

Blood loss in the NICU: The difficulty and tradeoffs of caring for the most fragile patients



Providing the best care for the most fragile NICU patients is full of challenges and tradeoffs. Sometimes the information doctors need to gather from their patients comes at a cost. When neonatal care teams need to assess how a patient is responding to the current level of ventilatory support, a blood draw is traditionally required. However, that blood draw can contribute to blood loss, pain, and infection risk for the infant.

Why do we need to ventilate NICU patients?

Caring for preterm infants requires 1) ventilating their underdeveloped lungs and 2) protecting their brains—which often have immature blood flow regulation—from intraventricular hemorrhage and other complications.

To determine whether or not the ventilation support that these patients are receiving is adequate, clinicians need to frequently measure and monitor the amount of indicative substances in the blood. One of the most critical is carbon dioxide (CO₂).

CO₂ levels can change quickly in neonates, and monitoring them is important because values too high (hypercarbia) or too low (hypocarbia), as well as fluctuations or sharp changes, have all been linked to intraventricular hemorrhage¹, which happens in as many as 25²–42%³ of neonates weighing less than 1500g at birth.

If ensuring CO₂ remains in a safe range helps support better outcomes for NICU patients, CO₂ levels must be measured and monitored closely.

How do we measure carbon dioxide levels in NICU patients' blood?

The gold standard for measuring CO₂ is through blood draws; Arterial Blood Gases (ABG) and capillary heel sticks are common in the NICU.

These blood samples, although accurate, offer only a point-in-time measurement and can miss periods of elevated or reduced levels of CO₂ in the blood. They also present an infection risk, cause pain and stimulation, and introduce iatrogenic blood loss: blood loss caused by medical examination or treatment.

Why is iatrogenic blood loss important?

We may not typically consider blood draws and heel sticks to be a large driver of patients losing blood, but the issue carries greater significance with neonatal patients, who don't have much blood to give in the first place. One study found that 30% of the circulating blood volume of neonates was drawn for lab work each week in their first six weeks of life⁴.

The significance of this blood loss in the NICU cannot be understated. As another study noted, "to further place this in perspective, 6–7 mL of blood drawn from an infant weighing 1 kg is equivalent to a 450 mL blood loss in an adult⁵." 450 mL is roughly one pint.



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If blood loss is so important, why do we draw it so frequently?

The answer, as studies have shown, is often to determine blood gases and pH levels, as well as some electrolytes, all stemming from the desire to monitor how patients are responding to treatment and/or their current level of ventilatory support.

One analysis saw that Very Low Birth Weight (VLBW) infants receive an average of nearly 57 blood gas measurements over the course of, roughly, one week⁶. The unfortunate reality of what happens next is that up to 63% of the blood lost by the infant is wasted⁴.



pH and Blood Gas measurements are the **highest driver of blood draws** in the NICU.

Transfusion, phlebotomy, and other issues with blood draws

Phlebotomy is well-established as the main nonphysiologic driver of anemia of prematurity⁵, shown through the direct relationship and high correlation values between the volume of blood drawn and the volume of blood transfused^{5,7}.

We know that blood taken in these fragile patients must eventually be replaced. Transfusion, however, presents a wide variety of risks and complications in neonates, including infection, vascular overload, lung injury, and sensitization⁸, and has even been linked to increased mortality in adult surgical patients^{9,10}.

Transfusion has a complex relationship to Necrotizing Enterocolitis (NEC), with one meta-analysis showing transfusion doubling the risk of developing the condition¹¹, and another stating “incidence of Transfusion-associated Necrotizing Enterocolitis varies from 20–35% of NEC cases and reports suggest that infants with TANEC are more likely to develop more surgical NEC”¹².

Patients with transfusion-associated NEC (TANEC) generally have higher mortality, longer hospital stays, and are more likely to require surgery than non-transfusion NEC patients¹¹. Some evidence has even connected transfusions with worsening intraventricular hemorrhages¹³.

Care teams in the NICU need the information that blood draws can deliver, but the cost of iatrogenic blood loss and other risks associated with those draws needs to be fully understood and weighed by the clinician.

How can we reduce blood loss in the NICU?

While this may paint a bleak picture, there are options and strategies for better blood management in the NICU – and small changes can have a big impact for these fragile patients.

In a study in the Journal of Maternal-Fetal and Neonatal Medicine, Clare E Counsilman and colleagues at Leiden University Medical Centre share strategies they’ve implemented to reduce iatrogenic blood loss in their NICU, such as using placental and umbilical cord blood to decrease blood loss on Day 1 of life and adopting transcutaneous CO₂ monitoring to minimize the frequency of blood draws.

Their study concluded that “extreme preterm infants lose almost one-third of their total blood volume in the first month of life as a result of blood loss due to multiple blood draws for laboratory investigations and procedures.”

Additionally, Counsilman et al. determined that “in-line point-of-care testing through arterial catheters... or transcutaneous CO₂ measurement might help to reduce the high blood loss associated with mechanical ventilation.”

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The role of transcutaneous CO₂

Transcutaneous monitors enable non-invasive measurement of patients' CO₂ levels, lessening the need for frequent blood draws without sacrificing visibility to this critical parameter¹⁴. Although blood draws provide crucial information and will likely never be eliminated from the NICU, efforts to reduce unnecessary blood loss are in the patient's best interest and are already underway in NICUs around the world.

As Counsilman et al. stated in their study, "decreasing the frequency and amount of phlebotomy loss is probably the area in the field of neonatology that can be changed the quickest. This will automatically decrease the risk of neonatal anemia and save substantial transfusions and complications."



1. Hochwald O, Borenstein-Levin L, Dinur G, Jubran H, Ben-David S, Kugelman A. Continuous Noninvasive Carbon Dioxide Monitoring in Neonates: From Theory to Standard of Care. *Pediatrics*. 2019;144(1):e20183640. doi:10.1542/peds.2018-3640
2. Database of Very Low Birth Weight Infants Born in 2012. Burlington, VT: Vermont Oxford Network, 2013. Nightingale Internet Reporting System, accessed April 4, 2014.
3. Ahn SY, Shim SY, Sung IK. Intraventricular Hemorrhage and Post Hemorrhagic Hydrocephalus among Very-Low-Birth-Weight Infants in Korea. *J Korean Med Sci*. 2015;30 Suppl 1(Suppl 1):S52-S58. doi:10.3346/jkms.2015.30.S1.S52
4. Carroll PD, Widness JA. Nonpharmacological, blood conservation techniques for preventing neonatal anemia—effective and promising strategies for reducing transfusion. *Semin Perinatol*. 2012;36(4):232-243. doi:10.1053/j.semperi.2012.04.003
5. Widness JA. Pathophysiology of Anemia During the Neonatal Period, Including Anemia of Prematurity. *Neoreviews*. 2008;9(11):e520. doi:10.1542/neo.9--e5206.
6. Alves-Dunkerson JA, Hilsenrath PE, Cress GA, Widness JA. Cost analysis of a neonatal point-of-care monitor. *Am J Clin Pathol*. 2002;117(5):809-818. doi:10.1309/04WC-GFVE-M7T3-4MGY
7. Valieva OA, Strandjord TP, Mayock DE, Juul SE. Effects of transfusions in extremely low birth weight infants: a retrospective study. *J Pediatr*. 2009;155(3):331-37.e1. doi:10.1016/j.jpeds.2009.02.026
8. Whitehead, N.S., Williams, L.O., Meleth, S. et al. Interventions to prevent iatrogenic anemia: a Laboratory Medicine Best Practices systematic review. *Crit Care* 23, 278 (2019). <https://doi.org/10.1186/s13054-019-2511-9>
9. Wedel C, Møller CM, Budtz-Lilly J, Eldrup N. Red blood cell transfusion associated with increased morbidity and mortality in patients undergoing elective open abdominal aortic aneurysm repair. *PLoS One*. 2019;14(7):e0219263. Published 2019 Jul 11. doi:10.1371/journal.pone.0219263
10. Kertai MD, Tiszai-Szűcs T, Varga KS, Hermann C, Acsády G, Gal J. Intraoperative use of packed red blood cell transfusion and mortality in patients undergoing abdominal or thoracoabdominal aortic aneurysm surgery. *J Cardiovasc Surg (Torino)*. 2009;50(4):501-508.
11. Mohamed A, Shah PS. Transfusion associated necrotizing enterocolitis: a meta-analysis of observational data. *Pediatrics*. 2012;129(3):529-540. doi:10.1542/peds.2011-2872
12. Gephart SM. Transfusion-associated necrotizing enterocolitis: evidence and uncertainty. *Adv Neonatal Care*. 2012;12(4):232-236. doi:10.1097/ANC.0b013e31825e20ee
13. Baer VL, Lambert DK, Henry E, Snow GL, Christensen RD. Red blood cell transfusion of preterm neonates with a Grade 1 intraventricular hemorrhage is associated with extension to a Grade 3 or 4 hemorrhage. *Transfusion*. 2011;51(9):1933-1939. doi:10.1111/j.1537-2995.2011.03081.x
14. Mukhopadhyay S, Maurer R, Puopolo KM. Neonatal Transcutaneous Carbon Dioxide Monitoring—Effect on Clinical Management and Outcomes. *Respir Care*. 2016;61(1):90-97. doi:10.4187/respcare.04212