Carter BloodCare
SPECIALTY SERVICES

Blood Matters

September/October 2022

News for Blood Bank Medical Directors, Physicians and the Lab

Blood Matters is a quarterly news *outlet with important medical information for you, our customers and colleagues, from Carter BloodCare. We hope you will share it with others interested in the work we do together.*

IN THIS ISSUE

HOT TOPICS

Monkeypox and the Community Blood Supply

Frances Compton, MD

Carter BloodCare continuously monitors any possible emerging infectious diseases or outbreaks, and routinely assesses their impact on the safety of the blood supply. We have been regularly evaluating the recent monkeypox outbreak and its effect on our community blood supply. Per the FDA and CDC, there have been no reports of transmission of monkeypox virus through transfusion, during this outbreak or any previous outbreak.[1, 2] There is currently no additional regulatory requirement for screening or testing of blood intended for transfusion.

However, Carter BloodCare remains vigilant in our role of maintaining a safe blood supply. The Association for the Advancement of Blood and Biotherapies (AABB) has issued informal recommendations which mirror CDC's monkeypox post-exposure monitoring recommendations.[3]

We have discussed the issue internally, and plan to comply with the following recommendations:

1) Individuals who have had exposure to monkeypox will be deferred from blood donation for 21 days.

2) Individuals who are sick or recovering from monkeypox will be deferred for 21 days after resolution of symptoms.

3) Those who have received the Jynneos monkeypox vaccine are eligible to donate unless they were vaccinated due to a recent monkeypox exposure.

Note: The first two deferrals will be based on donor information volunteered to screening staff since no formal donor screening question is advised by regulatory bodies at this time. Information on the third item will be collected from an existing question on vaccines and injections.

Carter BloodCare will track the situation and respond to new information and/or regulatory guidance as it emerges. As always, we will continue to preserve the safety of our community blood supply as the health and well-being of our patients is our utmost priority.

References:

1. FDA update, current as of 08/12/2022: Information for Blood Establishments Regarding the Monkeypox Virus and Blood Donation
https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/information-blood-establishments-regarding-monkeypox-virus-and-blood-donation

2. AABB Monkeypox interim Fact Sheet, updated 7/27/2022
https://www.aabb.org/docs/default-source/default-document-library/regulatory/interim-monkeypox-virus-fact-sheet.pdf

3. CDC website, updated 8/11/2022: Monitoring and Risk Assessment for Persons Exposed in the Community
https://www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html

Updates in Stem Cell Transplant and Gene Therapy for Sickle Cell Disease

Debra Smith, MD, PhD

The American Society of Hematology (ASH) recently published guidelines for stem cell transplantation in patients with sickle cell disease (SCD).[1] Allogeneic hematopoietic stem cell transplantation (HSCT) is currently the only curative treatment for SCD, but risks of transplant must be balanced with the potential patient benefits.

The ASH guidelines address the use of HSCT in SCD patients with neurologic injury, frequent pain, or acute chest syndrome (ACS). Guidelines also address type of transplantation, optimal donor and recipient age. The ASH guideline panel suggests matched related HSCT rather than standard of care (hydroxyurea/transfusion) in SCD patients who 1) have experienced an overt stroke or have an abnormal transcranial Doppler ultrasound, 2) have frequent pain, or 3) have recurrent episodes of ACS. The ASH guideline panel suggests for an allogeneic transplant to occur at an earlier age rather than an older age. The panel suggests the use of a high-quality HLA-identical sibling cord blood transplant when available over bone marrow.

SCD is the most prevalent single-gene disease, and has long been a target for gene therapy. Clinical trials for SCD treatment utilizing gene-addition therapy to modify patient CD34+ cells with the addition of a β-globin gene first began in 2006 with the French study protocol LG001 using a lentiviral vector for ex vivo transduction.[2] More recently, gene-editing technology has been developed that allows for correction of the point mutation in the β-globin gene or modification of regulatory genes to induce fetal hemoglobin (HbF or α2γ2) production, and numerous clinical trials for each of these gene-editing strategies are currently underway.[3]

The *BCL11A* gene represses expression of γ-globin, inhibiting production of HbF in adult red blood cells. The goal of *BCL11A*-targeted gene therapy is the reversal of hemoglobin switching, leading to an increase in HbF (and decrease of HbS). An increase in HbF level provides partial correction of SCD. An HbF fraction of 20 percent has been reported as the threshold level needed to significantly lessen the clinical severity in SCD.[4] A recent publication in the *New England Journal of Medicine* describes results for six patients enrolled in the *BCL11A* gene editing clinical trial NCT03282656.[5] Patients were enrolled in the single-center pilot study involving infusion of autologous stem cells after transduction with the BCH-BB694 lentiviral vector encoding a short hairpin RNA embedded in an endogenous microRNA (shmiRNA) targeting erythroid lineage-specific knockdown of *BCL11A*. Patients were eligible for this study if they had clinically severe SCD and no HLA-matched sibling available to serve as a stem cell transplant donor.

Study results describe the clinical and laboratory response and safety for six SCD patients followed for seven to 29 months after autologous gene therapy infusion. All patients engrafted after infusion with median times to engraftment of 22 days for neutrophils and 33 days for platelets. An increased HbF fraction was maintained in all patients. One patient continued regular transfusions but at a lower frequency than prior to gene therapy. For the five un-transfused patients, the median HbF fraction at the most recent study visit was 30.4 percent (range, 21.6 to 40.0). Hemolysis continued in all patients, but was reduced from baseline levels as measured by absolute reticulocyte count and lactate dehydrogenase levels. No patient had a vaso-occlusive crisis, ACS, or stroke after gene therapy infusion. One patient with left hip avascular necrosis prior to gene therapy, developed symptoms of right hip avascular necrosis nine months after gene therapy. One patient who had required frequent hospitalizations for priapism prior to gene therapy required two hospital admissions for recurrent priapism approximately four months after infusion. This patient did not require any emergency department visits or hospitalizations for priapism since month eight after gene therapy. The overall findings of this study demonstrate a favorable safety profile of this autologous gene therapy. Further, the HbF levels maintained in the study patients after BCL11A-targeted gene therapy are associated with meaningful reduction in the clinical severity of disease.

HOT TOPICS Continued

References:

1. Kanter J, Liem R, Bernaudin F, et al. American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation. *Blood Adv.* 2021;5(18): 3668-3689.
2. Negre O, Eggimann A, Beuzard Y, et al. Gene Therapy of the β-Hemoglobinopathies by Lentiviral Transfer of the $\beta^{A(T87Q)}$-*Globin* Gene. *Hum Gene Ther.* 2016;27(2):148-165.
3. Germino-Watnick P, Hinds M, Le A, et al. Hematopoietic Stem Cell Gene-Addition/Editing Therapy in Sickle Cell Disease. *Cells*. 2022;11:1843.
4. Powars DR, Weiss JN, Chan LS, et al. Is there a threshold level of fetal hemoglobin that ameliorates morbidity in sickle cell anemia? *Blood*. 1984;63(4):921-926.
5. Esrick EB, Lehmann LE, Biffi A, et al. Post-Transcriptional Genetic Silencing of BCL11A to Treat Sickle Cell Disease. *N Engl J Med.* 2021;384(3):205-215.

MEDICAL MINDS

What topics would you like to see in a future issue of Blood Matters?

Click **here** to submit your choice.

PHYSICIAN RESOURCES

Review Updates

- AABB Updated Deferral Recommendations for Medications to Prevent, Treat HIV Infection
- THOR-AABB Working Party Recommendations for a Prehospital Blood Product Transfusion Program
- FDA Recommendations to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease

HOT TOPICS Continued

Taking Action to Increase the Diversity of Blood Donors
William Crews, MD

September is Sickle Cell Awareness Month and National Hispanic Heritage Month began on September 15. This makes September a great month to highlight the efforts Carter BloodCare has made to recruit and increase the diversity of our donor base.

In the November/December 2021 edition of *Blood Matters*, I wrote about the importance of increasing the number of diverse blood donors at Carter BloodCare. Since then, we have worked to renew a campaign we first implemented in 2016 to recruit R0 donors. The campaign will kick off later this month that includes antigen typing select donors for the R0 phenotype,

sending an email or mailed postcard to donors with the R0 phenotype informing them their blood type is in popular demand, and encouraging them to visit **our dedicated webpage** to learn more and schedule an appointment for another donation.

Currently 7% of our donors have an R0 phenotype, so increasing the diversity of donors is important to this campaign for two main reasons. First, 44% of African American donors have an R0 phenotype. Increasing the number of African American donors provides the best opportunity to increase our percentage of R0 donors, thereby increasing the availability of R0 red cells for distribution to hospitals and patients. Second, more donations from African American donors should reduce the reagents and time used to manually screen RBC units to fill orders for R0 red cells.

We are working to increase the number of Hispanic donors, as well. Hispanic Americans make up 40% of the Texas population, but only 18% of Carter BloodCare donors are Hispanic.

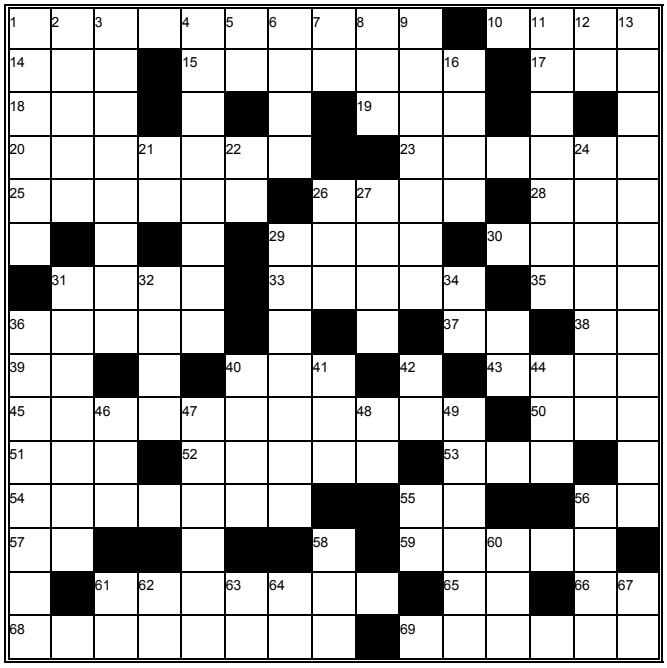
To increase our percentage of Hispanic donors, Carter BloodCare has improved our efforts to reach Hispanic donors by creating a **Spanish-language webpage.** We also **recognize National Hispanic Heritage Month on our website**, acknowledging the impact Hispanic donors can have on increasing the type O blood inventory. We designed Spanish language advertising and materials to promote blood donation and encourage the hosting of blood drives. To increase our number of multilingual staff, we partner with Spanish-language media company Univision, advertising our open jobs on their news station and through their social media channels.

As we observe the effectiveness of these campaigns in the coming months, we hope to learn, improve and expand upon their reach. By doing so, we can grow and sustain our efforts to have the diversity of our donor base more closely reflect the diversity of our communities.

Blood Matters

September/October 2022

CROSSWORD PUZZLE



Click **here** to download the answer key.

Across

1. Accumulations of activated platelets occasionally seen when stored at 1-6 degrees C
10. The plasticizer in your RBC bag (abbr)
14. What dieters count, for short
15. HIPAA requires a ____ officer
17. Humanitarian group not funded by our elected officials (abbr)
18. Head doctor at the hospital (abbr)
19. Site of 2016 summer Olympics, for short
20. An air ____ is a possible fatal complication of an IV line
23. The biggest one is the aorta
25. Possible side effect of citrate toxicity in apheresis donors
26. The first blood ____ was in Chicago in 1937
28. Documentation program towards keeping ASCP or ABP qualification (abbr)
29. Alert
30. Municipality
31. Partiality
33. Pertaining to the kidney
35. Garfield is a cartoon one
36. Spiffy
37. The first half of the day (abbr)
38. He won an Oscar for "Philadelphia" (init)
39. Universal donor type for plasma
40. Blood donor anemia screening analyte (abbr)
43. Soothing ointment for burns
45. Isotretinoin has this risky property
50. Where the antecubital fossa is
51. Drug banned in platelet apheresis donors (abbr)
52. Abnormal lung sounds heard with a stethoscope
53. Platelet specific antigen now part of HPA-4
54. _____ disequilibrium (genetic term)
55. Volume similar to 1 mL (abbr)
56. Per item (abbr)
57. Hawkeye state (abbr)
59. Bone marrow is aspirated from the ____ crest
61. NH_3
65. The drug tocilizumab inhibits ___-6 production (abbr)
66. A forensic pathologist often serves as one (abbr)
68. Brand name of axicabtagene ciloleucel (CAR-T product)
69. X-linked syndrome with abnormal XK gene

Down

1. Foreign travelers may speak with this
2. With *3 down*, blood derivative given for immunodeficiency (2 words)
3. See *2 down*
4. Convulsive disorder
5. Fred Astaire's dancing partner in "Top Hat" (init)
6. Disease associated with Kaposi's sarcoma (abbr)
7. Electronic appliance often found in blood donor rooms (abbr)
8. Site of blood donor hemoglobin sampling no longer allowed
9. The low incidence RBC antigen in this system was once called Bullee and is more common in Mennonites
11. The normal level of a disease in a community (vs epidemic or pandemic)
12. Element in old thermometers (abbr)
13. Condition requiring therapeutic phlebotomy
16. Old eponym for RBC antigen KN5
21. Anatomic name for an opening
22. Test done on bladder fluid (abbr)
24. Piece of equipment no longer needed with cold stored platelets
26. Modern slang for honey or sweetie
27. Italian river of Florence
29. What a worm on a hook may do
31. Parasite for which there is regional blood donor testing required
32. Latin name for journals or recorded proceedings
34. Cedars-Sinai Medical Center city (abbr)
36. Event reportable to FDA for donors or patients
40. Popular thriller author Tami
41. Word with spelling or quilting
42. Special reagent water used in the lab (abbr)
44. Type of WBC stimulated to kill cancer cells by culture in the presence of IL2 (abbr)
46. Raced on foot
47. Major indication for massive transfusion protocol
48. Crystalloid compatible with blood (abbr)
49. The "c" in cAMP (a molecule in regulating kinases)
55. Number of Disney's movie dalmations in Roman numerals
56. Lung bypass procedure (abbr)
58. Blood donor screening tests are often this methodology (abbr)
60. Individuals should not donate blood if they are ___
61. RBC extended life storage media (abbr)
62. The host of a game show or roast (abbr)
63. Surgical suite (abbr)
64. Abbreviation on lab printout for sample that wasn't run
67. Hospital triage area (abbr)