Implementation of a low titer group O whole blood program for a law enforcement tactical team

Andrew D. Fisher,[1,2,3] *John Dunn*,[4] *Jason R. Pickett*,[4,5] *Justine Garza*,[6] *Ethan A. Miles*,[7] *Vivian Diep*,[2] *and Mark Escott*[4,5]

The Texas Ranger Special Operations Group (SOG) performs high-risk warrant service and responds to callouts for evolving kinetic situations and special missions as required. These operations may occur many hours from a trauma center. Fresh whole blood (FWB) transfusions may offer a stopgap for those who are critically injured. To make FWB transfusions a viable option, several steps must be implemented. The following lays out how the Texas Ranger SOG will implement and conduct FWB transfusions using low titer group O whole blood. The techniques outlined may be useful for communities that may face critical blood shortage in disasters.

Prehospital trauma care in the United States can be directly attributed to the advances made in combat casualty care. These improvements in prehospital care, resuscitation, and surgery have helped increase the rate of survival to an unprecedented 90% in Afghanistan and Iraq; this can be attributed to the implementation of Tactical Combat Casualty Care (TCCC).[1] In response to evolving research, the Committee on TCCC changed the guidelines for fluid resuscitation in hemorrhagic shock in 2014; the guidelines call for whole blood (WB) as the fluid of choice.[2] Resuscitation with blood products in trauma has demonstrated to be beneficial when given early[3]; this might be equally important in settings where evacuation to surgical care will be prolonged past

ABBREVIATIONS: CPDA-1 = citrate-phosphate-dextrose-adenine; EMS = emergency medical services; FWB = fresh whole blood; HBV = hepatitis B virus; HCV = hepatitis C virus; LTOWB = low-titer group O whole blood; POI = point of injury; SOG = Special Operations Group; TACO = transfusion-related circulatory overload; TCCC = Tactical Combat Casualty Care; TRALI = transfusion-related acute lung injury; TROLO = Texas Ranger O Low program; TTDs = transfusion-transmitted diseases; WB = whole blood; WNV = West Nile virus.

From the [1]Medical Command, Texas Army National Guard; the [4]Texas Department of Public Safety; the [5]Austin-Travis County Office of the Medical Director; the [6]We Are Blood, Austin; [2]Texas A&M College of Medicine, Temple; [3]Prehospital Research in Military and Expeditionary Environments (PRIME2), San Antonio, Texas; and the [7]Maneuver Center of Excellence, Fort Benning, Georgia.

Address reprint requests to: Andrew D. Fisher, MPAS, 2401 S. 31st Street Temple, TX 76508; e-mail: fisherad@tamu.edu

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the Golden Hour concept.[4,5] The Golden Hour concept is a time previously described where critically injured patients should arrive at surgical care or be treated with more advanced care. The methods for the process of using low titer group O whole blood (LTOWB) at the point of injury (POI) have been described previously.[6,7] It is these lessons learned from combat that have substantially changed the approach and treatment of patients with hemorrhagic shock. There are currently several prehospital programs that use cold-stored LTOWB.[8,9] However, a description of how to optimally implement the use of low titer group O fresh whole blood (FWB) in the tactical civilian environment has not been described.

In austere operational settings, maintenance of cold storage for blood products can be challenging. WB and red blood cell (RBC) products must be stored within a tight temperature range (1-6°C) and continuously monitored to ensure safety of the blood products. The operational environment is often subject to wide temperature variations and extremes. Refrigerators require reliable power and have limited portability, which would compromise a unit's agility. The availability of coolers capable of storing blood products at the appropriate temperature ranges for long periods of time in the prehospital setting have increased over the past few years. Optimally, a team would use cold-stored WB or component therapy. However, when special operations teams perform infiltration by foot, there are constraints on what can be carried due to weight and/or space that limit the feasibility of carrying refrigerated containers or coolers. Furthermore, the availability of cold-stored blood is restricted to certain geographic areas. Finally, there may be a situation, where the available cold-stored blood products have been depleted, leaving FWB as the option. Although convenient, the use of crystalloid fluids such as 0.9% sodium chloride for trauma resuscitation has been challenged by a large body of data.[10–13] They have been attributed to adverse outcomes such acidosis, coagulopathies, and increased mortality in trauma patients.[14] Additionally, with the use of crystalloids, there are increased instances of acute kidney injury, acute lung injury, and acute respiratory distress syndrome.[15,16]

In an effort to find a solution for blood product storage, FWB transfusion protocols have been developed by military units to free operational units with use of a "walking blood bank." Donors within these organizations are identified before deployment through blood typing and screening for antibodies and infectious disease. When a casualty is encountered on the battlefield who requires blood, medical personnel immediately draw a unit of blood with a kit adapted for the field setting, this blood is then transfused at once to the casualty.[17] Other than a rapid blood typing of the casualty, no other point-of-care testing is performed at the time of this transfusion.

BACKGROUND

Current transfusion guidelines recommend the use of ABO group-specific blood products in transfusions when available. Several studies dating back to World War II on WB transfusions indicate that group O blood with low IgM anti-A and anti-B titers is safe and effective, regardless of the recipient's blood group.[18] During World War II, the American Red Cross Blood Donor Service determined from pools of donated plasma that group O blood was safe at titers below 1:250.[19] Additionally, the Army WB Procurement Program processed almost 1500 blood specimens daily. During this time, a study was conducted with use of group O plasma on healthy volunteers at the Colorado State Penitentiary to determine what titers would elicit a reaction.[19] The study evaluated the reactions of 39 recipients of high-titer group O plasma (1:400-1:4000); there were no deaths, and all recovered within hours to 4 days. With this data, Major Leslie H. Tisdall determined that group O blood was safe at titers below 1:200.[19] Though correlation between antibody levels and risk of hemolysis is imprecise, these antibodies can be measured in the laboratory setting to identify low-risk FWB donors.[20]

Approximately 37% to 53% of the US population is blood group O.[21] This number of potential donors could have significant benefits in a community. LTOWB is defined as low levels of anti-A and anti-B immunoglobulin G (IgG) and immunoglobulin M (IgM), though IgM levels are the primary concern since these are most closely associated with hemolysis. There is no universally accepted definition of "low titer," however, many experts suggest a level of 200 or lower for IgM. According to Berséus et al.,[18] a "universal donor" has IgM and IgG levels of 100 and 400, respectively. Furthermore, Strandenes et al.[5] stated that the Norwegian Naval Special Operations Commando use similar values to define their universal donor. Within the United States, emergency medical services (EMS) agencies that use LTOWB use IgM only and range from less than 1:50 to less than 1:256.[8] Acceptable titer levels for this protocol will be IgM anti-A and anti-B less than 1:200. There are no large-scale studies that address whether titer values change over time.

A recent study of soldiers (N = 2237) found that 266 (11.9%) had repeat titer testing more than once.[22] Up to 80% of donors had titer changes; however, it was rare to change more than one dilution, and there was a trend to for titers to decrease over time. Other studies evaluated the effects of titer levels of IgG and IgM titers in non–group AB donors and vaccinations titers over time.[23,24] The available data suggest relatively stable titers over time. With this information, the question of how often to titer a donor pool is valid.

There are over 600 RBC antigens with most of the concern surrounding RhD antigen.[25] The seriousness of a mismatch is often overstated and usually of little concern. It does not cause an immediate hemolytic reaction after the first exposure. According to the American Red Cross, 80% to 90% of the US population is D positive,[26] leaving a small percentage as D negative. If exposed to D-positive blood by transfusion, 20% to 26% develop a sensitivity, and 3% to 4% will develop a significant immune response to future exposures .[26] In this protocol, RhD is not taken into consideration for emergency WB transfusion but will be documented.

Use of untested WB entails a small but significant risk of disease transmission.[27] Risk can be mitigated through routine testing for diseases of concern. Jenkins et al.[28] recommended testing for HIV, hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis, West Nile virus (WNV), and Chagas. We Are Blood in Austin, Texas, tests for antibodies to human T-lymphotropic virus-I/II; hepatitis B core antibody and surface antigen; nucleic acid amplification test for HIV, HBV, HCV, WNV and Zika virus; antibodies to HCV; antibodies to HIV-1 and -2; syphilis; and antibodies to *Trypanosoma cruzi* and syphilis, with possible testing for cytomegalovirus. Rising vaccination rates for the hepatitis A and B viruses further increase the safety of FWB, though HBV testing is recommended, as the vaccine may produce an incomplete response.

Technologic advancements are in development to facilitate both point-of-care testing and rapid leukoreduction using a platelet-sparing leukoreduction filter. A leukoreduction filter would help to minimize febrile nonhemolytic transfusion reactions, human leukocyte antigen alloimmunization, and prevention of transmission of viruses such as cytomegalovirus.[29,30] While beneficial in theory, its use is time consuming and may result in decreased hemostatic potential.[31] Due to these potential issues, leukoreduction in its current form is not recommended. If this capability is eventually available at the POI, the tactical medic must take these factors into consideration.

Acute transfusion reactions appear within the first 24 hours of the transfusion. When transfusing FWB in the prehospital setting, the reaction of most concern is the immediate intravascular hemolytic transfusion reaction. This is due to the possibility of unreliable ABO confirmation at the point of injury (POI). This reaction between the donor's antigens and recipient's preexisting antibodies is mediated through complement fixation. This will be mitigated by having a roster of eligible low titer donors readily available by the leadership and medical personnel. The most severe sequelae that can follow is disseminated intravascular coagulation. However, this risk must be weighed against the risk of the patient dying on the battlefield before reaching definitive care. It is unlikely that this complication will be identified at the point of initial transfusion. A less severe febrile transfusion reaction can be easily managed in the field with antipyretics and antihistamines and does not require discontinuation of the transfusion. Typically, in a febrile nonhemolytic transfusion reaction, there is at least a 1°C increase in temperature that occurs within 4 hours of the transfusion. Anaphylaxis is an indication to stop the transfusion; the profound symptoms should be recognized immediately and managed with epinephrine, antihistamines, and crystalloids. It is important that medical personnel continue to monitor the patient for any delayed hemolytic transfusion reaction, but this monitoring is typically outside the capability of most prehospital providers' capabilities.

There are several advantages of FWB over stored blood and blood components. From the conflicts in Iraq and Afghanistan, FWB has demonstrated superiority over components[17,32,33] and it maintains complete hemostatic functionality.[34] Component therapy has approximately three times the anticoagulants and additives.[35] Although earlier studies of stored RBC use demonstrated some associations with increased mortality,[32,36–41] current literature suggest that stored RBCs are safe, with no difference in mortality.[42–45] Transfusion-related acute lung injury (TRALI), a cause of transfusion-related mortality, tends to be more related to stored blood components by antibodies to WBC antigens, lipids that accumulate during storage of cellular blood components, and a CD40 ligand.[42] TRALI also tends to have a higher association with female donors,[46] whereas this protocol will use male donors.

Several studies have discussed the decreased function of RBCs in stored blood.[36,43] In addition, the breakdown of RBCs has been linked to free hemoglobin and potassium leak.[43,47] Free hemoglobin subsequently binds to nitric oxide, a potent vasodilator, therefore causing microvasculature hypertension. Finally, transfusion-associated circulatory overload (TACO) typically presents within the 6 hours of a transfusion, and patients may have dyspnea, chest tightness, cyanosis, orthopnea, and increased blood pressure. TACO is responsible for the highest transfusion-related mortality; however, there is less concern for this due to lower fluid resuscitation volumes and duration in combat settings.[48,49] Patients who develop TACO are more likely to have comorbidities like congestive heart failure and kidney disease.[50,51] Several concerns about the potential for transfusion reaction and transfusion-transmitted diseases (TTDs) can be mitigated through regular and recommended testing.

THE POPULATION

The Texas Department of Public Safety, Texas Ranger Special Operations Group (SOG) performs high-risk warrant service, special reconnaissance, responds to callouts for evolving kinetic situations (barricaded subjects and hostage rescue), and performs other special missions. The high-risk nature of these operations and hostile persons encountered by the SOG make serious trauma a possibility. Though a low-frequency event (one demonstrated need in the past 4 years), the result of a need not met with WB can be catastrophic. The SOG's tactical medical personnel team includes paramedics, physicians, emergency medical technicians, and emergency care attendants. The SOG has a response area over a quarter-million square miles. Some of the areas where operations take place are remote, hours from definitive medical and surgical care. Furthermore, some of the response area is underserved by conventional ground-based EMS, and currently, very few EMS agencies in the state offer WB or component therapy. Stored WB was considered for use by SOG tactical medics but cost and the nature of operations rendered this impractical. Banked blood would allow transfusion to civilian patients and not

be limited to this current model of force protection only. While deployments, potentially including prolonged movements by foot or watercraft into remote regions do present challenges, these could be mitigated by portable coolers which would facilitate WB therapy. At present, there is an undeveloped supply, resupply, and rotation chain for banked WB. Even if there were abundant sources in the state, in the absence of a reliable rotation scheme, most WB would be unused for an infrequent albeit high-acuity event requiring prehospital transfusion. In time, as institutions (hospitals, ground and air EMS) field WB, SOG will consider adoption of a rotation system in each region with the aforementioned sources. These models may be adopted as primary and alternate plans, relegating the Texas Ranger O Low (TROLO) program to contingency status.

Logistically, a "walking blood bank" consisting of screened male donors and appropriately trained medics will minimize the disadvantages inherent to stored WB in a SOG mission set while fulfilling the need for emergent transfusion. With the potential possibility for prolonged evacuation, the capability to provide stabilization and early initiation of damage control resuscitation, including blood transfusion, is critical.

DEPLOYMENT AND MAINTENANCE

Initial deployment is with the Texas Department of Public Safety SWAT team based in Austin. Donor identification, screening, and briefings were finalized and appropriate

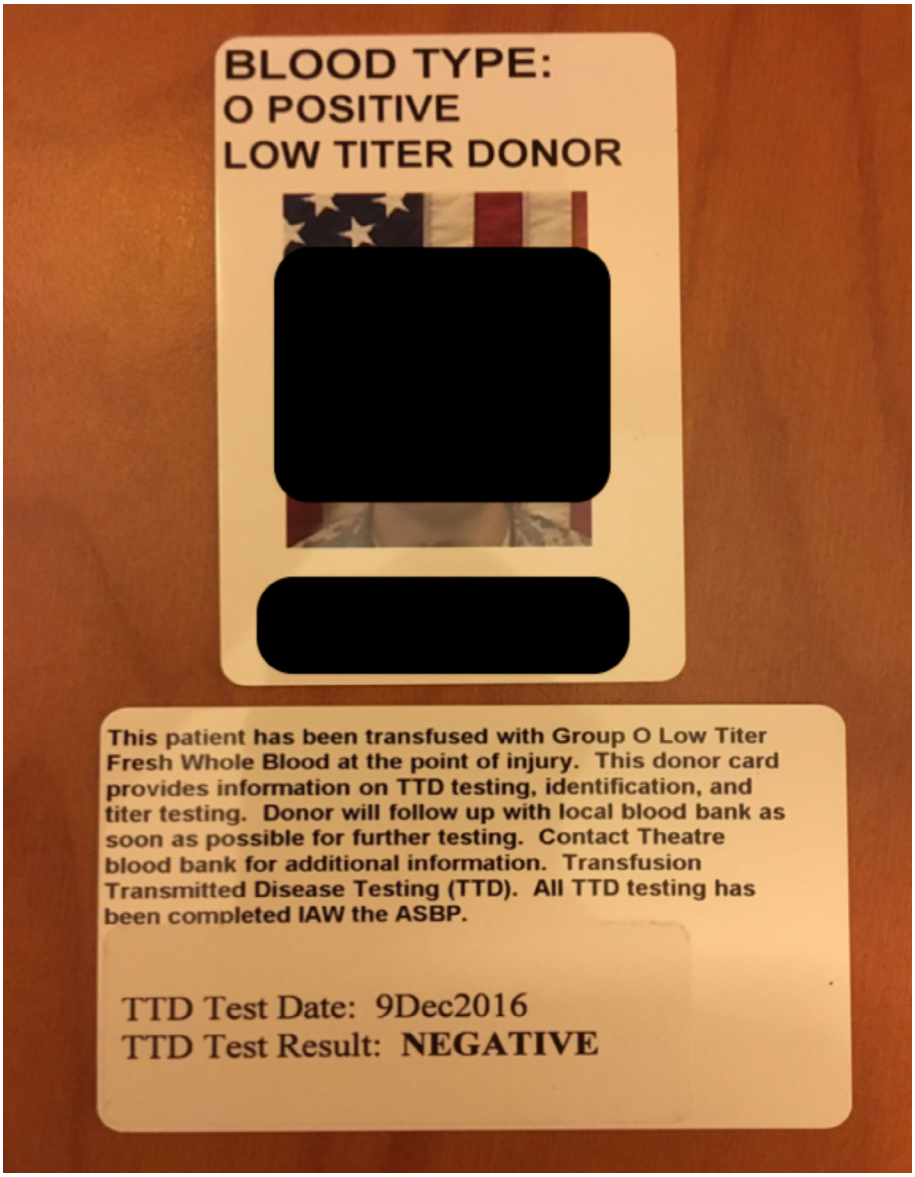

Fig. 1. TROLO identification.

testing performed. Now that the concept has been proven, this protocol will be rolled out statewide to all Texas Ranger Special Operation Group Special Response Teams, Ranger Recon, and SWAT South in the Rio Grande Valley. Since most of the SOG rotates through the Austin headquarters area at least once a year, using the regional blood center in Austin, We Are Blood, may be the preferred location for screening rather than turning to regional blood facilities. However, a working relationship with other blood banks is recommended and encouraged.

Arguably the most important aspect of the protocol after identifying the low titer group O donors is the administration and maintenance of the program. Initially, all SOG team members were screened for their blood group to construct a potential universal donor base. Two matching consecutive tests interpreted by medical staff provided ABO confirmation.[52] Since this is a volunteer program and has the potential to affect any trooper, the medical director or his designated representative gives all potential donors a brief on the background, indications, and any adverse effects associated with blood donation.

After the brief, all potential donors go to the We Are Blood center, where blood samples are drawn for ABO and infectious disease testing. Any potential donor identified to be group O blood has titer testing performed. All results are confidential, but if a trooper is notified by We Are Blood with a positive result for an infectious disease, they are encouraged to talk to the medical directors for treatment options. Testing was performed by preparing a single 1:200 dilution of the donor's serum to test for reactivity with reagent A and B cells by the tube method. Team members with titer levels of IgM anti-A and anti-B below 1:200 were identified and designated the universal donors or TROLO donors. In August 2019, the Texas Department of Public Safety began titer testing their SOG members. Of the 18 SOG members tested, eight were group O, five of which met inclusion criteria of TROLO. Ten were a blood group other than O.

Upon receiving the notification of their titer status, all universal donors receive counseling that outlines their responsibility and reporting requirements. All group O donor information is maintained by We Are Blood. The medical directors have restricted access to protect personal identifiable information and protected health information but also provide appropriate counseling to donors. TTD testing is recommended every 90 days; however, all universal donors are tested at a minimum frequency of every 6 months.

SOG members are required to undergo practical and written testing annually. The subjects include the recognition of hemorrhage and hemorrhagic shock, establishing vascular access, phlebotomy of the donor, blood administration, recognition and management of adverse reactions, documentation, and administrative concerns. Each medic maintains a separate roster of all personnel in their respective teams. The roster contains the member's name, low titer status, and date of communicable disease testing. This is based on the 75th Ranger Regiment's ROLO card (Fig. 1). Before each mission, universal donors are identified during the operations brief with the rest of the team. If a situation occurs where an operations brief was not completed, the medic will confirm with the team leader or deputy team leader of personnel on the operation. Each universal donor can donate one unit of FWB, collected in citrate-phosphate-dextrose (CPD) or citrate-phosphate-dextrose-adenine (CPDA-1) anticoagulant. In the future, it may be possible to either store the blood until expiration in approved containers or transfuse back to the donor. Donating a single unit of WB should not significantly impair the physical

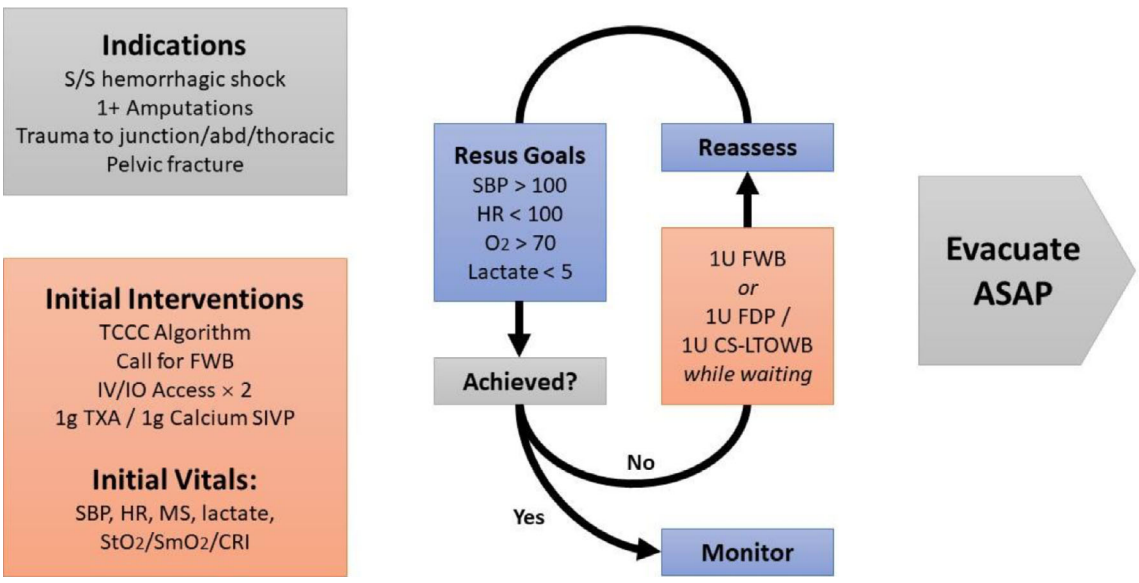

Fig. 2. Hemorrhagic shock algorithm.

or cognitive capacity of the donor. If tactically necessary, this donor may remain on station to continue participation in the tactical operation.

POI USE

When someone sustains one or more of the injuries listed below with hypotension, tachycardia, and other associated vital signs, the medic will begin the protocol (Fig. 2):

1. One or more major amputations
2. Penetrating or blunt torso trauma
3. Suspected pelvic fracture
4. Evidence of severe bleeding

The medic will then obtain intravenous (IV) access (or intraosseous if unable to gain IV access) preferably at two separate sites and give the patient 2 grams of tranexamic acid slow IV push. The universal donors will carry at least one 450-mL single blood pack unit with CPD or CPDA-1 with them in their bleeder kit; furthermore, the troopers with advanced medical skills will carry a commercially purchased FWB transfusion kit with one 450-mL single blood pack unit with CPD or CPDA-1. Blood collection from the donor will be immediately performed by another team member or medic following proper identification of the donor's full name. The medic or a designated person has the option of starting a 14-gauge saline lock and then placing the collection bag needle through the needle port (Fig. 3). This offers the advantage of access for replacement fluids and less positioning of the needle. Traditional blood collection uses hemostats or a similar device to "clamp" the collection bag line; however, the Norwegian Naval Special Operations Commando protocol has shown that this step is not necessary.[53] This eliminates unnecessary tasks and allows blood to immediately flow into the bag when the needle is placed inside the vein.

Fig. 3. Drawing a unit of blood through a 16-gauge catheter.

It is challenging to determine the precise volume of a blood collection bag. According to most commercially available FWB collection kits, a 9½-by-11-inch piece of paracord wrapped circumferentially around the collection bag is approximately 450 mL. This is a flawed method since the bag's circumference is uniform regardless of volume. A novel collection method was recently developed; by tying, for example, a 5½- to 6-inch paracord around the circumference, it is difficult to overfill the collection bag.[54] The beaded cable tie is the easiest and most accurate means to use during the donation. Blood sterility does not require refrigeration in the acute setting. However, if a unit of blood does not require administration, the blood can stay at ambient temperature for up to 6 hours before required cooling to 1 to 10°C.[53] It is important to note that this is a deviation from standard blood banking practices.

As outlined by Strandenes et al.,[53] after the donation, it is recommended that the donor consume an oral hydration solution and/or 0.5 L of water. Even without hydration, donor performance is not degraded after donating one unit of FWB.[55] However, this is donor specific, and the medic should evaluate the donor before allowing him to return to his duties.

Due to the relatively small size of SOG teams, team members with EMT or Emergency Care Attendant certifications are also cross trained in collecting the unit of blood. This protocol may utilize the nonparamedic to collect the donation. If the unit of blood was collected by a team member other than the paramedic or physician, once the blood has been collected and the donor has initialed the bag and attached his LTOWB donor card, they will move to the medic and patient. If the nonparamedic performs the phlebotomy, he and the paramedic will confirm the donor and recipient's blood group on the roster. The medic will then note the time and fill out the label (Fig. 4), place it on the bag, and administer the unit to the patient as required.

Blood transfusions during resuscitation can lead to profound hypocalcemia, a life-threatening condition secondary to the accumulating citrate from donor blood and chelation of calcium by myoglobin and lactate. The effects of hypocalcemia include long QTc, decreased cardiac output, coagulopathy, and seizures and eventually contribute to mortality. A 2015 study demonstrated 97% (n = 152) of patients requiring a massive transfusion had hypocalcemia and 111 (71%) exhibited severe hypocalcemia.[56] Furthermore, a 2017 study of patients receiving a massive transfusion revealed that hypocalcemia occurred in 35 (85%) of the patients.[57] Finally, a 2011 study correlates hypocalcemia and death in critical bleeding patients.[58] These studies were following the general rule of giving calcium after every four units of blood. This guideline recommends that calcium be given early with the administration of 2 g of calcium chloride or 6 g of calcium gluconate intravenous push (IVP) after the first unit.

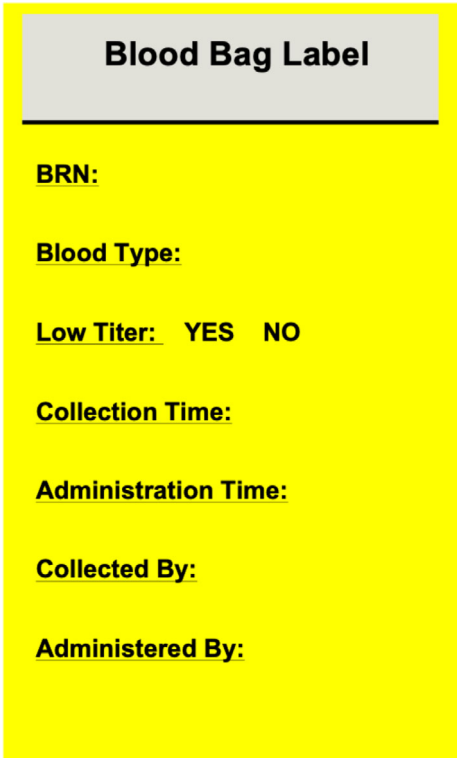

Fig. 4. Blood bag label.

LOGISTICS

For documentation, all universal donors have identification cards that list blood group and titer, in addition to last TTD testing dates, similar to the TROLO program (Fig. 1). During the phlebotomy and transfusion process, an identification card will be collected from the donor and given to the medic and patient receiving the FWB. Each blood bag will be labeled as described above as well as documented at time of injury on a DD1380, a laminated casualty record designed for austere settings. All blood bags, even if completely transfused, will accompany the patient to the hospital for further posttransfusion testing. Effective communication between the medic and local hospital is crucial to ensure that critical information and testing is captured in the patient's electronic medical record, including posttransfusion testing, associated documentation of testing results, transfusion details, product identification, any transfusion reactions, and disposition.

The significant logistical advantage to FWB is that it is readily available on target, does not require immediate storage, and is indefinitely maintained at approximately 98.6°F. The basic blood transfusion kit includes the basic material for a blood draw (one citrated collection bag with hard needle, one bag label for field use, chlorhexidine for prep, one Penrose drain to use as a venous constricting device, a black permanent marker, a beaded cable tie, and 4- × 4.5-inch dressing). The intermediate blood transfusion kit includes all items in the basic kit and adds a single inline filter infusion set. The advanced blood transfusion kit adds an additional citrated collection bag and blood bag label, and one ABO card for emergency blood group testing when working with an unknown population of donors in an extreme emergency when no identified donors are available or have been exhausted.

CONCLUSION

The use of fresh LTOWB eliminates logistical challenges, expense, and risk of general blood supply wastage, which are significant barriers to WB availability in austere conditions. Effective implementation requires physician medical oversight, quality assurance processes, operating procedures and protocols, appropriate training, and identification of a titer testing service. FWB is a viable option at the POI for resuscitation of the traumatically injured patient in the combat environment. Through appropriate training and troubleshooting, the FWB "battle drill" is potentially an efficient and safe protocol that civilian health care and public safety can implement during disasters or times of critical blood shortage.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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