1. **Principle**

To investigate suspected transfusion reactions.

1. **Scope and Related Policies**

The same test methods used for the crossmatch should also be used for the initial investigation.

* 1. There shall be policies and procedures for documentation, reporting, evaluation and follow-up of all transfusion reactions. A list of common signs and symptoms of suspected transfusion reactions must be included in both the nursing and hospital TS policy manuals.9.1
  2. In the event of a suspected transfusion complication, the personnel attending the patient shall immediately notify the TS and the physician ordering the transfusion. Records of the complication shall be maintained in the patient’s medical record.9.2
  3. The patient shall be observed during the transfusion and for an appropriate time thereafter for suspected adverse reactions.
  4. All suspected hemolytic transfusion reactions shall be investigated immediately. The transfusion must be stopped and the intravenous access maintained with 0.9% sodium chloride solution..9.1
     1. If there are symptoms or findings suggestive of an immediate transfusion reaction, the transfusion should be interrupted and evaluated. The evaluation shall not delay proper clinical management of the patient.
     2. Circulatory overload or mild allergic reactions (e.g., urticarial) need not be evaluated as possible hemolytic transfusion reactions.
  5. The hospital TS must maintain indefinitely the records of patients who have had serious transfusion complications or evidence of alloimmunization. Records of other transfusion complications should be retained for at least 5 years.9.1
  6. Interpretation of the reaction investigation shall be recorded in the patient medical record, and if suggestive of a hemolytic transfusion reaction (HTR), bacterial contamination or other serious complication of transfusion, shall be reported immediately to the attending physician.9.2
  7. All clinically significant transfusion reactions (including fatalities) shall be reported to the blood supplier within the required time frame for reporting to Health Canada or blood product manufacturer.9.1
  8. All cases of suspected transfusion transmitted disease shall be reported to the hospital TS and to the blood supplier or blood product manufacturer.9.1
  9. There shall be a system in place to identify all blood products implicated in cases of suspected transfusion-transmitted diseases. A record of these blood products and their unit numbers must be sent to the blood supplier.9.1
  10. Empty blood product containers should be returned to the TS on reported transfusion reactions as requested by the TS.
  11. When an error has resulted in the incorrect identification of a patient or specimen or a laboratory error is discovered, each step of the process shall be reviewed to find the source of error and corrective action initiated to prevent recurrence.

1. **Specimens**

# Pre-transfusion specimen

Post-transfusion specimen

Remainder of unit (or empty bag) with which the complication occurred, if available

Administration tubing, if available

Post-transfusion urine sample (if indicated)

1. **Materials**

# **Supplies:** Health Canada

# Canadian Transfusion Adverse Event Reporting Form

Worksheet or request form used for compatibility testing

1. **Quality Control**

## A clerical check must be performed to determine if any patient identification or blood product identification error has occurred.

* 1. All adverse reactions or incidents must be documented, investigated and corrective actions take if applicable.
  2. Although all types of transfusion reactions cannot be investigated in the laboratory, a comprehensive list of signs and symptoms associated with types of transfusion reactions is valuable in assisting personnel in determining the cause of the transfusion associated conditions. See table in Procedural Notes 8.8.

**TRANSFUSION REACTION CATEGORIES USED TO DETERMINE TESTING PROTOCOL**

|  |  |
| --- | --- |
| **CATEGORY** | **TYPE OF INVESTIGATION AND TESTING PROTOCOL** |
| PRODUCT  All Products | Visual and Clerical Check performed only if mild  If anaphylaxis may request IgA level and antibody testing  If consistent with TRALI, may request HLA testing |
| BASIC  For red cells only; Chills, Fever, Urticaria, Flushing | DAT, ABO, Rh and antibody screen performed on pre and post transfusion specimens |
| FULL  For red cells only: Hemolytic, Chills, Fever, Hypotension, Renal Failure  Moderate to Severe  Reactions of patients with known antibodies | ABO, Rh, DAT performed on Pre and Post transfusion specimens and implicated units  Repeat antibody screen and perform a serological crossmatch using pre and post transfusion specimens |
| BACTI  All products  Fever, Shock, DIC | Request return of implicated units and send for bacteria culture |

1. **Procedure**

When the TS is notified that a patient receiving a transfusion may be having a reaction, the technologist should perform the following steps.

|  |  |
| --- | --- |
| **STEP** | **ACTION** |
| 1. Determine type of reaction investigation indicated (PRODUCT, BASIC, FULL) | 1. Ask what the symptoms are  |  |  | | --- | --- | | ***If*** | ***Then*** | | the symptoms are that of a BASIC or FULL investigation | Go to step 6.2 | | symptoms are that of PRODUCT | Go to step 6.3 | |
| 1. Symptoms are that of a BASIC or FULL investigation | 1. Advise the nursing staff to:  * Stop the transfusion. Notify the attending physician of the symptoms. * Flush normal saline through the lines while they wait for the  physician's instructions * Determine that the patient information on the compatibility label matches the information on the patient identification wristband * Document the symptoms and the action taken on the Notification of Transfusion Reaction form – RT.012F1 * The completed form along with a post transfusion specimen (collected as per established procedure), product bag and  administration set implicated in the reaction are to be sent to the TS * If requested by physician, have first voided urine sent to the TS |
| 1. Symptoms are that of PRODUCT | 1. Advise the nursing staff to:  * Stop the transfusion. Notify the attending physician of the symptoms * Flush normal saline through the lines, maintaining I.V. access while they wait for the physician's instructions. The physician may prescribe an antihistamine * Determine that the patient information on the compatibility label matches the patient identification wristband * Document the symptoms and action taken on RT.012F1 – Notification of Transfusion Reactions and return the form to the TS * If symptoms disappear, have nurse contact physician to see if transfusion can resume. If symptoms do not disappear or if the physician requests a full investigation, discontinue the transfusion and follow step 6.2.1 |
| 1. Receive post-transfusion  specimens and bag  with attached administration set and form RT.012F1 | 1. Check for clerical errors:  * Retrieve the compatibility label (must be still attached to the blood product container) and check for errors. Ensure that the blood types of the donor and patient are compatible and that the correct tag is attached to the correct blood product container * Retrieve the pre-transfusion specimen and request form or worksheet. Ensure that the information on both coincides exactly and that they match the compatibility label  |  |  | | --- | --- | | ***If*** | ***Then*** | | a clerical error is discovered | * Notify the TS Medical Director or designate immediately * Initiate a search of appropriate records to determine whether misidentification or incorrect use of other specimens, or issue of components has put other patients at risk   Complete an incident report and submit it to a supervisor and/or TS Medical Director or designate |  1. Centrifuge the post-transfusion specimen and visually inspect the plasma for hemolysis.   Compare the plasma of the post-transfusion specimen with  the plasma of the pre-transfusion specimen.   |  |  | | --- | --- | | ***If*** | ***Then*** | | hemolysis is present in the  post-transfusion specimen | Contact the phlebotomist to  ensure that the venipuncture was not a difficult draw.   |  |  | | --- | --- | | ***If*** | ***Then*** | | a difficult collection is suspected | have a second specimen drawn and repeat visual inspection of plasma | | specimen was drawn more than 5-7 hours after the suspected reaction | see Procedural Notes 8.1 | |  1. Perform a direct antiglobulin test (DAT) on the post-transfusion EDTA specimen. See RT.007 – Direct  Antiglobulin Test and GM.009 – Direct Antiglobulin Test – Anti-IgG Gel Card  |  |  | | --- | --- | | ***If*** | ***Then*** | | post-reaction specimen DAT is positive | perform a DAT on the pre-transfusion specimen (unless this has already been done as a part of pre-transfusion testing) | | results are not as expected | continue as for a FULL reaction |  1. Perform ABO/RH and Antibody Screen. See ABO Grouping RT.004, Rh Typing RT.005 and Antibody Screen– Saline, LISS, Peg RT.008 and GM.004 – Antibody Screen – Anti-IgG Gel Card  * If results are not as expected continue as for a FULL reaction |
| 1. Receive urine sample | 1. Perform the following if a urine sample has been received  * Visually inspect the sample and record the results * If any segment of the stick is positive record results and send sample for a STAT complete urinalysis * Test the urine with a 'Multistick' using the directions on the container * If negative report the results * See Procedural Notes 8.2 |
| 1. Continue on to Full Reaction Investigation | 1. Examine the blood remaining in the unit and the administrative tubing for evidence of hemolysis, especially if a non-immune HTR is suspected. See also Procedural Notes 8.4 for non-immune hemolysis. 2. Perform Serological Crossmatch testing on the pre- and post-reaction specimens as well as on the donor unit(s) in question. See RT.011– Antiglobulin Crossmatch, Saline, LISS, PEG or GM.006 – Crossmatch – Anti-IgG Gel Card.  ***Note: use same method for crossmatch as was used for antibody screen***  |  |  | | --- | --- | | ***If*** | ***Then*** | | results are not as expected | Suspect a specimen mix up or mislabeling incident; another patient’s specimen may also have been incorrectly labeled. The person discovering the error must complete an incident report. The process should be reviewed to ensure that the root cause of errors is identified and, when applicable, procedures and processes revised to prevent recurrence | | a previously undetected antibody or positive DAT is discovered | Eluates and antibody identification testing should be done. If the antibody is discovered in the post-transfusion specimen but not the pre-transfusion specimen, suspect passively acquired antibodies from the blood product. In this situation perform an Antibody Screen on the donor unit plasma if possible. Alternatively, an anamnestic response resulting in antibody production following a previous transfusion or pregnancy may have occurred. All donor units transfused must be re-typed for the corresponding antigen that the patient has formed the antibody against. See NRT.009 – Antigen Typing – Direct and Indirect Agglutination | |
| 1. Complete paperwork | 1. Ensure that the results of the transfusion reaction investigation are reviewed by the TS Medical Director or designate 2. File the results of the investigation and the TS Medical Director or designate review |
| 1. Additional activities for special circumstances | |  |  | | --- | --- | | **Anaphylactic** | If the symptoms suggest an anaphylactic reaction, send a pre-transfusion specimen for quantitation of IgA levels and testing for anti-IgA. IgA deficient blood products should be provided until the results of the test for anti-IgA are available and have been evaluated (contact local CBS site for instructions on submitting sample for IgA testing). | | **Bacterial** | Examine the returned unit for any abnormal appearance, including clots or any brownish, opaque, muddy, or purple discoloration. If symptoms  suggest bacterial sepsis, a gram stain and aerobic and anaerobic culture of the contents of the bag should be done. See Procedural Notes 8.5, 8.6 and 8.7. | | **TRALI  .** | If symptoms and/or clinical presentation suggest TRALI, notify the blood supplier to test the donor plasma for HLA antibodies and send a pre- transfusion sample for HLA typing | | **Transfusion Transmitted Disease** | When a physician contacts the TS to report a suspected transfusion transmitted disease or any other type of transfusion complication as described in 8.8, fax a Notification of Delayed or Disease Transmission Transfusion Complication form– RT.012F2 to the physician’s office. Instruct the physician to return the form to the hospital TS as soon as possible. | | **Notification of Delayed Transfusion Reaction or Disease Transmission, Transfusion Complication form – RT.012F2** | |  |  | | --- | --- | | ***If*** | ***Then*** | | Delayed transfusion reaction is suspected | an antibody screen should be collected and tested on a post-transfusion specimen. If an antibody is identified, complete section “D” of the notification form. Sign and date the form and refer to a TS Medical Director or designate for review. Complete a history file record on the patient if the antibody is clinically significant | | Transmissible disease is suspected | a traceback should be initiated. Complete the blood supplier’s form for traceback notification and the hospital’s history record of units transfused to the patient | | |

1. **Reporting**
   1. Report all severe complications of transfusion to the blood supplier, manufacturer, and Provincial Surveillance (TTISS Ontario) as applicable. Fatalities must be reported within one working day and a written report submitted within seven days. Further information may be obtained from the CBS Circular of Information and Clinical Guidelines for the use of human blood and blood components.9.3
   2. Results of transfusion reactions should be reviewed by the TS Medical Director or designate and the interpretation of the results should be retained on the patient medical record.
2. **Procedural Notes**
   1. If the post-transfusion specimen is not drawn until 5-7 hours after an episode of acute hemolysis, hemoglobin degradation products, especially bilirubin, may be in the bloodstream and cause yellow or brown discoloration. Rising bilirubin may begin as early as one hour post reaction, peak at 5-7 hours and disappear within 24 hours if liver function is normal.
   2. The post-transfusion urine may be examined for hematuria, hemoglobinuria and myoglobinuria. In acute hemolytic transfusion reactions, free hemoglobin released from damaged cells can cross the renal glomeruli and enter the urine, but hematuria and myoglobinuria would not be expected. Urine examination should be done on the supernatant fluid after centrifugation of a freshly collected specimen; misleading free hemoglobin may be present if previously intact red cells in a specimen undergo in-vitro hemolysis during transportation or storage.
   3. If transfused incompatible cells have been coated with antibody but not immediately destroyed, the post-reaction specimen DAT is likely to be positive, often with a mixed field agglutination pattern. If the transfused cells have been rapidly destroyed, the post-transfusion DAT may be negative if there has been a delay in collection of the post-transfusion specimen. Non-immune hemolysis (e.g., overheating or freezing of the unit) causes hemoglobinuria but not a positive DAT.
   4. If blood in the administration tubing is hemolyzed and the blood in the unit is not, a faulty infusion device may be the cause. If the blood in both the unit and the administration set is hemolyzed, suspect a physically hemolyzed unit or the addition of a solution to the container that destroyed the cells.
   5. Investigation of blood components/products implicated in a suspected bacterial sepsis shall include a gram stain and culture of product (incubation at 25° C and 35° C). Segments should not be used as they may not be representative of the infused product.
   6. Treatment for suspected bacterial contamination should be based on clinical considerations as delay in therapy may result in severe morbidity or death. Treatment includes prompt intravenous administration of antibiotics after blood and other appropriate cultures are obtained, combined with therapy for shock.
   7. Notification of blood supplier must occur promptly if bacterial contamination of blood component/product is suspected as components from the same donor may also potentially be contaminated.
   8. The following chart identifies signs and symptoms associated with various types of transfusion reactions.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Reaction Type | | Etiology | | Signs and Symptoms |
| **Acute (<24 hours)** | | | | |
| Hemolytic (HTR) – Immune | Red cell incompatibility | | Chills, fever (at least 38°C and an increase of at least 1°C from baseline)  Hemoglobinuria, renal failure, hypotension, DIC, oliguria, oozing from IV site, back pain, pain along infusion vein | |
| Hemolytic (HTR) – non immune | Physical or chemical destruction of blood (freezing, heating, hemolytic drug or solution added to blood) | | Hemoglobinuria | |
| Sickle cell hemolytic transfusion reaction | Multiple theories; most common is bystander immune cytolysis or the development of autoantibodies | | Same symptoms as a sickle cell pain crisis. Development of a more severe anemia after transfusion than was present before transfusion | |
| Hypotensive episodes associated with ACE inhibition | Inhibited metabolism of bradykinin with infusion of bradykinin or activators of prekallikren | | Flushing, abrupt onset of hypotension with or without mild respiratory symptoms, shortly after the beginning of the transfusion | |
| Fever/chill, non hemolytic | Antibody to donor leukocytes;  accumulated cytokines in bag | | Rigors, fever (at least 38°C and an increase of at least 1°C from baseline), headache, malaise, vomiting | |
| Allergic | Antibody to donor plasma proteins | | Pruritis, rash, urticaria, flushing | |
| Anaphylactic | Antibody to donor plasma (most commonly anti-IgA) | | Urticaria, erythema, anxiety, respiratory distress, hypotension, laryngeal/pharyngeal edema, bronchospasm | |
| Circulatory overload | Volume overload | | Dyspnea, orthopnea, productive cough with pink frothy sputum, tachycardia, hypertension, headache | |
| Transfusion Related Acute Lung Injury (TRALI) | Anti HLA or anti-neutrophil antibody in donor plasma reacting with recipient antigens | | Acute respiratory distress with or without hypotension within 1-2 hours of the transfusion of plasma containing blood components | |
| Hypocalcemia | Massive transfusion of citrated blood and/or delayed metabolism of citrate | | Paresthesia, tetany, arrhythmia | |
| Bacterial contamination | Infusion of bacterially contaminated blood products | | Fever (at least 38°C and an increase of at least 1°C from baseline), tachycardia, rigors, shock, DIC, nausea, vomiting, shortness of breath, lumbar pain, rise or drop in systolic pressure, circulatory collapse. Any of these symptoms within four hours of the blood transfusion event. No evidence of hemoglobinemia or hemoglobinuria | |
| Hypothermia | Rapid infusion of cold blood | | Cardiac arrhythmia | |
| Air Embolism | Transfusion of air into vein | | Sudden onset of severe hypotension, breathlessness, cyanosis and collapse | |
| Hyperkalemia | Transfusion of large volumes of older blood with high supernatant potassium levels | | Cardiac arrhythmia | |

|  |  |  |
| --- | --- | --- |
| **Reaction Type** | Etiology | Signs and Symptoms |
| **Delayed (>24 hours)** | | |
| Alloimmunization | Immune response to foreign antigens on RBC, or WBC (HLA) and platelets | Usually none, but may result in platelet refractoriness, difficulty finding compatible blood for subsequent transfusion, delayed hemolytic transfusion reactions and hemolytic disease of the newborn |
| Hemolytic | Anamnestic immune response to RBC antigens | Weakness, unexplained fall in hemoglobin, elevated serum bilirubin |
| Graft versus host disease | Functioning lymphocytes transfused to immunosuppressed patient; may occur in immunocompetent patient receiving HLA-matched lymphocytes | Erythroderma, maculopapular rash, anorexia, nausea, vomiting, diarrhea, hepatitis, pancytopenia, fever |
| Post transfusion purpura | Platelet antibodies (usually against HPA-1a) | Purpura, bleeding, fall in platelet count 8-10 days following transfusion |
| Immunomodulation | Incompletely understood interaction of donor WBC or plasma factors with recipient immune system | Tolerance induction, post surgical wound infection, possibly other transfusion effects |
| Iron overload | Multiple transfusions in transfusion dependent patients | Cardiomyopathy, arrhythmia, hepatic and pancreatic failure |
| Hypocalcemia | Massive transfusion of citrated blood and/or delayed metabolism of citrate | Paresthesia, tetany, arrhythmia |

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| --- | --- | --- | --- |
| Bacterial contamination | Infusion of bacterially contaminated blood products | | Fever ((at least 38°C and an increase of at least 1°C from baseline), tachycardia, rigors, shock, DIC, nausea, vomiting, shortness of breath, lumbar pain, rise or drop in systolic pressure, circulatory collapse. Any of these symptoms within four hours of the blood transfusion event. No evidence of hemoglobinemia or hemoglobinuria |
| Hypothermia | Rapid infusion of cold blood | | Cardiac arrhythmia |
| Air Embolism | Transfusion of air into vein | | Sudden onset of severe hypotension, breathlessness, cyanosis and collapse |
| Hyperkalemia | Transfusion of large volumes of older blood with high supernatant potassium levels | | Cardiac arrhythmia |
| Other - Transfusion Transmitted Diseases | | | |
| Blood routinely tested for | | **Blood not routinely tested for** | |
| * Antibodies to Human Immunodeficiency Virus (HIV 1 and 2) Hepatitis C (HCV) * Human T-Cell Lymphotrophic Virus (HTLV I and II) Hepatitis B core antigen * Syphilis * WNV RNA * HIV, HCV and HBV nucleic acid testing | | * Hepatitis A (HAV) * Hepatitis D (HBV screening does reduce risk) * Hepatitis E * Hepatitis F * Hepatitis G * TT Virus (TTV) * Antibody to CMV (selected unit testing) * Epstein-Barr Virus (EBV) * Human Herpes Virus 6 (HHV-6) * Human Herpes Virus 7 (HHV-7) * Human Herpes Virus 8 (HHV-8) * Human Parvovirus B19 (HPV-19) * Creutzfeld-Jakob Disease (CJD) * Lyme disease * Malaria * Chagas disease (high risk donors tested) * Leishmaniasis * Babesiosis * Toxoplasmosis * Microfiliariasis | |

1. **References**
   1. Standards for Hospital Transfusion Services Version 3 – February 2011. Canadian Society for Transfusion Medicine, 7.1.1, 7.2, Appendix A..
   2. Standards for Blood Banks and Transfusion Service, 28th ed. Bethesda, MD: AABB, 2012; 7.4.1, 7.4.2, 7.4.3, 7.4.5.
   3. Circular of information for the use of human blood and blood components. Canadian Blood Services, http://blood.ca/CentreApps/Internet/UW\_V502\_MainEngine.nsf/page/E\_COI?OpenDocument.
   4. Roback JD, ed. American Association of Blood Banks Technical Manual, 17th ed. Bethesda, MD: AABB, 2011: 727-762.
   5. Ontario TTISS Transfusion Reaction Chart, version 1.1- June 2010
2. **Revision History**

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| --- | --- |
| **Revision Date** | **Summary of Revision** |
| January 31, 2014 | * Revised title to Investigation of Transfusion Complications for consistency * Global changes – TML to TS and Medical Chief to TS Medical Director * Revised wording to include “access maintained with 0.9% sodium chloride solution” in section 2.4. * Added clarification on category of reactions to table in 5.3. Changed reaction PLATLETS/PLASMA to PRODUCT to be consistent with 6.1.1 b) * Revised 6.1.1 and 6.2.1 to put Stop the transfusion first. * Revised 6.3.4 with corrected procedure numbers * Clarified wording in 6.5 * Added pregnancy to 6.5.2 * Added ‘contact local CBS… for IgA testing’ * Changed history/file card to history record in 6.12 * Changed National to Provincial and added Ontario to TTISS in 7.1 * Clarified wording in 8.5 and 8.7 * Updated table (section on transfusion transmitted diseases) in 8.8 * Revised wording to the table to include a fever of “at least 38ºC and an increase of at least 1ºC from baseline.” * Updated references 9.1, 9.2 & 9.4 to the most recent versions/ editions. |

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| **Revision Date** | **Summary of Revision** |
| January 31, 2014 | * Revised wording to include “maintain I.V. access with 0.9% sodium chloride” to the Instructions to Nursing Staff * Revised wording to the Signs and symptoms to include a fever of “at least 38ºC and an increase of at least 1ºC from baseline.” * Revised Pathologist to TS Medical Director |

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| **Revision Date** | **Summary of Revision** |
| January 31, 2014 | * Revised Pathologist to TS Medical Director |

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