Leukocyte reduction (LR) is a process applied to cellular blood products which removes the white blood cells from the product before it is transfused. The technology of LR was developed in the early 1960s and was refined in the early 1980s. Initially, the transfusion of LR blood products was reserved for selected patient subgroups; however, several European countries and Canada recently have implemented the use of LR of all allogeneic cellular blood components for transfusion.1 The proposal to introduce universal LR in the United States has been controversial and is not supported by all members of the transfusion medicine community.2

Achieving Leukoreduction

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Established Benefits of Leukoreduction

- Prevention/reduction in recurrent non-hemolytic transfusion reactions to RBC transfusions.
- Prevention/reduction or delay in alloimmunization to WBC antigens in transplantation candidates or long-term transfusion recipients.
- Prevention of CMV transmission.

Universal Prestorage Leukocyte Reduction

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After reading this article, the reader should be able to define blood product leukoreduction and list the established and potential benefits of this technology.

Hematology 0105 exam questions and corresponding answer form are located after the “Your Lab Focus” section, p 763.

Leukocyte reduction (LR) is defined by the American Association of Blood Banks (AABB) as fewer than 5 × 10^6 residual donor white blood cells (WBC) per final product. The Food and Drug Administration (FDA) guidelines at this time require quality control testing of leukoreduced units at a rate of at least 1% of products (or 4 per month for facilities preparing less than 400 units/month) with 100% of tested units containing less than 5 × 10^6 residual WBCs/unit. The FDA also requires the final product to contain at least 85% of the original therapeutic blood element.3 The European guidelines define leukocyte reduction as less than 1 × 10^6 WBCs/unit and recommend sufficient testing so as to be able to detect a 10% failure rate in the leukoreduction process.1 Current blood filters and apheresis systems are capable of consistently producing components with residual WBCs well below 1 × 10^6 when used properly, thus meeting either American or European cutoff standards.1

There are currently three basic approaches to leukoreduction of cellular blood components: prestorage leukoreduction performed by the blood collection facility, poststorage leukoreduction performed under laboratory conditions conducted by the hospital transfusion service, and bedside filtration.4 Bedside filtration is common and the least costly of the three methods, however, this method has several drawbacks. Bedside filtration results in poorer filter performance and is not easily adapted to current good manufacturing practices (cGMP).5,6 Bedside filtration of platelets has also been associated with infrequent hypotensive reactions.7

Prestorage leukoreduction, which is performed by the blood collection facility, has the advantage of process control and adherence to cGMP. Prestorage leukoreduction also prevents the accumulation of leukocyte-derived cytokines in platelet products which have been associated with a higher incidence of febrile non-hemolytic transfusion reactions.8 The main disadvantage of prestorage leukoreduction performed by the blood collection facility is cost. If one uses only leukoreduced blood at a facility, then costs increase at least about $30 more per unit.9 Several companies are currently exploring new ways to make leukoreduction more cost efficient. However, cost remains an area of concern even as regulatory agencies consider a universal policy on leukocyte reduction. Poststorage leukoreduction performed by the hospital transfusion service is the least common of the three methods employed.
Established Benefits of Leukoreduction

Leukocyte reduction of blood components has been shown to be clinically beneficial for selected patients and selected indications [T1]. Established indications include prevention of recurrent non-hemolytic febrile transfusion reactions to RBC transfusions, reduction of alloimmunization to leukocyte antigens in patients who are candidates for transplantation or those who may need transfusions on a long-term basis, and the reduction of transmission of cytomegalovirus CMV to patients at increased risk of CMV disease.1,4,10,12 Patients at risk for the development of CMV disease includes chemotherapy recipients for whom severe neutropenia is expected, recipients of hematopoietic progenitor cell replacement therapy, CMV seronegative recipients of CMV seronegative solid organ transplants, and low birth weight infants.

Potential Benefits of Leukoreduction

There is a growing list of potential, but not established, benefits of leukoreduction of cellular blood products [T2]. One such potential benefit of leukocyte reduction is decrease or delay in the development of HLA alloimmunization and the platelet-refractory state. Limited data also suggest that leukocyte reduction may show benefits by avoidance of immunosuppression in a transfusion recipient.11 This immunomodulatory effect is felt to be associated with the transfusion of allogeneic white blood cells. This clinical phenomenon has been referred to in the transfusion medicine literature as transfusion-associated immunomodulation (TRIM). The mechanism of this entity has yet to be defined and there is conflicting data in the literature as to its significance in clinical settings.1,2 It has been suggested that there is a decreased risk of development of post-operative infections with the peri-operative use of WBC-reduced blood products,13,14 but these data are also conflicting.2 Another potential benefit of leukocyte reduction is the reduction of the theoretical risk of transfusion-transmitted Creutzfeldt-Jacob disease (CJD) and new variant CJD.15 Situations in which leukocyte reduction is not considered appropriate include the prevention of transfusion-associated graft-versus-host disease. In this situation, irradiation of the blood product is the preferred method of preventing this serious complication.16

Conclusion

It seems clear that certain patient populations benefit from the use of leukoreduced blood products and that there are other populations in which a potential benefit exists; however, the data are not clear in these groups. Despite the conflicting data in the literature, there is mounting eagerness to implement universal leukoreduction of cellular blood products in the United States. The Blood Products Advisory Committee (BPAC) of the FDA voted “yes” by 13-0 in 1998 in answer to the question, “Is the benefit-to-risk ratio associated with leukoreduction sufficiently great to require universal reduction?” For now, the debate continues and additional data are being collected in hopes of shedding more light on this controversial subject.