ADVANCES IN HEMATOLOGY

Current Developments in the Management of Hematologic Disorders

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The Safety of the Blood Supply

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H&O About how many patients undergo blood transfusions?

PN Transfusions are used very commonly in the United States and around the world. In the United States in 2008, there were about 48.9 units of red cells transfused per thousand people, which is about 15 million units of red cell transfusions and about 2 million doses of platelets. Approximately 80% of the platelets in the United States are collected through single-donor apheresis procedures, and about 20% are made as a by-product of whole blood collections. At Johns Hopkins, approximately one third of our transfusions go to our oncology center, and approximately 60% of our platelets go to our oncology patients, mostly for hematologic malignancies and cancer therapy support.

H&O How safe is the blood supply in the United States?

PN In terms of viral infections, it is very safe. The virus that most people continue to worry about is HIV; we began the earliest testing for HIV in 1985. Currently, the risk of contracting AIDS from a transfusion in the United States is probably less than 1 in 2 million units, so it is very rare. Blood is now tested for HIV antibodies and HIV nucleic acid. This testing has shortened the window between the time a potential donor becomes infected with HIV and the time HIV testing will be positive, probably on the order of about 10 days.

We also test for hepatitis B, hepatitis C, human T-cell lymphotropic virus types 1 and 2 (HTLV-1, 2), and the agents that cause syphilis. More recently, we have begun testing for Chagas disease and for the West Nile virus, which is transmitted by mosquitoes in the United States. These tests, combined with a careful donor history—plus the fact that the donors are volunteers—have made the blood supply very safe.

We have not eliminated all infections. Internationally, pathogen reduction technologies for platelets and plasma are available that help sterilize blood. These technologies are not yet available in the United States, but they could potentially help reduce residual viruses and other agents that could emerge into the blood supply.

Another safety issue is the risk of septic reactions. Most blood components are stored in the refrigerator at 4°C. Platelets, however, are stored at room temperature, which can enable bacteria to contaminate the platelet, grow, and cause septic reactions in patients. This problem was addressed in 2003, when we began culturing platelets to reduce the risk of septic platelet transfusions. Occasional septic reactions can still occur, but culturing the platelets has reduced the problem substantially.

H&O How can hospitals optimize the safety of the blood supply?

PN Hospitals can take several steps to optimize blood supply safety. There are still problems in the United States and worldwide with misidentification of blood samples from patients who need transfusions; samples are collected from a patient different than the intended transfusion recipient, sent to the laboratory to be typed, and then blood of the incorrect type is given to the patient.

Administration of the wrong blood type can cause an ABO hemolytic transfusion reaction, a serious condition. Hospitals must develop rigid protocols for identification of samples from patients. Another step, already being taken by many hospitals, is to ensure that blood is given only to patients with appropriate indications for the transfusion. It is clear that over the past few years, the numbers that we used as indications for red cell transfusion were higher than they needed to be. For platelet transfusions, what we call the *transfusion trigger*—the point at which platelets are needed—was also presumed to be higher than it needed to be. In addition, in some cases, the doses of blood components were higher than necessary.

H&O Does storage affect the efficacy of blood?

PN This issue is a topic of ongoing controversy. Studies in the United States and around the world have suggested that blood stored for a longer period of time may have less efficacy than fresher blood and may increase the risk of transfusion-related adverse events, including effects on the immune system. There are ongoing, randomized, clinical studies in cardiac surgery in the United States and in Canada among patients in intensive care units to determine whether transfusing blood that is fresher is better than transfusing blood stored according to accepted guidelines. For example, according to regulations from the US Food and Drug Administration (FDA), red cells can be stored for 42 days. Studies are comparing transfusions with blood that is about 10 days old to transfusions with blood that is about 3 weeks old to identify any differences in patient outcomes, reactions, or efficacy. Until we know the answers to these questions, clinicians should follow the current transfusion guidelines and permissible storage protocols from the FDA.

H&O What are some ways that hospitals can effectively manage their blood supplies?

PN As I mentioned, a hospital-based transfusion committee that works with clinical departments can help ensure that blood is given only to patients who need it. Another important way to manage the blood supply is to return unused blood. In some cases, when blood is sent to the bedside but not used upon delivery, it is not returned appropriately, or it is returned too late for the blood bank to reissue it to another patient.

H&O What are some transfusion alternatives?

PN Soon after the HIV epidemic became a concern for transfusion—and before we could test for the virus—there was much interest in autologous blood. Currently, however, autologous blood is not that useful because most of the patients who would be eligible for this procedure are undergoing surgeries (eg, radical prostatectomies) that no longer routinely require transfusion. Cardiac surgery may still require transfusion, but, in general, these patients are not good candidates to give their own blood. In addition, autologous blood cannot be used by other patients and is frequently wasted. An important transfusion alternative is intraoperative blood salvage, which is used in open heart surgery and other types of surgery; it can save a lot of blood. Perioperative hemodilution is a surgical technique in which blood is collected in the operating room and then given back to the patient after surgery. This technique is not based on solid clinical evidence, and it is unclear whether it is helpful. The only group of patients who may have some benefit from this procedure are perhaps religious objectors who would not accept blood otherwise.

A transfusion alternative that we would like to have is a blood substitute that could be sterilized, would be free of ABO antigens, and could be used in emergencies in patients with an unknown blood type, in religious objectors, and in patients with autoimmune hemolytic anemia. Unfortunately, there is no licensed blood substitute in the United States, and we are not likely to have one in the near future. Hemoglobin-based oxygen carriers were being developed using hemoglobin outside of the red cell, but they were deemed unsafe due to the effects of nitric oxide scavenging by hemoglobin in the circulation.

Another approach to transfusions is drugs that avoid the use of blood. Erythropoietin is an important therapy that can stimulate red cell production in patients with anemia. It should be used in appropriate doses so that the hematocrit level is not raised too high. There are also drugs used during surgery to reduce bleeding complications, but some, such as aprotinin, have been withdrawn because of safety concerns.

Some of the earlier enthusiasm for transfusion alternatives seems to have lessened now that surgical blood loss has been decreased and some of the alternatives have been associated with risks that may not justify their use.

Suggested Readings

Ness PM. Does transfusion of stored red blood cells cause clinically important adverse effects? A critical question in search of an answer and a plan. *Transfusion*. 2011;51:666-667.

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Slichter SJ. Platelet transfusion therapy. *Hematol Oncol Clin North Am.* 2007;21:697-729.

Ness PM. Pharmacologic alternatives to transfusion. *Vox Sang.* 2002;83(suppl 1):3-6.