BLOOD GROUPING

Karl Landsteiner, in 1901 discover of blood groups

Determination of ABO blood groups depends upon the immunological reaction between antigen and antibody. Landsteiner found two antigens on the surface of RBCs and named them as A antigen and B antigen. These antigens are also called agglutinogens because of their capacity to cause agglutination of RBCs. He noticed the corresponding antibodies or agglutinins in the plasma and named them anti-A or α-antibody and anti-B or β-antibody. However, a particular agglutinogen and the corresponding agglutinin cannot be present together. If present, it causes clumping of the blood. Based on this, Karl Landsteiner classified the blood groups. Later it became the 'Landsteiner Law' for grouping the blood.

LANDSTEINER LAW

Landsteiner law states that:

- If a particular agglutinogen (antigen) is present in the RBCs, corresponding agglutinin (antibody) must be absent in the serum.
- If a particular agglutinogen is absent in the RBCs, the corresponding agglutinin must be present in the serum.

Though the second part of Landsteiner law is a fact, it is not applicable to Rh factor.

BLOOD GROUP SYSTEMS

More than 20 genetically determined blood group systems are known today. But, Landsteiner discovered two blood group systems called the ABO system and the Rh system. These two blood group systems are the most important ones that are determined before blood transfusions.

ABO SYSTEM

Based on the presence or absence of antigen A and antigen B, blood is divided into four groups:

1. 'A' group
2. 'B' group
3. 'AB' group
4. 'O' group.

- Blood having antigen A belongs to 'A' group. This blood has β-antibody in the serum.
- Blood with antigen B and α-antibody belongs to 'B' group.
- If both the antigens are present, blood group is called 'AB' group and serum of this group does not contain any antibody.
- If both antigens are absent, the blood group is called 'O' group and both α and β antibodies are present in the serum.

Group	Antigen in RBC	Antibody in serum
A	A	Anti-B (β)
B	B	Anti-A (α)
AB	A and B	No antibody
O	No antigen	Anti-A and Anti-B

DETERMINATION OF ABO GROUP

Determination of the ABO group is also called blood grouping, blood typing or blood matching.

Principle of Blood Typing –

Agglutination Blood typing is done on the basis of agglutination. Agglutination means the collection of separate particles like RBCs into clumps or masses. Agglutination occurs if an antigen is mixed with its corresponding antibody which is called isoagglutinin. Agglutination occurs when A antigen is mixed with anti-A or when B antigen is mixed with anti-B

IMPORTANCE OF ABO GROUPS IN BLOOD TRANSFUSION

During blood transfusion, only compatible blood must be used. The one who gives blood is called the 'donor' and the one who receives the blood is called 'recipient'.

- While transfusing the blood, antigen of the donor and the antibody of the recipient are considered.
- The antibody of the donor and antigen of the recipient are ignored mostly.
- Thus, RBC of 'O' group has no antigen and so agglutination does not occur with any other group of blood. So, 'O' group blood can be given to any blood group persons and the people with this blood group are called 'universal donors'.
- Plasma of AB group blood has no antibody. This does not cause agglutination of RBC from any other group of blood. People with AB group can receive blood from any blood group persons. So, people with this blood group are called 'universal recipients'.

MATCHING AND CROSS-MATCHING

Blood matching (typing) is a laboratory test done to determine the blood group of a person. When the person needs blood transfusion, another test called cross-matching is done after the blood is typed. It is done to find out whether the person's body will accept the donor's blood or not.

For blood matching, RBC of the individual (recipient) and test sera are used.

Cross-matching is done by mixing the serum of the recipient and the RBCs of donor. Cross-matching is always done before blood transfusion.

If agglutination of RBCs from a donor occurs during cross-matching, the blood from that person is not used for transfusion. **Matching = Recipient's RBC + Test sera.**

Cross-matching = Recipient's serum + Donor's RBC.

TRANSFUSION REACTIONS DUE TO ABO INCOMPATIBILITY

Transfusion reactions are the adverse reactions in the body, which occur due to transfusion error that involves transfusion of incompatible (mismatched) blood. The reactions may be mild causing only fever and hives (skin disorder characterized by itching) or may be severe leading to renal failure, shock and death.

In mismatched transfusion, the transfusion reactions occur between donor's RBC and recipient's plasma. So, if the donor's plasma contains agglutinins against recipient's RBC, agglutination does not occur because these antibodies are diluted in the recipient's blood. But, if recipient's plasma contains agglutinins against donor's RBCs, the immune system launches a response against the new blood cells. Donor RBCs are agglutinated resulting in transfusion reactions.

Severity of Transfusion Reactions Severity of transfusion reactions varies from mild (fever and chills) to severe (acute kidney failure, shock and death). Severity depends upon the amount of blood trans fused, type of reaction and general health of the patient.

Cause for Transfusion Reactions

Transfusion of incompatible blood produces hemolytic reactions. The recipient's antibodies (IgG or IgM) adhere to the donor RBCs, which are agglutinated and destroyed. Large amount of free hemoglobin is liberated into plasma. This leads to transfusion reactions.

Signs and Symptoms of Transfusion Reactions

Non-hemolytic transfusion reaction Non-hemolytic transfusion reaction develops within a few minutes to hours after the commencement of blood transfusion. Common symptoms are fever, difficulty in breathing and itching. Hemolytic transfusion reaction Hemolytic transfusion reaction may be acute or delayed. The acute hemolytic reaction occurs within few minutes of transfusion. It develops because of rapid hemolysis of donor's RBCs. Symptoms include fever, chills, increased heart rate, low blood pressure, shortness of breath, bronchospasm, nausea, vomiting, red urine, chest pain, back pain and rigor. Some patients may develop pulmonary edema and congestive cardiac failure. Delayed hemolytic reaction occurs from 1 to 5 days after transfusion.

The hemolysis of RBCs results in release of large amount of hemoglobin into the plasma. This leads to the following complications.

1. Jaundice Normally, hemoglobin released from destroyed RBC is degraded and bilirubin is formed from it. When the serum bilirubin level increases above 2 mg/dL, jaundice occurs.

2. Cardiac Shock Simultaneously, hemoglobin released into the plasma increases the viscosity of blood. This increases the workload on the heart leading to heart failure. Moreover, toxic substances released from hemolyzed cells reduce the arterial blood pressure and develop circulatory shock.

3. Renal Shutdown Dysfunction of kidneys is called renal shutdown. The toxic substances from hemolyzed cells cause constriction of blood vessels in kidney. In addition, the toxic substances along with free hemoglobin are filtered through glomerular membrane and enter renal tubules. Because of poor rate of reabsorption from renal tubules, all these substances precipitate and obstruct the renal tubule. This suddenly stops the formation of urine (anuria).

If not treated with artificial kidney, the person dies within 10 to 12 days because of jaundice, circulatory shock and more specifically due to renal shutdown and anuria.

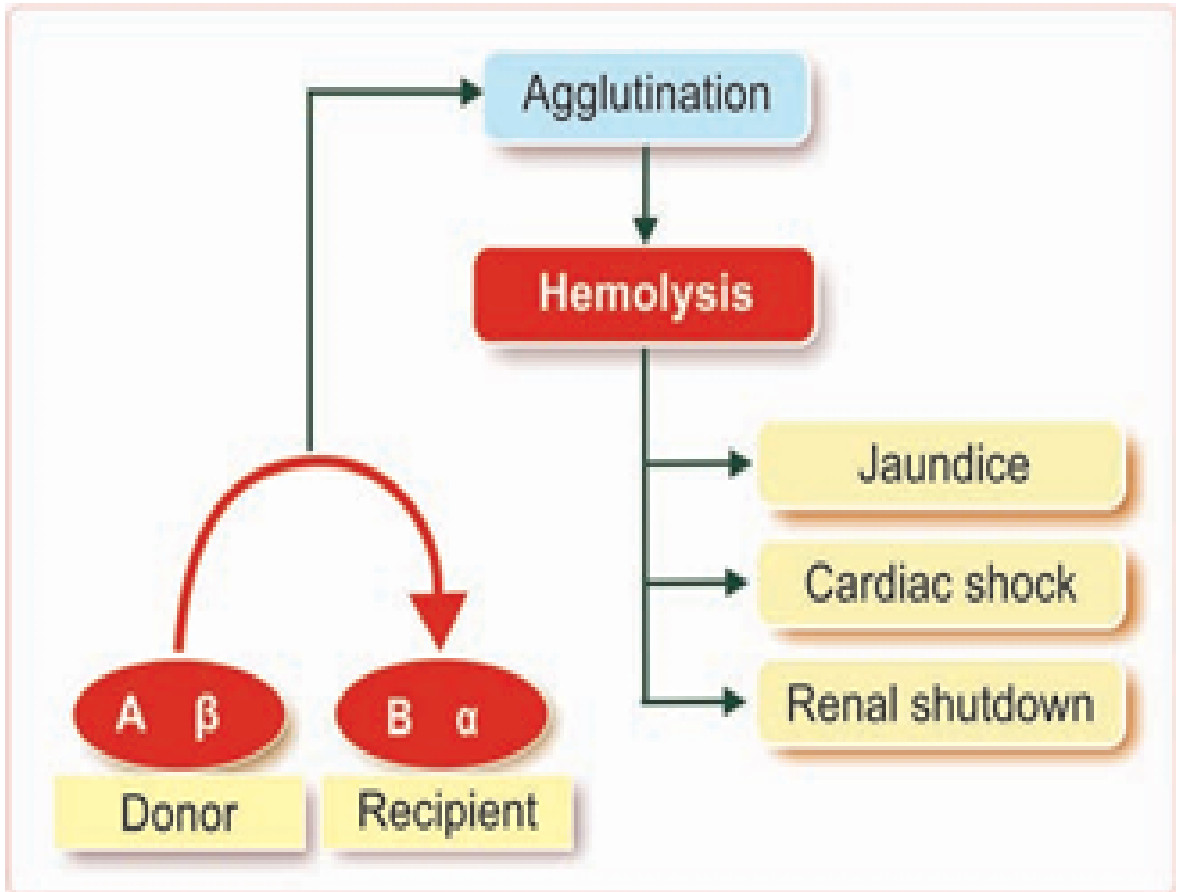

FIGURE 21.2: Complications of mismatched blood transfusion

Rh FACTOR

Rh factor is an antigen present in RBC. This antigen was discovered by Landsteiner and Wiener. It was first discovered in Rhesus monkey and hence the name ‘Rh factor’. There are many Rh antigens but only the D antigen is more antigenic in human. The persons having D antigen are called ‘Rh positive’ and those without D antigen are called ‘Rh negative’. Among Indian population, 85% of people are Rh positive and 15% are Rh negative. Percentage of Rh positive people is more among black people. Rh group system is different from ABO group system because, the antigen D does not have corresponding natural antibody (anti-D). However, if Rh positive blood is transfused to a Rh negative person anti-D is developed in that person. On the other hand, there is no risk of complications if the Rh positive person receives Rh negative blood.

INHERITANCE OF Rh ANTIGEN

Rhesus factor is an inherited dominant factor. It may be homozygous Rhesus positive with DD or heterozygous Rhesus positive with Dd (Fig. 21.3). Rhesus negative occurs only with complete absence of D (i.e. with homozygous dd).

TRANSFUSION REACTIONS DUE TO Rh INCOMPATIBILITY

When a Rh negative person receives Rh positive blood for the first time, he is not affected much, since the reactions do not occur immediately. But, the Rh antibodies develop within one month. The transfused RBCs, which are still present in the recipient's blood, are agglutinated. These agglutinated cells are lysed by macrophages. So, a delayed transfusion reaction occurs. But, it is usually mild and does not affect the recipient. However, antibodies developed in the recipient remain in the body forever. So, when this person receives Rh positive blood for the second time, the donor RBCs are agglutinated and severe transfusion reactions occur immediately (Fig. 21.4). These reactions are similar to the reactions of ABO incompatibility.

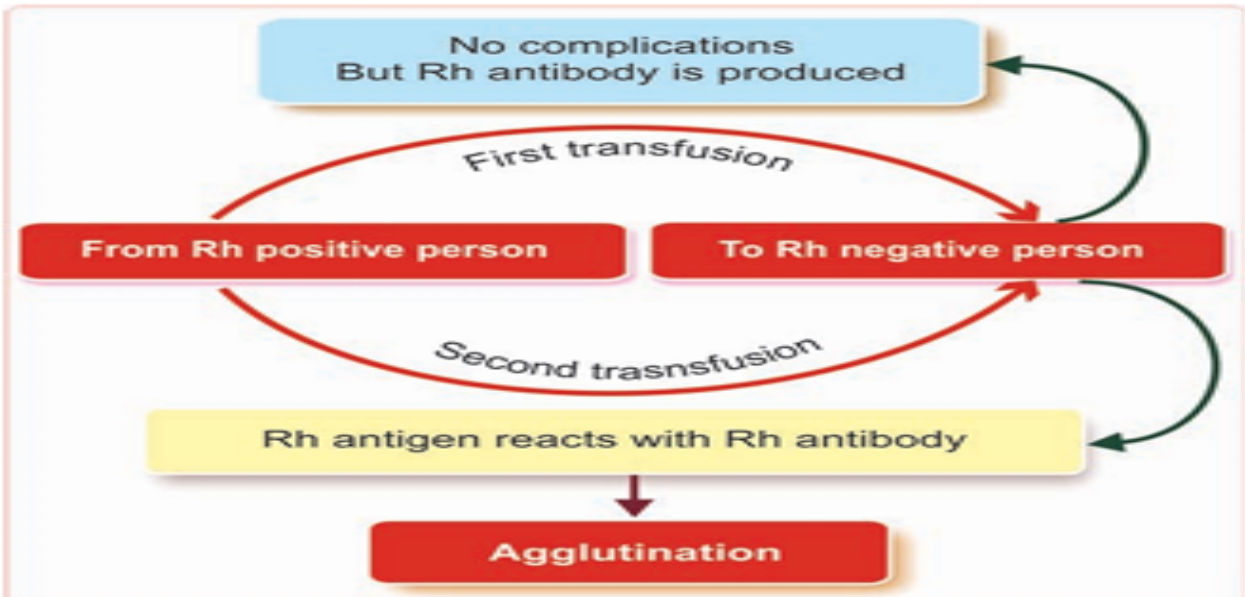

FIGURE 21.4: Rh incompatibility

HEMOLYTIC DISEASE OF FETUS AND NEWBORN – ERYTHROBLASTOSIS FETALIS

Hemolytic disease is the disease in fetus and newborn, characterized by abnormal hemolysis of RBCs. It is due to Rh incompatibility, i.e. the difference between the Rh blood group of the mother and baby. Hemolytic disease leads to erythroblastosis fetalis. Erythroblastosis fetalis is a disorder in fetus, characterized by the presence of erythroblasts in blood. When a mother is Rh negative and fetus is Rh positive (the Rh factor being inherited from the father), usually the first child escapes the complications of Rh incompatibility. This is because the Rh antigen cannot pass from fetal blood into the mother's blood through the placental barrier. However, at the time of parturition (delivery of the child), the Rh antigen from fetal blood may leak into mother's blood because of placental detachment. During postpartum period, i.e. within a month after delivery, the mother develops Rh antibody in her blood. When the mother conceives for the second time and if the fetus happens to be Rh positive again, the Rh antibody from mother's blood crosses placental barrier and enters the fetal blood. Thus, the Rh antigen cannot cross the placental barrier, whereas Rh antibody can cross it

Rh antibody which enters the fetus causes agglutination of fetal RBCs resulting in hemolysis. Severe hemolysis in the fetus causes jaundice. To compensate the hemolysis of more and more number of RBCs, there is rapid production of RBCs, not only from bone marrow, but also from spleen and liver. Now, many large and immature cells in proerythroblastic stage are released into circulation.

Because of this, the disease is called erythroblastosis fetalis. Ultimately due to excessive hemolysis severe complications develop, viz. 1. Severe anemia 2. Hydrops fetalis 3. Kernicterus.

1. Severe Anemia Excessive hemolysis results in anemia and the infant dies when anemia becomes severe.

2. Hydrops Fetalis is a serious condition in fetus, charact erized by edema. Severe hemolysis results in the develop ment of edema, enlargement of liver and spleen and cardiac failure. When this condition becomes more severe, it may lead to intrauterine death of fetus.

3. Kernicterus is the form of brain damage in infants caused by severe jaundice. If the baby survives anemia in erythroblastosis fetalis, then kernicterus develops because of high bilirubin content. The blood-brain barrier is not well developed in infants as in the adults. So, the bilirubin enters the brain and causes permanent brain damage. Most commonly affected parts of brain are basal ganglia, hippocampus, geniculate bodies, cerebellum and cranial nerve nuclei.

The features of this disease are:

i. When brain damage starts, the babies become lethargic and sleepy. They have high-pitched cry, hypotonia and arching of head backwards.

ii. As the disease progresses, they develop hypertonia and opisthotonus.

iii. Advanced signs of the disease are inability to suckle milk, irritability and crying, bicycling movements, choreoathetosis, spasticity, seizures, fever and coma.

Prevention or treatment for erythroblastosis fetalis

i. If mother is found to be Rh negative and fetus is Rh positive, anti D (antibody against D antigen) should be administered to the mother at 28th and 34th weeks of gestation, as prophylactic measure. If Rh negative mother delivers Rh positive baby, then anti D should be administered to the mother within 48 hours of delivery. This develops passive immunity and prevents the formation of Rh antibodies in mother's blood. So, the hemolytic disease of newborn does not occur in a subsequent pregnancy.

ii. If the baby is born with erythroblastosis fetalis, the treatment is given by means of exchange transfusion. Rh negative blood is transfused into the infant, replacing infant's own Rh positive blood. It will now take at least 6 months for the infant's new Rh positive blood to replace the transfused Rh negative blood. By this time, all the molecules of Rh antibody derived from the mother get destroyed.