DEPARTMENT OF THE NAVY
BUREAU OF MEDICINE AND SURGERY
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IN REPLY REFER TO
BUMEDINST 6530.17
BUMED-M3
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BUMED INSTRUCTION 6530.17

From: Chief, Bureau of Medicine and Surgery

Subj: USE OF LOW-TITER GROUP O WHOLE BLOOD AT UNITED STATES NAVY MEDICAL CENTERS

Ref: (a) 21 CFR

1. Purpose. To establish policy guidance for the use of cold-stored low-titer group O whole blood (LTOWB) for resuscitation at U.S. Navy medical centers.

2. Scope and Applicability. Applies to all U.S. Navy medical centers with blood banks and transfusion services. LTOWB will not normally be made available at hospitals and clinics due to the limited scope of use of the product for trauma patients.

3. Background

a. The use of whole blood as a therapeutic modality has for the past several decades been generally avoided in favor of component therapy. Recently, however, there has been increased interest in returning to the use of whole blood for managing hemorrhagic shock in trauma patients. On 15 May 2018, the Joint Trauma System published clinical practice guidelines for whole blood transfusion describing the rationale and guidelines for whole blood transfusion, available at https://jts.amedd.army.mil/.

b. There are many advantages of using whole blood in trauma resuscitation. A single unit of whole blood is logistically simpler to transfuse than multiple components while providing a 1:1:1 ratio of red blood cells (RBC), plasma, and platelets. The cold-stored platelets in whole blood may provide improved hemostasis compared to room-temperature platelets in trauma patients. Additionally, patients receiving whole blood will be exposed to fewer donors than patients receiving an equivalent volume of blood components, reducing the recipient's infectious disease risk.

c. Per the 31st edition of the AABB (formerly the American Association of Blood Banks) Standards for Blood Banks and Transfusion Services (available at http://www.aabb.org), whole blood no longer needs to be ABO identical to the recipient. Instead, it must be provided in a manner such that the RBC component is ABO compatible with the recipient. If whole blood is to be administered in a situation where the patient's ABO group is unknown and therefore the plasma component of the unit might be incompatible with the recipient, the standards mandate the Navy medical center must have certain policies and procedures in place to use LTOWB.

4. Policy. Navy Medicine supports the use of LTOWB for patients with clinically significant shock and when optimal blood component therapy is either unavailable or when component therapy is not adequately resuscitating a patient with immediate life-threatening hemorrhage. The use of LTOWB is a medical decision that must be made by a physician or an authorized health professional who has full knowledge of both the clinical situation and the availability of compatible blood products.

5. Responsibilities. U.S. Navy medical centers are not required to place LTOWB into available inventory for routine mission support. However, U.S. Navy medical centers have the discretion to utilize this product to augment facility massive transfusion protocols when deemed appropriate by the blood bank medical director of the U.S. Navy medical center. If a determination is made to place LTOWB into available inventory for patient transfusion, the U.S. Navy medical center must perform the following actions:

a. Commanding Officers and Officers in Charge of U.S. Navy Medical Centers must:

(1) Ensure compliance with applicable AABB accreditation standards and Federal regulations, as stated in reference (a), parts 606.121 and 640.1-6, available at https://www.ecfr.gov/cgi-bin/text-idx?SID=ba6f018034a90eae48e32f87e2a517f4&mc=true&tpl=/ecfrbrowse/Title21/21cfrv7_02.tpl#0.

(2) Define policies, processes, and procedures for the use of LTOWB. Prior to LTOWB use, there must be a protocol for the administration of LTOWB, including the use of blood filters, infusion devices, and ancillary equipment. Additional information regarding instructions for use, side effects, and hazards for whole blood transfusion can be found in the "Circular of Information for the Use of Human Blood and Blood Components." Paper copies of the document can be obtained from all transfusion services, or an electronic copy can be obtained online at http://www.aabb.org/tm/coi/Documents/coi1017.pdf.

(3) Define policies, processes, and procedures for the maximum number of LTOWB units allowed. It is not recommended to transfuse greater than six LTOWB units to non-group O hemorrhaging patients. This maximum volume will minimize the risk of a hemolytic transfusion reaction after the administration of potentially ABO-incompatible plasma in the LTOWB unit to a non-group O recipient. There is no maximum number of LTOWB units for group O recipients.

(4) Define policies, processes, and procedures for monitoring transfusion recipients for adverse events.

(5) Define policies, processes, and procedures for the use of O positive LTOWB in Rh-negative recipients.

(a) To avoid alloimmunizing Rh-negative recipients to the D-antigen, O-positive LTOWB should not be transfused to females of reproductive potential if she is Rh-negative or if her Rh-type is unknown. In these cases, Rh-negative LTOWB or Rh-negative RBCs should be transfused. Clinicians may consider the use of O-positive LTOWB in these patients, but must balance the risk of anti-D alloimmunization with the potential benefit of reducing mortality by transfusing Rh-positive LTOWB.

(b) O-positive LTOWB may be used in males that are Rh-negative or if their Rh-type is unknown. Clinicians must balance the risk of anti-D alloimmunization with the potential benefit of reducing mortality by transfusing Rh-positive LTOWB.

(6) Establish a peer-review program that monitors and addresses transfusion practices for all blood products, including LTOWB. Since LTOWB is a new blood product in the U.S. Navy medical centers, the following indicators must be carefully monitored for all LTOWB transfusions:

(a) Infectious and non-infectious adverse events, including near-miss events.

(b) Usage and discard.

(c) Appropriateness of use.

(d) Clinically relevant laboratory results.

b. Blood Bank Medical Director must:

(1) Ensure each donated unit of whole blood intended for LTOWB production is tested and found to have anti-A and anti-B titers of less than a 1:256 ratio by tube or equivalent method.

(2) Store LTOWB for up to 21 days if collected in citrate phosphate dextrose (CPD) or 35 days if collected in citrate phosphate dextrose adenine (CPDA-1). To reduce outdating, transfusion services are encouraged to store LTOWB for no more than 14 days after collection in citrate phosphate dextrose and 21 days after collection in CPDA-1. After this storage period has elapsed, the units should be returned to the blood donor center where they can be processed into RBC units. The platelet-rich plasma supernatant must be discarded. The final RBC units can be distributed to transfusion services. The RBC units must retain the original expiration date of the collection.

(3) Provide and document training on LTOWB policies, processes, and procedures. The laboratory must ensure all personnel performing critical tasks associated with LTOWB are

trained and evaluated for competence as described in local laboratory procedures. Additionally, an education plan for physicians and nurses on the use and availability of LTOWB should be delivered.

(4) Define policies, processes, and procedures for ensuring that when clinically significant red cell antibodies are detected in the recipient or the recipient has a history of such antibodies, LTOWB is prepared for transfusion that does not contain the corresponding antigen and is serologically crossmatch-compatible.

c. HealthCare Providers

(1) Nurses, physicians, and other authorized medical providers who transfuse LTOWB must be familiar with local policies to ensure appropriate utilization of LTOWB.

(2) On the day of LTOWB transfusion and for the next 2 days, measure the following biochemical markers of hemolysis as part of the LTOWB recipient protocol: haptoglobin concentration, lactate dehydrogenase activity, total bilirubin concentration, creatinine concentration, and serum potassium concentration. Medical staff should create an order set to facilitate consistent compliance with these post-transfusion monitoring requirements.

(3) Immediately report all adverse events during LTOWB transfusion to the transfusion service as defined by local procedures.

6. Records Management

a. Records created as a result of this instruction, regardless of format or media, must be maintained and dispositioned for the standard subject identification codes (SSIC) 1000 through 13000 series per the records disposition schedules located on the Department of the Navy/Assistant for Administration (DON/AA), Directives and Records Management Division (DRMD) portal page at https://portal.secnav.navy.mil/orgs/DUSNM/DONAA/DRM/Records-and-Information-Management/Approved%20Record%20Schedules/Forms/AllItems.aspx.

b. For questions concerning the management of records related to this instruction or the records disposition schedules, please contact your local records manager or the DON/AA DRMD program office.

7. Review and Effective Date. Per OPNAVINST 5215.17A, BUMED-M3, Healthcare Operations, will review this instruction annually around the anniversary of its issuance date to ensure applicability, currency, and consistency with Federal, Department of Defense, Secretary of the Navy, and Navy policy and statutory authority using OPNAV 5215/40 Review of Instruction. This instruction will be in effect for 10 years, unless revised or cancelled in the interim, and will be reissued by the 10-year anniversary date if it is still required, unless it meets

one of the exceptions in OPNAVINST 5215.17A, paragraph 9. Otherwise, if the instruction is no longer required, it will be processed for cancellation as soon as the need for cancellation is known following the guidance in OPNAV Manual 5215.1 of May 2016.

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Acting

Releasability and distribution:
This instruction is cleared for public release and is available electronically only via the Navy Medicine Web site, http://www.med.navy.mil/directives/Pages/BUMEDInstructions.aspx