NORMAL HUMAN INHERITANCE

I. MONOGENIC NORMAL HUMAN TRAITS

A. THEORETICAL DATA. DEFINITIONS.

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

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

3. MONOGENIC TRAITS - traits determined by a pair of allele genes.

PECULIARITIES:
- represent the produce of two allele genes action;
- are influenced by dominant \ recessive or codominance relations;
- action of one pair of allele 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 > POLYMORPHISM (explained by epistasis, multiple alleles) => every man is a unique biological individual;
- distribution in population = bimodal (trait is presented in one part of human population and is missing in another)
- the main monogenic traits are following::
  - blood types (groups)
  - tissue groups
  - secretory trait
  - serum groups
  - enzymatic groups
  - taste trait

B. HUMAN BLOOD TYPES

1. DEFINITION.

a. BLOOD TYPE is a hereditary trait (100%), which is determined by the presence of A ans B antigens (proteins or mucopolysaccarides) on the surface of red blood cells.

b. SYSTEM OF BLOOD TYPE is a totality of antigens, genes that determine them and relations between genotype and phenotype.

2. HISTORICAL BACKGROUND
- are studied for a long time because of its role in blood transfusion:
  1900 - Lansteiner described AB0 blood types,
  1940 - Lansteiner and Weiner described Rh factor (rhesus factor), which is implicated in a mother-fetus incompatibility,
- actually - different 19 systems are described, more important from them are the following: AB0, Rh, MN, Ss, Le, Xg.
3. ABO BLOOD TYPE SYSTEM

a. PHENOTYPES: blood types 0, A1, A2, B, A1B, A2B, Bombay’s phenotype
- are determined serologically (by the reaction of agglutination);
- are conditioned by the presence of 4 erythrocyte antigen types (MPS) (H, A1, A2, B) = agglutinogens and 4 plasma antibody types (anti-H, anti-A1, anti-A2, anti-B) = agglutinine
- relations between Ag and Ab on blood of some individ:
  1) normally, both homologous Ag and Ab don’t be presented;
  2) the absence of one agglutinogen implicates the presence of the respective agglutinin.

<table>
<thead>
<tr>
<th>BLOOD TYPES (phenotype)</th>
<th>AGGLUTINOGENS on the surface of erythrocytes</th>
<th>AGGLUTININS in plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>S</td>
<td>anti-H</td>
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<td>anti-A (alfa)</td>
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<td></td>
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<td>anti-B (beta)</td>
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<tr>
<td>0</td>
<td>H</td>
<td>anti-A (alfa)</td>
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<tr>
<td></td>
<td></td>
<td>anti-B (beta)</td>
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<tr>
<td>A</td>
<td>A</td>
<td>anti-B (beta) anti-H</td>
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<td>B</td>
<td>B</td>
<td>anti-A (alfa)</td>
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<tr>
<td></td>
<td></td>
<td>anti-H</td>
</tr>
<tr>
<td>AB</td>
<td>A, B, H</td>
<td>-</td>
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</tbody>
</table>

b. GENOTYPES
- are determined by the allele genes A1, A2, B, 0 in relations of epistasis with non-allele gene H (h)
- relations between these genes may be in form of:
  - codominance: A1 and B; A2 and B;
  - dominance/recesivity A1 > 0, A2 > 0, B > 0, A1 > A2, H > h
  - epistasiz: H and 0, A1, A2, B
    
    \[(A1>A2)=B \] > 0; H > h
- genes h and 0 are amorphic;
- gene H is obligatory for manifestation of genes A1, A2, B and 0;
- Bombay’s phenotype has the same serological manifestation as the 0 types, but hasn’t Ag H on the red blood cells surface.

c. FORMATION OF Ag IN ABO BLOOD SYSTEM

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  substance S
    gene H  substance H
    gene B  Substance B
    gene 0  Substance H
    hh  substance S
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d. GENOTYPE-PHENOTYPE RELATIONS IN ABO BLOOD TYPE SYSTEM

Transmission in this system is hereditary, according to the Mendel’s laws.

<table>
<thead>
<tr>
<th>PHENOTYPE</th>
<th>GENOTYPE</th>
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<tbody>
<tr>
<td></td>
<td>AB0 alleles</td>
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<td></td>
<td>homozygous</td>
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<tr>
<td>A1</td>
<td>A1A1</td>
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<td>A1 A2, A1 0</td>
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<td>A2</td>
<td>A2A2</td>
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<td>B</td>
<td>BB</td>
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<td>Bo</td>
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<td>A1B</td>
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<td>A2B</td>
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<td>BOMBAY’s</td>
<td>Any genotype AB0</td>
</tr>
</tbody>
</table>

3. Rh FACTOR’s SYSTEM

a. PHENOTYPES: - Rh+ (85%)
               - Rh- (15%)
               - Rh factor is determined by the presence of an antigen D on the surface of erythrocytes,
               - normally, antibodies D in blood plasma doesn’t exist, but they may be formed in the result of contact with Ag D in Rh-individuals.

b. GENOTYPES
   - there are three linked loci (D,C,A) and which of them has a few alleles,
   - each of as has 2 haplotypes, mostly Cde\cde and Cde\Cde,
   - gene D ia main in this group, it determines AgD that has most strong antigenic properties;
   - relations between D locus alleles:
     - dominancy\recesivity : D > d
     - gene d is amorific.

c. GENOTYPE-PHENOTYPE RELATION in RH SYSTEM
   - Rh+ individuals may be DD or Dd;
   - Rh- individuals may be only homozygous dd.

d. HAEMOLYTIC DISEASE OF THE NEWBORN
   - is appeared in result of reaction of a Rh-negative woman to the Rh-poizitive fetus same as if she was transfused Rh-poizitive blood. It produces antibodies that attack rhesus antigen. The first baby rarely suffers from haemolytic disease because during the first pregnancy antibodies in mother’s blood are not yet accumulated at the considerable level. Nevertheless during the second pregnancy of a Rh-negative woman, her antibodies can pass through placenta into fetus’s bloodstream and destroy his blood cells.
There is no problem if the father is Rh- and the mother Rh+. As d gene does not cause antibody formation, the fetus of either genotype will not suffer from the disease.

II. MONOGENIC NORMAL HUMAN TRAITS -II

1. MNSs BLOOD TYPE SYSTEM

a) PHENOTYPES: - MS; Ms; NS; Ns; MNS; MNs.
b) GENOTYPES: - 2 pairs of non-allelic genes (M,N and S,s), located in neighboring loci and transmitted together (linked).
c) GENOTYPE-PHENOTYPE RELATIONS:
   - M and N genes are co-dominant;
   - S and s genes are related by complete dominance;
d) SIGNIFICANCE: in medicine, criminology.

2. Xg BLOOD TYPE SYSTEM

a) PHENOTYPES:  \(Xg(a+)\) and \(Xg(a-)\) determined by the presence/absence of Ag Xg.
b) GENOTYPES:
   - determined by the two alleles: \(Xg^a\) (dominant) and Xg (recessive), located in X chromosome;
   - women may be both homozygous or heterozygous; men - hemizygous;
c) GENOTYPE-PHENOTYPE RELATIONS
   - women: \(XgXg \to Xg(a-)\)   - men: \(XgY \to Xg(a-)\)
   \(Xg^aXg \to Xg(a+)\) \(Xg^aY \to Xg(a+)\)
   \(XgXg^a \to Xg(a+)\)

3. SECRETORY GROUPS

a): PHENOTYPES
   - secretor and non-secretor
   - determined by the presence / absence of ABO and Le system’s antigens in different secrets (urine, gastric juice, saliva, milk, sweat, semen, etc.)
b): GENOTYPES
   - 2 alleles: Se (dominant) and se (recessive);
   - the product of Se gene determines the transformation of liposoluble Ag from the blood cells into hydrosoluble Ag which may be eliminated by the secretes;
c) GENOTYPE-PHENOTYPE RELATIONS:
   - SeSe and Sese \(\to\) secretor (78%)
   - sese \(\to\) non-secretor (22%)
   - relations of epistasis with the blood types.

4. SERUM AND ENZYMATIC GROUPS

a): PHENOTYPE:
   - the presence of some enzymes and structural proteins in serum or on the surface of red blood cells in multiple variants and combinations \(\xi\) the marked polymorphism;
   - each person has the definite protein structure, determined genetically and constant during all the period of life \(\xi\) biological individuality;
   - identification by - electroforesis;
     - immunoelectroforesis;
HAPTOGLOBINS - fixation and re-circulation of the hemoglobin - alfa-2 globulins
a) PHENOTYPES: Hp 1-1; Hp 1-2; Hp 2-2
b) GENOTYPES: 2 co-dominant alleles Hp-1 and Hp-2
c) GENOTYPE-PHENOTYPE RELATIONS:
   Hp-1Hp-1 -> Hp1-1
   Hp-1Hp-2 -> Hp1-2
   Hp-2Hp-2 -> Hp2-2

TRANSFERRINS - fixation and transport of metals (Fe, Cu etc) - beta-1 globulin
a) PHENOTYPES - there are 14 distinct forms;
b) GENOTYPES - many codominant alleles;
   - most frequent: TfC, TfD, TfB.

Gc (GROUP SPECIFIC COMPONENT) - alfa-2 globulin
a) PHENOTYPES: Gc 1-1; Gc 1-2; Gc 2-2;
b) GENOTYPES: there are 2 co-dominant alleles Gc-1 and Gc-2;
c) IMPORTANCE: it is used as an indicator in populational investigations.

IMMUNOGLOBULINS - gamma globulins;
a) PHENOTYPES: varied;
b) GENOTYPES - there are many alleles that occupy 3 different loci: Gm, Inv, Am.

ENZYMATIC GROUPS:
- the numerous enzymes from serum and red blood cells;
- presents the genetic polymorphism;
- ex: erythrocyte acid phosphatase (CPK).

5. HLA SYSTEM
a) PHENOTYPES:
   - multiple; the protein products of genes appear on most cell surfaces;
   - human leukocyte antigens (HLA antigens) are structurally distinct.
b) GENOTYPES:
   - HLA genes constitute rather typical gene families; all are clustered on chromosome 6;
   - these genes are very polymorphic, and their alleles are co-dominant;
   - any individual can express two alleles for each locus (one from the copy of chromosome 6 inherited from each parent;
   - theoretically may be over $10^7$ combinations;
   - concentrations of HLA haplotypes in specific populations are common.
c) IMPORTANCE:
   - biologic distinction of self-cells;
   - similarities in HLA haplotypes have been central to tissue and organ transplantation;
   - in criminology.

6. TASTE SENSIBILITY
a) PHENOTYPES: taste sensible \ taste non-sensible
b) GENOTYPES: 2 alleles - G (dominant) and g (recessive);
c) GENOTYPE-PHENOTYPE RELATIONS: GG, Gg, gg.
<table>
<thead>
<tr>
<th>Trait</th>
<th>Alleles</th>
<th>Chromosome localization</th>
<th>Relations between alleles</th>
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<td>Hp2Hp2</td>
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<td>Xg blood groups</td>
<td>Xg(a+), Xg(a-)</td>
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<td>Dominance / recessivity</td>
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<td>Xg(a-)Xg(a-), Xg(a-)Y</td>
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