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Policies for Providing Red Blood Cells to Patients with Unexpected Antibodies

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

The purpose of this document is to provide the Blood Bank staff with policies and procedure for providing red blood cells (RBCs) to patients with unexpected antibodies.

II. DEFINITIONS:

A. **Unexpected antibody:** Any antibody (other than naturally occurring anti-A or anti-B that is regularly found in normal serum or plasma) that is currently or was historically present in a patient's sample.

B. **Clinically significant antibody:** An antibody that:
   1. Is known to cause Hemolytic Disease of the Newborn (HDN) or shortened survival of antigen positive RBCs,
   2. Requires transfusion of antigen negative red blood cells, and
   3. Is usually IgG and best detectable with antihuman globulin (AHG).

C. **Clinically insignificant antibody:** An antibody that:
   1. Does not cause shortened red cell survival of antigen positive RBCs,
   2. Does not require transfusion of antigen negative red blood cells, and
   3. Is usually IgM and reacts best below 37°C.
   4. Antibodies that are usually considered clinically insignificant include the following specificities:

a. Anti-IH, anti-H, auto-anti-I, anti-I, anti-Le^a, anti-Le^b, anti-P_1, anti-M, anti-N, and anti-A_1.

D. **MSBOS / SBOS / MATRIX:** A document that identifies standard blood orders based on the patient's scheduled surgical procedure.

E. **Passively acquired antibodies:** Antibodies that are transferred from the donor(s) to a recipient through the transfusion or administration of plasma-containing components (i.e., RhIG, or IVIG administration). Passively acquired antibodies may also be transferred from mother to fetus through pregnancy, and may be present in the neonate after birth.

F. **Alloimmunization:** The process whereby a recipient forms antibodies in an immune response to foreign antigens on donor RBCs.

G. **Designee**: A Blood Bank technical director or Blood Bank fellow.

III. POLICIES:

A. General Policies for Providing RBCs to All Patients with Unexpected Antibodies

1. Patients with unexpected antibodies must be crossmatched by the gel crossmatch method unless directed otherwise in the Transfusion Medicine Policies or by Medical Director/ designee. This includes patients with autologous units who have unexpected antibodies.
    a. Some patients with warm autoantibodies or high titer low avidity (HTLA) antibodies shall be crossmatched by the 60-minute no-LISS method; see section III.D for additional information.
    b. Patients with a historical record or currently reactive anti-A_1 shall be crossmatched by the all-phase crossmatch method.
2. To ensure that electronic crossmatches cannot be performed in the Blood Bank computer system, the **NEXM** (not eligible for electronic crossmatch) antibody code should be added to the *Antibody* field of all patients with unexpected antibodies. Note: The NEXM code must be added to the *Antibody* field, not to the *Messages* field.
3. Obtain a patient history before RBCs are crossmatched.
    a. If a patient history is indicated, the Blood Bank shall attempt to obtain the patient's history before RBCs are crossmatched. Refer to site specific Transfusion Medicine policy, Obtaining Patient History.

B. Policies for Providing RBCs to Patients with Clinically Significant Antibodies

1. Patients with clinically significant antibodies must be crossmatched by the gel crossmatch method.
2. Generally, the RBC units that are crossmatched for patients with clinically significant antibodies must be negative for the antigens corresponding to the clinically significant

antibodies. However, three exceptions exist (when antigen negative RBCs may not be required):

a. If there is no corresponding antigen to a clinically significant antibody; for example, antibodies that are resolved as warm autoantibodies (WAA) or "too weak to identify" (TWTI).

b. If a patient has an antibody to a low frequency antigen, such as anti-Kp^a or anti-Js^a.

c. If any clinically significant antibody can not be ruled out in an antibody workup then antigen negative RBCs for the antibody are required.

3. If antigen negative units are required for a patient with clinically significant antibodies, then before selecting or crossmatching RBC units the technologist shall verify that the donor units are negative for the applicable antigens in both the Blood Bank computer and on the unit antigen tags attached to the units.

4. If the Blood Bank does not carry the antisera corresponding to a patient's antibody to a low incidence antigen, it may not be possible to provide antigen negative units. Therefore, the Blood Bank will proceed as follows:

    a. If the antibody is currently reactive, then gel crossmatch compatible RBCs shall be provided using units that are not tested for the corresponding antigen. Because the antibody is currently reactive, the gel crossmatch would likely be incompatible if the unit is antigen positive. Refer to Transfusion Medicine policy, *Interpretation of Antibody Investigations* in the section *Determining whether an Antibody to a Low Incidence Antigen is Reactive*.

    b. If it has been demonstrated that the antibody was reactive in the preceding 90 days, then gel crossmatch compatible RBCs shall be provided using units that are not tested for the corresponding antigen. Because the antibody was reactive in the preceding 90 days, it is unlikely that its level has dropped below detectable levels. The gel crossmatch would likely be incompatible if the unit is antigen positive.

    c. If the antibody is currently non-reactive and was not reactive in the preceding 90 days, it is unlikely that the crossmatch would be incompatible if an antigen positive unit was selected. Therefore, the Blood Bank will attempt to obtain antigen negative units from a blood supplier. If unable to provide antigen negative units, the blood supplier may:

        i. Provide units that are historically negative for the applicable antigen.

        ii. Provide units that are very likely to be antigen negative based on the donor's race (i.e., the V and Js^a antigens are extremely rare in the Caucasian population).

        iii. Indicate that there are no other options than to provide crossmatch compatible units.

    d. If the Blood Bank is unable to determine whether the antibody is currently reactive (i.e., test cells required to perform the testing are unavailable) then consider the antibody as currently non-reactive and proceed based upon the above recommendations.

C. Policies for Providing RBCs to Patients with Antibodies that are Usually Considered Clinically Insignificant

1. Antibodies that typically react only at temperatures less than 37°C are usually considered clinically insignificant. The following is a non-exhaustive list of antibodies that are usually considered clinically insignificant:
    a. Anti-IH, anti-H, auto-anti-I, anti-I, anti-Le^a, anti-Le^b, anti-P_1, anti-M, anti-N, anti-A_1, CRAUS (cold reacting antibody of undetermined significance), and CAA (cold autoantibody).
2. Patients with antibodies that are usually considered clinically insignificant must be crossmatched by the gel crossmatch method; however, see the exception for patients with anti-A_1 below. For patients with antibodies that are usually considered clinically insignificant, a compatible gel crossmatch indicates one of the following:
    a. That the antibody is not reactive at or above 37°C (and is therefore clinically insignificant), even though the unit may be positive for the corresponding antigen, or
    b. That the unit is negative for the corresponding antigen.
3. If incompatible crossmatches are observed, refer to Transfusion Medicine policy, Investigation of Incompatible Crossmatches before performing additional crossmatches.
4. Patients with antibodies that are usually considered clinically insignificant do not require transfusions of RBCs that are negative for the antigen corresponding to this antibody, as long as the gel crossmatch is compatible. However, three exceptions exist (when antigen negative units are required):
    a. Anti-A_1: If anti-A_1 was detected in the patient's sample (currently or historically), then the patient should be transfused with RBCs that are compatible by the all-phase crossmatch method.
        i. Group A_2 patients should receive group O or A_2 RBCs only.
        ii. Group A_2B patients should receive O, A_2, A_2B, or B RBCs.
        iii. For additional information refer to:
            A. Transfusion Medicine policy, Resolution of ABO Discrepancies for A Subgroups and Patients with Anti-A1.
    b. Anti-N: Anti-N may be considered clinically significant if the patient's red cells phenotype as N-S-s-. For additional information, refer to Transfusion Medicine policy, Interpretation of Antibody Investigations.
        i. If the patient's red cells phenotype as N-S-s-, then the RBCs provided for transfusion should be N-negative.
        ii. If anti-U is present, refer to Transfusion Medicine policy, *Policies Specific to Patient's with Anti-U*.
    c. Upon the Medical Director's (MD's) determination. On rare occasions, the Medical

Director may determine that a patient with an antibody that is usually considered clinically insignificant may require all future transfusions to consist of RBCs that are negative for the antigen that corresponds to the antibody. For example, this may occur if one of the above antibody specificities is suspected of causing a hemolytic transfusion reaction. Or, the MD may conclude that a patient's antibody is capable of causing shortened red cell survival in that patient. If the MD makes this determination, the technologist shall perform the following:

i. Confirm that the patient's antibody field is updated in the Blood Bank computer with the corresponding antibody.

ii. Add comments to the patient's computer record, indicating that the MD has instructed the Blood Bank to use antigen negative RBCs of the particular specificity.

D. Policies for Providing RBCs to Patients who Display Panreactivity (Patients with a WAA, Anti-CD38, HTLA Antibody, or receiving IVIG)

1. In some warm autoantibody cases, gel crossmatches are indicated unless there is panreactivity in gel panels. In this case, 60-minute no-LISS crossmatches are indicated. The appropriate crossmatch method is described in Transfusion Medicine policy, *Warm Autoantibody Investigation*. Note that in some cases, the use of phenotypically matched red cells may also be indicated.
2. For patients with anti-CD38 antibodies, refer to Transfusion Medicine policy, *Warm Autoantibody Investigation* and Transfusion Medicine policy, *DTT Treatment and Testing* if site applicable.
3. For patients with HTLA antibodies, refer to Transfusion Medicine policy, *HTLA / Anti-Bg^a Investigations*.

E. Policies for Providing RBCs to Patients with Passive Anti-D Due to Rh Immune Globulin (RhIG) or Other Passively Acquired Antibodies

1. Patients with passively acquired antibodies must be crossmatched by a gel crossmatch, this includes patients with currently reactive, passive anti-D due to RhIG. These RBCs are crossmatched per policy, after the Type and Screen and antibody investigations (if applicable) are completed.
2. Once the antibody screen of a patient with passive anti-D due to RhIG reverts to negative, gel crossmatches are no longer required and electronic crossmatches may be performed. This process is controlled by the appropriate updating of the patient's antibody field in the Blood Bank computer with the **NEXM** antibody code.
3. In some cases, it may be difficult to determine whether anti-D specificity is related to passive anti-D due to RhIG, or to alloimmunization. Refer to Transfusion Medicine policy, Policies

Specific to Patients with Passive Anti-D (Due to Recent RH Immune Globulin Administration).

4. Crossmatched RBCs must be negative for the antigen corresponding to the passively acquired antibody; i.e. RBCs crossmatched for patients with passive anti-D due to RhIG must be Rh(D) negative.
5. Crossmatching RBCs for neonates when passive anti-D due to RhIG is detected in the maternal sample.
    a. To crossmatch RBCs for neonates when passive anti-D due to RhIG is detected in the maternal or neonatal sample, refer to Transfusion Medicine policy, *Neonatal Compatibility Testing Guidelines*.

F. Determining the Number of RBCs to Crossmatch for Patients with Unexpected Antibodies

1. Inpatients should have at least two RBCs crossmatched.
2. Surgical patients should have at least two RBCs crossmatched before surgery. Refer to site Transfusion Medicine policy, *Review of the Surgical Schedule,* if applicable.

G. Communication of Extensive Delays in Providing Blood Products for Patients with Antibodies

1. The patient's caregiver will be notified when the Blood Bank is unable to provide blood products in a timely manner to a patient with a **potential need for transfusion within 24 hours**, due to an **extensive delay in providing RBCs** based on the patient's currently reactive, or historical antibodies. If there is any doubt about whether there is a "potential need for transfusion within 24 hours" or whether there is an "extensive delay", proceed as described to ensure that a physician is notified and that this is documented under the Antibody Screen using the **ADELX** canned message.
    a. Examples of a **potential need for transfusion within 24 hours**. Consider the following factors:
        I. Look at the patient's hemoglobin. If the hemoglobin is 10.0 g/dL or less, or is trending downward, proceed as if there is a potential need for transfusion within 24 hours.
        II. For **inpatients**, determine whether the patient is scheduled (or is being considered) for a surgical procedure within the next 24 hours.
        III. For **banded outpatients**, check EPIC visits for possible surgical or outpatient transfusion admits within the next 24 hours.
    b. Examples of an extensive delay in providing RBCs based on the patient's currently reactive or historical antibodies:
        a. When the patient has a warm autoantibody and an adsorption is required, or when 60-minute no-LISS testing is positive.
        b. When phenotypically matched RBCs are required, and the phenotype is incomplete or cannot be completed due to a positive DAT or recent

transfusion.

c. RBCs must be ordered from a blood supplier. For example, the patient has an antibody to a high frequency antigen or has multiple antibodies so that rare or hard-to-find RBCs are required.

d. RBCs must be deglycerolized.

2. If the *Urgent Request for Blood Product* form (F-1565) is received in the Blood Bank, do not delay. Provide emergency issue RBCs as described in Transfusion Medicine policy, Emergency Issue of Blood Products.

    a. If possible, provide RBCs that are negative (or preliminary negative) for any antigens corresponding to the patient's known clinically significant antibodies.

    b. If possible, provide phenotypically matched, partially phenotypically matched, or preliminary phenotypically matched RBCs, when indicated.

3. Continue working on the antibody investigation, and contact the Blood Bank Medical Director or designee.

IV. PROCEDURE:

A. Select appropriate RBCs for crossmatch, considering:

    1. The patient's ABO and Rh type. If necessary, refer to Transfusion Medicine policy, RBC Crossmatch Guidelines.

    2. The patient's clinically significant antibodies.

    3. Any special transfusion requirements. See Transfusion Medicine policy, Special Transfusion Requirements for Patients Greater than Four Months Old.

B. Perform a gel crossmatch as described in Transfusion Medicine policy, Serologic Crossmatching of Red Blood Cells.

C. If all units are compatible with the gel crossmatch, tag the units as described in Transfusion Medicine policy, *Tagging Blood Components*.

D. If any of the units are incompatible with the gel crossmatch, determine whether additional investigation is required before tagging any of the units that were crossmatched. See Transfusion Medicine policy, Investigation of Incompatible Crossmatches.

V. REFERENCES:

1. AABB, *Technical Manual*, current edition.
2. AABB, *Standards for Blood Banks and Transfusion Services*, current edition.
3. College of American Pathologist, *Transfusion Medicine Checklist*, current edition.

Approval Signatures

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