Modifications to Blood Components

When to Use them and What is the Evidence?

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KEYWORDS

• Red blood cells • Platelets • Transfusion medicine • Blood banking
• Transfusion reactions

KEY POINTS

- Blood components can be modified before issue to meet specific patient needs.
- Component modifications include leukoreduction, irradiation, volume reduction, splitting, and washing. With the exception of leukoreduction, which is nearly universally available in the United States and Canada, the other component modifications are time intensive.
- Transfusion medicine physicians can assist providers in selecting appropriate blood component modifications to meet patient needs.

TOPIC OVERVIEW INTRODUCTION

This article summarizes the benefits, drawbacks, and clinical considerations that should be factored into a decision to pursue specific blood component modifications.

LEUKOREDUCTION

Leukoreduction is the process of reducing the number of white blood cells (WBCs) in red blood cells (RBCs) and whole blood–derived or apheresis platelets (PLTs). In the United States and Canada, regulatory standards mandate that a leukoreduced blood component must contain fewer than 5×10^6 residual leukocytes ($<1 \times 10^6$ in Europe). Most leukoreduction in North America occurs during the blood component manufacturing process, either during apheresis collection or by using a specially designed filter that removes WBCs postcollection via adhesion.[1] These methods are commonly (and interchangeably) referred to as prestorage leukoreduction.

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Alternatively, it is also possible to perform leukoreduction as the blood component is being infused into a patient (ie, poststorage leukoreduction or bedside leukoreduction), although this practice is uncommon.

Leukoreduction has been shown to decrease alloimmunization to human leukocyte antigens (HLAs), which may reduce the risk of refractoriness to PLT transfusion. The Trial to Reduce Alloimmunization to Platelets (TRAP) study showed that poststorage leukoreduction of PLTs reduced the rate of development of lymphocytotoxic antibodies as well as the incidence of PLT refractoriness in patients being treated for acute myeloid leukemia.[2] Specifically, it was estimated that 45% of patients receiving nonleukoreduced PLTs developed lymphocytotoxic antibodies, compared with 18% ($P<.001$) of patients receiving leukoreduced, pooled PLT units and 17% ($P<.001$) of patients receiving leukoreduced, apheresis PLT units. Furthermore, the TRAP study investigators estimated that 16% of patients transfused with nonleukoreduced PLTs developed PLT refractoriness, compared with 7% ($P = .03$) of patients receiving leukoreduced, pooled PLT units and 8% ($P = .06$) of patients transfused with leukoreduced, apheresis PLT units. There was no significant difference in the rate of PLT refractoriness when patients with a history of pregnancy were removed from the study groups, showing that patient-specific factors (in addition to product modifications) influence alloimmunization and refractoriness.[3] Consistent with the results of the TRAP trial, prestorage leukoreduction of PLTs was shown to reduce the incidence of PLT alloimmunization and PLT refractoriness, without altering the incidence of hemorrhage, among patients undergoing bone marrow transplantation in Canada.[4]

Leukoreduction is also generally thought to be equivalent to the use of cytomegalovirus (CMV) seronegative blood components in terms of prevention of transfusion-transmitted CMV infection (TT-CMV). In a prospective, randomized study of CMV-negative patients undergoing bone marrow transplant, the use of leukoreduced blood components, compared with blood components collected from CMV-seronegative donors, was not associated with a statistically significant increase in CMV infection or CMV disease from day 21 until day 100 posttransplant.[5] Although this study did report a statistically significant increase in CMV disease in early (before day 21) transplant recipients receiving leukoreduced transfusions (2.4% vs 0%, $P = .03$), another retrospective study found that there was no difference in the incidence of CMV viremia among bone marrow transplant patients receiving leukoreduced versus CMV-negative transfusions.[6] Therefore, leukoreduced blood is often referred to as CMV safe and blood donors in the United States are not required to be tested for CMV in order to donate.[7] However, for select populations at high risk for TT-CMV, hematologists may request leukoreduced blood components collected from CMV-seronegative donors.[8,9]

In addition, leukoreduction is also associated with a reduction in febrile nonhemolytic transfusion reactions (FNHTRs). These transfusion reactions are thought to be mediated, at least in part, by cytokines released from WBCs during storage. One retrospective study showed that the incidence of FNHTRs was reduced from 0.33% to 0.19% after instituting universal leukoreduction of RBCs ($P<.001$) and from 0.45% to 0.11% after instituting universal leukoreduction of PLTs ($P<.001$).[10] A similar retrospective study of RBC leukoreduction also showed a statistically significant reduction in FNHTRs from 0.37% before leukoreduction to 0.19% afterward ($P = .0008$).[11]

Prestorage leukoreduction of RBCs and PLTs is universal in Canada and is the predominant practice in the United States. Blood components labeled with ISBT (International Society of Blood Transfusion) 128–compliant labels have “Leukocytes Reduced” printed in the lower left corner of the label if the component has been prestorage leukoreduced.[12] Blood components that have undergone prestorage