



LETTER TO BLOOD | MAY 26, 2022

Shortage of plasma-derived products: a looming crisis?

Mischa Li Covington, Chesinta Voma, Sean R. Stowell



Check for updates

Blood (2022) 139 (21): 3222–3225.<https://doi.org/10.1182/blood.2021015370>[Article history](#) 

Split-Screen

Share Tools 

PDF

Subjects: [Transfusion Medicine](#)

TO THE EDITOR:

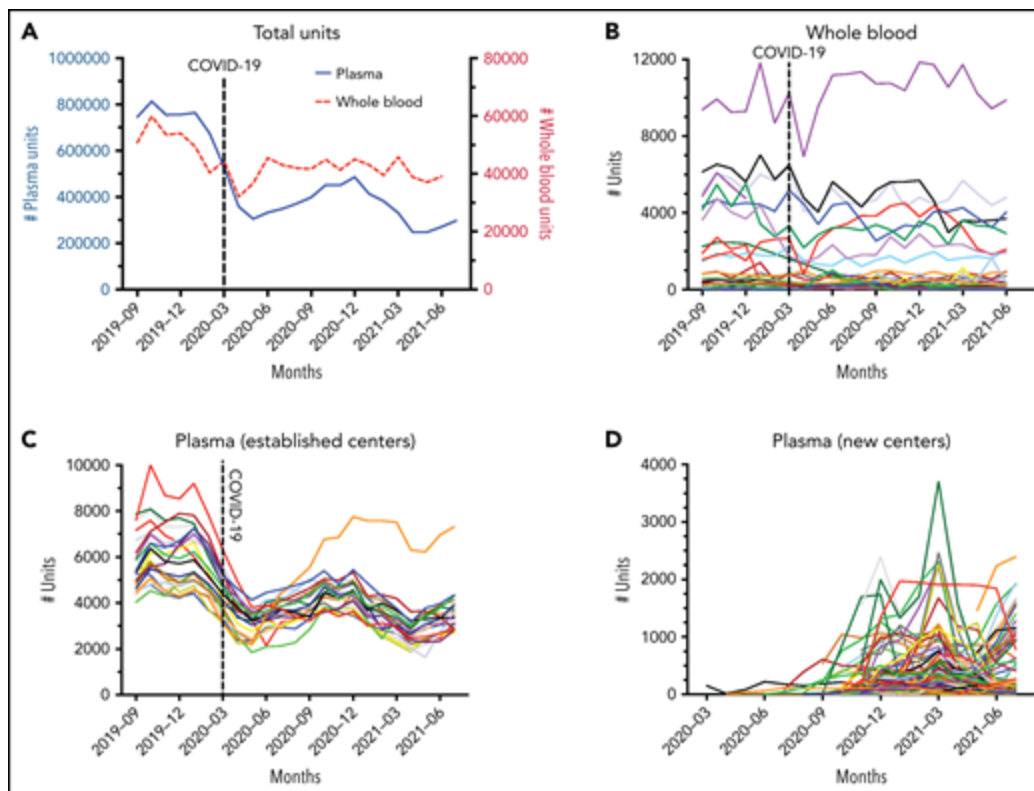
Plasma, the noncellular component of blood, contains many proteins important for homeostasis. Deficiencies in plasma components can contribute to the pathogenesis of different diseases. To overcome patient plasma deficits, plasma from healthy donors is often transfused. Plasma is also used to produce various plasma-derived medicinal products (PDMPs), which allow for a more tailored approach to treating specific plasma deficiencies. PDMPs include intravenous immunoglobulin (IVIg) and subcutaneous immunoglobulin, clotting factors, and albumin.^{1,2} Plasma and albumin are not only staples in surgical intervention but also serve as replacement fluid during therapeutic plasma exchange,³ a procedure to treat myriad immune-mediated hematologic, neurologic, renal, and transplant-associated conditions.⁴ Clotting factor concentrates are critical for treating coagulopathies,⁵⁻⁷ whereas IVIg is regularly used for immune modulation, whether to supplement immunosuppressed patients and prevent infection or to suppress autoimmune conditions.⁸⁻¹⁰ Over the years, the need for these PDMPs has steadily increased. However, source plasma supply has struggled to keep pace with PDMP demands.^{8,11}

Although PDMPs are routinely used to treat critical illnesses, as these products are derived from donor plasma rather than chemically synthesized or recombinantly generated, limitations in plasma donations directly impact PDMP availability. However, as PDMPs are commonly dispensed by hospital-based pharmacies, disruptions in [Supply Chain](#) may not be readily perceived by transfusion medicine services or the blood donation community, which understandably primarily focus on red blood cell (RBC) and platelet availability.^{12,13} Unlike

comes from the United States, 1 of only 5 countries where it is legal to financially compensate plasma donors.⁸ It takes 7 to 12 months for plasma to be processed into shelf-ready PDMPs.¹⁵ Thus, factors that impact plasma donations, particularly in the United States, may not be immediately appreciated despite far-reaching ramifications for health care worldwide in the ensuing years.

Following the onset of the COVID-19 pandemic, blood product donations decreased due to social restrictions and health concerns.^{16,17} Building upon opportunities designed to address prior blood shortages,¹⁸ health care centers and public campaigns have done excellent work raising awareness of RBC and platelet shortages and taking measures to conserve inventory. However, there is often little public awareness regarding the shortage of plasma products.³ Most plasma centers are not affiliated with academic or community blood centers, and unlike for whole blood and platelets, there are often no “plasma drives” or similar community outreach programs designed to raise awareness regarding possible shortages. Consequently, although PDMPs are as essential to health care as RBCs and platelets, the unique procurement strategies designed to obtain source plasma for PDMP manufacturing purposes prevent plasma shortages from receiving similar attention.³

Given the distinct mechanisms through which source plasma is procured, we hypothesized that the ongoing pandemic may have a unique impact on source plasma donation. To assess this, we examined the possible impact of COVID-19 on plasma donations by comparing source plasma to whole blood donations in the United States. This was accomplished by analyzing the number of units that were pathogen-tested by Qualtex (a large United States blood and plasma product-testing laboratory) from September 2019 to July 2021. The products came from more than 500 collection centers in the United States. As expected, there was a sharp drop in total units for both whole blood and plasma immediately following pandemic onset in March 2020 ([Figure 1A](#)). However, subsequently, the number of whole blood units quickly stabilized to a lower level (35 000-45 000 units per month postpandemic vs 50 000-60 000 prepandemic) and has remained largely stable ([Figure 1A](#)). In contrast, plasma donations did not rebound and then stabilize at near prepandemic levels ([Figure 1A](#)). Despite a minor recovery in the summer and fall of 2020, plasma donations continued to drop in 2021 compared with the same months in 2020 ([Figure 1A](#)). Part of the fluctuation in total units can be attributed to dropout of existing collection centers or emergence of new centers: some companies shifted away from Qualtex testing; others acquired additional centers. To control for these changes, we analyzed the units collected at each center. For whole blood donations, the individual centers did not experience drastic reduction in units following initial recovery after the onset of the COVID-19 pandemic ([Figure 1B](#)). In contrast, the 22 largest plasma centers demonstrated a pattern consistent with that seen for total plasma units: almost all demonstrate a sharp downturn in spring of 2020, modest recovery in summer and fall, recurrent drop after New Year’s 2021, and modest recovery again in the summer of 2021 ([Figure 1C](#)). The decrease in plasma donations at large centers is partially offset by the growth of new centers ([Figure 1D](#)). Although the volume from these new, smaller centers shows a promising trend, they are currently unable to fully compensate for the total decrease in plasma donations. With ongoing waves of SARS-CoV-2 variants, plasma donation volumes may not return to pre-



[VIEW LARGE](#)

[DOWNLOAD PPT](#)

Volume of blood product donations. (A) Cumulative units of whole blood (red dashed line, right y-axis) and plasma (blue solid line, left y-axis) tested by Qualtex from September 2019 to July 2021. (B) Volume of whole blood collected at each center. (C) Volume of plasma collected at the largest established centers. (D) Volume of plasma collected at new centers after March 2020. For panels B-D, each line represents a single collection center.

Although the data presented here reflect over 500 donor centers, they do not include all donor centers across the United States or internationally. However, assuming that the volume sampled by Qualtex reflects general trends, these data suggest that COVID-19 had a greater impact on the supply of plasma than of whole blood, and plasma donations continue to suffer despite the spread of vaccinations ([Figure 1A](#)). Because it can take up to a year for plasma to be processed into PDMPs, the health care impact of plasma shortages is not experienced as acutely as that of RBCs and platelets. Consequently, plasma deficits may continue unnoticed for long periods before the effects hit the health care system. Furthermore, due to the widespread policy in other nations of prohibiting payment for plasma donations, the reliance on the source plasma donations from the United States for PDMP manufacturing suggests that local shortages may have international consequences.^{19,20} Thus, the current paucity of plasma donations in the United States will manifest as global shortages in IVIg/subcutaneous immunoglobulin, factor concentrates, and albumin for years to come. As these products are routinely used in a wide variety of clinical settings, such shortages will negatively affect the care of many patients with hematologic, neurologic, rheumatologic, and transplant-associated conditions, with potentially significant consequences.

Acknowledgment

Authorship



already recognized the potential impact of the current plasma shortage on its members and are encouraging supporters to donate plasma. During times of RBC and platelet shortages, mitigation strategies are deployed, such as reducing nonessential procedures and triaging orders. We urge clinical care providers to adopt similar measures for PDMP use, substituting with alternative therapies when possible and critically evaluating the marginal benefit of PDMPs in the context of other therapies. Implementation of PDMP stewardship based on consensus guidelines by a multidisciplinary team may facilitate such endeavors. To conserve the long-term supply of PDMPs, these measures would need to be adopted across the medical field, not just at individual institutions.

Although the data presented here do not explain why plasma donations decreased more than whole blood, a variety of factors may converge to influence current plasma donation shortages (see [Table 1](#)). Payment for plasma donations propelled the United States to number 1 in volume, but it also indirectly targets lower-income populations, who may donate as frequently as twice a week.^{21,22} This may not only have unintended health consequences, because frequent donors exhibit altered plasma protein profiles compared with infrequent donors,²³ but may also create challenges with plasma donation pipelines that are distinct from whole blood donations, especially following unpredictable changes in global health and world economies during an ongoing pandemic. Although commercial companies increased the compensation per donation during the pandemic in an effort to achieve prepandemic levels, the current donor pool continues to fail to meet demand. Instead of increasing financial compensation, changes should be made to incentivize altruistic plasma donations. Public campaigns to educate and recruit donors for RBCs and platelets have been more successful, perhaps because of rather than despite the lack of financial remuneration. Education of the public about the necessity and uses of PDMPs may enhance the appeal of plasma donation but will require efforts from not only the transfusion medicine community but policy makers and the entire health care community.

Table 1. Possible factors influencing pandemic plasma donor trends

1. Relative lack of public awareness of the need for plasma and PDMPs.
2. Logistical challenges posed by homeschooling children and diminished transportation options, which may disproportionately impact plasma donors compared with whole blood donors.
3. Enhanced government benefits during the pandemic may have made plasma donation less appealing as a source of income.
4. Centers in border states may have had significant donor pools affected by border closures.
5. Donors who contracted COVID-19 may have donated convalescent plasma for clinical trials, which is not typically sourced for PDMP production.

We hope that these data raise awareness regarding possible immediate and long-term consequences of plasma shortages exacerbated by the pandemic. Now is the time to begin seriously considering conservation measures

and alternative or additional strategies to encourage plasma donations from a greater portion of the public.^{[9,22,24,25](#)}

Acknowledgment

The authors thank Vaishnavi Kunchala for facilitating data acquisition from Qualtex Laboratories.

Authorship

Contribution: M.L.C. was responsible for data analysis and writing the manuscript; C.V. facilitated data collection from Qualtex; S.R.S. oversaw study design and coordination; and all authors were involved in data interpretation and editing the manuscript.

Conflict-of-interest disclosure: The authors declare no competing financial interests.

Correspondence: Sean R. Stowell, Department of Pathology, Joint Program in Transfusion Medicine, Brigham and Women's Hospital, Harvard Medical School, 630E New Research Building, Boston, MA 02115; e-mail: srstowell@bwh.harvard.edu.

Full data are available by e-mail request to the corresponding author.

REFERENCES

1. Klein HG. Should blood be an essential medicine? *N Engl J Med*. 2013;368(3):199-201.

[Google Scholar](#) [Crossref](#) [PubMed](#)

2. Strengers PF, Klein HG. Plasma is a strategic resource. *Transfusion*. 2016;56(12):3133-3137.

[Google Scholar](#) [Crossref](#) [PubMed](#)

3. McLeod BC. Plasma and plasma derivatives in therapeutic plasmapheresis. *Transfusion*. 2012;52(suppl 1):38S-44S.

[Google Scholar](#) [Crossref](#) [PubMed](#)

4. Padmanabhan A, Connelly-Smith L, Aqui N, *et al*. Guidelines on the use of therapeutic apheresis in clinical practice – evidence-based approach from the Writing Committee of the American Society for Apheresis: the Eighth Special Issue. *J Clin Apher*. 2019;34(3):171-354.

[Google Scholar](#) [Crossref](#) [PubMed](#)

5. Lai M, Hough G, Tarrant J, Lillicrap D. Biological considerations of plasma-derived and recombinant factor VIII immunogenicity. *Blood*. 2017;129(24):3147-3154.

Acknowledgment

Authorship



6. Peyvandi F, Mannucci PM, Garagiola I, *et al.* A randomized trial of factor VIII and neutralizing antibodies in hemophilia A. *N Engl J Med.* 2016;374(21):2054-2064.

[Google Scholar](#) [Crossref](#) [PubMed](#)

7. Goldstein JN, Refaai MA, Milling TJ Jr, *et al.* Four-factor prothrombin complex concentrate versus plasma for rapid vitamin K antagonist reversal in patients needing urgent surgical or invasive interventions: a phase 3b, open-label, non-inferiority, randomised trial. *Lancet.* 2015;385(9982):2077-2087.

[Google Scholar](#) [Crossref](#) [PubMed](#)

8. Prevot J, Jolles S. Global immunoglobulin supply: steaming towards the iceberg? *Curr Opin Allergy Clin Immunol.* 2020;20(6):557-564.

[Google Scholar](#) [Crossref](#) [PubMed](#)

9. Brand A, De Angelis V, Vuk T, Garraud O, Lozano M, Politis D; European Mediterranean Initiative for Transfusion Medicine. Review of indications for immunoglobulin (IG) use: narrowing the gap between supply and demand. *Transfus Clin Biol.* 2021;28(1):96-122.

[Google Scholar](#) [Crossref](#) [PubMed](#)

10. Newburger JW, Takahashi M, Beiser AS, *et al.* A single intravenous infusion of gamma globulin as compared with four infusions in the treatment of acute Kawasaki syndrome. *N Engl J Med.* 1991;324(23):1633-1639.

[Google Scholar](#) [Crossref](#) [PubMed](#)

11. Hartmann J, Klein HG. Supply and demand for plasma-derived medicinal products – a critical reassessment amid the COVID-19 pandemic. *Transfusion.* 2020;60(11):2748-2752.

[Google Scholar](#) [Crossref](#) [PubMed](#)

12. Di Angelantonio E, Thompson SG, Kaptoge S, *et al*; INTERVAL Trial Group. Efficiency and safety of varying the frequency of whole blood donation (INTERVAL): a randomised trial of 45 000 donors. *Lancet.* 2017;390(10110):2360-2371.

[Google Scholar](#) [Crossref](#) [PubMed](#)

13. Stubbs JR, Homer MJ, Silverman T, Cap AP. The current state of the platelet supply in the US and proposed options to decrease the risk of critical shortages. *Transfusion.* 2021;61(1):303-312.

[Google Scholar](#) [Crossref](#) [PubMed](#)

14. Allen JG. Letter: Advantages of volunteer blood donors. *N Engl J Med.* 1974;291(25):1365-1366.

[Skip to Main Content](#) [PubMed](#)

Acknowledgment

Authorship



16. Al Mahmasani L, Hodroj MH, Finianos A, Taher A. COVID-19 pandemic and transfusion medicine: the worldwide challenge and its implications. *Ann Hematol.* 2021;100(5):1115-1122.

[Google Scholar](#) [Crossref](#) [PubMed](#)

17. Stanworth SJ, New HV, Apolseth TO, *et al.* Effects of the COVID-19 pandemic on supply and use of blood for transfusion. *Lancet Haematol.* 2020;7(10):e756-e764.

[Google Scholar](#) [Crossref](#) [PubMed](#)

18. Williamson LM, Devine DV. Challenges in the management of the blood supply. *Lancet.* 2013;381(9880):1866-1875.

[Google Scholar](#) [Crossref](#) [PubMed](#)

19. Puig Rovira L. Plasma self-sufficiency in Spain. *Transfus Apheresis Sci.* 2020;59(1):102700.

[Google Scholar](#) [Crossref](#)

20. Omokawa S, Abe M. The plasma supply in Japan. *Transfus Apheresis Sci.* 2020;59(2):102749.

[Google Scholar](#) [Crossref](#)

21. Thorpe R, Masser BM, Nguyen L, Davison TE. Understanding donation frequency: insights from current plasma donors. *Vox Sang.* 2020;115(2):174-181.

[Google Scholar](#) [Crossref](#) [PubMed](#)

22. Farrugia A, Penrod J, Bult JM. Payment, compensation and replacement – the ethics and motivation of blood and plasma donation. *Vox Sang.* 2010;99(3):202-211.

[Google Scholar](#) [Crossref](#) [PubMed](#)

23. Laub R, Baurin S, Timmerman D, Branckaert T, Strengers P. Specific protein content of pools of plasma for fractionation from different sources: impact of frequency of donations. *Vox Sang.* 2010;99(3):220-231.

[Google Scholar](#) [Crossref](#) [PubMed](#)

24. Kreil TR. Building blocks of the viral safety margins of industrial plasma products. *Ann Blood.* 2018;3(2):14.

[Google Scholar](#)

25. Gray AL, Wirtz VJ, 't Hoen EF, Reich MR, Hogerzeil HV. Essential medicines are still essential. *Lancet.* 2015;386(10004):1601-1603.

[Skip to Main Content](#)

[Google Scholar](#) [Crossref](#) [PubMed](#)

Acknowledgment

Authorship



[Sign in via your Institution](#)

[Add comment](#)

Volume 139, Issue 21

May 26 2022

[< Previous Article](#)

[Next Article >](#)

[Sign in via your Institution](#)

[View Metrics](#)

Cited By

[Web Of Science \(27\)](#)

[Google Scholar](#)

Email Alerts

[Article Activity Alert](#)

[First Edition Alert](#)

[Latest Issue Alert](#)

[Skip to Main Content](#)



Acknowledgment

Authorship



[About Blood](#)

[Abstracts](#)

[Advertising in Blood](#)

[Blood Classifieds](#)

[Collections](#)

[Contact Us](#)

[Permissions](#)

[Subscriptions](#)

[Submit to Blood](#)

[Alerts](#)

[All Issues](#)

[Author Guide](#)

[Current Issue](#)

[First edition](#)

[Newsroom](#)

American Society of Hematology / 2021 L Street NW, Suite 900 / Washington, DC 20036 / TEL +1 202-776-0544 /
FAX +1 202-776-0545

ASH Publications

American Society of Hematology

[ASH Home](#)

[ASH Image Bank](#)

[ASH Store](#)

[Advocacy](#)

[Education](#)

[Meetings](#)

[Research](#)

[Skip to Main Content](#)



[Acknowledgment](#)

[Authorship](#)

Blood

REFERENCES

Blood Advances

Blood Global Hematology

Blood Immunology &

Cellular Therapy

Blood Neoplasia

Blood Red Cells & Iron

Blood Vessels,

Thrombosis & Hemostasis

Hematology, ASH

Education Program

ASH Clinical News

ASH-SAP

The Hematologist

Copyright 2026 by American Society of Hematology

[Cookie Settings](#) [Privacy Policy](#) [Cookie Policy](#) [Terms of Use](#) [Contact Us](#)



Acknowledgment

Authorship