



Transfusion-Related Acute Lung Injury (TRALI)

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Transfusion-related acute lung injury (TRALI) is acute lung injury (ALI) that is temporally related to the transfusion of plasma-containing blood products and typically manifests with acute respiratory distress, hypoxemia, pulmonary edema, voluminous frothy airway secretions with elevated protein content, and fever. TRALI is a leading cause of transfusion-associated morbidity and mortality, with an estimated incidence of 0.02% to 0.05% per transfused blood product.¹

An international consensus conference in 2004 established clinical criteria for TRALI: acute onset, hypoxemia, bilateral infiltrates on frontal chest radiograph, absence of left atrial hypertension, no preexisting ALI prior to transfusion, onset of symptoms during or within six hours of transfusion, and the absence of a temporal relationship to an alternative risk factor for ALI. If an alternative risk factor for ALI exists, the reaction is designated “possible TRALI.”²

Although the pathogenesis of TRALI is not definitively known, three possible underlying mechanisms have been identified. Antibody mediated TRALI is caused by an antigen-antibody reaction. In 60%-80% of cases, donor antibodies react with the recipient’s leukocytes; a minority of cases may involve recipient antibodies and donor leukocytes. In both cases, antibodies are thought to bind to and activate leukocytes, which then aggregate in pulmonary capillaries. The cumulative effect of the offending antibodies is increased pulmonary vascular permeability and edema. The causative antibodies in TRALI may be directed against class I or II human leukocyte antigens (HLA) or human neutrophil antigens (HNA).¹

A second mechanism, non-antibody mediated TRALI, accounts for the 15% of TRALI cases where neither donor nor recipient antibodies are identified. This mechanism suggests that TRALI is caused by lipid products from cellular breakdown, which accumulate in stored blood products and prime and activate neutrophils. This theory is not readily applicable to acellular blood products and may work in conjunction with the “two-hit” hypothesis, described below.¹

The two-hit hypothesis suggests that two separate events are necessary to cause TRALI. The first hit can include recent surgery, hypoxia, infection, trauma, malignancy, massive transfusion, cardiopulmonary disease, or bypass. These underlying conditions are thought to activate the vascular endothelium and ultimately result in pulmonary neutrophil priming. The second hit is the transfusion of blood products containing lipids, antibodies, or cytokines that stimulate previously primed neutrophils. The result is endothelial cell damage and noncardiogenic pulmonary edema.¹

The diagnosis of TRALI is primarily clinical and radiographic and the majority of patients recover within days with only supportive care. If volume overload is excluded and TRALI is suspected,

evaluation of the donor serum can confirm the presence of anti-HLA or anti-HNA antibodies. Anti-HLA antibodies are a response to an immunologic challenge, and increased parity is known to be associated with increased antibody prevalence. Since the majority of donors associated with a TRALI reaction are multiparous females, many blood centers have moved toward using all-male plasma products and apheresis platelets. Research has yet to demonstrate a definitive reduction in the incidence of TRALI with the exclusion of multiparous donors. Donors involved in TRALI reactions, regardless of sex or antibody status, may be deferred from future donations.¹

References and Suggested Reading

1. Jawa RS, Anillo S, Kulaylat MN. Transfusion-related acute lung injury. *J Intensive Care Med.* 2008; 23(2):109-121.
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4. Goldman M, Webert KE, Arnold DM, et al. Proceedings of a consensus conference: toward an understanding of TRALI. *Transfus Med Rev.* 2005;19(1):2-31.