Lifeline for the front lines: blood products to support the warfighter

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BACKGROUND: Hemorrhage is the leading cause of death on the battlefield. Damage control resuscitation guidelines in the US military recommend whole blood as the preferred resuscitation product. The Armed Services Blood Program (ASBP) has initiated low-titer group O whole blood (LTOWB) production and predeployment donor screening to make whole blood more available to military forces.

STUDY DESIGN AND METHODS: ASBP donor centers updated procedures and labeling for LTOWB production. Donors are screened according to US Food and Drug Administration regulations and standard operating procedures. Group O donors are tested for anti-A and anti-B titer levels. Additionally, military personnel notified for pending deployment coordinate with their local ASBP donor center to complete whole blood donor prescreening. The process consists of completing a donor history questionnaire, processing of blood samples for blood group and infectious disease testing, and titer determination for group O personnel.

RESULTS: Since March 2016, 7940 LTOWB units have been manufactured at ASBP donor centers and shipped in support of combat operations. Additionally, ASBP donor centers have screened several thousand service members before deployment. From these screenings, the donor low titer rate was 68% and infectious disease reactive test rate was extremely low (≤0.004).

CONCLUSION: Whole blood is now the preferred blood product for resuscitation of combat trauma patients. The ASBP partnered with combat forces to screen personnel before deployment. Additionally, LTOWB is manufactured and shipped in support of combat operations. These efforts are expanding the availability of LTOWB for the warfighter.

Hemorrhage is the leading cause of death on the battlefield.[1] The sooner blood product transfusion can be initiated after injury, the better the chances of survival for a massively bleeding patient.[2] Both the Joint Trauma System and Committee on Tactical Combat Casualty Care recommend the use of whole blood or a balanced ratio of blood components to treat hemorrhage.[3–5] Whole blood was used extensively in World Wars I and II and the Korean and Vietnam wars. Over an 18-month period of the Vietnam War, more than 230,323 units of whole blood were transfused, with only one hemolytic reaction to a group O unit reported.[6,7] Following the Vietnam War, trauma resuscitation guidelines shifted to the use of blood components and crystalloids, and the production of whole blood greatly decreased.[8,9] The mission of the Armed Services Blood Program (ASBP) is to provide quality blood products and services to military health care

ABBREVIATIONS: ASBP = Armed Services Blood Program; CPD = citrate–phosphate-dextrose; CPDA-1 = citrate–phosphate-dextrose-adenine; LTOWB = low-titer group O whole blood; SOF = special operations forces; TMDS = Theater Medical Data Store; TTD = transfusion-transmitted disease; USCENTCOM = US Central Command.

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operations worldwide, and the program is committed to improving combat casualty care through advancement in blood product production and distribution on the battlefield. Since 2014, the ASBP has been heavily focused on renewing and improving access to whole blood for deployed military members. Whole blood initiatives within the ASBP include manufacturing and distributing low-titer group O whole blood (LTOWB) and prescreening service members prior to deployment to serve as potential donors in a walking blood bank (WBB) once deployed. Production of LTOWB by ASBP donor centers requires procedure and blood product label updates and identification of a titer-testing method. Prescreening of potential donors is performed by donor center staff and is closely coordinated with deploying military units. Donors must complete an abbreviated questionnaire and have samples drawn for standard blood donor testing along with anti-A/anti-B titer level determination for group O donors. Both LTOWB production and predeployment donor screening have seen a marked increase in scale with support by all three service blood programs. These whole blood efforts are key to providing advanced lifesaving blood products to our deployed warfighters. This article documents the development and implementation of these programs and ongoing advancements.

MATERIALS AND METHODS

Low-titer group O whole blood production

Volunteer donors were screened for donation using the ASBP Form 572 (donor screening record) and interviewed by ASBP personnel.[10–12] If determined to be eligible for donation, the donor was issued a unique donor identification number (DIN). Industry standard blood collection equipment was used for nonleukoreduced whole blood phlebotomy and processing. The tubes for the required viral marker and titer testing were collected and processed. Transfusion-transmitted disease (TTD) and titer-testing tubes were processed and shipped to the designated reference laboratories. Manual saline tube or automated gel technology analyzers were used as the titer-testing method to identify anti-A and anti-B IgM isohemagglutinin levels. Upon receipt of acceptable TTD and titer-testing results, the units were labeled per standard operating procedure and stored for 21 days for units collected in citrate–phosphate-dextrose (CPD) and 35 days for units collected in citrate–phosphate-dextrose-adenine (CPDA-1). Titer results had to be less than a titer of 1:256 for anti-A and anti-B for the unit to be designated as low titer. An additional label indicating low titer was added to the units meeting the low-titer criteria and the units were shipped through the ASBP Theater Distribution System (Fig. 1) as LTOWB for utilization in a theater of operation (Fig. 2). Whole blood units were stored at 1 to 6 °C without agitation and shipped at 1 to 10°C.

Predeployment donor screening for emergency walking blood bank

Volunteer donors were screened for donation using the ASBP Form 572 or ASBP 572-EWB (donor screening records) and interviewed by ASBP personnel.[13] Donor screening was conducted before deployment of the military unit. If determined to be eligible for donation, the donor was issued a unique donor identification number. The tubes for the required viral marker and titer testing were collected, processed, and shipped to the designated reference laboratories. Manual saline tube was the test method used for titer testing to identify anti-A and anti-B IgM isohemagglutinin levels. Military units were established in the Theater Medical Data Store (TMDS) for tracking and management of results and donations (Fig. 3). All results were placed in the TMDS by ASBP personnel. All results and deferrals were also placed into the ASBP blood establishment computer systems. Designated medical personnel were notified of ASBP deferrals and positive testing results. Donors with a positive TTD result were identified as deferred and counseled by Preventive Medicine as required. Donors determined through screening to be acceptable could then donate once deployed as part of emergency whole blood collection to support combat casualty care (Fig. 2). The screening performed is valid for 1 year with guidance to repeat screenings every 90 days while deployed if possible.[5]

RESULTS

Low-titer group O whole blood production

Since March 2016, 7940 LTOWB units have been manufactured by nine ASBP donor centers and shipped overseas in support of contingency operations. LTOWB units are shipped from a donor center to the Armed Services Whole Blood Processing Laboratories for packaging and shipment into active theaters of operation. Within the US Central Command (USCENTCOM) area of responsibility, LTOWB is flown into Al Udeid, Qatar, for initial receipt and inventory. From Qatar, the LTOWB units are further shipped to deployed medical facilities in support of Operations Freedom Sentinel, Spartan Shield, and Inherent Resolve. The majority of LTOWB units are distributed to special operations medical units, forward surgical teams, or used on board medical evacuation helicopters. The blood shipment process in theater can take several days as blood is moved further forward to more remote locations. At its final destination, the blood is delivered to a deployed hospital or surgical team and kept in inventory for patient use. In some cases, the LTOWB units are issued to individual medical providers to carry forward on designated missions. As of June 2018, 567 units of LTOWB have been transfused with no reported adverse events.[14]

Predeployment donor screening for emergency walking blood bank

During the period May 2015 to March 2018, 7177 potential donors were screened for infectious diseases as well as

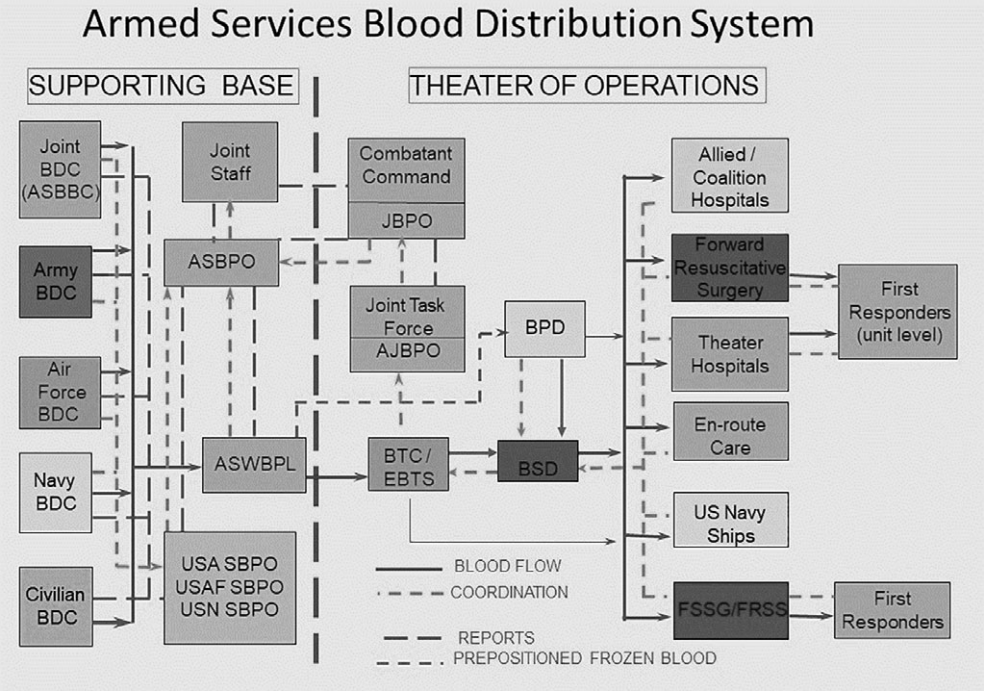

Fig. 1. ASBP distribution and reporting chart.

determinations of blood group, antibody screens, and, for group O donors, isohemagglutinin titer results. Based on these donor screenings, the overall infectious disease reactivity rate is low, with the highest being hepatitis B core antibody (Fig. 4). When titer testing is performed, potential blood group O WBB donors are evaluated for anti-A and anti-B isohemagglutinin titers based on an IgM tube reaction. The ASBP designates a "low-titer" blood group O donor as having an isohemagglutinin titer of less than 1:256. Potential donors are entered into the TMDS. The low-titer rate was found to be 68% in donors screened from May 2015 to March 2018.

A small subset of 32 group O donors, previously tested for isohemagglutinin titer levels, returned and repeat assessments were conducted. Repeat assessments occur due to service members having multiple deployments. Of the 32 blood group O soldiers with repeat assessments, a total of 7 exhibited a change in isohemagglutinin titer: 6 had a change in anti-A from high titer to low titer, and 1 had a change in anti-A titer from low to high titer (Fig. 5).

The US Army Rangers account for 3479 screening events, or roughly 48% of all US Army prescreening events. The 75th Ranger Regiment elected to screen only the blood group O donors for eligibility into this program. This program has identified a 97% accuracy rate in donor blood group self-reporting where the claimed group O blood types matched blood type testing results.

All screened personnel were available to serve as whole blood donors in the event of a patient emergency. These

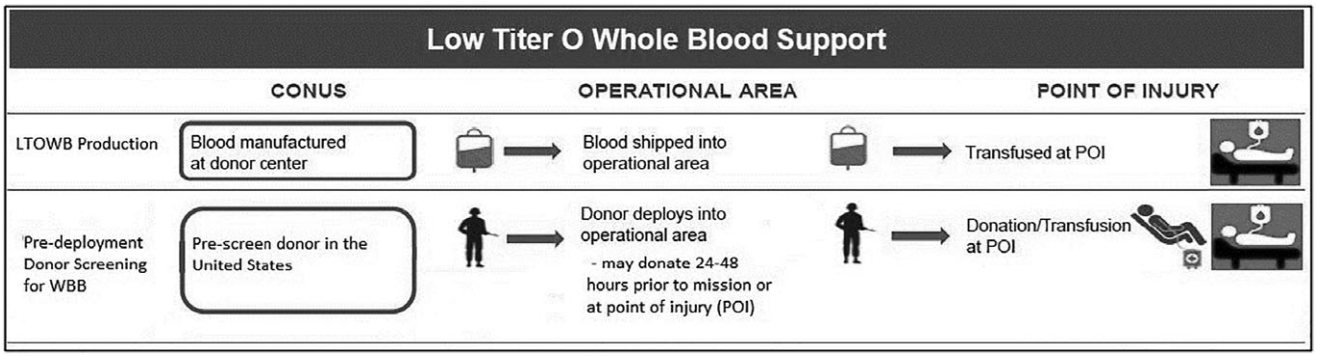

Fig. 2. ASBP methods of whole blood support.

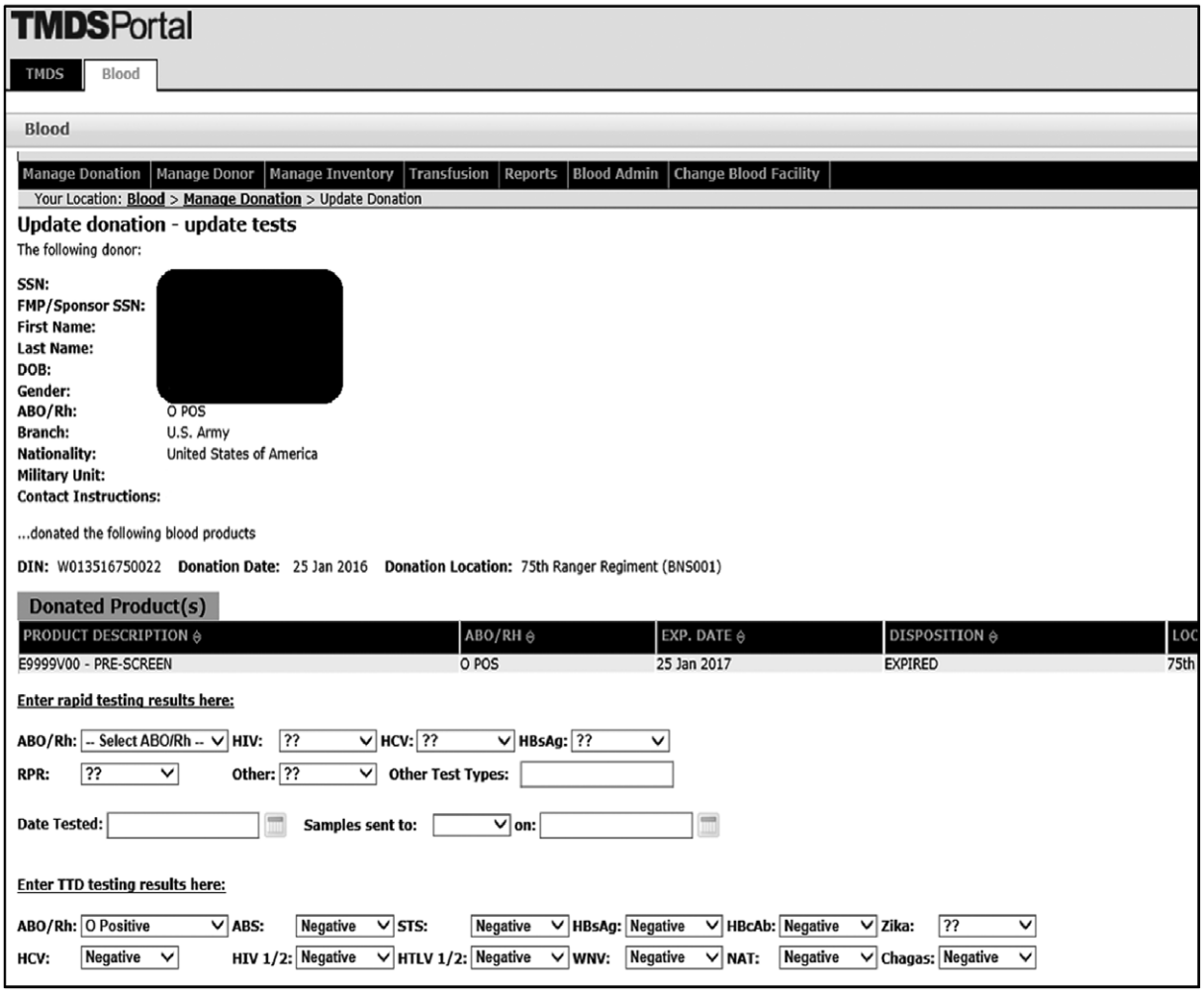

Fig. 3. Screen shot of the "Update Donation" page where the donor demographic, transfusion-transmitted disease, and comments in reference to the isohemagglutinin testing are documented.

emergency donations could occur at a deployed medical facility or further forward on the battlefield at the point of injury. Appropriate unit-level tracking is required to ensure that screened donors are used first in the event of a donation requirement.

DISCUSSION

Low-titer group O whole blood production

Shipment of LTOWB to USCENTCOM began in March 2016, with a shipment of 10 units per week. The initial production

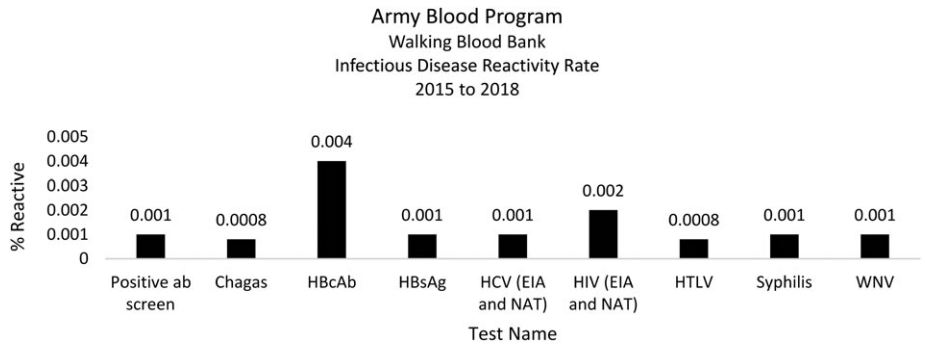

Fig. 4. The SOCOM infectious disease reactivity rates observed during the time period of May 2015 through March 2018. Reactivity rate was determined by dividing the number of positive tests by the total number of walking blood bank test screens.

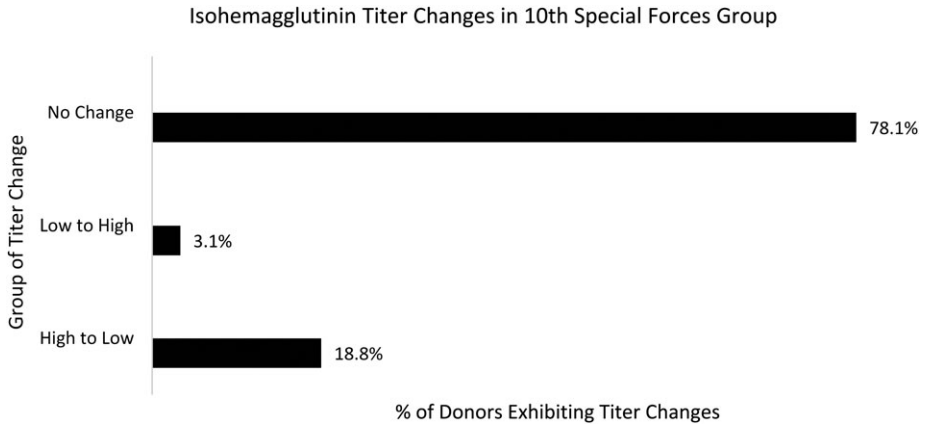

Fig. 5. When the 10th Special Forces Group blood group O soldiers were repeatedly screened for the walking blood bank program, roughly 22% of the 32 soldiers exhibited a change in the anti-A isohemagglutinin.

of LTOWB by ASBP blood donor centers focused on use of CPD as the anticoagulant, which allows for a 21 day shelf life of the blood product. Through 2016, requests for LTOWB from USCENTCOM continued to grow, resulting in gradual increases in the weekly quota required of the service blood programs. By the spring of 2017, all three service blood programs were manufacturing and shipping weekly LTOWB quotas in support of deployed forces. The weekly amount of LTOWB shipped has grown to over 100 units per week. With the increased focus on providing blood further forward on the battlefield, more medics and surgical units are being provided with LTOWB, although most still also keep RBCs and plasma in inventory.

Given the shipment time to fly blood products from the continental United States to USCENTCOM forces and use of CPD as the anticoagulant, LTOWB units were often arriving to their final destination with only a few days of shelf life remaining. ASBP donor centers have started to transition to production of LTOWB using CPDA-1 anticoagulant, which allows for a longer shelf life. The transition from CPD to CPDA-1 anticoagulant requires donor centers to use different bag sets and update standard operating procedures.

The production and distribution of LTOWB gives medical providers the preferred product for resuscitation while reducing reliance on emergency whole blood collections. ASBP-manufactured LTOWB is US Food and Drug Administration licensed and fully compliant with all donor screening and testing requirements. LTOWB also simplifies blood storing logistics as opposed to storing full component therapy products, which requires freezers and incubators in addition to a blood refrigerator. Although platelet and coagulation factor activity decreases during 21 or 35 day LTOWB storage, refrigeration attenuates the losses and preserves therapeutic benefit.[15]

LTOWB is preferred for deployed locations. However, the majority of Department of Defense garrison medical facilities require blood components. ASBP donor centers have to screen and direct donors to the appropriate donation group to ensure that quotas for both whole blood and components are met on a weekly basis. The military is working to update doctrine and policy guidance to establish planning factors for the amount of whole blood required for deployed forces.

Predeployment donor screening for emergency walking blood bank

One of the many challenges faced on the battlefield is the emergency collection, testing, processing, and transfusion of whole blood. To meet that challenge, treatment facilities must implement a WBB. This program is usually activated by the trauma surgeon or senior medical provider and is a medical decision made with full knowledge of the clinical situation and available blood products. There are risks associated with whole blood collected as part of a WBB, such as infectious disease transmission and blood group incompatibility.[5] However, these risks are outweighed by the therapeutic benefit of whole blood and can be mitigated with donor screening and regular WBB training. ASBP screening results indicate that the overall infectious disease risk is low in the screened US military population.

Currently, there are several locations that are participating in the whole blood donor screening program described in this paper. The Army Blood Program also sends teams of 8 to 12 personnel from a blood donor center to conduct mobile screening events. The donors are screened and samples are collected for testing at a contracted testing laboratory. Donors who are deferred or have positive test results are placed into the blood donor center enterprise computer system and communicated to the unit surgeon.

The program of screening donors prior to deployment initiated with Special Operations Forces (SOF). SOF screenings by ASBP centers have continued since 2014. Conventional forces are also starting to request screening for WBB program support. To meet the increased demand for

screenings, ASBP donor centers use combat medics assigned to the military units being screened to assist with the process. Medics with appropriate training can assist with sample collection and donor screening. The ASBP has developed an abbreviated donor screening questionnaire that can be used for both donor screening before deployment and in deployed locations for emergency whole blood collections.

Screened donors with acceptable TTD results can be used for LTOWB or group-specific emergency whole blood donation. LTOWB provides a universal blood product, while group-specific whole blood requires blood typing the patient to find a donor match. An overall low-titer rate of 68% of screened donors provides a substantial number of universal whole blood donors. Some military units may prefer to prioritize their LTOWB donors first and rely on group-specific donations as a secondary source of emergency whole blood.

Although only a small number of donors were assessed more than once for titers, there is evidence that titer levels for a service member can change over time. Currently, it is not clear what might cause the change in titer levels or to what degree the titers may change. With the understanding that titers can fluctuate, the practice of screening donors before each deployment will continue. Although testing every 90 days is preferred, a titer test is considered valid for 12 months.[5]

CONCLUSION

ASBP implementation of predeployment WBB donor screening and production of LTOWB have enhanced damage-control resuscitation options on the battlefield. These programs require dedicated resources and close coordination with deploying forces. Whole blood is simpler logistically to position far forward on the battlefield than blood components such as platelets and frozen plasma. ASBP leadership anticipates that the demand for whole blood will continue to grow and that future conflicts will see LTOWB as the primary blood product produced and shipped. Areas for further research should focus on enhanced blood product storage solutions, allowing for longer storage of whole blood and examination of donor titer changes.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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