Heredity of blood group systems

Blood groups are determined using specific antigens on the erythrocyte membrane. The presence of these antigens is conditioned genetically [1], while currently around 30 blood group systems are known. Knowledge of blood group systems for blood transfusions is of the greatest importance. The use of blood groups to confirm paternity is now obsolete and is completely replaced by DNA fingerprinting.

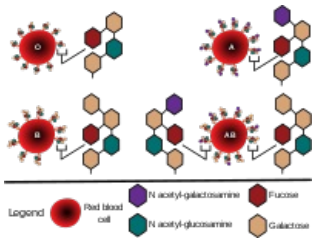
History

The Viennese doctor **Karl Landsteiner** was the first to discover blood groups (more precisely blood groups of the AB0 system) in 1900 (however, he identified only 3 groups). He received the Nobel Prize in Medicine and Physiology in 1930 for his discovery.[2] Together with Alexander Wiener, he participated in the discovery of the Rh system in 1937. Seven years later, independent of Landsteiner, the Czech psychiatrist **Jan Janský** also discovered blood groups (all four at once).

AB0 system.

🔎 *For more information see AB0 system.*

The most important antigens are **agglutinogen A** and **agglutinogen B**. The name agglutinogen refers to the ability of these antigens to be used in the process of clumping - blood agglutination. Depending on which of these agglutinogens are present, the blood group is determined:



The characteristic **presence of antibodies** – IgM a IgG – permanently present in the serum.

ABO antigens = glycolipids = short oligosaccharides protruding from the surface of lymphocytes - connected to a **lipid molecule** in the plasma membrane. **Molecules A a B** differ only in the last sugar residue:

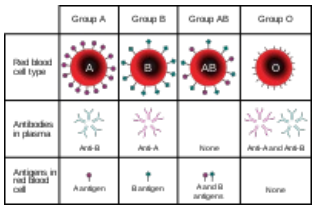
- **A** = N-acetyl-galactosamine
- **B** = galactose
- The last **sugar antigens** are responsible for the molecules being recognized as **different antigens**

- **Group A** – Only agglutinogen A is formed.
- **Group B** – Only agglutinogen B is formed.
- **Group AB** – Both agglutinogens are formed.
- **Group 0** – Not a single agglutinogen is formed.

More precisely, in the case of blood group 0, no agglutinogen (antigen) A or B is formed. However, we can find the so-called **H antigen**, which is actually a precursor for both A and B antigens. In some texts, therefore, group 0 is called group H.

For the expression of antigens of the ABO system the interplay of several genes is necessary - the main ABO locus (chromosome 9) and the H-locus (chromosome 19)

H – locus: 2 alleles – H / h; H, encodes a fucosyltransferase



Blood plasma, on the other hand, contains protein antibodies called **agglutinins** (anti-A, anti-B). A person's blood type again determines which types of antibodies are contained in the blood.

- **Group A** – Only anti-B agglutinin is formed.
- **Group B** – Only anti-A agglutinin is formed.
- **Group AB** – No agglutinin is formed.
- **Group 0** – Both agglutinins are formed (ie anti-A and anti-B).

Chemical nature of agglutinogens and agglutinins

Agglutinogens are antigenic structures on the membrane surface. The basic structural unit is an **oligosaccharide**, formed by a combination of 4 monosaccharides (L-fucose, D-galactose, N-acetylglucosamine, N-acetylgalactosamine). **Antigen H** (as a precursor to antigens A and B) is made up of 5 monosaccharides; if a 6th monosaccharide is attached to these - this is antigen A or B - depending on which monosaccharide is attached.

Agglutinins belong to immunoglobulins (gamma-globulins). Natural antibodies (such as anti-B antibodies for group A) belong to IgM antibodies, while antibodies that arose only when the individual was immunized (e.g. anti-D antibodies) are of the IgG type.

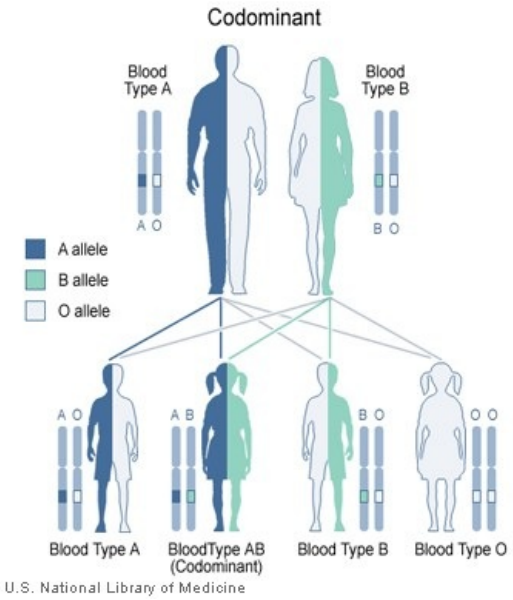
Subgroups

The antigenicity of group A may not be uniform. We distinguish several **subgroups** (A1–A6) according to the antigenicity of these groups (group A1 has the strongest antigenicity and therefore the strongest reaction with anti-A antibodies, A6 the weakest). The lower antigenicity is conditioned by the lower percentage of erythrocytes with antigen A (the remaining erythrocytes only have antigen H). The situation is similar with group B. In the case of group AB, we distinguish subgroups as well – we can meet, for example, group A2B1.

Inheritance of the AB0 system

Inheritance is relatively simple. Different alleles of one gene apply (***AB0* gene**; 9q34; OMIM: +110300 (https://omim.org/entry/110300)) Alleles that condition the formation of agglutinogen (either A or B) are dominant over the allele that does not condition the formation of any agglutinogen. They are codominant with each other. The following overview shows the relationship between genotype and phenotype:

- Phenotype – **blood group A** – Genotype *AA* or *A0*
- Phenotype – **blood group B** – Genotype *BB* or *BO*
- Phenotype – **blood group AB** – Genotype *AB*
- Phenotype – **blood group 0** – Genotype *00*



In some cases, we can rule out parentage based on the knowledge of the blood groups of the parents and the child. In practice, however, **we only know the phenotype**, not the genotype of an individual - so we have to consider all possible genotypes that determine the given phenotype. We have the following options:

- **A X A parents** – Child – A or 0
- **A X B parents** – Child – A, B, AB or 0
- **B X B parents** – Child – B or 0
- **A X 0 parents** – Child – A or 0
- **B X 0 parents** – Child – B or 0
- **AB X AB parents** – Child – A, B or AB
- **AB X A parents** – Child – A, B or AB
- **AB X B parents** – Child – A, B or AB
- **AB X 0 parents** – Child – A or B
- **0 X 0 parents** – Child – 0 only

Bombay phenotype

Even the formation of the **H antigen** is genetically determined (***FUT1* gene**; 19q13.3; OMIM: +211100 (https://omim.org/entry/211100)). There may be a rare case where an individual is an *hh* recessive homozygote and therefore does not form the H antigen. Since this antigen is a precursor for the formation of both A and B antigens, the synthesis of A or B antigens can be interrupted already at this step. As a result, the individual will have a group 0 phenotype (antigen A or antigen B will not be demonstrated), although the individual may carry the genes for the

production of one of these antigens (A or B, or both). Let's imagine a situation where an individual has the genotype *AA* but also *hh*. Phenotypically, he will be assigned blood group 0 (this particular phenotype is referred to as the Bombay phenotype). If he has an offspring with another individual with group 0 - this time, however, it is an individual with genotype *00* and *HH* – then this offspring will have blood group A (genotype *A0 Hh*). The result will therefore be a situation that contradicts the basic rules of blood group inheritance. However, this is a very rare phenomenon (generally falling under the concept of recessive epistasis, first identified in India.

Rh system

🔎 *For more information see Rh system.*

In addition to the AB0 antigen system, a large number of other systems are distinguished (Rh, MNSs, Lewis, P, etc.). The most famous is the Rh system, discovered by Wiener based on an experiment with the blood of the Maccacus Rhesus monkey. According to this system, we divide people into **Rh positive** (Rh+) and **Rh negative** (Rh-). Význam zde mají zejména antigeny C, D, E / c, d, e. Rozhodující je vliv antigenu D. Antigens C, D, E / c, d, e are particularly important here. The influence of antigen D is decisive. If antigen D is present in an individual, the individual is Rh positive. Individuals with the d antigen are Rh negative (actually d is not a specific antigen – it expresses the absence of the D antigen).

Antibodies against the Rh positive group (anti-D antibodies) do not occur naturally in an Rh negative individual (in contrast to the AB0 system), but only appear when **the individual is immunized** with Rh positive blood (e.g. during an inappropriate transfusion or during an incompatible pregnancy). In the Czech Republic, approximately four fifths of the population are Rh positive.

Inheritance of the Rh system

Two genes are involved in the inheritance of the Rh system: ***RHD*** (1p36.2-p34; OMIM: *111680 (https://omim.org/entry/111680)), which determines the presence / absence of the D antigen, and ***RHCE*** (1p36.2-p34; OMIM: +111700 (https://omim.org/entry/111700)), which determines the C/c and E/e antigens. As already said, the presence of antigen D is decisive for the Rh+ phenotype. We can therefore simply say that Rh+ is dominantly inherited and Rh negative persons are recessive homozygotes

- **Parents Rh+ X Rh+** = Child Rh+ or Rh-
- **Parents Rh+ X Rh-** = Child Rh+ or Rh-
- **Parents Rh- X Rh**- = Child only Rh-

Hemolytic disease of the newborn

🔎 *For more information see Hemolytic disease of the newborn.*

In an **incompatible** pregnancy, when the mother is Rh-, while the child (fetus) has inherited Rh+ from the father, the so-called fetal erythroblastosis occurs. Fetal erythroblastosis (now more commonly referred to as hemolytic disease of the newborn) is a condition in which the mother's immune system fights against the fetus (the fetus is Rh+, the mother's immune system does not recognize this antigen and considers it foreign) and begins to produce antibodies that cause various forms of neonatal jaundice (the cause is hemolysis), in the worst case also various nervous disorders. The first pregnancy is usually not risky (thanks to the placental barrier, there is no mixing of the mother's blood with the blood of the fetus), the blood of newborn enters the mother's circulation only during the birth itself. However, this amount is enough to immunize the mother, therefore any further incompatible pregnancy would be much more risky. Currently, this is prevented by **administering anti-D antibodies** within 72 hours after birth (or even after abortion or after performing invasive prenatal diagnostics).

Hemolytic disease of newborns can rarely be caused by incompatibility in other blood group systems.

Links

Related articles

- Blood groups
- AB0 system
- Rh system

- Fetal erythroblastosis

External links

- The Blood Group Antigen Gene Mutation Database (https://www.ncbi.nlm.nih.gov/gv/mhc/?cmd=bgmut/home)
- Blood Typing Systems Other Than ABO (http://www.bloodbook.com/type-sys.html)

Source

- ŠÍPEK, Antonín. *Genetika* [online]. [cit. 2009-05-31]. <http://www.genetika-biologie.cz/krevni-skupiny>.

Reference

1. BLUMENFELD, OO – PATNAIK, SK. Allelic genes of blood group antigens: a source of human mutations and cSNPs documented in the Blood Group Antigen Gene Mutation Database. *Human Mutation.* 2004, vol. 23(1), p. 8-16, ISSN 1059-7794.
2. The Nobel Foundation. *The Nobel Prize in Physiology or Medicine 1930* [online]. ©2009. [cit. 31. 5. 2009]. <https://www.nobelprize.org/?p=10275>.