More on the Changing Indications for Transfusion of Blood and Blood Components during Anesthesia

In little more than the past decade the human immunodeficiency virus (HIV) was discovered; the association between acquired immune deficiency syndrome (AIDS) and transfusion was established; transfusion of blood and blood components was determined to be an exceedingly efficient method of the transmission of the virus. These discoveries resulted in a burgeoning concern about the safety of blood and blood components, with attention concentrated principally on defining and decreasing the risk associated with these biologics. In fact, concern regarding the safety of blood antedates the introduction of HIV into the blood supply. During the past 20 yr, the overall risk of transfusion-transmitted viral disease has been reduced by a number of factors, including: exclusion of paid donations, improved screening procedures of donors and testing for the presence of viral antigens and antibodies to viruses, expansion of donor education programs, request for self-deferral among high-risk populations, implementation of "look-back" procedures, and provisions for confidential self-deferral of donors. As a result, blood and blood components are safer than ever. Hepatitis C (previously included in the group of hepatitis viruses described as "non-A, non-B"), the agent most likely to result in post-transfusion disease, has a current incidence of transmission of less than 0.03% per unit of blood, compared to the approximate incidence of 3% per unit (10% per recipient) 20 yr ago. In the United States, the risk of transmission of HIV by transfusion is approximately 0.00015%-0.0002% per unit transfused. The risk of fatal hemolytic transfusion reaction is similar. Other risks include alloimmunization, effects on cellular immune function, bacterial contamination, and white cell-mediated acute pulmonary injury.

However, these data define only the numerator of a risk/benefit ratio that provides the clinician with the information needed to judge therapy. Data regarding the benefit(s) or efficacy of blood and blood components are largely lacking. Although approximately 12 million units of red blood cells are transfused per year in the United States, the efficacy of this biologic has not been demonstrated in an appropriately controlled, prospective study, nor are there clear criteria by which one would judge the efficacy of red blood cells. Indeed, the U.S. Food and Drug Administration (FDA) is having difficulty deciding how to judge the efficacy of the asanguinous oxygen-carrying solutions now in various stages of development. Nevertheless, concern within the medical profession, the media, and the political arena (e.g., note the recent formation of the high-level post of "blood safety director" within the U.S. Department of Health and Human Services) has resulted in a number of consensus conferences, and the promulgation of transfusion guidelines (described in various terms) by a number of professional organizations, in an effort to reduce the perceived overtransfusion of blood and blood components and, thus, potentially reduce the incidence of post-transfusion infectious complications. The National Institutes of Health (NIH) published the conclusions of three consensus conferences regarding the indications for transfusion of red blood cells, fresh-frozen plasma, and platelets. Several medical societies also have produced guidelines. One of these societies, the American College of Physicians (ACP), published an algorithm for transfusion of red blood cells, which included their criteria for transfusion of patients during anesthesia (development of unstable vital signs in patients without "risks:" e.g., for myocardial or cerebral ischemia).

Since most blood transfusions occur during surgery, the concern regarding transfusion is immediately relevant to the anesthesiologist. During anesthesia, physiology is altered, symptoms of inadequate oxygen delivery are absent, and signs may be difficult to interpret. These problems have led to the conventional wisdom
that, whenever possible, inadequate oxygen delivery should be prevented (in preference to allowing its creation followed by treatment). Recognizing these issues, the American Society of Anesthesiologists in 1994 convened a task force (of which the undersigned was a member) comprised of representatives from societies of specialties other than anesthesia to develop practice guidelines for perioperative blood component therapy. That document appears in this issue of the Journal.21

Several points regarding these practice guidelines merit comment. Most importantly, the guidelines are just that; they are not a mandate. The task force recognized the lack of adequate data documenting efficacy of these biologics and the threshold(s) that demand therapy, the importance of biologic variation, the impact of disease, and the dynamic nature of surgery. The significance of these factors may be seen in several of the panel’s recommendations. The panel recognized such important practical issues as the rate and site of bleeding, the anticipation of bleeding, and the rapidity with which results of important laboratory tests are reported. The panel regarded the ACP’s recommendations for anesthetized patients as inappropriate, because the ACP panel apparently did not consider these issues or those that prompted the ASA to convene the task force (see above). The practitioner will note that the ASA task force recommended a range of thresholds above which it is unlikely (but not necessarily unacceptable) that transfusion of blood components would be required and below which it is likely (but similarly, not with certainty) that they would be required. It is conceivable that an anesthesiologist might rationally transfuse (or not transfuse) outside these parameters. The reasoning used by the task force should aid the reader in understanding how the recommendations were reached, and perhaps gauge when these recommendations might not apply. Practitioners choosing to administer (or not) these biologics outside the recommended limits should document their decision-making process.

The strength of this practice guideline is that it is an “evidence-based” product: an extensive literature search was conducted, and the strength of the conclusions of the culled articles was carefully reviewed by a multidisciplinary panel familiar with this literature and the practice imperatives of the specialty. However, the reader should also recognize omissions and limits of this practice guideline as well as those of previously published. This guideline did not address (1) the transfusion threshold of the pediatric population; (2) the use of autologous blood (a recent review by an NIH expert panel22 served that purpose); (3) techniques, such as controlled hypotension23 or hemodilution,24,25 that the anesthesiologist may employ in an effort to decrease blood loss and the need for blood or component therapy; (4) the special clinical circumstances of liver transplantation or special hemolitic disorders (e.g., sickle cell anemia); and (5) when the use of whole blood is appropriate.

Although the task force did not address sickle cell anemia, data have been published recently regarding preoperative transfusion of patients with this disease. These data indicate that preoperative reduction of the concentration of hemoglobin S to 30% (by exchange or multiple transfusion) increases the incidence of transfusion-related complications without altering the incidence of other serious perioperative complications.26

The task force also did not address the use of whole blood. Whole blood differs from packed red blood cells importantly in that the latter contains far less plasma and, thus, coagulation factors. Mathematical analysis predicts that loss of greater than one blood volume and its replacement by fluids with absent or greatly reduced coagulation factors is required to reduce the circulating factor concentrations to the level consistent with coagulopathy (concentrations less than 30% of normal). When that degree of blood loss is expected or achieved, transfusion with whole blood, in preference to a combination of packed red blood cells and fresh-frozen plasma, reduces the number of donors to which the recipient is exposed, thereby reducing the risks. Clinical data support that, when whole blood is used to replace massive blood loss, a coagulopathy does not result from decreased coagulation factor concentration, and therefore, administration of fresh-frozen plasma, in addition, is not efficacious.27 If a coagulopathy develops, it is likely a result of thrombocytopenia, which requires an even greater degree of blood loss and replacement.27,28 In contrast, the use of packed red blood cells for replacement of massive blood loss produces a coagulopathy secondary to coagulation factor deficiency earlier than that produced by thrombocytopenia.29

In addition, the risk of transfusion is not static. The rates of transmitted diseases may change with their epidemiology or improved detection technology. Other diseases may emerge. The risks of other complications of transfusion (e.g., transfusion reactions) have remained relatively stable. The possibility of human error
prevents these risks from reaching zero. While it is appropriate to educate our patients regarding the risks of blood component therapy, we must guard against overconfidence in the greatly improved safety of the U.S. blood supply. The recent decision by the FDA to test donated blood for HIV antigen § at substantial cost (perhaps $60,000,000–100,000,000 per year) and against the recommendation of its own extramural Blood Products Advisory Committee (in 1989 and 1995), may detect approximately five to ten antigen-positive, antibody-negative units per year but may increase the number of infected units in the blood supply because of the possibility of attracting potentially infected donors who desire to avail themselves of this test, which is not available elsewhere ("magnet" effect), or by increasing human error of other tests because of the increased number of tests and workload. It is a sobering thought that the majority of noninfectious transfusion-related deaths result from nothing more complicated than ABO group red blood cell incompatibility, a substantial fraction of these errors occur in the operating room, and the operating room is the most common site of physician error producing a fatal hemolytic transfusion reaction. The relative freedom of professional judgment afforded by the ASA Task Force’s guideline (compared to other guidelines) comes with an implied responsibility. Continued attention to this rapidly moving field is mandatory (the reader should note that the panel’s recommendations are based on information available as of mid-1994): Not only are risks likely to change, but undoubtedly, additional data is forthcoming regarding efficacy of blood and its components that might alter the thresholds for their administration.

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