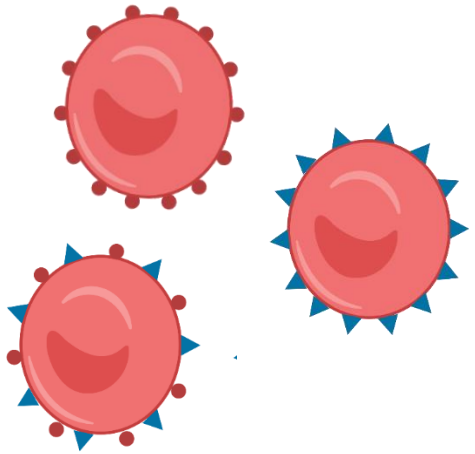
Blood Groups



Blood Types and Transfusion Reaction

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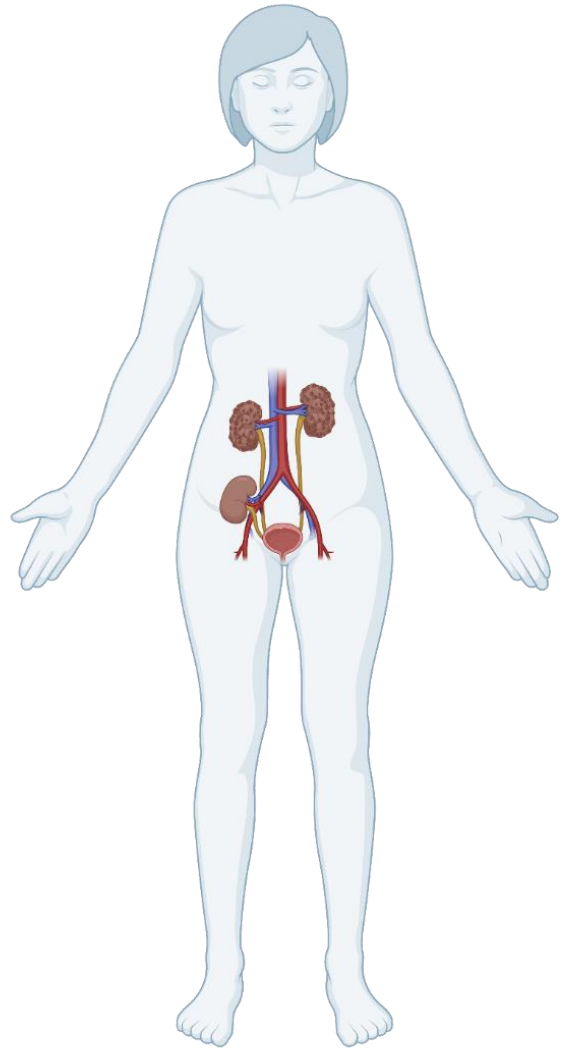

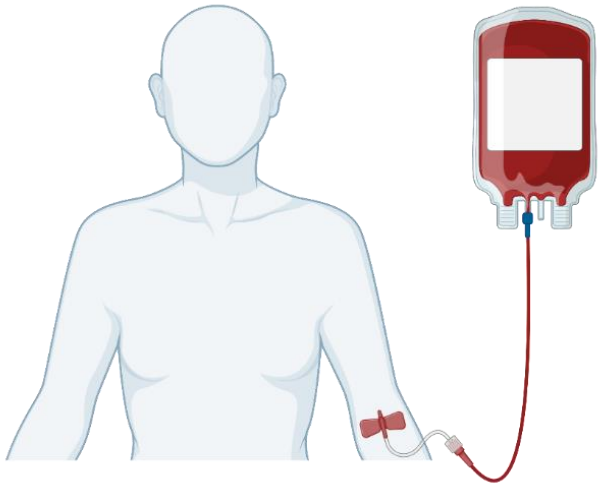

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Multiplicity of Antigens in the Blood Cells

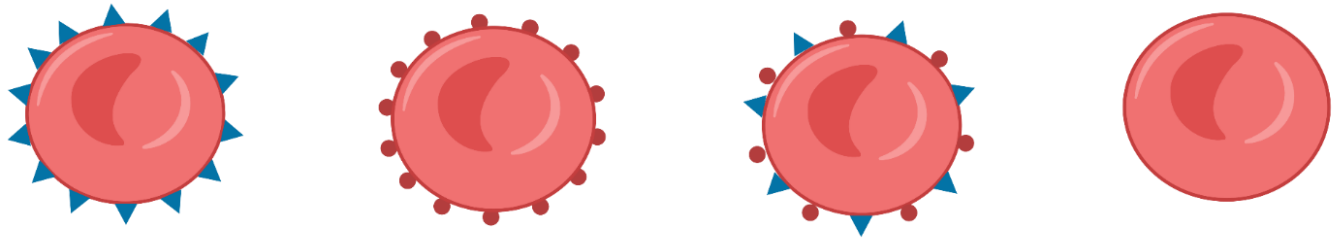
- At least **30 commonly occurring antigens** and hundreds of other rare antigens, each of which can at times cause antigen-antibody reactions.
- Two particular types of antigens are **much more likely** than the others to cause **blood transfusion reactions**. They are the **O-A-B system** of antigens and the **Rh system**.

Blood Groups

ABO System

- The ABO blood group is based on two glycolipid antigens called A and B.
- ABO blood group genetic locus has three alleles, which means three different forms of the same gene.
- These three alleles—I^A, I^B, and I^O.
- Only one of these alleles is present on each of the two chromosomes in any individual.
- The six possible combinations of genes OO, OA, OB, AA, BB, and AB.

O-A-B Blood Types

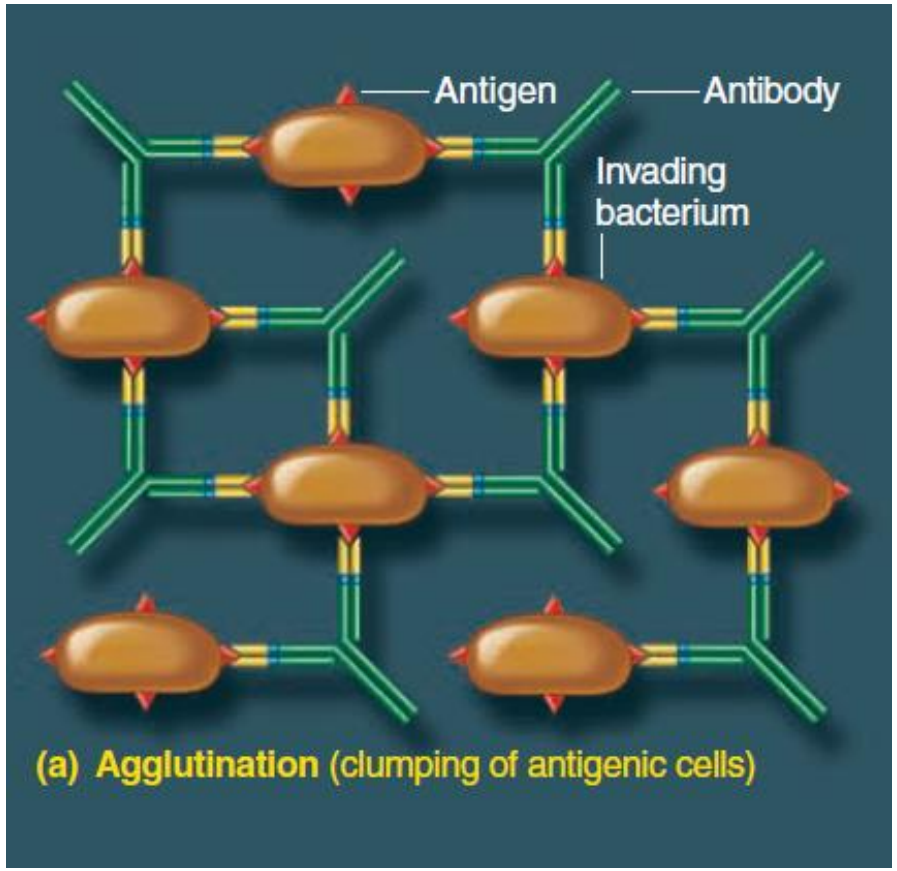


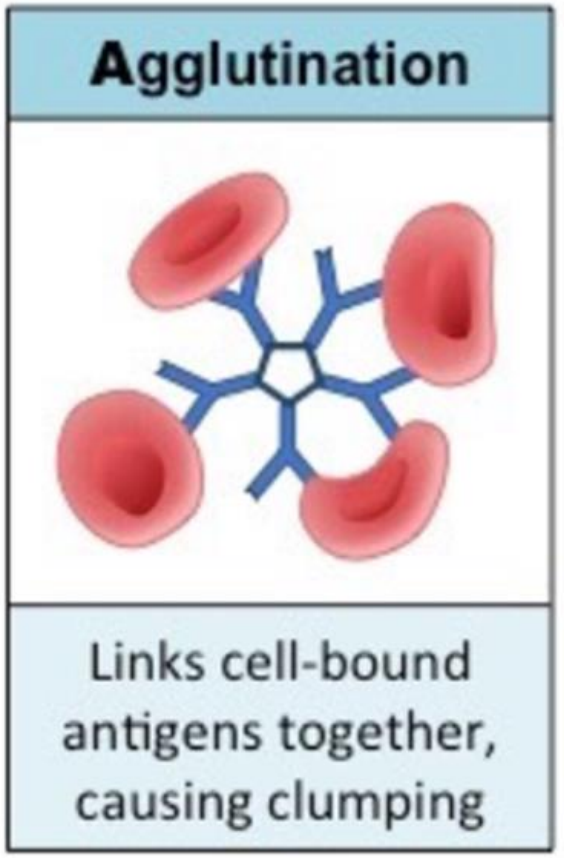
Genotype	**OA/ AA**	**OB/ BB**	**AB**	**-**
Antigen	**A**	**B**	**AB**	**-**
Blood group	**A**	**B**	**AB**	**O**

Relative Frequencies of the Different Blood Types

O	47%
A	41%
B	9%
AB	3%

Blood Groups — Agglutination



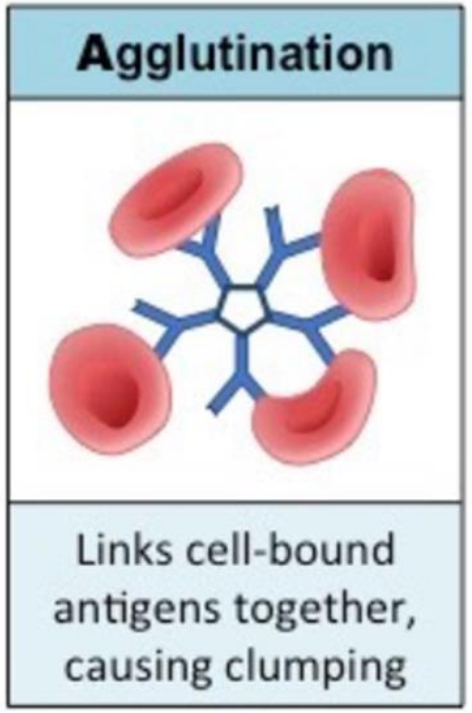


Because the agglutinins have **two binding sites (IgG type) or ten binding sites (IgM type),** a single agglutinin can attach to **two or more RBCs** at the same time, thereby causing the **cells to be bound together** by the agglutinin. This binding causes the cells **to clump,** which is the process of agglutination.

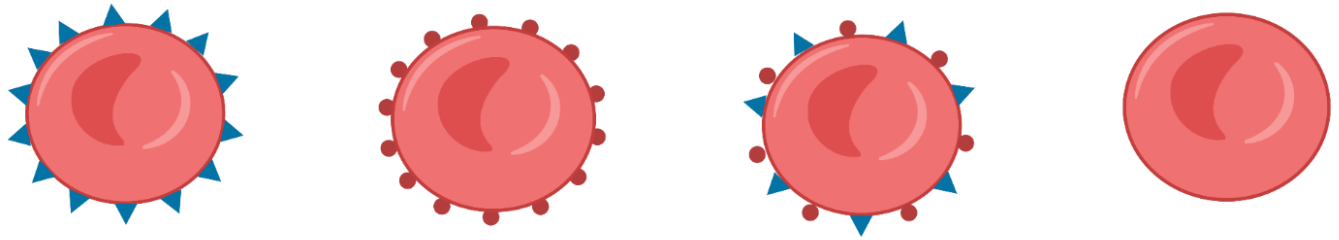
Antigen (Agglutinogen)
Antibody (Agglutinin)

Agglutinins (antibodies)

- The agglutinins are **gamma globulins**, as are almost all antibodies.
- Most of them are **IgM and IgG** immunoglobulin molecules.
- When type A agglutinogen is not present in a person's RBCs, antibodies known as anti-A agglutinins develop in the plasma.



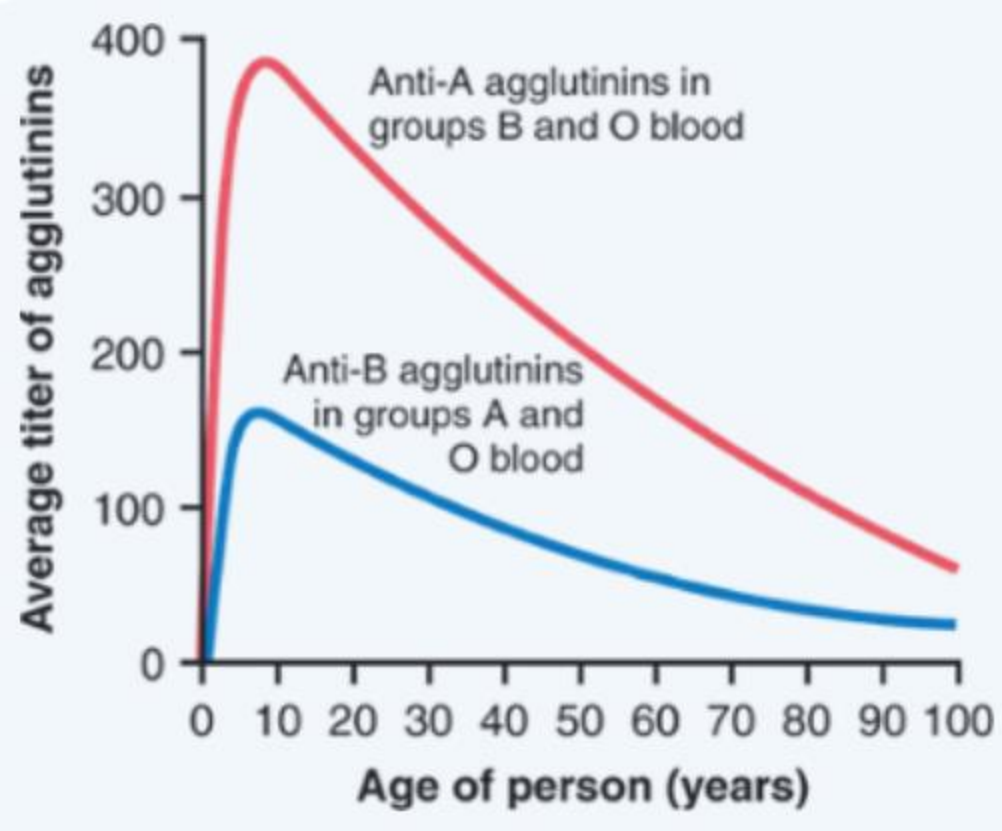
O-A-B Blood Types



Antigen (Agglutinogen)	**A**	**B**	**AB**	**-**
Genotype	**OA/ AA**	**OB/ BB**	**AB**	**-**
Blood group	**A**	**B**	**AB**	**O**
Antibody (Agglutinins)	**anti-B**	**anti-A**	**-**	**Anti-A & anti-B**

Agglutinins (antibodies)

- Immediately after **birth**, the quantity of agglutinins in the plasma is almost **zero.**
- **Two to 8 months** after birth, an infant **begins** to produce agglutinins.
- A **maximum** titer is usually reached at **8 to 10 years** of age, and this gradually declines throughout the remaining years of life.



Also, the neonate has few, if any, agglutinins, showing that agglutinin formation occurs almost **entirely after birth.

Agglutinins (antibodies)

- But **why** are these **agglutinins** produced in people who do not have the **respective agglutinogens** in their RBCs?

- The answer to this is that small amounts of type A and B antigens enter the body in food, in bacteria, and in other ways, and these substances initiate the development of the anti-A and anti-B agglutinins.

Agglutination Process in Transfusion Reactions

- The clumps plug small blood vessels throughout the circulatory system.
- During the ensuing hours to days, **physical distortion** of the cells or attack **by phagocytic white blood cells** destroys the membranes of the agglutinated cells, **releasing hemoglobin into the plasma**, called **hemolysis** of the RBCs.

Agglutination followed by delayed hemolysis

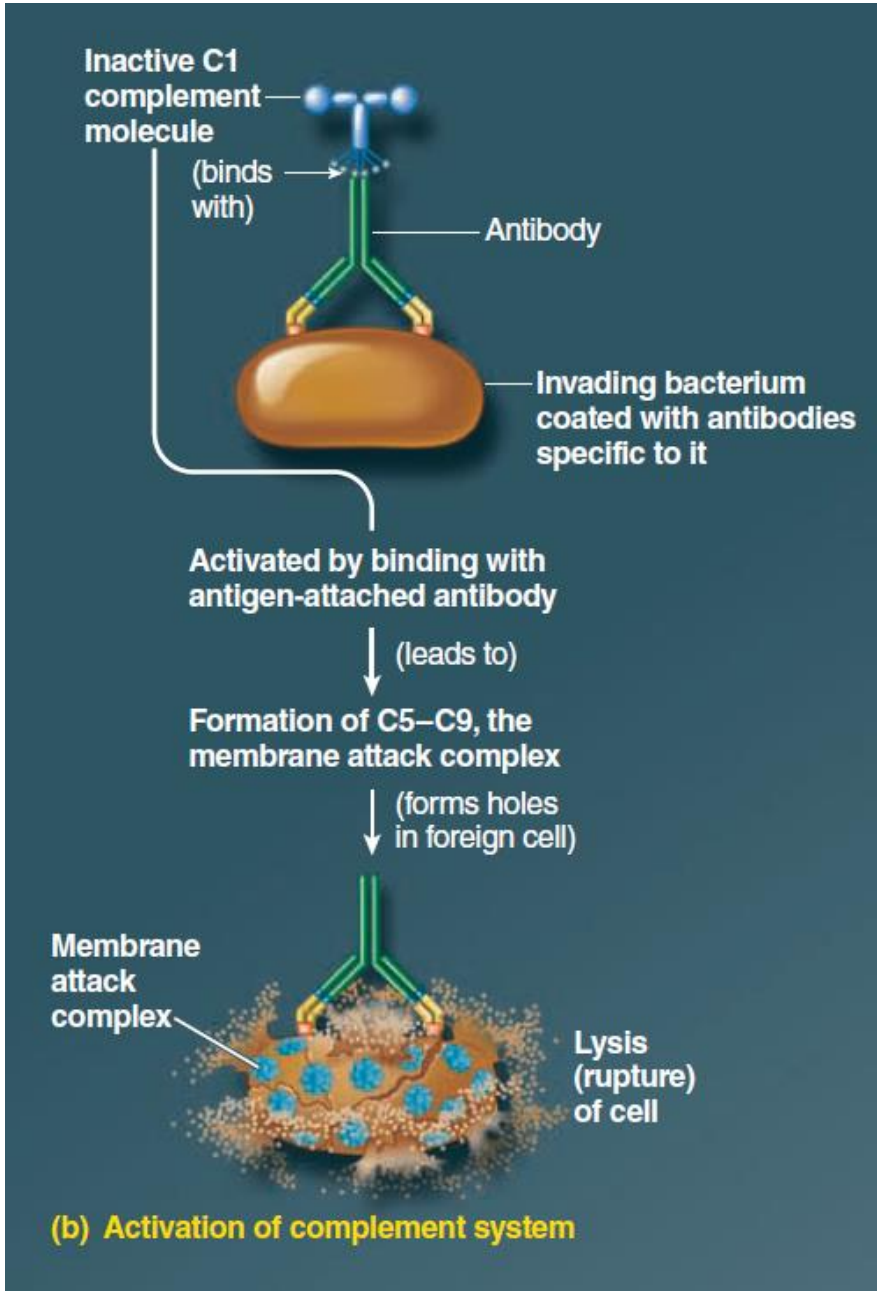
Acute Hemolysis Occurs in Some Transfusion Reactions

→ **Immediate** intravascular hemolysis.

→ In this case, the antibodies cause lysis of the red blood cells by activating **the complement system**, membrane attack complex.

→Less common

→ have to be a **high titer** of antibodies for lysis to occur, but also a different type of antibody seems to be required, mainly the **IgM antibodies.**



Blood Groups — Rh System

- There are **six common types of Rh antigens**, each of which is called an *Rh factor*. These types are designated C, D, E, c, d, and e.
- Each person has **one** of each of the three **pairs** of antigens.
- The type **D antigen** is widely **prevalent** in the population and considerably more antigenic than the other Rh antigens
- Anyone who has the **D antigen** is said to be Rh positive, whereas a person who does **not have type D antigen** is said to be **Rh negative**.
- The worldwide frequencies of **Rh-positive** and Rh-negative blood types are **95%** and 6%, respectively.

However, it must be noted that even in Rh-negative people, some of the other Rh antigens can still cause transfusion reactions, although the reactions are usually much milder.

Blood Groups — Rh System

The **major difference** between the **O-A-B system** and the **Rh system** is the following:

In the **O-A-B system**, the plasma **agglutinins** responsible for causing transfusion reactions **develop spontaneously**, whereas in the **Rh** system, spontaneous agglutinins almost **never occur.**

Instead, the person must first be massively exposed to an Rh antigen.

Formation of Anti-Rh Agglutinins

- When RBCs containing Rh factor are injected into a person whose blood does not contain the Rh.
- Anti-Rh agglutinins **develop slowly**, reaching a **maximum** concentration of agglutinins about **2 to 4 months** later.
- This immune response occurs to a much greater extent **in some people** than in others.
- With **multiple exposures** to the Rh factor, an Rh-negative person eventually becomes **strongly sensitized** to Rh factor.

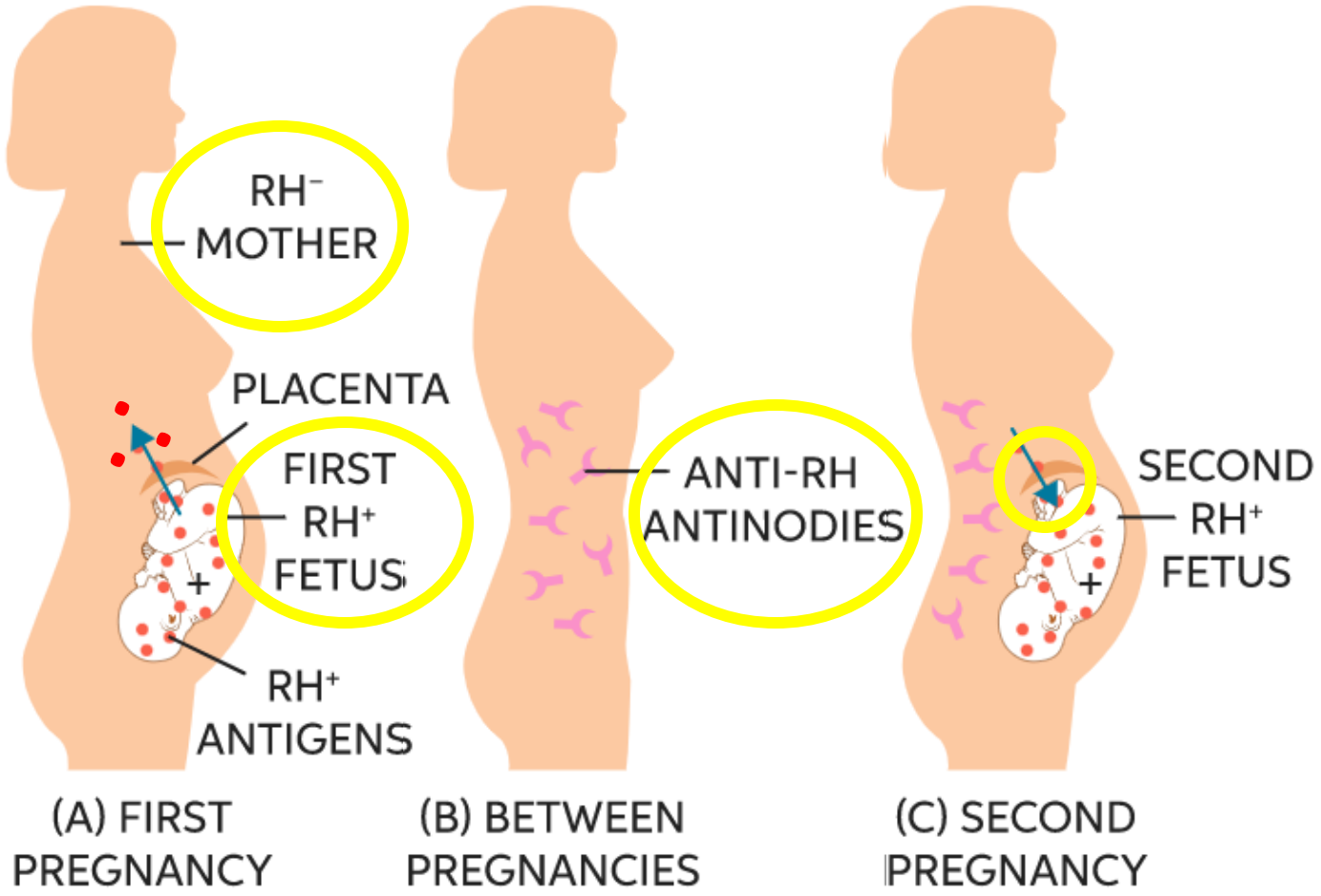
Characteristics of Rh Transfusion Reactions.

- likely cause **no immediate reaction**.
- **Anti-Rh antibodies** can develop in sufficient quantities during the next **2 to 4 weeks** to cause **agglutination** of those **transfused cells** that are still circulating in the blood.
- These cells are then hemolyzed by the tissue macrophage system. Thus, a **delayed transfusion reaction** occurs, although it is usually **mild.**

Characteristics of Rh Transfusion Reactions.

- On **subsequent transfusion** of Rh-positive blood into the same person (**sensitized)**, who is now already immunized against the Rh factor, the transfusion reaction is **greatly enhanced** and can be **immediate** and as **severe** as a transfusion reaction caused by mismatched type A or B blood.

Hemolytic Disease of the Newborn Erythroblastosis Fetalis



Hemolytic Disease of the Newborn Erythroblastosis Fetalis

- The mother is Rh negative and the baby has inherited the Rh-positive antigen from the father.
- The mother develops anti- Rh agglutinins from exposure to the fetus's Rh antigen.
- In turn, the mother's agglutinins diffuse through the placenta into the fetus and cause red blood cell agglutination.
- 3% of second Rh -positive babies exhibit some signs of erythroblastosis fetalis
- 10% of third babies exhibit the disease; and the incidence rises progressively with subsequent pregnancies.

Hemolytic Disease of the Newborn Erythroblastosis Fetalis

- Hemolytic anemia.
- Jaundice.
- The liver and spleen become greatly enlarged.
- Presence of nucleated blastic red blood cells.
- Permanent mental impairment or damage to motor areas of the brain.

Although the severe anemia of erythroblastosis fetalis is usually the cause of death, many children who barely survive the anemia exhibit permanent mental impairment or damage to motor areas of the brain because of precipitation of bilirubin in the neuronal cells, causing the destruction of many of these cells, a condition called kernicterus.

Treatment of the Erythroblastotic Neonate

- One treatment is to **replace the neonate's blood with Rh-negative blood.**
- This procedure may be repeated several times during the first few weeks of life
- Anti-Rh agglutinins from the mother usually circulate in the infant's blood for another 1 to 2 months after birth, destroying more and more red blood cells.
- This keeps the bilirubin level low and thereby prevent complications.

**By the time these transfused Rh-negative cells are replaced with the infant's own Rh-positive cells, a process that requires 6 or more weeks, the anti-Rh agglutinins that had come from the mother will have been destroyed.

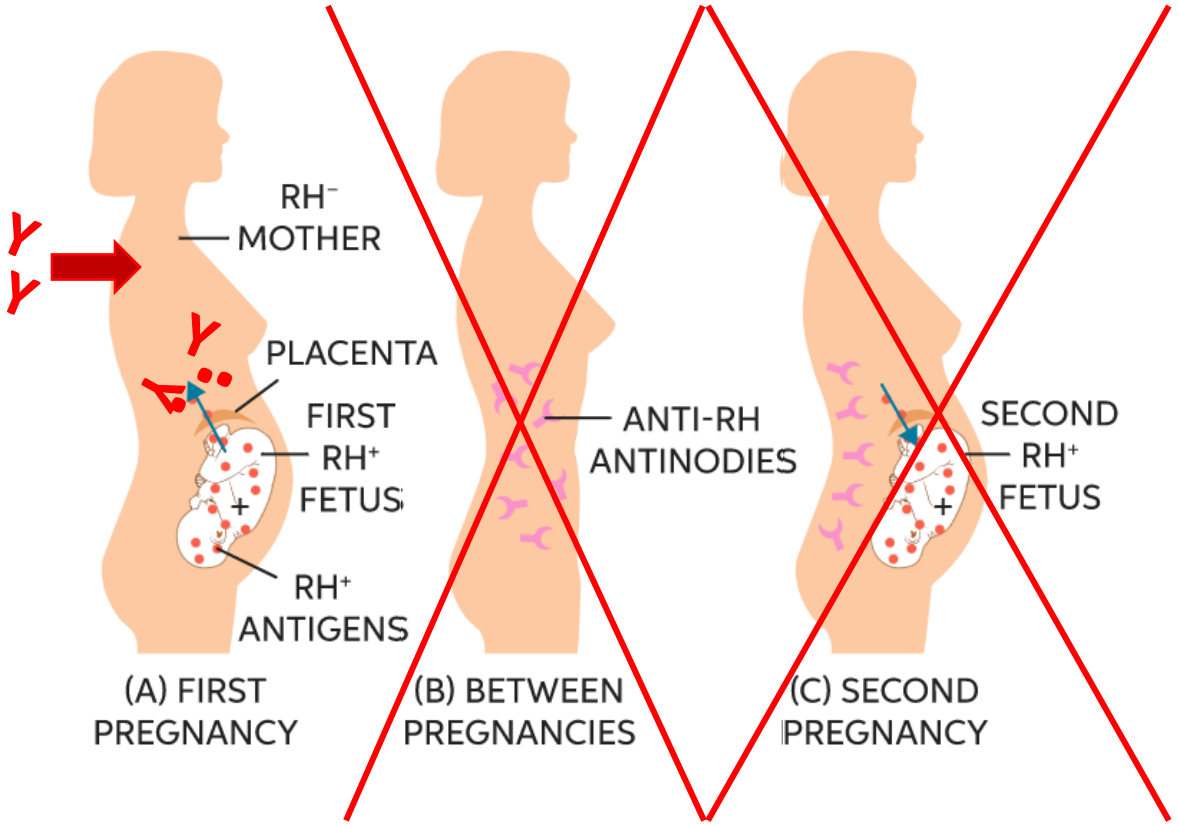
Prevention of the Erythroblastotic Neonate

- By administration of **Rh immunoglobulin globin, an anti-D antibody** to the expectant mother starting at **28 to 30 weeks of gestation.**

**women should receive RhoGAM® before delivery, and soon after every delivery, miscarriage, or abortion.

Prevention of the Erythroblastotic Neonate

The mechanism whereby Rh immunoglobulin globin prevents sensitization of the D antigen is not completely understood, but one effect of the anti-D antibody is to inhibit antigen-induced, B lymphocyte antibody production in the expectant mother. The administered anti-D antibody also attaches to D antigen sites on Rh-positive fetal RBCs that may cross the placenta and enter the circulation of the expectant mother, thereby interfering with the immune response to the D antigen.

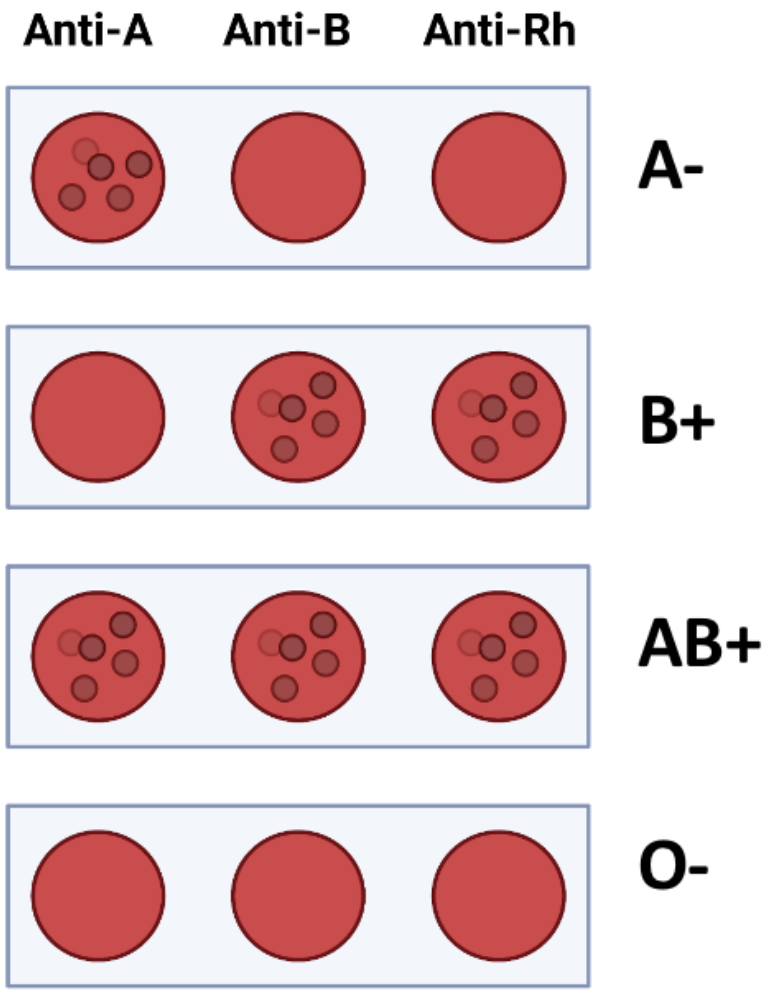


Blood Groups

Blood Typing

Blood Groups

Blood Typing



Blood Groups > Blood matching

- Before giving a transfusion to a person, it is necessary to determine the **blood type** of the **recipient** and **donor** blood so that the bloods can be appropriately matched.

- In a cross-match, the possible **donor RBCs** are **mixed** with the **recipient's serum.** If **agglutination does not occur**, the recipient does not have antibodies that will attack the donor RBCs.

- Alternatively, the **recipient's serum** can be **screened** against a test panel of RBCs having **antigens** known to cause blood transfusion reactions to detect any antibodies that may be present.

Except in extreme emergencies, it is safest to individually cross-match blood before a transfusion is undertaken even though the ABO and Rh typing is already known, because there are approximately 23 other minor human erythrocyte antigen systems, with hundreds of subtypes.

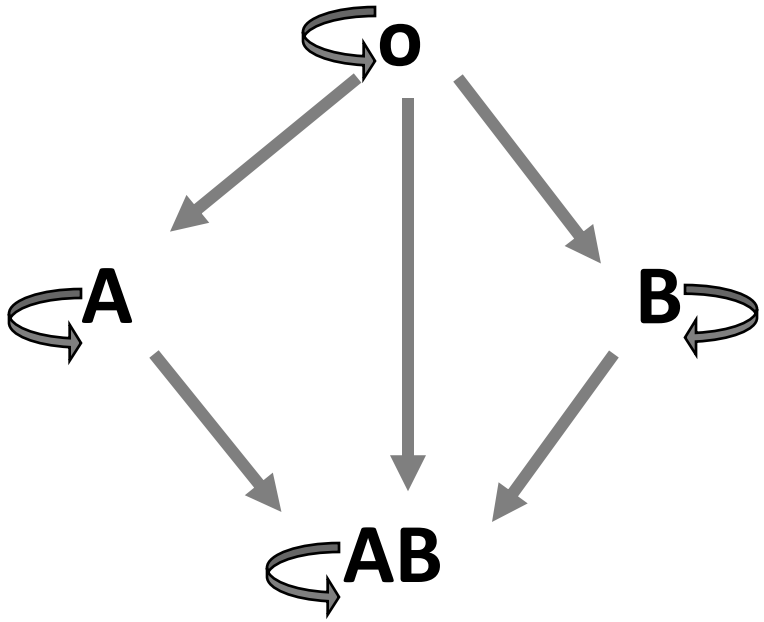
Blood Groups

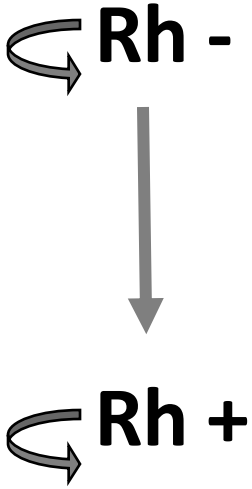
Blood matching

Blood group	Donate	Receive
B+ (anti-A)	AB+, B+	B- (B+) O- (O+)
O- (anti-A and anti-B)	To all blood group	O-
AB+	AB+	From all blood group

Blood Groups

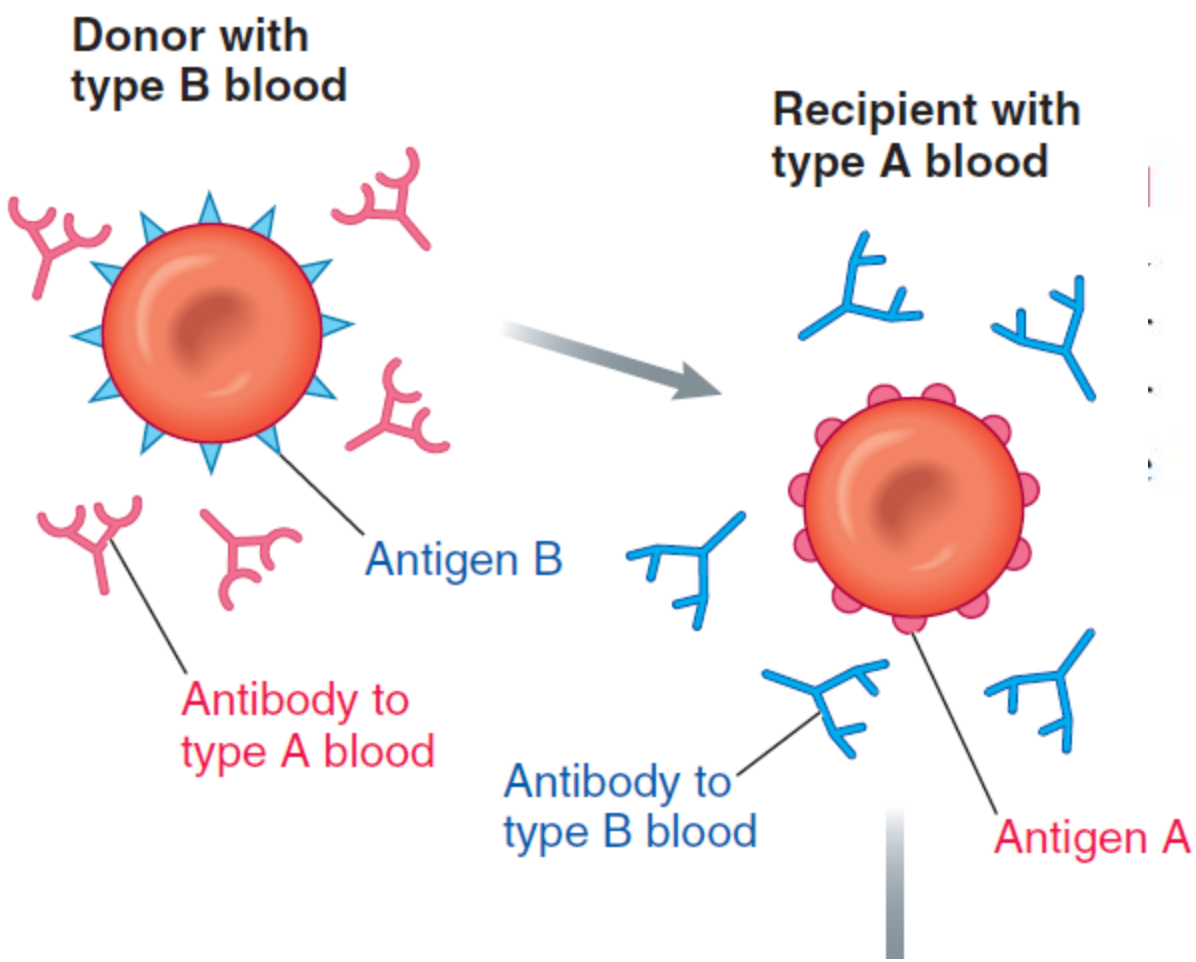
Blood matching



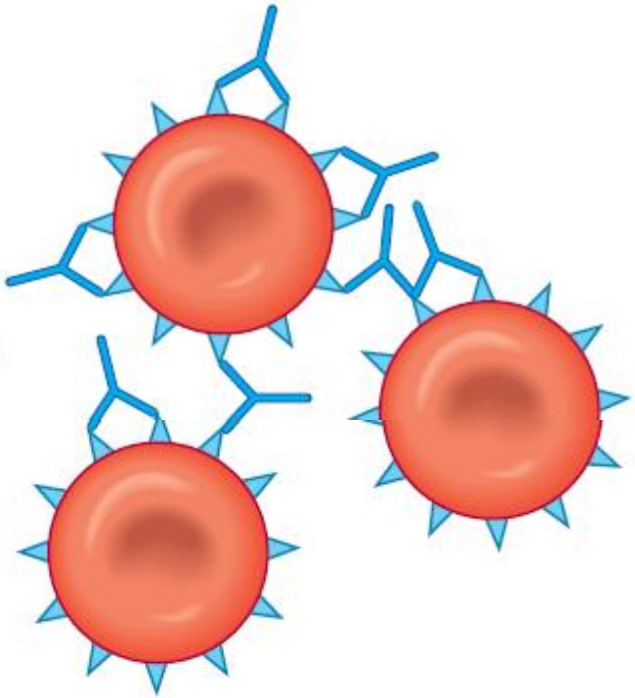


Blood Groups

Transfusion reaction

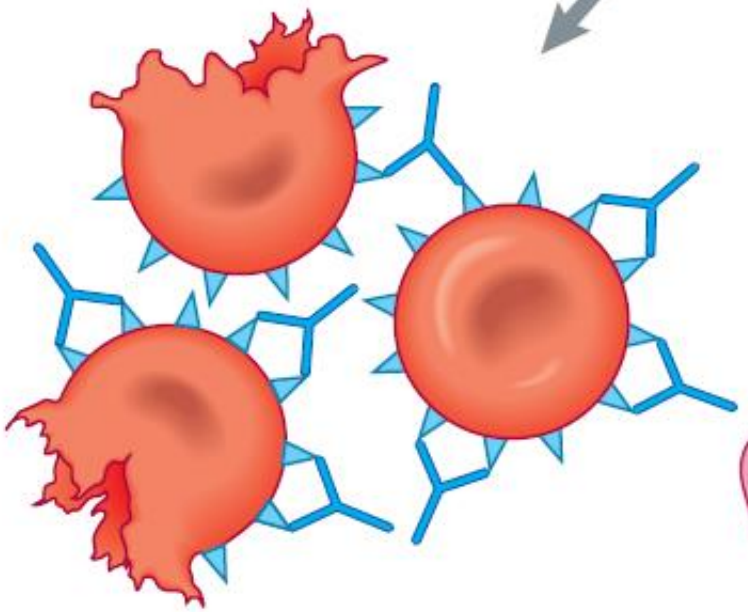


Red blood cells from donor agglutinate



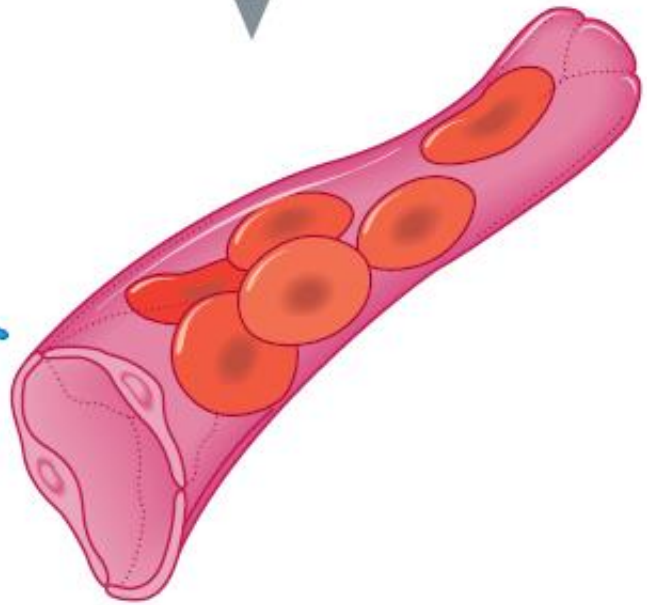
Blood Groups

Transfusion reaction



Red blood cells usually rupture

Hemoglobin precipitates in kidney, interfering with kidney function



Clumping blocks blood flow in capillaries

Oxygen and nutrient flow to cells and tissues is reduced

Transfusion Reactions Resulting from Mismatched Blood Types

- If **donor blood** of one blood type is transfused into a recipient who has another blood type, a transfusion reaction is likely to occur in which the red blood cells **of the donor blood are agglutinated**.
- The plasma portion of the donor blood immediately becomes diluted by all the plasma of the recipient (decreasing the titer of the infused agglutinins)
- The small amount of infused blood does not significantly dilute the agglutinins in the recipient's plasma.

Transfusion Reactions Resulting from Mismatched Blood Types

- Cause either **immediate hemolysis** or **delayed hemolysis** resulting from phagocytosis of agglutinated cells.
- Jaundice
- Acute Kidney Shutdown

Transfusion Reactions Resulting from Mismatched Blood Types- Acute Kidney Failure After Transfusion Reactions

The kidney shutdown seems to have three causes:

1. The **antigen-antibody reaction** of the transfusion reaction releases **toxic substances** from the hemolyzing blood that cause powerful **renal vasoconstriction.**

2. **Loss of circulating RBCs** in the recipient, along with production of toxic substances from the hemolyzed cells and the immune reaction, often cause **circulatory shock**. The **arterial blood pressure falls very low**, and renal blood flow and urine output decrease.

3. Much of the excess **free hemoglobin** leaks through the glomerular membranes into the kidney tubules.