

NORMAL HUMAN INHERITANCE

NORMAL MONOGENIC HUMAN TRAITS

General Data

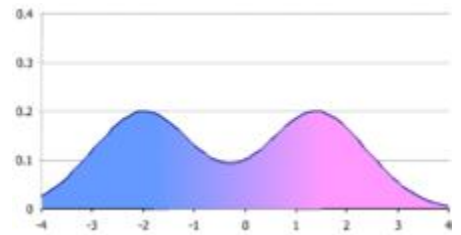
1. **NORMAL TRAITS** define an individual from the biological point of view. They represent biochemical, physiological and morphological traits. They are determined by the action of hereditary factors combined with environmental factors in different proportions.

2. **HEREDITARY TRAITS** are genetically determined traits (50-100%).

3. **MONOGENIC TRAITS** are determined by a pair of allele genes.

PECULIARITIES:

- represent the produce of action of two alleles;
- are characterized by dominant \ recessive or codominant relations;
- action of one pair of alleles may be influenced by the action of other non-allele genes (epistasis) or environment;
- **transmission** = according to the Mendel's laws (monohybrid crosses);
- **manifestation** = a large variability of phenotypes > POLYMORPHISM (explained by epistasis, multiple alleles) => every man is a unique biological individual;
- **distribution in population** = bimodal (a probability distribution with two different values that are markedly more frequent than neighbouring values);
- the **main monogenic traits** are the following:
 - blood types (groups)
 - serum groups
 - tissue groups
 - enzymatic groups
 - secretor trait
 - taste trait



Bimodal distribution

HUMAN BLOOD TYPES

Blood group is a hereditary trait (100%), which is determined by the presence of A and B antigens (proteins or mucopolysaccharides) on the surface of red blood cells.

Blood group system is the classification of human blood based on the inherited properties of red blood cells (erythrocytes) as determined by the presence or absence of the antigens A and B, which are carried on the surface of the red cells.

The blood types are studied for a long time because of their role in blood transfusion:

1900 - Lansteiner described AB0 blood types,

1940- Lansteiner and Weiner described Rh factor (Rhesus factor), which is involved in mother-fetus incompatibility,

Nowadays 19 different blood type systems are described, the following being more important: AB0, Rh, MN, Ss, Le, Xg.

ABO BLOOD TYPE SYSTEM

PHENOTYPES represent the blood types: 0, A1, A2, B, A1B, A2B, Bombay phenotype. They are tested serologically (by the reaction of agglutination).

The phenotype is determined by the presence of 4 types of erythrocyte antigens (H, A1, A2, B) = **agglutinogens (Ag)** and 4 types of plasma antibodies (**Ab**) (anti-H, anti-A1, anti-A2, anti-B) = **agglutinins**. So, agglutinogens are present in the cell membrane of erythrocytes, while agglutinins (antibodies) are in the plasma and are formed after birth. If agglutinogens from the surface of erythrocytes combine with the agglutinins from the plasma, the result is agglutination or clumping of erythrocytes.

Relations between Ag and Ab in the blood of some individuals:

- 1) Normally, the homologous Ag and Ab are not present;
- 2) The absence of one agglutinogen (Ag) involves the presence of the respective agglutinin.

GENOTYPES are determined by the alleles A1, A2, B, and 0 in relation of epistasis with non-allele gene H (h)

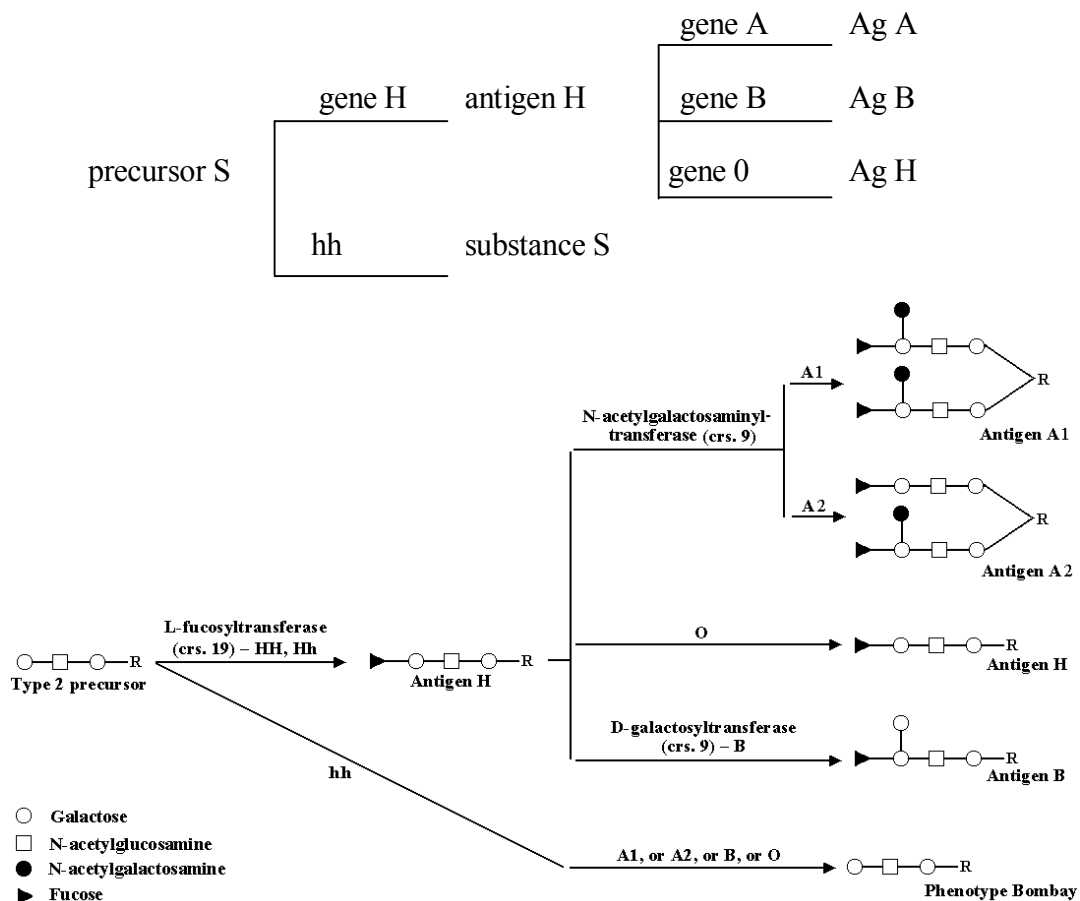
Relations between these genes may be in form of:

- **codominance**: A1 and B; A2 and B;
- **dominant/recessive**: A1 > 0, A2 > 0, B > 0, A1 > A2, H > h
- **epistasis**: H and 0, A1, A2, B

$$[(A1>A2)=B] > 0; H > h$$

- genes h and 0 are **amorphic**;
- A2 is hypomorphic as compared to A1;
- gene H is obligatory for manifestation of genes A1, A2, B and 0;
- Bombay phenotype has the same serological manifestation as the 0 types, but has no Ag H on the surface of red blood cells.

FORMATION OF ANTIGENS IN ABO BLOOD SYSTEM



GENOTYPE-PHENOTYPE RELATIONS IN ABO BLOOD TYPE SYSTEM

Transmission of ABO blood types is inherited according to the Mendel's laws.

PHENOTYPE	GENOTYPE			
	ABO alleles		H alleles	
	homozygous	heterozygous	homozygous	heterozygous
A1	A1A1	A1 A2, A1 0	HH	Hh
A2	A2A2	A2 0	HH	Hh
B	BB	Bo	HH	Hh
A1B	-	A1B	HH	Hh
A2B	-	A2B	HH	Hh
0	00	-	HH	Hh
BOMBAY	Any genotype ABO		hh	-

Rh FACTOR SYSTEM

PHENOTYPES: - **Rh+** (85%)
 - **Rh-** (15%)

Rh+ blood type is determined by the presence of antigen D on the surface of erythrocytes. Antibodies D do not usually exist in blood plasma, but they may be formed as a result of contact with Ag D in Rh- individuals.

GENOTYPES

Chromosome 1 includes three loci (D, C, A), with a few alleles each, that form a haplotype. Every person contains 2 haplotypes (on each of homologous chr.), the most frequent being CDe/cde and CDe/Cde. Gene D is the main in this group. It determines AgD with the strongest antigenic properties. Allele D is dominant over d (D > d). Recessive allele is amorphic.

GENOTYPE-PHENOTYPE RELATIOND IN RH SYSTEM

- Rh+ individuals may be DD or Dd;
- Rh⁻ individuals may be only homozygote dd.

HAEMOLYTIC DISEASE OF THE NEWBORN (HDNB)

HDNB appears as a result of reaction of a Rh-negative woman to the Rh-positive fetus. It determines the mother-fetus incompatibility. The reaction is similar to the transfusion of Rh-positive blood. The antibodies that attack rhesus antigen are produced. The first baby rarely suffers from haemolytic disease because during the first pregnancy antibodies are not yet accumulated at the considerable level in mother's blood. Nevertheless during the second pregnancy of an Rh-negative woman, her antibodies can pass through placenta into the bloodstream of the fetus and destroy his blood cells.

No incompatibility problem exists in couples with Rh- father and Rh+ mother.

MNSs BLOOD TYPE SYSTEM

- a) PHENOTYPES: - *MS; Ms; NS; Ns; MNS; MNs*.
- b) GENOTYPES: - 2 pairs of allelic genes (M, N and S, s), located in neighboring loci of chromosome 4, forming a haplotype and inherited together (linked).
- c) GENOTYPE-PHENOTYPE RELATIONS:
- M and N genes are co-dominant;
 - S and s genes are in complete dominance interaction;
- d) SIGNIFICANCE: This blood group system is important for forensic medicine.

Xg BLOOD TYPE SYSTEM

- a) PHENOTYPES: $Xg(a+)$ and $Xg(a-)$ determined by the presence/absence of Ag Xg in the membrane of erythrocytes.
- b) GENOTYPES are determined by two alleles: Xg^a (dominant) and Xg (recessive), located on X chromosome. Female may be both homozygous or heterozygous; male only hemizygous;
- c) GENOTYPE-PHENOTYPE RELATIONS
- | | | | |
|-----------|-------------------------------|---------|----------------------------|
| - female: | $XgXg \rightarrow Xg(a-)$ | - male: | $XgY \rightarrow Xg(a-)$ |
| | $Xg^aXg \rightarrow Xg(a+)$ | | $Xg^aY \rightarrow Xg(a+)$ |
| | $Xg^aXg^a \rightarrow Xg(a+)$ | | |

SECRETORY GROUPS

- a): PHENOTYPES: *secretor* and *non-secretor*. The phenotypes are determined by the presence / absence of ABO and Le systems' antigens in different secrets (urine, gastric juice, saliva, milk, sweat, semen, etc.). The product of Se gene transforms liposoluble Ag into hydrosoluble Ag. So, Se/se gene is in epistatic interaction with the genes of ABO system.
- b): GENOTYPES are determined by 2 alleles: **Se** (dominant) and **se** (recessive), located on chromosome 19.
- c): GENOTYPE-PHENOTYPE RELATIONS:
- SeSe and Sese \rightarrow secretor (78%)
 - sese \rightarrow non-secretor (22%)

SERUM AND ENZYMATIC GROUPS

The phenotype is determined by the presence of some enzymes and structural proteins in serum or on the surface of red blood cells in multiple variants and combinations \rightarrow the marked polymorphism. Each person has a definite protein structure, determined genetically and constant during the whole life characterizing the biological individuality.

HAPTOGLOBINS are alfa-2 globulins, involved in fixation and re-circulation of the hemoglobin. The phenotypes are: Hp 1-1; Hp 1-2; Hp 2-2, which are based on 2 co-dominant alleles Hp-1 and Hp-2, localized on chromosome 16.

GENOTYPE-PHENOTYPE RELATIONS:

Hp-1Hp-1 \rightarrow Hp1-1

Hp-1Hp-2 \rightarrow Hp1-2

Hp-2Hp-2 \rightarrow Hp2-2

TRANSFERRINS are beta-1 globulins involved in fixation and transport of metals (Fe, Cu etc). Fourteen distinct phenotypic forms exist. The phenotype is controlled by a number of co-dominant alleles, the most frequent being TfC, TfD, TfB.

Gc (GROUP SPECIFIC COMPONENT) is characterized by alfa-2 globulins. The phenotypes are: Gc 1-1; Gc 1-2; Gc 2-2, determined by 2 co-dominant alleles Gc-1 și Gc-2.

SIGNIFICANCE: These globulins are used as an indicator in population genetics investigations.

IMMUNOGLOBULINS are gamma globulins with various phenotypic manifestations, controlled by many alleles that occupy 3 different loci: Gm, Inv, and Am on chromosomes 2, 14, 22.

ENZYMATIC GROUPS are represented by numerous enzymes from serum and red blood cells; The groups are characterized by the genetic polymorphism. Ex: erythrocyte acid phosphatase, G6PD.

TISSUE GROUPS - HLA SYSTEM

HLA (human leukocyte antigens) are structurally distinct. HLA system is characterized by multiple phenotypes. The protein products of genes appear on most cell surfaces and have structural role, cell signaling and protection.

HLA genes constitute rather typical gene families, occupying 4 loci (A, B, C, D); all are clustered on chromosome 6, short arm, forming a haplotype. These genes are very polymorphic and their alleles are co-dominant. Concentrations of HLA haplotypes in specific populations are common.

c) IMPORTANCE: HLA genes are involved in biologic distinction of self-cells. Similarities in HLA haplotypes have been central to tissue and organ transplantation. This system is also used for forensic medicine.

TASTE SENSIBILITY

The phenotypes are: taste sensible (approximately 2/3 of population) and taste insensible (1/3), which are determined by the ability or disability of some people to feel the bitter taste of phenylthiocarbamide (PTC). The genotypes are determined by 2 alleles - G (dominant) and g (recessive).

GENOTYPE-PHENOTYPE RELATIONS: GG, Gg – taste sensible; gg – taste insensible.

MONOGENIC NORMAL HUMAN TRAITS

Trait	Alleles	Chromosome localization	Relations between alleles	Genotypes	Phenotypes
Rh factor	D, d	1	Dominance / recessivity	DD, Dd dd	Rh+ Rh-
Taste sensibility	G, g	?	Dominance / recessivity	GG, Gg gg	Taste sensible Taste non-sensible
Secretory groups	Se, se	19	Dominance / recessivity	SeSe, Sese sese	Secretor Non-secretor
Antigen H	H, h	19	Dominance / recessivity	HH, Hh hh	H antigen Bombay phenotype
AB0 blood types	0, A ₁ , A ₂ , B	9	Dominance / recessivity	00 A ₁ A ₁ , A ₁ A ₂ , A ₁ 0 A ₂ A ₂ , A ₂ 0 BB, B0	0 (I) A ₁ (II) A ₂ (II) B (III)
			Co-dominance	A ₁ B A ₂ B	A ₁ B (IV) A ₂ B (IV)
MN blood types	M, N	4	Co-dominance	MM MN NN	M MN N
Haptoglobin	Hp1, Hp2	16	Co-dominance	Hp1Hp1 Hp1Hp2 Hp2Hp2	Hp1-1 Hp1-2 Hp2-2
Xg blood groups	Xg(a+), Xg(a-)	X	Dominance / recessivity	Xg(a+)Xg(a+), Xg(a+)Xg(a-), Xg(a+)Y	Xg+
				Xg(a-)Xg(a-), Xg(a-)Y	Xg-