

## 11.0 TRANSFUSION REACTIONS

<b>Policy</b>	The Transfusion Medicine Service has established policies, processes and procedures for the identification, investigation and management of suspected transfusion reactions. All transfusion reactions should be reported according to Health Canada requirements. All transfusion reactions should also be reported to the national surveillance programs to which the hospital is a reporting participant.
<b>Reason</b>	While the care of the recipient is primarily the responsibility of the attending physician(s), some immediate and delayed transfusion reactions are sufficiently uncommon that physicians and nurses may be unfamiliar with their recognition and management. Thus, the Medical Director, Transfusion Medicine has an important role in the education of clinical staff in the diagnosis and management of transfusion reactions. Transfusion safety, transfusion practice and accreditation standards all require that facilities detect, manage, investigate and report such reactions.
<b>Applies to</b>	Recipients with suspected adverse reactions to blood components or products.  The Public Health Agency of Canada (PHAC) defines an adverse reaction as: <b><i>“An undesirable and unintended response to the administration of blood, blood components, or blood products (plasma protein products) that is considered to be definitely, probably or possibly related to these components/products.”</i></b>
<b>Responsibilities of the Medical Director, Transfusion Medicine</b>	<ul style="list-style-type: none"> <li>• Liaise with, communicate with, and promote the education of, clinical staff regarding the recognition, management, investigation and reporting of transfusion reactions</li> <li>• Determine the extent of investigation required on possible adverse reactions as defined above</li> <li>• Provide direction as necessary to technologists regarding the examinations to be performed</li> <li>• Report the final conclusion regarding the type of reaction in a timely manner</li> <li>• Sign off on all required documentation</li> <li>• Review the clinical and laboratory information on all transfusion reactions, assess the probability of a causal relationship between transfusion and the signs and symptoms, and if applicable (TTISS/TESS) categorize the reaction according to PHAC definitions (see users manual at PHAC website)</li> <li>• Advise the treating physician, when appropriate, on the investigations, possible management and strategies to avoid future adverse reactions</li> <li>• Ensure that CBS or the plasma protein product manufacturer is immediately informed in cases where a component/product-attribute issue (e.g. bacterial contamination) is linked to a transfusion and another recipient may be at risk</li> <li>• Ensure that CBS or the plasma protein product manufacturer is contacted promptly, and in any case within 24 hours, if a death is linked to transfusion</li> <li>• Report the result of assessment of the putative adverse reaction to the required surveillance programs. There are currently two national surveillance programs: The Transfusion Transmitted Injury Surveillance System (TTISS) and the Transfusion Error Surveillance System (TESS). Not all hospitals report through these systems. Contact PHAC for more information if your hospital does not currently report to these systems and would like to do so</li> <li>• Engage clinical staff in the development of clinical practice documents for reporting transfusion reactions</li> </ul>



**Responsibilities of clinical staff**

- Recognize and manage the signs and symptoms of a transfusion reaction
- Confirm all unique identifiers for recipient and component/product to determine whether the transfused component/product was intended for the recipient
- Complete a transfusion reaction report form and submit to the Transfusion Medicine Service
- With any signs and symptoms for which the transfusion is to be terminated (i.e. other than urticaria/pruritis or mild non-hemolytic febrile reaction controlled with antipyretics) including IVIG-related reactions not resolved by ongoing transfusion care, send the following to the Transfusion Medicine Service:
  - » The blood component/product with the remaining contents, sealed to avoid contamination
  - » The attached administration set
  - » Recipient post-reaction blood samples or a request for their collection
  - » Recipient blood culture samples or request for their collection, if indicated by the nature of the reaction
  - » Epinephrine should be readily available wherever transfusion is carried out (see also section 11.1)
  - » First post-transfusion voided urine sample
- Collaborate with laboratory staff in the development of clinical practice documents for reporting transfusion reactions

**Responsibilities of Transfusion Medicine Service staff**

- Based on the clinical information provided, complete an investigation in accordance with the policies, processes and procedures, and the guidelines laid out in sections 11.8 below
- Send copies of completed transfusion reaction investigations to the required surveillance agencies (PHAC, TTISS/TESS; CBS, Plasma protein product manufacturers)
- At the request of the Medical Director, participate in the development of clinical practice and laboratory documents for the investigation and reporting of transfusion reactions



General Policies		
<b>Clinical and Laboratory Teams</b>	Every effort should be made to create and maintain a transfusion leadership team with clinical, technical and transfusion medicine physician representation that coordinates information in regard to transfusion practice and develops detailed documents that inform all staff involved in transfusion care on standardized optimal practice.	
<b>Immediate contact – clinical staff with the Transfusion Medicine Service</b>	The nursing staff in the clinical area will immediately contact the Transfusion Medicine Service to report reactions when: <ul style="list-style-type: none"> <li>• A recipient identity check error is found in relation to a transfused recipient or</li> <li>• A transfused recipient shows any of the following; <ul style="list-style-type: none"> <li>» Sudden spike in fever &gt;1.5 C from pre-transfusion temp</li> <li>» Sudden onset of hypoxemia/dyspnea</li> <li>» Sudden onset of hypotension</li> <li>» New onset of red/brown urine</li> </ul> </li> </ul>	
<b>Immediate contact – Transfusion Medicine Service staff with Medical Director, Transfusion Medicine (or delegate):</b>	The Transfusion Medicine Service staff will immediately contact the Medical Director, Transfusion Medicine or delegate if they receive a report of a transfusion reaction with the following: <ul style="list-style-type: none"> <li>• Recipient or component/product identity check error</li> <li>• Suspected bacterial contamination of the component/product</li> <li>• Sudden onset of hypoxemia/dyspnea</li> <li>• Sudden onset of hypotension</li> <li>• Hemoglobinuria reported in recipient’s post-transfusion urine sample</li> <li>• If and when, the transfusion reaction investigation shows: <ul style="list-style-type: none"> <li>» Abnormal results after completion of the primary investigation</li> <li>» Component/product is requested before the investigation is completed</li> </ul> </li> </ul>	
<b>Premedication of recipient</b>	<ul style="list-style-type: none"> <li>• Premedication of recipients with anti-histamines or anti-pyretics is NOT recommended in the absence of a history of repeated allergic or febrile reactions</li> <li>• “Fever” is defined as a temperature <math>\geq 38^{\circ}\text{C}</math> AND an increase of <math>\geq 1^{\circ}\text{C}</math> above recipient’s baseline temperature (oral temperature)</li> </ul>	
<b>Restarting transfusions</b>	<b>Signs &amp; Symptoms</b>	<b>Ongoing transfusion care</b>
	Urticaria/pruritis with any component/product: <ul style="list-style-type: none"> <li>• Minor allergic reaction.</li> <li>• Absence of clerical error, anaphylaxis, serious symptoms.</li> </ul> Medical assessment indicates transfusion may proceed.	<ul style="list-style-type: none"> <li>• Close monitoring of vital signs</li> </ul>
	<ul style="list-style-type: none"> <li>• Fever <ul style="list-style-type: none"> <li>» Temperature <math>&lt;39^{\circ}\text{C}</math> or fever is a consequence of an underlying condition.</li> <li>» Absence of clerical error, serious symptoms.</li> <li>» Medical assessment indicates transfusion may proceed.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Close monitoring of vital signs</li> </ul>



<b>Use of surveillance data</b>	<ul style="list-style-type: none"> <li>Track changes in reaction patterns for the institution and assess reactions in the wider hospital population for comparison</li> <li>Provide information for the institution's Transfusion Committee to facilitate: <ul style="list-style-type: none"> <li>» Identification of opportunities for improvement in clinical or laboratory transfusion practice</li> <li>» Initiation of process improvement projects</li> </ul> </li> </ul>		
<b>Recipient assessment and monitoring</b>	The recipient is directly observed during initiation of the transfusion, and for the first 15 minutes of the transfusion. Vital signs are recorded as indicated below		
	<b>Recipient category</b>	<b>Frequency of Vitals/Observation</b>	<b>Vital signs include</b>
	ALL	<ul style="list-style-type: none"> <li>Vital signs within 30 minutes prior to transfusion</li> <li>Observe for first 15 minutes, starting the transfusion slowly if clinical circumstances permit</li> <li>Vital signs 15 minutes after start of transfusion</li> <li>Vital signs at end of transfusion of each unit</li> <li>Vital signs and observation if a transfusion reaction is suspected</li> </ul>	<ul style="list-style-type: none"> <li>Temperature</li> <li>Blood pressure</li> <li>Pulse rate</li> <li>Respiratory rate</li> </ul>
	High Risk: Those with risk of cardiac overload, history of previous transfusion reaction, or clinically unstable recipients	<ul style="list-style-type: none"> <li>All of the above plus: <ul style="list-style-type: none"> <li>» Oxygen saturation</li> <li>» Auscultation for recipients at risk for circulatory overload (TACO), e.g. elderly, pediatric, cardiac disease</li> </ul> </li> <li>More frequent monitoring and observation as prescribed by the ordering physician</li> </ul>	
Unconscious	<ul style="list-style-type: none"> <li>Continuous monitoring</li> </ul>		
<b>Laboratory investigation of suspected transfusion reactions</b>	<ul style="list-style-type: none"> <li>Laboratory investigation of transfusion reactions will depend on the type of reaction and the differential diagnostic possibilities</li> <li>All laboratories should have an algorithm and process for determining the investigation that is required</li> </ul>		
<b>Retention of records of transfusion reactions</b>	<ul style="list-style-type: none"> <li>Indefinitely for recipients who have had serious transfusion complications or reactions</li> <li>Minimum of 5 years for all other recipients with transfusion reactions</li> </ul>		
<b>Reporting of reactions to external agencies</b>	<ul style="list-style-type: none"> <li>All serious transfusion reactions must be reported within 24 hours to: <ul style="list-style-type: none"> <li>» Fresh blood and blood components: CBS</li> <li>» Manufactured blood products: report to the individual manufacturer <ul style="list-style-type: none"> <li>» It is the manufacturer's responsibility to report all serious adverse reactions to Health Canada within 24 hours</li> </ul> </li> </ul> </li> </ul>		

## REFERENCES

26. Callum, J.L. 2011.
29. "Standards for Hospital Transfusion Services." 2011.
30. "Standards for Blood and Blood Components. CAN/CSA-Z902-10."
77. Lima, A. 2011.
105. "Transfusion Transmitted Injuries Surveillance System. User's Manual." 2007.
126. "The 2011 Annual SHOT Report." 2012.



**Table 11.1 – Ontario TTISS Transfusion Reaction Chart**  
[http://www.transfusionontario.org/media/TTISS%20version1\\_1%20final.pdf](http://www.transfusionontario.org/media/TTISS%20version1_1%20final.pdf)

**ONTARIO TTISS\* TRANSFUSION REACTION CHART**

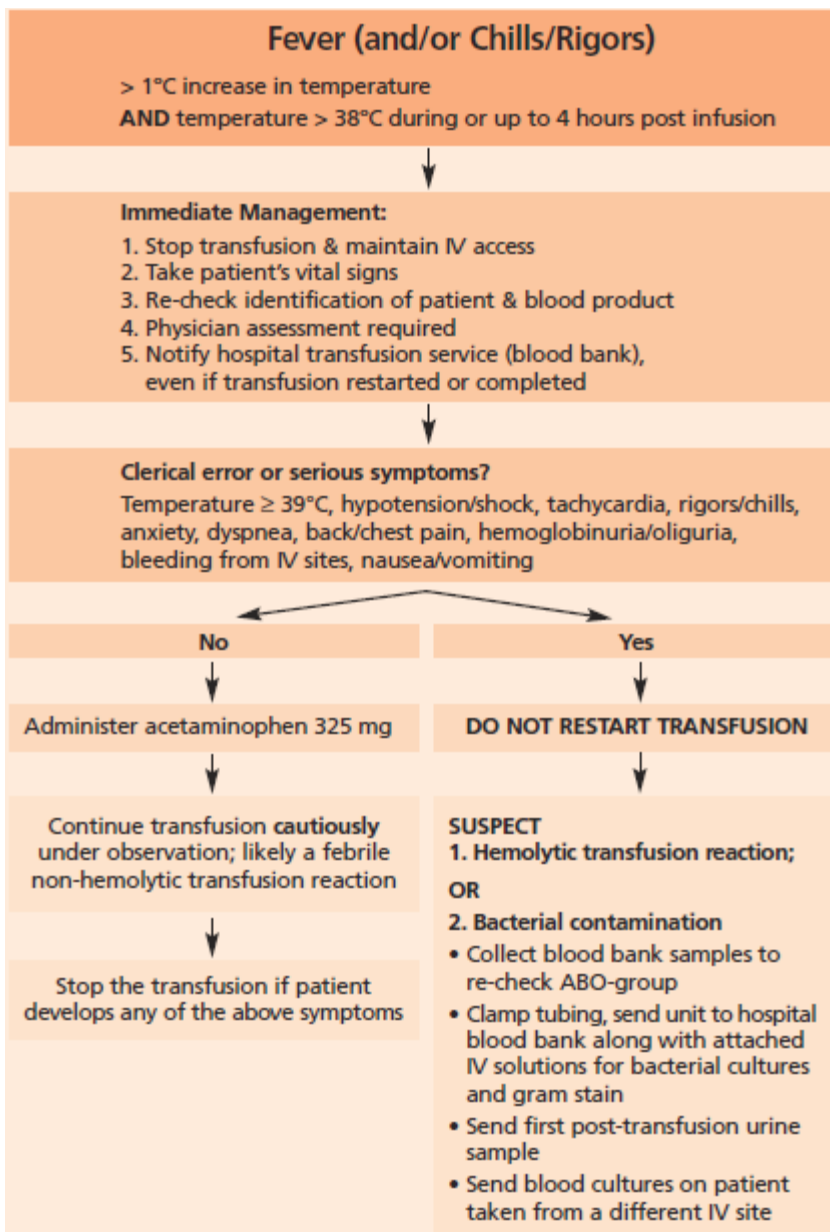
SIGNIS & SYMPTOMS		USUAL TIMING	POSSIBLE ETIOLOGY	RECOMMENDED INVESTIGATIONS	SUGGESTED TREATMENT AND ACTIONS
<b>IMMEDIATE ACTIONS!</b> 1. STOP the transfusion 2. Maintain IV access 3. Check vital signs 4. Re-check patient ID band and product label 5. Notify physician 6. Notify Transfusion Laboratory	Fever (at least 38° C and an increase of at least 1° C from baseline) <b>and/or</b> Shaking Chills/Rigors	During or up to 4 hours post transfusion  Usually within first 15 minutes but may be later	Febrile non-hemolytic transfusion reaction  Febrile non-hemolytic transfusion reaction Bacterial contamination Acute hemolytic transfusion reaction	No testing required  ▲ Group & Screen, DAT ▲ Patient blood culture (s) ▲ Urinalysis If hemolysis suspected (e.g. red urine or plasma) ▲ CBC, electrolytes, creatinine, bilirubin, LDH, aPTT, INR, fibrinogen, haptoglobin, plasma Hb	▲ Antipyretic ▲ With physician approval transfusion may be resumed cautiously if product still viable  <b>Do not restart transfusion</b> ▲ Antipyretic ▲ Consider Meperidine (Demerol®) for significant rigors ▲ If bacterial contamination suspected, antibiotics should be started immediately ▲ Monitor for hypotension, renal failure and DIC ▲ Return blood product to Transfusion Laboratory ▲ For additional assistance, contact _____
	38° C to 38.9° C but <b>NO</b> other symptoms  Less than 39° C but with other symptoms (e.g., rigors, hypotension) <b>or</b> 39° C or more	During or up to 4 hours post transfusion  Usually early in transfusion	Minor allergic  Severe allergic	No testing required  No testing required	▲ Antihistamine ▲ With physician approval transfusion may be resumed cautiously if product still viable  <b>Do not restart transfusion</b> ▲ Antihistamine ▲ May require steroid  <b>Do not restart transfusion</b> ▲ Epinephrine ▲ Washed/plasma depleted blood products pending investigation ▲ Return blood product to Transfusion Laboratory ▲ For additional assistance, contact _____
Urticaria (hives) Itching <b>or</b> Rash	Less than 2/3 body but <b>NO</b> other symptoms  2/3 body or more but <b>NO</b> other symptoms  Accompanied by other symptoms (e.g., dyspnea hypotension)	Usually early in transfusion	Anaphylaxis	▲ Group & Screen, DAT ▲ Chest X-Ray (if dyspneic) ▲ Blood gases (if dyspneic) ▲ Haptoglobin ▲ Anti-IgA testing	<b>Do not restart transfusion</b> ▲ Diuretics, oxygen, High Fowler's position ▲ Return blood product to Transfusion Laboratory ▲ Slow transfusion rate with diuretics for future transfusions  <b>Do not restart transfusion</b> ▲ Assess chest X-Ray for bilateral pulmonary infiltrates ▲ If TRALI may require vasopressors and respiratory support ▲ If bacterial contamination suspected, antibiotics should be started immediately ▲ Monitor for hypotension, renal failure and DIC ▲ If anaphylaxis suspected, epinephrine ▲ Return blood product to Transfusion Laboratory ▲ For additional assistance, contact _____
Dyspnea <b>or</b> Decrease in SpO <sub>2</sub> %	Typically with Hypertension  Typically with Hypotension	Within several hours of transfusion  Within 6 hours of transfusion  Usually within first 15 minutes but may be later	Transfusion associated circulatory overload (TACO)  Transfusion related acute lung injury (TRALI)  Bacterial contamination Acute hemolytic transfusion reaction Anaphylaxis	▲ Group & Screen, DAT ▲ Chest X-Ray ▲ Blood gases ▲ Urinalysis If sepsis suspected: ▲ Patient blood culture (s) If hemolysis suspected: ▲ CBC, electrolytes, creatinine, bilirubin, LDH, aPTT, INR, fibrinogen, haptoglobin, plasma Hb If anaphylaxis suspected: ▲ haptoglobin, Anti-IgA	▲ For additional assistance, contact _____

\* TTISS (Transfusion Transmitted Injuries Surveillance System) Transfusion Reaction Chart

version 1.1 June 2010 Originally printed in *Bloody Easy Blood Administration*



Table 11.2 Algorithm for management of transfusion – associated fever



## REFERENCES

18. Brecher, M.E. 2005.
26. Callum, J.L. 2011.
31. Capon, S.M. 1989.
42. Davenport, R.D. 2007.
67. Heddle, N.M. 2007.
77. Lima, A. 2011.
94. Perotta, P.L. 2001.
108. Ramirez-Arcos. 2007.
134. Vamvakas, E.C. 2009.

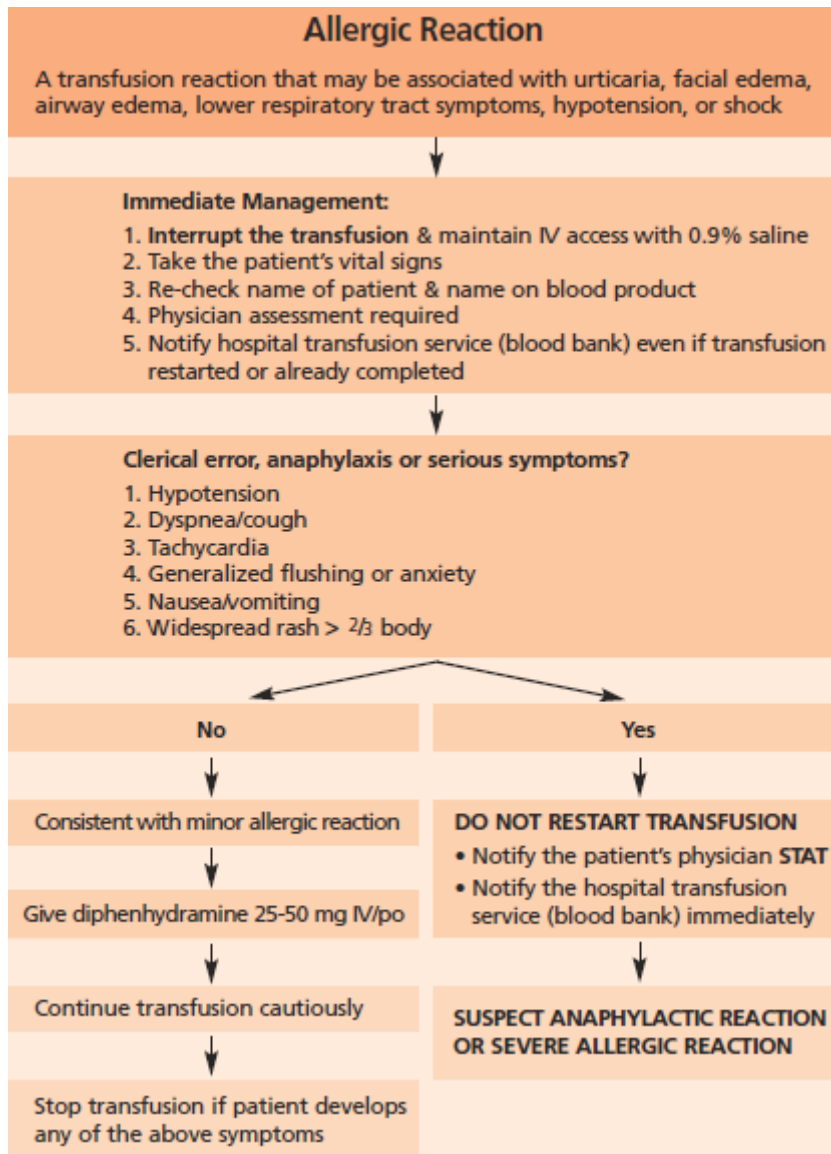


## 11.1 URTICARIA AND OTHER ALLERGIC REACTIONS

<b>Minor allergic reaction – urticaria/pruritus</b>	<ul style="list-style-type: none"> <li>Etiology: <ul style="list-style-type: none"> <li>Unclear, but relates to factors in plasma portion of component or in the product</li> </ul> </li> </ul>
<b>Clinical features</b>	<ul style="list-style-type: none"> <li>A single to widespread urticarial lesions</li> <li>May be associated with pruritus, erythema, mild upper respiratory symptoms, nausea, diarrhea</li> </ul>
<b>Management</b>	<ul style="list-style-type: none"> <li>Interrupt the transfusion</li> <li>Give diphenhydramine 25-50 mg po or IV depending on severity of the reaction</li> <li>Transfusion may be restarted slowly if the urticarial rash involves less than 2/3 of body surface and no associated symptoms suggesting severe allergic reaction</li> </ul>
<b>Prevention</b>	<ul style="list-style-type: none"> <li>For recurrent urticarial reactions, the following measures (of uncertain efficacy) may be used: <ul style="list-style-type: none"> <li>Premedication with diphenhydramine and/or corticosteroids</li> <li>Plasma depletion of red blood cells or platelets</li> <li>Washing red blood cells or platelets (see section 6.9)</li> </ul> </li> </ul>
<b>Severe Allergic Reaction/ Anaphylaxis</b>	<ul style="list-style-type: none"> <li>Usually unexplained</li> <li>Sensitivity to IgA or haptoglobin in a patient with deficiency of these</li> <li>Sensitivity to polymorphic forms of plasma proteins</li> <li>Sensitivity to allergens or drugs in donor plasma</li> </ul>
<b>Clinical features</b>	<ul style="list-style-type: none"> <li>Immediate to 45 minutes after start of transfusion</li> <li>Severe urticaria - &gt;2/3 body area</li> <li>Upper or lower airway obstruction, may be severe</li> <li>Hypotension</li> <li>Gastrointestinal symptoms</li> <li>Potentially life-threatening</li> </ul>
<b>Management</b>	<ul style="list-style-type: none"> <li>Stop the transfusion. Do not restart</li> <li>Severe allergic reaction – urticaria &gt;2/3 of body area <ul style="list-style-type: none"> <li>25-50 mg diphenhydramine IV</li> </ul> </li> <li>Anaphylaxis <ul style="list-style-type: none"> <li>Promptly administer epinephrine, corticosteroids, diphenhydramine, vasopressors and supportive care as required</li> <li>Ventilatory support as required</li> <li>Epinephrine should be readily available wherever transfusion is carried out</li> </ul> </li> </ul>
<b>Prevention</b>	<ul style="list-style-type: none"> <li>Premedication with intravenous steroids and diphenhydramine</li> <li>Determine IgA status of the patient</li> <li>Test for anti-IgA regardless of status</li> <li>Where the patient is IgA deficient with anti IgA the following products may be recommended: <ul style="list-style-type: none"> <li>IgA deficient components available from CBS</li> <li>Washed red blood cells or platelets (see section 6.9)</li> <li>If patient is of Asian extraction, test for haptoglobin deficiency</li> </ul> </li> </ul>



Table 11.3 Management Algorithm for Allergic Reactions



**REFERENCES**

26. Callum, J.L. 2011.  
 57. Gilstad, C.W. 2003.  
 94. Perotta, P.L. 2001.  
 116. Sandler, S.G. 1995.  
 132. Vamvakas, E.C. 2007.



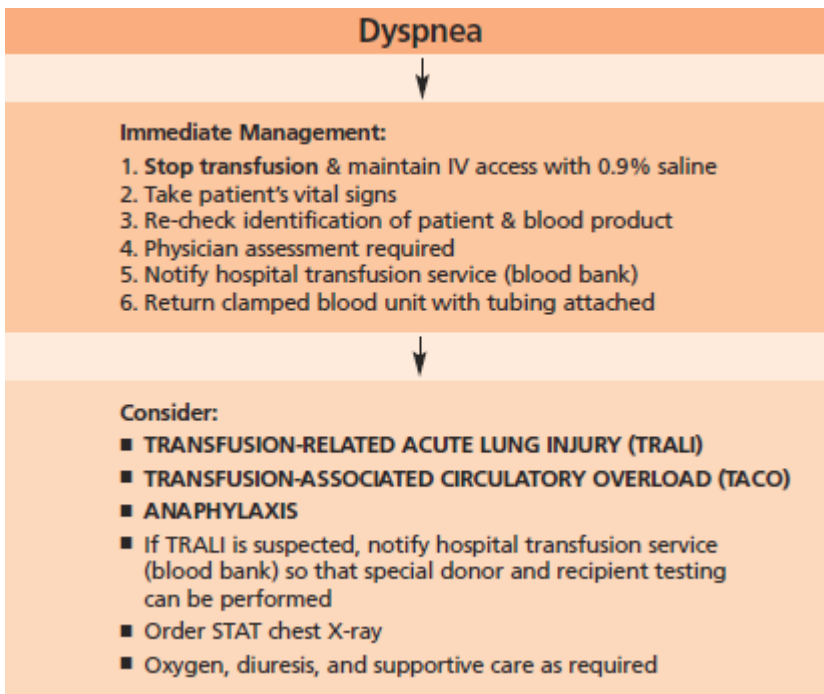


## 11.2 DYSPNEA

<b>Transfusion-related acute lung injury (TRALI)</b>	<b>Etiology</b> Two mechanisms have been postulated: <ul style="list-style-type: none"><li>• Passive transfer of HLA or granulocyte antibodies to recipient from a donor sensitized by previous pregnancy or transfusion</li><li>• Biologic response modifiers in the transfused component</li></ul>
<b>Clinical features</b>	<ul style="list-style-type: none"><li>• Acute onset of dyspnea during or within 6 hours of transfusion.</li><li>• Hypoxemia</li><li>• Bilateral lung infiltrates on radiograph</li><li>• No evidence of circulatory overload (see 11.3)</li><li>• Predisposing factors include direct lung injury (e.g. aspiration, pneumonia, toxic inhalation) and indirect lung injury (e.g. severe sepsis, multiple trauma, burn injury)</li></ul>
<b>Investigation</b>	<ul style="list-style-type: none"><li>• Accurate diagnosis and reporting to the hospital Transfusion Medicine Service is essential to identifying implicated donors</li><li>• Patient and donor testing for implicated antigens/antibodies should be arranged through CBS</li></ul>
<b>Management</b>	<ul style="list-style-type: none"><li>• Stop the transfusion and check vital signs</li><li>• Check identification of patient and component label</li><li>• Return residual component and clamped tubing to the Transfusion Service laboratory</li><li>• Supportive care, including mechanical ventilation as necessary</li><li>• Diuretics and steroids are not believed to be useful</li></ul>
<b>Prevention</b>	<ul style="list-style-type: none"><li>• Deferral of donors confirmed to be implicated in an episode of TRALI</li><li>• Component strategies to reduce the risk of TRALI include:<ul style="list-style-type: none"><li>» Plasma for transfusion from male donors only</li><li>» Buffy coat platelet pools re-suspended in male plasma</li><li>» Apheresis single donor platelets collected only from male and never pregnant females</li></ul></li></ul>



Table 11.4 Management Algorithm for Dyspnea



## REFERENCES

10. Benson, A.B. 2009.
26. Callum, J.L. 2011.
58. Goldman, M. 2005.
75. Kopko, P.M. 2007.
103. Popovsky, M.A. 2010.
134. Vamvakas, E.C. 2009.



### 11.3 TRANSFUSION-ASSOCIATED CIRCULATORY OVERLOAD (TACO)

<b>TACO</b>	<b>Etiology</b> <ul style="list-style-type: none"> <li>• Impaired cardiac or renal function</li> <li>• Excessively rapid rate of transfusion</li> <li>• Elderly patients, infants and euvolemic severely anemic patients</li> <li>• Common and under-diagnosed</li> </ul>
<b>Clinical features</b>	<ul style="list-style-type: none"> <li>• Dyspnea and orthopnea</li> <li>• Cyanosis</li> <li>• Increased venous pressure</li> <li>• Tachycardia, hypertension</li> </ul>
<b>Investigation</b>	<ul style="list-style-type: none"> <li>• Cardiac assessment</li> <li>• Chest X-ray</li> </ul>
<b>Management</b>	<ul style="list-style-type: none"> <li>• Interrupt the transfusion</li> <li>• Administer diuretics intravenously and oxygen as needed</li> <li>• Consider restarting transfusion at reduced rate if clinical status allows and component is still within standard time limits</li> </ul>
<b>Prevention</b>	<ul style="list-style-type: none"> <li>• Pre-transfusion assessment to identify patients at risk</li> <li>• Measures at time of transfusion include: <ul style="list-style-type: none"> <li>» Transfuse only one unit at a time and over longer time period up to 4 hours</li> <li>» Pre-emptive diuretics</li> <li>» Oral furosemide in low risk patients</li> <li>» IV furosemide in high risk patients</li> <li>» Transfuse components in smaller (“split”) aliquots</li> </ul> </li> </ul>
<b>Anaphylaxis</b>	See section

#### REFERENCES

26. Callum, J.L. 2011.  
88. Narick, C. 2012.  
94. Perotta, P.L. 2001.  
102. Popovsky, M.A. 2007.  
103. Popovsky, M.A. 2010.



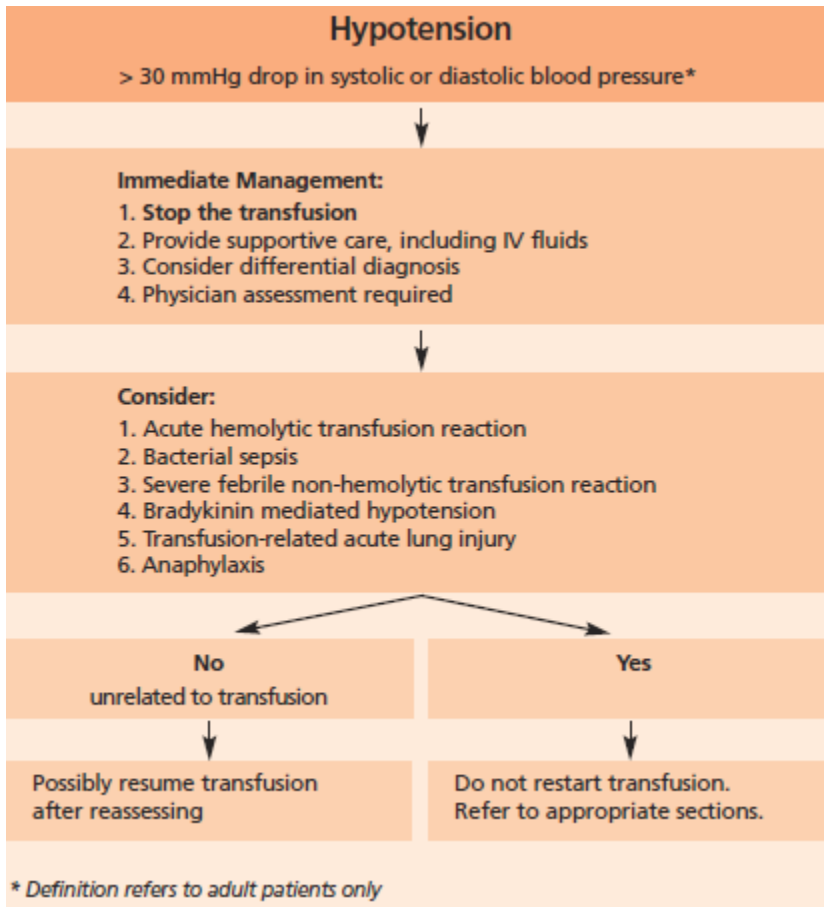
## 11.4 HYPOTENSION (BRADYKININ MEDIATED)

Defined as a >30 mmHg fall in systolic or diastolic blood pressure (in adults only).

<b>Hypotension</b>	<b>Etiology</b> <ul style="list-style-type: none"><li>• Genetic polymorphism leading to decrease in bradykinin degradation</li><li>• Use of angiotensin converting enzyme inhibitors<ul style="list-style-type: none"><li>» Hypotension may be a part of the constellation of signs in other transfusion reactions, including acute hemolytic reactions, bacterial sepsis, severe febrile non-hemolytic transfusion reactions, TRALI or anaphylaxis</li></ul></li></ul>
<b>Clinical features</b>	<ul style="list-style-type: none"><li>• Majority occur with platelet transfusions</li><li>• Often associated with use of ACE inhibitors</li><li>• Other symptoms may include nausea and vomiting dyspnea, urticaria</li><li>• Rarely associated with significant morbidity</li></ul>
<b>Investigation</b>	<ul style="list-style-type: none"><li>• Consider other potential causes of hypotension listed above</li></ul>
<b>Management</b>	<ul style="list-style-type: none"><li>• Detect early, during the monitoring of transfusion in the first 15 minutes</li><li>• Stop the transfusion and do not restart</li><li>• Provide supportive care including IV fluids</li><li>• Consult with an expert in transfusion medicine if further transfusion is required</li></ul>
<b>Prevention</b>	<ul style="list-style-type: none"><li>• Where ACE inhibitors have been implicated, consider alternative anti-hypertensive agents</li></ul>



Table 11.5 Management Algorithm for Hypotension



## REFERENCES

4. Arnold, D.M.
5. Arnold, D.M. 2004.
26. Callum, J.L. 2011.
39. Cyr, C. 2001.
50. Eastland, T. 2007.



## 11.5 CYTOPENIAS AFTER TRANSFUSION

<b>Post-transfusion purpura (PTP)</b>	<b>Etiology</b> <ul style="list-style-type: none"> <li>• Transfusion of a platelet antigen positive component to a patient who lacks that antigen</li> <li>• 75% of cases involve HPA-1a positive platelets transfused to an HPA-1a negative recipient</li> <li>• Autologous platelet destruction occurs but the mechanism is unclear</li> </ul>
<b>Clinical features</b>	<ul style="list-style-type: none"> <li>• Occurs 1-24 days (median 9 days) after transfusion.</li> <li>• Female:male ratio 5:1 as a consequence of sensitization in pregnancy</li> <li>• Platelet count &lt;10 x 10<sup>9</sup>/L in 80% of cases</li> <li>• Mortality about 8%, mainly intra-cranial hemorrhage</li> <li>• Thrombocytopenia lasts about 2 weeks if untreated with IVIG</li> </ul>
<b>Investigation</b>	<ul style="list-style-type: none"> <li>• Test patient plasma for platelet-specific antibodies (refer to CBS)</li> </ul>
<b>Management</b>	<ul style="list-style-type: none"> <li>• IVIG 1g/kg daily for 2 days; response expected within 4 days</li> <li>• Patients with PTP should be warned that they (and possibly relatives) are at risk for neonatal immune thrombocytopenia</li> </ul>
<b>Prevention</b>	<ul style="list-style-type: none"> <li>• Transfuse only with components negative for the appropriate antigen</li> </ul>

### REFERENCES

26. Callum, J.L. 2011.  
 82. McFarland, J.G. 2007.  
 94. Perrotta, P.L. 2001.  
 136. Waters, A.H. 1989.

## 11.6 TRANSFUSION-ASSOCIATED GRAFT-VERSUS-HOST DISEASE (GVHD)

<b>GVHD</b>	<b>Etiology</b> <ul style="list-style-type: none"> <li>• Due to an immune response mounted by donor lymphocytes against the recipient's HLA determinants</li> <li>• Occurs in immuno-compromised recipients, and</li> <li>• Immuno-competent recipients receiving a haplo-identical product</li> </ul>
<b>Clinical features</b>	<ul style="list-style-type: none"> <li>• Fever, rash, hepatic dysfunction and diarrhea 1-2 weeks post-transfusion</li> <li>• Overwhelming infections with mortality &gt;99%</li> </ul>
<b>Investigation</b>	<ul style="list-style-type: none"> <li>• Diagnosis can be confirmed by skin, liver or bone marrow biopsy</li> <li>• Confirmation requires documentation of presence of donor lymphocytes (HLA typing or DNA analysis)</li> </ul>
<b>Management</b>	<ul style="list-style-type: none"> <li>• Treatment mostly ineffective</li> <li>• Survival is rare, and is attributed to immunosuppressive therapy</li> </ul>
<b>Prevention</b>	<ul style="list-style-type: none"> <li>• For patients at risk, irradiation of cellular components (red blood cells and platelets) is critical</li> <li>• Pre-storage leukoreduction does not completely eliminate the risk of GvHD</li> <li>• Indications for irradiation are detailed in section 6.8</li> <li>• Patient at risk should have a card indicating the requirement for irradiated cellular components</li> </ul>

### REFERENCES

1. Alyea, E.P. 2007.  
 26. Callum, J.L. 2011.  
 94. Perrotta, P.L. 2001.  
 114. Ruhl, H. 2009.  
 134. Vamvakas, E.C. 2009



## 11.7 RARE CAUSES OF TRANSFUSION-ASSOCIATED CYTOPENIA

- Transfusion-associated alloimmune thrombocytopenia:
  - Due to platelet-specific donor antibodies to recipient platelet antigens
- Transfusion-associated alloimmune neutropenia:
  - Due to neutrophil-specific donor antibodies to recipient neutrophil antigens

## 11.8 HEMOLYSIS AFTER TRANSFUSION

<b>Delayed hemolytic transfusion reactions (DHTR)</b>	<b>Etiology</b> <ul style="list-style-type: none"> <li>• Results from formation of antibodies in the recipient to red blood cell allo-antigens from transfusion or exposure during pregnancy</li> <li>• Concentrations of antibody are below the level of detectability of antibody screen testing</li> <li>• Incidence is about 1 in 7000 units of red blood cells transfused</li> </ul>
<b>Clinical features</b>	<ul style="list-style-type: none"> <li>• Appear 3 – 14 days post-transfusion</li> <li>• Fall in hemoglobin, spherocytosis, reticulocytosis, elevated bilirubin, hemoglobinuria, elevated LDH</li> <li>• Positive DAT and antibody screen</li> <li>• Most are relatively benign, but occasional DHTRs present with severe hemolysis and renal failure may occur</li> </ul>
<b>Investigation</b>	<ul style="list-style-type: none"> <li>• Identification of the offending allo-antibody</li> <li>• Confirmation of the presence of the corresponding antigen on one or more of donor red blood cell units transfused</li> <li>• Confirmation of the absence of the corresponding antigen on the recipient's red blood cells</li> </ul>
<b>Management</b>	<ul style="list-style-type: none"> <li>• Supportive therapy as needed</li> <li>• Select only red blood cells "negative" for the antigen involved for subsequent transfusions</li> </ul>
<b>Prevention</b>	<ul style="list-style-type: none"> <li>• Avoid transfusion if possible</li> <li>• Use antibody screening methods with maximal sensitivity</li> <li>• Notify the patient and supply a wallet card and recommend medical alert bracelet with antibody information</li> </ul>
<b>Other possible causes of hemolysis after transfusion</b>	<ul style="list-style-type: none"> <li>• Transfusion-transmitted malaria or babesiosis</li> <li>• Use of hypotonic IV solutions with red blood cell transfusion</li> <li>• Medical device (warmer, cell saver) malfunction</li> <li>• Freezing or overheating of red blood cells</li> <li>• Transfusion of outdated red blood cells</li> <li>• Transfusion through small bore needle under pressure</li> </ul>

### REFERENCES

26. Callum, J.L. 2011.  
 42. Davenport, R.D. 2007.



Table 11.5 Example chart of response to notification of suspected transfusion reaction from Sunnybrook Transfusion Service

IMMEDIATE ACTIONS!	SIGNS & SYMPTOMS	USUAL TIMING	POSSIBLE ETIOLOGY	RECOMMENDED INVESTIGATIONS	SUGGESTED TREATMENT AND ACTIONS
<p><b>REACT</b></p> <ol style="list-style-type: none"> <li>1. STOP the transfusion</li> <li>2. Maintain IV access</li> <li>3. Check vital signs</li> <li>4. Re-check patient ID band and product label</li> <li>5. Notify patient's physician</li> <li>6. Notify Blood Bank</li> </ol>	<p>Fever (at least 38° C and an increase of at least 1° C from baseline)</p> <p><b>and/or</b></p> <p>Shaking Chills/Rigors</p>	<p>During or up to 4 hours post transfusion</p> <p>Usually within first 15 minutes but may be later</p>	<p>Febrile non-hemolytic transfusion reaction</p> <p>Febrile non-hemolytic transfusion reaction</p> <p>Bacterial contamination</p> <p>Acute hemolytic transfusion reaction</p>	<p>Reaction slip only</p> <p>No testing required</p> <p>▲ Group &amp; Screen, DAT</p> <p>▲ Patient blood culture(s)</p> <p>▲ Urinalysis</p> <p>If hemolysis suspected (e.g. red urine or plasma)</p> <p>▲ CBC, electrolytes, creatinine, bilirubin, LDH, aPTT, INR, fibrinogen, haptoglobin, plasma Hb</p>	<p>▲ Antipyretic</p> <p>▲ With physician approval transfusion may be resumed cautiously if product still viable</p> <p><b>Do not restart transfusion</b></p> <p>▲ Antipyretic</p> <p>▲ Consider Meperidine (Demerol®) for significant rigors</p> <p>▲ If bacterial contamination suspected, antibiotics should be started immediately</p> <p>▲ Monitor for hypotension, renal failure and DIC</p> <p>▲ Return blood product to Blood Bank</p> <p>▲ For additional assistance, contact Transfusion Medicine Physician on call</p>
<p>Urticaria (hives)</p> <p>Itching</p> <p><b>or</b></p> <p>Rash</p>	<p>Less than 2/3 body but <b>NO</b> other symptoms</p> <p>2/3 body or more but <b>NO</b> other symptoms</p> <p>Accompanied by other symptoms (e.g. dyspnea, hypotension)</p>	<p>During or up to 4 hours post transfusion</p> <p>Usually early in transfusion</p> <p>Usually early in transfusion</p>	<p>Minor allergic</p> <p>Severe allergic</p> <p>Anaphylaxis</p>	<p>Reaction slip only</p> <p>No testing required</p> <p>Reaction slip only</p> <p>No testing required</p> <p>▲ Group &amp; Screen, DAT</p> <p>▲ Chest X-Ray (if dyspneic)</p> <p>▲ Blood gases (if dyspneic)</p> <p>▲ Haptoglobin</p> <p>▲ Anti-IgA testing</p>	<p>▲ Antihistamine</p> <p>▲ With physician approval transfusion may be resumed cautiously if product still viable</p> <p><b>Do not restart transfusion</b></p> <p>▲ Antihistamine</p> <p>▲ May require steroid</p> <p><b>Do not restart transfusion</b></p> <p>▲ Epinephrine</p> <p>▲ Washed/plasma depleted blood products pending investigation</p> <p>▲ Return blood product to Blood Bank</p> <p>▲ For additional assistance, contact Transfusion Medicine Physician on call</p>
<p>Dyspnea</p> <p><b>or</b></p> <p>Decrease in SpO<sub>2</sub> %</p>	<p>Typically with Hypertension</p> <p>Typically with Hypotension</p>	<p>Within several hours of transfusion</p> <p>Within 6 hours of transfusion</p> <p>Usually within first 15 minutes but may be later</p>	<p>Transfusion associated circulatory overload (TACO)</p> <p>Transfusion related acute lung injury (TRALI)</p> <p>Bacterial contamination</p> <p>Acute hemolytic transfusion reaction</p> <p>Anaphylaxis</p>	<p>Group &amp; Screen, DAT</p> <p>Chest X-Ray</p> <p>Blood gases</p> <p>Urinalysis</p> <p>If sepsis suspected:</p> <p>▲ Patient blood culture(s)</p> <p>If hemolysis suspected:</p> <p>▲ CBC, electrolytes, creatinine, bilirubin, LDH, aPTT, INR, fibrinogen, haptoglobin, plasma Hb</p> <p>If anaphylaxis suspected:</p> <p>▲ Haptoglobin, Anti-IgA</p>	<p><b>Do not restart transfusion</b></p> <p>▲ Diuretics, oxygen, High Fowler's position</p> <p>▲ Return blood product to Blood Bank</p> <p>▲ Slow transfusion rate with diuretics for future transfusions</p> <p><b>Do not restart transfusion</b></p> <p>▲ Assess chest X-ray for bilateral pulmonary infiltrates</p> <p>▲ If TRALI, may require vasopressors and respiratory support started immediately</p> <p>▲ If bacterial contamination suspected, antibiotics should be started immediately</p> <p>▲ Monitor for hypotension, renal failure and DIC</p> <p>▲ If anaphylaxis suspected, epinephrine</p> <p>▲ Return blood product to Blood Bank</p> <p>▲ For additional assistance, contact Transfusion Medicine Physician on call</p>

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## 11.9 ADVERSE REACTIONS TO INTRAVENOUS IMMUNOGLOBULIN (IVIG)

<p><b>General policy</b></p>	<ul style="list-style-type: none"> <li>• In the event of an adverse reaction, stop the transfusion and assess the patient</li> <li>• If the reaction is minor, the transfusion may be continued at a reduced infusion rate</li> <li>• Report all adverse reactions to the Transfusion Medicine Service</li> </ul>																																				
<p><b>Clinical features and management of reactions to IVIG</b></p>	<table border="1"> <thead> <tr> <th colspan="4" data-bbox="451 296 1279 338">ADVERSE REACTIONS TO IVIG <sup>235,241,242,243</sup></th> </tr> <tr> <th data-bbox="451 338 667 380">REACTION</th> <th data-bbox="667 338 792 380">SEVERITY</th> <th data-bbox="792 338 959 380">FREQUENCY**</th> <th data-bbox="959 338 1279 380">COMMENT/TREATMENT</th> </tr> </thead> <tbody> <tr> <td data-bbox="451 380 667 558">Anxiety, chills/fever, rash, flushing, headache, chest, back or abdominal pain, nausea/vomiting, tachycardia, hypo- or hypertension</td> <td data-bbox="667 380 792 558">Mild-moderate</td> <td data-bbox="792 380 959 558">Common</td> <td data-bbox="959 380 1279 558">Slow or pause IVIG treatment. Symptomatic treatment. Recurrent reactions – pre-medicate and/or change to another manufacturer's IVIG product</td> </tr> <tr> <td data-bbox="451 558 667 642">Aseptic Meningitis</td> <td data-bbox="667 558 792 642">Moderate</td> <td data-bbox="792 558 959 642">Rare</td> <td data-bbox="959 558 1279 642">Stop infusion. Administer analgesics. Usually resolves spontaneously in 24-48 hours</td> </tr> <tr> <td data-bbox="451 642 667 747">Anaphylaxis</td> <td data-bbox="667 642 792 747">Severe</td> <td data-bbox="792 642 959 747">Rare</td> <td data-bbox="959 642 1279 747">Stop infusion. <b>May require epinephrine promptly.</b> Often reaction to IgA in an IgA-deficient patient</td> </tr> <tr> <td data-bbox="451 747 667 873">Acute renal failure</td> <td data-bbox="667 747 792 873">Severe</td> <td data-bbox="792 747 959 873">Rare (120 cases reported to FDA in 13 years)</td> <td data-bbox="959 747 1279 873">Usually with sucrose-containing product (none currently licensed in Canada). Predisposing factors: age &gt; 65, diabetes mellitus, pre-existing renal insufficiency</td> </tr> <tr> <td data-bbox="451 873 667 936">Hemolysis<sup>244</sup></td> <td data-bbox="667 873 792 936">Mild-Severe</td> <td data-bbox="792 873 959 936">Uncommon</td> <td data-bbox="959 873 1279 936">More common in non-blood group O patients</td> </tr> <tr> <td data-bbox="451 936 667 1020">Thrombo-embolic events<sup>245</sup></td> <td data-bbox="667 936 792 1020">Severe</td> <td data-bbox="792 936 959 1020">Rare (anecdotal reports)</td> <td data-bbox="959 936 1279 1020">Causative relationship not clearly established. Possibly related to increases in viscosity</td> </tr> <tr> <td data-bbox="451 1020 667 1167">Infectious disease transmission</td> <td data-bbox="667 1020 792 1167">Severe</td> <td data-bbox="792 1020 959 1167">No reported case since HCV in 1995,<sup>246</sup> No known case of transmission of HIV or HBV</td> <td data-bbox="959 1020 1279 1167">Modern viral reduction measures are robust. Prion (vCJD) transmission remains an entirely theoretical risk</td> </tr> </tbody> </table> <p data-bbox="451 1188 1279 1232">** Reactions are more likely with faster rates of infusion.</p>	ADVERSE REACTIONS TO IVIG <sup>235,241,242,243</sup>				REACTION	SEVERITY	FREQUENCY**	COMMENT/TREATMENT	Anxiety, chills/fever, rash, flushing, headache, chest, back or abdominal pain, nausea/vomiting, tachycardia, hypo- or hypertension	Mild-moderate	Common	Slow or pause IVIG treatment. Symptomatic treatment. Recurrent reactions – pre-medicate and/or change to another manufacturer's IVIG product	Aseptic Meningitis	Moderate	Rare	Stop infusion. Administer analgesics. Usually resolves spontaneously in 24-48 hours	Anaphylaxis	Severe	Rare	Stop infusion. <b>May require epinephrine promptly.</b> Often reaction to IgA in an IgA-deficient patient	Acute renal failure	Severe	Rare (120 cases reported to FDA in 13 years)	Usually with sucrose-containing product (none currently licensed in Canada). Predisposing factors: age > 65, diabetes mellitus, pre-existing renal insufficiency	Hemolysis <sup>244</sup>	Mild-Severe	Uncommon	More common in non-blood group O patients	Thrombo-embolic events <sup>245</sup>	Severe	Rare (anecdotal reports)	Causative relationship not clearly established. Possibly related to increases in viscosity	Infectious disease transmission	Severe	No reported case since HCV in 1995, <sup>246</sup> No known case of transmission of HIV or HBV	Modern viral reduction measures are robust. Prion (vCJD) transmission remains an entirely theoretical risk
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- 23. Callum, J.L. 2007.
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