

Section L: Adverse Effects of Blood Transfusion

(Notify BTL if patient has any adverse effect to blood transfusion)

IMMEDIATE ACTIONS

1. STOP transfusion pending further physician order
2. Maintain IV access with saline TKVO
3. Check vital signs
4. Re-check name and PIN of patient with product label
5. Notify patient's physician.
6. Go to TRAC visual aid to access additional recommended clinical actions.

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T R A C

Transfusion ReAction Course

Clinical Management

IMMEDIATE ACTIONS

1. STOP transfusion pending further physician order
2. Maintain IV access with saline TKVO
3. Check vital signs
4. Re-check name and PIN of patient with product label
5. Notify patient's physician

Click on symptoms below to access recommended Clinical Actions.

Suspected Transfusion Reaction Signs and Symptoms:

Fever ($\geq 38^{\circ}\text{C}$ & increase of more than 1°C from baseline)
and/or Chills / Rigors

NO known underlying cause for fevers / chills / rigors

Urticaria (Hives) Rash Other Allergic symptoms

Dyspnea OR Decreased SpO_2

Hypotension

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Fever and/or Chills/Rigors

Fever ($\geq 38^{\circ}\text{C}$ & increase of more than 1°C from baseline) and/or Chills / Rigors without an underlying cause

Suspected Transfusion Reaction Signs & Symptoms	Recommended Clinical Actions	"Possible" Etiology	Timing of Symptoms	Actions and Suggested Treatment or Investigations
38°C to < 39°C and NO other symptoms	Order test TRX Complete TRAC Report (fax to BTL) No testing required	FNHTR (febrile non hemolytic transfusion reaction)	During or up to 4 hours post transfusion	Consult with patient's physician – Administer Antipyretic and continue transfusion cautiously if product still viable Premed with antipyretic only after 2 episodes
< 39°C and other symptoms (eg. rigors, hypotension) or $\geq 39^{\circ}\text{C}$	Order tests TRX, GS, .DATG Send to BTL: - Completed TRAC Report - Labeled patient sample - Offending unit(s) Blood culture (to Micro) Urinalysis (to Core Lab)	Severe FNHTR , Bacterial sepsis , or AHTR (acute hemolytic transfusion reaction)	Usually within first 15 minutes but may be later	STOP & DO NOT RESTART Administer Antipyretic If bacterial contamination suspected start antibiotics immediately If PLASMA HEMOLYSIS reported by BTL send: INR, PTT, CBC, electrolytes, creatinine, bilirubin, LDH, and fibrinogen to core lab Urinalysis (to Core Lab) for hemoglobinuria Monitor for hypotension, renal failure and DIC For additional assistance contact Hematologist on call

Link to LEGEND

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Urticaria(Hives) / Rash / Other Allergic Symptoms

Suspected Transfusion Reaction Signs & Symptoms	Recommended Clinical Actions	“Possible” Etiology	Timing of Symptoms	Actions and Suggested Treatment or Investigations
<2/3 body surface and NO other symptoms	Order test TRX Complete TRAC Report (fax to BTL) No testing required	Minor Allergic	Usually during transfusion; or up to 4 hours after completion of transfusion	Consult with patient’s physician – Administer Antihistamine and continue transfusion cautiously if product still viable Premed with antihistamine only after 2 episodes
≥2/3 body surface and NO other symptoms	Order test TRX Complete TRAC Report (fax to BTL) No testing required	Severe Allergic	Usually during transfusion; or up to 4 hours after completion of transfusion	STOP & DO NOT RESTART – Administer Antihistamine Premedication with antihistamine with/without corticosteroid Consider plasma depletion if recurrent – Discuss with BTL MD
With other symptoms (ie. dyspnea, hypotension)	Order tests TRX, GS, .DATG Send to BTL: - Completed TRAC Report - Labeled patient sample - Offending unit(s) Chest X-Ray (optional) Consider PCCOT/CCOT	Severe Allergic or Anaphylaxis	Usually early in transfusion	STOP & DO NOT RESTART Administer Epinephrine (MD order) Requires washed blood until investigation complete Send haptoglobin & IgA testing to immunology (via Core lab) Send anti-IgA testing to BTL For additional assistance contact Hematologist on call

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Dyspnea or Decreased SpO₂

Suspected Transfusion Reaction Signs & Symptoms	Recommended Clinical Actions	“Possible” Etiology	Timing of Symptoms	Actions and Suggested Treatment or Investigations
Cardiac Risk Factors	Order tests TRX, GS, .DATG Send to BTL: - Completed TRAC Report - Labeled patient sample	TACO (transfusion associated circulatory overload)	Within several hours of transfusion	Administer Diuretics, O ₂ , Elevate head of bed to 45° May resume transfusion if adequate response Resume transfusion slowly & cautiously (as per physician order) Appropriate use of diuretics for subsequent transfusions
	- Offending unit(s) Chest X-Ray Capillary blood gases	TRALI (transfusion related acute lung injury)	Within 6 hours of transfusion	STOP & DO NOT RESTART Assess Chest X-Ray for pulmonary infiltrates Administer O ₂ , may require vasopressors, intubation and ventilation
	Urinalysis (to Core Lab) Consider PCCOT/CCOT	AHTR (acute hemolytic transfusion reaction)	Usually within first 15 minutes but may be later	If bacterial contamination suspected start antibiotics immediately If PLASMA HEMOLYSIS reported by BTL (bloodwork as above) For additional assistance contact Hematologist on call

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Hypotension

Adult: ≥ 30 mmHg drop in SBP or DBP AND SBP < 80 mmHg

Pediatric: 0-28 days SBP < 60
 1-12 months SBP < 70
 1-10years SBP $< 70 + (2x \text{ age})$
 > 10 years SBP < 90

Suspected Transfusion Reaction Signs & Symptoms	Recommended Clinical Actions	“Possible” Etiology	Timing of Symptoms	Actions and Suggested Treatment or Investigations
Another cause identified	Reporting NOT required	Underlying cause identified	Any time	Manage and correct underlying cause Proceed with transfusion cautiously
No other cause identified or Shock	Order tests TRX, GS, .DATG Send to BTL: - Completed TRAC Report - Labeled patient sample - Offending unit(s) Urinalysis (to Core Lab) Capillary blood gases (optional) Consider PCCOT/CCOT	AHTR Bacterial sepsis Anaphylaxis TRALI	See above descriptions	STOP & DO NOT RESTART (unless alternate cause identified) Determine cause and treat as described above for each possible etiology
		Bradykinin mediated		Bradykinin mediated, consider alternate ACE inhibitor (if applicable)

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LEGEND for TRAC

BTL	Blood Transfusion Laboratory
TKVO	To Keep Veins Open
SpO₂	Saturation of Peripheral Oxygen
TRX	Transfusion Reaction Investigations (selection on PowerChart)
GS	Group and Screen
.DATG	Direct Antiglobulin Test
BTL TRI form	<u>Internal BTL</u> Transfusion Reaction Investigation form
FNHTR	Febrile Non-Hemolytic Transfusion Reaction
AHTR	Acute Hemolytic Transfusion Reaction (seen more often in RBC transfusions)
TACO	Transfusion Associated Circulatory Overload
TRALI	Transfusion Related Acute Lung Injury (seen more often in plasma transfusions)
PCCOT/CCOT	Paediatric or Adult Critical Care Outreach Team.

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Immediate Adverse Effects of Transfusion: Incidence and Cause(s)

FNHTR: Febrile Non-Hemolytic Transfusion Reaction

Incidence: 1 in 300 for RBC transfusions¹
1 in 10 for platelet transfusions¹

Cause: Recipient antibodies directed against donor white cell (or platelet) antigens
Soluble factors e.g. cytokines in the plasma of the blood component

AHTR: Acute Hemolytic Transfusion Reaction

Incidence: 1 in 7000² to 1 in 38,000¹
Fatal outcomes: 1 in 600,000² to 1 in 1.8 million¹

Cause: Recipient antibodies directed against donor red cell antigens.
Antibodies to A and B antigens are usually most severe because they cause intravascular hemolysis.
May be a result of error in the identification of a patient, a specimen or unit(s) of blood.
On occasion, may be due to transfused ABO antibodies (generally in platelet transfusion or Intravenous Immune Globulin – IVIG).

Allergic Reaction

Incidence: 1 in 250²
1 in 100 mild allergic reactions with plasma containing blood components¹

Cause: Relates to factors in the plasma portion of the blood component, possibly recipient antibodies to donor plasma proteins.

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Anaphylaxis:

Incidence: Rare^{1,2}

Cause: Recipient antibodies to specific plasma proteins, most often IgA.
May also occur due to recipient antibodies to polymorphic forms of serum proteins (IgG, haptoglobin, a-1-antitrypsin, transferrin, C3, C4 etc)¹.
There are rare reports of a passive transfer of donor antibody (drug or food allergy transferred to recipient during transfusion of plasma products).

TACO: Transfusion Associated Circulatory Overload

Incidence: 1 in 700 (1 in 100 in older orthopedic surgical patients)¹

Cause: Circulatory overload resulting from blood products administered faster or in greater amount than the circulation can accommodate, often due to impaired cardiac function.

TRALI: Transfusion Related Acute Lung Injury

Incidence: True incidence unknown because often not recognized or reported
Estimated incidence: 1 in 1,200 to 1 in 5,000 plasma-containing transfusions¹.

Cause: May be due to HLA or granulocyte antibodies in the donor reacting with recipient white cells.
Also postulated that biologically active lipids in transfused blood component may have a role in TRALI.

Bacterial Sepsis:

Incidence: 1 in 10,000 (symptomatic septic reaction to platelets)¹
1 in 1,000,000 (symptomatic septic reaction to RBC)¹

Cause: Bacterially contaminated blood component.
Platelets are the most susceptible to bacterial growth due to room temperature storage.

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Massive Transfusion: Complications / Adverse Events

Definition of Massive Transfusion: > 10 units of RBC in a 24 hour period, or replacement of 50% of blood volume in 3 hours.

Dilutional Coagulopathy:

- 50% of massively-transfused patients develop an INR >2.0¹
- 33% of massively-transfused patients develop platelet count < 50 X 10⁹ ¹
- Lab values should be used to determine need for component therapy
- Ratio of red cells:plasma:platelets should only be used when transfusion is so aggressive that lab values are not “real time”

Hypothermia:

- During massive transfusion, an approved and properly maintained blood warmer should be used
- Mortality after massive transfusion is inversely related to core temperature:
 - <34°C - 40%
 - < 33°C - 69%
 - < 32°C - 100% ¹
- Consequences of hypothermia include platelet dysfunction, reduced clearance of citrate, decreased cardiac output, hypotension, arrhythmias and ECG changes ¹

Citrate Toxicity (Hypocalcemia, hypomagnesemia)

- Citrate is the anticoagulant used in blood components
- Citrate binds calcium and magnesium

Metabolic acidosis

- Rare, but may result from the acid pH of blood products.

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Hyperkalemia

- Potassium is released from stored red cells, and the amount of potassium increases with storage time
- For pediatric patients < 10kg who are receiving > 20mL/kg of packed cells in a 24 hour period, packed cells are spun down and the supernatant (extra-cellular potassium) is removed
- ALL other patients who are receiving massive transfusion – potassium should be monitored.

Delayed Adverse Effects of Blood Transfusion

Sensitization and development of antibodies

- Antibodies to red cell antigens, platelet antigens, HLA and plasma proteins may develop following transfusion.
- This may result in destruction of red cells, febrile or allergic reactions and platelet refractoriness.

Delayed Hemolytic Transfusion Reactions

Incidence: 1 in 6715 units of RBCs¹
1 in 5500²

Note: Detection of new antibodies following transfusion (often due to amnestic response) and/or development of a positive Direct Antiglobulin Test is more common, but does not usually result in a hemolytic reaction, although there may be reduced survival of transfused red cells.

Transfusion Associated Graft versus Host Disease (TA-GVHD)

Incidence: Rare (leucoreduction of red cells and platelets reduces incidence)^{1,2}

Cause: Donor's lymphocytes in the blood product transfused, mount a reaction against HLA determinants on the recipient's cells in the immunoincompetent patient.
In immunocompetent patients, HLA similar (Directed donation from parent to child) blood products places the recipient at risk for developing TA-GVHD.

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Prevention: Patients at risk (immunoincompetent) must receive irradiated blood products.
All blood products that are HLA matched, or from a first degree relative must be irradiated.

Post-transfusion Purpura (PTP)

Incidence: Unknown, more frequent with female patients due to sensitization from previous pregnancies¹

Cause: 75% of cases reported are due to HPA-1a positive red cells, plasma or platelets transfused to a patient that has developed anti-HPA-1a
Clinical presentation includes decreased platelet count (usually $< 10 \times 10^9/L$) following transfusion of either red cells, plasma or platelets
Laboratory confirmation of platelet antibody is required to confirm PTP

Viral Infections

Incidence: HIV: 1 in 4.7 million¹
HCV: 1 in 3.1 million¹
HBV: 1 in 82,000¹ (Risk of clinical disease is 1 in 1.2 million)²
HTLV: 1 in 3 million¹
WNV: <1 in 1 million¹
CMV: Low, but not quantifiable; significant clinical disease is rare²

Blood Transfusion Lab should be contacted if transfusion transmitted viral infection is suspected
Continued vigilance in both donor screening and testing of donors is required to maintain and reduce any viral infection risk to the blood supply. Whenever possible, blood components/products that are virally inactivated should be chosen above blood components that are not virally inactivated

Immune Modulation

Several studies have noted an increase in the frequency and severity of infection in patients receiving allogeneic blood²
There is continued controversy as to whether allogeneic blood transfusion contributes to cancer recurrence²
Leukoreduction of the blood supply should reduce these possible risks of transfusion

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References

1. Callum JL, Pinkerton PH. BloodyEasy2: Blood transfusions, blood alternatives and transfusion reactions: a guide to transfusion medicine. 2nd ed:2005.
2. Physician's Guide 2004: Physician's guide for blood and blood product utilization. British Columbia Provincial Blood Coordinating Office. <http://www.pbco.ca/images/Resources/Publications/ic%202003%20final%20with%20changes.pdf>