## Physiology of Blood

Lec. 4

## Blood groups

bloods of different people have different antigenic and immune properties, so that antibodies in the plasma of one blood will react with antigens on the surfaces of the red cells of another blood type. If proper precautions are taken, one can determine ahead of time whether the antibodies and antigens present in the donor and recipient bloods will cause a transfusion reaction.

### • 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, have been found in human blood cells, especially on the surfaces of the cell membranes. Most of the antigens are weak and therefore are of importance principally for studying the inheritance of genes to establish parentage.
- 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. The ABO blood group consists of blood types A, B, AB, and O, depending on the presence or absence of two antigens

### O-A-B Blood Types:

- A and B Antigens—Agglutinogens:
- Two antigens—type A and type B—occur on the surfaces of the red blood cells in a large proportion of human beings. It is these antigens (also called agglutinogens because they often cause blood cell agglutination) that cause most blood transfusion reactions. Because of the way these agglutinogens are inherited, people may have neither of them on their cells, they may have one, or they may have both simultaneously.

### Major O-A-B Blood Types:

• In transfusing blood from one person to another, the bloods of donors and recipients are normally classified into four major O-A-B blood types, as shown in Table below, depending on the presence or absence of the two agglutinogens, the A and B agglutinogens. When neither A nor B agglutinogen is present, the blood is type O. When only type A agglutinogen is present, the blood is type A. When only type B agglutinogen is present, the blood is type B. When both A and B agglutinogens are present, the blood is type AB.

#### Table 35-1

### Blood Types with Their Genotypes and Their Constituent Agglutinogens and Agglutinins

Genotypes	Blood Types	Agglutinogens	Agglutinins
OO	О	_	Anti-A and Anti-B
OA or AA	A	A	Anti-B
OB or BB	В	В	Anti-A
AB	AB	A and B	_

# • Genetic Determination of the Agglutinogens:

• Two genes, one on each of two paired chromosomes, determine the O-A-B blood type. These genes can be any one of three types but only one type on each of the two chromosomes: type O, type A, or type B. The type O gene is either functionless or almost functionless, so that it causes no significant type O agglutinogen on the cells. Conversely, the type A and type B genes do cause strong agglutinogens on the cells.

• The six possible combinations of genes, as shown in Table above, are OO, OA, OB, AA, BB, and AB. These combinations of genes are known as the genotypes, and each person is one of the six genotypes. One can also observe from Table above that a person with genotype OO produces no agglutinogens, and therefore the blood type is O. A person with genotype OA or AA produces type A agglutinogens and therefore has blood type A. Genotypes OB and BB give type B blood, and genotype AB gives type AB blood.

### Relative Frequencies of the Different Blood Types:

The prevalence of the different blood types among one group of persons studied was approximately:

- O:47 %
- A:41 %
- B:9%
- AB:3%
- It is obvious from these percentages that the O and A genes occur frequently, whereas the B gene is infrequent.

### • Agglutinins:

• When type A agglutinogen is not present in a person's red blood cells, antibodies known as anti-A agglutinins develop in the plasma. Also, when type B agglutinogen is not present in the red blood cells, antibodies known as anti-B agglutinins develop in the plasma. Thus, referring once again to Table above note that type O blood, although containing no agglutinogens, does contain both anti-A and anti-B agglutinins; type A blood contains type A agglutinogens and anti-B agglutinins; type B blood contains type B agglutinogens and anti-A agglutinins. Finally, type AB blood contains both A and B agglutinogens but no agglutinins

### Titer of the Agglutinins at Different Ages :

• 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—anti-A agglutinins when type A agglutinogens are not present in the cells, and anti-B agglutinins when type B agglutinogens are not in the cells. Figure below shows the changing titers of the anti-A and anti-B agglutinins at different ages. A maximum titer is usually reached at 8 to 10 years of age, and this gradually declines throughout the remaining years of life.

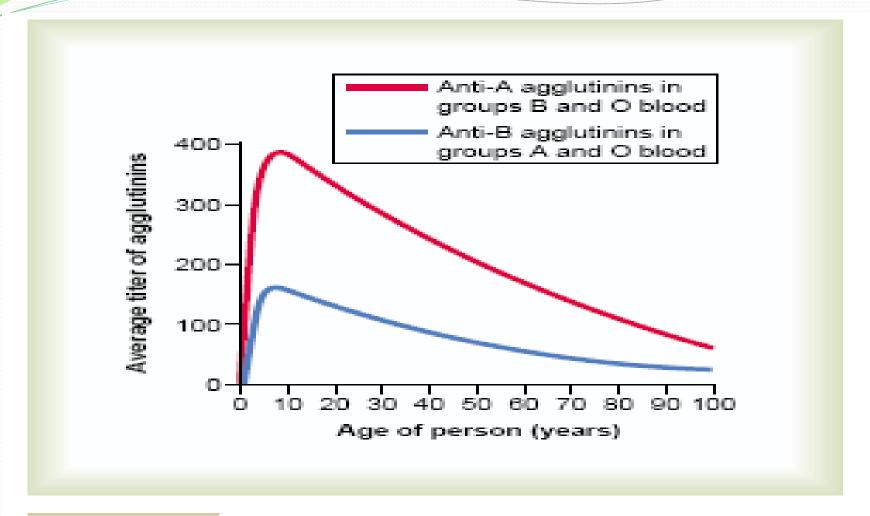


Figure 35-1

Average titers of anti-A and anti-B agglutinins in the plasmas of people with different blood types.

### Origin of Agglutinins in the Plasma:

• The agglutinins are gamma globulins, as are almost all antibodies, and they are produced by the same bone marrow and lymph gland cells that produce antibodies to any other antigens. Most of them are IgM and IgG immunoglobulin molecules. But why are these agglutinins produced in people who do not have the respective agglutinogens in their red blood cells?

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. For instance, infusion of group A antigen into a recipient having a non-A blood type causes a typical immune response with formation of greater quantities of anti-A agglutinins than ever. Also, the neonate has few, if any, agglutinins, showing that agglutinin formation occurs almost entirely after hirth.

# Agglutination Process In Transfusion Reactions:

 When bloods are mismatched so that anti-A or anti-B plasma agglutinins are mixed with red blood cells that contain A or B agglutinogens, respectively, the red cells agglutinate as a result of the agglutinins' attaching themselves to the red blood cells. Because the agglutinins have two binding sites (IgG type) or 10 binding sites (IgM type), a single agglutinin can attach to two or more red blood cells at the same time, thereby causing the cells to be bound together by the agglutinin.

This causes the cells to clump, which is the process of "agglutination." Then these clumps plug small blood vessels throughout the circulatory system. During ensuing hours to days, either physical distortion of the cells or attack by phagocytic white blood cells destroys the membranes of the agglutinated cells, releasing hemoglobin into the plasma, which is called "hemolysis" of the red blood cells.

### Acute Hemolysis Occurs in Some Transfusion Reactions:

• Sometimes, when recipient and donor bloods are mismatched, immediate hemolysis of red cells occurs in the circulating blood. In this case, the antibodies cause lysis of the red blood cells by activating the complement system, which releases proteolytic enzymes that rupture the cell membranes.

• Immediate intravascular hemolysis is far less common than agglutination followed by delayed hemolysis, because not only does there 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; these antibodies are called hemolysins.

### • Blood Typing:

• Before giving a transfusion to a person, it is necessary to determine the blood type of the recipient's blood and the blood type of the donor blood so that the bloods can be appropriately matched. This is called blood typing and blood matching, and these are performed in the following way: The red blood cells are first separated from the plasma and diluted with saline. One portion is then mixed with anti-A agglutinin and another portion with anti-B agglutinin.

- After several minutes, the mixtures are observed under a microscope. If the red blood cells have become clumped—that is, "agglutinated"—one knows that an antibody antigen reaction has resulted.
- Table below lists the presence (+) or absence (-) of agglutination of the four types of red blood cells. Type O red blood cells have no agglutinogens and therefore do not react with either the anti-A or the anti-B agglutinins. Type A blood has A agglutinogens and therefore agglutinates with anti-A agglutinins. Type B blood has B agglutinogens and agglutinates with anti-B agglutinins.

- Type AB blood has both A and B agglutinogens and agglutinates with both types of agglutinins. O red blood cells have no agglutinogens and therefore do not react with either the anti-A or the anti-B agglutinins. Type A blood has A agglutinogens and therefore agglutinates with anti-A agglutinins. Type B blood has B agglutinogens and agglutinates with anti-B agglutinins. Type AB blood has both A and B agglutinogens and agglutinates with both types of
- Agglutinins.

• A mismatched transfusion causes a transfusion reaction the agglutinated R.B.C.s block small blood vessels, hemolyze, and release their Hb over the next few hours to days. Free Hb can block the kidney tubules and cause death within a week or so from acute renal failure. For this reason, a person with type A (anti-B) blood must never be given a transfusion of type B or AB blood. Type "AB" is called universal recipient while "O" is universal donor.

#### Table 35-2

#### Blood Typing, Showing Agglutination of Cells of the Different Blood Types with Anti-A or Anti-B Agglutinins in the Sera

Red Blood Cell Types	Sera		
	Anti-A	Anti-B	
0	_	_	
A	+	_	
В	_	+	
AB	+	+	

### Rh Blood Types:

• Along with the O-A-B blood type system, the Rh blood type system is also important when transfusing blood. 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, such as by transfusion of blood containing the Rh antigen, before enough agglutinins to cause a significant transfusion reaction will develop.

- Rh Antigens—"Rh-Positive" and "Rh-Negative" People:
- 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.A person who has a C antigen does not have the c antigen, but the person missing the C antigen always has the c antigen. The same is true for the D-d and E-e antigens. Also, because of the manner of inheritance of these factors, 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 this type of antigen is said to be Rh positive, whereas a person who does not have type D antigen is said to be Rh negative. 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. About 85% of all white people are Rh positive and 15%, Rh negative. In American blacks, the percentage of Rh-positives is about 95, whereas in African blacks, it is virtually 100 per cent.

- Rh Immune Response:
- Formation of Anti-Rh Agglutinins:
- When red blood cells containing Rh factor are injected into a person whose blood does not contain the Rh factor—that is, into an Rh-negative person—anti-Rh agglutinins develop slowly, reaching 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:

 If an Rh negative person has never before been exposed to Rh positive blood, transfusion of Rh-positive blood into that person will likely cause no immediate reaction. However, 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. On subsequent transfusion of Rh-positive blood into the same person, 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.

## 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. It is rare that the transfused blood causes agglutination of the recipient's cells, for the following reason: The plasma portion of the donor blood immediately becomes diluted by all the plasma of the recipient, thereby decreasing the titer of the infused agglutinins to a level usually too low to cause agglutination. Conversely, the small amount of infused blood does not significantly dilute the agglutinins in the recipient's plasma. Therefore, the recipient's agglutinins can still agglutinate the mismatched donor cells. As explained earlier, all transfusion reactions eventually cause either immediate hemolysis resulting from hemolysins or later hemolysis resulting from phagocytosis of agglutinated cells.

The hemoglobin released from the red cells is then converted by the phagocytes into bilirubin and later excreted in the bile by the liver, The concentration of bilirubin in the body fluids often rises high enough to cause jaundice—that is, the person's internal tissues and skin become colored with yellow bile pigment. But if liver function is normal, the bile pigment will be excreted into the intestines by way of the liver bile, so that jaundice usually does not appear in an adult person unless more than 400 milliliters of blood is hemolyzed in less than a day.

### Transplantation of Tissues and Organs:

 Most of the different antigens of red blood cells that cause transfusion reactions are also widely present in other cells of the body, and each bodily tissue has its additional complement of antigens. Consequently, foreign cells transplanted anywhere into the body of a recipient can produce immune reactions. In other words, most recipients are just as able to resist invasion by foreign tissue cells as to resist invasion by foreign bacteria or red cells.

## Thank you..