

Bombay Blood Group- Understanding Genetics

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The blood group serology plays an imminent role in transfusion medicine. The discovery of the rarest blood group (only found in 0.0004 percent of Indian population), Bombay (O_h) Phenotype, also known as hh blood type or ABO blood group by Dr Bhende et al in 1952 in Mumbai formerly (Bombay) was important in the field of immunohematology.

At present over 33 blood grouping systems representing over 300 antigens are known but ABO remains the most significant in transfusions and transplantations. In the year 1900-1902, K. Landsteiner divided the human blood into four groups namely; A, B, AB and O. Where A, B and AB groups have corresponding antigens except the O blood group which doesn't have any. Therefore O is called the universal donor as it can donate blood to any blood group. Similarly AB can take blood from A, B, AB and O i.e. from all blood groups and so is called Universal Recipient.

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Table 1.1 ABO blood grouping

Blood Group	Can donate blood to	Can receive blood from
A	A and AB	A and O
B	B and AB	B and O
AB	Only AB	AB, A, B and O
O	AB, A, B and O	Only O

Discovery: Only ABO blood grouping was known until the discovery of Bombay phenotype in 1952 by Dr Bhende et al of the Seth Gordhandas Sunderdas Medical College, Mumbai published a note in The Lancet (pp.903-4, May 3, 1952) about two patients in need of blood transfusion. To their amazement none of the blood types known until then worked for them i.e. each blood type showed immediate agglutination when mixed with their blood. The blood samples of over 160 donors were tested by the doctors and ultimately the blood from a resident of Bombay suited both the patients. This donor blood type was then named by Dr Bhende et al as the 'Bombay blood type.'

This discovery later helped Watkins and Morgan (1959) and Gerard et al (1982) to elucidate biosynthetic pathway for ABH and Lewis (Le) antigens proposing that the secretor (Se) and H are closely linked structural genes. The Recent molecular genetic studies clearly depicted the role of the H, Se and Le genes in the expression of H antigen in secretions and Lewis blood group antigen on RBCs. It is known that the precursor protein from which all blood groups are formed is the H Antigen which either translates into A antigen (blood group A), B Antigen (blood group B), both A and B Antigens (blood group AB) or it remains as H (blood group O). In the case of Bombay blood group, H antigen itself is absent. Therefore A, B, AB and O which are all different manifestations of H are alien to people with Bombay blood group. Its also known as O_h meaning absence of H Antigen.

Basic ABO antigen synthesis: There are two chains responsible for carrying the antigens and three genes that modify the chains:

- > H also called FUT 1 (located on chromosome 19)
- > Se also called FUT 2 (located on chromosome 19)
- > ABO (located on chromosome 9)

The two chains are;

1. Type 1: They float around freely and are primarily found as glycoproteins in secretions e.g. saliva (except cerebral spinal fluids). They are also found to float around in plasma but ain't bound to RBCs. β 1-3 linkage is present between terminal galactose (Gal) and sub terminal N-acetyl glucosamine.

Se or FUT 2 activity: The various combinations of alleles possible are:

- > SeSe (active)
- > Sese (active)
- > sese (inactive)

Hence at least 1 copy of Se gene must be present to show the activity i.e. if Se allele is present it produces FUT 2 enzyme that acts specifically on type 1 chain and catalyzes the addition of Fucose to terminal galactose, making H antigen. Around 80% people make H antigens on type 1 chain, they're called secretors (SeSe, Sese) and 20% (sese) are non secretors.

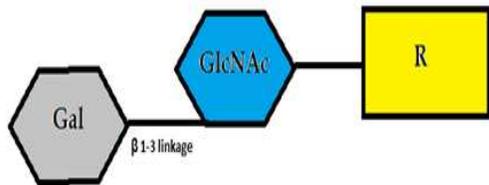


Figure 1.1 Type 1 chain

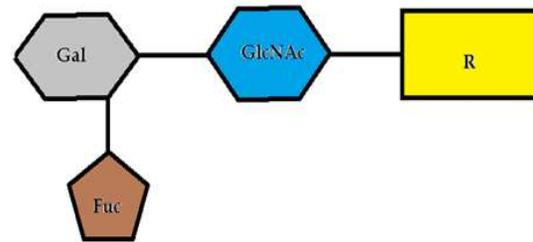


Figure 1.5 H antigen (precursor)

2. Type 2: They're primarily attached to RBC membranes where they can be either glycolipids or glycoproteins. β 1-4 linkage is present between terminal galactose and sub terminal N-acetyl glucosamine.

H or FUT 1 activity: Its composed of H and Se gene. H gene has several different types of genotypes:

- HH (active)
- Hh (active)
- hh (inactive, Bombay phenotype)

In presence of HH or Hh gene, the FUT 1 enzyme is produced that acts specifically on type 2 chain and catalyzes the addition of fucose to terminal galactose forming H antigen



Figure 1.2 Type 2 chain

Blood group A: If alleles AA or Ai are present on the chromosomes, it facilitates secretion of A transferase that causes addition of N-Acetyl galactosamine on Galactose and changes the H antigen to A antigen. Hence the blood group of the person will be of A type.

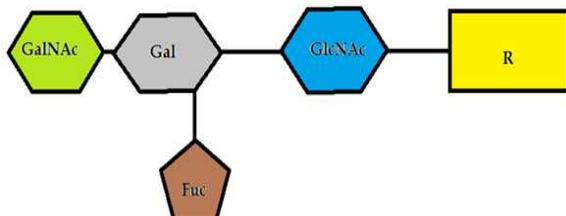


Figure 1.3 A antigen

Blood group B: Similarly if a person has blood group B then either BB or Bi alleles are present, producing B transferase that facilitates the attachment of galactose to the terminal galactose on the precursor chain, thereby leading to the formation of B antigen from H antigen.

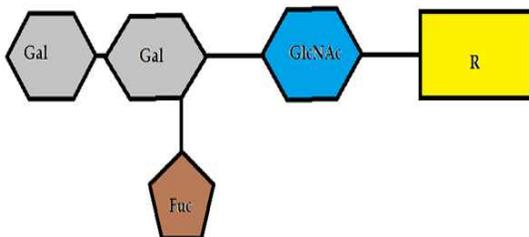


Figure 1.4 B antigen

O blood group: If a person has O blood type, two copies of 'i' alleles are present or in other words only H antigen is present with nothing attached to it (as transferase enzyme isn't produced in such case).

H deficient types:

1. H - Deficient, non secretors (Bombay/O_h): They have hh and sese genotypes (inactive). People having FUT1 and FUT2 gene mutations possess such phenotype. Usually what happens is someone having H antigen and AA or AO alleles will add GalNAc in presence of A transferase to make A antigen. However those having hh have no FUT1 enzyme, hence on the surface of RBC, fucose was never added so GalNAc won't also be added. Similarly in people having blood group B, if hh is present there's no FUT1 enzyme hence fucose is absent and galactose won't be added as a result the carbohydrate chains on their surface won't carry A, B or H activity.

Note: They seem to be like blood group O but there's a huge difference between the two blood types i.e. People with Bombay phenotype have abundant anti - H unlike people with blood group O that lack anti - H in their serum.

Leukocyte adhesion deficiency Type II (LAD II): Such individuals are H - Deficient due to the inhibition of fucosylation of RBC type 2 chains. Its an incredibly rare syndrome as only few cases have been reported so far. It also leads to infections and mental retardation.

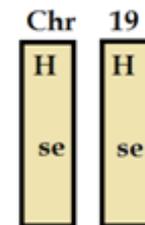


Figure 1.6 H - Deficient, non secretors (chromosome 19)

2. H - Deficient, secretors (Para Bombay): These individuals have hh by definition (like O_h) but SeSe or Sese (unlike O_h). Therefore they don't make H on the surface of blood cells just like the people with Bombay blood type. However they don't have deletion of secretor allele Se so unlike Bombay people, they're capable of attaching fucose on type 1 chain and making H antigen both in secretions and plasma and thus some A and/B antigens can attach to RBC.

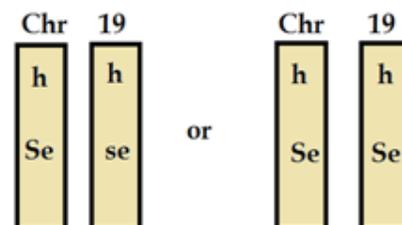


Figure 1.7 H - Deficient, secretors (chromosome 19)

3. Mostly H – Deficient, non secretors (H^w): These individuals have weak H (FUT1) and are non secretors (sese). Thus act more like O blood type.

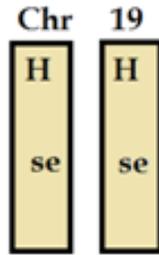


Figure 1.8 Weak H/H – Deficient, non secretors (chromosome 19)

Antibodies in Bombay phenotype: The individuals don't have H antigen so they've anti – A, anti – B, and anti – H.

Bombay case example: A couple with blood groups O and B respectively had their 1st baby with blood group B (as expected).

	B (Female)		X	O (male)	
	O	O		O	O
B	BO	BO	B	BO	BO
B	BO	BO	O	OO	OO

But the second baby had blood group A so it was concluded that the father had blood group A.

	O (Female)		X	A (Male)	
	A	O			
B	AB	BO			
O	AO	OO			

Scientists were curious to know why it showed blood group O in the first case and A in the second. It was found that the person actually had Para Bombay phenotype (hh, Sese/SeSe) and thus had strong anti-H in their blood.

Transfusion: It depends on how antigen - H is reacting i.e. the people with Bombay phenotype will essentially always need blood from another Bombay and those who're Para Bombay, can accept blood from either another Bombay individual or their own autologous blood cells when healthy.

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