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Editorial

# COVID-19-Related Blood Shortages and Cardiac Surgery: Do We Have Too Many Eggs in One Basket?

THE UNITED STATES BLOOD SUPPLY (Fig 1) is built on volunteer donations, a system that dates to World War II. It is estimated that there are 200 million potential blood donors in the United States, or roughly two-thirds of the population.[1] The number of eligible donors has grown during the past 15 years, mainly through the inclusion of older persons (age ≥65 years) in the donor pool.[1] Despite this, blood supply has decreased as more donor restrictions have been put into place and demand has fallen, offsetting growth in the potential donor pool.[1,2] It currently is estimated that <5% of eligible donors or around 7 million persons annually donate blood. This fact, coupled with an aging donor population, highlights vulnerabilities in the national blood supply.[1]

The American Red Cross, which supplies approximately 40% of the nation's blood supply, estimates the demand for red blood cells (RBCs) is approximately 14 million units per year.[3] In addition, annually, 2 million platelet and 2.5 million plasma units are transfused. Surgical patients, particularly cardiac surgical patients, continue to be major consumers of allogeneic blood products. There are more than 300,000 cardiac surgical procedures performed with cardiopulmonary bypass each year in the United States, with conservative estimates suggesting that at least one-third of adult patients undergoing cardiac surgery are transfused. [4,5] However, transfusion risk varies greatly with surgical complexity, and transfusion rates for complex surgeries (eg, combined valve replacement and coronary artery bypass grafting) exceed 80%.[6] Given the trend of increasing surgical complexity, it is likely that allogeneic transfusion rates will remain high in cardiac surgery for the foreseeable future.

The COVID-19 pandemic has dramatically impacted nearly all aspects of life in the United States, including the national blood system. Supply chain disturbances have been numerous, affecting the building industry, auto industry, food industry, and healthcare. In June 2020, industry leaders from across the United States were surveyed regarding these challenges, with 93% of respondents acknowledging a need to make supply chains more "flexible, agile, and resilient."[7] These disturbances have magnified blood collection challenges in the United States, leading to blood shortages that have worsened progressively throughout the pandemic. In this setting, the United States Department of Health and Human Services issued a report to Congress on the adequacy of the national blood supply, describing multiple "stressors" in the current system (Table 1).

These include a lack of "real-time" monitoring of the national blood inventory, reliance on a loosely connected system of nonprofit blood centers and hospital-based collection centers without robust integration or central coordination, an aging donor pool, disparate local collection and supply models, and regulations that do not promote innovation and rapid adoption of new technology.[8] By late 2021, numerous blood collections across the nation, including critically important mobile drives at high school and college campuses, had been canceled because of COVID-19. Staffing shortages and associated social and economic disturbances resulted in a 10% drop in the United States blood collections from prepandemic levels. When coupled with high volumes of surgical and intensive care unit admissions, this resulted in the depletion of local and regional blood inventories. The American Red Cross and other blood collection organizations offered numerous incentives to attract donors to available blood donation sites, including opportunities to win Super Bowl tickets, luxury travel packages to popular music festivals, gift cards, and home electronic devices. Nevertheless, blood shortages worsened, and in January 2022, the American Red Cross declared a "National Blood Emergency" for the first time in its history.[3]

In response, the American Medical Association, American Nurses Association, and American Hospital Association issued a joint statement outlining the dire nature of the national blood crisis and encouraging all eligible persons to donate blood. Shortly thereafter, the Association for the Advancement of Blood and Biotherapeutics, in collaboration with 17 leading American healthcare and blood collection organizations including but not limited to the American Society of Anesthesiologists, American College of Emergency Physicians, American College of Surgeons, American Society of Hematology, America's Blood Centers, Blood Centers of America, American Red Cross, Federation of American Hospitals, and the Society for the Advancement of Patient Blood

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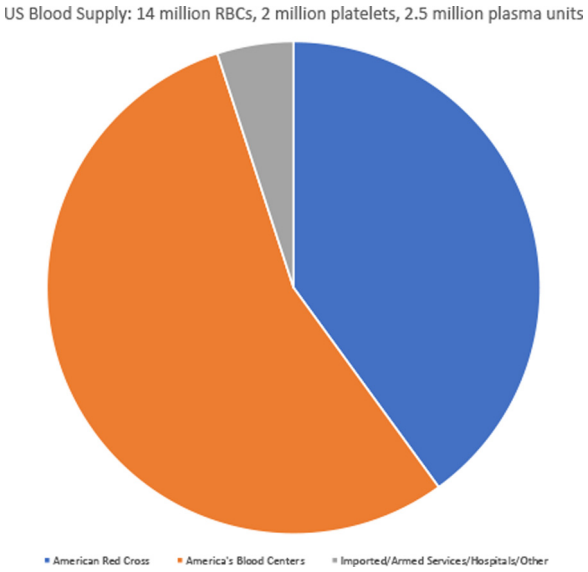


Fig 1. Figure shows approximate contributions from various United States blood suppliers.

Management, launched the "Alliance for a Strong Blood Supply" to facilitate communication regarding the state of the United States blood supply, share best practice initiatives, and coordinate public communications and advocacy efforts.

Although strengthening the United States blood supply is critically important and receives appropriate media coverage, far less attention is given to equally important efforts to decrease the demand for allogeneic blood products. In light of the national blood crisis, coupled with the multitude of well-described benefits to patients and the broader healthcare system that accompany reduction in allogeneic transfusion, it is past time for hospitals across the nation, including cardiac surgery programs, to evaluate current transfusion practices and further invest in evidence-based patient blood management (PBM). PBM can be loosely defined as evidence-based clinical practice and educational tools to optimize the blood health of each patient, minimize transfusion exposure, and improve clinical outcomes. These initiatives are a win-win for patients and hospitals—conserving blood resources for those most in need, reducing transfusion, expenditures and waste, and improving patient outcomes.[9,10]

In 2021, the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists published an updated joint guideline outlining contemporary PBM practices in cardiac surgery.[11] In the guideline, the authors provided multiple recommendations, including the evaluation and treatment of preoperative anemia (Class IIa), minimization of phlebotomy for the prevention of iatrogenic anemia (Class IIa), implementation of standardized transfusion protocols (Class IIa), appropriate withholding of anticoagulation (Class I and Class IIa), employment of antifibrinolytics in cardiopulmonary bypass cases (Class I) and off-pump coronary artery bypass grafting (Class IIa), appropriate utilization of factor concentrates (Class IIa), retrograde autologous priming (Class I), acute normovolemic hemodilution (Class IIa), and cell salvage (Class I), and goal-directed hemostasis management based on coagulation testing (Class I).[11] Simply stated, these evidence-based tools are readily available in nearly all cardiac surgery practices to augment red cell production, prevent and treat coagulopathy, and minimize perioperative bleeding, thereby reducing the need for allogeneic transfusion.

Beyond these immediately available interventions, there are other long-term aspirational goals that may help to stabilize the United States blood supply (Table 2). These include efforts to prolong the shelf-life of blood components (eg, mitigation strategies for the RBC storage lesion, delayed cold-storage of platelets), enhancing research into RBC-like products (eg, hemoglobin-based oxygen carriers, encapsulated hemoglobin products) and pooled products with longer storage durations (eg, cryopreserved platelets, freeze-dried plasma), and expanding use of fibrinogen concentrates and factor concentrates for the treatment of acquired coagulation abnormalities. Further, it is essential to establish a strong pool of recurring blood donors rather than relying on surges in one-time donations in response to critical events, as such highly publicized calls for donations may be unnecessary to meet current transfusion demand,

Table 1
Key Themes From the 2020 Health and Human Services Report on the Adequacy of United States Blood Supply.

| Vulnerability | Recommendation |
|---|---|
| Lack of "real-time" data on national blood availability | • Create an apparatus for "real-time" monitoring of the national blood supply |
| Dependence on volunteer donations and eroding culture of donation, particularly among young adults | • Nurture a culture of donation, particularly among young adults and those with lesser access to healthcare<br>• Better understand through research the reasons people donate blood and whether there is equitable access to blood donation |
| Fragmented/disparate local models for blood donation and supply | • Modernize the business model for blood donation, storage, and supply |
| Current regulations may stifle innovation and rapid adoption of important technology | • Create novel regulatory approaches to foster innovation and move important technology into practice more quickly<br>• Create a public-private partnership that, in coordination with FDA, reviews how current regulations impact innovation, safety, and outcomes |
| Revenue losses and negative balance sheets for many blood collection centers | • Move away from treatment of blood as a commodity and move towards treatment of nation's blood supply as a public health program |

Abbreviation: FDA, United States Food and Drug Administration.

Table 2
Aspirational Goals to Stabilize the United States Blood Supply.

| Blood Product | Potential Solution | Challenge |
|---|---|---|
| RBC | • Mitigate RBC storage lesion and increase the safe duration of refrigerated RBC storage | • Refrigerated RBC storage duration has not been able to successfully expand beyond 42 d; limited literature suggests that "old" RBCs may be harmful to patients |
| | • Enhance the safety of HBOCs | • Concerns about adverse effects of HBOCs when compared against RBCs (eg, hypertension, methemoglobinemia, circulatory overload, gastrointestinal side effects)<br>• Producers of HBOCs have had difficulty maintaining financial solvency |
| | • Bring innovative RBC alternatives to FDA approval and/or licensure (eg, CRISPR edited universal donor RBCs, bioengineered encapsulated hemoglobin products) | • Products are in development, but have not entered clinical trials at this time |
| Plasma | • Continue to develop freeze-dried plasma products with increased shelf life | • Freeze-dried plasma remains poorly studied compared to liquid plasma and there are no contemporary phase 3 studies comparing against liquid plasma in the United States |
| Cryoprecipitate | • Move towards fibrinogen concentrate as the standard of care for treatment of acquired hypofibrinogenemia (as has been done in Canada and Europe) | • Phase 3 study of fibrinogen concentrate has not yet been completed in the United States<br>• Cryoprecipitate remains modestly cheaper than fibrinogen concentrate and also provides other useful pro-coagulant proteins (ie, von Willebrand factor, factors VIII and XIII) |
| Platelets | • Continue to develop and study alternative products, including cryopreserved platelets and cold-stored platelets, which would allow for longer storage durations | • Clinical trials are ongoing, but current efficacy of these products is unknown.<br>• Cold-stored platelets may be effective for hemostasis, but they have a shorter circulation time and/or life span |

Abbreviations: CRISPR, Clustered Regularly Interspaced Short Palindromic Repeats; FDA, United States Food and Drug Administration; HBOC, hemoglobin-based oxygen carriers; RBC, red blood cell.

overwhelm local blood collection capacity, and ultimately lead to increased blood waste.[12]

Although these aspirational goals will take years to achieve, common-sense PBM tools to decrease blood demand and improve the blood health of each patient are available for broad adoption now. Each provider (cardiothoracic anesthesiologist, cardiac surgeon, intensivist) can have an immediate impact on ongoing blood shortages by critically evaluating the appropriateness of each transfusion, becoming a recurrent blood donor if they are eligible, and by advocating for PBM initiatives in their own institution. Although the national blood crisis will continue to challenge the United States healthcare system for the foreseeable future, it should serve as a unifying call to improve blood-banking systems, promote coordination between diverse blood collection and distribution organizations, and invest in research, quality improvement, and practice optimization efforts to reduce blood demand by embracing the core principles of PBM.

## Conflict of Interest

Matthew A. Warner and Prakash A. Patel serve on the Board of Directors for the Society for the Advancement of Patient Blood Management. Matthew A. Warner, Nadia B. Hensley, and Michael Mazzeffi serve on the American Society of Anesthesiologists Committee on Patient Blood Management. Nadia B. Hensley and Michael Mazzeffi are on the scientific advisory board for Octapharma USA, which is involved in patient blood management.

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