Bloody white cells—no problem: Let's solve hemorrhage out of the operating room

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In this issue of the *Journal*, McQuilten and colleagues¹ report the effects of the introduction of universal leukodepletion of red blood cells on patient outcomes after cardiac surgery. Whole blood and red blood cell (WB-RBC) units and units of apheresis platelets are usually leukocyte depleted to decrease the perceived risk of febrile nonhemolytic reactions, leukotropic virus infection such as cytomegalovirus (CMV), and HLA alloimmunization.² Leukodepleted units have less than 0.83 million leukocytes per WB-RBC unit and less than 5 million leukocytes per unit of apheresis platelets. Universal prestorage leukodepletion of red blood cell and platelet products was instituted by the Canadian Blood Services by 1999, was put into practice in Australia in 2008, and is currently the practice in most European countries.

The majority of WB-RBC units transfused in the United States are leukocyte depleted, but not all are. The biannual United States National Blood Collection and Utilization Survey for 2011³ reported that 84.8% of the 13,785,000 WB-RBC units transfused in the United States in 2011 and 86.6% of the 2,179,000 unit equivalents of apheresis platelets were leukocyte depleted. Apheresis platelets are leukocyte depleted by the method of collection, so it is likely that their rate was 100% but that reporting was incomplete. The rate of leukocyte depletion at the bedside has declined to nearly zero. Of the institutions that responded to the United States National Blood Collection and Utilization Survey of 2011, 73% reported that they had a policy of transfusing only leukocyte-depleted components. Of the remaining institutions, fewer than 3% reported that they transfused only leukocyte-depleted components to cardiac surgical patients.³ It is therefore likely that about 2,000,000

leukocyte-rich WB-RBC units are still transfused in the United States each year.

Leukocyte depletion may have some effect on the risks of febrile nonhemolytic reactions, transmission of CMV, and HLA alloimmunization, but it is not entirely clear how effective universal leukocyte depletion is in preventing these adverse events.⁴ The rates of adverse transfusion reaction and of severe adverse donor reactions in the United States during the last 15 years have remained steady, at 0.24% and 0.13%, respectively. Febrile nonhemolytic reactions occurred at a rate of 1 reaction per 957 units of any blood component transfused. Current data for the rate for only red blood cell-containing products is unavailable. Similarly, current data for reduction in CMV infection and HLA alloimmunization after WB-RBC or platelet transfusion are also not available. CMV infection is a greater risk for patients who are immunosuppressed and have no evidence of CMV resistance, such as CMV-seronegative bone marrow and organ transplant recipients and neonates with an anti-CMV-seronegative mother. Lastly, HLA alloimmunization—the development of anti-HLA antibodies—induced by leukocyte-rich transfusion may be ameliorated by leukodepletion. Thus patients who are likely to receive heart, bone marrow, or other transplant should routinely receive leukocyte-depleted units.

Cardiac surgeons, however, generally worry most about nonspecific proinflammatory immune modulation by transfused leukocytes, notably possible effects on end-organ dysfunction, infection, and mortality. As detailed in the article of McQuilten and colleagues,¹ the evidence that immune modulation by transfused leukocytes has an effect on clinical outcomes is weak, or at best controversial, and this article adds another tick to the “no” column. The observed reduction in acute kidney injury may be a specific effect of leukodepletion, or it may mirror the overall reduction in adverse events and mortality observed during the 2000s. It does not appear enough on its own to justify leukodepletion. It is hard to get too worried, however, because the technology is cheap and effective for leukodepletion, even if the benefit is marginal, and its use is generally routine for most transfusions.

There is another way of looking at the value or lack thereof of leukodepletion. If there is no need to transfuse because you have been effective at reducing blood wastage, then no one need care whether an untransfused unit is leukodepleted or not. There are 2 sources of avoidable

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blood loss out of the operating room that can be favorably impacted by cardiac surgeons.

Avoidance of the usual approximately 5% reduction in hematocrit after femoral cardiac catheterization and the occasional but significant risk of femoral access site bleeding complications should be possible by a change to performing radial instead of femoral cardiac catheterization.⁵ The primary advantage of transradial cardiac catheterization is reduced access site bleeding, as opposed to the sometimes catastrophic complications associated with femoral arterial cannulation, along with decreased cost and patient burden.⁶⁻⁸

There are concerns with a steep learning curve,⁹ cannulation difficulty, technical issues with coronary artery engagement, use of the radial artery for subsequent coronary revascularization, and ischemic hand complications; however, these concerns should not limit the use of radial cannulation for most cardiac catheterization procedures.^{10,11} Although radial catheterization is common,¹² it is not routine in every US institution; however, it is a valuable means of transfusion avoidance. It is time to encourage our interventional colleagues.

The volume of blood used for laboratory testing in association with cardiac surgical procedures is an unmeasured and little-recognized source of blood loss. This is not a new idea,¹³ but large-volume blood sampling, equivalent to a unit of whole blood for routine cardiac surgery, persists even the most sophisticated centers.¹⁴ What would happen if 1.5-mL phlebotomy tubes were routinely used instead for all perioperative testing? The technology has no additional cost, may have benefit, and can easily be routine for all patients.

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