LEUKOCYTE REDUCTION OF BLOOD COMPONENTS

Leukocytes (WBC) are present in varying concentrations in all cellular blood components, including modified whole blood, red blood cells, platelets prepared from units of whole blood, and platelets collected by apheresis. The average unit of red blood cells contains 2.0-5.0 x 10^6 leukocytes, a platelet concentrate from a unit of whole blood contains 0.5-2.5 x 10^8 leukocytes, and some apheresis platelet collections using older technology may contain up to 5.0 x 10^9 leukocytes. As much as a 3 to 4 log reduction of contaminating WBC can now be achieved in both red cell and platelet products using either leukocyte filters or, in the case of single donor platelets, apheresis devices designed to reduce the number of WBC collected, resulting in fewer than 10^6 WBC/product. The FDA permits blood products to be labeled "leukocytes reduced" if they contain less than 5.0 x 10^6 WBC. Depending on the method, leukocyte reduction may be carried out at the Blood Center shortly after or during collection (pre-storage), after storage but before issue from the Blood Center, or at the bedside (post-storage). Although bedside filtration has been shown to be effective, it has drawbacks: for example, as blood warms during transfusion, filtration becomes less efficient. In addition, this process can only be quality-controlled on products at the Blood Center.

Clinical Indications for the Use of Leukocyte-Reduced Blood Components

Established Indications

- Preventing non-hemolytic febrile transfusion reactions
- Preventing CMV transmission by cellular blood components
- Preventing anaphylactic (hypersensitivity) transfusion reactions
- Preventing transfusion-associated graft vs. host disease
- Preventing transfusion-related acute lung injury due to passive administration of anti-leukocyte antibody
- Preventing CMV transmission by cellular blood components
- Preventing cancer mortality in immuno-compromised patients
- Preventing HLA alloimmunization to platelets in patients receiving induction chemotherapy

Leukocyte Reduction is not Indicated for

- Reducing HLA alloimmunization to platelets in patients receiving induction chemotherapy
- Reducing CMV transmission by cellular blood components
- Reducing recurrent febrile non-hemolytic transfusion reactions to cellular blood components
- Reducing CMV transmission by cellular blood components
- Reducing HLA alloimmunization to platelets in patients receiving induction chemotherapy
- Preventing alloimmunization and the refractory state to platelets
- Preventing HLA alloimmunization in organ or bone marrow transplant candidates

Preventing CMV transmission by cellular blood components. CMV is an important cause of morbidity and mortality in immuno-compromised patients. Since CMV is a lymphotropic virus, leukocyte reduction has received significant attention as a method to reduce the risk of primary CMV infection in certain groups of patients. In clinical trials, leukoreduction prevents transfusion-transmitted CMV infection in low birth weight infants. In bone marrow transplant recipients, it is as effective as CMV-seronegative blood components in preventing CMV transmission.

Preventing or delaying alloimmunization to leukocyte antigens in selected patients who are chronic transfusion candidates. Platelet survival is frequently diminished in patients who require repeated transfusions. This is most commonly due to antibodies directed against HLA Class I antigens expressed both on white cells and platelets. There is evidence that it is the leukocytes in platelet concentrates,
rather than the platelets, which induce the formation of HLA antibodies. Rates of platelet alloimmunization can be reduced if the white cell content of red cells or platelets is less than 5.0 x 10^9/unit. Leukodepletion of this order can be achieved with most of the third generation filters, and also with newer apheresis platelet collection procedures.

Recent data from the TRAP study (Trial to Reduce Alloimmunization to Platelets) have shown that the incidence of HLA antibody formation can be reduced by about 50 percent in patients with AML receiving high-dose induction chemotherapy; i.e., from 45 to 18 percent (p < 0.001). However, the incidence of alloimmune platelet refractoriness was very low, and the influence of antibodies on platelet responses could not be determined.

**Indications Under Review**

Preventing alloimmunization and the refractory state to platelets. It is not clear whether leukocyte-reduction would also be effective in preventing platelet alloimmunization in chronically-transfused patient groups who are not concurrently receiving immunosuppressive chemotherapy. The TRAP study patients were receiving induction chemotherapy and, thus, the applicability of leukocyte-reduction techniques to decrease alloimmunization rates in non-immunosuppressed patients has not been demonstrated.

Avoiding transfusion related immunosuppressive effects. Animal studies as well as infection rates and cancer recurrence in transfused patients suggest an immunosuppressive effect of transfusion. This appears to be mediated by residual white blood cells in blood components and may be abolished by their removal. Several studies, however, have failed to find an independent effect of transfusion. A difficulty with the investigations is that both the number of transfusions given and the risk of cancer recurrence are highly correlated with the extent of the primary tumor. Whether or not postoperative wound infections or tumor recurrence might be reduced through the use of leukoreduced blood components is being studied (cf Ref. 6).

Preventing viral reactivation. Preliminary evidence also suggests that exposure to allogeneic donor leukocytes may reactivate latent viruses. For example, the incidence of CMV infection after transfusion in CMV positive recipients was the same whether blood products were from CMV seropositive or seronegative donors. This suggests that transfusion may reactivate latent CMV infection or that seronegative donors harbor low levels of CMV that is activated following transfusion. In vitro, HIV-infected lymphocytes display viral activation only when cultured with allogeneic leukocytes but not with erythrocytes, platelets or plasma, raising the possibility of HIV activation by transfusion.

**Conditions for Which Leukoreduction is Not Indicated**

Although leukodepleted components for transfusion contain low numbers of white cells, leukodepletion cannot be relied on to prevent graft versus host disease (GVHD). It is essential that recipients at risk of GVHD (e.g. bone marrow transplant recipients, immuno-compromised patients or recipients of transfusions from family members) receive products irradiated prior to transfusion.

Leukodepletion also is ineffective in preventing transfusion related acute lung injury (TRALI). In patients experiencing this rare complication of transfusion, acute respiratory distress syndrome is attributable to a reaction between leukoagglutinating or HLA specific antibodies in the donor's plasma and the patient's leukocytes, resulting in complement mediated leukocyte aggregation and pulmonary leukostasis.

Leukocyte reduction does not prevent antibody mediated transfusion reactions such as hemolytic or hypersensitivity reactions not involving donor leukocytes.

**References**
