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Unit 9: Immunohaematology

Module Name: ABO blood Group System

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❖ **ABO Blood Group System**

- Most important blood group system in human blood transfusion
- Found on platelets, epithelium and cells other than erythrocytes
- AB antigens can also cause an adverse immune response to organ transplantation.

- **KARL LANDSTEINER** discovered the ABO Blood Group System in 1901.
- He and five co-workers began mixing each other's red blood cells and serum together and accidentally performed the first forward and reverse ABO groupings.

- The ABO system contains four blood groups and is determined by the presence or absence of two distinct antigens, A and B, on the surface of erythrocytes.
- Red cells of group A carry antigen A, cells of group B antigen B and cells of group AB have both A and B antigens, while group O cells have neither A nor B antigen.
- Group O is the most common group and group AB is the rarest.
- The 4 groups are also distinguished by the presence or absence of two distinct isoantibodies in the serum.
- The serum contains the isoantibodies specific for the antigen that is absent on the red cell.
- The serum of group A individual has anti-B antibody, group B has anti-A and group O both anti-A and anti-B, while in group AB both anti-A and anti-B are absent.

Table 3.6. Classification of the ABO blood groups

Antigen on Red Cells	Antibodies in Serum	Blood Group
A	Anti-B	A
B	Anti-A	B
Neither A nor B	Anti-A and Anti-B	O
A and B	Neither anti-A nor anti-B	AB

- Group A is subdivided into A1 and A2.
- Antiserum of group A agglutinates group A1 cells powerfully but A2 cells only weakly.
- The subgroups of A are also represented in group AB.
- Therefore, by recognition of group A subgroups, the number of ABO phenotypes increases from 4 to 6: A1, A2, B, A1B, A2B and O.

➢ **Inheritance of the ABO Groups**

- Blood group antigens are inherited according to simple Mendelian Laws.

- The ABO blood type is controlled by a single gene (the ABO gene) with three types of alleles i, I^A, and I^B.
- The I designation stands for isoagglutinogen, another term for antigen.
- The gene encodes a glycosyltransferase.
- The gene is located on the long arm of the ninth chromosome.
- I^A allele gives type A, I^B gives type B, i gives type O.
- I^A and I^B are dominant over i.

Genotypes	Blood groups
$I^A I^B$	AB
$I^A I^A$ or $I^A i$	A
$I^B I^B$ or $I^B i$	B
i i	O

- $I^A I^B$ people have both phenotypes, because A and B express a special dominance relationship: co dominance, which means that type A and B parents can have an AB child.

- **Types of Blood Group Antibodies**

- Blood group antibodies are classified into Natural and Immune antibodies, based on their development.

1. Natural Antibodies

- Anti-A and Anti-B isoantibodies appear in the serum of infants by about the age of 6 months and persist thereafter.
- These are called 'natural' antibodies because they seem to arise under genetic control without any apparent antigenic stimulation.
- It is believed that these antibodies must be the result of some kind of outside stimulus.
- Natural anti-A and anti-B antibodies belong to IgM class.
- They are saline agglutinating antibodies
- They react optimally between $4^{O}C$ and $18^{O}C$. Hence, they are called cold agglutinins.
- For this reason, these do not give rise to severe transfusion reactions.

2. Immune Antibodies

- Immune isoantibodies may develop due to antigenic stimulation following incompatible pregnancy or transfusion., i.e., as a result of immunization by red cells.
- They belong to the IgG class.
- Immune isoantibodies are 'albumin agglutinating' antibodies.
- They react optimally at $37^{O}C$.
- They act as hemolysins in the presence of complement.
- They are clinically more important than natural IgM antibodies and may cause more severe transfusion reactions.

- **H Antigen**

- Red cells of all ABO groups possess a common antigen, the H antigen or H substance which is a precursor for the formation of A and B antigens.
- The presence or absence of the ABH antigens on the red blood cell membrane is controlled by the H gene.

Gene	Enzyme
H	L- fucosyltransferase
A	3 N-acetyl- D- galactosaminyl transferase
B	3-D- galactosyl transferase
O	None

- H gene (HH/Hh) leads to production of an enzyme α-2-L- Fucosyl transferase, which transfers fucose to the terminal galactose of the precursor substance in red cells forming H antigen or H substance.

- A gene codes for an enzyme that adds GalNAc (N-Acetyl-D galactosamine) to the terminal sugar of the H Antigen which convert H substance in to A red cell antigen.
- B gene codes for an enzyme that adds D-Galactose to the terminal sugar of the H Antigen which convert H substance in to B red cell antigen.
- O gene encodes for an inactive enzyme, which results in no conversion of the substance in-group O red cells.
- Hence, Group O cells have the most amount of H antigen whereas AB has the least.

- Persons who do not inherit H gene (very rare hh genotype) are unable to produce H substance and therefore even when A and B genes are inherited, A & B antigens cannot be formed.
- This rare group is referred to as OH (**Bombay group**).
- Such individuals have anti-A, anti-B antibodies and their sera are incompatible with all red cells except of those with the same rare blood group.
- This blood (phenotype) was first discovered in Bombay by Dr. Y.M Bhende in 1952.

➢ **Secretors and Non-Secretors**

- The term secretor and non-secretor only refer to the presence or absence of water-soluble ABH antigen substances in body fluids (saliva, semen, urine, sweat, tears, gastric juice, etc).
- In addition to blood group antigens being present on tissues and cells, when water soluble (glycoprotein) form of antigens appears in most body fluids, then the person is called a secretor.
- Those who lack blood group antigens in secretions are called 'non-secretors'.
- The secretion of ABH antigens is controlled by allelic genes Se and se.
- Individuals who are homozygous or heterozygous for Se are secretors, while those who are se-se are non -secretors.

➢ **ABO Typing**

- ABO typing involves both antigen typing and antibody detection.
- The antigen typing is referred to as the **forward typing** (Direct Blood Grouping) and the antibody detection is the **reverse typing** (Indirect Blood Grouping)
- The direct blood grouping also called cell grouping employs known reagent anti sera to identify the antigen present or their absence on an individual's red cell.
- The indirect blood grouping, also called serum grouping employs red cells possessing known antigen to see the type of antibodies (anti A & -B) present, or absence of these antibodies in serum.