Ensuring a Safe and Sufficient Global Blood Supply Jeremy W. Jacobs, M.D., M.H.S., Imelda Bates, F.R.C.P., F.R.C.Path, Bridon M'baya, M.B., B.S., Quentin Eichbaum, M.D., Ph.D., M.P.H., Vernon J. Louw, M.B., Ch.B., M.Med, Ph.D., Arwa Z. Al-Riyami, M.D., F.R.C.P.C., Claude Tayou, M.D., M.P.H., Silvano Wendel, M.D., Ph.D., Aaron A. R. Tobian, M.D., Ph.D., and Evan M. Bloch, M.B., Ch.B.

Words 1425

A safe and sustainable blood supply remains elusive for many low- and middle-income countries (LMICs). The World Health Organization (WHO) considers blood and blood components to be essential medicines, which underscores their importance to health systems. Essential medicines are products that are deemed to be necessary to meet the health care needs of the majority of the population and that therefore must be in adequate supply, accessible, affordable, and quality-assured. Yet nearly two thirds of all countries — including countries in central, eastern, and western sub-Saharan Africa, Oceania, and South Asia — lack sufficient blood to meet clinical demand.¹

There are substantial disparities in the availability and safety of blood between high-income countries and LMICs. Forty percent of the global blood supply is collected in high-income countries, despite these countries having less than 20% of the world's population.¹ The WHO recommends collecting a minimum of 10 units of blood per 1000 population; as of 2018 the donation rate in high-income countries was 31.5 units per 1000 people, as compared with 6.6 units and 5.0 units per 1000 people in lower-middle-income countries and low-income countries, respectively. Evidence supporting both the WHO's minimum target and the application of a single global target is weak, however. Limited availability of blood in LMICs has meant that transfusion practices differ between high-income countries and LMICs. For example, hemoglobin thresholds for administering transfusions to children are lower in LMICs (4 to 5 g per deciliter) than in high-income countries, although recent trials indicate that this cutoff may be appropriate for some children.²

The global blood deficit has wide-ranging adverse effects, given that many clinical disciplines (e.g., obstetrics, pediatrics, hematology, oncology, emergency medicine, and surgery) depend on blood transfusion. There are notable effects on maternal and child health. For example, one quarter of maternal in-hospital deaths caused by peripartum hemorrhage in sub-Saharan Africa have been attributed to blood shortages.³ The Fluid Expansion As Supportive Therapy (FEAST) trial, conducted in Uganda, Kenya, and Tanzania, found that more than half of children who presented with febrile illness and severe anemia (i.e., a hemoglobin level below 5 g per deciliter) died when transfusion was delayed for more than 8 hours after admission, whereas only 4% died when transfusion occurred within 8 hours.⁴ Lack of adequate blood is an impediment to achieving the United Nations' Sustainable Development Goals for reducing the burden of maternal death and deaths among children younger than 5 years of age. Treatment strategies that are considered to be the standard of care in high-income countries (e.g., hematopoietic stem-cell transplantation and cardiac surgery) are severely limited or unaffordable in many LMICs.

We believe three challenges deserve specific attention. The first relates to the composition of the donor pool, which affects both safety and sustainability of the blood supply. Voluntary, nonremunerated blood donors have long been considered to be the safest donor group. But replacement donors (i.e., friends or family members of the intended recipient) and, to a lesser extent, paid donors account for a substantial portion of donors in many LMICs. Members of these groups are known to have a higher risk of transfusion-transmissible infections than voluntary, nonremunerated donors, since opportunities for replacement and paid donation may discourage donors from admitting to high-risk behaviors. However, there is some nuance to this concern. When controlling for first-time versus repeat donor status, infection risk (as measured by the prevalence of transfusion-transmissible infections) doesn't differ dramatically between voluntary and

replacement donors.⁵ There is geographic variation in risk. For example, paid donation in Africa may be employed when blood is in short supply. By contrast, paid donation in some former Soviet Bloc countries is routine practice; while the infectious risk is not as low as that of voluntary donors in this setting, it may be acceptable for repeat donors, given their ease of recruitment. We are not advocating for paid donation: voluntary donation should remain the goal. However, there is support for emphasizing donor retention rather than categorization of donors according to voluntary or replacement status alone, at least pending attainment of a voluntary donor pool.

Second, the inappropriate use of blood — which can involve administering transfusions for improper indications, transfusing too much or too little blood, or failing to consider alternative treatment options (e.g., iron supplementation for patients with iron deficiency who are in stable condition) — is an important area for improvement. There are evidence-based transfusion thresholds for a wide range of clinical indications, which — in general—favor restrictive transfusion but lack of adherence to guidelines can result in blood wastage..., ... The third challenge involves dependence on external funding, which is vulnerable to changes in politics and policy. For example, selected countries received massive infusions of funding for transfusion services in the mid-2000s as part of HIV/AIDS-mitigation initiatives. Despite the success of this support in bolstering blood-transfusion safety, funding has since diminished, which has impeded further progress. Deliberate, phased transitions to self-reliance in LMICs should be carefully considered as part of funding efforts.

Inattention to blood transfusion reflects broad neglect of pathology and laboratory services in LMICs. Deficiencies include a lack of government support for national blood services, limited infrastructure and staffing, suboptimal or incomplete laboratory-based donor testing with quality assurance, limited or absent post-transfusion surveillance, and insufficient regulatory oversight. Challenges also extend beyond structural considerations. Outside of major disasters, such as earthquakes, laboratory services and blood transfusion often fail to capture public attention — and, consequently, support from funding agencies — despite being indispensable to modern medical practice.

We believe blood transfusion should be considered a global health priority. Despite limited resources and myriad systemic challenges, access and safety have been advanced in some instances. A partnership between the Eswatini National Blood Transfusion Services and the U.S. Centers for Disease Control and Prevention led to a near tripling of the number of donated units of blood after education and operational outreach. In Rwanda, government support for the National Centre for Blood Transfusion yielded an exclusively volunteer, nonremunerated donor pool as part of a centralized-blood-center model that included an expanded network of blood-collection sites. In Georgia, blood-transfusion services have been prioritized under a national hepatitis C elimination program; this focus has spurred a complete overhaul of the blood-donation system, from policy and regulatory oversight to donor-selection and testing and post-transfusion-surveillance procedures. In Zimbabwe, an innovative, low-cost initiative known as the Pledge 25 Club has recruited schoolage students (a group that is at relatively low risk for HIV infection) to be repeat blood donors. This approach has been adopted regionally. Nicaragua transitioned from a hospital-based collection model to regional blood center-collections, achieving 100% voluntary donation within three years. Interventions included raising public awareness regarding blood donation, donor education, and training of physicians, nurses and allied health professionals within the framework of a nascent national blood system. Contemporaneously, the blood collection rate rose by almost 20% and the prevalence of infectious markers decreased by more than half. In Cambodia, a collaboration between the Cambodian Blood Service and the Australian Red Cross has advanced its goal toward accreditation by meeting international standards, such as those of the African Society for Blood Transfusion (AfSBT). AfSBT has introduced a stepwise approach to accreditation for blood services for LMICs. Interventions in Cambodia included training and education, donor selection and counseling, strengthening manufacture of blood components and clinical blood use.

Global indicators of blood safety and availability suggest improvement, but such metrics may be biased by success in a subgroup of countries. Furthermore, accurate data are difficult to obtain because both donations and transfusions happen at the level of individual hospitals. Successful models have yet to be implemented widely to a number of countries.

Though we acknowledge that there are numerous competing priorities in global health, we believe steps should be taken to ensure blood safety and availability. This demands a holistic approach to address each element of the blood collection-transfusion continuum. One solution could be to implement more effective messaging that involves promoting the status of blood products as essential medicines, akin to antibiotics and anesthetics. Another is engagement of stakeholders to prioritize transfusion within national health systems, which would include development of guidelines for evidence-based transfusion practice. Finally, situational analysis is imperative to provide robust evidence about the actual deficit in LMICs. Under the current circumstances, the continued neglect of blood safety and availability represents a tacit acceptance of suboptimal standards for LMICs.