ABO and H Blood Group Systems

Dr Ali Maleki
PhD in Laboratory Hematology & Transfusion Sciences

Ali.maleki@kums.ac.ir
Maleki.hem@gmail.com
**Introduction**

- **A blood group (BG) system:**
  - antigens produced by alleles at a single genetic locus or at loci so closely linked that genetic crossing over rarely occurs

- **BG antigens are molecules located primarily on RBC membrane.**
  - These molecules can be:
    1. Proteins
    2. Glycolipid
    3. Glycoprotein
Introduction

- With adequate immunologic exposure, a BG Ag may elicit production of Ab (in individuals who lack Ag)
  - Example: during transfusions

- ISBT has assigned genetically based numeric designations for RBC Ags
  - Presently it has defined 36 BG systems

- According to ISBT criteria, genetic studies and serologic data are required before an Ag is assigned to a BG system.
  - ABO BG system → ISBT number 001 with 4 Ags.
  - H BG system → ISBT number 018 with 1 Ag.

Ag: antigen / Ab: antibody / ISBT: International Society of Blood Transfusion
# Examples of ISBT Blood Group System Assignments

<table>
<thead>
<tr>
<th>BLOOD SYSTEM NAME</th>
<th>ISBT GENE NAME</th>
<th>ISBT NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO</td>
<td>ABO</td>
<td>001</td>
</tr>
<tr>
<td>MNS</td>
<td>MNS</td>
<td>002</td>
</tr>
<tr>
<td>P1PK</td>
<td>P1</td>
<td>003</td>
</tr>
<tr>
<td>Rh</td>
<td>RH</td>
<td>004</td>
</tr>
<tr>
<td>Lutheran</td>
<td>LU</td>
<td>005</td>
</tr>
<tr>
<td>Kell</td>
<td>KEL</td>
<td>006</td>
</tr>
<tr>
<td>Lewis</td>
<td>LE</td>
<td>007</td>
</tr>
<tr>
<td>Duffy</td>
<td>FY</td>
<td>008</td>
</tr>
<tr>
<td>Kidd</td>
<td>JK</td>
<td>009</td>
</tr>
<tr>
<td>Diego</td>
<td>DI</td>
<td>010</td>
</tr>
</tbody>
</table>
ABO blood group system

- **Discovery**: by Landsteiner in 1900 → in a series of experiments designed to show serologic incompatibilities between humans
  - He described blood groups as A, B, and O.
  - Several years later → von Decastello added group AB.

- Landsteiner noted the presence of agglutinating Abs in serum of individuals who lacked the corresponding ABO antigen.

*Ag*: antigen / *Ab*: antibody
Relationship between ABO Ags and Abs

- **Landsteiner’s rule (or Landsteiner’s law)**
  - **group A** RBCs → possess A- Ag, lack B- Ag ⇒ possess anti-B Abs
  - **group B** RBCs → possess B- Ag, lack A- Ag ⇒ possess anti-A Abs

- **ABO BG system:**
  - the first BG system to be described
  - the most important BG system for transfusion purposes.
  - accurate donor and recipient ABO types are fundamental to transfusion safety
  - transfusion of ABO-incompatible blood to a recipient can result in IV-hemolysis ⇒ an **acute hemolytic transfusion reaction**.
ABO and H blood group system antigens

- ABO antigens are found:
  1. in association with **cellular membranes**:
     - RBCs exist as either glycolipid or glycoprotein
     - lymphocytes & PLTs adsorbed from plasma
     - most epithelial and endothelial cells
     - organs such as kidneys
  2. **Soluble forms** → can also be synthesized and secreted by tissue cells
     - detected in secretions and body fluids (except CSF)
     - are primarily glycoproteins
ABO and H blood group system antigens

- **ABO antigens:**
  - are detectable at 5–6 weeks in utero
  - newborns possess fewer Ag copies per RBC (compared with adults)
    - Newborns’ RBCs → also lack the fully developed Ag structures of adults’ RBCs
  - In cord blood → ABO Ags have fewer numbers and partially developed Ag structures → may demonstrate weaker ABO phenotyping reactions.

- **Ag development** → occurs slowly
  - full expression of adult levels is reached at ~2–4 years of age
ABO and H blood group system antigens

- ABO phenotype frequencies differ in populations and ethnic groups:
  - Example: group B has a higher frequency in blacks and Asians (compared with whites)

<table>
<thead>
<tr>
<th>ABO PHENOTYPE</th>
<th>WHITE (%)</th>
<th>BLACK (%)</th>
<th>ASIAN (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>40</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>B</td>
<td>11</td>
<td>20</td>
<td>27</td>
</tr>
<tr>
<td>AB</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>O</td>
<td>45</td>
<td>49</td>
<td>40</td>
</tr>
</tbody>
</table>
Inheritance and formation of ABO antigens

- Occurrence and location of ABO antigens → influenced by 3 independent loci: ABO, H, Se.
  1. **H gene** (Ch: 19):
     - Controls production of H Ag inherited independent of ABO antigens
  2. **ABO genes** (Ch: 9)
     - Controls production of A, B, AB, O Ags
  3. **Se gene** (Ch: 19)
     - expression of soluble ABO Ags → is influenced by inheritance of Se gene (in addition to ABO and H genes) genetically influences formation of ABO Ags in saliva, tears, and other body fluids.
Inheritance and formation of ABO antigens

- ABO Ags → assembled on a common carbohydrate structure it also is a base for formation of H, Lewis, I/i, P1 antigens.
  - this common carbohydrate structure → is capable of Ag expression for >1 BG system.
  - the action of genes of one BG system → can affect expression of Ags in another system.
Common Structure for A, B, H Antigens

- Common structure (Ag building block) for A, B, H Ags → an **oligosaccharide chain** attached to a protein or a lipid carrier molecule.
  - comprises **4 sugar molecules** → linked in **linear** or **branching** forms

- The 2 terminal sugars $\mathcal{D}$-galactose (Gal) and N-acetylglucosamine (GLcNAc), may be linked together in **2 different linkages**:
  1. **Linkage: $\beta 1 \rightarrow 3$ (C1 of Gal is linked with C3 of GLcNAc) → Type 1 oligosaccharide chains** $\mathcal{C}$ associated primarily with **body fluids**
  2. **Linkage: $\beta 1 \rightarrow 4$ (C1 of Gal is linked with C4 of GLcNAc) → Type 2 oligosaccharide chains** $\mathcal{C}$ are associated primarily with glycolipids and glycoproteins on **RBC membrane**

- Some type 2 glycoprotein structures → are located in **body fluids & secretions**.

**Type 1:** Body Fluids and Secretions

---

**Type 2:** Red Blood Cells*

Body Fluids and Secretions
Development of H Antigen

- H Ag → is the only Ag in H BG system (Ch. 19, closely linked with Se locus)
- H locus has 2 alleles:
  1. H allele → is dominant, with high frequency (>99.99%)
  2. h allele is → is amorph, with rare frequency
- product of H allele is: L-fucosyltransferase (FUT-1) transfers a L-fucose, to type 1 & 2 common oligosaccharide chains (added to terminal Gal)
  - FUT-1 → adds L-fucose to both oligosaccharide chains on RBCs and in secretions.

![Diagram of H antigen]

**Gene product:**
L-Fucosyltransferase

**Immunodominant sugar:**
L-Fucose
Development of H Antigen

- L-fucose $\rightarrow$ the **immunodominant sugar** for H antigens

- Formation of H Ag $\Leftrightarrow$ is crucial to expression of A & B Ags (as an acceptor molecule)

- h allele is with no detectable gene product $\Leftrightarrow$ RBCs from hh genotype classified as **Bombay phenotype**.
  - These rare individuals lack H and ABO antigen expression on their RBCs.
Three major alleles exist within ABO locus (Ch. 9): A, B, O:

1. A allele → produces N-acetylgalactosaminytransferase ☻ transfers GalNAc to H antigen.
2. B allele → produces D-galactosyltransferase ☻ transfers D-Gal to H antigen
3. O allele → is nonfunctional ☻ gene product is an enzymatically inactive protein ⇒ O RBCs carry no A or B antigens ☻ but are rich in H antigens.

Gene product: N-Acetylgalactosaminytransferase
Immunodominant sugar: N-Acetylgalactosamine

GalNAc: N-acetylgalactosamine

Gene product: D-Galactosyltransferase
Immunodominant sugar: D-Galactose
Type 1: Body Fluids and Secretions

H antigen

\[ \text{Gal} \rightarrow \text{GlcNAc} \rightarrow \text{Gal} \rightarrow \text{R} \rightarrow \text{Protein or Lipid} \]

\[ \beta_1 \rightarrow 3 \text{ linkage} \]

\[ \alpha_1 \rightarrow 2 \]

\[ \text{Fuc} \]

Gene product:
L-Fucosyltransferase

Immunodominant sugar:
L-Fucose

A antigen

\[ \text{GalNAc} \rightarrow \text{Gal} \rightarrow \text{GlcNAc} \rightarrow \text{Gal} \rightarrow \text{R} \rightarrow \text{Protein or Lipid} \]

\[ \beta_1 \rightarrow 4 \text{ linkage} \]

\[ \alpha_1 \rightarrow 3 \]

\[ \alpha_1 \rightarrow 2 \]

\[ \text{Fuc} \]

Gene product:
N-Acetylgalactosaminyltransferase

Immunodominant sugar:
N-Acetylgalactosamine

B antigen

\[ \text{Gal} \rightarrow \text{Gal} \rightarrow \text{GlcNAc} \rightarrow \text{Gal} \rightarrow \text{R} \rightarrow \text{Protein or Lipid} \]

\[ \alpha_1 \rightarrow 3 \]

\[ \alpha_1 \rightarrow 2 \]

Gene product:
D-Galactosyltransferase

Immunodominant sugar:
D-Galactose

Type 2: Red Blood Cells

Body Fluids and Secretions
Development of A & B Antigens

- N-acetylgalactosamine → the immunodominant sugar for A specificity
- D-galactose → the immunodominant sugar for B specificity

- Adult group O RBCs → have about 1.7 million H-Ag copies / RBC (greatest concentration of H Ags)
- Other ABO phenotypes → have fewer copies of H antigens ⊥ Group A₁B possesses the lowest number of unconverted H sites.
ABO subgroups

ABO subgroups differ in:

1. quantitative difference \(\rightarrow\) amount of Ag expressed on RBC membrane
2. qualitative differences in antigen expression
   - some subgroups possess more highly branched forms of Ag
   - others have simplified linear forms of Ag
ABO subgroups

- Group A → is classified into 2 major subgroups: A1 and A2
  - differ slightly in their glycosyltransferase ability to convert H→A Ag.
- A1 phenotype → encoded by A1 gene → exists in ~80% of A individuals
  - A–Ags are highly concentrated on branched and linear oligosaccharide chains
  - A1 gene effectively acts on H–Ag in production of A–Ag
- A2 phenotype → encoded by A2 gene → constitutes ~20% of group A individuals
  - A–Ag copies: in A2 < A1 phenotype
  - A2 phenotype is assembled on linear forms of oligosaccharide chains.

- Allo-anti-A1, can be detected in:
  - 1–8% of A2 individuals
  - 22–35% of A2 B individuals
ABO subgroups

- both $A_1$ & $A_2$ RBCs agglutinate with commercially anti-A reagents

- $A_1$ & $A_2$ RBCs can be distinguished → only with Dolichos biflorus lectin.
  - This lectin possesses anti-$A_1$ specificity.
  - diluted Dolichos biflorus lectin (anti-$A_1$ lectin) agglutinates $A_1$, but not $A_2$, RBCs.

- Anti-$A_1$ lectin:
  - not used in routine ABO testing (of donors and recipients)
  - it is unnecessary to distinguish between $A_1$ and $A_2$ phenotypes for transfusion purposes
  - is useful in:
    - resolving ABO typing problems
    - identifying infrequent subgroups of A
ABO subgroups

**A₁ Phenotype**
- Branched A antigens
- 2 million A antigens/adult red cells
- Positive with anti-A
- Positive with anti-A₁ lectin

**A₂ Phenotype**
- Linear A antigens
- 500,000 A antigens/adult red cells
- Positive with anti-A
- Negative with anti-A₁ lectin
Additional Subgroups of A & B

- are genetically controlled by rare alleles at ABO locus (<1% frequency)
- A subgroups → $A_{in}$, $A_{3}$, $A_{x}$, $A_{m}$, $A_{end}$, $A_{el}$, and $A_{bantu}$ based on: reactivity of RBCs with human anti-A and anti-A,B.
- amount of H-Ag present on weak subgroups of A → is usually equivalent to group O RBCs (3+ to 4+ reactions)

- Serologic classification of rare A subgroups is determined by:
  - Weak or no RBC agglutination → with anti-A & anti-A,B commercial reagents
  - No agglutination → with anti-A$_{1}$
  - Presence or absence of → anti-A$_{1}$ in serum
  - Strong agglutination → with anti-H
  - Presence of A and H → in saliva
  - Adsorption and elution studies → for presence of A-Ag
### Additional Subgroups of A and B

- **Weak A-subgroups**: are difficult to classify using serologic techniques
  - definitive classification requires molecular techniques

- **B-subgroups**: are rarer than A-subgroups
  - demonstrate weak or no agglutination with anti-B reagents

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Anti-A</th>
<th>Human Anti-A, B</th>
<th>Anti-H Lectin*</th>
<th>Anti-A&lt;sub&gt;1&lt;/sub&gt; Lectin†</th>
<th>Soluble Antigens in Saliva‡</th>
<th>Anti-A&lt;sub&gt;1&lt;/sub&gt; in Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>A&lt;sub&gt;3&lt;/sub&gt;</td>
<td>++mf</td>
<td>++mf</td>
<td>+++</td>
<td>0</td>
<td>A and H</td>
<td>0 to ++§</td>
</tr>
<tr>
<td>A&lt;sub&gt;x&lt;/sub&gt;</td>
<td>weak/0</td>
<td>+ to ++</td>
<td>++++</td>
<td>0</td>
<td>H</td>
<td>0 to ++§</td>
</tr>
<tr>
<td>A&lt;sub&gt;el&lt;/sub&gt;</td>
<td>0</td>
<td>0</td>
<td>+++++</td>
<td>0</td>
<td>H</td>
<td>0 to ++§</td>
</tr>
</tbody>
</table>

*mf, Mixed field.

*Ulex europaeus.*

†Dolichos biflorus.

‡If secretor.

§Variable occurrence of anti-A<sub>1</sub>.
Importance of Subgroup Identification

- Although subgroups of A and B are of academic interest, failure to detect a weak subgroup could have serious consequences:
  - If a weak subgroup in a recipient be classified as group O, it would probably not harm.
  - If a weak subgroup in a donor be classified as group O, subsequent labeling of donor unit as group O (rather than group A) → ↓ survival of transfused RBCs in a group O recipient.
Genetic feature of ABO blood group system

- Inheritance of genes from ABO locus (on Ch. 9) follows laws of Mendelian genetics
- An individual inherits 2 ABO genes (one from each parent).
- The 3 major alleles of ABO BG system are A, B, and O.
  - The A gene divided into A\(^1\) and A\(^2\) alleles.
  - The A and B genes codominant mode of inheritance O allele is recessive.
  - The A\(^1\) allele is dominant over A\(^2\) allele both are dominant over O allele.

- Correct use of terminology regarding ABO blood group system:
  - for alleles A\(^1\) and A\(^2\) the numbers superscripts
  - for A\(_1\) and A\(_2\) phenotypes the numbers subscript
Genetic feature of ABO blood group system

O allele is recessive → it is not always possible to determine ABO genotype from corresponding phenotype without family studies or molecular analysis.

✓ RBCs can be phenotyped only for presence or absence of antigens

✓ RBCs cannot be genotyped → unless a family study has been performed with conclusive results ⇒ a genotype is only a probable interpretation of a phenotype.

<table>
<thead>
<tr>
<th>ABO Phenotypes and Possible Genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHENOTYPE</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Group A₁</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Group A₂</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Group B</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Group A₁B</td>
</tr>
<tr>
<td>Group A₂B</td>
</tr>
<tr>
<td>Group O</td>
</tr>
</tbody>
</table>
Group A and group B phenotypes → may produce offspring with group AB, O, B, and A phenotypes ☞ if the parents’ genotypes are AO and BO.
ABO blood group system antibodies

- **Landsteiner’s rule:**
  - Checkmark: individuals possess ABO Ab against ABO Ag absent from their RBCs.
  - Checkmark: an important consideration in selection of blood products for transfusion.
  - ABO antibodies exist in healthy individuals.

- ABO Abs → were originally thought to be “naturally occurring.”

- Biochemical structures similar to A & B antigens are present in environment (in bacteria, plants, and pollen) environmental exposure to these → produce ABO Abs → non-RBC stimulated Abs is more appropriate.
ABO blood group system antibodies

- **Newborns** → **do not produce ABO Abs until 3–6 months of age.**
  - ✓ ABO Abs detected prior to this time → are maternal in origin.
- **Maximal ABO titors** → **have been reported in children 5–10 years old.**
  - ✓ As a person ages → ‼ Ab titers ↘ may cause problems in ABO phenotyping.

<table>
<thead>
<tr>
<th>Reduction in ABO Antibody Titers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age-Related</strong></td>
</tr>
<tr>
<td>Newborn</td>
</tr>
<tr>
<td>Elderly</td>
</tr>
<tr>
<td><strong>Pathologic Etiology</strong></td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
</tr>
<tr>
<td>Congenital hypogammaglobulinemia or acquired hypogammaglobulinemia</td>
</tr>
<tr>
<td>Congenital agammaglobulinemia or acquired agammaglobulinemia</td>
</tr>
<tr>
<td>Immunosuppressive therapy</td>
</tr>
<tr>
<td>Bone marrow transplant</td>
</tr>
<tr>
<td>Multiple myeloma</td>
</tr>
</tbody>
</table>
ABO blood group system antibodies

- **Ig Class**
  - anti-A (in group B) and anti-B (in group A) are primarily of IgM, along with small amounts of IgG.
  - anti-A & anti-B in group O are primarily of IgG class

- **Hemolytic Properties and Clinical Significance**
  - IgG & IgM forms of anti-A and anti-B are capable of binding & activation of complement → hemolysis of RBCs (in-vivo or in-vitro)
  - ABO Abs are clinical significance in transfusion precipitating an acute-HTR

- **In Vitro Serologic Reactions**
  - ABO Abs directly agglutinate RBCs suspension in a physiologic saline (do not require potentiators)
    - optimally reactive → in IS-phases at RT (15–25°C)
    - do not require an incubation period

**HTR**: hemolytic transfusion reaction / **IS**: immediate-spin / **RT**: room temperature
**ABO blood group system antibodies**

- **Human anti-A,B:**
  - in group O individuals → possesses unique activities beyond mixtures of anti-A and anti-B
  - is capable of recognizing a common antigenic determinant (a structure shared by A and B Ags) agglutinate RBCs of group A, B, and AB
  - also agglutinate RBCs of infrequent subgroups of A (particularly A_x)
  - before advent of mAbs human anti-A,B was widely used to detect these infrequent subgroups in routine ABO typing.
ABO blood group system antibodies

- **Anti-A<sub>1</sub>**
  - Anti-A produced by group O and B → can be separated (by adsorption and elution techniques) into 2 components: anti-A and anti-A<sub>1</sub>.
  1. **Anti-A<sub>1</sub>:**
     - ✓ is specific for A<sub>1</sub> RBCs ₂ does not agglutinate A<sub>2</sub> RBCs
     - ✓ optimal reactivity: at RT or lower
     - ✓ not clinically significant for transfusion purposes
  
  - Anti-A<sub>1</sub> becomes a concern when
    1. it causes problems with ABO phenotyping results
    2. incompatible crossmatches on IS

 2. **Anti-A<sub>2</sub>** does not exist

---

**IS:** immediate-spin / **RT:** room temperature
ABO phenotyping

- ABO phenotyping is performed by 2 methods:
  1. Forward grouping → testing of RBCs for presence of ABO- Ags
  2. Reverse grouping → testing of serum (plasma) for expected ABO- Abs

- According to Standards for Blood Banks and Transfusion Services → both methods must be performed for donor and recipient:
  - RBCs → must be tested using anti-A and anti-B reagents
  - serum or plasma → must be tested for expected ABO Abs using reagent A1 and B RBCs

### ABO Phenotype Reactions

<table>
<thead>
<tr>
<th>PHENOTYPE</th>
<th>RED CELL REACTIONS WITH</th>
<th>SERUM OR PLASMA REACTIONS WITH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ANTI-A</td>
<td>ANTI-B</td>
</tr>
<tr>
<td>Group A</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Group B</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Group O</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Group AB</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

+ Agglutination; 0, no agglutination.
ABO phenotyping

- Anti-A, B reagent (Human or mAb blend) → is not required in ABO typing

- for cord blood and infants <4 months → only Forward grouping

- Serum testing (reverse grouping) provides a control for RBC testing
  - ABO discrepancy occurs when RBC testing does not agree with expected serum testing.
  - any discrepancy in ABO testing should be resolved:
    1) before transfusion of recipients or
    2) before labeling of donor units
Selection of ABO-compatible RBCs and Plasma products for transfusion

- In routine transfusion practices:
  - ABO-identical (ABO-specific) blood products (RBCs and plasma) → are usually transfused to recipient

- when identical ABO phenotype is unavailable:
  - ABO-compatible blood → may be issued to recipient
  - for RBC transfusions, ABO compatibility is defined as serologic compatibility between ABO-Abs in recipient’s serum and ABO-Ags on donor’s RBCs.

- ABO compatibility applies to RBC transfusions not to whole blood (WB)
  - for WB → ABO-identical units must be transfused

- Persons with group O are called universal donors → their RBC product can be transfused to any ABO phenotype.
  - Group O RBCs → can be used for emergency release of donor units

- Recipients with group AB are considered universal recipients → can receive RBCs from any ABO phenotype
Selection of ABO-compatible RBCs and Plasma products for transfusion

- When **plasma products** are transfused:
  - the ideal situation ⊗ selection of ABO-identical phenotype
  - when ABO-identical phenotype is unavailable ⊗ compatible plasma (is the reverse of RBC transfusion)

- For transfusion of plasma:
  - group AB → the universal donor
  - group O → the universal recipient

### Practical Application: ABO Compatibility for Whole Blood, Red Blood Cells, and Plasma Transfusions

<table>
<thead>
<tr>
<th>ABO PHENOTYPE</th>
<th>WHOLE BLOOD</th>
<th>RED BLOOD CELLS</th>
<th>PLASMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>Group A</td>
<td>Groups A, O</td>
<td>Groups A, AB</td>
</tr>
<tr>
<td>Group B</td>
<td>Group B</td>
<td>Groups B, O</td>
<td>Groups B, AB</td>
</tr>
<tr>
<td>Group AB</td>
<td>Group AB</td>
<td>Groups AB, A, B, O</td>
<td>Group AB</td>
</tr>
<tr>
<td>Group O</td>
<td>Group O</td>
<td>Group O</td>
<td>Groups O, A, B, AB</td>
</tr>
</tbody>
</table>
Classic Bombay phenotype

- Both RBCs and secretions → are deficient in H and ABO antigen expression.
  - RBC testing → group O
  - Serum testing → reactions similar to group O individuals.
  - Anti–H in Bombay phenotype is of clinical significance → is capable of activity at 37°C and complement activation ⇒ hemolysis.

- >130 Bombay phenotypes have been reported ⇐ greater incidence in India.
- An individual with homozygous for h allele (hh) (Bombay phenotype) → does not produce L-fucosyltransferase ⇒ not H-Ag on RBCs.
- H antigen is the building block for development of A and B antigens ⇒ lacks expression of H and ABO antigens.
- Transfusion for these individuals → an especially difficult problem ⇐ they are compatible only with Bombay phenotype.
  - If transfusion is necessary → stored autologous units, siblings, and rare donor files are potential options.
Secretor status

- There are 2 allelic genes at this locus: Se and se.
- The gene Se allele product $\rightarrow$ FUT2 (L-fucosyltransferase):
  - preferentially adds L-fucose to type 1 oligosaccharide chain structures in secretory glands.
  - may also act on type 2 chains in the secretory glands.
  - FUT1 (H gene) $\rightarrow$ preferentially adds fucose to type 2 chains.
- The FUT2 gene $\rightarrow$ responsible for regulating expression of soluble A, B, and H antigens on glycoprotein structures located in body secretions such as saliva.
Secretor status

- An individual with genotype SeSe or Sese → is classified as a **secretor**.
  - ~80% of population are secretors ≈ express soluble forms of H antigens in secretions → can be converted to A or B antigens (by A and B glycosyltransferases) → found in saliva, urine, tears, bile, amniotic fluid, breast milk, exudate, and digestive fluids.
- An individual with genotype sese → is classified as a **nonsecretor** ≈ ~20% of population.
- allele se, is amorph ⇒ a homozygote does not convert antigen precursors to soluble H → no soluble H, A or B antigens present in body fluids.

<table>
<thead>
<tr>
<th>Example 1</th>
<th>Genes inherited</th>
<th>Antigen expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB HH SeSe</td>
<td>RBC A, B, H</td>
<td>Saliva A, B, H</td>
</tr>
<tr>
<td>AB HH sese</td>
<td>RBC A, B, H</td>
<td>None</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Example 2</th>
<th>Genes inherited</th>
<th>Antigen expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>OO HH Sese</td>
<td>RBC H</td>
<td>Saliva H</td>
</tr>
<tr>
<td>OO HH sese</td>
<td>RBC H</td>
<td>None</td>
</tr>
</tbody>
</table>
Thank You