a place of agency. And in the chaos of the NICU, agency is everything. It allows them to stand tall, to participate, and to know they did everything they could for their infant. That's a powerful thing.

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New Product Spotlight: Nurse Angele's Wipes™

Jessica Harnish, MSN, NNP-BC, President and Inventor WarriorNP

Nurse Angele's Adhesive Remover™ and skin massage wipes are 100% non-toxic, organic, medical-grade virgin coconut oil, individually packaged for single-patient use. (Table 1) Invented by a Neonatal Nurse Practitioner and a NICU RN, they are designed for the safe, easy, and pain-free removal of medical adhesives, such as tape, electrodes, stoma wafers, hydrocolloids, silicone adhesives, bandages, and wound or surgical dressings, while also minimizing the risk of epidermal stripping and medical adhesive-related skin injuries. Nurse Angele's Wipes™ are the only non-toxic adhesive remover on the market today. In addition to adhesive removal, Nurse Angele's Wipes™ may be used for infant massage, helping to decrease trans-epidermal water loss (TEWL), assist with weight gain, aid in the prevention of sepsis, and reduce medical device-related pressure injuries.

Virgin coconut oil (VCO) is an edible oil extracted from mature coconuts. It is a colorless, water-insoluble liquid obtained through both hot and cold extraction processes.[26] VCO is composed entirely of medium-chain fatty acids (MCFAs), which are a source of highly efficient cellular food: caprylic acid C-8:0 (8%), capric acid C-10:0 (7%), lauric acid C-12:0 (49%), myristic acid C-14:0 (8%), palmitic acid C-16:0 (8%), stearic acid C-18:0 (2%), oleic acid C-18:1 (6%) and 2% of C-18:2 linoleic acid.[22] VCO is believed to have medicinal qualities, including but not limited to antifungal, antioxidant, antibacterial, antiviral, hepatoprotective, low glycemic index and immune system-enhancing properties.[23]

The skin is one of the most important organs at birth, responsible for the following functions: (1) barrier protection against water loss and absorption control of substances, including light; (2) temperature regulation; (3) acid-mantle formation and infection control; (4) water and electrolyte regulation; and (5) tactile sensory function. Therefore, during the first days and months of life, neonatal skin care focused on protection and integrity is an essential component to nursing care for both healthy and sick newborns. The overall goal of skin care is to prevent skin alterations, including injury, and the accompanying morbidities, such as dehydration and nosocomial infection.[1]

Topical oil massage is routinely practiced in many countries. For hundreds of years, populations, especially in the Indian subcontinent, have routinely applied natural oils to the skin of newborns. The practice of oil massage has also gained favor in neonatal intensive care units in the developed countries.[2] The putative benefits to the newborn are twofold: those related to the oil application itself, and those related to the tactile kinesthetic stimulation from the massage. Topical oil application has been shown to improve skin barrier function, thermoregulation and is also suggested to have a positive effect on growth.[3,4]

Topical emollient application is known to reduce TEWL in preterm neonates. Results from a study conducted by Nangia et al. (2015) support this claim. Based on significantly lower TEWL, favorable skin scores, and low colonization rate in the oil group in this study population of preterm VLBW neonates, it can be concluded that coconut oil application reduces TEWL, improves skin maturity and integrity without compromising the sterile milieu of the baby and thus can be recommended to be used in small preterm neonates in the NICU.[12]

When coconut oil is applied topically, the cells absorb the MCFAs, converting them into energy, thus promoting weight gain. Therefore, it can be used for nutritional purposes and faster weight gain in low-birthweight (LBW) infants.[11] Oil massage for newborns has been reported to improve weight gain by enhancing thermoregulation, with transcutaneous absorption suggested as a possible mechanism. A recent study compared the effects of massage with coconut oil versus mineral oil and placebo (powder) on growth velocity and behavior in preterm infants.[6] Coconut oil massage resulted in significantly greater weight gain velocity as compared to mineral oil and placebo in the preterm infants' group. The preterm infants receiving coconut oil massage also showed a greater length gain velocity compared to the powder group. A similar study compared the effects of essential fatty acid (EFA)-rich safflower oil and saturated fat-rich coconut oil on the fatty acid profiles of massaged infants.[10] Post-oil triglyceride values were significantly increased in both oil groups and the control group. However, the increase was significantly greater in the oil groups as compared to the control group. Fatty acid profiles (gas chromatography) suggested a significant increase in EFAs (linoleic acid and arachidonic acid) in the safflower oil group and saturated fats in the coconut oil group. This study showed that topically applied oil could be absorbed in neonates and is probably available for nutritional purposes. The fatty acid constituents of the oil can influence changes in the fatty acid profiles of the massaged babies.[5] The skin of a preterm baby allows significant absorption of fat, as it is thinner and more vascular.[7,8] This may also result in greater caloric intake and hence better weight gain.[9] The greater weight gain documented by several investigators is associated

Provided by WarriorNP, 2211 South Telegraph Road, #7230 Bloomfield Hills, MI 48301. jessica@warriornp.com

Table 1. Safety Data Sheet

SAFETY DATA SHEET

According to OSHA Regulation 29 CFR 1910.1200

SDS No: 1162 **Revision No:** 00 **Date of Revision:** 02/14/24

SECTION 1: IDENTIFICATION OF PRODUCT AND OF THE COMPANY

- **Product Name:** NURSE ANGELE'S ADHESIVE REMOVER WIPES
- **Product Code:** F8103PKT [101343-OG]
- **Relevant identified uses:** Cleaning
- **Contact:** regulatory@diamondwipes.com
- **Company Telephone/Fax No:** 909-230-9888 / 909-230-9885
- **Emergency Contact No:** Infotrac Domestic: 1-800-535-5053
  Infotrac International: 1-352-323-3500

SECTION 2: HAZARD IDENTIFICATION

- **CLASSIFICATION:** This product is not classified using OSHA GHS SDS HAZCOM Standard
- **LABELING**

Signal Word:	N/A
Hazard Pictogram	N/A
Hazard Statement:	N/A
Precautionary Statements	Keep out of reach from small children

SECTION 3: COMPOSITION / INFORMATION ON INGREDIENT

Ingredient	CAS #	%
Coconut Oil	**8001-31-8**	**> 99.00**

This product does not contain carcinogens as listed by NTP, IARC, or OSHA.

SECTION 4: FIRST AID MEASURES

- Skin: This product is expected to contact with skin. If irritation is experienced, discontinue use of product. If discomfort persists, seek medical attention.
- Eye: Hold eyelid open and flush with water for at least 15 minutes. If irritation persists, seek medical attention.
- Ingestion: Wipes may present a choking hazard. Accidental ingestion may necessitate medical attention.
- Inhalation Not likely to be inhaled. If symptomatic, remove to fresh air.

SECTION 5: FIREFIGHTING MEASURES

- Flammability Classification: Non-flammable
- Extinguishing Media: Carbon Dioxide, dry chemical powder, water spray
- Special Fire Fighting Procedures: None required
- Unusual Fire and Explosion Hazard: None known

SECTION 6: ACCIDENTAL RELEASE MEASURES

- **For non-household setting:** Prevent entry into waterways, sewers, or confined areas. It is preferable to contain and collect large spillages with non-combustible absorbent materials and place in a clearly labeled suitable container for disposal in accordance with local waste control laws.
- **For household setting:** Pick up wipe and place in a suitable container for disposal

SECTION 7: HANDLING AND STORAGE

- Use according to package label instructions.
- Keep out of reach of children except under adult supervision. Keep in cool storage.

SECTION 8: EXPOSURE CONTROLS / PERSONAL PROTECTION

- This is a personal care product that is safe for all users under normal and reasonably unforeseen use.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES (of the liquid absorbed on the wipes)

- Appearance: Clear oily liquid, impregnated into white nonwoven material
- Flash Point >104 ^{O}C (220 ^{O}F)
- Vapor Pressure: Not determined

SECTION 10: STABILITY AND REACTIVITY

- **Stability:** Stable
- **Materials to avoid:** None expected
- **Conditions to Avoid:** Avoid freezing or excessive heat
- **Hazardous Decomposition Products:** None

SECTION 11: TOXICOLOGICAL INFORMATION

- No data is currently available. This product has not been tested on animals to obtain toxicological data. There are toxicological data for the components of this product which are found in the scientific literatures.

SECTION 12: ECOLOGICAL INFORMATION

- No data is currently available. The components of this product are expected to be safe for the environment at concentrations predicted under normal use and accidental spill scenarios. Packaging components are compatible with the conventional solid waste management practices.

SECTION 13: DISPOSAL CONSIDERATIONS

- Dispose wipes and packaging according to state, local, and federal regulations.

SECTION 14: TRANSPORT INFORMATION

- **Ground Shipping Name (US DOT):** Not regulated as hazardous for transport
- **Air Shipping Name (IATA):** Not regulated as hazardous for transport
- **Ocean Shipping Name (IMDG):** Not regulated as hazardous for transport

SECTION 15: REGULATORY INFORMATION

- The product described in this Safety Data Sheet is regulated by the Federal Food, Drug and Cosmetic Act and is safe to use as per directions on container, box or accompanying literature (where applicable)
- All of the components of this product are listed on the TSCA Inventory or exempted from TSCA.
- California Proposition 65 Warning: This product does not contain substances known to the State of California to cause cancer, birth defect, or other reproductive harm, at levels which would require a warning under the statute

SECTION 16: OTHER INFORMATION

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as guidance for the safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific materials designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

with 3-6 days' shorter hospital stays. A recent cost-benefit analysis suggested a hospital cost savings of approximately $10,000 per infant (or 4.7 billion dollars across the 470,000 preterm infants born each year).[21]

The structure and function of infant skin are not fully developed until 34 weeks of gestation, and this immaturity is associated with an increased risk of late-onset sepsis (LOS).[19] Ghouri et al. (2023) investigated the effect of topical coconut oil emollient on the skin microbiome in preterm infants born at <30 weeks of gestational age. The coconut oil intervention was associated with lower bacterial diversity within samples and an overall increase in the density of colonization with *Coagulase Negative Staphylococcus* (*CoNS*). The reduction in diversity with age is likely due to a combination of host and environmental factors. *CoNS* secrete products, such as lipoteichoic acid and proteases, that enhance skin barrier function and immunity,[13] limiting colonization by *S. aureus* and other pathogenic microbes. Hence, the increased abundance of the *Staphylococcus* genus may play an important role in the development of the skin's immune function and in competing with other microbes. Ghouri et al. (2023) previously reported that the implementation of topical coconut oil skin care in their NICU was associated with a lower frequency of late-onset sepsis, without a change in the pattern of causative organisms.[14] The reduction in late-onset sepsis due to coconut oil may be related to a key component of coconut oil, monolaurin, a chemical made from lauric acid. They previously demonstrated that, in preterm infants, topical coconut oil administration resulted in higher plasma monolaurin levels compared to skin care without coconut oil,[15] with potential direct antimicrobial and immunomodulatory effects. Monolaurin inhibits toxin production and biofilm formation in several bacteria, including *Staphylococcus aureus.*[16,17] *Staphylococcus aureus* has previously been reported to be inhibited by monolaurin in coconut oil.[18]

Due to immaturity, the nose of preterm infants can easily be injured, even with a short application of a nasal device. However, 20% to 60% of preterm infants suffer nasal damage while using nasal continuous positive airway pressure (NCPAP) due to weak skin tissue, prolonged use of nasal devices, and improper nursing practices, leading to increased risk of infection and decreased compliance and tolerance. Fifty percent of newborn medical device-related pressure injuries (MDRPI) occur on the nose, which is also the most common site. Using moisturizing oil to massage the nose during the switching period can moisturize the skin, protect the stratum corneum, and enhance the epidermal barrier function.[20] (Table 2)

Table 2. Guidelines for Use of Nasal Continuous Positive Airway Pressure

- Bubble CPAP therapy will be initiated with a mask interface.
- The Respiratory Therapist will alternate between mask and prong interfaces every 3 hours unless the patient is on minimal touch the interface changes will occur Q6 (Sivandan & Ballambattu, 2022).
- The Respiratory Therapist will coordinate touches and repositioning of all patients with bedside RNs.
- The patient's skin integrity will be assessed. The device will be completely removed once per shift and a brief assessment will be completed every 3-6 hours with interface changes.
  - Tip of the Nose
  - Nares
  - Nasal Septum
  - Nostrils
  - Bridge of the Nose
  - Nose shape
  - Upper lip
  - Forehead
  - Scalp
- Respiratory Therapist will gently massage any area that the interface rests on including nasal areas, bridge of nose, forehead, and upper lip using **Nurse Angele's Wipes**™ every 3-6 hours with interface changes (Fu, Li, Li, & Shi, 2024).

In conclusion, Nurse Angele's Wipes™ can be used for numerous applications in the NICU and for patients of all ages. By incorporating our product into practice, institutions can take a significant step in safeguarding the health and well-being of their staff and patients, while limiting exposures to harmful adhesive remover chemicals. For more information, or to order free samples, please visit www.warriornp.com/nurse-angeles-wipes

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Neonatal Thermoregulation: A Critical Intervention in the 'Golden Hour'

Constance Girgenti, MSN, RN, VA-BC

Thermoregulation is paramount in the care of preterm infants, particularly during the "Golden Hour," the first hour of life. Maintaining an optimal body temperature (36.5-37.5°C or 97.7-99.5°F) is one of the first and most crucial interventions to improve neonatal outcomes. However, preterm infants face significant challenges in achieving thermal stability due to their physiological immaturity and environmental factors.

Challenges in Thermoregulation for Preterm Infants

Preterm infants are particularly vulnerable to hypothermia due to several physical factors:

- Inadequate stores of subcutaneous fat, which serves as insulation.
- Limited brown adipose tissue, impairing their ability to generate heat.
- An inability to shiver.
- An immature epidermal barrier and unbalanced skin surface-to-weight ratio.

Environmental factors further exacerbate heat loss through:

1. **Convection** – heat loss to surrounding air.
2. **Conduction** – heat transfer to colder surfaces in direct contact.
3. **Evaporation** – loss of heat as water evaporates from the skin.
4. **Radiation** – heat loss to cooler objects not in direct contact.

Incidence and Impact of Hypothermia

Hypothermia remains a significant concern for neonatal morbidity and mortality. Upon admission to the NICU, hypothermia is common, with the following incidence rates:

- Over 56% of infants weighing < 750g.
- Over 25% of infants weighing ≤ 2500g.

For every 1°C (1.7°F) drop in admission temperature, the odds of late-onset sepsis increase by 11%, and the risk of death rises by 28% (Lyu et al., 2015). Alarmingly, more than 40% of infants at 24 weeks of gestation have an admission body temperature below 35°C (Bell et al., 2019). Zanelli et al. (2021) emphasize the importance of tailored thermoregulation strategies to prevent heat loss and improve outcomes in preterm infants.

Risks Associated with Hypothermia

Hypothermia in neonates leads to several short- and long-term complications, including:

- **Metabolic Acidosis:** The increased metabolic demand due to hypothermia can lead to lactic acidosis.
- **Respiratory Distress:** Hypothermia can exacerbate pulmonary issues by increasing oxygen consumption.
- **Hypoglycemia:** The neonate's glucose stores are rapidly depleted as their metabolism accelerates to generate heat.
- **Neurological Damage:** Prolonged hypothermia may impair brain development and increase the risk of intraventricular hemorrhage.
- **Mortality:** The correlation between hypothermia and neonatal death underscores the critical need for effective interventions (World Health Organization [WHO], 2022).

Benefits of Achieving Normal Thermoregulation

When normal thermoregulation is achieved, neonates experience improved outcomes across various health domains:

- **Reduced Mortality Rates:** Maintaining a stable body temperature is associated with significantly lower neonatal death rates (Anderson et al., 2020).
- **Enhanced Growth and Development:** Proper thermoregulation minimizes energy expenditure, allowing for better utilization of nutrients for growth.
- **Lower Risk of Infections:** Maintaining normothermia reduces the risk of late-onset sepsis, a critical concern in preterm infants (Smith et al., 2018).
- **Improved Neurological Outcomes:** Stable thermal environments support optimal brain development during critical early-life stages.
- **Efficient Respiratory Function:** Normothermia decreases oxygen demand, reducing the workload on immature lungs.

Current Interventions and Limitations

To combat heat loss, radiant warmers, transport beds, prewarmed surfaces, and plastic wraps or bags are routinely employed. These interventions, while inexpensive, are not without limitations. Plastic wraps and sandwich bags, though widely used, are off-label and often ineffective. When wraps are opened for umbilical catheter placement or physical assessments, significant heat is lost via convection and evaporation.

Constance Girgenti is an influential nurse leader renowned for her expertise in NICU care, particularly in advocating for human milk and advancing vascular access. She is a sought-after speaker at conferences worldwide and has authored publications on vascular access. Connie has received prestigious awards, including the AVA 2016 "Impact Award" and the Lasallian Nursing Graduate Award in 2021. She is also a distinguished member of Sigma Global Nursing Excellence.

An Innovative Solution

The development of a thermoregulation suit offers a more dignified and effective solution for these vulnerable patients. This suit includes an attached hat to minimize head heat loss, a foam pad for proper positioning, a central opening for umbilical catheter access, and double-layered protection to address all four environmental heat loss mechanisms. Unlike makeshift solutions, this suit is specifically designed for preterm infants, ensuring a comprehensive approach to thermoregulation.

Conclusion

Hypothermia prevention is a vital component of neonatal care, particularly for preterm infants. While traditional methods like plastic wraps may provide some protection, innovative and purpose-built solutions are needed to address the multifaceted challenges of neonatal thermoregulation. By prioritizing thermal stability, we can significantly improve outcomes for our tiniest and most vulnerable patients.

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Extracorporeal Membrane Oxygenation for Chinese Neonates With Severe Respiratory and Cardiac Failure

Xiao-Juan Zhang[1], Ying-Yue Liu[2], Hui Wang[2] and Xiao-Yang Hong[2,3*]

Introduction

Extracorporeal membrane oxygenation (ECMO) is a life-saving procedure for critically ill neonates with severe cardiac and/or respiratory failure and refractory to maximal conventional management. The primary function of ECMO is to act as a surrogate for the cardiopulmonary system of a patient, facilitating the circulation of oxygenated blood throughout the body. Now ECMO remains an important support treatment tool for neonates with reversible congenital cardiopulmonary diseases.[1,2] The use of ECMO to support neonates with cardiorespiratory failure in China has a relatively recent change in care strategy. The overall survival rate in cardiac ECMO is lower, with congenital heart defect representing the main indication. This review provides an overview of the available evidence in the field of neonatal ECMO. ECMO is a life support with a potential impact on long-term patients' outcomes. In the past years, clinical technology, and expertise have push neonatal ECMO towards more premature, but also complex, all doctors want to reduce the burden of ECMO-related complications and improve the outcomes.[3] The ECMO centers doctors should keep on learning, to know as much as possible of the experience. Therefore, we reviewed our institutional experience with Neonatal ECMO support, showed our experiences and our problems, shared our work to explore potential areas for improvement.

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Method and material

Study participants

From 2012 to 2016, 28 neonates diagnosed with severe respiratory and cardiac failure at the BaYi Children's Hospital of PLA Army General Hospital, were provided with ECMO support. Among them, there were 6 females and 22 males with a median age was 5 days (ranging from 1 to 28 days) and a median weight was 3.3 kg (ranging from 2.4 to 4.2 kg). All neonates experienced severe respiratory or cardiac failure post CHD operation, whose clinical symptoms were unresponsive to conventional treatments and had no contraindications for ECMO. Among them, 14 neonates required ECMO support for cardiac conditions, while another 14 required it for respiratory issues. The decision for ECMO support was made after obtaining consent from the families of the neonates.

Indications for ECMO support in this study were as follows:

- Indications for respiratory failure: Oxygenation index > 40 for > 4 h; Oxygenation index > 20 without improvement after prolonged duration (> 24 h), severe hypoxic respiratory failure with abrupt decompensation (PaO2 < 40) resistant to intervention, and progressive respiratory failure and/or pulmonary hypertension with signs of right ventricular dysfunction or sustained high inotropic demand.
- Indications for heart failure: Inability to be weaned from extracorporeal circulation following surgery for congenital heart disease, severe low cardiac output syndrome persisting after surgery for congenital heart disease, and unsuccessful cardiopulmonary resuscitation (CPR) after a cardiac arrest.

Contraindications

Gestational age < 34 weeks, weight < 2 kg, irreparable cardiopulmonary injury, irreversible nerve injury, multiple organ failure, fatal chromosomal anomalies, and refusal of ECMO support by the families.

Methods

The ECMO setup utilized a Medtronic ECMO bio-console 560 and a water tank, along with a Medtronic Minimax Plus Oxygenator (CB2503R1). The cannulation sites for respiratory support were right jugular vein for venous outflow and the jugular arterial for arterial inflow. For cardiac support, the right atrium served as the venous outflow, and the aorta was used for arterial inflow. Cardiac support was initiated through the chest, following a

V-A model configuration. The flow rate range was 100-150 ml/kg/min. Anticoagulation was maintained through a heparin infusion at a rate of 5-10 u/kg.h, aiming to keep activated clotting times within the range of 150-200 s. Blood routine and blood gas samples were monitored, ensuring PLT levels were above 75×10^9/L, HCT ranged between 30 and 40%, and SvO2 levels remained above 50%. During ECMO support, active vascular drug dosage was decreased, with the end-expiratory volume between 5 and 8 ml/kg, high peep pressure between 5 and 8 mmHg, and end-expiratory pressure between 18 and 25 mmHg, in an effort to maintain lung inflation. Hemodynamic stability, blood gas samples, chest X-rays, urine output, and mixed venous oxygen saturation were continuously monitored to assess cardiopulmonary function. If these indicators improved, the ECMO flow rate was gradually reduced. Once the flow rate fell below 10–30 ml/kg/h and both circulation and oxygenation remained stable, the ECMO support was discontinued. The lactide levels in different group were compared by ANOVA using the SPSS version 16 software.

Results

In this study, 28 infants underwent ECMO support, comprising 6 females and 22 males, with ages ranging from 1 day to 28 days, The duration of support varied, ranging from 11 h to a maximum of 173 h. .Out of the 14 cases supported for cardiac-related issues, 9 neonates survived, resulting in a 65% survival rate. For the 14 cases supported for respiratory conditions, 6 neonates survived, leading to a survival rate of 42%. Among the cases, 3 neonates had meconium aspiration syndrome, 2 had respiratory distress syndrome (RDS) due to sepsis, and 1 had diaphragmatic hernia (CDH), as outlined in Table 1. In the 15 successful weaning neonates, four neonates died at the end of the study. One was given up for the cardiac function failure; two were given up for the respiratory failure; one was given up for Bipedal necrosis; the other 11 neonates were successful discharge.

The neonates whose lactate levels declined significantly in the first 24 h had a better prognosis, while those whose lactate levels decreased slowly or did not change had a worse prognosis (see Table 2).

Among the ECMO cases, 5 experienced complications: 2 cases developed diffuse intravascular coagulation, 1 suffered a pipeline accident, and 2 faced venous cannula obstruction, leading to lower limb ischemia necrosis in those instances. Notably, no instances of bleeding or other complications were observed, resulting in a complication rate of 17%.

Discussion

ECMO plays a pivotal role in rapidly and effectively improving severe cardiopulmonary function loss, providing a critical window for recovery. Its widespread application in severe respiratory and heart failure treatment is well-established, encompassing neonates, children, and adults. Specifically in neonatal settings, ECMO serves as a valuable tool for heart support, ventilator assistance, and in vitro cardiopulmonary resuscitation (CPR). The neonatal ECMO requiring specific expertise and technical skill, especially for the special pathophysiological characteristics of neonates. it becomes nearly impossible to separate the role of pediatric surgeons from the continuous involvement with and management of neonatal ECMO patients. This technology, well-established overseas, has recently gained traction in China's clinical landscape. Data from the External Life Support Organization (ELSO, 2016)[4] indicates

Table 1 The neonates requiring ECMO support and survival rate

		Died	Survived	Survival rate
Cardiac		5	9	64%
Respiratory	RDS/SEPSIS	4	2	42%
	MAS	1	3	
	PH	2	0	
	PPHN	1	0	
	CDH	0	1	
Sex (f/m)		3/10	1/14	
Weight (kg)		3.40 ± 0.75	3.54 ± 0.84	

ECMO: Extracorporeal Membrane Oxygenation; CDH: Diaphragmatic hernia; MAS: Meconium aspiration syndrome; PPHN: Neonatal persistent pulmonary hypertension; RDS: Respiratory distress syndrome; PH: Pulmonary hypoplasia

Table 2 Lactate levels (mmol/L) during the initial 24 h of ECMO support

	0 h	6 h	12 h	24 h
Survival group	12.83 ± 2.77	8.31 ± 3.73[1]	6.06 ± 3.83[1,2]	3.01 ± 0.97[1, 3, 4]
Death group	10.33 ± 4.80	9.97 ± 4.83[5]	10.47 ± 5.32[5,6]	10 ± 1.97[5,6,7]

Note Survival group: 1 was 24 h compared with 0 h, $p < 0.05$

2 was 12 h compared with 6 h, $p > 0.05$

3 was 24 h compared with 6 h, $p < 0.05$

4 was 24 h compared with 12 h, $p > 0.05$

Death group : 5 was compared with 0 h, $p > 0.05$

6 was compared with 6 h, $p > 0.05$

7 was compared with 12 h, $p > 0.05$

that 36,946 neonates have undergone ECMO support, comprising 29,153 cases for cardiac support with a 42% survival rate, 6,475 cases for respiratory support with a 72% survival rate, and 1,336 cases for external cardiopulmonary resuscitation (ECPR) with a 41% survival rate,[1,3-10] ESLO(In January 2016) data revealed that there were only 9 neonates who received ECMO, 3 for respiratory support with a 0% survival rate and 6 for cardiac assistance with a 50% survival rate; hence, ECMO for neonates in China lags Western countries. Since 2012, our hospital has developed ECMO for neonates; we have performed ECMO on 28 infants, 14 for cardiac support with a 64% survival rate and 14 for respiratory conditions with a 42% survival rate. So many years passed, the data of 2023 from ESLO shows 167 neonates who received ECMO, 70 for respiratory support with a 68.6% survival rate, 78 for cardiac assistance with a 42.3% survival rate and 19 for ECPR assistance with a 11.4% survival rate. In our center, the survival rate for cardiac support (41%) was marginally higher than that for respiratory support, not consistent with ESLO data., maybe due to the limited number of cases in our center, the comparability is weak, and it is essential to collect more cases for a comprehensive analysis.

The survival rate for respiratory assistance was significantly lower than what is published internationally; potential factors include the following:

1) In our study, the initiation of ECMO procedures was delayed, resulting in fewer than 15 cases annually. This indicates a need to enhance our management and operational proficiency. Freeman et al. demonstrated a correlation between patient survival rate and the volume of cases managed by a center.[11] Notably, centers handling approximately 22 cases annually exhibited a significant decrease in mortality rates.
2) The initiation of ECMO support for neonates in our center

was considerably delayed, predominantly due to the limited knowledge and experience with ECMO among neonatal physicians. While surfactant therapy, high-frequency ventilation, and inhaled nitric oxide are commonly employed in clinical settings, by the time neonates were considered for ECMO intervention, their physiological status had often deteriorated significantly. The majority of these neonates presented with profound internal environmental imbalances, marked hypoxemia (arterial oxygen tension less than 20 mmHg), and cardiac insufficiency. Out of the total cohort, 20 out of 28 neonates exhibited lactate levels exceeding 15 mmol/L prior to ECMO intervention. Consequently, a significant proportion of these neonates experienced severe fluid leakage following ECMO initiation, leading to circulatory instability. This rendered resuscitative measures ineffective, resulting in an inability to rescue these neonates. Within the first 24 h of ECMO intervention, neonates whose lactate levels normalized exhibited a favorable prognosis. Conversely, those who maintained elevated lactate levels or experienced a further rise demonstrated a poor prognosis.

3) In our center, the veno-arterial (V-A) ECMO model was exclusively employed for neonatal patients. While it is widely recognized that the venous-venous (V-V) model is optimal for patients with primary respiratory ailments, the absence of a V-V circuit in our institution necessitated our reliance on the V-A configuration for neonatal interventions.[12] The intricacies associated with the administration of the V-A model, coupled with its potential impacts on circulatory dynamics, may be contributory factors to the observed diminished survival rates.

During the ECMO support phase, lung management plays a pivotal role in patient prognosis, with particular emphasis on modifications in patient positioning, such as adopting the prone position. Kredel conducted a retrospective case analysis in 2014 and scrutinized 9 patients diagnosed with ARDS who were positioned prone during their ECMO support.[13] Based on the comparison of the oxygenation index and lung compliance, there were notable improvements post-proning. Specifically, the oxygenation index improved from a median value of 47 (ranging from 41 to 47) before proning, to 12 (ranging from 11 to 14) after. Similarly, lung compliance revealed enhancement from 20 (ranging from 17 to 28) before proning, to 42 (ranging from 27 to 43) after the intervention, now there also some opinion shows the prone positioning did not facilitate earlier weaning from ECMO.[14] In our center, beginning from June 2016, two patients were placed in the prone position during ECMO support, the lung of two babies occurred hypostatic pneumonia, so we tried the prone intervention. Remarkably, these patients did not encounter complications such as facial edema, pipeline issues, or pump failure. This indicates that positioning patients supported by ECMO in the prone orientation is both safe and practicable. However, we did not find the benefit from the prone position, so we acknowledge the necessity for additional data collection to definitively assess the effects of this positioning on parameters such as the oxygenation index and lung compliance.

Neonates requiring ECMO mechanical intervention present with a diverse array of clinical conditions including congenital diaphragmatic hernia (CDH), meconium aspiration syndrome (MAS), neonatal persistent pulmonary hypertension (PPHN), respiratory distress syndrome (RDS), sepsis, neonatal pneumonia, and air leakage, among others.[15,16] A review of existing literature indicates that MAS has the highest association with ECMO use, followed by CDH, followed by PPHN, sepsis, RDS, pneumonia, and air leakage. Survival rates were most favorable for MAS, estimated around 94%, followed by RDS (84%), PPHN (77%), and sepsis (73%), with CDH registering the lowest at approximately 51%. The reduced survival rate in CDH may be attributed to concurrent pulmonary hypoplasia (PP). In our center, 14 neonates had ECMO support primarily for respiratory issues, 6 had SEPSIS/RDS, 4 had MAS, 2 displayed PP, and 1 was diagnosed with CDH. The distribution of conditions diverges from commonly cited literature, potentially due to unique admission patterns and national circumstances. Our center has proficiency in neonatal transport, but the presented state of the neonate with CDH was critically compromised, and the capabilities of primary healthcare facilities are restricted. Consequently, many neonates were deprived of opportunities for escalated care in tertiary healthcare centers. While the patient volume is insufficient to facilitate a comparison with the ELSO data, it is evident from our observations that neonates with sepsis/MAS generally have a favorable prognosis.

Since the 1970s, technology, management, and clinical applications of neonatal ECMO have improved. Pulmonary diseases still represent the principal neonatal diagnosis, with an overall 74% survival rate, and up to one-third of cases are due to congenital diaphragmatic hernia. The overall survival rate in cardiac ECMO is lower, with congenital heart defect representing the main indication.[3] However, in our center the survival was lower with the pulmonary diseases, the reason may be the seriously ill, or maybe the example was small. Yu et al.[17] reported 23 neonates who received ECMO support for cardiac failure in their center from January 2017 to June 2019, The successful weaning rate was 78.26% and discharge rate was 52.17% in their center, the survival rate was similar with ours, So ECMO is a safe and efficacious therapeutic modality, emblematic of the critical emergency technological capabilities of a hospital, region, or even a country. It was Bartlett, who, in 1976, pioneered the successful application of ECMO for neonates with ARDS.[18] Subsequent to this achievement, the clinical utilization of ECMO expanded, leading to significant improvements in survival rates for patients who are critically ill. In China, while ECMO has been extensively adopted for adult patients, its implementation in pediatric settings has been comparatively gradual.[19,20]

Conclusion

As ECMO becomes increasingly integrated into neonatal critical care, the technology will undergo continuous refinement, paving the way for a new era in neonatal critical care in China.

Abbreviations

ECMO	Extracorporeal Membrane Oxygenation CPB Extracorporeal circulation
CPR	Cardiopulmonary resuscitation CDHDiaphragmatic hernia
MAS	Meconium aspiration syndrome
PPHN	Neonatal persistent pulmonary hypertension RDS Respiratory distress syndrome
PH	Pulmonary hypoplasia

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Author contributions

Conception and design of the research: Xiao-juan Zhang, Xiao-

yang Hong. Acquisition of data: Hui Wang, Ying-yue Liu. Analysis and interpretation of the data: Hui Wang, Ying-yue Liu. Statistical analysis: Xiao-juan Zhang. Obtaining financing: Xiao-yang Hong. Writing of the manuscript: Xiao-juan Zhang.

Critical revision of the manuscript for intellectual content: Ying-yue Liu. All authors read and approved the final draft.

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Data availability
The datasets used and analysed during the current study available from the corresponding author on reasonable request.

Ethics approval and consent to participate
This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of BaYi Children's Hospital of PLA Army General Hospital.

Consent for publication
Written informed consent was obtained from the minor(s)' legal guardian for the publication of any potentially identifiable images or data included in this article.

Competing interests
The authors declare no competing interests.

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News…continued from page 41
amoxiclav (impetigo and cellulitis). The infant was receiving prophylactic iron and multivitamins, phosphate supplements, and alginic acid. Results of cultures, skin swabs, and bloodwork were normal/negative, except for mild thrombophilia and a low alkaline phosphatase level. The infant was started on zinc supplements based on clinical suspicion of deficiency, resulting in rapid resolution of symptoms, including near-complete resolution of the rash within 1 week. When results for a pre-supplementation zinc level became available, they showed a value of 1.8 µmol/L (normal range, 5-21.5 µmol/L); the level after 1 week of supplementation was 11 µmol/L. "Consider nutritional zinc deficiency in a premature infant presenting with an erythematous scaly, well demarcated circumoral, anogenital, and acral skin changes unresponsive to treatments of common differential diagnoses. Risk factors…include prematurity [and] exclusive breastfeeding especially with a deficient or restrictive maternal diet," the authors wrote. "Start zinc supplementation before confirmation with a low zinc level as test results can take time. In children unable to maintain zinc levels after stopping supplements, genetic testing for primary acrodermatitis enteropathica should be considered," they concluded.

US Med-Equip, Sentec Team Up to Support Clinicians Nationwide

As hospitals across the United States navigate the challenges of delivering patient care in increasingly high-acuity environments, a new partnership between US Med-Equip (USME), a leading provider of medical equipment rentals and services, and Sentec, a global leader in respiratory monitoring technology, is set to help more clinicians with real-time insights into the conditions of critically ill respiratory patients, including newborns in Neonatal Intensive Care Units (NICUs). Under the new partnership, USME added Sentec's transcutaneous monitoring (TCM) devices as part of its extensive portfolio of life-saving medical equipment. Sentec's TCM devices provide continuous, non-invasive monitoring of a patient's carbon dioxide levels and oxygen saturation to help clinicians make better-informed decisions in real-time — particularly vital in the care of patients, such as those in the NICU, where precise monitoring of respiratory function is crucial. In addition to transcutaneous monitoring, Sentec's Intrapulmonary Percussive Ventilation (IPV) technology will also be available through this partnership. IPV therapy supports the front-line care of critically ill respiratory patients as a management tool to restore lung function and mobilize secretions. By adding both TCM and IPV technology into USME's rental and service offerings, healthcare providers gain greater access to non-invasive equipment often preferred by clinicians, especially in intensive care units, emergency departments, and during transport of critically ill patients. "Partnering with US Med-Equip enables us to better support our shared hospital customers dedicated to providing the highest quality care for respiratory-compromised patients, especially during periods of high patient census and urgent capital needs," Sentec CEO Bob Cormier said. This partnership reflects a growing trend in healthcare, where the integration of advanced technology with on-demand service is increasingly essential. Under the new partnership, US Med-Equip, known for its rapid response and high-quality service, is offering Sentec's devices with the level of support that has made them a trusted partner for hospitals nationwide. "Sentec shares our unwavering commitment to supporting clinicians in delivering exceptional patient care," Greg Salario, CEO of USME, said. "This collaboration enhances our ability to provide healthcare partners with access to the most advanced patient monitoring solutions, precisely when they need them most."

Beyond Air Provides LungFit PH System to hospital

Beyond Air, Inc., a commercial stage medical device and biopharmaceutical company focused on harnessing the power of nitric oxide (NO) to improve the lives of patients, is proud to announce the deployment of its groundbreaking LungFit PH system to the US Naval Hospital Guam. This partnership, made possible through collaboration with TrillaMed, marks a significant advancement in the neonatal critical care unit, offering enhanced care for newborns in need of respiratory support. The LungFit PH system is an innovative device designed to generate Nitric Oxide (NO) from room air and deliver NO for the treatment of persistent pulmonary hypertension in neonates (PPHN), a condition that affects the lungs and heart of newborns. The system provides a safe, efficient, and user-friendly solution to address critical respiratory conditions, ensuring that the hospital's youngest and most vulnerable patients receive the highest standard of care. **Key Features of the LungFit PH System:** Portable and compact design, making it ideal for intensive care settings; advanced nitric oxide generating technology with no need for high-pressure cylinders; rapid response for improved oxygenation in neonates with PPHN; easy integration into existing hospital infrastructure. "We are honored to support the US Naval Hospital Guam in their mission to provide top-tier neonatal care," said Steve Lisi, CEO of Beyond Air. "Through our partnership with TrillaMed, we are able to extend the reach of our LungFit PH, delivering critical solutions to the healthcare community. This collaboration is a testament to our commitment to advancing neonatal care and improving patient outcomes." The US Naval Hospital Guam serves as a critical care provider for the military community in the region. More than 17,000 active-duty military personnel and family members currently are stationed on Guam, which is expected to increase by 2,500 in the next two years. The US Naval Hospital Guam delivers an average of 315 babies per year, with that number expected to rise to 487 births by 2033. The introduction of the LungFit PH system underscores the hospital's dedication to utilizing state-of-the-art technologies in neonatal care, ensuring military families have access to the latest in respiratory treatment options.

ART Linked With Congenital Heart Defects in Newborns

The rate of congenital heart defects is higher in newborns conceived using assisted reproductive technologies (ART) than in newborns conceived without assistance. This finding comes from a population-based cohort study led by Dr Nona Sargisian, a gynecologist at the University of Gothenburg, Gothenburg, Sweden, and colleagues, which was published in the *European Heart Journal.* The researchers analyzed more than seven million results of all live-born children in Denmark, Finland, Sweden, and Norway between 1984 and 2015. They found that congenital heart defects occurred more frequently in the ART newborn group (1.85%) than in naturally conceived newborns (1.15%). The study also revealed that the risk for congenital heart defects in multiple births is higher than in single births, with and without the use of ART. However, the result that congenital heart defects occur more often in ART newborns remained significant when comparing single births from both groups (1.62% vs 1.11%). Dr Barbara Sonntag, a gynecologist at Amedes Fertility Center in Hamburg, Germany, referred to a "clinically relevant risk increase" with a relatively low prevalence of the condition. "When 1000 children are born, an abnormality occurs in 18 children after ART, compared with 11 children born after

natural conception," she told the *Science Media Center*. Sonntag emphasized that the risk is particularly increased by a multiple pregnancy. A statement about causality is not possible based on the study, she said. But multiple pregnancies are generally associated with increased risks during pregnancy and for the children. The large and robust data set confirms long-known findings, said Dr Georg Griesinger, medical director of the fertility centers of the University Medical Center Schleswig-Holstein in Lübeck and Manhagen, Germany. The key figures can be found in single births, he explained. "Among single births conceived by ART, the rate of severe congenital heart defects was 1.62% compared with 1.11% in spontaneously conceived single births, an increase in risk by 1.19 times. For severe heart defects, the rate was 0.31% in ART single births, compared with 0.25% in spontaneously conceived single births." The increased risks are consistent with existing literature. Therefore, the current study does not reveal any new risk signals, said Griesinger.

Weight Loss Surgery Before Pregnancy Tied to Smaller and Premature Infants

The type of weight loss surgery women undergo before becoming pregnant may affect how much weight their children gain in the first three years of life, suggests a study presented at ENDO 2024, the Endocrine Society's annual meeting in Boston, Mass. Researchers found children born to women who underwent the bariatric procedure known as sleeve gastrectomy before they became pregnant gain more weight per month on average in the first three years of life compared with children born to women who had the less common Roux-en-Y gastric bypass weight loss procedure. Maternal obesity is a risk factor for obesity in children. Women are more likely to conceive following weight loss procedures, but less is known about the early growth of the children born after pre-pregnancy weight loss procedures. Sleeve gastrectomy and Roux-en-Y gastric bypass are two of the more common types of weight loss surgery, also known as bariatric and metabolic surgery. These surgeries result in sustained weight loss and improve the body's metabolism in the majority of patients. In vertical sleeve gastrectomy (also called gastric sleeve surgery), a surgeon removes most of the stomach, leaving only a banana-shaped section that is closed with staples. By removing a part of the stomach that makes hormones that drive hunger, this procedure also decreases appetite. In gastric bypass, the surgeon divides the stomach into two parts, sealing off the upper section from the lower. The surgeon then connects the upper stomach directly to the lower section of the small intestine. This creates a shortcut for food, bypassing part of the stomach and the small intestine. Skipping these parts of the digestive tract means the body absorbs fewer calories and nutrients. The researchers examined the weight and length of offspring born after pre-pregnancy weight loss procedures in the first three years of life. The study used data from 20,515 deliveries over three years, of which 450 had pre-pregnancy weight loss procedures. Among the mothers who underwent weight loss surgery, 57% had sleeve gastrectomy and 41% had Roux-en-Y gastric bypass. Long-term weight and length data were available for about half of the babies in each group. The researchers found there was no difference in birth weight among the babies born after weight loss surgery. The pace of weight gain was higher in those born after pre-pregnancy sleeve gastrectomy compared to those born following Roux-en-Y gastric bypass, while adjusting for several other variables including pre-pregnancy body mass index.

New Urgency Over Pregnant Women With Epilepsy

Pregnant women with epilepsy are at higher risk for severe maternal, foetal, and neonatal outcomes, including death, according to the largest study to date of 4.5 million deliveries in five Nordic countries. This study was a prospective cohort of 4,511,267 deliveries, of which 35,283 were to mothers with epilepsy and 4.475 million were to mothers without epilepsy in Denmark, Finland, Iceland, Norway, and Sweden (1996-2017). The study also was of antiseizure medication use (n = 16,240) vs non-use (n = 19,043) among mothers with epilepsy. The primary outcomes were a composite of severe maternal outcomes and a composite of severe perinatal (foetus and neonatal) outcomes. Findings were adjusted for maternal age, parity, birth year, number of chronic conditions, among other confounders. There was a 23% increase in composite maternal death and morbidity (adjusted odds ratio [aOR], 1.23; 95% CI, 1.16-1.31) among mothers with epilepsy vs those without. The three greatest maternal risks were for mortality (aOR, 3.86; 95% CI, 1.84-8.10), cerebrovascular accidents (aOR, 5.81; 95% CI, 4.27-7.89), and severe mental health conditions (aOR, 1.81; 95% CI, 1.50-2.19). Adverse perinatal outcomes included a 44% increase in composite perinatal death/severe neonatal morbidity (aOR, 1.44; 95% CI, 1.37-1.52), including a 48% increase in composite severe neonatal morbidity (aOR, 1.48; 95% CI, 1.40-1.56), and an 18% increase in stillbirth (aOR, 1.18; 95% CI, 1.00-1.40) compared with outcomes among mothers without epilepsy. Antiseizure medication use vs non-use by women with epilepsy was associated with a higher risk for neonatal death (aOR, 2.40; 95% CI, 1.44-4.00), cerebrovascular accidents (aOR, 1.99; 95% CI, 1.13-3.50), and perinatal death (aOR, 1.40; 95% CI, 1.03-1.89). With regard to specific antiseizure medication vs non-use, the likelihood of severe maternal morbidity was increased for valproate (aOR, 1.67; 95% CI, 1.26-2.23), carbamazepine (aOR, 1.46; 95% CI, 1.14-1.87), and oxcarbazepine (aOR, 1.53; 95% CI, 1.08-2.17).

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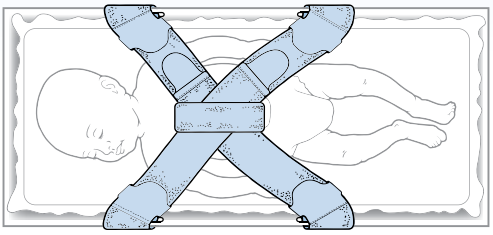

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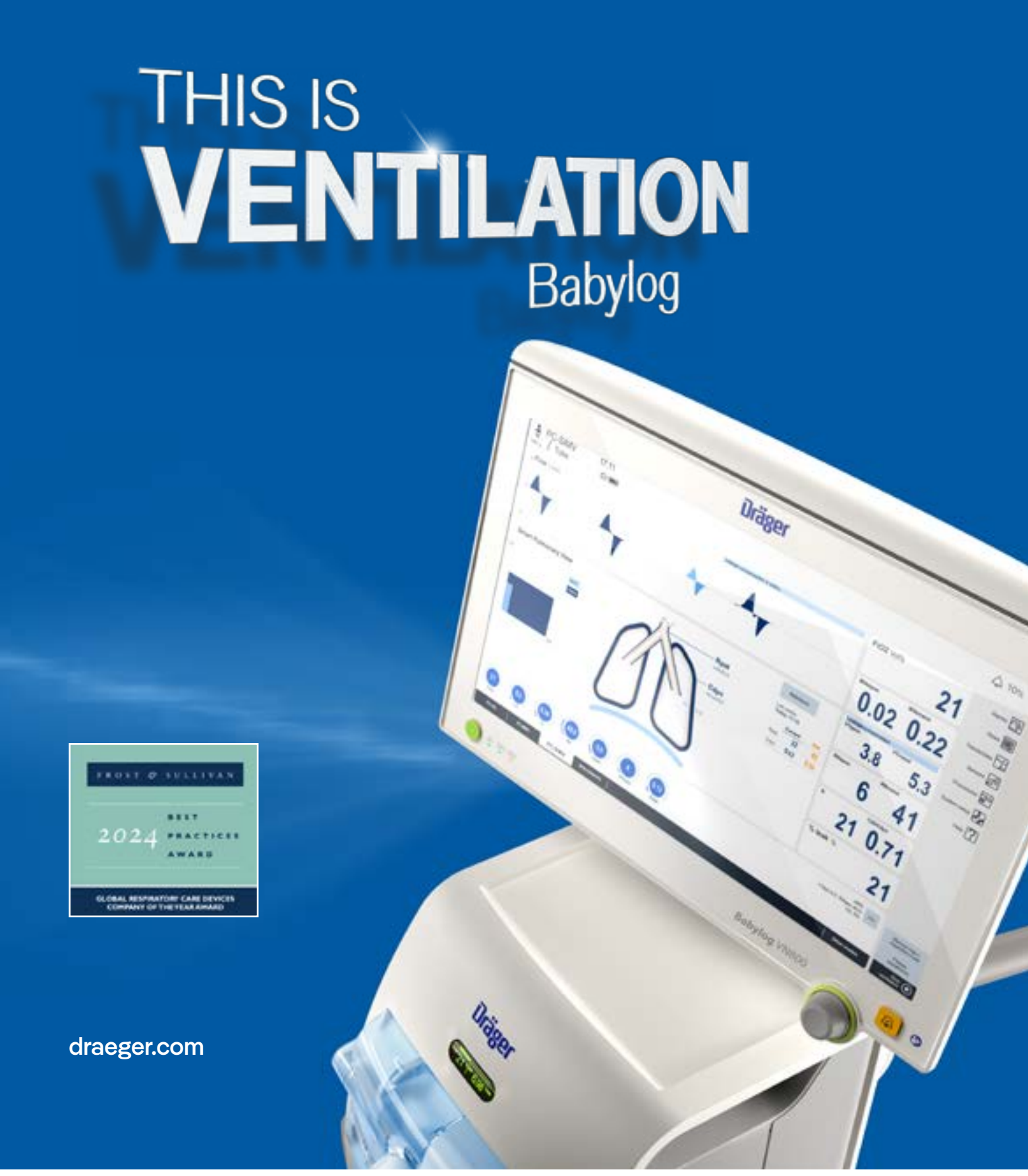

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