11.0 TRANSFUSION REACTIONS

Policy	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.
Reason	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.
Applies to	Recipients with suspected adverse reactions to blood components or products. The Public Health Agency of Canada (PHAC) defines an adverse reaction as: ***"An undesirable and unintended occurrence during or after the administration of blood, blood components, or blood products (plasma derivatives) whether or not considered to be related to the administration of these products."***
Responsibilities of the Medical Director, Transfusion Medicine	• Liaise with, communicate with, and promote the education of, clinical staff regarding the recognition, management, investigation and reporting of transfusion reactions • Determine the extent of investigation required on possible adverse reactions as defined above • Provide direction as necessary to technologists regarding the examinations to be performed • Report the final conclusion regarding the type of reaction in a timely manner • Sign off on all required documentation • 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 categorize the reaction according to PHAC definitions (see users manual at PHAC website) • Advise the treating physician, when appropriate, on the investigations, possible management and strategies to avoid future adverse reactions • 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 • 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 • 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 • Engage clinical staff in the development of clinical practice documents for reporting transfusion reactions

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 (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. With Health Canada regulations, hospitals are required to report any reaction to a component where the hospital has modified it (washed, plasma reduced etc).

General Policies		
Clinical and Laboratory Teams	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.	
Immediate contact – clinical staff with the Transfusion Medicine Service	The nursing staff in the clinical area will immediately contact the Transfusion Medicine Service to report reactions when: • A recipient identity check error is found in relation to a transfused recipient or • A transfused recipient shows any of the following; » Sudden spike in fever >1.5 C from pre-transfusion temp » Sudden onset of hypoxemia/dyspnea » Sudden onset of hypotension » New onset of red/brown urine	
Immediate contact – Transfusion Medicine Service staff with Medical Director, Transfusion Medicine (or delegate):	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: • Recipient or component/product identity check error • Suspected bacterial contamination of the component/product • Sudden onset of hypoxemia/dyspnea • Sudden onset of hypotension • Hemoglobinuria reported in recipient's post-transfusion urine sample • If and when, the transfusion reaction investigation shows: » Abnormal results after completion of the primary investigation » Component/product is requested before the investigation is completed	
Premedication of recipient	• Premedication of recipients with anti-histamines or anti-pyretics is NOT recommended in the absence of a history of repeated allergic or febrile reactions • "Fever" is defined as a temperature ≥ 38°C AND an increase of ≥ 1°C above recipient's baseline temperature (oral temperature)	
Restarting transfusions	**Signs & Symptoms**	**Ongoing transfusion care**
	Urticaria/pruritis with any component/product: • Minor allergic reaction. • Absence of clerical error, anaphylaxis, serious symptoms. Medical assessment indicates transfusion may proceed.	• Close monitoring of vital signs
	• Fever » Temperature <39°C or fever is a consequence of an underlying condition. » Absence of clerical error, serious symptoms. » Medical assessment indicates transfusion may proceed.	• Close monitoring of vital signs
Use of surveillance data	• Track changes in reaction patterns for the institution and assess reactions in the wider hospital population for comparison • Provide information for the institution's Transfusion Committee to facilitate: » Identification of opportunities for improvement in clinical or laboratory transfusion practice » Initiation of process improvement projects	

<table>
<tr><td rowspan="4">Recipient assessment and monitoring</td><td colspan="3">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</td></tr>
<tr><td>Recipient category</td><td>Frequency of Vitals/Observation</td><td>Vital signs include</td></tr>
<tr><td>ALL</td><td>• Vital signs within 30 minutes prior to transfusion
• Observe for first 15 minutes, starting the transfusion slowly if clinical circumstances permit
• Vital signs 15 minutes after start of transfusion
• Vital signs at end of transfusion of each unit
• Vital signs and observation if a transfusion reaction is suspected</td><td>• Temperature
• Blood pressure
• Pulse rate
• Respiratory rate</td></tr>
<tr><td>High Risk:
Those with risk of cardiac overload, history of previous transfusion reaction, or clinically unstable recipients</td><td>• All of the above plus:
» Oxygen saturation
» Auscultation for recipients at risk for circulatory overload (TACO), e.g. elderly, pediatric, cardiac disease
• More frequent monitoring and observation as prescribed by the ordering physician</td><td></td></tr>
<tr><td>Unconscious</td><td>• Continuous monitoring</td><td></td></tr>
<tr><td>Laboratory investigation of suspected transfusion reactions</td><td colspan="3">• Laboratory investigation of transfusion reactions will depend on the type of reaction and the differential diagnostic possibilities
• All laboratories should have an algorithm and process for determining the investigation that is required</td></tr>
<tr><td>Retention of records of transfusion reactions</td><td colspan="3">• 10 years for recipients who have had serious transfusion complications or reactions
• Minimum of 5 years for all other recipients with transfusion reactions</td></tr>
<tr><td>Reporting of reactions to external agencies</td><td colspan="3">• All serious transfusion reactions must be reported within 24 hours to:
» Fresh blood and blood components: CBS
» Manufactured blood products: report to the individual manufacturer
» It is the manufacturer's responsibility to report all serious adverse reactions to Health Canada within 24 hours
• Preliminary report with full investigation to follow and complete report within 15 days. If fatality report must be complete within 24 hours</td></tr>
</table>

RESOURCES

1. TTISS-ON Ontario Guide for Reporting Transfusion Reactions, March 2017.
2. Health Canada regulations Guidance Document: Blood Regulations (mod Mar 2016) Health Products and Food Branch, Health Canada.

REFERENCES

25. Callum JL, 2016.
30. CSTM, version 4, 2017
31. CAN/CSA-Z902-5.
80. Lima A, 2015.
112. Transfusion Transmitted Injuries Surveillance System User's Manual, 2007.
122. Serious Hazards of Transfusion (SHOT), 2017.
131. Tinegate A, 2012.

TTISS-ON Transfusion Reaction Chart

Immediate Actions!

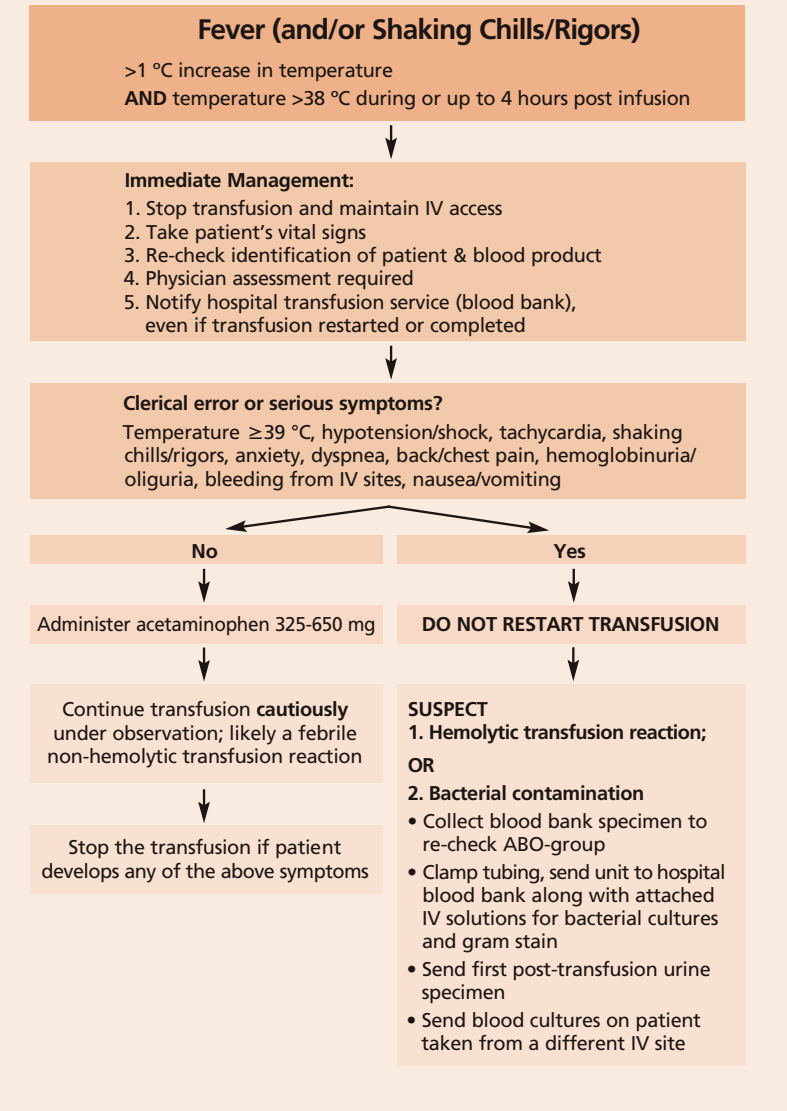
1. STOP the transfusion
2. Maintain IV access
3. Check vital signs
4. Re-check patient ID band and product label
5. Notify physician
6. Notify Transfusion Laboratory

Signs & Symptoms		Usual Timing	Possible Etiology	Recommended investigations	Suggested Treatment and Actions
Fever (at least 38° C and an increase of at least 1° C from baseline) **and/or** Shaking Chills/ Rigors	38°C to 38.9°C but **NO** other symptoms	During or up to 4 hours post transfusion	Febrile non-hemolytic transfusion reaction	No testing required	▲ Antipyretic ▲ With physician approval transfusion may be resumed cautiously if product still viable
	Less than 39°C but with other symptoms (e.g. rigors, hypotension) **or** 39° C or more	Usually within first 15 minutes but may be later	Febrile non-hemolytic transfusion reaction Bacterial contamination Acute hemolytic transfusion reaction	▲ 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	**Do not restart transfusion** ▲ 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_____
Urticaria (hives) Itching **or** Rash	Less than 2/3 body but **NO** other symptoms	During or up to 4 hours post transfusion	Minor allergic	No testing required	▲ Antihistamine ▲ With physician approval transfusion may be resumed cautiously if product still viable
	2/3 body or more but **NO** other symptoms	Usually early in transfusion	Minor allergic (extensive)	No testing required	**Do not restart transfusion** ▲ Antihistamine ▲ May require steroid
	Accompanied by other symptoms (e.g. dyspnea hypotension)	Usually early in transfusion	Anaphylactoid reaction/Anaphylaxis	▲ Group & Screen, DAT ▲ Chest X-Ray (if dyspneic) ▲ Blood gases (if dyspneic) ▲ Haptoglobin ▲ Anti-IgA testing	**Do not restart transfusion** ▲ Epinephrine ▲ Washed/plasma depleted blood products pending investigation ▲ Return blood product to Transfusion Laboratory ▲ For additional assistance, contact_____
Dyspnea **or** Decrease in SpO_2% to 90% or less (and change of at least 5% from baseline)	Typically with Hypertension	Within several hours of transfusion	Transfusion associated circulatory overload (TACO)	▲ 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	**Do not restart transfusion** ▲ Diuretics, oxygen, High Fowler's position ▲ Return blood product to Transfusion Laboratory ▲ Slow transfusion rate with diuretics for future transfusions
	Typically with Hypotension	Within 6 hours of transfusion	Transfusion related acute lung injury (TRALI)		**Do not restart transfusion** ▲ 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_____
		Usually within first 15 minutes but may be later	Bacterial contamination Acute hemolytic transfusion reaction Anaphylaxis		

* Ontario Transfusion Transmitted Injuries Surveillance System (TTISS-ON)

version 2.1 January 2016 *Originally printed in Bloody Easy Blood Administration*

Table 11.2 Algorithm for management of transfusion – associated fever



REFERENCES

4. AABB, 2012.
18. Brecher ME, 2015.
23. Callum JL, 2011.
37. Cohen, 2017.
44. Delaney M, 2016.
80. Lima A, 2015.
102. Perotta PL, 2001.
134. Vamvakas EC, 2009.

11.1 URTICARIA AND OTHER ALLERGIC REACTIONS

Minor allegic reaction – urticaria/pruritus	• Etiology: • Unclear, but relates to factors in plasma portion of component or in the product
Clinical features	• A single to widespread urticarial lesions • May be associated with pruritus, erythema, mild upper respiratory symptoms, nausea, diarrhea
Management	• Interrupt the transfusion • Give diphenhydramine 25-50 mg po or IV depending on severity of the reaction • 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

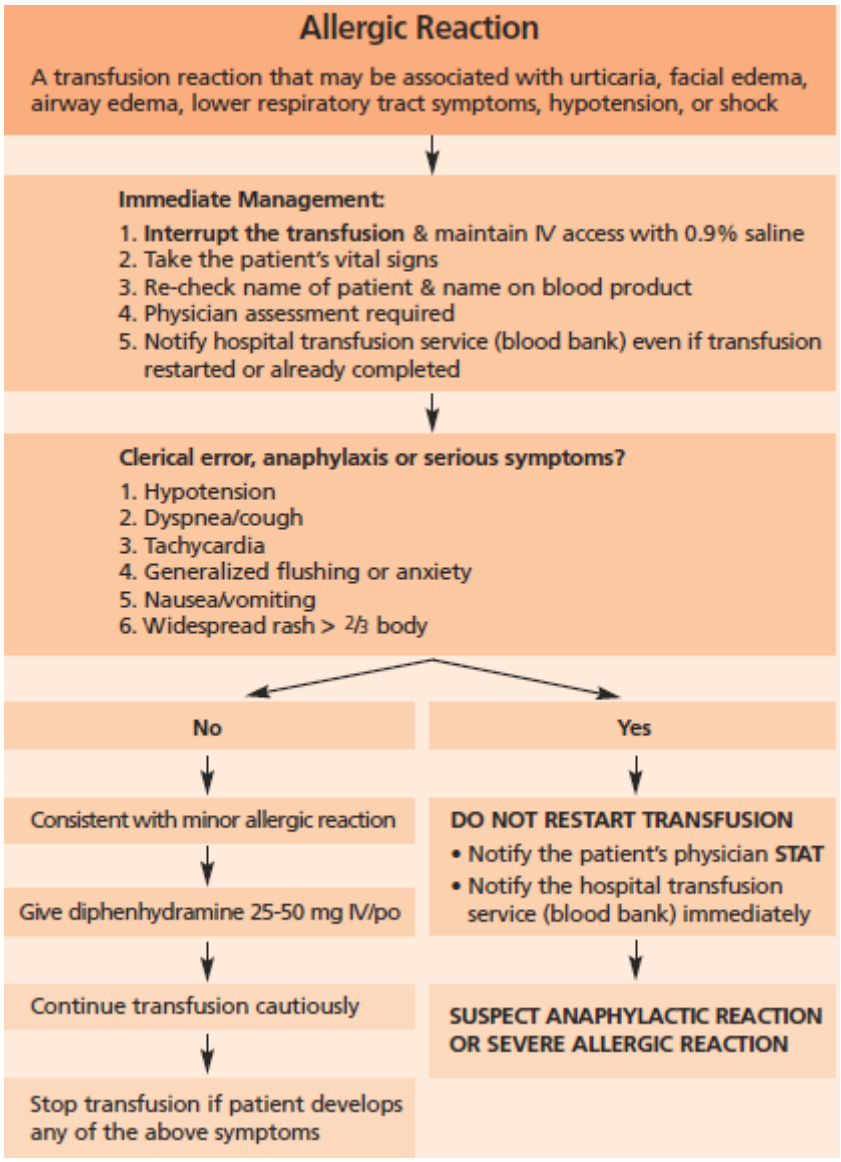
Prevention	• For recurrent urticarial reactions, the following measures (of uncertain efficacy) may be used:
	  » Premedication with diphenhydramine and/or corticosteroids
	  » Plasma depletion of red blood cells or platelets
	  » Washing red blood cells or platelets (see section 6.9)

Severe Allergic Reaction/ Anaphylaxis	• Usually unexplained • Sensitivity to IgA or haptoglobin in a patient with deficiency of these • Sensitivity to polymorphic forms of plasma proteins • Sensitivity to allergens or drugs in donor plasma
Clinical features	• Immediate to 45 minutes after start of transfusion • Severe urticaria - >2/3 body area • Upper or lower airway obstruction, may be severe • Hypotension • Gastrointestinal symptoms • Potentially life-threatening

Management	• Stop the transfusion. Do not restart
	• Severe allergic reaction – urticaria >2/3 of body area
	  » 25-50 mg diphenhydramine IV
	• Anaphylaxis
	  » Promptly administer epinephrine, corticosteroids, diphenhydramine, vasopressors and supportive care as required
	  » Ventilatory support as required
	  » Epinephrine should be readily available wherever transfusion is carried out

Prevention	• Premedication with intravenous steroids and diphenhydramine
	• Determine IgA status of the patient
	• Test for anti-IgA regardless of status
	• Where the patient is IgA deficient with anti IgA the following products may be recommended:
	  » IgA deficient components available from CBS
	  » Washed red blood cells or platelets (see section 6.9)
	  » If patient is of Asian extraction, test for haptoglobin deficiency

Table 11.3 Management Algorithm for Allergic Reactions



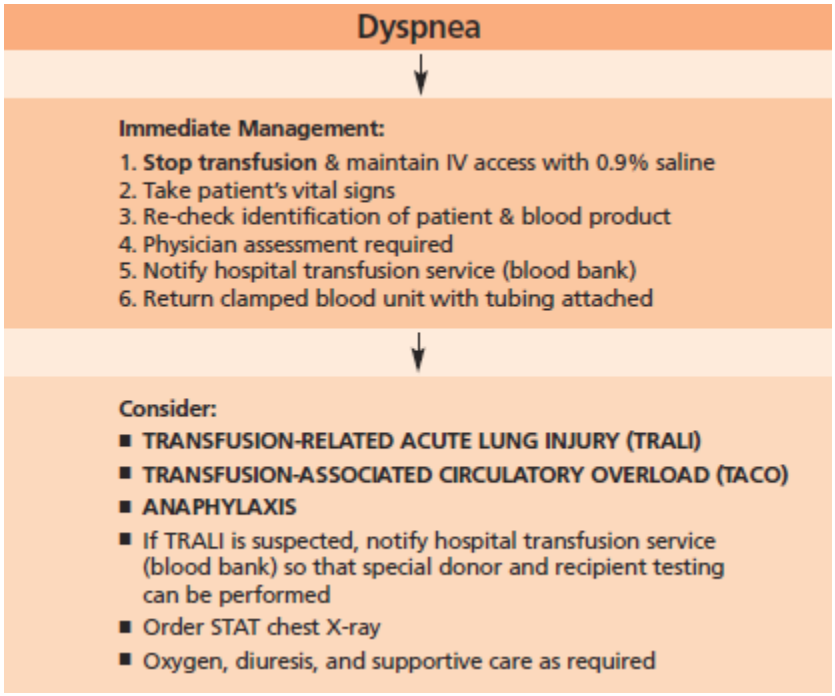
REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
57. Gilstad CW, 2003.
102. Perotta PL, 2001.

11.2 DYSPNEA

Transfusion-related acute lung injury (TRALI)	**Etiology** Two mechanisms have been postulated: • Passive transfer of HLA or granulocyte antibodies to recipient from a donor sensitized by previous pregnancy or transfusion • Biologic response modifiers in the transfused component with a susceptible recipient
Clinical features	• Acute onset of dyspnea during or within 6 hours of transfusion. • Hypoxemia • Bilateral lung infiltrates on radiograph • No evidence of circulatory overload (see 11.3) • Predisposing factors include direct lung injury (e.g. aspiration, pneumonia, toxic inhalation) and indirect lung injury (e.g. severe sepsis, multiple trauma, burn injury)
Investigation	• Accurate diagnosis and reporting to the hospital Transfusion Medicine Service is essential to identifying implicated donors • Patient and donor testing for implicated antigens/antibodies should be arranged through CBS
Management	• Stop the transfusion and check vital signs • Check identification of patient and component label • Return residual component and clamped tubing to the Transfusion Service laboratory • Supportive care, including mechanical ventilation as necessary • Diuretics and steroids are not believed to be useful
Prevention	• Deferral of donors confirmed to be implicated in an episode of TRALI • Component strategies to reduce the risk of TRALI include: » Plasma for transfusion from male donors only » Buffy coat platelet pools re-suspended in male plasma » Apheresis single donor platelets collected only from male and never pregnant females

Table 11.4 Management Algorithm for Dyspnea



REFERENCES

4. AABB, 2012.
11. Benson AB, 2009.
25. Callum JL, 2016.
58. Goldman M, 2005.
109. Popovsky MA, 2010.
134. Vamvakas EC, 2009.

11.3 TRANSFUSION-ASSOCIATED CIRCULATORY OVERLOAD (TACO)

TACO	Etiology • Impaired cardiac or renal function • Excessively rapid rate of transfusion • Elderly patients, infants and euvolemic severely anemic patients • Common and under-diagnosed
Clinical features	• Dyspnea and orthopnea • Cyanosis • Increased venous pressure • Tachycardia, hypertension
Investigation	• Cardiac assessment • Chest X-ray
Management	• Interrupt the transfusion • Administer diuretics intravenously and oxygen as needed • Consider restarting transfusion at reduced rate if clinical status allows and component is still within standard time limits
Prevention	• Pre-transfusion assessment to identify patients at risk • Measures at time of transfusion include: » Transfuse only one unit at a time and over longer time period up to 3.5 hours from time of issue from Transfusion Medicine Service » Pre-emptive diuretics » Oral furosemide in low risk patients » IV furosemide in high risk patients » Transfuse components in smaller (“split”) aliquots
Anaphylaxis	See section 11.1

REFERENCES

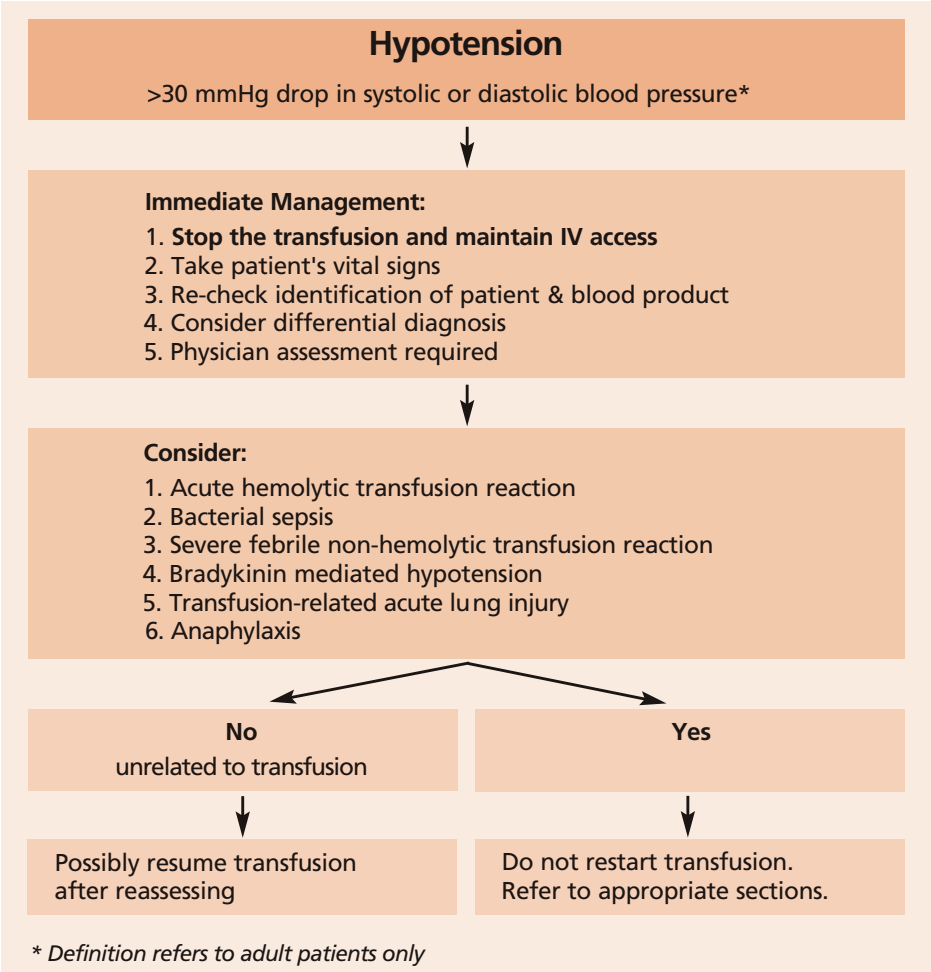
25. Callum JL, 2016.
35. Clifford L, 2017.
79. Lieberman L, 2013.
91. Narick C, 2012.
102. Perotta PL, 2001.
109. Popovsky MA, 2010.

11.4 HYPOTENSION (BRADYKININ MEDIATED)

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

Hypotension	**Etiology** • Genetic polymorphism leading to decrease in bradykinin degradation • Use of angiotensin converting enzyme inhibitors » 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
Clinical features	• Majority occur with platelet transfusions • Often associated with use of ACE inhibitors • Other symptoms may include nausea, vomiting, dyspnea and urticaria • Rarely associated with significant morbidity
Investigation	• Consider other potential causes of hypotension listed above
Management	• Detect early, during the monitoring of transfusion in the first 15 minutes • Stop the transfusion and do not restart • Provide supportive care including IV fluids • Consult with an expert in transfusion medicine if further transfusion is required
Prevention	• Where ACE inhibitors have been implicated, consider alternative anti-hypertensive agents

Table 11.5 Management Algorithm for Hypotension



** Definition refers to adult patients only*

REFERENCES

4. AABB, 2012
6. Arnold DM, 2004.
25. Callum JL, 2016.
39. Cyr C, 2001.
50. Eastland T, 2007.

11.5 CYTOPENIAS AFTER TRANSFUSION

Post-transfusion purpura (PTP)	**Etiology** • Transfusion of a platelet antigen positive component to a patient who lacks that antigen • 75% of cases involve HPA-1a positive platelets transfused to an HPA-1a negative recipient • Autologous platelet destruction occurs but the mechanism is unclear
Clinical features	• Occurs 1-24 days (median 9 days) after transfusion • Female:male ratio 5:1 as a consequence of sensitization in pregnancy • Platelet count <10 x 10^9/L in 80% of cases • Mortality about 8%, mainly intra-cranial hemorrhage • Thrombocytopenia lasts about 2 weeks if untreated with IVIG
Investigation	• Test patient plasma for platelet-specific antibodies (refer to CBS)
Management	• IVIG 1g/kg daily for 2 days; response expected within 4 days • Patients with PTP should be warned that they (and possibly relatives) are at risk for neonatal immune thrombocytopenia
Prevention	• Transfuse only with components negative for the appropriate antigen

REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
86. McFarland JG, 2007.
102. Perrotta PL, 2001.

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

GVHD	**Etiology** • Due to an immune response mounted by donor lymphocytes against the recipient's HLA determinants • Occurs in immuno-compromised recipients, and • Immuno-competent recipients receiving a haplo-identical product
Clinical features	• Fever, rash, hepatic dysfunction and diarrhea 1-2 weeks post-transfusion • Overwhelming infections with mortality >90%
Investigation	• Diagnosis can be confirmed by skin, liver or bone marrow biopsy • Confirmation requires documentation of presence of donor lymphocytes (HLA typing or DNA analysis)
Management	• Treatment mostly ineffective • Survival is rare, and is attributed to immunosuppressive therapy
Prevention	• For patients at risk, irradiation of cellular components (red blood cells and platelets) is critical • Pre-storage leukoreduction does not completely eliminate the risk of GvHD • Indications for irradiation are detailed in section 6.8 • Patient at risk should have a card indicating the requirement for irradiated cellular components

REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
76. Kopolovic I, 2015.
102. Perrotta PL, 2001.
119. Ruhl H, 2009.
134. Vamvakas EC, 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

Delayed hemolytic transfusion reactions (DHTR)	**Etiology** • Results from formation of antibodies in the recipient to red blood cell allo-antigens from transfusion or exposure during pregnancy • Concentrations of antibody are below the level of detectability of antibody screen testing • Incidence is about 1 in 7000 units of red blood cells transfused
Clinical features	• Appear 3 – 14 days post-transfusion • Fall in hemoglobin, spherocytosis, reticulocytosis, elevated bilirubin, hemoglobinuria, elevated LDH • Positive DAT and antibody screen • Most are relatively benign, but occasional DHTRs present with severe hemolysis and renal failure may occur
Investigation	• Identification of the offending allo-antibody • Confirmation of the presence of the corresponding antigen on one or more of donor red blood cell units transfused • Confirmation of the absence of the corresponding antigen on the recipient's red blood cells
Management	• Supportive therapy as needed • Select only red blood cells "negative" for the antigen involved for subsequent transfusions
Prevention	• Avoid transfusion if possible • Use antibody screening methods with maximal sensitivity • Notify the patient and supply a wallet card and recommend medical alert bracelet with antibody information
Other possible causes of hemolysis after transfusion	• Transfusion-transmitted malaria or babesiosis • Use of hypotonic IV solutions with red blood cell transfusion • Medical device (warmer, cell saver) malfunction • Freezing or overheating of red blood cells • Transfusion of outdated red blood cells • Transfusion through small bore needle under pressure

REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
42. Davenport RD, 2011.

11.9 ADVERSE REACTIONS TO INTRAVENOUS IMMUNOGLOBULIN (IVIG)

General policy	• In the event of an adverse reaction, stop the transfusion and assess the patient • If the reaction is minor, the transfusion may be continued at a reduced infusion rate • Report all adverse reactions to the Transfusion Medicine Service
Clinical features and management of reactions to IVIG	

Table 11.6 Adverse Reactions to IVIG

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	7 in 10,000[272]	Stop infusion. Administer analgesics. Usually resolves spontaneously in 24-48 hours
Anaphylaxis	Severe	Rare	Stop infusion. **May require epinephrine promptly.** Consider testing for IgA and anti-IgA (see page 63)
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	Mild-Severe	10%[273,274]	More common in non-group O patients
Thrombo-embolic events	Severe	0.5-1%[275]	Causative relationship not clearly established. Possibly related to increases in viscosity
Infectious disease transmission	Severe	No reported case since HCV in 1995.[276] No known case of transmission of HIV or HBV	Modern viral reduction measures are robust. Prion (vCJD) transmission remains an entirely theoretical risk

** Reactions are more likely with faster rates of infusion.

REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
33. Cherin P, 2016.
106. Pierce LR, 2003.
129. Stiem ER, 2013.