Carter BloodCare
SPECIALTY SERVICES

Blood Matters

March/April 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

Update on Bacterial Platelet Contamination – Focus on Bag Damage and Late Environmental Bacterial Contamination

Laurie J. Sutor, MD, MBA

In April 2019, the Food and Drug Administration (FDA) released a memo to blood establishments and transfusion services alerting them to the recent reports of four cases of sepsis in apheresis platelets, despite bacterial screening or pathogen reduction techniques. These four cases were notable for being with the bacterium *Acinetobacter.* These cases were written up in the journal *Morbidity and Mortality Weekly Report* (MMWR) in detail (reference below).

The four cases were from May to October 2018 and included patients from three states (California, Utah, and Connecticut). All of the platelets were apheresis products and were transfused on days 4 or 5. Product number one was a pathogen reduced platelet. The other two platelets (one was a split that went to two patients) were tested negative by culture originally. Each part of the split product actually was tested negative again by a rapid bacterial test on day 4, prior to transfusion. All products and patients in this investigation grew *Acinetobacter calcoaceticus-baumannii* complex and *Staphylococcus saprophyticus.* One patient died. Despite being drawn from different donors, whole genome sequencing of the *Acinetobacter* from bags, patients and blood bank environmental samples from these widely different locations suggested that these bacteria were highly related. No common source could be identified. The conclusions of this investigation were that these organisms were unusual to see in contaminated platelets, that this *Acinetobacter* species is an environmental contaminant that adheres to plastics, and that further monitoring of this situation was warranted.

One of the four cases (the California case) is detailed further in a *Transfusion* case report by Fridey et al. published in 2020. In this report, the authors show evidence that the infection did not come from the donor and that the pathogen reduction technology was effective against the organisms.

In early December 2021, the FDA issued another announcement about this ongoing concern. They reported that they had been made aware of three more cases of platelet contamination involving *Acinetobacter* species, *Staphylococcus saprophyticus*, and/or *Leclercia adecaboxylata.* These cases were again geographically dispersed, occurring in North Carolina, Ohio and Virginia, yet were apparently genetically related, again with no common source identified. Two of the cases were fatal and the third resulted in a septic transfusion reaction. Additional reports were being investigated. The FDA urged any transfusion service identifying a similar case to save the platelet bags and samples and to report them to the FDA for investigation.

The first possible explanation for this series of platelet contaminations came to light in a report by Fadeyi et al. in late 2021. These authors reported another case of fatal sepsis due to *Acinetobacter baumannii* complex, *Staphylococcus saprophyticus* and *Leclercia adecarboxylata.* The apheresis product had been pathogen reduced, and the authors showed that the pathogen reduction process would have been effective on these organisms, suggesting that the contamination occurred late in the product's life.

They then demonstrated that a leak, visible only microscopically after application of pressure, was present in the bag. This could explain how environmental contaminants could enter and contaminate the platelet.

Finally, an online only (at the time of this writing) article in *Transfusion* by Gammon et al. looked at platelet bag manufacturers' records to see how commonly leaks were reported. For the period January 2019 to July 2020, they found 23 reports of leaks in the U.S. from post-manufacturer damage out of 546,310 containers - a rate of 44 per million distributed. The damage ranged from pin holes, to damage from objects placed on or between bags (e.g. hemostats) during shipping or storage, to scratches apparently made from poor placement on platelet agitators. The authors strongly recommended greater care from facilities in handling and storing platelets.

Possible actions to take to protect platelets from such damage and contamination might include:

- Avoid having sharp objects near platelets
- Don't use box cutters to open shipping containers
- Have a regular cleaning schedule for incubators and other surfaces
- Inspect rotators for sharp edges or damage
- Don't put clips on bags
- Control how platelets are folded
- Don't put hard objects between or onto bags
- Carefully pack into pneumatic tubes
- Be careful manipulating the ports

In summary, facilities should be aware of this new development in platelet contamination, watch for any cases in their institution for proper reporting and investigation, and be more cautious in handling apheresis products and cleaning surfaces to help avoid the contamination.

References:

- https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/important-information-blood-establishments-and-transfusion-services-regarding-acinetobacter-sp April 2019
- https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6823-H.pdf (The issue with four cases of *Acinetobacter* sepsis from 2018)
- Fridey JL, Stramer SL, Nambiar A et al. Sepsis from an apheresis platelet contaminated with *Acinetobacter calcoaceticus/baumannii* complex bacteria and *Staphylococcus saprophyticus* after pathogen reduction. *Transfusion* 2020; 60:1960-1969. https://doi.org/10.1111/trf.15951
- https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/important-information-blood-establishments-and-transfusion-services-regarding-bacterial December 2021
- Fadeyi EA, Wagner SJ, Goldberg C et al. Fatal sepsis associated with a storage container leak permitting platelet contamination with environmental bacteria after pathogen reduction. *Transfusion* 2021; 61:641-648. https://doi.org/10.1111/trf.16210
- Gammon RR, Reik RA, Stern M et al. Acquired platelet storage container leaks and contamination with environmental bacteria: a preventable cause of bacterial sepsis. *Transfusion* early view online 20 Dec 2021. https://doi.org/10.1111/trf.16776

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

Click **here** to submit your choice.

PHYSICIAN RESOURCES

Download updates

- Blood Bulletin Vol. 21, No. 3: Today's Platelet Products — Not Your Grandfather's Platelets
- Blood Bulletin: Blood Shortages — How Can Hospitals Help?

HOT TOPICS Continued

COVID-19 Convalescent Plasma: A Look Back and Current Status
Geeta Paranjape, MD

Carter BloodCare began collecting COVID-19 Convalescent Plasma (CCP) in March of 2020 and continued until March 2021. We also had a brief period when we resumed collection of CCP from August 2021 to October 2021 due to high demand.

The Food and Drug Administration (FDA) has always regarded this component as "investigational" and issued a letter in August 2020 stating that an "Emergency Use Authorization – EUA" had been granted for use of the component. In order for a plasma component to be classified as CCP, donors had to meet select criteria in addition to meeting regular blood donor guidelines. The plasma had to contain a defined concentration of anti-SARS-CoV-2 antibodies in order to be CCP. In the beginning, the FDA allowed only one particular test to be utilized for performing the antibody levels (this was the test that Carter BloodCare utilized while performing CCP collections).

As more data became available during the period of August 2020 to March 2021, the EUA letter was updated and an additional 11 tests were approved for blood centers to perform the anti-SARS-CoV-2 antibody levels.

As new information and studies became available, the FDA updated the EUA letter again on December 28, 2021. Out of the 11 previously approved tests, only four were approved and included on the list (the test that had been used by Carter BloodCare was not on the new list) and two new ones were added. The titer (level of antibodies needed) required to qualify a plasma component as CCP was also higher with the new document.

The patients who qualified to receive CCP transfusion also changed with the current EUA letter. The original letter allowed for "hospitalized" patients to receive CCP, and also recommended patients be transfused early in the course of the disease. The current EUA allows CCP to be used only for "patients with immunosuppressive disease OR receiving immunosuppressive therapy in an outpatient or inpatient setting."

In addition to the EUA letter, the FDA published an accompanying guidance to clarify who was eligible to donate CCP. The previous document, published in February 2021, was updated to follow the release of the EUA on Jan. 7, 2022. CCP donors still had to meet all regular blood donor criteria, in addition to either being unvaccinated for COVID-19 or, if vaccinated, must have had a COVID-19 infection in the last six months. Donors who met these criteria must also have the required antibody concentration before the plasma could be labeled as CCP.

So far, the studies that have been completed about the benefit of CCP for patients have been inconclusive, with studies showing some benefit as well as no benefit. Blood centers are receiving very few requests for CCP at this time.

Based on the most recent FDA changes, Carter BloodCare had to re-label previously collected, tested and labeled CCP units as plasma, since the antibody test that was performed to qualify donors was excluded from the list of approved tests. This was permissible by the FDA as a way to preserve the components. Hospital customers were made aware of the operational changes in December 2021, following the FDA updates. Additionally, hospitals were notified that Carter BloodCare did not have intentions to resume collection of CCP.

Cold-Stored Platelets: Ready for Transfusion

Frances Compton, MD

It is official: as of January 17, 2022, we have cold-stored platelets (CSPs) available for use for all of our hospital customers. We are encouraging all of our customers to be ready to accept these products. Please remember that per our FDA variance, CSPs are intended to be used for actively bleeding patients and may be distributed for STAT platelet orders.

CSPs have already shown to be of great benefit for the stability of the blood supply. They were a valuable resource when Carter BloodCare was unable to collect blood for two days during the recent February ice storm. As they have a shelf-life of two weeks, we had over 40 units of in-date CSPs which had been collected within the prior two weeks before the storm. Hospitals who could receive these products had access to this additional inventory.

CSPs have clinical benefits beyond inventory support. Randomized clinical trials are ongoing, but *in vitro* and preliminary clinical studies suggest that these products are superior at bleeding control when compared to their room temperature counterparts. It is thought that the cold storage temperature pre-activates the platelets so that they are ready for clot formation immediately upon transfusion.

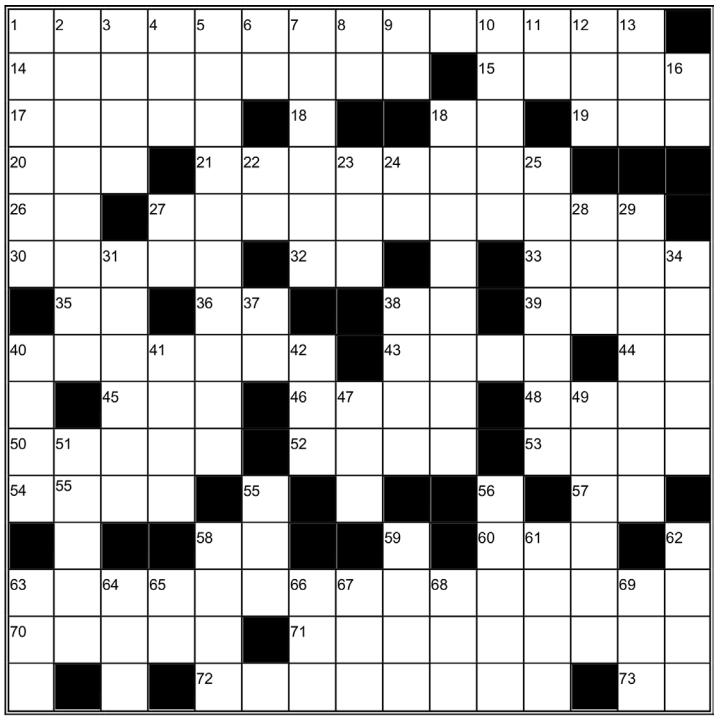
If you have not already done so, please make sure that you are able to receive these life-saving products. CSPs are available, based on inventory, for all of our hospital customers. We want you to take advantage of the clinical benefit as well as the additional inventory reinforcement that CSPs provide for our community.

Reference:

- Reddoch-Cardenas KM, Bynum JA, Meledeo MA *et al*. Cold-stored platelets: A product with function optimized for hemorrhage control. *Transfusion and Apheresis Science.* 2019; 58: 16-22.

Blood Matters

CROSSWORD PUZZLE



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

Across

1. Antifibrinolytic agent made of synthetic lysine (two words)
14. IV monoclonal antibody treatment approved for CLL, non-Hodgkin lymphoma and rheumatoid arthritis
15. Screening ____: privacy area for blood donors
17. Blood bank finding patients may form after exposure to pigeons
18. Element used in outdated donor hemoglobin screening method (abbr)
19. "To the ___ degree"
20. College football NCAA champions, 2022 (abbr)
21. Pulse will do this during hypovolemia
26. Type of cutaneous T-cell lymphoma (abbr)
27. _____ - Jakob disease
30. Biggest artery
32. Old name for the blood collector in Milwaukee: Blood Center of ___ Wisconsin (abbr)
33. A 500 ml bag of whole blood is equal to one ___ collected from a donor
35. Blood grouping for transfusion routinely includes ABO and __ (D).
36. Polyagglutinable antigen that may be associated with acquired B antigen
38. Ex-Dallas Cowboys' player Jason Witten's position (abbr)
39. It may be used to hold needles or tubing in place during blood collection
40. Blood Centers of _____: group purchasing organization
43. Online site that is built and edited collaboratively with user input over time
44. A physician delegate must perform for frequent source plasma donors (abbr)
45. ___ Paulo, Brazil
46. Average
48. Kiln
50. Do a ____: make a 180º change in direction
52. Misplace
53. Brooklyn NBA team
54. Ask, as a question
57. 20-24ºC in common parlance (abbr)
58. Country where the AABB was founded (abbr)
60. Hospital quality metric for duration of patient visit (abbr)
63. Handy reference book from AABB (2 words)
70. Adult stage of winged insect
71. What flow cytometry markers often do when exposed to the laser
72. Signs and _____ of disease
73. What you might call your divorced spouse

Down

1. Major reason for massive transfusion protocol
2. Shape of malarial parasite (2 words)
3. ____ girl! Rah-rah statement.
4. Rapa ___ : native name for Easter Island
5. _____ date for RBCs is 42 days
6. Clotting factor in Intrinsic path called plasma thromboplastin
7. One of the two major apheresis machines in the U.S.
8. State where Brigham and Women's Hospital is located (abbr)
9. He wrote the song "White Christmas" (init)
10. Blood donor arms are examined for signs of drug ____
11. This toxic substance in the blood can cause cherry red lips (abbr)
12. Na^+ or Cl^-
13. Blood bank reagent used in daratumumab workups (abbr)
16. Common diagnosis of person needing therapeutic phlebotomy (abbr)
18. Drink additive that can transiently raise blood pressure
22. Its state capital is Lincoln (abbr)
23. GPS picks out a good one for you (abbr)
24. Ad lingo for "a breeze"
25. Lui freeze, for example
27. A common medical scan (abbr)
28. The genetic material in hepatitis B (abbr)
29. Dr. Patricia _____, Rh gene theory researcher.
31. Monkey for whom blood group is named
34. Age group prone to vasovagal donor reactions
37. ___ and the Sunshine Band
38. ____ the Night Before Christmas
40. Large reference lab in Salt Lake City (abbr)
41. American ___ Donor Program
42. Blood malignancy often needing bone marrow transplant (abbr)
47. Leukocytes with bright red granules, for short
49. Graft ___ host disease
51. ___ pole: carved monument created by indigenous peoples of the Pacific Northwest
55. 23rd letter of the Greek alphabet
56. Storage devices for blood must have one per AABB Standards
58. Non profit organization that manages the U.S. solid organ transplant system (abbr)
59. Overabundance
61. Low denomination bills
62. Lectin that detects H antigen
63. Spasm, usually of the face
64. Most labs order proficiency test surveys from this group (abbr)
65. Element that used to be in thermometers (abbr)
66. Measure for air flow through hoods (abbr)
67. The Matterhorn is one
68. Cow sound
69. High card in the deck