This National Blood Donor Month, AABB celebrates all you do to support donors and patients across the country. Thanks to you, patient lives are saved every day.

From all of us at AABB, Thank you!

AABB will be celebrating National Blood Donor Month throughout January. Follow AABB and share your celebration stories using #AABBGiveRed.
Management Strategies for Bleeding in Neonates

Although neonates are one of the most frequently transfused populations, there are numerous factors that make diagnosing and treating them complex.

Special Concerns in Neonatal Transfusion

Neonatal patients are not just small children. Their needs differ quantitatively and qualitatively from older pediatric and adult patients.
Happy New Year! I hope the year is off to a great start for all of you. 2020 is going to be an exciting year for AABB and I look forward to sharing it with all of you – our supportive members, many of whom are incredible volunteers... Thank you!

As we announced at the 2019 Annual Meeting in San Antonio in October, AABB has a new strategic plan, one that will guide our focus for the next three years. As 2020 continues to unfold, you will see more of this strategic plan come to fruition. The plan was designed to ensure that AABB is providing optimal value for its members and helping to drive the field forward. You’ll see various new initiatives and updates throughout 2020 as AABB puts the strategic plan into practice.

Celebrating our community

One of the cornerstones of the strategic plan that I am particularly enthusiastic about is the emphasis on celebrating our community. The blood community is diverse and dynamic and comprises thousands of dedicated professionals throughout the world working in many critical areas.

In this month’s issue of AABB News, we look at a vital but sometimes overlooked area of the field: transfusion medicine in neonatal patients. I am often reminded of the need for more medical research examining pediatric transfusion medicine; this dearth is even more apparent when it comes to neonatal patients.

But in the pages of this issue, we highlight some of the prominent physicians and researchers working in this area of our community. They are treating patients and conducting research, working tirelessly to better address the needs of the youngest patients.

This issue’s first feature article, beginning on page 10, focuses on the causes and symptoms of bleeding in neonates and provides an overview about differentiating among possible diagnoses and choosing the appropriate treatment strategy. The second feature article, starting on page 16, highlights some of the differences that make neonates unique among patient populations.

2020 Annual Meeting

The 2019 Annual Meeting may still be fresh in your memories, but AABB is already planning for the 2020 Annual Meeting, to be held in Baltimore Oct. 3-6. The call for education session submissions is open until Jan. 31; I encourage any interested member to submit a proposal and help AABB continue to capitalize on its success in 2020. Your input is vital to creating another engaging and cutting-edge program.

Beth Shaz, MD
AABB President
A concise and practical guide for all members of the health care team who support apheresis.

Therapeutic Apheresis: A Handbook, a joint publication of AABB and the American Society for Apheresis (ASFA), provides a thorough account of common apheresis procedures and indications for their use — including cytapheresis, therapeutic plasma exchange, erythrocytapheresis and selective depletion.

Available now in the AABB Marketplace
aabb.org/marketplace
Neonatal Platelet Transfusion

By Martha Sola-Visner, MD
Guest Contributor

Historically, it has been widely accepted that thrombocytopenic preterm neonates should receive platelet transfusions at higher platelet count (PC) thresholds than older children and adults due to their high incidence of spontaneous intracranial bleeding, particularly intraventricular hemorrhage (IVH). Throughout the past decade, several surveys and observational studies revealed a striking worldwide variability in neonatal platelet transfusion thresholds and an overall more liberal approach to platelet transfusions in United States compared with European neonatal intensive care units. This variability was, at least in part, due to the paucity of high-level evidence in the field. Until recently, there was only one randomized trial of platelet transfusion thresholds in preterm neonates, published 25 years ago. That study randomized 152 very-low-birth-weight (VLBW, < 1500 g at birth) neonates to receive platelet transfusions for PCs < 150x10^9/L or < 50x10^9/L in the first week of life, and found no differences in the incidence of new IVH or extension of existing IVH (the primary outcome) between the two groups. These results likely formed the basis for the use of 50x10^9/L as the most frequent threshold for platelet transfusions in preterm neonates.

The recently published much larger PlaNeT-2 multicenter trial randomized 660 thrombocytopenic neonates with a median gestational age of 26.6 weeks and a median birth weight of 740 g to receive platelet transfusions at PC thresholds of < 50x10^9/L (< 50 group) or < 25x10^9/L (< 25 group). Infants were randomized at any time during their NICU hospitalization when the PC fell below 50x10^9/L, and the primary outcome was a composite of death or new major bleeding within 28 days of randomization. Ninety percent of infants in the < 50 group and 53% in the < 25 group received at least one platelet transfusion. Unexpectedly, infants in the < 50 group had a significantly higher rate of mortality or major bleeding within 28 days of randomization compared with those in the < 25 group (26% versus 19%, respectively; odds ratio 1.57, 95% CI 1.06-2.32). In a subgroup analysis, findings were similar for neonates < 28 weeks gestation, the group at highest risk of bleeding and death. Furthermore, among secondary outcomes, infants in the liberally transfused group also had a higher incidence of bronchopulmonary dysplasia, a complication of prematurity characterized by abnormal lung development and persistent oxygen requirement. While these findings might have seemed surprising at first, they were in fact consistent with a growing number of observational studies describing a poor association between severity of thrombocytopenia and bleeding risk, a lack of effectiveness of platelet transfusions to prevent bleeding in neonates and an association between number of platelet transfusions and neonatal mortality and morbidity.

The results of PlaNeT-2 provided high-level evidence in support of these concepts, although the possibility that the benefits of the lower transfusion threshold would be limited to clinically stable infants with a low risk of bleeding and/or death led to initial skepticism. This question was largely addressed in a follow-up study in which a multivariable logistic regression model was developed (incorporating factors known to influence neonatal bleeding risk and mortality, such as gestational age) and used to predict the baseline bleeding/mortality risk of neonates enrolled in PlaNeT-2. Based on their model-predicted baseline risk, 653 neonates in PlaNeT-2 were divided into four quartiles (very low, low, moderate and high risk), and the absolute risk difference between the < 50 group and the < 25 group was assessed within each quartile. Interestingly, the lower transfusion threshold was associated with an absolute risk reduction in all four groups, varying from 4.9% in the lowest to 12.3% in the highest risk group. These results suggested that using a lower (< 25x10^9/L) prophylactic
platelet transfusion threshold is beneficial even in high risk neonates. While these studies provide strong support for the use of lower platelet transfusion thresholds in non-bleeding preterm infants, some uncertainties remain. First, only 37% of infants in the study were randomized by the fifth day of life and 59% by the tenth, the period when most clinically significant hemorrhages occur in preterm neonates. While this might have simply reflected the time of onset of thrombocytopenia in the study population, 39% of infants in PlaNeT-2 received one or more platelet transfusions prior to randomization, for unknown reasons and at non-specified PCs. This raises the question of whether these transfusions were given during the first few days of life, the highest risk period for IVH in preterm neonates. Second, the study required obtaining a head ultrasound within 6 hours of randomization and excluded infants with a significant IVH for 72 hours (after which they could be randomized). Thus, by design, PlaNeT-2 did not assess the effects of a restrictive versus liberal platelet transfusion threshold on the potential extension of an existing IVH. Taken together, these limitations leave some lingering uncertainty around the translatability of the findings to extremely preterm neonates in the first few days of life, particularly in the absence of a just-in-time head ultrasound.

The results of PlaNeT-2 also provided strong support for the hypothesis that platelet transfusions may have deleterious effects in neonates that can be mediated by various potential mechanisms. Consistent with routine neonatal practices, neonates in PlaNeT-2 were transfused with 15 mL/Kg of a platelet suspension. This is a substantially higher volume than that used in older children or adults, who usually receive ~5 mL/Kg of a standard platelet suspension. This high transfusion volume, combined with the fragile vasculature of preterm neonates, raises the possibility that the platelet transfusion itself could have caused or extended a pre-existing hemorrhage, thus providing a potential explanation for the higher incidence of major bleeding in the < 50 compared to the < 25 group. Adult platelets have also been shown to be functionally hyperreactive compared to neonatal platelets, and in vitro mixing studies have found that adult platelets added to neonatal thrombocytopenic blood can induce a prothrombotic phenotype. Finally, it has become increasingly clear throughout the past decade that platelets have important functions beyond hemostasis, including as central mediators and modulators of inflammation. Thus, it is plausible that some of the pathogenic effects of platelet transfusions on neonates could be mediated through inflammatory pathways. Additional work is needed to elucidate which of these potential mechanisms contribute to the increased mortality and morbidity associated with the liberal use of platelet transfusions in neonates.

Martha Sola-Visner, MD, is director of the newborn medicine clinical research program at Boston Children’s Hospital and associate professor in pediatrics at Harvard Medical School.
REFERENCES


