The Lecture’s topics

Blood groups
- ABO system
  * Transfusion reaction
- Rhesus factor
  * Hemolytic disease of newborn

Blood transfusion and Tissue transplant
The ABO System Discovered in 1901 by Dr. Karl Landsteiner

- Experiments with blood transfusions have been carried out for hundreds of years. Many patients have died and it was not until 1901, when the Karl Landsteiner (from Austria) discovered human blood groups and blood transfusions became safer. Landsteiner found that mixing blood from two individuals can lead to blood clumping. The clumped RBCs can hemolyzed and cause toxic reactions. This can be fatal.

- Karl Landsteiner discovered that blood clumping was an immunological reaction which occurs when the receiver of a blood transfusion has antibodies against the donor blood cells. For this discovery he was awarded the Nobel Prize in Physiology or Medicine in 1930.
Blood groups

• There are 30 common blood group systems (genetically determined) and hundreds rare groups known today. Most of them are weak and are practically not important.

• The AB0 and Rh systems are the most important ones and must be considered in blood transfusions.

• Mixing incompatible blood groups leads to blood clumping or agglutination, which is dangerous for individuals.
What are the ABO blood groups?

- The differences in human blood are due to the presence or absence of certain protein molecules called antigens (agglutinogens) and antibodies (agglutinins).

- The antigens are located on the surface of the red blood cells and the antibodies are in the blood plasma. Individuals have different types and combinations of these antigens and antibodies. The blood group you belong to depends on what you have inherited from your parents.
Blood groups according to ABO system

• Blood is divided into four groups according to presence or absence of certain antigen on the surface of RBCs.

• We have two types of antigens on RBC
  - A antigen
  - B antigen

*** We have four possibilities of presence or absence of these two types of antigens

1. Presence of A antigen .........................group A
2. Presence of B antigen .........................group B
3. Presence of both A and B antigens .......group AB
4. Absence of both A and B antigens ........group O
Genetic determination of ABO antigens

- Humans have three different gens for expression ABO genes (A, B and O genes). Gene O is functionless.
- These genes are on two chromosomes (pair 9).
- 6 possible combinations (genotypes) and four groups
  1. AA .................. group A
  2. AO .................. group A
  3. AB .................. group AB
  4. BB .................. group B
  5. BO .................. group B
  6. OO .................. group O
Example for inheritance of Blood groups
Agglutinins (antibodies)

- Found in plasma
- Are mostly of IgM type (gamma globulin).
- Landsteiner’s Law (for ABO system) States that if an antigen is absent, the corresponding antibody is present.
- Conversely, if an antigen is present on the surface of the RBC, the corresponding antibody is absent in the plasma.

No antibodies
AB0 blood grouping system

According to the AB0 blood typing system there are four different kinds of blood types: A, B, AB or 0.

**Blood group A**
people belong to the blood group A have A antigens on the surface of red blood cells and anti B antibodies in blood plasma.

**Blood group B**
people belong to the blood group B have B antigens on the surface of red blood cells and anti A antibodies in blood plasma.

**Blood group AB**
people belong to the blood group AB have both A and B antigens on the surface of red blood cells and no anti A or anti B antibodies at all in blood plasma.

**Blood group 0**
belong to the blood group 0 have neither A or B antigens on the surface of red blood cells but have both anti A and anti B antibodies in blood plasma.
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<thead>
<tr>
<th>Erythrocytes</th>
<th>Antigen A</th>
<th>Antigen B</th>
<th>Antigens A and B</th>
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<tr>
<td>Plasma</td>
<td>Anti-B antibodies</td>
<td>Anti-A antibodies</td>
<td>Neither anti-A nor anti-B antibodies</td>
<td>Both anti-A and anti-B antibodies</td>
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<td>Blood type</td>
<td>Type A</td>
<td>Type B</td>
<td>Type AB</td>
<td>Type O</td>
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<td>Erythrocytes with type A surface antigens and plasma with anti-B antibodies</td>
<td>Erythrocytes with type B surface antigens and plasma with anti-A antibodies</td>
<td>Erythrocytes with both type A and type B surface antigens, and plasma with neither anti-A nor anti-B antibodies</td>
<td>Erythrocytes with neither type A nor type B surface antigens, but plasma with both anti-A and anti-B antibodies</td>
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Origin and Development of Agglutinins

- The antibodies are developed in response to antigens A and B in food and bacteria (these antigens will enter our body). Remember if the body has no antigen A, it will produce antibodies against this antigen introduced to the body. Infants rapidly develop antibodies against the antigens not present in their own cells.

- At birth there is no agglutinins in the plasma
- At 2-8 months of age the titer of antibodies starts to increase
- Maximal antibodies is found at age 8-10 years of age.
- After age 10, the titer is decreased progressively with age
Transfusion of mismatched blood (transfusion reaction)

- If blood group A is given to a person whose blood group is B, donor RBCs will be attacked by antibodies (anti A agglutinin) which are already present in the recipient blood. The donor RBCs agglutinate (forming a mass). The agglutinated RBCs can block small blood vessels and are liable for phagocytosis and hemolysis.
Transfusion reaction (cont.)

• Transfusion of mismatched blood type causes either

• Agglutination of donor RBCs followed by delayed hemolysis (resulted from phagocytosis of agglutinated RBCs by macrophages).

• Immediate hemolysis of donor RBCs (occurs if the titer of the antibodies (of IgM type) is high and if complements system is activated).
Consequences (outcome) of hemolysis of RBCs followed transfusion reaction

- The hemolyzed RBCs will liberate Hb which is eventually converted to bilirubin. If bilirubin level is increased jaundice will develop.
- A possibility of acute renal shutdown (renal failure). This occurs in large hemolysis.

- Some of liberated Hb can be carried by plasma protein called haptoglobin. If haptoglobin is saturated, the free Hb filtered through glomerular membrane and precipitates in renal tubules closing them and causing renal failure.

*** other causes of renal shutdown followed transfusion reaction
1. Release of toxic substances from hemolyzed RBCS. These substances cause vasoconstriction in renal vessels and less filtration and less urine production.
2. Large hemolysis causes circulatory shock and a decrease in blood pressure and this leads to less urine formation.
Rh factor blood grouping system

- Rh from Rhesus monkey
- **Discovered in 1940 after work on Rhesus monkeys**
- Antigens – C, D, E (only in RBCs)
- **D is the most antigenic component**
- **Rh positive individuals have agglutinogen D.**
- They have **no antibodies** against antigen D in the plasma.
- Rh negative persons have **no D antigen.**
- Anti D agglutinins formed only when these persons are injected with D+ ve cells.
- A person with Rh+ blood can receive blood from a person with Rh- blood without any problems.
- **The majority of people have Rh+ blood**
Inheritance of blood groups

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Characteristics of transfusion reaction due to Rh factor

• It is possible in Rh\textsuperscript{-} person only
• If Rh\textsuperscript{-} person is injected by Rh\textsuperscript{+} RBCs, the body produces antibodies against Rh factor in 2-8 weeks. If these antibodies are in sufficient amount they can cause agglutination of donor RBCs.
• If that Rh\textsuperscript{-} person (who developed antibodies from previous transfusion) receives Rh\textsuperscript{+} RBCs, a strong transfusion reaction occurs (between antibodies in the plasma and transfused RBCs) causing agglutination of these cells and subsequent hemolysis.
Problems associated with Rh antibodies in pregnancy:

• Rh- woman with an Rh+ fetus or transfusion of Rh+ blood
• no problems with first transfusion or pregnancy.
• Reaction occurs if mother has formed antibodies and is pregnant with 2nd Rh+ child. The possibility of reaction is increased with successive pregnancies.
• Rh antibodies can cross placenta and attack fetal blood causing severe anemia.
Hemolytic disease of newborn (erythroblastosis fetalis)

- Could developed in Rh+ fetus of Rh- mother.
- The mother developed anti D antibodies. These antibodies cross the placenta to the fetus’s blood causing agglutination and hemolysis of the fetal RH+ RBCs.

Clinical picture of erythroblastosis fetalis

1. Hemolysis of RBCs leading to anemia and jaundice.
   ***Jaundice could lead to KERNICTERUS (bilirubin crosses blood brain barrier and deposited in motor areas of the brain causing permanent motor and mental abnormalities).

2. Because of loss of RBCs, the process of hematopoiesis is greatly accelerated (in attempt to replace the hemolyzed RBCs) leading to:
   a. appearance of erythroblasts in blood
   b. liver and spleen regain their ability to produce RBCs and their size increases (hepatomegaly and splenomegaly).
Transplantation of tissues or organs

• Every cell in our body has its antigenic properties. If tissue or organ from one person is transplanted in another person, the transplanted tissue or organ will be rejected.

Types of transplanted tissues:

**Autograft**: tissue from a person is transplanted into the same person. The chance of rejection is zero. Both recipient and donor have same antigens.

**Isograft**: tissue from one identical twin is transplanted to other identical twin. The chance of rejection is zero. Both recipient and donor have same antigens.

**Allograft**: tissue from one person to another. If proper matching is done the chance of graft survival is high.
Tissue typing- HLA complex of antigens

- Cell membrane of all body cells has complex called human leukocyte antigens (HLA). There are six of these HLA found in the cell membrane and are responsible for graft rejection.

- Matching of these HLA between the recipient and donor is important for successful transplant.

- The HLA are screened in T lymphocytes because these lymphocytes are responsible for attacking and destroying the transplanted tissues.