Carter BloodCare
SPECIALTY SERVICES

Blood Matters

Feb/March 2019

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

Is it OK to Transfuse ABO and Rh Mismatched Platelets?

William Crews, MD

Many factors put demands on platelet availability in our facility and our community. These include the need for quality control and bacterial testing, the short shelf life, an increase in utilization over recent years, and loss of donors with new regulations. For all these reasons we encourage transfusion services and transfusing physicians to consider the use of non-ABO matched platelets in adult patients as described below whenever necessary and reasonable.

Platelets are often transfused regardless of their ABO group because ABO antigens are only weakly expressed on platelets. Most adults have soluble A or B antigenic substances in their blood that are capable of neutralizing the antibodies in small amounts of ABO-incompatible plasma, such as one platelet transfusion. For high-risk patients (neonates and young pediatric patients, stem cell transplant patients, and organ transplant patients) a special effort to use plasma-compatible platelets is preferred to prevent possible hemolysis.

It is known that ABO major incompatibility platelet transfusion is associated with lower rates of post-transfusion corrected count increment and accelerated destruction of platelets in the recipient. But studies have shown the transfusion of PLTs with major ABO-incompatibility is equally effective in preventing clinical bleeding compared to ABO-identical and platelets with ABO-minor incompatibility. If a patient has an indication to receive a platelet transfusion and an ABO compatible platelet is not immediately available, the benefit of transfusing an ABO incompatible platelet may outweigh the risk of waiting for a compatible platelet. Even in high-risk patients this is possible since any anti-A or anti-B would be diluted into 2 to 3 L of recipient plasma in adult patients. In pediatric patients, if a major ABO incompatible transfusion is unavoidable, the unit should have the plasma removed before transfusion as an alternative approach. Close monitoring of the patient should take place to ensure the incompatible plasma does not cause hemolysis.

Platelets do not express Rh antigens on their surface, and with the majority of platelets being collected by apheresis technology, the amount of (passenger red cells) contaminating red cells are felt to be negligible enough that anti-D alloimmunization after RhD-incompatible platelet transfusion does not warrant serious concern. The red cell content in apheresis platelets is estimated to be less than 0.001 mL per unit. An exception for RhD negative females of childbearing age is made by some clinicians. Although the cases of documented immunization which have been documented for patients getting a low number of modern apheresis platelets is very low. Administration of the lowest dose of RhIG is sufficient for one apheresis platelet if deemed necessary.

Summary of Platelet component selection

- ABO type of platelets:
  - ABO-identical platelets can be given if plentiful, especially for smaller patients or for repeated transfusions
  - ABO-mismatched platelets may result in lower corrected count increments but this difference is not usually clinically significant
  - ABO-incompatible plasma in platelets may cause a positive DAT or may rarely cause hemolysis

HOT TOPICS Continued

- Rh type of platelets:
  - Rh negative males and females past childbearing age may receive Rh positive apheresis platelets if Rh negative platelets are in short supply
  - Females of childbearing potential can receive Rh-positive platelets if needed. Although, RhIG should be given for pooled platelets and may be given following apheresis platelets, especially if multiple units are used.
  - Rh negative platelets may be given to Rh negative patients if plentiful

References:

1) Valsami S, Dimitroulis D, Gialeraki A, Chimonidou M, Politou M, Current trends in platelet transfusions practice: The role of ABO-RhD and human leukocyte antigen incompatibility. Asian Journal of Transfusion Science 2015; 9(2) 117-123

2) Mintz, P. D. (2011) Transfusion Therapy: Clinical Principles and Practice Bethesda, MD. AABB Press

3) Absence of anti-D alloimmunization in hematologic patients after D-incompatible platelet transfusions" J Cid, X Ortin, E Elies et al. Transfusion 2002 42(2): 173-176

4) Absence of D alloimmunization in D- pediatric oncology patients receiving D-incompatible single-donor platelets" R Molnar, R Johnson, LT Sweat,TL Geiger. Transfusion 2002, 42(2):177-182

5) Low incidence of anti-D alloimmunization following D+ platelet transfusion: the anti-D alloimmunization after D-incompatible platelet transfusion (ADAPT) study" J Cid, M Lozano, A Ziman et al. Br J Haematol 2015, 168(4):598-603.

MEDICAL MINDS

What topic do you want included in the next issue of Blood Matters?

A) Texas New Maternal Care Levels

B) Cellular Therapy

C) Therapeutic Apheresis Applications

D) Other

Click **here** to submit your choice. If you answered ***D (Other)***, remember to include your topic.

A Brief Review of Transfusion Practice in Sickle Cell Disease (SCD)

Laurie J Sutor, MD, MBA

1) When to transfuse. Consensus recommendations support transfusion for the prevention and treatment of stroke in high-risk patients. There is also some evidence that transfusion is helpful in patients to treat acute chest syndrome and for splenic sequestration with anemia. However, transfusion has not shown to be helpful routinely for treatment of pain crises, priapism, acute renal failure, or in pregnant women. Transfusion may be used pre-operatively to bring the hemoglobin level to 10 g/dL prior to surgery involving anesthesia. Patients receiving chronic transfusion to prevent stroke should maintain a HbS level below 30%. Patients receiving infrequent transfusions should avoid surpassing a hemoglobin level of 10 g/dL or risk the hyperviscosity syndrome.

2) How closely to match the blood. Since these patients are at high risk for forming alloantibodies, there is much discussion on prophylactically matching antigens of the donor blood to the patient to prevent alloantibody formation. An NHLBI expert panel as well as the British Society of Haematology guidelines both recommend prophylactically matching for Rh (D, C, c, E, e) and Kell antigens. Other institutions try to match for all of the clinically significant antigens for which the patient could make antibodies. Which strategy the facility chooses is often based on the resources available to that institution. A very recent (2019) publication by Fasano et al in *Transfusion Medicine Reviews,* that looked at 303 different publications on red cell matching in SCD, found that none of the studies were prospective randomized controlled trials to compare different matching strategies and therefore, high quality evidence is lacking to scientifically make a recommendation one way or another. Low quality observational studies support extended matching to decrease the risk of alloimmunization.

3) When to use molecular genotyping. Any patient who is at high risk for having serological problems should have a complete red cell phenotype done, and the sickle cell patient certainly falls into this category with so many forming multiple red cell alloantibodies. Up to one third or more of sickle cell patients make alloantibodies after transfusion. Serological testing, while readily available, is labor intensive and somewhat subjective in its interpretation. Molecular red cell typing provides the advantage of providing a panel of a larger number of red blood cell antigens screened for at one time. The one used at our facility looks for 29 polymorphisms-predicting 37 phenotypes, representing 10 red blood cell groups. Molecular typing also works in patients recently transfused, those with positive direct antiglobulin tests, and for others with complex serological problems. It is also advantageous when commercial serologic reagents are not available for certain red cell antigens. Casas et al showed improved accuracy of red cell typing when DNA methods were used (see references). Fasano's review of the literature mentioned above did not find any randomized controlled trials to compare the use of molecular genotyping and serological testing on rates of alloimmunization or cost.

4) When to do simple transfusion vs. red cell exchange. The advantage of red cell exchange (virtually always by apheresis technology) is that the sickle cells can be removed and normal cells supplied without significantly increasing the hemoglobin and increasing the viscosity of the blood. In addition, in these patients who often require multiple, chronic transfusions, iron can be removed through exchange transfusion-decreasing the dangerous accumulation that can be seen with life-long transfusion. On the other hand, exchange transfusion requires more expensive resources which are not available at all hospitals and clinics, and also can result in the need for more matched units and increased donor exposures. In general, red cell exchange should be performed in sickle cell patients needing chronic transfusion whenever possible, as the advantages outweigh the disadvantages if this option is available.

HOT TOPICS Continued

5) What are the different types of red cell exchange? Few facilities perform manual red cell exchange these days, so the choices are really between traditional automated red cell exchange and isovolemic hemodilution followed by automated red cell exchange. At least one apheresis instrument currently on the market has a program designed to perform the hemodilution type of red cell exchange without manual intervention. The advantages of the isovolemic hemodilution type of procedure are that it can increase the interval between exchange procedures (from approximately 4-5 weeks to 6-8 weeks) and requires less units of red cells per treatment. It also may improve iron removal over traditional red cell exchange. It does this by removing some of the patient's blood and replacing it with normal saline prior to the start of the red cell exchange. It is recommended that patients undergo traditional red cell exchange at least once to demonstrate they can tolerate an apheresis procedure, before proceeding to hemodilution.

References:

Yawn BP, Buchanan GR, Afenyi-Annan AN et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA 2014; 312(10):1033-48.

Davis BA, Allard S, Qureshi A et al. Guidelines on red cell transfusion in sickle cell disease. Part I: principles and laboratory aspects. Br J Haematol 2017; 176:179-91.

Vichinsky EP, Earles A, Johnson RA et al. Alloimmunization in sickle cell anemia and transfusion of racially unmatched blood. N Engl J Med 1990; 322:1617-21.

Fasano RM, Meyer EK, Branscomb J, White MS, Gibson RW, Eckman JR. Impact of red blood cell antigen matching on alloimmunization and transfusion complications in patients with sickle cell disease: a systematic review. Trans Med Rev 2019; 33:12-23.

Danielson CFM. The role of red blood cell exchange transfusion in the treatment and prevention of complications of sickle cell disease. Ther Apher 2002; 6(1):24-31.

Casas J, Friedman DF, Jackson T et al. Changing practice: red cell typing by molecular methods for patients with sickle cell disease. Transfusion 2015; 55(6):1388-93.

Feldman A, Siniard R, Staley E et al. Cost savings with isovolemic hemodilution red cell exchange in sickle cell disease patients: a single center experience. Am J Clin Pathol 2016; 146:327.

Sarode R, Matevosyan K, Rogers ZR et al. Advantages of isovolemic hemodilution-red cell exchange therapy to prevent recurrent stroke in sickle cell anemia patients. J Clin Apher 2011; 26(4):200-7.

PHYSICIAN RESOURCES

Download updates.

- **December 2018 Blood Bulletin - Patient Blood Management (PBM) in the Setting of Adult Cardiovascular Surgery (CVS)**
- **Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion**

New Draft Guidance and the Potential Impact on Platelet Inventories

Geeta Paranjape, MD

Background

The reported rates of septic transfusion reactions from platelets vary from 1/100,000 by passive surveillance to 1/10,000 by active surveillance when testing with primary culture alone. Surveillance data on platelets stored up to five days have shown that the majority of platelet transfusion-related septic reactions and associated fatalities have occurred with transfusion of day four and day five stored platelets.

The FDA has established regulations to address the control of bacterial contamination of platelets. Under 21 CFR 606.145(a), blood establishments and *transfusion services* must assure that the risk of bacterial contamination of platelets is adequately controlled using FDA approved or cleared devices, or other adequate and appropriate methods found acceptable for this purpose by the FDA.

Currently, this risk can be controlled by bacterial testing or pathogen reduction methods.

Bacterial testing includes the use of culture-based or rapid detection tests. While primary testing is typically performed by culture and within 24 hours of collection, secondary testing is performed at later times of storage and prior to transfusion. Pathogen reduction is performed shortly after platelet collection.

Under 21 CFR 610.53(b), the dating period for platelets with a storage temperature between 20 and 24 degrees Celsius is five days from the date of collection. The current maximum dating period for platelets can be extended to seven days provided the storage container is FDA approved for seven days and rapid testing is performed. Current expiration date for platelets treated with pathogen reduction technology is five days. In the draft guidance document (published December of 2018 and open for comments), the FDA has proposed the following methods.

Table 1. Summary Table of FDA's Recommendations

Recommendations to control the risk of bacterial contamination in platelets		
Dating	Method	Applicable components
5-day storage	Primary culture + secondary culture (no earlier than Day 3)	Pre-storage pools; Apheresis
	Primary Culture + secondary rapid testing	Pre-storage pools; Apheresis
	Pathogen Reduction Technology	Apheresis
7-day storage	Primary culture+ secondary culture (no earlier than Day 4)	Apheresis
	Primary Culture + secondary rapid testing	Apheresis
	Large volume delayed sampling*	Apheresis

*currently no licensed method available

The recommendations posed by the FDA will result in a disruption to the current manner that platelet inventories are managed, add cost to provide the final component, and most likely require hospital transfusion services to implement rapid testing to meet urgent transfusion needs.

Pathogen reduction option

Currently, there is only one approved pathogen reduction technology available for use in the U.S. The technology is not comprehensive in its use and cannot be used for testing of pre-storage whole-blood derived pools or triple apheresis collections. Additionally, the processing method has content and volume limitations for effective treatment that cause a decrease in the apheresis split rate. As a blood collection facility, without major changes to how we collect, the option to use and distribute pathogen reduced platelets could significantly impact our ability to meet the current need for platelet components.

5-day or 7 day storage primary culture + secondary culture/rapid testing

Currently, Carter BloodCare elects to rotate and restock apheresis platelets maintained on site at multiple healthcare facilities in order to meet the daily, unpredictable demand for platelets. This model allows Carter BloodCare to maximize the use of this limited resource and minimize outdates. While there is currently no additional charge for this service, this model is most likely unsustainable with the need to re-test (secondary culture or rapid point of issue testing) and re-label. Secondary culture and rapid testing is not feasible as the component is at the hospital transfusion service and would need to be returned to the blood center and then delivered back to the hospital for use after sampling. The logistics involved present a challenge, but of more importance is the available transfuseable inventory that will be reduced due to the time period to re-test and re-label. Hospital transfusion services should be prepared to implement rapid testing to ensure a readily transfuseable platelet is always maintained on-site.

7–day storage large volume delayed sampling

Large volume delayed sampling at 48 hours post collection and incubating for an additional 12 hours means that platelets will not be available for 60 hours post collection. Additionally, the large volume requirements could result in a reduced platelet yield per component. While this option is promising and places fewer burdens on the hospital transfusion service, there is currently no methodology licensed for this option. We encourage you to urge the FDA not to finalize the guidance until this option is available.

To review the guidance in its entirety, please visit the FDA website at
https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM627407.pdf

Any of the final recommendations will result in a strain on the current platelet supply, which is already challenged by the unpredictability in usage. The hospital's burden to implement rapid testing may increase; some methods will result in a decreased number of platelet products that can be made available from a single donation which creates additional pressures on the blood center to recruit more donors. Overall, the final guidance will inevitably require a more collaborative and innovative platelet management model than we have seen in the past.

Table 1. Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion, FDA draft guidance, December 2018.

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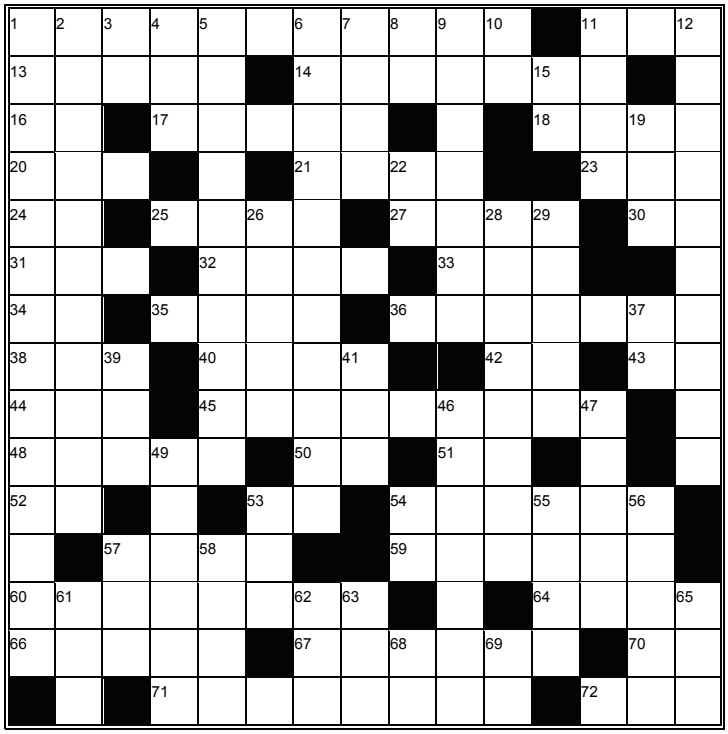
CROSSWORD PUZZLE - *Created by Dr. Laurie Sutor*



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

Across

1. Multiple myeloma drug that interferes with serological testing
11. Infection that is associated with post-transplant lymphoproliferative disorder (abbr)
13. Prefix for -uterine or -operative
14. Found commonly in an area, such as an infection
16. Media mogul who started CNN (init)
17. Gut bacterium that commonly causes disease, for short
18. First name of early Nobel Prize winners von Behring and Fischer
20. Colloid used in granulocytopheresis to improve the RBC interface (abbr)
21. Prefix for -sphere
23. Community donor center 206 miles north of Dallas on I-35 (abbr)
24. Lead character in The Legend of Sleepy Hollow (init)
25. Renowned immunohematologist Moulds who passed away in 2011
27. Haemonetics platelet screening kit recently taken off the market (abbr)
30. Johns Hopkins state (abbr)
31. "___ Town", Thornton Wilder play
32. ____ lock – IV line connection
33. Procedure for administering blood to a fetus (abbr)
34. Mycobacterium all hospital workers get screened for (abbr)
35. Intentions or goals
36. Word preceeding payable or receivable
38. Joint often replaced
40. River running through Frankfurt Germany
42. Blood group that includes McCoy antigens (abbr)
43. Physician specialist who would treat celiac disease (abbr)
44. What comes up on your GPS device (abbr)
45. Nickname for terrorist Ted Kaczynski
48. Takes home, such as a wage
50. Continent where babesiosis is most prevalent (abbr)
51. What nurses measure to keep track of patient fluids (abbr)
52. Molecule that is overproduced in cytokine release syndrome (abbr)
53. Dar-__-Salaam, largest city of Tanzania
54. Part of name of 20 across
57. ____ lumen catheter – used for therapeutic apheresis procedures
59. Pay attention
60. Part of name of TACO
64. What complement can do to RBC membranes
66. Kind of advice you might get if you get a demand letter
67. Fluid tested for secretor status
70. Term for things you can copyright protect (abbr)
71. Action required under 21 CFR 610.46 for HIV
72. Potentiating reagent (abbr)

Down

1. Reagent used for resolving workups with 1 across
2. _____ fossa, site for phlebotomy
3. Assay condition for ABO testing but not Rh (abbr)
4. Movie of 2010: "The Kids ___ All Right"
5. Immunosuppressive drug also called FK506
6. Population in whom Gerbich antigen is most commonly missing
7. Term for a bag of RBCs
8. Physician's degree (abbr)
9. Type of bacteria that grow using oxygen
10. One source of hematopoietic progenitor cells for transplantation (abbr)
11. Lung bypass procedure (abbr)
12. Process by which new equipment or reagents are shown to work properly
15. For example (abbr)
19. Computer company nicknamed "Big Blue"
22. "__ too" social movement of 2017
26. Anti-____ globulin used in DAT testing
28. Craft involved in Branson MO fatal accident in July 2018
29. What's crushed in a lithotripsy
37. How a negative blood culture may be reported out (abbr)
39. Each
41. Carmelo Anthony's league (abbr)
46. Description of a dividing cell
47. Actress Christina of the Addams Family movie
49. Type of tissue in the brain
53. Band with the 1977 hit "Mr. Blue Sky" (abbr)
54. Chemical symbol for tin
55. Supplemental test for hepatitis C antibody no longer available for blood donors (abbr)
56. Norwegian figure skater Sonja ____
57. Academic attainment at graduation (abbr)
58. Prefix for -geneic or -antibody
61. Blood group antigen first recognized in 1952 by Sussman and Miller
62. What we do of donors for their time, blood, health history
63. "Just a little ___'ll do ya" – old Brylcreem slogan
65. Molecule 2,3-___ releases oxygen to the tissues (abbr)
68. State where 25 across worked (abbr)
69. He played Iceman in Top Gun (init)