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Document Contact	Kelly Sartor: Mgr, Division Laboratory
Area	Laboratory-Blood Bank
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Transfusion Reaction Investigation & Workup

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

This document will provide instructions for the Blood Bank staff to perform a suspected Transfusion Reaction investigation.

II. SCOPE

A. A suspected transfusion reaction investigation involves the patient's nurses and physicians, the laboratory staff, and the Blood Bank Medical Director.

B. The scope of this document is primarily on the medical technologist's and pathologist's roles and responsibilities in the process.

III. INTRODUCTION:

A. Although it is believed that today's blood supply is safer than at any time in history, it is still impossible to prevent or predict all transfusion risks. Therefore, it is imperative that all staff involved with the blood transfusion process recognize possible adverse reactions to a transfusion.

B. The standard transfusion reaction evaluation includes clerical checks, testing on the post-reaction sample and possible testing on the pre-transfusion sample and donor unit. At the conclusion of the evaluation, the Medical Director considers the patient's adverse reactions and laboratory results and classifies the type of reaction.

C. There are numerous transfusion reaction classifications. These include febrile non-hemolytic, acute or delayed hemolytic, delayed serologic, bacterial contamination, allergic, TACO (Transfusion Associated Circulatory Overload), and TRALI (Transfusion Related Acute Lung

Injury) among others.

D. Urticarial reactions occur in 1-3% of all transfusions and are believed to be caused by antibodies in the recipient to donor plasma proteins. Urticarial reactions are characterized by urticaria (hives) and/or pruritus (itching). If an urticarial reaction resolves with antihistamine therapy, the transfusion may be resumed and serologic testing is not indicated. Urticarial reactions that resolve with antihistamine therapy are the only type of reaction in which the transfusion may be resumed.

IV. ADVERSE REACTION SIGNS AND SYMPTOMS:

A. fever (38°C or greater **AND** at least 1°C or 2°F above pre-transfusion temperature)
B. chills, with or without rigors (shaking)
C. hives, itching
D. respiratory distress including wheezing, coughing, or dyspnea (shortness of breath)
E. changes in systolic blood pressure (↑ or ↓ of 30 mm Hg)
F. tachycardia (≥ 120 bpm or ↑ 40 bpm)
G. hemoglobinuria (red urine)
H. jaundice
I. shock
J. skin manifestations, including color changes and localized edema
K. abdominal, chest (angina), back, flank, infusion site, or other unusual pain

V. DEFINITIONS:

Use this section to define words and/or phrases, which may be unfamiliar or not readily understood by all users. Your intent should be that users clearly understand what the policy or procedure says. Not every policy and procedure will require definitions.

A. Pathologist: Transfusion Medicine/Blood Bank (TM/BB) Medical Director or Pathologist or any pathologist or fellow on TM/BB service.
B. Pre-transfusion sample: the sample drawn *before* the transfusion reaction, and tested according to Operating Procedures.
C. Post-reaction sample: the sample drawn *after* the transfusion reaction and tested according to the procedures in this document .
D. WBIT: wrong blood in tube, when a sample is drawn from the wrong patient so that the identifying information on the label does not correlate with the blood in the tube.
E. Mistransfusion: when a blood component is transfused to a patient who was not the intended recipient.
F. Hemolytic transfusion reaction: the immunologic destruction of transfused RBCs, nearly always due to incompatibility of an antigen on transfused cells with an antibody in the

recipient's circulation; i.e., transfusion of ABO incompatible RBCs. Laboratory indications of a hemolytic transfusion reaction include a positive DAT and hemolysis in the 2nd post-reaction sample.

G. EHR: Electronic Health Record

H. BBIS: Blood Bank Information System

I. LIS: Laboratory Information System

J. TRALI: Transfusion Related Acute Lung Injury, a transfusion reaction associated with acute increased permeability of the pulmonary microcirculation, usually occurring within 6 hours of transfusion and requiring aggressive respiratory support.

K. TACO: Transfusion Associated Circulatory Overload, an event associated with the transfusion of excessive volumes or at excessively rapid rates which can lead to pulmonary edema, especially in elderly patients.

L. TAD: Transfusion Associated Dyspnea, characterized by respiratory distress occurring within 24 hours of transfusion that does not meet the criteria of TRALI, TACO, or allergic reactions. Note: respiratory distress should not be explained by the patient's underlying condition.

M. TTI: Transfusion Transmitted Infection

VI. SPECIMEN COLLECTION AND HANDLING:

The preferred specimen is a properly labeled 6 mL EDTA sample. The post-transfusion specimen must be collected after the transfusion is stopped. The pre-transfusion specimen (if available) will also be evaluated. See Transfusion Medicine policy Identifying and Triaging Acceptable Samples for Testing

VII. FORMS:

A. Blood Culture Order Form

B. Transfusion Reaction investigation Form

VIII. POLICIES:

A. **Training of Personnel Involved in the Transfusion of Blood Components**

1. All personnel involved in transfusion must be trained in the identification of transfusion recipients and blood components, and in the observation of recipients during and after transfusion for adverse reactions, with in-service education at least annually.
2. All personnel who administer blood components must be trained to identify transfusion recipients and components and to closely observe patients during and for a period of time after blood administration.

B. This training includes a mandatory on-line, self-paced course *Blood Product Administration*. This course includes the recognition of transfusion reactions and must be completed every year by nurses and by the Blood Bank medical technologists.

C. Suspected transfusion reactions should be reported immediately to the Blood Bank by the

caregivers.

D. **Notification of the Medical Director**

1. Blood Bank staff will notify the Medical Director immediately in the following cases:
2. Transfusion of an incompatible RBC product (consider ABO, Rh, and other blood group systems)
3. Bacterial contamination of a transfused blood product, refer to Transfusion Medicine policy, Suspected Bacterial Contamination of a Transfused Component.
4. "Wrong Blood in Tube" collection errors coupled with a suspected transfusion reaction
5. Mistransfusion of a blood component (refer to the *Definitions* section / mistransfusion)
6. Significant adverse reaction to transfusion (i.e. Significant hemolysis in the post transfusion specimen)
7. Suspected acute hemolytic transfusion reactions

E. **Critical Value Notification**

A suspected acute hemolytic transfusion reaction is defined as a critical value. The Blood Bank Medical Director (or designee) and the patient's caregiver will be notified of the critical value immediately. The **CVRXN** code is used to document the notification. For additional information, refer to, Critical Value Notification Policy – Transfusion Medicine.

F. **Communication with the Blood Supplier**

In some cases, the Blood Bank Medical Director or supervisor is required to notify the blood supplier and/or outside agencies. Refer to section, Roles and Responsibilities of the Blood Bank Medical Director for Transfusion Reaction Evaluations.

G. **Serologic Indications for Possible Delayed Transfusion Reaction**

1. Blood Bank staff will consult the pathologist to determine whether a transfusion reaction evaluation should be ordered if each of the following conditions is met:
    a. The patient has a positive antibody screen on the current sample in which new, unexpected antibody reactivity is detected, and
    b. An antibody screen performed within last four (4) weeks was negative, or did not demonstrate the same unexpected reactivity present in the current sample, and
    c. The patient received a RBC transfusion in the last four (4) weeks, and
    d. Either transfused RBC is antigen positive (via testing of RBC segments, or statistical probability of antigen exposure if >6 RBC units transfused over 4 weeks) or the new antibody is detectable in the patient eluate.
2. The Medical Director's instructions will be documented in the blood bank computer as a comment.

H. **Reporting of Fatal Transfusion Reactions**

Any transfusion reactions that are thought to have contributed to a patient’s death must be reported, preferably by the Pathologist, to the United States (U.S.) Food and Drug

Administration (FDA) in accordance with Transfusion Medicine, Notification Process for Transfusion Related Fatalities.

IX. PROCEDURE:

A. Nursing

1. The nurse administering the blood component should:
    a. Stop the transfusion.
    b. Notify patient's provider and the blood bank of suspected transfusion reaction.
    c. The patient's physician or any Blood Bank personnel (Medical Director, Supervisor, Medical Technologist) have discretion to initiate a transfusion reaction workup.
    d. A transfusion reaction work up will be placed STAT if indicated.
    e. Refer to clinical policies *Blood/Blood Components Administration - Adults and Pediatrics* and *Blood/Blood Components Administration-Neonatal Services* for additional information.
2. Reaction symptoms should be documented in the EHR or documented on a downtime transfusion form if the EHR is not available.

B. Blood Bank

1. If a call or an order is received in the blood bank reporting a suspected transfusion reaction, verify:
    a. The blood has been stopped.
        i. For any symptom(s) except urticaria (hives/itching), communicate that the transfusion cannot be continued.
    b. A clerical check of the unit and the patient being transfused has been made by the transfusionist.
    c. A Transfusion Reaction Workup (LAB647) has been ordered in the EHR.
        i. If urticaria (hives/itching) is the ONLY symptom, the transfusion may be resumed with clinical provider's approval after treatment and resolution of symptoms. However, a Transfusion Reaction Workup still needs to be initiated but a post-transfusion sample does not need to be collected.
2. Request that the transfusionist return the component bag back to the blood bank, along with the attached tubing and IV solutions. Note: Units Retrieval of a transfused unit discarded in biohazard bin should not occur.
3. Request nursing staff and/or lab phlebotomy collect the post transfusion EDTA specimen.
4. Document the Communication Log or Board with a notation about the pending reaction investigation.

a. **Additional blood products can not be issued until after completion of clerical/technological components of the serological investigation or if the investigation identifies positive findings (i.e. positive DAT).** Exception: Pathologist may approve the issue of products prior to the completion of the serological investigation in an emergent or urgent situation when requested by clinician. Document the approval in the BBIS and follow Transfusion Medicine procedure, Emergency Issue of Blood Products.

5. Gather the following items:
    a. The dispense form and retained portion of the P-Tag
    b. The blood component bag; including (whenever possible), the entire administration set and the intravenous solutions, with the needle removed. The bag tag should still be attached.
    c. The pre-transfusion sample
    d. The post-reaction sample
    e. *Transfusion Reaction Investigation Form*
6. With a Sharpie, write the words "pre" and "post" on the corresponding patient samples.
7. Reprint and affix a Beaker accession label for the TXRX Workup sample in the space provided on the reaction investigation form.
8. **Perform Clerical Checks.**
   These steps will documented in section I of the Transfusion Reaction Form and in the BBIS as described in the Transfusion Medicine policy, SafeTrace (Blood Bank Application). After performing each of the following steps, place your initials in the space provided in Section I on the *Transfusion Reaction Investigation Form* to signify that you performed the step.
9. **Patient Verification**:
    a. Document the patient's name in the space provided. Verify that the patient's name matches and is accurate in for each of the locations listed (in the non shaded areas) on the workup form. Place a check mark in the appropriate boxes on the form to signify that the clerical check for the patient's name is satisfactory.
    b. Repeat step above for the patient's medical record number (MRN), B#, patient's ABORh, donor unit #, and donor ABORh.
    c. If patient verification is confirmed enter "Yes"
    d. If there are any discrepancies in any of these checks, notify the Pathologist.
10. **Unit Verification:**
    a. Verify that the correct kind of blood product was issued and transfused by comparing the dispense form with the returned blood product.

b. If product identification was verified, enter Yes. Enter unit number involved in the reaction in the comment.

c. If product identification was not verified or was incorrect, enter No and document details in result comment.

d. If unable to perform unit verification, enter "Not Tested" and document description of unit could not be verified.

11. **Unit Condition:** Perform a visual inspection of the returned blood product and any attached tubing, solutions, etc. as described in Transfusion Medicine policy, Visual Inspection of Blood Products - Blood Bank.

    a. Check the solutions returned. If any solution was used other than 0.9% normal saline, Plasma-Lyte-A Injection pH 7.4 (Baxter Healthcare), Plasma-Lyte-148 (Multiple Electrolytes Injection, Type 1, USP, Baxter Healthcare), or Normosol-R pH 7.4 (Hospira) for red blood cell transfusion (e.g. D5W, lactated ringers) notify the pathologist immediately.

    b. If condition of blood unit and infusion set are verified as satisfactory, enter Satisfactory.

    c. If condition of unit or infusion set was not satisfactory; enter Unsatisfactory and document description in the result comment and/on the form.

    d. If the blood product was not returned to the blood bank, enter "Not Tested".

12. Determine the approximate volume that was transfused if available and document this volume on the form.
    The nurse may have documented this information in the EHR or on a downtime blood product administration form.

13. Determine if the returned product should be send for culture. Refer to Procedure IX.C *Investigation of Suspected Bacterial Contamination* section below.

    a. Indicate whether unit was sent for culture (Y/N) in Section I of the *Transfusion Reaction Investigation Form.*

14. Place the returned product and any attached tubing, solutions, etc. on the quarantine shelf. Do not quarantine the unit in Blood Bank Information System (BBIS); do not return the unit in the BBIS.

15. If investigation was initiated for symptoms of hives/itching only, serological investigation steps are not required.

16. **Perform the serological investigation**
    These steps will documented in section II of the *Transfusion Reaction Investigation Form* and in the BBIS as described in the Transfusion Medicine policy, SafeTrace (Blood Bank Application). After performing each of the following steps, place your initials in the space provided in Section II on the *Transfusion Reaction Investigation Form* to signify that you performed the step.

    a. Document the clerical checks of the post- and pre-reaction samples.

i. The clerical check is documented as "OK" and the interpretation is "pass" if the information noted during the clerical check is complete, accurate, and in agreement (as described above).

ii. The clerical check is documented as "NotOK" and the interpretation is "fail" if the information noted during the clerical check is incomplete, inaccurate, or not in agreement (as described above).

iii. If there are any discrepancies in any of these checks, notify the Pathologist.

17. Spin down the post transfusion sample.
18. Inspect the post- and pre-reaction samples for hemolysis, document the hemolysis check as "-" (hemolysis absent) or "+" (hemolysis present), and interpret as "neg" (hemolysis absent) or "pos" (hemolysis present).
    a. If the post-transfusion sample has greater hemolysis than the pre-transfusion sample then request a second post sample to determine if the first was a result of a traumatic draw.
    b. If the second sample is not hemolyzed, result the non-hemolyzed finding in the BBIS.
    c. If the second sample is still significantly more hemolyzed then the pre-transfusion sample, then:
        i. Result the finding in the BBIS
        ii. Communicate this critical value to the Medical Director and to the patient(s) caregiver immediately. Refer to above policy, *Critical Value Notification*.
        iii. Instruct the caregiver(s) to collect a first post-reaction urinalysis
        iv. Obtain a patient history. Refer to Transfusion Medicine Policy, Obtaining a Patient History
19. Perform ABORh typing (automated or tube method is acceptable) on the post-reaction sample and document the results.
    a. If the pre and post sample ABO and Rh results are not in agreement, then repeat the ABO/Rh testing on the pre and post samples.
    b. If a typing discrepancy still exists notify the Pathologist immediately.
    c. Consider the possibility of a wrong-blood-in-tube (WBIT) collection error, an additional sample may be required for resolution.
20. Perform a DAT on the post-reaction sample and document the results. Refer to Transfusion Medicine policy, Direct Antiglobulin (DAT) Test by Tube Method - Blood Bank
    a. If the DAT on the post-reaction sample is positive, also perform a DAT on the pre-reaction sample and document the results. Note: In a Transfusion Reaction workup the age of the Pre sample can be >24 hours.

b. If the DAT with polyspecific AHG is positive, then a differential DAT shall be performed with anti-IgG and anti-C3b,-C3d AHG.

21. **Additional Studies (Antibody Screen /Eluate) ? :**

a. Compare the strength of post-reaction DAT and the pre-transfusion DAT to determine whether additional studies of the post-reaction sample are indicated.

DAT of the POST Reaction Sample	DAT of the PRE Reaction Sample	Antibody Screen & Eluate on Post Sample Required?
negative	any result or not tested	No
positive, less than or equal strength to the pre-transfusion strength	positive	No
positive with IgG	negative	Yes
positive with IgG, strength greater than strength of pre-transfusion DAT strength.	positive	Yes
Note: If the DAT is positive with complement only consult with pathologist to determine whether to perform eluate.		

i. If an antibody screen is indicated, order the testing in the BBIS and perform testing in accordance with Transfusion Medicine Policy, Antibody Screening

ii. If an eluate is indicated, order the testing in the BBIS and perform testing in accordance with Transfusion Medicine Policy, Eluates.

1. If eluate testing is indicated and the patient's transfusion history indicates that the patient has received ABO-incompatible-plasma components (e.g., plasma, platelets, or cryoprecipitate), then eluate testing with A1 and B cells should also be performed.
2. Eluate Samples from Taylor, Trenton and Wayne will be sent to Dearborn Blood Bank for testing when indicated.

22. **Antigen Typing of Donor Units**

a. If a new antibody was identified in this investigation (e.g., in a panel or eluate), then the segments of any units transfused in the last 2 months should be typed for the antigen corresponding to the newly identified antibody. If a pre-transfusion sample is available (no transfusions in the preceding 90 days), then antigen type the pre-transfusion sample.

b. If the patient had known, historical antibodies at the time of the transfusion reaction and additional testing is indicated, then repeat the antigen typings of the unit implicated in the transfusion reaction.

c. Either transfused RBC is antigen positive (via transfusion of RBC segments, or statistic probability of antigen exposure if >6 RBC units transfused over 4 weeks) or the new antibody is detectable in the patient eluate.

23. **Serologic Crossmatch of the Transfused Unit**

    a. Perform serologic crossmatches with the unit implicated in the transfusion reaction if:

        i. The 2nd post sample is hemolyzed, or

        ii. A new antibody was detected (in a panel or eluate), or

        iii. A transfused unit is found to be positive for an antigen corresponding to the patient's clinically significant antibody.

        iv. Unexplained positive DAT on post transfusion sample with reaction stronger than pretransfusion sample.

    b. Perform a serologic crossmatch using *pre-transfusion* plasma vs. transfused donor cells, and also perform a serologic crossmatch using the *post-reaction* plasma vs. transfused donor cells. Document the crossmatch results on a *Downtime Crossmatch Worksheet*.

    c. Contact medical director immediately for any positive serologic crossmatch after confirming donor unit has a negative DAT.

24. **Result Preliminary Investigation Results in BBIS**

    a. Click Orders tab and select the Order ID of the Transfusion Reaction Order

    b. Select **Edit TxRx**

    c. In **Treatment Code** drop down menu, select "See Progress Note"

    d. In **Reaction Type** drop drown menu, select "Preliminary Complete"

    e. Check **Clerical Check Ok** box

    f. Confirm completion in BBIS by completing Section III of the *Transfusion Reaction Investigation Form* and initial/date.

25. **Submission for Pathologist Review**

    a. Place all paperwork in the review box.

    b. Report will be reviewed for completeness by the Supervisor, Lead Technologist or designee.

    c. Scan or deliver all paperwork associated with this transfusion reaction evaluation to the Medical Director.

C. **Investigation of Suspected Bacterial Contamination**

Bacterial contamination of blood units may occur due to bacteremia in the donor, incomplete

disinfection of the skin site at the time of collection, or breaches of aseptic technique during processing or handling of blood components. Components stored at room temperature, such as platelets, have been particularly associated with bacterial contamination events.

1. Bacterial contamination of a blood product should be considered if:
    a. Patient temperature increases to at least 39°C or greater and at least 2°C over pre-transfusion temperature
    b. Rigors (shaking/chills) with decreased blood pressure
    c. Sepsis or septic shock
    d. The blood unit involved in the reaction is visibly discolored, cloudy or hemolyzed.
2. If indicated send the blood product to Royal Oak Microbiology department for culture.
    a. Complete the attached *Manual Requisition* for "Sterility Culture" with the unit number and date.
3. The Microbiology laboratory will call the Blood Bank and/or Pathologist immediately with all positive results.
4. Immediately notify the patient's nurse as follows:
    a. Inform the nurse that "the Microbiology *Lab has reported growth in a blood component that was returned to the Blood Bank as part of a suspected transfusion reaction; this may or may not represent a contaminated blood component."*
    b. Ask the nurse for the name and pager number of the person who he or she would contact if the patient's condition deteriorates; i.e. the patient's physician or resident.
    c. Immediately notify the pathologist, and provide them with the name and pager number of the person that the nurse would contact.
    d. Document the nurse's employee number, the name and pager of the nurse's contact person, and the laboratory physician's name on the work up report.
    e. If the Pathologist indicates that there is sufficient evidence suggesting that bacterial contamination may have occurred, quarantine any products in house from the same donor and notify Blood Supplier of the possible bacterial contamination so that they can quarantine concurrent products from the same donor.

D. **Suspected TRALI Reaction**:
TRALI is a sudden onset of acute noncardiogenic pulmonary edema. The symptoms occur within 6 hours of the transfusion and mimic acute respiratory distress syndrome. The symptoms include acute respiratory distress, dyspnea, tachycardia, fever, hypotension, pulmonary edema, and hypoxemia. It is often caused by HLA antibodies in the donor's plasma reacting with the patient's neutrophils.

1. If a TRALI Reaction is suspected, contact or call the Pathologist immediately.

2. If upon review the Pathologist believes the symptoms warrant a TRALI investigation, do the following:
    a. Have the provider or nurse order a Reference Lab Send Out for Miscellaneous Tests, with the comment “1 red top and 1 EDTA top; send to blood bank for TRALI rule-out by Blood Supplier”.
    b. Have one 6mL EDTA tube and one 6mL red top tube drawn from the patient and sent to the blood bank.
    c. Notify the blood supplier of the possible TRALI so that they can quarantine any concurrent products from the same donor and quarantine any products in house from the same donor as well.
    d. Blood Bank staff, along with the Pathologist, will complete an Adverse Recipient Event (ARE) form and send it to blood supplier along with the specimens. Note: If evening, night or weekend, this task may wait until the following weekday morning.

E. **Pathologist Review**

1. The Pathologist will assess symptoms and serological workup and direct staff if additional testing is needed.
2. Pathologist will communicate with clinical staff as soon as possible, dependent upon the transfusion reaction assessment.
3. Pathologist will complete the *Pathologist Consult of Reaction (CRXN)* and enter impression directly in the LIS.
4. All paper work will be retained in the Blood Bank.

Refer to Transfusion Medicine procedure, Roles and Responsibilities of Medical Director for Transfusion Reaction Evaluation.

X. REFERENCES:

1. AABB*, Technical Manual*, current edition.
2. AABB, *Standards for Blood Banks and Transfusion Services*, current edition.
3. AABB Circular of Information for the use of Human Blood and Blood Components, current edition.
4. College of American Pathologists, Transfusion Medicine Checklist, current edition.

Attachments

Blood Culture Request Form _4093 JUN 07

Transfusion Reaction Evaluation Form (rev. 07/11/2024)

Approval Signatures

Step Description	Approver	Date
	Kristina Davis: Staff Physician	Pending
	Jeremy Powers: Chief, Pathology	Pending
	Ryan Johnson: OUWB Clinical Faculty	Pending
	Hassan Kanaan: OUWB Clinical Faculty	Pending
	Ann Marie Blenc: System Med Dir, Hematopath	Pending
	Muhammad Arshad: Chief, Pathology	Pending
	Masood Siddiqui: Staff Pathologist	7/16/2024
	John Pui: Chief, Pathology	7/16/2024
Policy and Forms Steering Committe (if needed)	Kelly Sartor: Mgr, Division Laboratory	7/16/2024
	Kristen DiCicco: Mgr, Laboratory	7/16/2024
	Fatima Bazzi: Medical Technologist Lead	7/16/2024
	Katherine Persinger: Mgr, Laboratory	7/16/2024
	Karrie Torgerson: Medical Technologist Lead	7/13/2024
	Hilary Morey: Medical Technologist Lead	7/12/2024
	Ashley Beesley: Mgr, Laboratory	7/12/2024
	Suzanne Chahine: Medical Technologist Lead	7/12/2024
	Teresa Lovins: Supv, Laboratory	7/12/2024
	Kelly Sartor: Mgr, Division Laboratory	7/11/2024

	Kelly Sartor: Mgr, Division Laboratory	7/11/2024

Applicability

Dearborn, Farmington Hills, Grosse Pointe, Royal Oak, Taylor, Trenton, Troy, Wayne