



# OHIO ASSOCIATION OF BLOOD BANKS



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## *From The OABB President*

Dear OABB members,

In the last newsletter, I mentioned that the OABB Annual Meeting not only provided us with an educational opportunity but gave many of us the chance to make new friends and visit with "old" friends from around the state. Shortly after the Annual Meeting I received an article about workplace friendships, "Challenging Long-Held Assumptions about Workplace Friendships" published June 04, 2008 by [Knowledge@W.P.Carey](mailto:Knowledge@W.P.Carey).

The author of the article refers to a quote by Tom Rath, "Throughout my professional life, I have attended countless development programs that aimed to make me more productive...I had it all wrong. The potential was hiding within each relationship in my life." Tom Rath has published a book, "Vital Friends: The People You Can't Afford to Live Without." Rath leads Gallup's Workplace and Leadership Consulting worldwide. He tells us that not only is it nice to have friends at work—but that workplace friends are essential to an employee's happiness and being engaged and productive in one's job.

Rath had worked on a special homelessness project in 1991 and had interviewed many "street people." One story from Rath's book is about a homeless man (Roger) who had been a successful worker with a good family. Roger's work colleague and best friend was fired and eventually lost touch with Roger. Roger's world fell apart; he began to drink, lost his job and

got divorced—ending up homeless and on the streets. What Rath found in working on this project was that so many of the downward turns for the people he interviewed seemed to involve a key relationship. And in the same manner a key relationship with a caring person led some of the homeless back to a more normal life.

It has been shown those who take the time and effort to build and nurture friendships are happier and healthier. Rath's research found that people who had workplace friendships were happier overall AND there was also a direct correlation between friendship in the workplace and overall job satisfaction, performance and productivity!

Rath gives some ideas of the type of friend you can be or the types of persons you might want to build a friendship with: someone who motivates, someone who accepts you as you are, someone who has the same interests as you, someone who will defend you no matter what, someone who will expand your horizons, someone you can laugh with, someone who will make you a better person, someone who gives good advice and points you in the right direction.

Friends play a vital role in our lives. Rath invites us to assess our current workplace friendships, determine what friends we need to cultivate at work and ask ourselves what kind of friend we can be to others.

Mary Schumacher  
OABB President

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## TRALI – Proposed Mechanisms and Current Suggested Prevention Techniques

Transfusion-related acute lung injury (TRALI) was first reported in the 1950's. In the early 1970's antibodies to HLA and non-HLA antigens were thought to cause TRALI reactions. By 1985, the "term" TRALI was first proposed and recognized as a distinct clinical condition referring to pulmonary edema related to blood transfusions.<sup>1</sup> Since 2001, TRALI is the leading cause of transfusion-associated mortality reported to the FDA. Even with aggressive transfusion support and increased recognition, up to 10% of patients with TRALI die. The exact cause of TRALI remains unclear.<sup>2</sup>

TRALI typically occurs within 6 hours of transfusion. Symptoms include acute respiratory distress characterized by a rapid onset of abnormal shallow breathing, shortness of breath or difficulty breathing, chest crackles, decreased breath sounds, and decreased oxygen levels. The bilateral pulmonary edema on chest x-rays is described as "fluffy infiltrates".<sup>3</sup> The majority of cases occur during transfusion or within an hour or two of completion. Treatment consists of respiratory support including administration of oxygen and mechanical ventilation. Steroids and diuretics do not provide any benefit to a patient suffering from TRALI. Most patients recover within 72 hours.<sup>1</sup>

TRALI is under-diagnosed and under-reported because of a lack of awareness. It is actually more common than expected and may be caused by transfusion of a single unit of any blood product. It should be considered as a diagnosis when the signs and symptoms occur within 6 hours of transfusion.<sup>4</sup> It is not necessary to identify the presence of donor antibodies against HLA or granulocyte antigens in the transfused product or specific antibodies directed against the donor leukocytes in the host for transfusion reaction to be considered TRALI.<sup>1</sup>

The two proposed theories receiving the most attention as the causes of TRALI are the antibody hypothesis and the two-event hypothesis. The common pathway in all of the proposed theories of TRALI is the increased permeability of the pulmonary capillaries, which results in movement of the plasma into the alveolar space causing pulmonary edema.<sup>5</sup>

### The antibody hypothesis for TRALI

The antibody hypothesis proposes that TRALI is due to infusion of donor antibodies towards the recipient's leukocyte antigens, or the infusion of donor's leukocytes into a recipient who has antibodies directed against the donor's leukocytes.<sup>1</sup> In the majority of TRALI cases, antibodies specific for HLA class I or granulocyte antigens were reported.<sup>1</sup> The antigen-antibody interactions activate complement which causes the activation and sequestering of neutrophils in the lungs. This results in endothelial cell damage and capillary leakage which leads to TRALI.<sup>4</sup>

In 1970, Ward was the first to propose that the transfusion of donor antibodies was the cause of TRALI. This was confirmed by Popovsky and Moore in 1985. In the cases examined, antibodies to granulocytes were documented in 89%, and antibodies to HLA antigens in 72%. Most of the granulocyte antibodies did not show specificity, but 59% of the HLA class I antibodies did.<sup>1</sup>

Early studies of donors involved in TRALI reactions did not include testing for antibodies against HLA class II antigens. However, as better techniques became available, class II HLA antibodies were identified in the plasma from both donors and recipients.<sup>5</sup> Kopko *et al.* proposed, and was confirmed by others, that TRALI was due to the infusion of HLA class II antibodies that were specific to class II antigens in the recipient. They demonstrated that HLA class II antibodies involved in TRALI could actually activate the circulating monocytes that expressed these antigens. This caused the synthesis of a large amount of tumor necrosis factor- $\alpha$ , inter-leukin-1 $\beta$ , and tissue factor. These cytokines could activate neutrophils, leading to damage of the endothelial cell that result in leakage of the capillaries and TRALI.<sup>1</sup>

Most of the literature focuses on the antibody hypothesis. However, antibodies have not been detected in all cases of TRALI.

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### **The two-event hypothesis for TRALI**

Silliman *et al.* proposed an alternative theory of TRALI that does not require the presence of leukocyte antibodies. It is the two-event hypothesis that is also called the biologically active mediator model. The first event is the pre-existing condition of the patient that causes activation of the endothelial cells of the lungs. These conditions include sepsis, cardiac bypass surgery, hematological malignancies, burns and trauma. This results in the sequestering of neutrophils in the lungs. The second event is the transfusion of cellular blood components containing various cytokines and/or lipid based, biologically active substances known as biological response modifiers, or BRMs. The BRMs stimulate the neutrophils to release proteases that cause damage to the endothelial cells and results in pulmonary edema.<sup>2</sup> These cytokines and lipids accumulate during storage of platelets and red blood cells. Platelet-derived CD40 ligand may also be a cofactor in the cause of TRALI. CD40 ligand accumulates during storage of packed red blood cells, whole blood and platelet concentrates (especially plateletpheresis products). CD40 ligand primes the neutrophils and this causes the endothelial damage to the lungs.

Because antibodies can play a role in either of the proposed hypotheses, it appears as though the two are not mutually exclusive. However, there are areas where the two theories differ and yield different approaches to the prevention of TRALI. In the antibody-based theory, components with the highest amount of antibodies, such as plasma products, would be more likely to cause TRALI. Therefore, products containing the most plasma, such as FFP, would be the main target for prevention. In the two-event hypothesis, it is the cellular products that are usually considered to contain the BRMs.

### **Prevention**

The two categories for the prevention of TRALI are donor management strategies and blood component processing strategies to reduce the risk.<sup>2</sup>

Donor management strategies include the disqualification of donors implicated in TRALI reactions until leukocyte antibody testing can be completed. If these donors have antibodies to high incidence antigens, such as HNA-3a, HLA-A2, and HLA-B12, they should be disqualified from plasma or platelet donations. If the results of these tests are negative, then they should be returned to the donor pool.<sup>1</sup>

Problems with trying to test for HLA and granulocyte antigens are that these tests are labor intensive and difficult to perform on a large scale that would be needed by blood collection facilities. The additional expense would be prohibitive, and the cost-effectiveness of testing only high-risk donors has not been studied.<sup>2</sup>

Several other donor management strategies have been proposed. They include:

- ◆ Preventing donation by individuals who are at risk for developing, or known to have, leukocyte antibodies. This includes multiparous females and transfused donors.
- ◆ Banning donation by donors who were previously implicated in any confirmed TRALI case, or in two or more suspected cases of TRALI, or in a fatal case of TRALI.

Even though the number of multiparous women with circulating antileukocyte antibodies may approach 26% and up to 5% of all plasma-containing blood products may contain antileukocyte antibodies, most recipients of these products do not develop TRALI.<sup>2</sup> This observation suggests that prohibiting multiparous females from donating could have serious consequences on the availability of blood.<sup>2</sup> Although these recent data have demonstrated that female plasma is not disproportionately implicated in TRALI reactions; the United Kingdom has still decided to adopt a policy to disqualify all multiparous females from plasma donations.<sup>1</sup>

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Blood component processing strategies are an alternative method of preventing TRALI. They involve the production of components that are less likely to cause acute lung injury and include the following suggestions:

- ◆ Products from donors with known leukocyte antibodies or from donors likely to have these antibodies (for example-multiparous females) are diverted to plasma fractionation or are plasma reduced and only the red cells are used.
- ◆ Blood components are leukoreduced to remove any leukocytes that might react with the recipient's antibodies. This also decreases the development of biologic response mediators (BRMs) in the cellular component.
- ◆ Fresher cellular components are used in order to reduce the accumulation of cytokines and other BRMs.
- ◆ Cellular components are washed.

Recently a new study suggested that packed red cells with added preservative solutions could also be an acceptable use of blood from donors implicated in TRALI.

In the United Kingdom, the Serious Hazard of Transfusion (SHOT) study estimated that the risk of TRALI from platelets and FFP was five to seven times higher than that seen with red cells and cryoprecipitate. However, the amount of antibody needed to cause a reaction, and the amount of antibody removal needed to prevent it, is currently unknown because red cells and other plasma-poor components are known to cause TRALI.

Because packed red cells develop biologically active lipids and cytokines during storage, some suggest that patients with pre-existing illnesses should receive fresher blood. This could minimize the accumulation of and exposure to BRMs that act as a "second hit" in TRALI. Washing red cells has also been considered as another way of reducing BRMs. However, this changes the shelf life and decreases the quantity of cells.

In 2004 the FDA Blood Product Advisory Committee (BPAC) recommended delaying the implementation of donor management strategies for TRALI. They felt more information was needed to link female donors with TRALI and more research should be done to establish the role of leukocyte antibodies. They emphasized that it is the blood collection centers' responsibility to identify and defer donors implicated in TRALI.

However, in 2005 AABB provided written guidelines for management of donors involved in more than one TRALI reaction. They stressed that the goal of donor management strategies should be to prevent TRALI while limiting the disqualification of donors.

Finally, a recent international conference entitled "Toward an Understanding of TRALI" agreed that the only method to prevent TRALI is to decrease the number of blood transfusions. They felt there was not enough data or evidence to consider other strategies and that more research is needed.<sup>2</sup>

Marlene Friedman, MT(ASCP)SBB

#### References:

1. Silliman CC, McLaughlin NJD. Transfusion-related acute lung injury. *Blood Reviews* 2006; 20:139-159
2. Mair DC, Hirschler N, Eastlund, T. Blood donor and component management strategies to prevent transfusion-related acute lung injury (TRALI). *Critical Care Medicine* 2006; 34:S137-S143
3. Sachs UJH, Hattar K, Weissmann, Bohle RM, Weiss T, Sibelius U, Bux J. Antibody-induced neutrophils activation as a trigger for transfusion-related acute lung injury in an ex vivo rat lung model. *Blood* 2006; 107:1217-1219
4. Barrett NA, Kam PCA. Transfusion-related acute lung injury: a literature review. *Anaesthesia* 2006; 61:777-785
5. Curtis BR, McFarland, JG. Mechanisms of transfusion-related acute lung injury (TRALI): anti-leukocyte antibodies. *Critical Care Medicine* 2006; 34:S118-S123

## OABB Continuing Education Activity

### Neonatal Exchange Transfusion (0.5 CH)

After reading this Continuing Education article, the participant shall be able to:

- ◆ State the incidence of mortality from neonatal exchange
- ◆ Identify the volume of a single and double volume transfusion
- ◆ State why FFP is used rather than 24-hour plasma in exchange transfusion
- ◆ Define fresh red blood cells for exchange transfusion
- ◆ Calculate the volume of plasma to reconstitute red blood cells for exchange transfusion.

#### The history of neonatal exchange transfusion

Exchange transfusion (ET) was introduced in the late 1940s to decrease infant mortality from hemolytic disease of the newborn (HDN) and to prevent kernicterus in surviving newborns. ET was subsequently applied to remove antibody-coated red blood cells (for example, due to Rhesus incompatibility and ABO incompatibility), to remove products of hemolysis in various immune or non-immune hemolytic anemias (for example, G6PD deficiency and other red cell enzyme deficiencies), and to remove bacterial toxins in severe sepsis cases. It quickly became one of the most commonly performed neonatal procedures. However, over the last 30 years ET has declined, primarily due to development of Rh-immunoglobulin, improvements in diagnostic ultrasound and postnatal phototherapy, and greater use of intrauterine transfusions. Some institutions may have recently observed a change in the use of ET after the publication describing the management of hyperbilirubinemia in newborn infants (*Pediatrics*. 2004;114:297 –316).

#### The exchange transfusion process

The ET process involves incremental blood removal from the affected infant and replacement with fresh donor blood. If a newborn's blood volume is estimated as 80 - 90 mL/kg, a single volume exchange transfusion (SVET) involves replacement of 80-90 mL/kg, and a double volume exchange transfusion (DVET) is 160 - 180

mL/kg. Ideally, blood should be infused through a peripheral vein at a rate equal of blood being withdrawn from the umbilical venous catheter (UVC). If only a single catheter is used, the "push-pull" technique, no more than 5 mL/kg of body weight should be withdrawn at any one time. Mortality directly attributable to ET, reported to be at least 1%, is often due to unexplained cardiac arrest, cardiac arrhythmia or air embolism. Severe necrotizing enterocolitis and bowel perforation requiring surgery occur in about 1%. Other major complications include severe bleeding or coagulopathy requiring intervention, and severe bradycardia or apnea during or following exchange. There are several reports of portal vein thrombosis and portal hypertension.

#### Products used for exchange transfusion

The products utilized by the Transfusion Service may vary, however, there are general principles that most institutions follow. Relatively fresh (less than 7 days old) units of red blood cells (RBCs) are used. They may be screened negative for hemoglobin S. Irradiation and CMV status of the products vary depending on the institution's protocol, the history of in-utero transfusions, birth weight of the infant, and risk of congenital immunodeficiency. ET uses a red blood cell product reconstituted with plasma to a 45-55% hematocrit (hct). The RBCs must be type compatible with the infant and serologically compatible with the mother's serum, for example antigen-negative when the mother has a red cell antibody. RBCs may be either CPD or Adsol units, but if Adsol is used, the Adsol solution should be removed by centrifugation of the unit and removing the supernatant. For reconstitution of the unit, fresh frozen plasma is more desirable than saline since ET is technically considered a "massive transfusion". Due to the immaturity of the infant's liver, FFP rather than 24 hour plasma should be used. FFP is selected to be either group specific or group AB when the infant's blood type is unknown. A platelet transfusion will most likely follow the exchange, due to the dilutional effects.

#### Reconstitution of RBCs with plasma for exchange transfusion

Below is an example of the formula used to prepare 'reconstituted whole blood' (RWB) from a unit of RBCs and plasma for ET.

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If using CPD unit(s), adjust the red cell hct using the following calculation:

- Use 70% as the average hct of a CPD unit.
- Weigh the unit before any further manipulation to determine the initial weight (Wt).
- Assume 1 gm weight is equal to 1 mL plasma/rbcs.
- Calculate the amount of plasma to add to the RBCs by using the following formula:

(Initial Wt of CPD unit x hct) divided by desired hct = Final Wt of RWB

Final Wt - Initial Wt = Wt in grams (mL) of plasma to add to CPD unit

**EXAMPLE:**

CPD unit initial weight = 250gm, CPD hct = 0.70 (70%), Desired hct = 0.55 (55%)

$$\frac{(250\text{gm}) \times (0.70)}{0.55} = X \text{ (final weight of RWB)}$$

$$318 \text{ gm} = X$$

318 (final weight) – 250 (initial weight) = 68 gm (mL) of FFP to add to the CPD unit

Suggested reading:

American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 weeks or more of gestation. *Pediatrics*. 2004; 114: 297 –316.

A Decline in the Frequency of Neonatal Exchange Transfusions and Its Effect on Exchange-Related Morbidity and Mortality. *Pediatrics*. 2007;120: 27-32.

Prepared by Kathy Nicol, MD

Answers will be given in the next issue of the OABB Newsletter

Questions

- The percentage of infant mortality due to exchange transfusion is
  - 1%
  - 5%
  - 7%
  - 10%
- A one volume exchange would be:
  - 50-60mL/kg
  - 60-70 mL/kg
  - 70-80 mL/kg
  - 80-90 mL/kg
- FFP rather than 24 hour plasma is used for exchange transfusion because
  - it is more readily available
  - it has a longer shelf life
  - the newborn has an immature liver
  - it has a higher concentration of proteins
- Fresh blood for exchange transfusion is considered as units less than \_\_\_ days old.
  - 3
  - 5
  - 7
  - 10
- A unit of CPD blood weighs 300 gm. You need to prepare a RWB with a hematocrit of 55%. How much plasma must you add to the unit of RBCs?
  - 40 mL
  - 60 mL
  - 80 mL
  - 100 mL



**Answers to *Serologic Approach to Identifying an Antibody to a High-Incidence Antigen*  
(0.5 CH)**

**Questions**

1. What is the first step to determine if reactivity observed in a panel of cells is multiple antibodies or an antibody to a high-incidence antigen?
  - a. Adsorb the antibody onto phenotypically-matched cells
  - b. Enzyme treat test cells and run with the patient's plasma
  - c. **Test a phenotypically similar cell with the patient's plasma**
  - d. Test an auto control to determine if the antibody is allo
  
2. If a patient has Hispanic ethnicity and has an antibody to a high-incidence antigen, which test cells would be tested first?
  - a. Co<sup>a</sup> and Js<sup>b</sup>
  - b. **Di<sup>b</sup> and Ge2**
  - c. hrB and Kp<sup>d</sup>
  - c. Yt<sup>a</sup> and Ge2
  
3. When a patient has an antibody identified to a specific high-incidence antigen and determining whether antigen-negative blood is needed, the next step is to:
  - a. Chemically treat the cells for crossmatch and issue crossmatch compatible
  - b. Give antigen-negative blood if the antibody reacts by the indirect antiglobulin test
  - c. Inform the physician and allow them to sign for incompatible blood
  - d. **Research textbooks on whether the antibody is responsible for rapid red cell clearance.**
  
4. When high-incidence antigen-negative blood is needed the next day and is unavailable at the local blood center, the best option for the blood center IRL is to call:
  - a. AABB
  - b. **American Rare Donor Registry**
  - c. Family members
  - d. Other blood centers



**News from the Proficiency Coordinator:**

This month's proficiency sample (07-2008) was intended as an ABO discrepancy. The sample was an A subgroup with an anti-A<sub>1</sub> reactive at room temperature. It was interesting to note that very few participants detected the antibody, most likely due to Gel ABO typing. Thanks to everyone who participated and look for the next sample in October!

Suzanne M. Davisson, BS SBB(ASCP)<sup>CM</sup>

**Teleconferences Sponsored By  
American Red Cross Central Ohio Region  
995 East Broad Street  
Columbus, Ohio  
Call (614) 253-2740, ext. 2215 to Attend**

Date	Teleconference Title
Feb 27 2:00 – 3:30 PM	Mechanisms of Drug-Induced Hemolytic Anemia
Mar 19 2:00 – 3:30 PM	Serological to Molecular Testing: Points to Consider for Successful Conversion
May 16 2:00 – 3:30 PM	(ASCP) Eliminating ABO Incompatible Transfusions—No More Excuses!
Jun 4 2:00 – 3:30 PM	(ASCP) The US Biovigilance System: Surveillance, Safety, and Savings
Jun 26 2:00 – 3:30 PM	(ASCP) Transfusion-Transmitted Cytomegalovirus (CMV) Infection
Jul 30 2:00 – 3:30 PM	Coagulation Case Studies for Blood Bankers
Sep 10 2:00 – 3:30 PM	Managing Massive Transfusion: Clinical and Blood Bank Perspectives
Oct 22 2:00 – 3:30 PM	Intravenous Immunoglobulin (IVIG): Intended Use and Administration
Nov 19 2:00 – 3:30 PM	Platelet Refractoriness: Causes and Treatments
Dec 10 2:00 – 3:30 PM	Differential Diagnosis of Suspected Pulmonary Transfusion Reactions



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Submissions**

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