

Transfusion Reactions

Case 1

An 88 year-old group O+ man with chronic lymphocytic leukemia (CLL) presented to ER with a 2d history of weakness, oliguria, and chills.

He has a history HTN, CAD, and CHF;

His outpatient medications are ASA, furosemide, ramipril, & metoprolol.

In ER, BP is 92/60. He is given 1L NS, antibiotics, and antipyretics.

His diuretic and antihypertensives are held.

CBC shows Hb 79 g/L; one month prior his Hb was 100 g/L.

2 units RBC were ordered, each to be given over 1h. A 21 day old unit is hung.

Pre-transfusion HR 121, BP 100/60, T 37.3 O₂ sat 100% R/A

After 1st unit: HR 140, BP 127/72, T 37.3 O₂ sat 78% R/A;





→97% on 2L/min NP.

The 2nd unit is cancelled.

His JVP is at the angle of the jaw, his chest fields have crackles, and bipedal pitting edema is up to the knees. CXR shows bilateral infiltrates with cardiomegaly, in keeping with pulmonary edema.

- Which of the following might have been his *best defense* against TACO?
 - Fresh (<14 day old) RBC
 - Pre-transfusion furosemide
 - CLL treatment to recanalize obstructed pulmonary lymphatics
 - Slower administration of the unit (over 3-4h instead of 1h)

This patient had tachypneic, hypoxic respiratory distress with features of pulmonary edema (crackles, radiographic CHF) and cardiovascular system changes (increased HR, BP, JVP with pedal edema) within 12h of blood product exposure. He meets diagnostic criteria for TACO by the minimum of 3 domains.

<p>≥ 1 REQUIRED:</p> <p>OCCURRING DURING OR UP TO 12H AFTER TRANSFUSION</p>	 <p>Respiratory Distress</p> <p>eg-</p> <ul style="list-style-type: none"> tachypnea dyspnea cyanosis ↓spO₂ % without other causes bronchospasm/wheezing 	<p>AND/OR</p>	 <p>Pulmonary Edema</p> <p>Clinical Physical Examination</p> <p>L heart failure findings without other specific causes, eg-</p> <ul style="list-style-type: none"> crackles orthopnea cough S3 frothing pink sputum <p>Radiography:</p> <p>CXR and/or other non-invasive cardiac function testing</p> <p>new/worsening changes, eg-</p> <ul style="list-style-type: none"> effusions widened vascular pedicle lobar vessel enlargement peribronchial cuffing Kerley lines alveolar edema with nodular opacities cardiac silhouette enlargement
	<p>AND:</p>  <p>Cardiovascular system changes unexplained by underlying condition</p> <ul style="list-style-type: none"> tachycardia ↑BP, PP (or ↓ if cardiogenic shock) JVP distension/↑ CVP/↑ cardiac silhouette peripheral edema 		<p>Fluid overload</p>  <ul style="list-style-type: none"> + fluid balance or weight gain diuretic or dialytic response

In the context of withheld diuretics, cardiac risk factors, and volume loading, he has significantly desaturated.

A. Fresher blood has not been shown to reduce the risk of TACO (be it across fresh-blood RCTs or in data beyond preclinical animal models)

B. A definitive study to establish the role or effect of furosemide as a premedication has not yet been done beyond pilot form; as this patient was oliguric and hypotensive, the strategy favoured volume restoration rather than reduction (at the expense of further intravascular collapse).

C. We can only speculate that the CLL contributed to his susceptibility to TACO by impairing fluid clearance by pulmonary lymphatic “impaction.” The extent to which lymphatics play a role in mitigating TACO, or the extent to which lymphatics are impaired in lymphomas, is not known.

*D. Though prospective studies on the efficacy of slower vs faster infusion rates in blood transfusion have not been performed, and though TACO can still occur with low volume loads (ie- the typical 1u RBC order), a **slowdown would have been the most feasible, intuitive, and affordable approach from among the choices listed.***

2. Which one of the following is true of TACO?

- A. An RBC unit is more “TACO-genic” than a platelet transfusion
- B. Fever with a suspected TACO argues for another diagnosis
- C. It is the 2nd commonest cause of transfusion-related death
- D. It is the 2nd commonest cause of respiratory transfusion reactions

A. Is true for a variety of reasons.

- *Packed cell volumes (PCV) in cellular components are intravascularly retained (ie- RBC: >65% PCV, vs PLT: <1% PCV), exerting more effect per mL than cell-free, isotonic/iso-oncotic infusions;*
- *indeed, the typical volume in TACO is 250-300cc in adults, and is “RBC-disproportionate” (ie- even when corrected for the number of RBC units issued in relation to other products); and*
- *RBC transfusions may follow fluid loading, wherein hemodilution reduces the Hb (truly ± artefactually), thereby triggering the order for a RBC unit that the circulatory system is even less able to accommodate*

B. is false. In TACO, fever is NOT a rule out criterion (like “alternative explanations” in the HIT 4T score). In fact, a third of TACO presentations co-manifest with fever. As well, pre-transfusion fever increases the odds or apparent susceptibility to TACO. Which mediators are responsible (in which products, and in what amounts)... remain to be determined.

C. was once true but is now false, ie- TRALI historically bore this distinction. With mitigation strategies against TRALI, versus casemix changes (ie- more TACO-susceptible patients in modern times) and awareness/reporting, TACO is the #1 cause of reported transfusion fatalities in the US (FDA), UK (SHOT), and Canada (TTISS).

D. TACO occurs more often than originally appreciated. Though passive systems historically captured TACO at rates of 1 in 1000 or less, more active reporting systems recognize this as a top-tier-frequency risk (at 1-10% per encounter). TACO is more common than TRALI, TAD, and severe (cardiopulmonary-involving) allergic spectrum reactions.

Suggested Reference:

Case 2

You are called to the hematology ward to review an 87 year old woman admitted with febrile neutropenia after myeloma therapy. She is a grand multipara (G8) with hypertension.

She experienced fevers, rigors, and tachycardia following a 7-day-old platelet transfusion.

	Pre-transfusion	Post-transfusion
HR	75	110
BP	104/62	130/80
Temp	37.3°C	39.9 °C
RR	16	30
SpO ₂	98% (room air)	95% (room air)

Labs:

Pre-transfusion: Hb 68, WBC 0.2, platelets <10

Patient blood group A, RHD positive

Platelets transfused: Group O, day 7, single donor apheresis collection

3. Which one of the following is indicated at this time for investigation and management of this patient?
- A. repeat CBC, LDH, creatinine, PT/aPTT, and urinalysis
 - B. review chart (temperature trends, antibiotics, cultures)
 - C. repeat G&S, do DAT, culture patient & residual product
 - D. no investigation needed; already admitted with febrile condition

Choice A is only sensitive to hemolysis (and not its mechanism), with no regard for sepsis.

Choice B is directed only at finding an underlying cause to this disturbance.

Choice C addresses serologic AND microbiologic causes of high-risk fever, meeting our obligations on the 2 sinister transfusion-attributable possibilities (acute hemolysis or bacterial contamination).

Choice D would be under-investigation.

This is a high- risk febrile reaction, marked by both rigors, and a $T_{max} > 39^{\circ}C$ (with $> \Delta 1^{\circ}C$ to achieve that fever [and a $2.6^{\circ}C$ rise in this specific case]).

If she had no symptoms and no vital sign disturbances, with $T_{max} < 39^{\circ}C$, she would have qualified as a "low-risk" fever, thereby freeing her from further tests. (This is due to the low odds of finding something, while sparing costs). Waiving tests also removes reporting disincentives (ie - willingness to report minor fevers may be low if patients are punished with testing and aborted transfusions).

Acute hemolytic transfusion reactions (AHTR) may manifest with fever, chills, rigors, N/V, pain (at infusion site or in flanks), dyspnea \pm hypoxia, hypotension, tachycardia,

visible hemoglobinuria and/or pigment nephropathy/acute tubular necrosis, and disseminated intravascular coagulation.

Note that this case is serologically at-risk for a passive AHTR (with the platelets being minor/plasma-incompatible [group O: bearing anti-A, -B] towards the patient [group A]), with her red cells at risk of hemolytic sensitization.

Transfusion-associated sepsis (TAS)/Bacterial contamination (BaCon) may likewise manifest with fever, chills, rigors, nausea, or vomiting, dyspnea \pm hypoxia, hypotension/septic shock, tachycardia, oliguria, and disseminated intravascular coagulation. This case is microbiologically at-risk as a last-day shelf-life platelet.

She lacks shock or hypoxia, this do not rule out BaCon or AHTR.

The diagnosis of exclusion for a high-risk fever is the underlying disease (eg. incipient/pre-existing febrile neutropenia) or a febrile non-hemolytic transfusion reaction (FNHTR), the latter of which would dominate as the explanation for fevers not due to underlying illness.

The rise in HR and BP may be confounded directly by the fever and rigors, or may reflect an additional, independent cardiovascular insult (such as TACO). Fevers occur in 1/3rd of TACO cases (Parmar, Vox Sanguinis 2016); the reason for this remains unknown.

The dyspnea with the reduced O₂ saturation may be an artefact of rigors, or reflect a respiratory insult (such as a dyspneic febrile non-hemolytic transfusion reaction [FNHTR], and/or a change due to the underlying condition).

Based on the differential diagnosis above, the approach is:

- Hematologic: A “transfusion reaction specimen” is assessed for the colour of the spun plasma, and subjected to a DAT with a repeat G&S [+/- Coomb’s phase post-reaction re-crossmatching if relevant]), while a clerical check of labels is also performed with a review of the typing records. Outside of the Blood Bank, tests for hemolysis can be implemented “in reasonable part” or “all at once”.
 - Evidence of a new, product-attributable antibody (passive anti-A) may include ABO typing discrepancy, or a positive DAT with eluted anti-A. The product may have had a high titer of anti-A.
 - If there is a significant drop in Hb with associated hemolytic changes, ie-
 - reticulocytosis/polychromasia +/- bloodfilm spherocytosis;
 - increased LDH/AST/bilirubin [indirect predominating];
 - diminished haptoglobin;
 - reddened urine +/- hemosiderin / increased creatinine; and
 - consumptive markers [high PT/INR, aPPT, TT; low fibrinogen]), this would suggest AHTR.
- Microbiologic: The implicated product, and the patient (by infusion line, other catheters, and by peripheral blood venous stab) should be cultured. Note should be made of any pre-transfusion cultures for comparison with post-reaction cultures. Suspected BaCon is reported to CBS (+/- Canada Vigilance Program if the blood bank may have contaminated the product by its own modification activities [like washing]). CBS co-verifies the final results of the parallel pre-release culture performed on platelets, and can check for any post-donation

donor reports of illnesses, and launch recall notifications on any co-components (i.e. red blood cells).

- Clinical case review should include: Pre-existing VS trends (fevers, daily Tmax), WBC/ANC trends (onset date for severe neutropenia), pre-existing microbiology, symptoms/signs of a pre-existing focus of infection, antibiotic initiations, and radiologic investigations suggesting a focus. CBS defines hemolysis as the 10g/L drop with at least 2 of the above findings.

Repeat blood group, IAT, and DAT all negative.

Repeat CBC was unchanged.

LDH, bilirubin, and haptoglobin were all within normal limits.

The product and the patient's cultures were all negative.

Review of her chart reveals that she presented with fever 4 days ago and was started on piperacillin/tazobactam. She defervesced over the last 2 days.

4. Which one of the following is recommended to prevent future febrile reactions in this patient?
 - A. plasma volume reduction (PVR) of platelet products
 - B. pre-medication with acetaminophen
 - C. washing of RBC and platelet cellular products
 - D. no interventions recommended

This was a transfusion-associated high-risk fever, probably due to a febrile non-hemolytic transfusion-reaction (FNHTR), with recently remitting/actively treated febrile neutropenia.

FNHTR has traditionally been defined as a rise in temperature of greater than or equal to 1°C that cannot be explained primarily by the patient's condition, accompanied (or instead characterized) by chills, rigors, cold, discomfort, or some combination thereof. Occasionally, symptoms such as headache, nausea, vomiting, and dyspnea have also been described (Cohen, Transfusion 2017), & appear soon (during/right after) product.

The frequency of FNHTR varies according to the type of product administered, its modifications (eg. prior leukoreduction), and the sensitization or exposure history of the recipient.

Platelet components provoke a roughly 2 to 20 -fold higher reaction rate than do red cells (0.06 to 37.5 reactions per 100 transfusions ["1 in 20"], versus 0.04 to 6.8 per 100 units respectively ["1 in 300"]).

FNHTR due to plasma is rare.

Two well-described mechanisms cause FNHTRs:

- *host anti-leukocyte antibodies confronting residual product leukocytes*
 - *This grand multipara has a significant "exposure history" to foreign blood antigens and likely has a broad repertoire of HLA antibodies; and*
- *storage-generated pyrogenic mediators.*

Since 1999, Canada has had a policy to universally prestorage leukoreduce blood, which has reduced the rate of FNHTR by roughly 50%.

Premedication with an antipyretic drug, although standard practice in high-risk populations and in patients with recurrent febrile reactions, has been called into question, with failures to demonstrate effectiveness in several studies. (Marti-Carvajal, Cochrane 2010)

For some in whom recurrent reactions occur, blood bank consultation may determine if there are any special product attributes or modifications to implement.

In most cases, we do NOT recommend any routine modifications of the patient or product to prevent future reactions, due to the nature of their still-low frequency and general tolerability, ESPECIALLY IN A FIRST TIME REACTOR.

- ***D is favoured over B in this first instance.***
- *If reactions recur in this individual, a trial of B (cheap, low-risk) may enable her to complete (rather than abort) her necessary product sittings in the future, saving inventory and time (and better achieving goals of transfusion).*
- *If B fails, and reactions are repeatedly platelet-associated, then A (PVR) is reasonable.*
- *If A fails in platelets, and reactions are recurrent in RBCs and platelets alike, then C is the last resort.*

Antipyretics are best reserved for treatment. In severe rigors, there may be a role for meperidine (Demerol®). Note that other opioids do not have the same effect as Demerol (re: cross-effects on cholinergic, serotonergic, dopaminergic, and adrenergic receptors to blunt shivering; Friedlander & Noble, CJA 1989: 460 [U of T anesthesiologists]). If unavailable, maximum dose oral acetaminophen (500-1000mg) with a warming blanket may help.

Note also that antihistamines (eg. diphenhydramine [Benadryl]) is NOT a treatment for rigors, which are NOT an allergic phenomenon. We suspect that clinicians are using this either as a placebo or to exploit the drowsiness-inducing (sedating) properties.

Case 3

An athletic 17 year old male with ALL is undergoing induction chemotherapy (day 3 of the Dana Farber protocol, with no infusion reactions yet).

His CBC today shows WBC 0.4, plt <10, Hb 69.
He is ordered 1 adult dose of platelets and 1u RBC.

The platelet transfusion is completed and the RBC unit is hung.
After 100mL of RBC have been transfused, the patient becomes febrile, dyspneic, tachypneic, and his spO2 drops to 78% on room air.

The transfusion is stopped and he transfers to the ICU.
He is given furosemide and salbutamol with no effect, and requires intubation.
CXR shows new bilateral infiltrates.

5. Which one of the following is the most likely diagnosis?
- A. type 1 ("definite") TRALI
 - B. type 2 ("possible") TRALI
 - C. chemotherapy-related ARDS
 - D. atypical pneumonia due to immune compromise

A. Definite (type 1) TRALI is the diagnosis if there is no alternative explanation. *Though he has a new diagnosis of leukemia, there is no hyperleukocytosis (leukostasis), and his neutropenia has not (yet) presented with an apparent infection.*

B. While possible (type 2) TRALI acknowledges priming by background factors or an already compromised baseline, these are stable in the preceding 12h. Had he been hypoxic but on a stable level of supplemental oxygen, this may have been a consideration.

C. ARDS in hematologic malignancy occurs more commonly in the neutrophil count recovery phase, so this is unlikely now.

D. Atypical pneumonia is not impossible, but CXR shows new infiltrates (by contrast with a normal admitting CXR). This would doubtful present so rapidly and severely (and in such temporal correlation with the blood product).

INCIDENCE:

TRALI accounts for ~1% of reported reactions, (and 4% of the serious ones), but it has not been eliminated, and it is still a leading cause of transfusion-related death (at 15%, second to TACO [36%]). After TRALI reduction measures, incidence has decreased by ~50% to less than 1 in 10,000. Plasma (antibody) – containing products have associated most strongly with TRALI.

6. The patient's parents are upset and want to know why this happened and what can be done to prevent it from happening again.
 - A. IVIG and steroid will mitigate recurrence risk
 - B. irradiation of cellular products prevents TRALI
 - C. antihistamine, acetaminophen, and furosemide reduce severity
 - D. supportive care is mainstay; most recover within 48-96 hours

With prompt and rigorous respiratory support, death rates from TRALI are 5-50%, in contrast with ARDS (27-45%).

- a. *is incorrect. Though murine models show some attenuation of lung injury with IVIG given before leukoagglutinin infusion, it is impractical to administer IVIG before all transfusions for such a rare reaction type, and IVIG is not without its own adverse effects. (Note that case reports of TRALI are also described with IVIG.) Steroids are neither a prevention nor definitive treatment of TRALI.*
- b. *is incorrect. Irradiation is indicated to prevent TA-GVHD in those at risk of engraftment by potentially viable contaminating/residual lymphocytes in cellular components. Irradiation induces DNA damage, thereby stopping division/proliferation. Irradiation does not kill the bacteria that can cause BaCon, nor alter antibody molecules capable of causing hemolysis or TRALI.*
- c. *is incorrect.*
 - i. *Based on the most recent systematic review/meta-analysis of antipyretic and antihistamine premedications, there is insufficient evidence to prescribe acetaminophen to prevent FNHTR, or antihistamine to prevent allergic reactions, let alone other wishful bystander benefits in TRALI.*
 - ii. *Furosemide as a pre-medication is of intuitive appeal for preventing TACO, but its role is yet to be definitively established.*
 1. *Furthermore, furosemide is not expected to help TRALI, insofar as non-cardiogenic pulmonary edema is not a volume problem, and may in fact progress to iatrogenic (or worsening) hypotension by diuretic administration.*
 2. *While ARDS may benefit from diuretics, unconditional diuresis of suspected TRALI may be harmful, and is not recommended. In real-life practice, the temptation to administer empiric diuretics is understood, but may be a poor substitute to personalized assessments (ie- proper volume status assessment with overload clues as the gate).*

D. is correct

As TRALI is donor- or product-attributable, improvement is expected as long as the patient has adequate reserves; the harmful mediator was passive and finite. If ALI/ARDS continues beyond 4-7 days, one should consider pathologies other than TRALI.

7. Based on what is known about TRALI, which of the following is the strongest measure by which to protect other recipients?
- A. placing an alert in the patient's allergy profile
 - B. reporting the suspected TRALI to blood bank
 - C. launching an incident report
 - D. informing the Transfusion Transmitted Injuries Surveillance System (TTISS)
- a. *is incorrect. TRALI is not an allergic reaction, and labelling the patient as having a blood allergy may cause the harm of undertransfusion or delay to transfusion with the next instance that blood products are indicated.*
- b. ***is CORRECT.** By reporting to the blood bank, a series of actions follows. Every effort is made to quarantine co-components (wherever they may be) so that any humors responsible for the observed severe reaction are not administered to others by in-date products from the implicated donor/donation. A TRALI Review Working Group assesses for whether the donor ought to be investigated, and if so, is contacted for tests of the anti-leukocyte antibody (HLA PRA) repertoire, and for whether or not it is cognate with the recipient's (HLA) profile. Alignment would support the provisional diagnosis of immune complex TRALI. If the case is suspicious enough, then the donor is deferred. If moderate doubt and concern co-exist, then the donor may be flagged ("on surveillance") so that a future adverse occurrence triggers deferral by proof of reproducibility.*
- c. *is incorrect. TRALI is not a medical error but an intrinsic biologic hazard in the product. Ad hoc corrective action meetings on hospital processes will not change the fate of this reaction having occurred in the patient or in others, unless there was indeed a process of concern (ie- infusing too quickly without supervision, or ordering a product that was unnecessary in retrospect).*
- d. *is incorrect; though reporting to TTISS enables the country to have data to inform risk discussions and observe trends over time, it does not link to donors or producers and products for testing and isolating problematic materials.*

PREVENTION:

Blood supply systems world-wide have reacted with donor selection and component production adjustments. In Canada, non-nulliparous females are deferred from apheresis (plasma or platelet) donations. Whole blood from females is manufactured in such a way that the plasma is "recovered", ie-diverted to the fractionation industry for pooling, while whole blood buffy coat-derived platelets are pooled in a pack suspended with a male donor's plasma ("buffy coat platelets"). These changes were implemented in Canada in 2008.

Case 4

A 52 year old male was in the OR for a 4-vessel CABG.

He received a 400mg dose of protamine at 17:15,
then 1 dose of platelets, 2u FP, and 1u RBC.

As he was coming off bypass pump, he developed an extensive urticarial rash (75% TBSA) with shock (BP 70-80/40) and bradycardia (20-80).

He had no known history of allergies and no prior exposures to blood products.

He was bolused phenylephrine 40 mcg IV with dopamine at 3 mcg/kg/min IV & norepinephrine at 0.1 mcg/kg/min IV.

He was also given diphenhydramine 50 mg IV + hydrocortisone 100 mg IV.

There were no respiratory/oxygenation changes, with P/F ratio remaining >300 with FiO2 30 – 50% during mechanical ventilation, which was continued, as he had significant airway and peri-orbital angioedema.

On transfer to the CVICU at 19:15, he was hypothermic (33.1C), and required ongoing boluses, pressors, and inotropes for a period of 12h.

8. Which one of the following investigations yields a result most likely to guide future transfusion advice to the patient?
- A. CBC, PT, aPTT, fibrinogen
 - B. culture patient and blood products
 - C. baseline IgA level and presence of anti-IgA IgG
 - D. repeat blood group, IAT, and DAT

This patient appears to have suffered an anaphylactic transfusion reaction, although a coincident exposure to protamine could also be possible.

Caution is needed on any re-exposure to protamine or to blood products. He may need blood products again during his lifetime so it is important to determine the culprit of the anaphylactic reaction if possible.

This presentation is unlikely to reflect RBC incompatibility/hemolysis, which is what A) or D) test for.

Because of the shock, bacterial sepsis should be ruled out (B).

However, for the management implications, choice C is preferred.

It is important to determine if the patient has severe IgA deficiency because:

- IgA deficiency-related anaphylaxis was thought to be a major cause of anaphylaxis [-- although >80% of anaphylaxis cases remain unexplained in hemovigilance systems despite this testing!], and*
- Knowing the cause allows for specific treatment/products to be secured e.g. IgA deficient products or washed products.*

He recovers and is extubated on POD1.

He is discharged home on POD7 after an uneventful post-operative course.

Laboratory testing reveals evidence of IgA deficiency (on a pre-transfusion specimen) and post-reaction detection of anti-IgA IgG in the patient's serum.

Two years later he is back, needing a hip replacement.

9. Which strategy would you adopt for this case?
- A. cancel surgery
 - B. bloodless surgery
 - C. fractionated blood substitutes
 - D. stock 2u washed RBC ± 4u IgA-deficient donor FP

It is not true that he cannot be transfused (ie- although Hb optimization to prevent transfusion is key). Banning blood may be detrimental to him in both (A) & (B).

(C) may not be safe. Firstly, we do not have licensed RBC substitutes. Secondly, although plasma can be contrived by its purified protein products (eg PCC, fibrinogen, albumin), these are not guaranteed to be as free of IgA as components donated from individuals who are known to be IgA deficient.

If we assume that IgA deficiency is the basis of his previous reaction, we would favour safe-for-IgA deficiency products (D).

The IgA deficient plasma can be brought to the hospital and only thawed if needed.

The bigger question is the relevance of IgA deficiency in any given anaphylactic reaction.

Individuals with a reassuring exposure history (ie- many uneventful transfusions, with one anaphylaxis event) may be re-exposed without testing; if a reaction recurs, then testing & special management are justified, but if a reaction does not recur, then the patient has proven themselves tolerant.

However, in someone who has reacted early (and especially serially) into their blood product exposure history, the precautionary principle would be to assume that IgA deficiency may be at play.

If tests reveal IgA deficiency, then managing with IgA deficient or washed blood products is justified.

If there is no IgA deficiency (or IgA sensitization), then exposures to unmodified products may resume, although if reactions recur, then modifications (such as washing to remove other mediators in the plasma) may be required.

If this was not a reaction case, but we were told that the patient was incidentally noted to be IgA deficient, (as may occur on pre-operative chart review), it is NOT necessary to test for anti-IgA IgG, nor to provide IgA-free products.

The risk of testing in a patient who has not had a previous reaction is that up to 1/3rd of IgA deficient individuals may be found to be sensitized (having anti-IgA IgG). Though having anti-IgA IgG may be a predictor of the experience of anaphylaxis, the positive predictive value is poor (ie- twice as many examples of non-reactors as reactors in a scoping review of exposures [Rachid & Bonilla, J Allergy Clin Immunol 2012]).

However, if anti-IgA IgG is tested for, and it is absent, then some reassurance may be gained on unmodified exposures.

Contingencies/Options for Transfusion Support & Challenges

	Give un-altered/ routine products & observe what happens	"plasma" (supernatant) volume reduction (PVR)	Washing	Sourcing from IgA deficient donors	Solvent-detergent- treated
Platelets	(riskiest of these options)	(though performed at some blood banks, will not deplete IgA)	(few banks offer, and action strips product)	Usually at least 1 dose available in national inventory at any given time, but not guaranteed, and delivery may not be immediate	Not an option
Plasma	(riskiest of these options)	Not applicable! (PVR = no plasma left!)	Not applicable (washing = no plasma left!)	Frozen stock usually available but may be scarce & need to be transported in	SDP (eg Octaplas) may help in recurrent (non-IgA-deficient) reactors
RBC	(risky, but less so than platelets or plasma, due to low plasma content in the product [2- 20cc]; this may arguably be the safest "unmodified starter/re- exposure" product)	(though performed at some blood banks, will not deplete IgA)	Feasible at some blood banks, or may be ordered as such from CBS	Feasible, but IgA deficient donors will be favoured for apheresis plasma and platelet donations; RBC stock may take more time to amass, especially if there are also RBC antigen matching needs	Not an option