Carter BloodCare
SPECIALTY SERVICES

Blood Matters

May/June 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

Texas Hospital Level of Care Designation for Maternal Care: Blood Bank Effects

Laurie J. Sutor, MD, MBA

Area hospitals and the community blood center have become aware of new sections of the Texas Administrative Code and the Health and Safety Code that, in their standard-setting for maternal care for the state, are having significant effects on blood banks. The legislation was first passed in 2013 and modified slightly in 2015. It took effect in March of 2018 with a window period for facilities to become compliant.

A nineteen-member perinatal advisory council set the requirements for four levels of care for hospitals seeking maternal designation for Medicaid reimbursement. Level I is the most basic and Level IV is the most advanced. Level I ("Basic Care"), which assumes care of essentially healthy obstetric patients with no underlying illnesses or risk of morbidity or mortality, will still require 24-hour blood bank coverage and massive transfusion capability. Levels II to IV, which cover increasing complexity of care and risk to the obstetric patient, require (in addition to the above) the following to be available on site at all times:

- ABO and Rh specific or Group O, Rh negative red cells
- Cryoprecipitate
- Frozen plasma
- Apheresis platelets

The effect of these new designations has become apparent in recent months. Many hospitals, who never stocked cryoprecipitate or apheresis platelets previously, have been requesting them from the blood center in the process of applying for their new level of care designation. It is anticipated this change will put a strain on the apheresis platelet community inventory by requiring more units to be out at hospitals, even though many of these units will probably never be needed for transfusion.

Reference:

1. Subchapter H of the Health and Safety Code, Sections 241.182 (Level of Care Designations) through 241.187(Perinatal Advisory Council)
2. Texas Administrative Code, Title 25, Part 1, Chapter 133, Subchapters C and K

PHYSICIAN RESOURCES

Download updates.

- **Final Babesiosis Guidance Published by FDA**
- **February 2019 Blood Bulletin - The Appropriate Use of Liquid Plasma**

CAR-T: An Emerging Cellular Therapy

Geeta Paranjape, MD

Cellular therapy is a rapidly progressing field with new clinical trials for novel products being added all the time.

Autologous and allogeneic hematopoietic stem cell transplants have been used for many hematological malignancies as treatment. The new kid on the block is CAR T-cell (Chimeric Antigen Receptor T) therapy. Development of cancer is usually attributed to the failure or exhaustion of T lymphocyte surveillance, which leads to persistence and proliferation of malignant cells and development of clinically detectable cancer.

Since the 1980s, researchers have been looking for ways to re-direct or re-educate a patient's own T lymphocytes so they can attack cancer cells more effectively. CAR T is one form of this adoptive cell therapy. Cancer cells may express tumor associated antigen (TAA) or tumor specific antigen (TSA). The concept is to genetically modify T-cells so they express a fragment of the antibody to this TAA on their surface as a receptor. This is not a naturally-occurring antigen (hence referred to as Chimera). T-cells expressing this receptor are able to interact and kill tumor cells with no need of HLA recognition. They are also able to secrete cytokines that recruit more killing cells to the tumor. However, cytokines are a double-edged sword. They can lead to cytokine release syndrome (CRS) seen in many CAR T patients.

A patient's own mononuclear cells (which contain lymphocytes as well as monocytes) are collected by apheresis (leukapheresis). They are transported to the manufacturing site, and are genetically modified by transfecting them with replication incompetent retrovirus or lentivirus vector carrying the genetic code for the chimeric antigen. Once transfected, the T-cells are grown and expanded to achieve a minimum number. Following the completion of all quality and sterility tests, the CAR T product is returned to the patient. The entire process takes weeks and may be a rate limiting factor for patients who are very ill. Another issue limiting access to this therapy is that some patients may have an insufficient number of T-cells for initial collection, due to previous therapies and the cancer itself.

The therapy is autologous and hence does not carry the risk of GvHD as allogeneic stem cell transplant does. And yet, it has its own risks. Patients need to receive lymphodepletion therapy in order for CAR T cells to effectively live and expand in the patient's body. These cells can cause CRS, as well as neurotoxicity and other severe side effects. Patients with severe CRS need to be treated with an IL6 inhibitor in order to survive.

Currently, there are two products licensed by the FDA: KYMRIAH® – for B Acute Lymphoblastic Leukemia (patients up to 25 years of age) and adults with diffuse B Cell Lymphoma, and YESCARTA® for adults with diffuse B Cell Lymphoma. In both cases, patients must have refractory/relapsed disease or must have failed previous therapies. Both drugs target CD19 on B cells and, when effective, can lead to B cell aplasia needing immunoglobulin treatment.

While the results for pediatric patients with B ALL have been impressive, researchers are discovering that cancer cells get smarter and learn to "escape" CAR T-cells. Research is ongoing to find CAR T-cells that can target more than one antigen and last longer, so the anti-tumor effect will be long lasting. There are also ongoing efforts to combine different adoptive immunotherapies to achieve the best results. The focus so far has been hematological malignancies, but scientists are asking if this can be applied to solid tumors. This approach presents more challenges. Autologous T-cell use requires weeks to get the product. Can an allogeneic CAR T be developed for "off-the-shelf" use? How is GvHD avoided, if this is possible? Will this therapy ever become affordable?

Like any novel therapy, there are more questions than answers - but this is an exciting development in cell therapy.

HOT TOPICS Continued

Wait! Some of the information on the product label is missing or different, why?

William Crews, MD

There are two ways to collect blood products from donors. For red blood cells, the most common way is performing a venipuncture and allowing blood to fill a blood bag by gravitational force. This initial bag contains a standard amount of anticoagulant and the preset target volume for collection is 500mL of blood. After the bag is filled with blood, this is known as whole blood. The whole blood is leukoreduced, and then further separated into blood components such as red cells, plasma, platelets, and cryoprecipitate. After the red cells have been separated into a new satellite blood bag, an additive solution is added to the red cells to replace the plasma. The additive solution allows for better flow through the administration system when being transfused to a patient, and also extends the shelf life of the red cells.

Another method of collecting blood products from donors is by automated apheresis. This involves performing a venipuncture, and then a machine automatically separates the blood by centrifugal force and retains the individual blood component being donated; either red cells, platelets, or plasma, while returning the other blood components back to the donor. The apheresis machine automatically calculates the volume of the blood component retained along with the volume of anticoagulant used, so the precise volume of the blood bag is known. Once all post-donation testing and quality control measurements are satisfactory, the unit is ready to be labeled. For red cells prepared from a whole blood donation, since collecting and processing of blood components are done manually, there is an expected, but acceptable amount of variability in the volume of each red cell. For this reason, the preset target volume of 500mL will be printed on the label. If the red cells were collected by apheresis, the precise volume of red cells/anticoagulant will be printed on the label.

Another reason the information on the product label may be different is when demand for blood in our service area is higher than our ability to collect enough blood (this typically occurs during the summer, Thanksgiving and the Christmas season). In this situation, we will purchase blood products from other blood centers to meet the increased demand. A good example is when we purchase platelets from another blood center - they may collect the platelet unit in a manner where the platelet count will not be on the label. This can occur when the initial platelet product is determined to have an adequate platelet count and volume; this initial product can be split and labeled as two or, possibly, three separate units. Since an acceptable platelet count was taken on the initial product, it is not a requirement to perform a platelet count on the split units. In such cases, the platelet count will not be printed on the unit label and instead may contain a sticker that says the platelet count is $\geq 3.0 \times 10^{11}$.

At Carter BloodCare, we consider printing the platelet count on every unit label a value-added service, so we perform platelet counts on the initial bag as well as any split units from the initial bag. Any platelet product collected by Carter BloodCare, using automated apheresis, will include the platelet count on the unit label. When we purchase platelet products from other blood centers to meet increased demand, the platelet count may not always be printed on the unit label.

MEDICAL MINDS

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

A) Highlights from the 2019 ASFA meeting
B) Proposed changes to AABB standards for 2019
C) Cold stored platelets
D) Other

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

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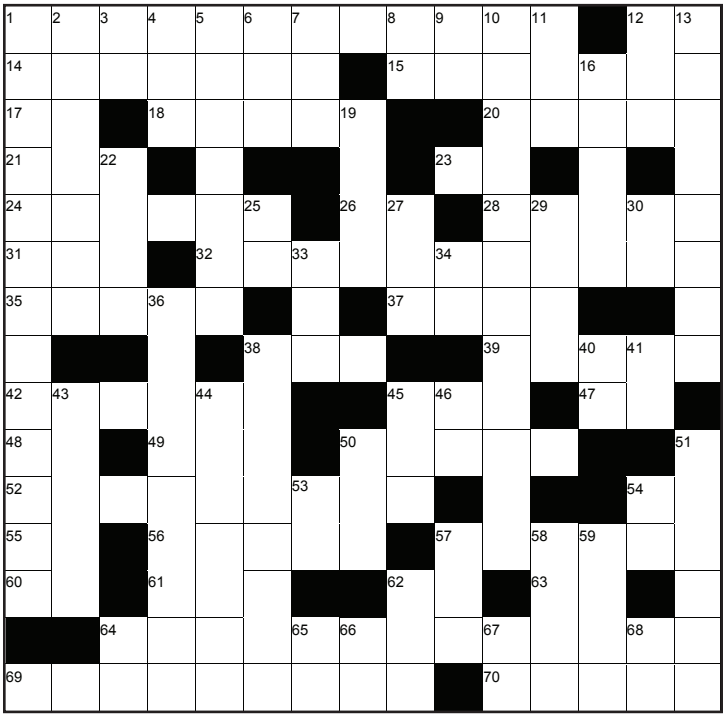
CROSSWORD PUZZLE - *Created by Dr. Laurie Sutor*



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

Across

1. Epitope displayed in polyagglutination
12. Chemical element that is also a drug for mania (abbr)
14. Another name for blood component expiration
15. What one calls milky looking plasma
17. Element used in blood irradiator shielding (abbr)
18. ____ mortis, sign of death
20. Equipment used at a blood drive to know when to end a collection
21. Immunohematology potentiating reagent (abbr)
23. Fiftieth U.S. state (abbr)
24. Lui freeze makes one, for example
26. Famous fictional resident of plantation Tara (init)
28. Deciduous conifer tree of Canada
31. Segment of the lung (abbr)
32. Red blood cell
35. Healthy lunch order
37. A Cooper or Clubman
38. ___-3 (Muromonab-CD3) first monoclonal antibody drug, once used for transplant rejection.
39. HTLV-I can cause ____ T-cell Leukemia Lymphoma
42. The LD-50 is the ____ dose of radiation to 50% of people at 30 days
45. Beaver construction
47. Status checked in saliva for soluble antigens (abbr)
48. Its state song is "Old Folks at Home" (abbr)
49. QB Manning
50. Texas town with zip code 75098
52. Person in whom Australia antigen (HBsAg) first described
54. Legendary Dallas Cowboy coach (init)
55. Cowboy recently initiated into the NFL Hall of Fame who didn't show up for the ceremony (init)
56. Sugar substitute
57. Eponym for DAT test
60. She played Hermione at Hogwarts (init)
61. Big ___, California
62. ___ and behold!
63. Egyptian sun god
64. Describing a software tool or method for understanding biologic data
69. Nosebleed
70. Put bacteria on a petri dish

Down

1. Old technique for checking donor hemoglobin levels (2 wds)
2. Vaccine requiring 4 week donor deferral
3. Blood bank abbreviation for Cartwright
4. Common medication office manual (abbr)
5. Contaminated or blemished
6. Medication of polyclonal horse or rabbit antibodies for transplant rejection (abbr)
7. Prefix for –sporin or –antigen
8. Molecule implicated in cytokine release syndrome (abbr)
9. Related to the gut (abbr)
10. ____-____ caproic acid; Amicar (2 wds)
11. Infant gut condition predisposing to polyagglutination (abbr)
12. ___ Wayne, rap music artist
13. Container to ship cooled blood components (2 wds)
16. Wed
19. What platelets must do after being centrifuged
22. Sea bird
25. Location for trauma blood use (abbr)
27. Unit of electrical resistance
29. Type of red cell elution
30. Yale state (abbr)
33. Old name for HPA-4
34. Smallest state (abbr)
36. Cell separation technology used for donors and patients
38. Little urine output
40. You and me
41. Blood group related to secretor type (abbr)
43. Joint close to the antecubital fossa
44. Neonatal blood "serving"
45. Trypan blue is one
46. He's on the penny (init)
50. Lab abbreviation for "this result is in the usual range"
51. Region of France where Strasbourg is
53. Hawkeye state (abbr)
54. Infection for which healthcare workers are tested annually (abbr)
57. ____ pulmonale, type of heart failure
58. Type of body temperature still measured by most blood centers
59. _____ Hari, WWI spy
62. _____ Alamos, New Mexico
64. Metallic element (83) used in fire extinguishing systems (abbr)
65. Lexus small SUV model
66. Fee ___ fo fum
67. Swimmer with 28 Olympic medals (init)
68. Computer department (abbr)