Death by Transfusion: Sinister Sabotage at the Hands of TACO and TRALI

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WHILE THE TITLE MAY seem a bit dramatic, consider that the FDA cites Transfusion Associated Cardiac Overload (TACO) and Transfusion Related Acute Lung Injury (TRALI) as the most common causes of transfusion-related death. TRALI has historically been the leading cause of death, but in the most recent data available, TACO is now the leader based on mandated reporting of transfusion-associated deaths.[(1)]

The FDA's Center for Biologics Evaluation and Research is responsible for tracking transfusion-related complications (including deaths) and provides a fascinating look at the epidemiology of these events. Consider the FDA's table below, revealing how TRALI and TACO have clearly been the major players in mortality related to blood transfusion, but how TACO, in the most recent years, has overtaken TRALI as the primary cause of death.

Complication	FY14 Cases	FY15 Cases	FY16 Cases	FY17 Cases	FY18 Cases	Total Cases
Anaphylaxis	2 (7%)	2 (5%)	5 (12%)	3 (8%)	2 (6%)	**14 (8%)**
Contamination	1 (3%)	5 (14%)	5 (12%)	7 (19%)	7 (23%)	**25 (14%)**
HTR* (ABO)	4 (13%)	2 (5%)	4 (9%)	1 (3%)	2 (6%)	**13 (7%)**
HTR (non-ABO)	4 (13%)	4 (11%)	1 (2%)	6 (16%)	4 (13%)	**19 (11%)**
Hypotensive Reaction	1 (3%)	1 (3%)	1 (2%)	0	0	**3 (2%)**
TACO	5 (17%)	11 (30%)	19 (44%)	11 (30%)	12 (39%)	**58 (32%)**
TRALI†	13 (43%)	12 (32%)	8 (19%)	9 (24%)	4 (13%)	**46 (26%)**

*HTR: Hemolytic Transfusion Reaction
†FY2014–FY2018 numbers combine both TRALI and Possible TRALI cases.

It's also interesting that TRALI represented 26% of transfusion-associated fatalities reported to the FDA over the last five fiscal years and 13% in FY2018. Looking back even further reveals a rise in TRALI cases over the years 2004–2007, followed by an abrupt decline in 2008, with a downward trend up to the present time.

Blood donation and resultant transfusions are generally safe, and the number of donation-associated fatalities reported to the FDA remains small compared to the total number of donations. FDA data (which always lags a few years in terms of its publication) reveals that allogeneic blood donations provided over 12 million whole blood and apheresis red blood cell components, about 2.5 million platelet components, and nearly 4 million plasma components for distribution over the five years up to 2018. Over the same period, there were 52 reported donation-associated fatalities. Despite mandated reporting, there are always the risks of underreporting due to compliance failures as well as incorrect attribution to the causes of death.

CRNAs manage perioperative anemia and blood loss across the perioperative continuum. Fresh frozen plasma, cryoprecipitate, and platelets are vital for coagulopathic patients, and transfusion is a common intervention in the operating room and intensive care unit. Depending on the institution, the anesthesia provider may be directly involved in transfusion practices to a greater extent than any other hospital provider.

So, what exactly are TACO and TRALI? Let's begin with actual case reports of each (the cases are real, with minor edits to alter potential identifiers).

A fatal case of TACO

A 73-year-old female was admitted to the ICU with an upper gastrointestinal bleed, marked anemia, and alcoholic cirrhosis. An invasive procedure under general anesthesia was scheduled as the first case of the following day. She was transfused with 6 units of plasma overnight to correct an INR of 1.8, likely prolonged by her chronic use of naproxen. Immediately before the procedure, she was given an additional 2 units of FFP at 250 mL/hr. Anesthetic induction and maintenance proceeded without complication, and endoscopy revealed two small ulcerations with active arterial bleeding, which were repaired. One additional unit of FFP was administered along with a slow infusion of packed red blood cells. At the end of the procedure, the patient was extubated and appeared to do fine during her stay in the PACU. Approximately 2 hours later, on the ward, the nursing staff observed and reported that her hemoglobin saturation had declined to 91% even though she was receiving oxygen by nasal cannula.

A second unit of packed red cells was administered fairly rapidly through a fluid warmer. Within a few minutes of its completion, she was in severe respiratory distress, with a SpO_2 value of 82–85%. Jugular vein distension and an S-3 gallop were observed, along with tachycardia and hypertension. Her chest radiograph demonstrated congestive heart failure, and diffuse crackles were heard with auscultation of her lungs. She was lightly sedated, emergently intubated, and placed on positive pressure ventilation. IV administration of 80 mg of furosemide briefly improved the clinical picture with arterial blood gas results that were still concerning but moving in the right direction. The sudden appearance of blood-stained froth in the endotracheal tube was noted, and she was suctioned, given an additional 60 mg of furosemide, and continued on 100% O_2 and PEEP. While plans were underway to move her to the medical ICU, she coded, and resuscitation was unsuccessful.

A fatal case of TRALI

A 33-year-old man was ejected from his motorcycle without cranial protection. He was urgently transferred to the ED by ambulance with multiple orthopedic fractures, including a basilar skull fracture. His admission Glasgow Coma Score was 3 to 4. A CT scan revealed a diffuse intraparenchymal cerebral injury, a small subarachnoid hemorrhage, and splenic laceration. Additional medical findings included a positive toxicology screen for ethanol, a 2-decade use of cigarettes, well-controlled hypertension with a calcium channel blocker, a hemoglobin of 6.1 g/dL, and radiographic evidence of pulmonary contusions. He was preoperatively transfused with 2 units of packed RBCs and had urgent surgical stabilization of his femur fracture under general anesthesia with ketamine, propofol, and rocuronium. Laparoscopic exploration of the abdomen was also performed. He was then transferred directly to the surgical ICU for supportive care. During his initial postoperative course, the patient became lucid, followed commands, weaned from mechanical ventilation, and extubated. However, ongoing laboratory findings included a decreasing hemoglobin level to a nadir of 7.1 g/dL that was treated with an additional transfusion of 2 units of packed RBCs. He underwent a repeat abdominal CT for a reassessment of his splenic injury.

Approximately 5 hours following administration of the second unit, he developed dyspnea, tachypnea, fever, hypotension, frothy sputum, diffuse crackles, decreased bilateral breath sounds, and marked confusion. He was hypoxemic and acidotic with pulmonary infiltrates on two chest radiographs. Signs of congestive heart failure, such as increased jugular venous pressure and a third heart sound were absent. His respiratory distress necessitated reintubation and positive pressure ventilation. ARDS ensued, rapidly progressing to renal dysfunction. Over the next 24-hours, he suffered multiple organ dysfunction syndrome and died on day 12 of his admission.

TACO: its pathophysiology and clinical course unveiled

TACO is defined as a cluster of signs and symptoms of acute pulmonary edema associated with left atrial hypertension or volume overload occurring within 6 hours of blood transfusion. The classic signs of TACO include

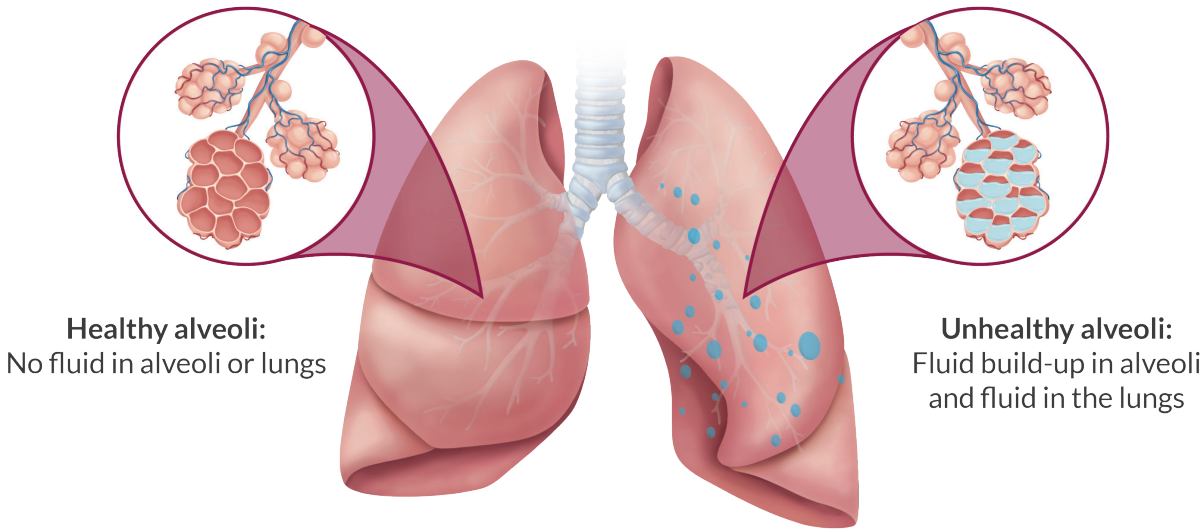
- acute onset of respiratory distress.
- signs of congestive heart failure:
  - S3 heart sound.
  - jugular vein distension.
  - cough/wheezing.
  - dyspnea.
  - frothy sputum tinged with blood.
- hypertension.
- hypoxemia.
- chest radiographic evidence:
  - bilateral opacities.
  - Kerley B lines (distinctive, 1–2 cm long in the lung periphery).

Due to the difficulty of differentiating TACO from TRALI, the Centers for Disease Control and Prevention (CDC) published guidelines for diagnosing TACO. The guidelines included a definitive diagnosis of pulmonary edema occurring within 6 hours of a blood transfusion that can't be attributed to other known causes of acute lung injury.[2]

It is tempting to attribute all TACO cases to the blood product administration that is too fast or too high a volume. In the largest case series found in our review of TACO, there is general agreement that females and those over 60 years of age appear the most vulnerable. It seems implicit that a positive fluid balance is a factor as well as underlying renal dysfunction and pre-transfusion cardiac impairment.

Pathophysiology insights

First, let's consider what is going on in a healthy person. In the pulmonary capillary beds, hydrostatic pressure is counterbalanced by colloid osmotic pressure. Any excessive transudate is mopped up from the alveoli by the pulmonary lymphatic system. We can think of this as a kind of "janitorial service" that typically works quite well, but as in all biological systems, there is a "tipping point' where any process can fail when pushed beyond its limits. In the case of the alveoli, there is a predictable relationship between rising left atrial pressure and the rate of pulmonary edema formation.



Consider this: not all patients who experience heart failure have an excessive blood volume. It is often some "event" that "tips" them into failure sufficient enough to cause pulmonary edema. Examples include an exacerbation of a comorbidity or even a small cardiac ischemic event.

In the patient with compensated (or undiagnosed) cardiac dysfunction or chronic renal failure experiencing TACO, even a moderate increase in circulating volume and a concomitant increase in pulmonary capillary pressure may exceed that tipping point. Conversely, patients with normal renal and cardiac function require considerably larger transfusion amounts to tip them into pulmonary edema.

In essence, TACO is a form of circulatory system volume overload that can occur in any individual who receives a transfusion of red blood cells, platelets, fresh frozen plasma, or cryoprecipitate. Indeed, there is a strong correlation between the volume transfused and the subsequent risk of TACO.

An even more exacting set of risk factors for TACO is provided by a study that took a deep dive using published reports and databases involving patients who experienced TACO or "probably" experienced TACO.[3] The authors composed a list of their findings of patient-specific and practice-specific conditions that may set the stage for TACO.

Patient factors

- Age > 60 years
- Female sex
- White race
- Higher APACHE-II score†
- Shock state
- Heart failure
- Pre-existing cardiac dysfunction
- Renal dysfunction/failure
- Chronic pulmonary disease

†APACHE-II is an acute physiology score that includes a variety of measured values. For more information and an example calculation, see: https://www.mdcalc.com/apache-ii-score

Practice factors

- Volume of blood products infused
- Administration rate (faster = worse)
- Positive fluid balance
- Insufficient use of diuretics

Biomarkers

- B-type natriuretic protein (BNP)
- N-terminal pro-BNP (NT pro-BNP)

The two biomarkers noted above are indirect markers of TACO. B-type natriuretic peptide (BNP) is one member of a family of hormones called natriuretic peptides. Each member of the family is produced by a different part of the circulatory system. For example, there are also "A," "C," and "D" types of natriuetic peptides. ANP is produced by the muscle cells in the heart's atria, CNP is produced mainly in the vasculature, and DNP is found in the plasma but likely originates in the heart.

BNP is produced in the heart's ventricles, and while all have roles in regulating the circulation and participate in both homeostasis and pathology, BNP seems to have a significant role in TACO. BNP (like ANP) acts on blood vessels, causing them to dilate, and it causes the kidneys to excrete salt and water. In addition, the natriuretic peptides influence adrenaline, angiotensin, and aldosterone function.

The net effect of these peptides is to reduce myocardial workload by promoting vasodilation and urine excretion. Natriuretic peptides are part of the body's natural defense mechanisms designed to protect the heart from harm, and they surge into action when the heart is under siege.

N-terminal (NT)-prohormone BNP (NT-proBNP) is a non-active prohormone (like a pro-drug conceptually) that is released from the same molecule that produces BNP. Both BNP and NT-proBNP are released in response to changes in intracardiac pressures. These markers can be related to heart failure, and they provide value in their ability to help rule-in or rule-out TACO.

The use of these biomarkers in clinching a diagnosis of TACO is far from certain. Studies have found overall higher BNP and NT-proBNP levels in TACO patients in comparison to those in patients with TRALI. However, levels of these biological markers alone were found to have variable ability in differentiating these groups of patients from one another.[4]

The hunt for more exacting biomarkers continues. These go by the usual odd nomenclature we see in biomedical studies like "cystatin C", "GDF-15", "ST-2" etc., but all have the common theme of being in the general family of cytokines that fluctuate based on cardiac and renal function, thus remaining as indirect or associated markers of TACO.[5]

Demystifying clinical decision making: deciding if it's really TACO

It's increasingly clear that distinguishing TACO from some other disorder (like TRALI) isn't always clear-cut. What is fairly well accepted is that symptoms of TACO generally occur within 6 hours of blood product transfusion, and common signs like tachycardia, tachypnea, and often, hypertension, can be subtle in their development.[6] Identifying the onset of TACO can be particularly difficult in the patient recovering from anesthesia and surgery due to the lingering effects of drugs, the routine use of supplemental oxygen, and the presence of pain.

Hypoxemia is another frequent accompanying sign of TACO. When there isn't a clear explanation for it (e.g., hypo-ventilation, active bleeding, significant V/Q mismatch), we often order a chest radiograph. Doing so helps identify the root of the problem, such as pulmonary edema or a cardiac origin such as cardiomegaly. A study of 100 documented TACO patients revealed that 80 patients did not have a post-transfusion chest radiograph ordered when, in retrospect, such a diagnostic aid would have proven useful.[7] It is always interesting to read reports like this one, when in retrospect, it seems so obvious what should have happened. We can learn a lot from the mistakes of others.

Hypoxemia can be obscured by the use of oxygen during surgery, in the PACU, or on the ward. Arterial blood gas analysis is important in managing the clinical course of the pathophysiology. Still, specific blood gas thresholds haven't been defined for TACO, and arterial blood gas analysis is not routinely employed due to its invasive nature. As a singular measure, blood isn't likely to serve as a differentiating test between TACO and TRALI. Instead, arterial blood analysis yields insight into the degree of pulmonary dysfunction, whether from TACO of TRALI, and can help gauge a therapeutic intervention.

EKG and echocardiography analysis have merit as diagnostic tools, with the latter perhaps having greater utility. Echocardiography, in particular, may provide useful noninvasive information regarding the pathogenesis of post-transfusion pulmonary edema. Observation of any respiratory variation of the inferior vena cava flow in a spontaneously breathing patient is useful for assessing volume status. Likewise, systolic or diastolic dysfunction or elevations in right or left-sided filling pressures may lend credence to a cardiogenic mechanism underlying the patient's symptoms.[8]

The clinical management and prevention of TACO

The following summarizes the major preventative and therapeutic strategies relevant to TACO.

Prevention interventions for TACO

- Transfusion decisions exclusively on evidence-based practice
- Single-unit transfusion
- Identification of high-risk patients
- Maintaining a high index of suspicion
- Slower rates of infusion, especially in those deemed high risk
- Prophylactic diuretic therapy

Treatment interventions for TACO

- Early suspicion and recognition are vital
- Cessation of transfusion
- Elevation of the head of the bed
- Oxygen supplementation
- Diuretic therapy
- Vasodilators
- Intubation and positive pressure ventilation as needed
- Consideration given to noninvasive ventilation

The literature describing management principles is uniform in employing interventions similar to those used for patients experiencing cardiogenic pulmonary edema. As noted above, these include oxygen therapy, gravity-assistance with the head of the bed elevation, diuretics, nitrates, and discontinuation of blood product transfusion.[9] The benefits of nitrates are based on their ability to reduce preload, particularly in the patient with significant hypertension.

Essentially, the management of TACO is based on supportive measures, as specific therapies are lacking. Potential therapies await a deeper understanding of the underlying pathophysiology that will likely be based, at least in part, on the creation of appropriate animal models. Additionally, work continues in the domain of identifying pre-transfusion risks for TACO that might lead to improved screening for subclinical cardiac insufficiency, which may predispose to its occurrence. Lastly, having a very high index of suspicion and slowing the rate and volume of transfusions will continue to be targets of clinical research.

TRALI: its pathophysiology and clinical course unveiled

From the preceding sections, it is clear that while TACO and TRALI are potentially catastrophic life-threatening responses to transfusion, there are significant challenges in diagnosing and differentiating these conditions. That both TACO and TRALI present with hypoxemia, respiratory embarrassment, and chest radiographs characterized by pulmonary edema within five or six hours of transfusion suggests differentiation is a part of the problem.

So, what do we know about TRALI that might make its differentiation somewhat clearer? First, TRALI is strictly noncardiogenic in nature and isn't characterized by blood pressure elevations. Second, there is an absence of a timely relationship to other factors causing lung injuries, such as pneumonia, sepsis, aspiration, and multiple trauma.

Based on several authoritative sources, the following table describe diagnostic and clinical presentation differences between TRALI and TACO that we may use in our decision making.[10, 11]

Clinical Concern	Diagnostic Clue	TRALI	TACO
Hypoxemia	SpO_2 <90% PaO_2 /FiO_2 <300 on room air	yes	yes
Rapid onset	Onset within 6 hours of blood transfusion	yes	yes
Pulmonary edema	Characteristic infiltrates Bilaterally on chest x-ray	yes	yes
Alternative cause?	Pneumonia, trauma, aspiration, sepsis	no	no
Hydrostatic lung P	Pulmonary artery occlusion P >18 mmHg	no	yes
Cardiac involvement	BNP elevated NT pro-BNP elevated	no	yes
Diuretic Response	Rapid Improvement	no	yes
Non-lab clues	Hypertension Ejection fraction < 45	no	yes
Cardiac ischemia	New EKG changes	no	no

Interestingly, we know more about TRALI-related mechanisms and clinical concerns than we do about TACO. The injury resulting from TRALI causes non-cardiogenic permeability edema that is protein-rich in its composition.

The use of animal models and *in vitro* cultures of human lung endothelial cells has greatly advanced our understanding of TRALI but has, at the very same time, created tremendous controversy. We must be careful about how to apply animal models to humans, in part because of differences in antibodies formed and species-dependent cellular signalers and modifiers. And while cell cultures can provide a useful bench research tool, they aren't quite the same as the variations encountered in the real deal (the living, breathing TRALI victim).

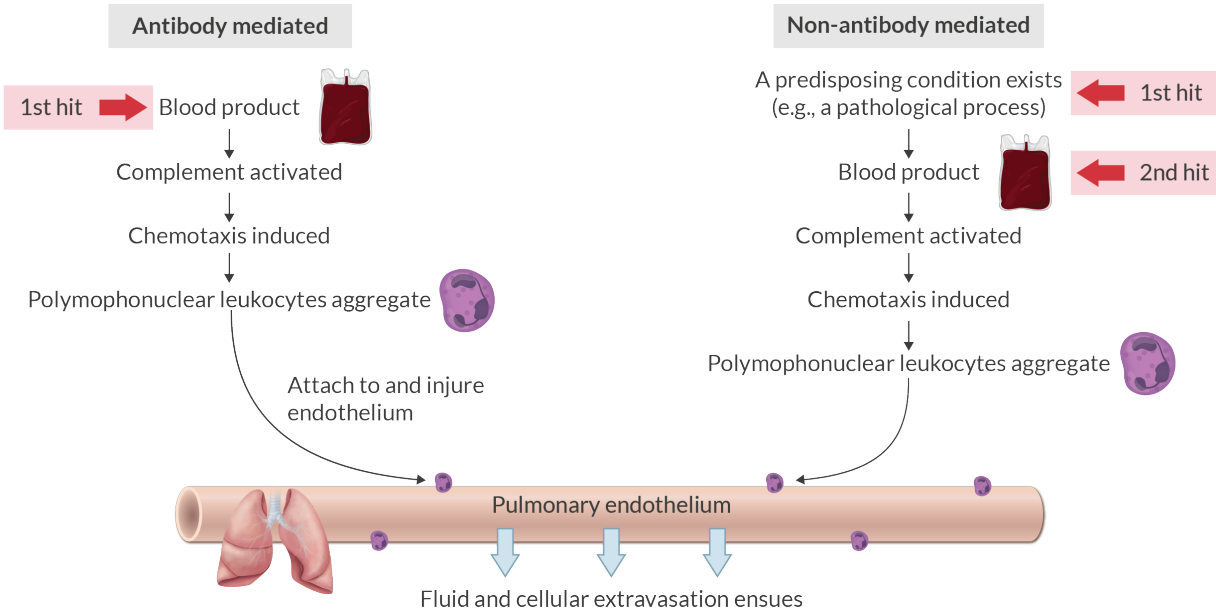
TRALI is an incredibly complex pathological process due to the many moving parts and players. For example, it's been known for a long time that polymorphonuclear leukocytes (PMNs) are found at autopsy in the TRALI-affected lung.[12] Like the PMNs, platelets appear to be involved in TRALI's pathogenesis, but all authorities don't embrace this thinking.[13] Other contributors to TRALI's pathophysiologic mechanisms depend on the type of antibodies (of which there are many, including anti-HLA class I, anti-HLA class II, or anti- HNA antibodies‡ and response modifiers, such as lipids from stored platelets or red blood cells.

‡HLA is Human Leukocyte Antigen; HNA is Human Neutrophil Antigen

The one- and two-hit model of TRALI

Similar to TACO, the risk and severity of TRALI are likely increased by the presence of certain conditions. With this line of thought, there is a so-called "first-hit" that involves a comorbid clinical condition or some physiological perturbation. This is followed by the "second-hit", which is the administration of what amounts to a provocative blood product in the susceptible recipient.

The prevailing view is that both "hits" are essential for TRALI to manifest. The first "hit" factor for TRALI is thought to be one (or more in combination) of several factors, including chronic alcohol abuse, shock, major surgery, tobacco use, higher peak airway pressures during mechanical ventilation, positive intravascular fluid balance, low interleukin-10 level, and systemic inflammation.[14]



Hypotheses abound regarding the mechanism of TRALI. A single inflammatory injury to the endothelium may occur. Additionally a 2-hit model may also account for the injured lung endothelium. Besides complement, white cells, oxidative stress, even certain cell lipids can create a second hit.

C-reactive protein (CRP) increases acutely during inflammatory processes such as TRALI, so it can be used clinically as a biomarker of inflammation. It's also used in murine models, where it parallels PMN accumulation in the lungs.[15] In 80% of TRALI cases, the "second hit" involves antibodies that are present in the transfused product.[16] The remaining 20% of cases have other suggested "hit" substances that include lipid mediators, extracellular vesicles, and older blood cells.[16]

How antibodies promote the development of TRALI

TRALI's insidious origins that involve antibody mediation are quite complex, and only a brief description of identified pathways are mentioned below:[13, 18]

- Certain antibodies can bind to the pulmonary endothelium and attract, sequester, and activate PMNs.
- Antibodies associated with platelets may directly induce a toxic injury to the pulmonary endothelium enabling TRALI.
- Antibodies may bind to certain receptors on monocytes / macrophages, attracting these cells to the lungs and inducing them to produce reactive oxygen species that damage the pulmonary endothelium.
- There is also evidence in animal models that GI flora contribute to the development of antibody-mediated lung injury.

These are just some of the proposed antibody-mediated phenomena thought to contribute to TRALI. Further description of the complexities of these paths is beyond the scope of our discussion. The bottom line is that all blood components have been implicated in TRALI, but those containing large amounts of plasma are mainly responsible. Most TRALI cases have white blood cell antibodies that can be identified in the implicated blood donor, and most implicated donors have been women with a history of pregnancy. White blood cells (e.g., B lymphocytes) produce antibodies, which can only be removed through expensive blood processing methods. It's well known that pregnancy results in alloimmunization against paternal white blood cell antigens in almost 25% of women, with three main antibody specificities: human leukocyte antigen (HLA) class I, HLA class II, and human neutrophil antigens (HNAs).[19]

How non-antibody mechanisms promote the development of TRALI

Mechanisms that may be operative in TRALI include, but are likely not limited to, lipids from stored red blood and plasma and lipids from stored platelets. Lipids from stored red blood cells activate the pulmonary endothelium setting the stage for lung injury. Additionally, several biological response modifiers, such as lyso-PC (from stored platelets) may cause pulmonary and systemic coagulopathy.[20] Even microparticles from platelets and red blood cells can activate PMNs and mediate TRALI in human pulmonary cell cultures and animal models.[21]

It is important to emphasize that the overwhelming support of these mechanisms comes from animal models, and still, many questions remain. TRALI is a complex pathophysiological syndrome with a great deal of fog that needs to clear.

The clinical management and prevention of TRALI

As is the case with TACO, currently, only supportive therapies are available in treating TRALI; these include oxygen, positive pressure ventilation (intubation or noninvasive ventilation), and use of fluid and pressor interventions to manage hemodynamic changes.

Preventing TRALI has an important upstream intervention that involves donor deferral based on several factors.[22] These include donor antibody screening as well as donor deferral if there is a history of pregnancy or a history of transfusion. There are also advocates of deferring all female donors, where only male plasma donors are used. This approach leads to obvious supply issues.

In a very recent large study of relevance to donor deferral programs, a retrospective multicenter study included analysis of TRALI rates from 2007 through 2017 involving definite or probable TRALI reports from five blood centers serving nine states.[23] One-hundred four TRALI cases were reported from 10,012,707 components distributed. The TRALI rate was well over double for female versus male donated components. Of great interest was that the TRALI rate declined extraordinarily from 2007 to 2017 by over 300%.

As the data was teased out, another interesting observation was a significantly higher TRALI rate associated with female versus male plasma. From 2014 through 2017, following the implementation of donor prevention strategies, a nearly four-fold higher TRALI rate was seen in female-donated plateletpheresis.

The authors concluded that while the TRALI rates have substantially decreased secondary to multiple strategies over the past decade, a residual risk remains, particularly with female-donated plateletpheresis products. They suggested that there may be other mitigation strategies that may offer a further reduction in TRALI. Those mentioned in the study included the use of buffy coat pooled platelets suspended in male donor plasma or platelet additive solution due to the lower amounts of residual plasma. You may recall that the "buffy coat"' is the fractionfraction of an anticoagulated blood sample containing much of the white blood cells and platelets following density gradient centrifugation.

Summary of the CRNA's role in preventing/managing TRALI

Prevention

- Use evidence-based practices & avoid transfusion unless essential.
- Talk to blood bank personnel about donor deferral program.
- Use washed RBCs from which plasma is removed.
- Use washed platelets (note: their function is decreased).

Treatment (more difficult from our vantage as onset is hours)

- Oxygen supplementation
- Mechanical ventilation may be needed
- ICU, close monitoring
- Circulatory support may be needed
- Possible corticosteroids
- Cessation of transfusion

Another center reported on their experience with mitigation strategies noting that TRALI has become a relatively rare event. This work, emerging from a large urban center well known for its aggressive use of plasma in the setting of trauma, hemorrhagic shock, and massive transfusion protocols, reported on a decade of transfusion experience.

They reported seven cases of TRALI in a sample of 714,757 units of blood products transfused. In this particular setting, the acute duration of symptoms averaged about 2 days and patients usually improved with supportive care. Reactions were observed predominantly in plasma products, both type-specific and non-type specific.

The authors concluded that while TRALI still occurs, clinically meaningful cases are rare. Moreover, TRALI rates remain low despite the increasingly aggressive use of plasma and platelets in the trauma setting. The authors noted that blood banks have moved toward male-predominant plasma or female donors who are carefully screened to reduce exposure to implicated human leukocyte antigen (HLA) antibodies.

On the drawing board: advanced TRALI treatment strategies

There are several interventions, either hypothesized or in clinical trials, that target the actual lesion(s) of TRALI. The most promising of these include

- IL-10 therapy.
- downregulation of CRP levels.
- neutralizing/preventing reactive oxygen species.
- blocking instigating receptors such as IL-8.
- targeting complement factors.
- anti-platelet therapy.

As is the case with virtually all therapeutic interventions, the aforementioned treatments carry the potential for serious adverse effects. For instance, IL-10 administration can significantly impair host resistance to infectious pathogens, which might be catastrophic in a surgical patient at risk for infection.

Clinical contemplations

- What, if any, donor mitigation strategies are in place at your institution?
- Can you elaborate on the management of TACO or TRALI in a patient that you or a colleague cared for?
- Do you think that discussions about the risks TACO or TRALI should be part of the preoperative blood consent process? Why?
- Should there be more restrictive guidelines or other modifications to transfusion practice in regards to TRALI or TACO?
- If caring for a patient who is at risk for TACO or TRALI, how (if at all) might that influence your clinical decision making?

Summary

As our understanding of TRALI and TACO improves, it's increasingly clear that both impose significant risks to transfusion recipients. This is the case even if there is a sense that their uncommonness in everyday clinical practice seems to render these complications to a lower status of consideration.

Further research into TRALI's pathophysiological mechanisms will be critical to improve diagnostic approaches and to design best-evidence treatment strategies. Health care personnel, especially those at the sharp end (like the CRNA), should be trained to recognize the signs and symptoms of TACO and TRALI and to respond appropriately. Such approaches may significantly contribute to combating these life-threatening complications of blood transfusion.

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