Vol. 23, No. 1 March 2023

BLOOD BULLETIN

Directed Donations and COVID-19 mRNA Vaccinated Blood Donors

Authors: Daniela Hermelin, MD, Chief Medical Officer at ImpactLife; Louis Katz, MD, Chief Medical Officer Emeritus at ImpactLife; Nancy Van Buren, MD, Medical Director at Innovative Blood Resources and Community Blood Center of Kansas City, divisions of New York Blood Center; Kip Kuttner, DO, Vice President and Medical Director at Miller-Keystone Blood Center; Richard Gammon, MD, Medical Director at OneBlood; Debra Smith, MD, PhD, Medical Director at Carter BloodCare; Kirsten Alcorn, MD, Co-Chief Medical Officer at Bloodworks Northwest.

Contributors: Rita Reik, MD, FCAP, Chief Medical Officer at OneBlood; Claudia S. Cohn, MD, PhD, Professor of Laboratory Medicine and Pathology at the University of Minnesota; Theresa Nester, MD, Co-Chief Medical Officer at Bloodworks Northwest.

The authors disclose no conflicts.

versiti™

America's Blood Centers®
It's About *Life.*

Directed Donations and COVID-19 mRNA Vaccinated Blood Donors

KEY POINTS

- Hospitals and blood centers have been confronted with a growing number of directed donation requests for individuals asking for blood components from COVID-19 unvaccinated blood donors.
- Blood donors who have received the SARS-CoV-2 mRNA vaccine do not pose a risk for the safety of the blood supply.
- Information on COVID vaccination or the type of vaccine used is not collected during the donor interview because it is not medically relevant. Hence, it is not possible to label or segregate blood accordingly.
- While not medically indicated, providing directed donations from COVID-19 unvaccinated donors is also logistically arduous and costly for blood centers and hospitals alike. Health care providers should strongly discourage legislation that requires collection facilities to provide a medically unjustified service.

A growing number of requests are being received to provide blood from donors not immunized against COVID-19.

This *Blood Bulletin* is a resource for health care providers and hospital transfusion medicine medical directors and blood center staff to respond.

DEFINITIONS:

Directed donations are from donors generally selected by the potential recipient. In some cases, there is a valid medical indication for this request, however, more often there is the mistaken assumption that the recipient can select a safer donor than the collection facility. In many cases, the donor and recipient know one another and are often related. The donor must meet all allogeneic criteria to undergo collection.

mRNA vaccine is a type of vaccine that uses a copy of a molecule called messenger RNA to produce an antigen that provokes an immune response. Vaccines using mRNA do not contain transmissible virus.

During the human immunodeficiency virus (HIV) pandemic, the concern for infection by transfusion prompted an increased demand for directed donations. This risk has been essentially eliminated for HIV and other important transfusion-transmitted infections (TTI) after decades of continuous improvements in donor testing. The remaining risks from HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) are less than one per one million donations.[1]

With the COVID-19 pandemic, concerns have been raised about the potential adverse effects from transfusion of blood from donors having received SARS-CoV-2 vaccines, especially mRNA. These include the potential for passive transmission of the vaccine through transfusion with alleged but unsubstantiated adverse events (e.g., myocarditis). There are also fears that free circulating mRNA may cause changes in our DNA leading to oncogenic mutations, sterility, or birth defects. There is no evidence for any of these concerns.[2] Others have expressed religious reservations of receiving blood from a COVID-19-vaccinated donor because the vaccine was developed using embryonic or fetal tissue.[3]

COVID-19 mRNA vaccines were developed relatively recently, but mRNA vaccine technology has been studied for over 15 years. Two of the four U.S. Food and Drug Administration (FDA)-approved and authorized COVID-19 vaccines use mRNA. Current evidence indicates that after injection the mRNA **does not** enter the cell's nucleus and **cannot** interact with DNA. While vaccine components can be detected beyond the injection site for days after the shot, at picogram levels, this is many orders of magnitude below what is initially injected (microgram levels).[4] While fetal tissues were involved in previous mRNA vaccine research, they are not used in the production of available mRNA vaccines.[5] A fetal cell line used in the Janssen (Johnson & Johnson) vaccine (less than 3 percent of vaccine doses given in the U.S.) has been propagated for decades in tissue culture and no longer contains actual fetal tissue.

The donor questionnaire assures safe and effective blood donations by interrogating those who have recently received live vaccines. Because live vaccine viruses (e.g. measles or smallpox) can replicate and presumably circulate after injection, donors recently immunized with live viral vaccines are excluded for an appropriate interval. Since the COVID-19 mRNA vaccines are not live and cannot replicate SARS-CoV-2 in a donor, blood centers, in accordance with federal requirements and professional standards, do not defer donors based on vaccination status. Since a donor's COVID-19 vaccination status does not impose a safety risk for transfusion, it is not recorded and cannot be conveyed to hospitals, physicians, or patients. The FDA finds no current evidence to support concerns related to the safety of vaccinated

individuals.[6] Hence, recent requests for blood from non-vaccinated donors are medically unfounded.[7]

What are the logistical challenges and risks associated with directed donations?

The request for a directed donation begins with a patient, parent, or legal guardian who has been advised that a blood transfusion is anticipated. At this point, rather than accepting blood products from the hospital "shelf" inventory, the transfusion recipient may request family members or friends to donate blood on their behalf. The ordering physician must submit an order to collect from selected donors for a documented medical indication. All standard donor eligibility criteria must be met for these collections and the patient's blood type must be compatible with the donor's blood type. The timing from order to shipment of blood to the participating transfusion service can take several days or more, so directed requests are not useful for acute transfusion, e.g., for hemorrhaging patients. In addition, the logistical challenges of directed donations add strain and cost to an already overtasked system in the absence of medical justification.

Past studies have demonstrated that directed donors had higher rates of TTI markers than general donors.[8, 9] This was likely because directed donors are more likely to be first-time donors who have never been screened. There may also be a component of undisclosed, potentially stigmatizing, donor TTI risk. Additionally, a separate study showed that first-time parental directed donors had significantly higher rates of TTI positivity than first-time non-parental and community donors.[10] Also, directed donations from family members carry a risk of transfusion associated graft-versus-host disease and must undergo irradiation,[11] adding both complexity and expense.

Further:

- Mother-to-child directed donation poses an increased risk of transfusion-associated acute lung injury (TRALI).[12]
- Male partner to female partner directed donation poses risk of hemolytic disease of the fetus and newborn and alloimmune thrombocytopenia to future children. Therefore, husbands or potential fathers, may not serve as directed donors for women of childbearing potential.
- Blood donation by a family member who is a potential future stem cell or solid organ transplant donor may cause the patient/recipient to develop red cell or human leukocyte antigen (HLA) antibodies against that donor's antigens.

By contrast, designated donations are limited to patients with a medically justifiable need for blood products requiring attributes not found or exceedingly rare in the standard blood bank inventory. These blood products are requested from the transfusion service and fulfilled by the blood center. This process may require screening and recruiting family members of the recipient who may be the only easily accessible source in rare situations. They are medically justifiable due to the inability to supply compatible blood readily from the general donor base.

How should health care providers respond to patients requesting blood from unvaccinated donors?

Discourage these requests and encourage patients to accept blood from the general inventory and/or offer bloodless alternatives to transfusion.

There is no scientific evidence that demonstrates adverse outcomes from transfusions of blood products collected from COVID-19 vaccinated donors and, therefore, no medical reason to distinguish or separate blood donations from individuals who have received a COVID-19 vaccination. Accordingly, that information is neither collected nor is it on the blood product label.

For more information, we recommend referring to materials recently published by the Association for the Advancement of Blood & Biotherapies (AABB) and America's Blood Centers (ABC) that provide additional talking points.[13, 14]

Are hospitals legally obligated to provide directed donations to patients who request them?

The legal guidelines regarding the obligation of a hospital to satisfy the request for directed donations are state dependent. Review of one's hospital transfusion consent and updating hospital policies in conjunction with key hospital administration and its legal department regarding these issues is recommended.

Are there additional fees incurred for providing a directed donation for my patient who is requesting them?

Yes, depending on the blood center there will be additional fees incurred for directed donations that are added to the transfusion service's fees. These might not be covered by insurance.

If a directed donation was not transfused to the intended recipient, may it be allowed into the general inventory to be transfused to another patient?

Depending on the hospital transfusion service policy, a directed donation may be allowed into the general inventory. However, practically speaking, it is difficult to know when the directed donation will be required by the recipient and many hospitals keep them for that recipient until product outdate. It is recommended that the hospitals develop policies to release directed donations into the general inventory after a defined period to prevent wastage.

CONCLUSION

Requests for blood components from unvaccinated donors have no medical foundation and impose costly operational challenges for the collection facility. In addition, directed donations of platelets, plasma, and cryoprecipitate are logistically difficult.

More than 80 percent of people old enough to donate blood in the U.S. have received one or more doses of a COVID-19 vaccine.[15, 16] The very large majority have gotten one or more doses of an mRNA vaccine.[17] If donors were spuriously deferred for COVID-19 vaccination based on unfounded concerns, the blood supply would be significantly decreased, putting many thousands of patients' lives at risk.

AABB, ABC, and the American Red Cross recently issued the following joint statement: "All Americans, including both blood donors and blood recipients, should feel confident that receiving a blood transfusion is safe. COVID-19 vaccines do not replicate, and all blood donations offer the same life-saving therapeutic benefits, regardless of the vaccination status of the donor."[18]

REFERENCES

1. Busch MP, Bloch EM, Kleinman S. Prevention of transfusion-transmitted infections. Blood. 2019;133(17):1854-64.
2. CDC. COVID-19: Myths and facts. Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html?s_cid=11760:covid%20vaccine%20facts:sem.ga:p:RG:GM:gen:PTN:FY22. [Accessed 5 February 2023].
3. Zimmerman RK. Helping patients with ethical concerns about COVID-19 vaccines in light of fetal cell lines used in some COVID-19 vaccines. Vaccine. 2021;39(31):4242-4.
4. Ogata AF, Cheng CA, Desjardins M, et al. Circulating Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccine Antigen Detected in the Plasma of mRNA-1273 Vaccine Recipients. Clin Infect Dis. 2022;74(4):715-8.
5. CDC. Finding credible vaccine information. Available at: https://www.cdc.gov/vaccines/vac-gen/evalwebs.htm. [Accessed 5 February 2023].
6. CBER. Updated Information for Blood Establishments Regarding COVID-19. U.S. Food and Drug Administration. Available at: https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/updated-information-blood-establishments-regarding-covid-19-pandemic-and-blood-donation. Published 11 Jan 2022. [Accessed 5 February 2023].
7. Jacobs JW, Bibb LA, Savani BN, et al. Refusing blood transfusions from COVID-19-vaccinated donors: are we repeating history? Br J Haematol. 2022;196(3):585-8.
8. Starkey JM, MacPherson JL, Bolgiano DC, et al. Markers for transfusion-transmitted disease in different groups of blood donors. JAMA. 1989;262(24):3452-4.
9. Dorsey KA, Moritz ED, Steele WR, et al. A comparison of human immunodeficiency virus, hepatitis C virus, hepatitis B virus, and human T-lymphotropic virus marker rates for directed versus volunteer blood donations to the American Red Cross during 2005 to 2010. Transfusion. 2013;53(6):1250-6.
10. Jacquot C, Seo A, Miller PM, et al. Parental versus non-parental-directed donation: an 11-year experience of infectious disease testing at a pediatric tertiary care blood donor center. Transfusion. 2017;57(11):2799-803.
11. AABB. Blood Transfusion Therapy: A Physician's Handbook. 13th ed. Bethesda, MD: AABB Press; 2020.
12. Dunbar N, Cooke M, Diab M, et al. Transfusion-related acute lung injury after transfusion of maternal blood: a case-control study. Spine (Phila Pa 1976). 2010;35(23):E1322-7.
13. AABB. Vaccination and blood donation. Available at: https://americasblood.org/wp-content/uploads/2023/02/FAQ-COVID-Vaccines-and-Blood-Donation-2.23.pdf. [Accessed 13 February 2023].
14. ABC. Frequently asked questions: COVID vaccines and blood donation. Available at: https://americasblood.org/wp-content/uploads/2023/02/FAQ-COVID-Vaccines-and-Blood-Donation-2.23.pdf. [Accessed 5 February 2023].
15. CDC. COVID Data Tracker. Available at: https://covid.cdc.gov/covid-data-tracker/#vaccine-delivery-coverage. [Accessed 5 February 2023].
16. US Coronavirus vaccine tracker. Available at: https://usafacts.org/visualizations/covid-vaccine-tracker-states. [Accessed 5 February 2023].
17. COVID-19 vaccine doses administered by manufacturer. Available at: https://ourworldindata.org/grapher/covid-vaccine-doses-by-manufacturer. Published 6 Feb 2023. [Accessed 7 February 2023].
18. Blood community issues new joint statement to combat misinformation regarding vaccines and the blood supply Available at: https://www.aabb.org/news-resources/news/article/2023/01/30/blood-community-issues-new-joint-statement-to-combat-misinformation-regarding-vaccines-and-the-blood-supply. [Accessed 5 February 2023].

Blood Bulletin is issued periodically by America's Blood Centers. Publication Editor: Mack Benton. The opinions expressed herein are opinions only and should not be construed as recommendations or standards of ABC, ABC SMT Committee, or its board of directors. Publication Office: 1717 K St. NW, Suite 900, Washington, DC 20006. Tel: (202) 393-5725; Fax: (202) 393-1282; E-mail: memberservices@americasblood.org.

America's Blood Centers®
It's About *Life.*

versiti™