ON THE FRONT LINES of Transfusion Medicine

The Armed Services continues to adapt transfusion medicine to meet the needs of combat casualties.
Although the use of blood transfusion for military traumatic hemorrhage dates back to the first and second World Wars, the ins and outs of where and how transfusions are given in combat continue to progress today.

This evolution became evident in 2014 when the United States Armed Forces updated its Tactical Combat Casualty Care (TCCC) guidelines to recommend the use of whole blood as the preferred product for resuscitating casualties in hemorrhagic shock and for administering blood products as far-forward (close to combat) as feasible. These updates reflected a growing awareness of the importance of timely fluid resuscitation for combat casualties who can potentially be treated.

“Put simply, even if you can’t stop the bleeding, sometimes you can keep people alive by replacing what is lost,” explained Army Col. Andrew “Andre” P. Cap, MD, PhD, FACP, chief of blood research for the U.S. Army Institute of Surgical Research. “It’s like, if you have a bucket with a hole in it, water will leak out, but if you keep pouring water in, even though there is still a leak, the bucket will at least always have water in it until the hole can be fixed.”

In order to provide this timely resuscitation, the Armed Services Blood Program (ASBP) has worked to advance the science of blood banking and transfusion, including in whole blood transfusion, freeze-dried plasma and cold-stored platelets. These innovations have reduced recent combat mortality rates to their lowest levels in any conflict.

Timely Transfusions

“Whether it’s from a blast or a gunshot wound, many combat injuries require blood transfusion, with approximately 350,000 blood products having been transfused over the past 18 years of U.S. military involvement in the Middle East,” said Army Lt. Col. Jason B. Corley, MT(ASCP)SBB, MS, director of the Army Blood Program. In the last decade, evidence has mounted to support the idea that the faster blood products are given, the better the odds of survival.

In 2009, a study looking at in-hospital deaths at modern combat support hospitals found that among deaths deemed highly preventable, 90% were related to delays in hemorrhage control during transportation or resuscitation phases. That same year, then Secretary of Defense Robert M. Gates issued a mandate calling for a standard of 60 minutes or less — dubbed the “golden hour” — from call for prehospital helicopter transport for U.S. military casualties to arrival at the treatment facility.

In 2016, a study confirmed that implementing the “golden hour” goal had reduced casualties. The percentage of those killed in action and the case-fatality rates both significantly decreased after implementation of the mandate. The median transport time had been reduced from 90 minutes to 43 minutes.

“More recent research looking at MEDEVAC [medical evacuation] blood transfusion has shown that the ‘golden hour’ is important, but the difference between life and death could come down to minutes,” Corley said.

A retrospective study of military combat casualties in Afghanistan who were transported on MEDEVAC helicopters showed that blood transfusion occurring in a prehospital setting or within minutes of the injury was associated with better 24-hour and 30-day survival compared with delayed transfusion.

Giving Whole Blood

Part of the transition from transfusing blood in a hospital to the battlefield has involved a growing use of whole blood. Historically, the move from whole blood to blood components occurred to provide optimal use of a limited blood supply. Patients could receive only the blood component that they needed most, allowing several patients to benefit from the same unit of whole blood.

“In some military settings with a lot of staff, you could pick and choose which components are necessary, but this is less reasonable in a far-forward setting,” Cap said. Additionally, a 2009 study retrospectively comparing combat casualty patients transfused with either warm fresh whole blood or component therapy showed that use of warm fresh whole blood improved both 24-hour and 30-day survival. Using whole blood instead of components also has fewer logistical challenges, Cap added.

“Administering a bag of red cells, a bag of plasma, and a bag of platelets in the back of a helicopter, or on the ground, for a medic, is hard to do,” Cap said. “We recognized that whole blood actually has everything you need and comes in one convenient package.”
Low-Titer O

Because whole blood has antibody components, collecting low-titer type O whole blood (LTOWB) is key to having whole blood available in emergency situations.

When using ABO group-specific whole blood in emergency medicine, treatment may be delayed because of the need for ABO typing, and there is an increased risk for hemolytic transfusion reactions. Cap coauthored a 2014 study assessing the use of whole blood for life-threatening hemorrhagic shock, which recommended the use of group O whole blood donors with low anti-A/B titers in emergency situations when ABO group-specific typing is unavailable or unfeasible.6

LTOWB — defined by the Department of Defense (DOD) as coming from donors with titers of less than 1:256 anti-A/B blood group antibodies — can be manufactured at a donor center and shipped into an operational area. However, the military has also created programs for collecting low-titer O blood in theater. The first option collects blood from pre-screened donors 24 to 48 hours prior to a mission, with rapid testing for HIV and hepatitis B and C viruses done at the time of donation. A second option has been dubbed the “walking blood bank.”

“In cases where the existing supply is gone due to a mass casualty event, or more casualties are coming in prior to a blood resupply, a decision might be made to collect fresh whole blood on the scene,” said Army Col. Audra L. Taylor, MS, SBB(ASCP), division chief of the Armed Services Blood Program.

According to Cap, the idea of the walking blood bank was first used in the special forces community when teams were being deployed into dangerous situations where they were expected to take casualties but would be far beyond the capability for immediate MEDEVAC. These units would not be able to carry more than a few units of blood with them. “We identified personnel within each team that were low-titer O so that person would be available to take a unit of blood off at the point of injury,” Cap said. “That way they are not trying to do type-specific transfusion in a far-forward setting or keeping track of units of blood in the middle of a rainy night.”

In the U.S. population, group O donors represent about 40% of all individuals, and a low-titer population might make up about 90% of those individuals, depending on the age of the donor population, said Cap. In fact, in an early rollout of the concept, the Ranger O Low Titer Whole Blood Program was recognized in 2017 for winning the Army’s Greatest Innovation Award at the Association of the United States Army Global Welfare Symposium.

“More than 20 major trauma systems in the U.S. have instituted whole blood in emergency resuscitation protocols and, in some cases, in prehospital treatment protocols through EMS systems,” Cap said. In San Antonio, for example, ground ambulances, air ambulances and trauma centers all keep LTOWB on hand for hemorrhaging patients.

Plasma Products

Another important military advance is an improved availability of plasma products on the battlefield, according to Navy Cmdr. Jonathan Hoiles,
stasis decreases over time. There are lots of disadvantages to this product that are critical to hemostasis.”

Room-temperature platelets were adopted to limit clearance from the blood and maintain high platelet count for as long as possible. However, in cases of severe trauma, rapid formation of clots is the priority. In emergency situations, adoption of cold-stored platelets would meet more of the needs of far-forward injuries. Cold-stored platelets maintain their hemostatic function, have a reduced risk for bacterial growth and can be moved around theater more easily, Cap explained.

In 2015, FDA approved cold-stored apheresis platelets for resuscitation of bleeding patients. Platelets can be stored for three days at refrigeration temperature between 1 to 6 degrees C. In 2016, the DOD began transfusing cold-stored platelets in Iraq, Afghanistan and other combat areas. The three-day storage limit was restricting, and the shelf-life of the platelets was extended to 10 days, and, more recently, to 14 days. Researchers are studying whether or not platelet shelf-life can be safely extended beyond the currently approved three days, possibly up to a period of two to three weeks.

Advances Continue
The military has been pushing the lines of technology and medicine for hundreds of years, and looking to the future, this is not likely to change. “We continue to have a focused effort to gather data and increase the training of our forces in both blood collection and administration, and the recognition of patients that require transfusions,” Cap concluded. “All this work is to continue to get the right blood products to the right place as quickly as possible.”

Cold-Stored Platelets
Early administration of platelets after severe trauma can provide rapid control of hemostasis and help treat platelet dysfunction. Typically, platelets are stored at room temperature with an FDA-mandated storage restriction of five days, according to Cap. “The problem is, if you collect platelets in Texas and need to get them to Afghanistan in five days, that isn’t going to happen,” he said. “In addition, it is well documented that the ability of the platelets to form hemo-

MSC, director of the Navy Blood Program. Plasma can serve as a bridging product until whole blood is available.

Transfusion with fresh frozen plasma has several limitations, including the need for refrigeration and allowance for adequate thawing time, Hoiles explained. “The goal is to have a dried plasma product that we can deliver to the front-line medic or corpsman so they have a readily available product on the battlefield without having to store fresh frozen plasma,” he said.

Last summer, an important step toward this goal was met when the Food and Drug Administration granted an emergency use authorization (EUA) to the DOD enabling emergency use of pathogen-reduced leukocyte-depleted freeze-dried plasma, or French freeze-dried plasma.9 The product is collected from volunteer donors and manufactured in France. After being reconstituted with sterile water, it can be administered intravenously. The freeze-dried product is intended for use on individuals with hemorrhage or coagulopathy during a life-threatening situation when the use of fresh plasma is not possible or practical.

Unlike fresh frozen plasma, the French freeze-dried plasma can be stored for 2 years from manufacture date at temperatures between 36 to 77 degrees F.

ENDNOTES