3 .0 Blood group system

Inheritance

- ✓ Inheritance of blood group system is determined by the allelomorphic genes A, B & O.
- ✓ These genes are concerned with the passing of blood group from one generation to another.
- ✓ The allelomorphic genes A& B are dominant and therefore control the entire ABO system.
- ✓ The O gene is considered a morph or recessive gene since it doesn't exert any effect on the basic antigenic structure.
- ✓ There are 4 blood group systems namely A, B, AB&O. There are 3 antibodies in the system e.g. Antibody A, A1 &B.
- ✓ These antibodies are naturally distributed among individuals of various blood groups according to Landsteiner rule.

Landsteiner rule.

The rule states that an individual will always have in their serum antibodies directed to the missing antigen.

Blood group	Antigen on RBCs	Antibody in the serum
A	A	Anti –B
B	B	Anti A & anti A1
AB	A&B	None
O	None	Anti A, anti A1 & anti B

3 .1 Genotypes and phenotypes

- ✓ The allelomorphic genes of the ABO group system are found in pairs in the same locus of a pair of chromosomes, the gametes of an individual after meiosis will therefore contain one of the 2 pairs which he can pass onto the offspring.
- ✓ When a dominant gene pair up with a recessive gene on the same locus, only the resultant qualities of the dominant gene will be demonstrable as the visible expression.
- ✓ The entire ABO blood group system therefore has got 6 genotypes (AO, AA, BB, BO, OO & AB) and 4 phenotypes (A, B, O &AB)

Phenotype	Possible genotype
A	AA & AO
B	BB & BO
AB	AB
O	OO

- ✓ During the inheritance process an individual receives one gene from one parent among the A, B or O genes.

- ✓ When an individual inherits identical gene on the same locus on a pair of chromosome, he/she is said to be **Homozygous** for the character e.g. AA, AB, OO. If he/she receives different genes on the same locus, the person is said to be **Heterozygous** e.g. AO, BO,AB

Parental phenotype	A	A
Parental genotype	AO	AO

Offspring genotype	AA	AO	AO	OO
Offspring phenotype	A	A	A	O

- ✓ It can therefore be seen from the above flow diagram that it's possible to have blood group O offspring from parents who are both blood group A.

Formation of blood group antigens

- ✓ The process entirely depends on the presence of the H-gene which has a role to play before the A, B, &O genes can exert their presence.
- ✓ H-gene is very common in human being and most individuals are Homozygous for it (HH) although there is Heterozygous form (Hh).
- ✓ The Homozygous recessive (hh) is very rare and when present, results into Bombay phenotype (O^h) which lacks visible expression of A, B & O genes.
- ✓ The H-gene and A, B & O genes are inherited independently but they join to form blood groups of ABO system. The A, b &H antigens are all formed from the same precursor substance (ps)

- ✓ The **H gene** acts first on the basic precursor substance by attaching a sugar (**L-fucose**) through enzyme fucosyl transferase to form H-active substance. The A, B&O genes present then follow by attaching specific sugar to the H active substance to form the blood group antigens

- ✓ The **A gene** attaches a sugar (**N-acetylgalactosamine**) through N-acetylgalactosaminal transferase into the H active substance to form both antigens A & H with terminal sugars being L-fucose and N-acetylgalactosamine.

- ✓ The **B gene** attaches a sugar (**D-galactose**) through D-galactosyl transferase into the H active substance to form both antigens B & H with terminal sugars being L-fucose and D-galactose

- ✓ When both A& B genes are present, each attaches its specific sugar through relevant transferases to the H active substance to form A,B&H antigens with three terminal sugars (L-fucose, D-galactose and N-acetylgalactosamine)

- ✓ The **O gene** is **a morph** and attaches **no sugar** to the H-active substance resulting in the formation of only the H antigen with terminal sugar being L-fucose.

NB: The H antigen is found on all human red cells except the subjects of Bombay phenotype (O^h). The A&B phenotypes have less H antigen than O subjects. The order of reactivity with anti- H is as follows:-

$$O > A_2 > A_2B > B > A_1 > A_1B$$

Bombay phenotypes (ABH Null / O^h)

- ✓ This is a rare blood group in which the A, B&H antigens are lacking on the Red cells while antibodies A, B &H are present in the serum. This was discovered by Dr. Bhende in 1952 among the Amarathi speaking Indians.
- ✓ The subjects lack the H-gene which is instrumental in the formation of A, B&O antigens. Instead they posses the recessive (h) gene in homozygous form (hh).
- ✓ The gene attaches no sugar to precursor substance hence the (ps) remain unchanged. The individual may have inherited ABO genes from the parents but these have no where to attach their specific sugars since the H-active substance is lacking.
- ✓ The person ends up lacking A, B&H antigens & according to Landsteiner rule, the person develops Abs. AB&H
- ✓ Bombay individuals can only receive blood from fellow Bombay donors. They cannot receive blood from other blood groups because they posses corresponding antibodies in their serum.
- ✓ The Bombay phenotypes shows similar reactions to blood group O in forward grouping techniques, but on reverse grouping, shows a difference by reacting with O cells since it has anti-H and O cells posses H antigen.
- ✓

	Anti -A	**Anti -B**	**Anti -H**	**A cells**	**B cells**	**O cells**
ABH Null (O^h)	---	---	---	+	+	+
Blood group O	---	---	+	+	+	---

The sub-groups of ABO system

- ✓ These subgroups were discovered by Von Dungem and Hiss Field in 1911 and the four major groups are A_1, A_1B, A_2, A_2B. All these can be put into two major groups of (A_1& A_1B) and (A_2 &A_2B).
- ✓ Anti-A_1 is used to differentiate the two groups. It agglutinates antigens of A_1 only but not A_2.
- ✓ Anti-A can be obtained from serum of blood groups O &B and also from plant lectins (Dolichus biflorus).
- ✓ Nearly all anti-A sera from group O &B persons contain two antibodies namely: - Anti-A & Anti A_1.
- ✓ The Anti A agglutinates the cell of A_1, A_1B, A_2, A_2B…. Anti A_1 agglutinates only the cells of A_1& A_1B.
- ✓ The antigen A2 reacts more weakly with anti-A serum than A_1 antigen because it has less antigenic sites for the anti-A to attach to.
- ✓ The Antibody-A_1 occurs naturally in about 2% of A2 individuals and in 25% of A_2B individuals.
- ✓ Blood group A2 is generally referred to as group A as antibody A2 is also referred to as anti-A.
- ✓ Normally anti-A is routinely used for grouping. Anti-A agglutinates all cells with antigen A (A_1, A_1B, A_2 & A_2B).
- ✓ The inheritance of subgroups is similar to ABO and offspring will inherit one of these genes from each parent to have one of these 8 possible genotypes: -

Phenotype	**Genotypes**
A_1	A_1 A_1, A_1O, A_1 A_2 (A_2 is the same as Antigen A)
A_2	A_2 A_2, A_2O A_1 A_2
A_1B	A_1B
A_2B	A_2B

Antigen on RBC's	**Antibody in Serum**
A_1	Anti -B
A_2	Anti -B & Anti -A_1 (2%)
A_1B	None
A_2B	Anti -A_1 (25%)
O	Anti -A_1, Anti- A_2 & anti -B

- ✓ Critically, the subgroups are more than two and are A_1, A_2, A_3, A_x and A_o. They differ in the amount of the antigenic sites on red cells membrane.

A_1	810,000—1,170,000 antigenic sites
A_2	240,000 - 440,000 antigenic sites
A_3	70,000—100,000 antigenic sites
A_x	1400—10,300 antigenic sites

Other groups are;-

A	800,000 - 1,000,000 antigenic sites
B	750,000 – 1,000,000 antigenic sites
D	110,000 – 202,000 antigenic sites