BLOOD GROUP AND RH FACTOR

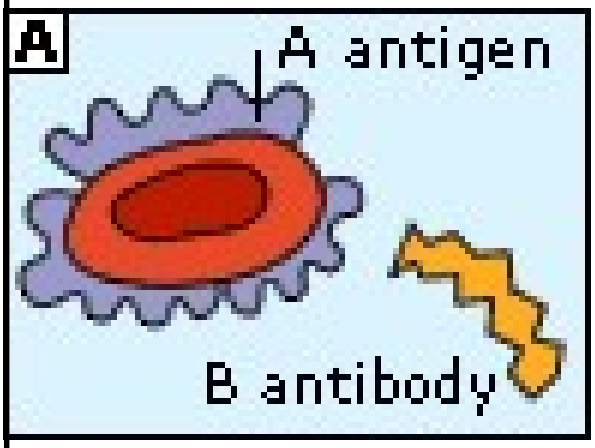
ABO BLOOD GROUPS

- ABO blood group in Human was discovered by LANDSTEINER in 1901.
- The ABO system is characterized by the presence or absence of antigens on the surface of Red Blood Cells.
- Individuals will naturally develop antibodies against the ABO antigens they do not have.
- For example, individuals with blood group A will have anti-B antibodies, and individuals with blood group O will have both anti-A and anti-B.

RBC Surface proteins (Ag)	Plasma Antibody (Ab)	Blood Type
A	b	A
B	a	B
AB	--	AB
--	a & b	O

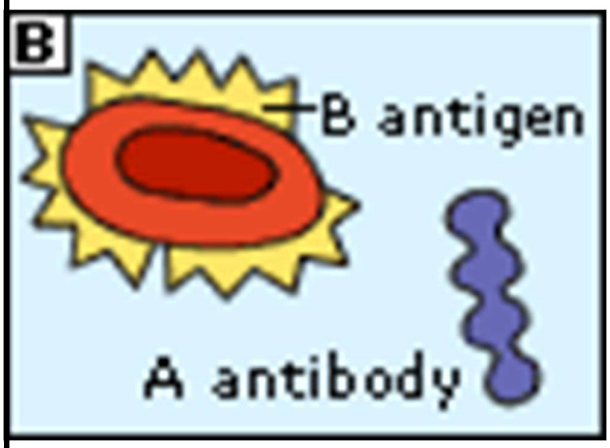
- The ABO phenotype of any individual is ascertained by mixing a blood sample with antiserum containing type A or type B antibodies. If the antigen is present on the surface of Red Blood Cells of the person, then it will react with the corresponding antibody and cause clumping or agglutination of the Red Blood Cells.

Blood group A



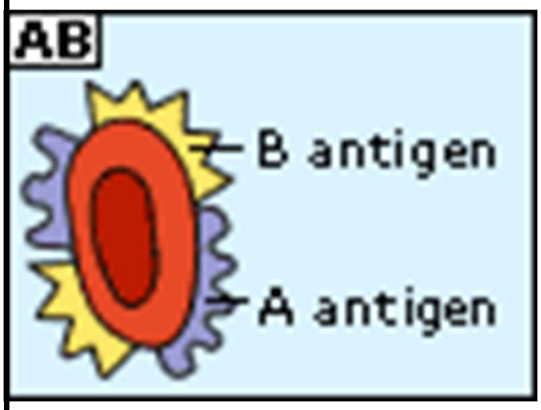
If you belong to the blood group A, you have A antigens on the surface of your RBCs and B antibodies in your blood plasma.

Blood group B



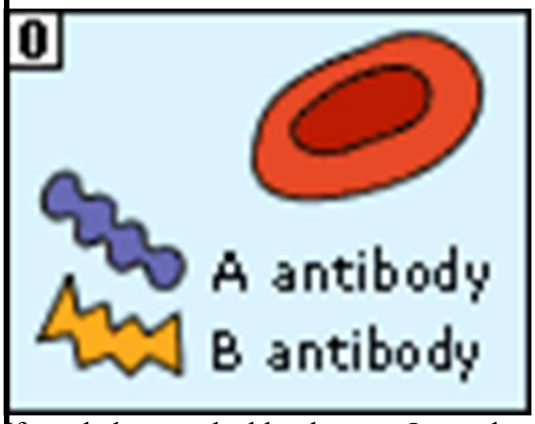
If you belong to the blood group B, you have B antigens on the surface of your RBCs and A antibodies in your blood plasma.

Blood group AB



If you belong to the blood group AB, you have both A and B antigens on the surface of your RBCs and no A or B antibodies at all in your blood plasma.

Blood group O



If you belong to the blood group O, you have neither A or B antigens on the surface of your RBCs but you have both A and B antibodies in your blood plasma.

GENETICS OF ABO BLOOD SYSTEM

- The ABO blood type is inherited in an Autosomal Co-Dominant fashion.
- The ABO locus is located on **chromosome 9** at 9q34.1-q34.2 consisting 18 kb of genomic DNA (Exon 7).
- The A and B alleles differ from each other by seven nucleotide substitutions
- The gene controlling ABO blood type is labeled as I.
- The alleles are designated as I^A, I^B and I^O (or i).
  Where, I → Isoagglutinogen (antigen)
  I^A → Allele for A antigen
  I^B → Allele for B antigen I^O
  → Allele for o antigen
- Dominance Hierarchy among alleles; $\mathbf{I^A = I^B > I^O}$
  i.e., Alleles I^A & I^B are dominant over I^O
  Alleles I^A & I^B are Co-dominant

Genotype	Antigen on RBC	Blood type
$I^A I^A / I^A I^O$	A	A
$I^B I^B / I^B I^O$	B	B
$I^A I^B$	A & B	AB
$I^O I^O$	--	O

- Further, studies suggest that I^A allele may occur in at least FOUR allelic forms; I^A1, $IA2$, I^A3 & I^A4
- Thus, Dominance Hierarchy among 6 alleles; $\mathbf{I^A}$ $[I^A1 > IA2 > I^A3 > I^A4] = \mathbf{I^B > I^O}$

Note:
Recent data reports over 80 ABO alleles.

- The blood groups are defined by the presence of specific carbohydrate sugars [oligosaccharide chains] on the surface of red blood cells.
- The specificity of A and B antigens are based on the terminal sugars of carbohydrate group [i.e., precursor molecule - H antigen]
- The H locus is located on chromosome 19 at 19q13.3 (>5 kb of genomic DNA, three exons), and it encodes a fucosyltransferase that produces the H antigen on RBCs.
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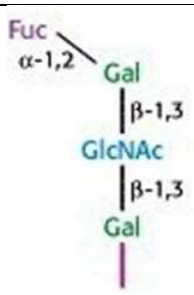
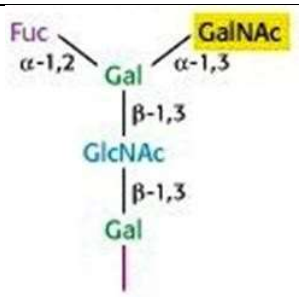
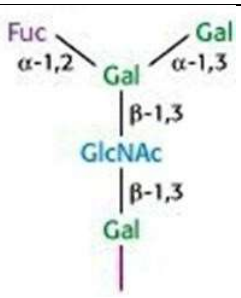
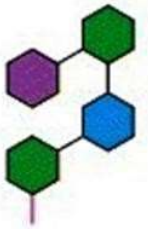
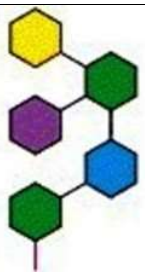
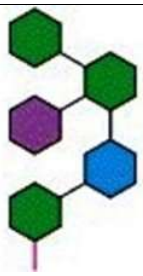
- H-antigen consists of 3 sugar molecules; galactose (Gal), N-acetylglucosamine (GlcNAc) and fucose (Fuc)
- I^A and I^B alleles each encode a specific glycosyl-transferring enzyme, which catalyzes the final step in the synthesis of the A and B antigen.
- The I^A allele encodes a glycosyltransferase (i.e., N-acetylgalactose transferase) that produces the A antigen (by adding terminal N-acetylgalactosamine - immunodominant sugar)
- The I^B allele encodes a glycosyltransferase (i.e., galactose transferase) that creates the B antigen (by adding terminal D-galactose - immunodominant sugar).
- The I^O allele encodes an enzyme with no function (*might be, not yet discovered*), and therefore neither A or B antigen is produced, leaving the underlying precursor (the H antigen) unchanged.

Allele ↓*translation* Glycosyl transferase ↓*Function* Terminal-sugar	**I^O** ↓ --- ↓ ---	**I^A** ↓*translation* N-acetylgalactose transferase ↓*Function* N-acetyl galactosamine	**I^B** ↓*translation* galactose transferase ↓Function D-galactose
Oligosaccharide chains			
Symbolic form of Antigen			

Rh FACTOR IN HUMAN

- Rh system most polymorphic of all human blood group systems comprised of > 50 independent antigens.
- The Rh factor genetic information is also inherited from our parents, but it is inherited independently of the ABO blood type alleles.

HISTORY

- The Rh-factor was discovered by **K LANDSTEINER** in 1940 along with **A.S. WEINER**.
- They immunized rabbits with blood of a monkey (***Macaca rhesus***).
- The rabbits developed antibodies that could agglutinate not only rhesus blood, but also the blood of human beings.
- The antigens of both monkeys and humans were called **Rhesus (Rh antigen)**.
- The antigen responsible for this reaction was consequently called as Rhesus (Rh) factor.
- Rhesus proteins are expressed only in the membranes of red blood cells and their immediate precursors.
- The gene is denoted as R-r or Rh-rh.
- Formation of Rh antigen is controlled by dominant gene (R) and its absence by recipient gene (r).
- People having this antigen with genotype (RR or Rr) were called Rh positive (Rh^+) and those whose blood is devoid of it with genotype (rr) were Rh negative (Rh^-).
- About 95% in India are Rh^+.

Genotype	**Rh factor**
Rh^+/Rh^+	Rh^+
Rh^+/Rh^-	Rh^+
Rh^-/ Rh^-	Rh^-

CURRENT STATUS

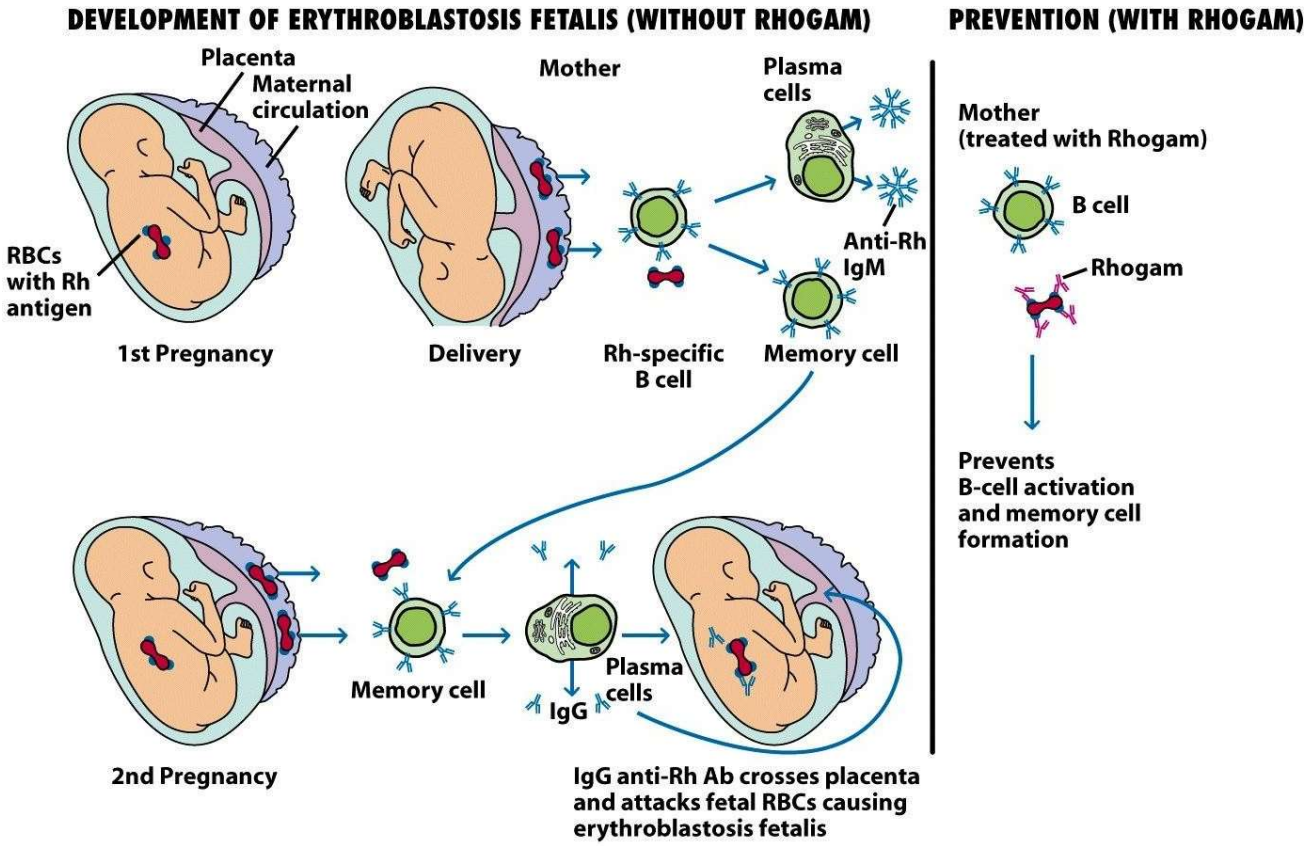
- The Rh system is one of the most complex genetic systems, and certain aspects of its genetics, nomenclature and antigenic interactions are unsettled.
- The descriptive terms **D positive** and **D negative** refer only to the presence or absence of the red cell antigen "D".
- **The terms Rh positive and Rh negative are the old terms used**.
- The early name given to the D antigen, "Rho", is less frequently used.

GENETICS OF Rh FACTOR

- The first Rhesus gene, the **RHCE gene**, was discovered in 1990.
- The **RHD gene** was found two years later (1992).
- These 2 genes controlling antigen expression are located on **Chromosome 1**.
- The two Rhesus proteins, RhD and RhCE, are very similar, differing in only 36 of the 417 amino acids, which they each comprise.
- More than **170 alleles** have been found on the **RHD gene** since. The site has still not been explored fully.
- Depending on the phenotype and their molecular structure, these RHD alleles are classified as partial D, weak D or DEL….
- The Rh antigens are transmembrane protiens, whose structure is similar to the ion channels,
- Function of Rh protein is Cation transportation, RBC Membrane stability…

PREGNANCY COMPLICATIONS WITH Rh FACTOR

- If a **woman** who is **Rh-negative** and a **man** who is **Rh-positive** conceive a baby.
- The child inherits the Rh+ trait from the father.
- Rh-incompatibility usually isn't a problem if it's the mother's first pregnancy. Because, unless there's some sort of abnormality, the fetus's blood does not normally enter the mother's circulatory system during the course of the pregnancy.
- However, during delivery, the mother's and baby's blood can intermingle.
- If this happens, the mother's body recognizes the Rh-protein as a foreign substance and can begin producing antibodies (protein molecules in the immune system that recognize, and later work to destroy, foreign substances) against the Rh-proteins introduced into her blood.
- Rh antibodies are harmless until the mother's second or later pregnancies.
- If she is ever carrying another Rh-positive child, her Rh-antibodies will recognize the Rh-proteins on the surface of the baby's blood cells as foreign, and pass into the baby's bloodstream and attack those cells.
- This can lead to haemolysis of the normal blood cells.
- A baby's blood count can get dangerously low when this condition, known as haemolytic disease of the newborn, "**Erythroblastosis foetalis**" occurs.



Blood Group	Antigens	Antibodies	Can give blood to	Can receive blood from
AB	A and B	None	AB	AB, A, B, O
A	A	B	A and AB	A and O
B	B	A	B and AB	B and O
O	None	A and B	AB, A, B, O	O

O- = UNIVERSAL DONOR
AB+= UNIVERSAL RECEPIENT

Possible Blood group Genotypes

Parent Allele	A	B	O
A	AA	AB	AO
B	AB	BB	BO
O	AO	BO	OO

NOTE:

- The **ABO gene is autosomal** (the gene is not on either sex chromosomes)
- The **ABO gene** locus is located on the **chromosome 9.**
- **A** and **B** blood groups are **dominant** over the **O** blood group
- **A** and **B** group genes are **co-dominant**
- Each person has **two copies of genes** coding for their ABO blood group (one maternal and one paternal in origin)