Case 24 Transfusion Reaction

HPI: A 61-year-old man with coronary artery disease and hypertension underwent a coronary artery bypass graft (CABG) procedure. Before the operation the surgeon ordered four units of packed RBCs to be cross-matched to the patient's type A, Rh negative blood. The patient required three units during the surgery. The patient had an uneventful recovery until the fifth postoperative day, at which time his Hb dropped from 15 to 8 g/dL. The patient appeared jaundice and spiked a temperature of 39.1°C; his urine appeared "tea-colored." As part of a work-up for a suspected hemolytic anemia, a direct Coombs' test was ordered.

Thought Questions

- What are blood groups and why are they important in transfusion medicine?
- What is an indirect Coombs' test and what other tests are used to match transfusion products?
- What are some common transfusion reactions?

Basic Science Review and Discussion

Blood Groups The major **blood types, A, B, O,** and **AB,** are based on the presence or absence of carbohydrate antigens on the RBC surface. Type A blood has the "A" antigen, type B blood has "B" antigen, type AB has both antigens, and individuals with type O blood have neither of these antigens. Individuals have "naturally" occurring antibodies in their serum (stimulated by the environment) directed against the AB antigen(s) that are *not* found on their red cells. For example, a person who is type B blood has anti-A in her plasma. These antibodies are usually IgM, which react at room temperature, bind complement, but do not cross the placenta. IgG forms of anti-A and anti-B are produced when individuals are exposed to red cells by pregnancy or transfusion.

The presence of the AB antigens on the surface of the red cell and the presence of AB antibodies in the plasma dictates what blood products can be safely transfused. Red cell products must be transfused only to recipients who lack the corresponding AB antibody in their plasma. Plasma products containing AB antibodies must be transfused only to recipients who lack the corresponding antigen on their red cell membranes. Since group O individuals lack any A or B antigens on their red cells, they are considered **universal blood donors.** Group AB individuals are **universal plasma donors** as they lack AB antibodies.

Another type of blood grouping is the **Rh** system. Of the numerous antigens in the Rh system, the D antigen is the most important. Rh(+) blood denotes the presence of the D antigen on the red cells of an individual's blood. The D antigen is strongly immunogenic and anti-D (anti-Rh) antibodies are the leading cause of **hemolytic disease of the newborn.** When a Rh-negative pregnant woman carries a Rh-positive fetus, small amounts of D-positive red cells can enter her circulation. Her body can then produce anti-D IgG antibodies. If she becomes pregnant in the future with an Rh-negative fetus, the antibodies can cross the placenta and attack the red cells of the fetus. Rh-negative pregnant women are given a small amount of Rh immunoglobulin (anti-D), RhoGAM, which prevents their own formation of anti-D antibodies.

Over 600 red cell antigens are known, but only a small amount are considered clinically significant (capable of stimulating IgG antibodies), and may cause hemolytic transfusion reactions. Some examples are Kell, Duffy, or Kidd antigens.

Blood Testing When a patient requires a blood transfusion, there are several tests that are done to find a compatible match in the blood bank. First, the patient's red cells are tested for the presence of A, B, and D antigens (blood typing). Next, an antibody screen (also known as an **indirect Coombs' test**) is performed by mixing a patient's serum with reagent red cells with known antigens (Figure 24-1). If the patient has serum antibodies directed against any of the red cell antigens, the specimen will agglutinate (clump) after antiglobulin is added. Another test is the **direct Coombs' test,** during which the patient's RBCs are mixed directly with antiglobulin (Figure 24-2). Patients with delayed hemolytic transfusion reactions or with autoimmune hemolytic anemias have red cells coated with antibodies that agglutinate, yielding a positive reaction.

Transfusion Reactions Reactions to blood transfusions do occur and can even result in death. Reactions can be acute (immediate) or delayed, occurring days or weeks after transfusion. **Febrile nonhemolytic transfusion reactions (FNHTRs)** are one of the most common acute transfusion events. The patient often experiences chills, rigors, and a temperature increase of 1°C or more during or after the transfusion. This reaction is due to pyrogenic cytokines [interleukin-6 (IL-6) or tumor necrosis factor (TNF)] that are stimulated in the recipient by leukocytes in the transfused product or that have

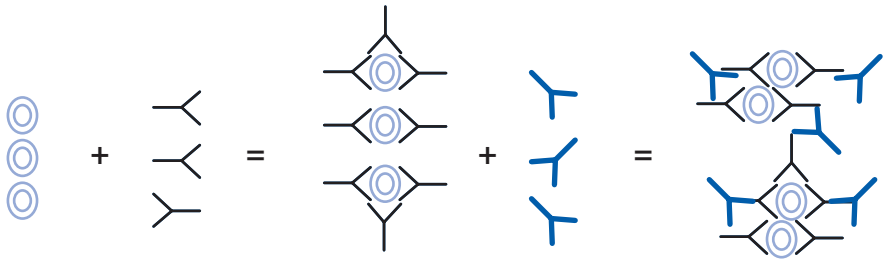

Figure 24-1 Indirect Coombs' test.

already been produced in the transfusion product during storage. Most patients are pretreated with an antipyretic (e.g., acetaminophen) to avoid this reaction.

A **hemolytic transfusion reaction,** a less common but more serious transfusion reaction, also causes fever. These reactions can be acute or delayed. Acute hemolytic transfusion reactions occur most commonly when ABO incompatible blood is transfused. The most common cause is human error in matching identification of the patient and appropriate blood product! Antibodies in the patient's serum react with antigens on the transfused cells and complement-mediated **intravascular hemolysis** occurs. Along with fever, patients may have chills, chest pain, hypotension, and diffuse bleeding. Renal failure, shock, and DIC can follow. This is an extremely serious reaction, as death occurs in 10% to 40% of cases. Delayed reactions occur when a person is sensitized during a previous transfusion but has undetectable antibodies on pretransfusion testing. Several days to weeks after the second transfusion, the patient produces more antibodies, which coat the surface of the transfused cells. Presenting symptoms are fever, anemia, and jaundice due to **extravascular hemolysis** as the antibody-coated RBCs are removed in the spleen. A direct Coombs' test is often positive. These reactions may go undetected due to their delayed nature. Treatment includes a procedure, called *elution,* that removes antibodies from the surface of the red cells.

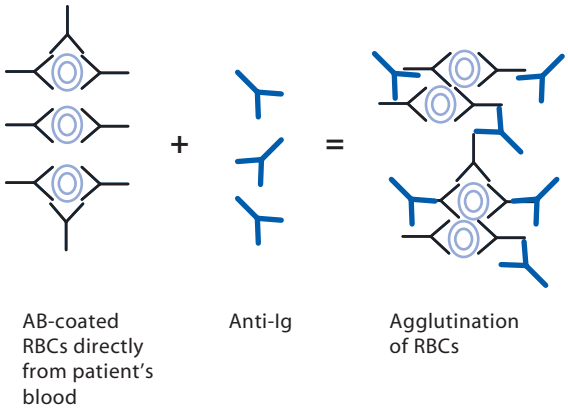

Figure 24-2 Direct Coombs' test.

Another common reaction is an **allergic transfusion reaction,** occurring in 1% to 3% of all transfusion recipients. These are mediated by preformed IgE in the recipient to some transfused allergen. Hives and pruritus are common, but reactions can progress to bronchospasm, hypotension, and anaphylaxis. Treatment is with antihistamines, which are often given to all patients before a transfusion to prevent this event.

Case Conclusion The direct Coombs' test was positive. According to the patient's records, he had been transfused two units of red cells the previous year for his first CABG procedure. A formal investigation of a suspected transfusion reaction was performed. There was no evidence of clerical or laboratory error. The pretest direct Coombs' test of the transfused blood was negative. As a part of the patient's treatment, an elution was performed and the antibodies were then identified in the laboratory as JKb, a Kidd antigen. It was determined that the patient underwent a delayed hemolytic transfusion reaction. He was sensitized to the Kidd antigen during the previous transfusion, but his antibody titer was too low to be detected on pretransfusion testing. The patient was given further supportive care and was discharged from the hospital on day 9. It was noted in his records that all future transfusion products be screened for this antigen and avoided.

Thumbnail: ABO Blood Group Antigens, Antibodies, and Compatibility

Group	ABO antigens of red cells	Compatibility of red cells	Antibodies in plasma	Compatibility of plasma
O	None	Transfuse to all patients *(universal donor)*	Anti-A, Anti-B	O patients only
A	A	A and AB only	Anti-B	A or O
B	B	B and AB only	Anti-A	B or O
AB	A and B	AB only	None	Transfuse to all patients *(universal donor)*

Key Points

- ABO blood types are based on red cell antigens. Patients receiving blood products from another person must have a compatible blood type.
- An antibody screen (also known as an indirect Coombs' test) is performed by mixing a patient's serum with reagent red cells with known antigens to determine which RBC antibodies are present in the patient's serum.
- A direct Coombs' test detects the presence of pre-formed antibody-coated RBCs in the patient's blood and can be positive in autoimmune hemolysis and delayed transfusion reaction.
- Hemolytic disease of the newborn occurs when Rh-negative mothers are sensitized by Rh-positive babies. If pregnant with a subsequent Rh-positive child, anti-D (Rh) antibodies can cross the placenta and attack the newborn's RBCs. RhoGAM is given early to prevent this occurrence.
- Acute hemolytic transfusion reaction is caused by direct ABO incompatibility. Delayed hemolytic transfusion reactions can be caused by antibody sensitization during pregnancy or prior transfusions.
- Allergic transfusion reactions, mediated by IgE, can cause hives and, in severe cases, shock and anaphylaxis.

Questions

1. Which of the following correctly describes how a direct Coombs' test is performed?
   - **A.** The patient's serum is mixed with test RBCs and agglutination is measured.
   - **B.** The patient's serum is mixed with mouse RBCs and agglutination is measured.
   - **C.** The patient's RBCs are mixed with anti-human immunoglobulin/complement mouse antibodies and agglutination is measured.
   - **D.** The patient's RBCs are mixed with anti-mouse immunoglobulin/complement human antibodies and agglutination is measured.
2. Which of the following statements is correct regarding Rh immunoglobulin (RhoGAM)?
   - **A.** It prevents the production of anti-D antibodies.
   - **B.** It is given to all Rh-positive pregnant women at the time of delivery.
   - **C.** It blocks IgM antibodies from crossing the placenta.
   - **D.** It can trigger hemolytic disease of the newborn in some patients.