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TRM.4200

TRANSFUSION REACTION

EVALUATION AND COMPLETE WORK UP

Test Code: TRXNV

I. PRINCIPLE

To provide guidelines for suspected transfusion reaction workups and reporting information to the pathologist evaluating the reaction, the FDA and the Compliance/Quality Assurance Committee to trigger a root cause analysis, if indicated.

An acute hemolytic transfusion reaction is triggered by an antigen-antibody reaction and mediated by neuroendocrine responses and by activation of the complement and coagulation systems. Clinically, catastrophic events that may occur include shock, disseminated intravascular coagulation (DIC) and acute renal failure. Life-threatening hemolytic transfusion reactions are almost always due to ABO mismatch attributable to an identification error that results in the recipient receiving the wrong blood. Incompatibility in other blood groups may also cause acute hemolysis or a delayed transfusion reaction in a recipient with alloantibodies stimulated by previous transfusions or pregnancy. These reactions, however, are rarely as severe as those involving ABO incompatibility. Clinically serious nonimmunologic causes of hemolysis include bacterial contamination of the unit of blood, infusion of hypotonic solutions or transfusion of donor blood damaged by excessive pressure, freezing, or overheating.

UnityPoint Health-Pekin will investigate and report transfusion reactions. This includes the Lab/Nursing procedures to report initial signs and symptoms and stop progression by stopping unit transfusion and initiating a transfusion reaction evaluation. The pathologist will interpret the results.

II. CLINICAL SIGNIFICANCE

Some of the initial signs and symptoms that may occur with an acute hemolytic transfusion reaction include fever (rise of ≥2°F), chills, back or chest pain, headache, heat at infusion site, apprehension (feeling of impending doom), tingling, numbness, shortness of breath, cough, wheezing, nausea, vomiting, abdominal pain, bradycardia, tachycardia, hypotension, hypertension, cyanotic color, facial flushing, cool/clammy, edema, and changes in urine color. The most common initial symptom noted in recipients is fever, frequently accompanied by chills. Reactions may occur when as little as 10 - 15 ml of incompatible blood has been infused. The onset of symptoms may be misleadingly mild, such as vague uneasiness or an aching back. The first sign the patient observes may be red urine, which may or may not be accompanied by back

pain. The severity of initial symptoms is often related to the amount of blood transfused and may presage the severity of the ensuing clinical problems. In unconscious or anesthetized recipients the only manifestations of an acute hemolytic transfusion reaction may be bleeding at the surgical site (due to DIC), hypotension or the presence of hemoglobinuria.

III. SPECIMEN

A. Pre-transfusion Pink K2EDTA sample
B. Post-transfusion Pink K2EDTA sample
C. Plasma/serum (Gold or Green tops-for Chemistry testing) samples labeled:
    1. Pre-transfusion sample (if one was collected)
    2. Immediate post-transfusion sample (if indicated)
    3. 12 – 24 hours post-transfusion sample (if indicated)
D. Donor bag with segments, attached tubing, IV solution, and attached crossmatch card.
E. Urine sample

IV. REAGENT

A. ABO Rh Retyping:
    1. Anti - A
    2. Anti - B
    3. Anti - D
    4. ABO+Rh Control
    5. A_1 cells
    6. B cells
B. Direct antiglobulin testing
    1. Anti-IgG & C3d, Polyclonal Coombs
    2. Coombscell-E, IgG-coated pooled red cell antiglobulin control
C. Crossmatch and Antibody Testing:
    1. Low Ionic-Strength Additive Solution for Antibody Detection Tests
    2. Anti-IgG Monoclonal Coombs
    3. Coombscell-E IgG-coated pooled red cell antiglobulin control
    4. Red cells from involved product(s)
    5. Screen Cells 1, 2, and 3
    6. Panel Cells (if indicated)
    7. Appropriate Anti-sera (if indicated)

V. INSTRUMENTATION/EQUIPMENT

A. Centrifuge
B. Cell washer
C. Microscope
D. Urine analyzer

E. 12x75mm glass test tubes
F. Disposable plastic transfer pipettes
G. Glass microscope slides

VI. QUALITY CONTROL

A. QC as stated and reagents must be within expiration dates:
   1. Perform a Negative and Positive control on the Anti-IgG, & C3d, Polyclonal Coombs (using Bio-Rad Screen Cells 1, 2, or 3 for the Neg control and Bio-Rad Coombscell-E for the Positive control).
   2. Immucor CorQC -Daily QC of reagents
   3. Coombscell-E -used on all, negative at coombs phase, AB screen tubes, crossmatch tubes, and all negative weak D tests
   4. ABO+Rh control -used with repeat ABO+Rh typings

VII. PROCEDURE:

A. Nursing Protocol:

1. If a reaction occurs, the following actions must be taken immediately by nursing personnel:
   a. Stop the transfusion to limit the amount of blood infused. Notify the patient's physician.
   b. Keep the intravenous line open with infusion of normal saline.
   c. Check all labels, forms and patient's identification to determine if the correct patient received the correct blood or component.
   d. Report the suspected transfusion reaction to blood bank personnel immediately.
   e. Send the discontinued bag of blood, the administration set, attached IV solutions, and all the related forms and labels to the laboratory.
   f. Send a urine specimen to the laboratory.
   g. Have the phlebotomist draw a blood sample (pink EDTA top tube carefully to avoid mechanical hemolysis).
   h. Document thoroughly in EPIC.

IF ANY OF THE INITIAL STUDIES SHOW EVIDENCE OF A HEMOLYTIC REACTION, OR BACTERIAL CONTAMINATION, A PATHOLOGIST AND THE PATIENT'S PHYSICIAN MUST BE NOTIFIED IMMEDIATELY.

B. Laboratory Blood Bank Protocol (Evaluation/Initial Workup):

1. When a suspected transfusion reaction is reported to the blood bank, the technologist is to complete the pertinent information on the Transfusion Reaction Worksheet (UPPK BB 0100.01).

a. **Check for clerical errors on the following:**
   1) Check patient identification and information.
   2) The unit of donor blood bag and tag
   3) Blood Bank Worksheet (if computer downtime)
   4) LIS entry
   5) If there is a discrepancy, **immediately notify the pathologist**, the patient's physician or other responsible health care professional.
   6) Search appropriate records to find if other patient samples or donor units have been misidentified or incorrectly issued. After ascertaining if other patients are at risk, and after performing appropriate diagnostic and therapeutic procedures, trace each step of the transfusion process to a possible error.

b. **Check color of the specimen.**
   1) Compare the patient's pre-reaction specimen and post-reaction specimen for color of serum or plasma. Pink or red discoloration (indicative of possible hemolysis) present in the post-reaction specimen, but not in the pre-transfusion specimen, usually indicates the presence of free hemoglobin and destruction of red cells. Intravascular hemolysis of as little as 5 ml of red cells can produce visible hemoglobinemia.
   2) Mechanical hemolysis occurring during blood sample collection can produce pink or red-tinged serum. If this is suspected, a repeat STAT blood draw is to be requested; but a slightly hemolyzed sample can still be used for the direct antiglobulin test.
   3) If the repeat blood draw is positive for hemolysis or change of color of the serum, **immediately notify the pathologist** about the possibility of a hemolytic transfusion reaction.
   4) In samples drawn 4 to 10 hours after transfusion, yellow or brown discoloration, from increased bilirubin and other hemoglobin breakdown products, may indicate recent hemolysis.

c. **Retest ABO/Rh type on pre- and post-reaction specimen.**

d. **Perform a Direct Antiglobulin Test on the pre and post-reaction specimen using Polyspecific Coombs.** The

Direct Antiglobulin Test must allow for detection of RBC-bound compliment as well as IgG.

1) If antibody or complement coated transfused incompatible cells are not immediately destroyed, the direct antiglobulin test on the post-reaction specimen will be positive, with a mixed-field appearance. (Refer to DAT procedure UPPK BB-0519 for sending out positive DAT's for an elution.)
2) Since circulating antibody or complement-coated cells may be very rapidly destroyed, the direct antiglobulin test may be negative.
3) Non-immune hemolysis can produce hemoglobinemia without a positive direct antiglobulin test. These and other causes of non-immune hemolysis should be considered whenever hemoglobinemia occurs without an obvious immune etiology.

e. **Check the urine sample for occult blood (perform a urine dipstick).** If positive, do microscopic for intact RBCs. If no intact RBCs are present or the number is minimal compared to the occult blood result, **notify the Medical director or pathologist on-call.**

2. If the initial testing is negative and there are no clerical errors, no further testing is necessary unless specifically requested.
   a. Phone floor to inform nurse that no evidence of a hemolytic transfusion reaction is found. This will minimize the delay in completing the transfusion and allow the nurse to notify physician with preliminary results.
   b. Skip to step VIII REPORTING RESULTS
3. If there are any positive reactions or any clerical errors, call the pathologist **IMMEDIATELY** and the patient's physician.
4. If determined by the pathologist and /or patient's physician that further testing needs to be performed, continue with the extended workup below.

C. Laboratory Blood Bank Protocol (Complete/Extended Workup):

1. Send discontinued units to the Blood Bank.
   a. Examine the donor bag for discoloration, clots or masses, opaque or muddy looking plasma, and fuzziness of the interface between the plasma and the red cells, and for evidence of hemolysis. If present, **notify the Medical Director or the pathologist on-call**.

b. Confirm tubing is specifically for blood transfusion and the fluid is only normal saline. If not, **notify the Medical Director or the pathologist on-call.**

2. Repeat the antibody detection tests on the pre-reaction and post-reaction samples. If any tests are positive, identify the antibody. Test donor units for the presence of the corresponding antigen. If the patient's pre-reaction sample has an unexpected antibody not previously reported, check records to see how the discrepancy occurred.

Possible Scenarios:

PRE-TRANSFUSION ANTIBODY SCREEN	POST-TRANSFUSION ANTIBODY SCREEN	REASONING
Negative	Negative	No evidence of serologic incompatibility
Negative	Positive	Possible mix up of patient specimens Mislabeled specimen pre or post Possible drug effect Possible transfusion of antibody in prior blood component
Positive	Positive	AHG not used at time of original screen Incubation time too short at time of original screen
Positive	Negative	Possible drug effect Diluted post specimen

Notify the Medical Director or pathologist on call if the antibody screen on either the pre or post reaction specimen is different than the antibody screen done prior to transfusion.

3. Repeat the crossmatch, testing both the pre-reaction serum sample and the post-reaction serum sample against a sample of red blood cells from the bag or from a segment still attached to the unit.

Possible Scenarios:

PRE-REACTION CROSSMATCH	POST-REACTION CROSSMATCH	REASONING
Compatible	Compatible	No evidence of serologic incompatibility
Compatible	Incompatible	Possible mix up of patient specimens, unit pigtails Wrong unit hung on wrong patient Mislabeled specimen pre or post Fast anamnestic response
Incompatible	Compatible	Possible mix up of patient specimens, unit pigtails Mislabeled specimen pre or post
Incompatible	Incompatible	AHG not used at time of original crossmatch Shaking tube too hard at time or original crossmatch Incubation time too short during original crossmatch

Notify the Medical Director or pathologist on call if either the pre or post reaction crossmatch is not compatible.

4. Perform the following tests on the pre, the immediate post transfusion specimen and a 12 – 24 post transfusion peripheral blood specimen:
    a. Bilirubin
    b. BUN
    c. LDH
    d. Gram stain on the unit
    e. Culture of the blood unit (inoculate 2 bottles-send to UPH Methodist)
    f. Any other test the pathologist requests
5. Investigation for Other Problems - To evaluate the possibility of nonimmunologic hemolysis:
    a. Consider bacterial contamination of the donor unit if:
        1) The cells or plasma have brownish or purple discoloration.
        2) There are clots or abnormal masses in the liquid blood.
        3) Delineation between cells and plasma in a spun sample is fuzzy or blurred.
        4) The plasma is opaque or mudding looking.
        5) There is a peculiar odor.

b. Before manipulating the bag excessively, take specimens from the bag for cultures following blood culture protocol in microbiology.
c. Examine a smear of the blood stained with gram stain.
d. Examine the supernatant plasma of the blood from the donor blood container for presence of free hemoglobin. If present, the unit may have been damaged by improper temperatures in shipping or storage or at the time of administration by the injection of drugs or hypotonic solutions or by bacterial contamination.
e. Consider the possibility of mechanical hemolysis. Mechanical red cell lysis can occur with the use of roller pumps such as those used in cardiac bypass surgery, pressure infusion pumps, pressure cuffs or small-bore needles.

VIII. REPORTING RESULTS

All results should be entered on the Transfusion Reaction Worksheet (UPPK BB 0100.01) and into the computer (SEE UPPK BB 0100.04 FOR AN EXAMPLE). The reports should be submitted to the pathologist for final evaluation. After pathologist's final evaluation is done, enter it into the computer (if the pathologist has not already entered it), and keep the original in the blood bank file cabinet.

IX. PROCEDURAL NOTES/PROBLEM-SOLVING TIPS

A. If it is determined that the product is at fault for causing a transfusion reaction, report it to the American Red Cross.

You should report:

1. All transfusion reactions where a problem with manufacturing (which includes donor selection) may have been the cause. Possible septic reactions, transfusion-related acute lung injury (TRALI), serious allergic reactions and some hemolytic reactions (for example, hemolysis in a group A recipient of a Group O platelet with high titer anti-A) should be reported.
2. Reactions due to compatibility problems (e.g. acute and delayed hemolytic reactions) if a Red Cross Immunohemotology laboratory performed any of the testing or provided specially selected (e.g. antigen-negative) components.
    - The Red Cross form for submitted transfusion reaction cases follows (UPPK BB 0100.02 and UPPK BB 0100.03).

Please make copies for use as cases arise, and return the completed reports to the address on the form.

Reactions that are related solely to blood administration (e.g. fluid overload or mis-transfusion) or recipient factors (e.g. typical febrile non-hemolytic non-septic reactions) do not need to be reported to the American Red Cross unless the transfusion reaction workup discloses a possible manufacturing problem.

B. Transfusion Related Fatality Reporting to the FDA:
   1. Transfusion related fatalities, the issuance of infectious disease reactive (or positive) products, or the reinfusion of wrong red blood cells to a donor during plasmapheresis must be reported in writing to the Director, Center of Biologics Evaluation and Research within seven working days of the discovery. Fatalities must also be reported immediately by telephone. If corrective actions include procedural revision, the report should include a description of the new procedure. If the incident involves infectious disease reactive (or positive) products, the patient's follow up must be long enough to determine if infection occurred and the final report must indicate whether or not the patient(s) contracted the disease.
   2. Contact the Medical Director or pathologist on call. Before calling, gather the following information and have it readily available:
      a. Date of collection, transfusion and date of death.
      b. Product and unit number and where collected.
      c. A brief description of the incident.
      d. What you believe at that time to have been the cause.
   3. An immediate report should be made by telephone to:

      Director
      Center for Biologics Evaluation and Research (CBER)
      1401 Rockville Pike
      Suite 200 N, HFM - 650
      Rockville, MD 20852-1448
      (301) 594-1191

      State to the person answering the phone, "I wish to report a fatality associated with a blood transfusion." The individual receiving the message will immediately transfer you to the proper person, or if the proper person is not available, they will take your name, telephone number and return your call as soon as possible.
   4. The person receiving the call will advise you at that time of what action is necessary.
   5. Immediate notification may also be made by e-mail at fatality@al.cber.fda.gov

6. Notify Risk Management at (309) 672-4680 or (309) 672-4819 and complete an event report in RL solutions if the hemolytic transfusion reaction involves administration of blood or blood products having major blood group incompatibilities.

X. REFERENCES RANGE VALUES:

A. Expected values are the normals in the Lab Information System for BUN, total bilirubin, LDH and urine occult blood.
B. Crossmatch results should be compatible.
C. ABO/Rh testing of post-transfusion samples should match pre-transfusion.

XI. REFERENCES:

A. AABB Technical Manual, 19th Edition, American Association of Blood Banks, Bethesda, MD, 2017.
B. Food and Drug Administration: Code of Federal Regulations, 21 CFR 606.17(b), Office of the Federal Register.

POLICY CREATION :	***Date***
Author: Sharrol Brisbin, MT (ASCP)	***03/01/1995***
Medical Director: Sheikh, MA, MD	***03/01/1995***

MEDICAL DIRECTOR		
DATE	NAME	SIGNATURE
12-5-18	Kathy McKramer MD	
SECTION MEDICAL DIRECTOR		

REVISION HISTORY (began tracking 2011)			
Rev	Description of Change	Author	Effective Date
12/4/18	"Or a delayed transfusion reaction " to Section I.	Jenny Turner	12/4/18

Reviewed by

Lead	Date	Coordinator/ Manager	Date	Medical Director	Date
[signature]	12-4-18				