TRALI Mitigation Strategy for High Plasma Volume Components

Purpose

To provide a description of the measures being taken by the Indiana Blood Center (IBC) to mitigate the risk of TRALI.

This policy was first drafted and approved in March 2009 to be written documentation of IBC’s policy and was made available to requesting hospital customers and/or regulatory agencies (i.e., AABB). It was formalized into IBC’s document control process (as Policy IBC5300) in January 2011.

Rationale

Transfusion-associated acute lung injury (TRALI) is a serious non-infectious hazard of transfusion with significant risk associated with all blood components, but especially with high plasma volume components (plasma for transfusion, apheresis platelets). TRALI incidence is commonly estimated in the literature to be 1/5000 recipients, but there is general consensus it is probably under-reported. More recent studies suggest incidence may be closer to 1/1000 recipients, although reported rates are highly influenced by the surveillance methods and by patient characteristics that may predispose to TRALI under certain circumstances.

The pathogenesis of TRALI is controversial, and multiple pathophysiologic mechanisms have been proposed. One such mechanism centers on antibody-mediated activation of neutrophils in the pulmonary endothelium, with such antibodies being predominantly of donor origin. Rare cases of recipient antibody-mediated TRALI, and even TRALI mediated by antigen-antibody interaction between transfused products have been reported. In a large number of reported cases, there is an association with the transfusion of components from donors alloimmunized against human leukocyte (HLA) and/or human neutrophil (HNA) antigens. Multiparous female donors are most commonly alloimmunized against HLA antigens, and the probability of alloimmunization increases with parity. HNA antibodies are naturally occurring in men and women. It is important to note, however, that the diagnosis of TRALI remains solely a clinical diagnosis, and absence of serologic findings does not rule out TRALI occurring by other mechanisms. Likewise, serologic findings do not definitively secure a TRALI diagnosis, but are rather considered a diagnostic adjunct. There is some bias in the literature toward reporting TRALI cases associated with positive serology, so the relative proportion of TRALI cases associated with alloimmunized donors versus TRALI occurring by other mechanisms is difficult to assess. In addition, since HLA antibodies occur commonly, the coincidental occurrence of positive serology findings in some cases of TRALI-like reactions should be considered.

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Rationale (cont.)

As many as 80% of well-characterized cases reported in the literature describe donors with antibodies against these antigens. A causal association is, however, difficult to impute in most cases due to a failure to demonstrate recipient antigen expression corresponding to donor antibody, and the fact that HLA antibodies are infused in blood products much more commonly than TRALI is recognized or reported. It is clear that certain HNA antibodies are more closely correlated with clinical reactions (e.g. HNA 3a), and suggest that HLA class II antibodies may be more frequently associated with TRALI than the more commonly recognized class I. Yet studies show even transfusion of a high plasma component from a donor known to be alloimmunized against HNA 3a is insufficient alone to cause TRALI. It is clear that a donor antibody-recipient antigen pairing is neither necessary nor sufficient to cause TRALI. As yet uncharacterized recipient factors in addition to expression of cognate antigen appear to play a key role in determining whether a TRALI reaction occurs.

There are both EIA and flow cytometric assays for HLA antibodies that are adaptable to the production environment of the blood center. There are no available assays for HNA antibodies suitable for screening. These assays were generally developed for high sensitivity for transplantation applications. There is no data set that establishes appropriate cutoffs in the distinct application of donor screening for TRALI mitigation, and positive predictive values for these assays remain uncharacterized. Positive predictive value, however, is expected to be low, as numerous lookback studies have demonstrated many women known to be alloimmunized have provided large numbers of components to recipients who did not experience TRALI. Again, this lack of response has been noted even when the cognate antigen has been demonstrable in the recipient.

The AABB published an Association Bulletin (#06-07 “Transfusion-Related Acute Lung Injury”) that recommended collection facilities have TRALI mitigation strategies for plasma and apheresis platelets. IBC has implemented their TRALI mitigation strategy in five phases. The original implementation began in 2006. Plasma production (from donors of whole blood) for transfusion was converted from fresh frozen plasma to plasma frozen within 24 hours of phlebotomy with restriction of the latter’s production source to male donors. Plasma from female donors was generally diverted to fractionation for derivative manufacture. However, occasionally the supply of male-derived plasma was insufficient to meet demand. Therefore, when necessary, the male plasma supply was supplemented with AB plasma derived from female donors.

For apheresis platelets, IBC focused recruitment efforts on male donors capable of donating double or triple products in a single donation event, and discontinued active recruitment of female platelet donors. This resulted in a shift of the donor pool toward males and an even greater shift in apheresis platelet components distributed toward male-derived. Therefore, the probability of a recipient receiving a platelet component from a female donor, let alone one positive for HLA antibodies was reduced.

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Rationale (cont.)

IBC’s second TRALI mitigation initiative was implemented February 1, 2012 to allow the male plasma supply to be supplemented with plasma derived from female donors who have been tested and found negative for HLA antibodies. HLA testing was limited to female donors of apheresis platelets and/or plasma at IBC’s Main Branch facility only. Female plasma donors who were found to have HLA antibodies are deferred (strong antibodies) or converted to whole blood donors (weakly positive antibodies).

IBC’s third TRALI mitigation initiative was implemented on September 4, 2012. This initiative expanded the HLA testing of female plasma and/or plateletpheresis donors to all IBC collection facilities.

IBC’s fourth TRALI mitigation initiative was initiated December 1, 2013. This initiative expanded the HLA testing of female donors to include female type AB whole blood donors.

<table>
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<tr>
<th>Blood Group</th>
<th>% Distributed Plasma (that meets mitigation criteria)</th>
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<td>AB Plasma from WB</td>
<td>&gt;99.9% (derived from males or HLA tested females)</td>
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<tr>
<td>O, A, B Plasma from WB</td>
<td>&gt;99.5% (derived from males)</td>
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<tr>
<td>All blood groups Pheresisplasma</td>
<td>&gt;99.9% (derived from males or HLA tested females)</td>
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The AABB published an Association Bulletin (#14-02 “TRALI Risk Mitigation for Plasma and Whole Blood for Allogeneic Transfusion”) and implemented Standard 5.4.1.2 (29th edition of BBTS Standards) that requires collection facilities to provide plasma and whole blood for allogeneic transfusion that is collected from males or females who have either never been pregnant or who have been tested/found to be negative for HLA antibodies after their most recent pregnancy.

IBC’s fifth TRALI mitigation initiative was initiated August 5, 2014. This initiative identifies female donors’ pregnancy history. Those females who have never been pregnant are not tested for HLA antibodies. Female donors of plasma and/or plateletpheresis as well as type AB whole blood who have been pregnant subsequent to their last HLA antibody screen are retested for HLA antibodies.

The IBC TRALI mitigation policy has developed over time in response to TRALI study data. THE AABB 2006 recommendation was made chiefly on the strength of the UK SHOT data, which suggested that strategies providing solely male donor plasma for transfusion resulted in significant decrease in TRALI incidence. However, release of 2008 data suggests that reporting issues artificially inflated the apparent magnitude of the intervention’s ability to mitigate TRALI.
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Policies

1. IBC has enhanced surveillance and investigation for TRALI by providing education at the Medical and Technical Advisory Committee meetings, hospital client transfusion committee meetings, and didactic lectures for customer hospital personnel. IBC physicians take a more active consultative role in evaluation of the clinical scenario of reported possible reactions.

2. Donors implicated in a TRALI reaction will be indefinitely deferred for all blood components. An implicated donor is defined as a donor associated with a transfusion reaction clinically consistent with TRALI, in whom an HLA antibody with a specificity matching recipient antigen has been identified, or in whom an HNA antibody has been identified.

3. Investigation of all alleged TRALI events is standardized with a reporting form, and the IBC Medical Staff will make a determination of implicated donor status after completion of each investigation.

4. The presence of HLA antibodies in a donor, absent a cognate antigen in the recipient, is not, in and of itself cause for donor deferral. When such donors are identified in the course of a TRALI investigation, where possible they will be redirected to whole blood donation as appropriate.

5. Continuous review of data regarding antibody screening and evidence reflecting a causative role of HLA antibodies in TRALI reactions is the responsibility of IBC Medical Staff.

6. Female plateletpheresis donors who have not been tested for HLA antibodies are not actively recruited. In addition, deliberate recruitment efforts are underway to increase both the absolute proportion of male/tested female apheresis donors, as well as the proportion of apheresis components derived from males/tested females. This approach has been underway since 11/07, and includes continuation of the “purple top program” for the identification and recruitment of donors capable of donating doubly and triply split plateletpheresis components. This will minimize the impact of TRALI mitigation on the adequacy of the platelet supply.

7. Production of prestorage pooled platelets derived from whole blood from male donors is currently not planned as a further strategy, but will remain under consideration.

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References


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References


**DOCUMENT REVIEW AND REFERENCES PAGE**

**NUMBER:** IBC5300  
**TITLE:** TRALI Mitigation Strategy for High Plasma Volume Components  
**VERSION DATE:** 08/05/2014  
**SUPERSEDES:**  
**AUTHOR:** Julie Cruz, MD Revised: Beth Hughes

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**References**  
- AABB Association Bulletin #12-02 “TRALI Risk Mitigation Update”  
- AABB Association Bulletin #14-02 “TRALI Risk Mitigation for Plasma and Whole Blood for Allogeneic Transfusion”  
- AABB BBTS Standards, 29th edition; April 1, 2014.

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**SCOPE**

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**APPROVAL**

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**ANNUAL REVIEW**

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**CHANGE CONTROL FORM**

**Date**: 6/18/2014  |  **Department**: QA  |  **Completed By**: BH  

**Type**:  
- [x] New/revised/retired controlled document(s) (attach NRDocument Worksheet(s) for Process documents)  
- [ ] One-time exception to procedure  
- [ ] Temporary deviation from procedure  
- [ ] Other:  

**Description of Change**:  
(If a controlled document change, list all documents being changed unless NRD Worksheet attached.)  

**Revised Policy**:  
IBC5300 TRALI Mitigation Strategy for High Volume Plasma Components  

**Reason for Change**:  
(List Deviation #, Audit name; or Pending CCF # (if applicable) that initiated this change.)  

- Added 5th mitigation strategy: Testing all targeted female donors for HLA antibodies after each pregnancy. To ensure compliance with 29th edition of AABB BBTS Standard 5.4.1.2.  

**Proposed Date of Implementation**: 8/5/2014  

- [ ] Impact Assessment performed and no impacts identified that require completing a CAF (no CAF needed/attached)  
- [x] Impacts identified, but no Risk Assessment required (page 2 of CAF not needed/attached)  

**Are other documents impacted (besides any identified above)?**  
- [x] Yes  
- [ ] No  
- [ ] NA  

**Document(s) affected**:  
See CAF for TRALI Mitigation Project  
Documents to be revised by: 8/5/2014  

**PIC required/valuable? (MD011-05)**  
- [x] NA  
- [ ] Yes  

**PIC Number (generated by T21)**  

**Communication**:  
- [ ] NA  
- [x] Self-Read  
- [ ] Training Plan (see attached)  
- [ ] Other – describe: Specific instruction for staff provided in departmental procedures (see CAF)  

**Request Urgent Notification of Approval?**  
- [ ] Yes (Phone ext:  |  or email: )  

**Change approved by**:  
- [ ] Department Head/designee  |  ↓ 6/19/14  
- [ ] VP/Executive Officer  |  ↓ 7/22/14  

**QA Processing**:  
- [ ] Validation/Qualification performed as needed?  
- [ ] Communication/Training Plan adequate?  
- [ ] ISDH/FDA notification required?  
- [ ] Customer/Vendor notification required?  
- [ ] If CLIA regulated / Lab Director signature?  

**CCF Status**:  
- [ ] Done  
- [ ] Pending  

**QA Comments**:  

**Change approved by**:  
- [ ] QA Management  |  ↓ 7/22/14  
- [ ] IBC Physician  |  ↓ 7/21/14  

If not approved, why:  

**Date Returned to Dept:**  

**Copies to**:  
- [ ] Originating Department  
- [x] QA  
- [ ] Training  
- [ ] Other  

**Distributed By**:  

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**FORM MD003-06.1e  |  Revised 05/20/2014**