Multiple alleles and Pseudoalleles

Contents: Definition and characteristics of multiple alleles; Examples of multiple alleles; ABO blood groups in man; Other blood antigens in man; Pseudoalleles; Rh antigen in man; Differences between multiple alleles and pseudoalleles; Medico-legal applications of blood groups in man; Suggested reading.

Definition of multiple alleles

A series of three or more genes that occupy the same locus in a given pair of homologous chromosomes are referred to as multiple alleles.

Note: Multiple alleles were unknown to Mendel; but the alleles follow Mendel's laws of inheritance

Characteristics of multiple alleles

1. The multiple alleles always occupy the same locus on the homologous chromosomes;
2. No crossing-over takes place between the members of the multiple alleles;
3. Each member of the multiple alleles has its own phenotype, but together they control the same character;
4. The wild-type (normal) is dominant or codominant to mutant alleles, and two such alleles may express an intermediate trait (*e.g*. AB blood group);
5. Crosses between any two mutant alleles result in a mutant-like phenotype, but not like the wild-type phenotype.

Examples of multiple alleles

1. ABO blood groups in man: Three alleles (I^A, I^B and I^O) control four blood groups: A, B, AB and O.
2. Coat colour in rabbits: Four alleles (C^+, C^{ch}, C^h and C^a) control four coat colours: agouti, chinchilla, Himalayan and albino.
3. Genes for haemoglobin variants in man: Numerous alleles control Hb variants, important ones are Hb^A, Hb^S, Hb^C, Hb^G etc.

ABO blood groups in man

Blood components of vertebrates: Blood corpuscles, plasma and blood serum

1. Blood corpuscles: Cellular part; composed of erythrocytes (RBC), leucocytes (WBC) and thrombocytes (blood platelets);

2. Plasma: Non-cellular, colourless and liquid part;

3. Blood serum: Transparent, pale yellow part; blood serum= (plasma-fibrinogen)

*Fibrinogen is the blood coagulating component.

ABO blood groups: Antigen-antibody reaction

- Human blood contains two antigens: Antigen A and antigen B;
- Blood antigens (=agglutinogens) are mucopolysaccharides (protein + sugar) that are present on the surface of the RBC. The protein is identical in both blood antigens A and B, but sugar in the basis for antigen-antibody reaction specificity;

- Antibodies (= immunoglobulins) are also proteins, produced in blood serum by the immune system of the body in response to a particular antigen;
- So, human RBC has two blood antigens: A and B, and blood serum produces two antibodies: anti A (σ) and anti B (β).

Discovery of ABO blood groups

- Dr. Karl Landsteiner (1900) discovered two types of blood antigens, A and B, and he divided human blood into three groups: A, B and O; He was awarded the Nobel Prize in 1930.
- Two years later (1902), two students of Dr. Landsteiner: Alfred Von DeCastello and Adriano Sturli discovered the 4th blood group AB;
- So, human blood is divided into four blood groups: A, B, AB and O.

Classification of ABO blood groups in man

Depending on the antigen-antibody reactions, humans belong to the following four blood groups:

Blood groups	Antigens in RBC	Antibodies in blood serum	Can donate to	Can receive from
A	A	Anti B (β)	A, AB	A, O
B	B	Anti A (σ)	B, AB	B, O
AB	AB	None	AB only	AB, A, B, O
O	None	Both σ & β	O, A, B, AB	O only

Note: AB$^+$ is a universal recipient and **O$^-$** is a universal donor. But, another blood antigen (Rh + or -) must be taken into consideration during blood transfusion.

Inheritance of ABO blood groups in man

- ABO blood groups are controlled by three multiple alleles: I^A, I^B and I^O (=i);
- where I= isohaemagglutinogen or isoagglutinogen;
- The gene responsible for blood groups is located on the long arm of chromosome 9 in man;
- The dominance relationship between the alleles: $(I^A = I^B) > I^O$;
- So, there are 4 phenotypes and 6 genotypes of the human blood groups as follows:

Phenotypes	Genotypes
A	$I^A I^A$ (homozygote), $I^A I^O$ (heterozygote)
B	$I^B I^B$ (homozygote), $I^B I^O$ (heterozygote)
AB	$I^A I^B$ (always heterozygote)
O	$I^O I^O$ (always homozygote)

Inheritance of ABO blood groups in man

Probable crossing types of ABO blood groups can be shown in the following table.

♀♀/♂♂	I^AI^A	I^AI^O	I^BI^B	I^BI^O	I^AI^B	I^OI^O
I^AI^A						
I^AI^O						
I^BI^B						
I^BI^O						
I^AI^B						
I^OI^O						

Note: There are 6♀♀ × 6♂♂ =36 blood group types × (3♀♀ ×3♂♂) =9 Rh antigen types (Rh^{++}, Rh^{+-} and Rh^{--}) = 324 crossing types.

	AA	AO	BB	BO	AB	OO
AA	A	A	AB	A,AB	A,AB	A
AO	A	A,O	AB,B	A,B, AB,O	A,B,AB	A,O
BB	AB	B,AB	B	B	B,AB	B
BO	A,AB	A,B, AB,O	B	B,O	A,B,AB	B,O
AB	A,AB	A,B	B,AB	A,B	A,B,AB	A,B
OO	A	A,O	B	B,O	A,B	O

Checkerboard showing possible crosses between the blood groups of males and females resulting in blood groups in their progenies.

	You Can Receive							
If Your Type Is	O-	O+	B-	B+	A-	A+	AB-	AB+
AB+	YES	YES	YES	YES	YES	YES	YES	YES
AB-	YES		YES		YES	YES		
A+	YES	YES			YES	YES		
A-	YES				YES			
B+	YES	YES	YES	YES				
B-	YES		YES					
O+	YES	YES						
O-	YES							

Table showing donors and recipients of different blood groups in man.

Blood Type:	Can Receive:	Can Donate to:
O+	O+, O-	O+,A+,B+,AB+
O-	O-	ALL TYPES,UNIVERSAL DONOR
A+	A+,A-,O+,O-	A+,AB+
A-	A-,O-	A+,A-,AB+,AB-
B+	B+,B-,O+,O-	B+,AB+
B-	B-,O-	B+,B-,AB+,AB-
AB+	ALL	AB+
AB-	AB-,A-,B-,O-	AB+,AB-

Different blood groups and who can receive from and who can donate to

Frequency of ABO blood groups in man

O group ~ 48%
A group ~ 37%
B group ~ 11%
AB group ~ 4%

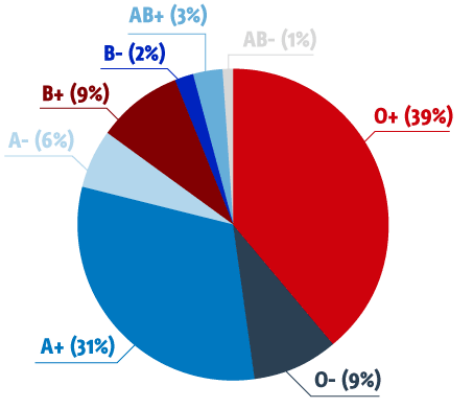

Fig 7.1 Pie diagram showing the frequency (%) of ABO blood groups in man

Subtypes of A and B blood groups

Blood groups	Subtypes
A	A_1, A_2 and A_3
AB	A_1B, A_2B and A_3B

Other blood antigens in man: Apart from A and B blood antigens, there is a large number of other blood antigens in man. These include: Rh, MN, Bombay, Cellano, Diago, Duffy, Kidd, Kell, Lervis, Lewis, Lutheran and Xg etc.

A couple of problems and their solutions

Problem 1: A woman of blood group A married a man of blood group O. They have three children bearing O, A and AB blood groups. Which child does not belong to the couple? (Or, which child is adopted?)

Solution: The genotype of the man is I^OI^O.

(a) If the woman is homozygous A: $I^AI^A \times I^OI^O$ = Children will be A (I^AI^O) only;
(b) If the woman is heterozygous A: $I^AI^O \times I^OI^O$ = Children will be A (I^AI^O) and O (I^OI^O).

So, the possible blood groups of the children are A and O. The child with blood group AB does not belong to the couple, which means he/she is adopted.

Problem 2: A female belongs to blood group A and she married a person having blood group B. What would be the possible blood groups of their children?

Solution: The female is either I^AI^A or I^AI^O and the male is either I^BI^B or I^BI^O. So, the possible blood groups of the children from this couple would be: A, B, AB and O which is shown below:

♂♂/♀♀	I^AI^A	I^AI^O
I^BI^B	AB	B, AB
I^BI^O	A, AB	A, B, AB, O

Pseudoalleles

Definition

Pseudoalleles occupy different loci that are very close to each other, but not exactly the same loci. As a result, crossing-over between the pseudoalleles takes place at extremely low frequencies.

Examples of traits controlled by pseudoalleles

1. Rh antigen in man (3-10 alleles): Rh^{++}, Rh^{+-}. Rh^{--} are major ones.

2. Eye colour in *Drosophila* (up to 16 alleles): white eye (w), apricot (w^a), coral (w^c), chery (w^{ch}), ivory (w^i) etc are common ones.

Rh antigen (Rh factor) in man

Discovery: Landsteiner and Wiener (1940) discovered Rh antigen in man. Rhesus monkeys *Macaca rhesus* have the same antigen, hence the name. Subsequently, it was found that about 85% people have similar antigen (Rh^+) and about 15% people lack this antigen (Rh^-) in the blood. The responsible gene for the Rh antigen is located on the short arm of chromosome 1 in man.

Number of alleles: Rh antigen forms a complex system involving over 45 antigens. According to Fisher and Wiener, however, 3-10 pseudoalleles regulate the Rh antigen in man. For simplicity, we may assume that there are 3 genotypes: Rh^{++}, Rh^{+-} and Rh^{--} in the human population.

Importance of Rh antigen in man: Rh antigen is very important for blood groupings in man, because mixing of Rh+ and Rh- blood (incompatible match) may cause blood clotting as well as death of the blood recipients and foetus/ newborn babies.

Rh incompatibility in man

An example:

P: Husband Rh positive (Rh^{++}/Rh^{+-})	×	Wife Rh negative (Rh^{--})		
G:	Rh^+ and Rh^-		Rh-	
F_1:	Rh^{+-}	Rh^{--}	Rh^{+-}	Rh^{--}
	Mother sensitized	Normal	Die of *Erythroblastosis*	Normal
	baby	baby	*foetalis*	baby

Features of *Erythroblastosis foetalis* in man:

- The foetus suffers from haemolytic anaemia;
- It has severe jaundice; and
- It results in stillbirth or neonatal death.

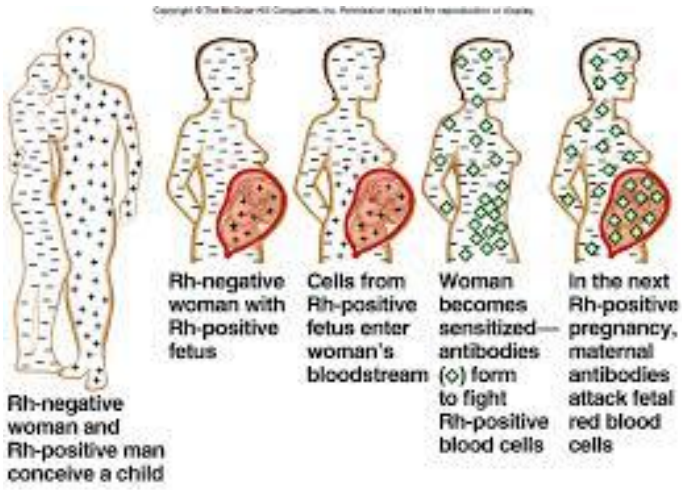

Fig 7.2 Diagram showing the consequence of an incompatible marriage between a Rh negative woman and a Rh-positive man.

Solution to Rh incompatibility cases

- If the mother is Rh^- and father is Rh^+
- Administration of anti-D antibody injection (Rh^o immunoglobulin) during pregnancy or shortly after delivery of the first Rh^+ child
- This may solve the problem for her second and subsequent Rh^+ babies

Differences between multiple alleles and pseudoalleles

Multiple alleles	Pseudoalleles
1. Multiple alleles always occupy the same locus on the homologous chromosomes	1. Pseudoalleles always occupy different loci on the homologous chromosomes
2. No crossing-over takes place between the members of the multiple alleles	2. Crossing-over takes place at extremely low frequencies between the members of the pseudoalleles
3. These do not show *cis*- and *trans*- position effect	3. These show *cis*- and *trans*- position effect
4. Examples include ABO blood groups in man and coat colour in rabbits.	4. Examples include Rh antigen in man and eye colour in *Drosophila*.

Medico-legal applications of blood groups in man

Medical applications:

1. Both AB and Rh antigens are very important for blood groupings and blood transfusion cases;
2. These are also important for Rh incompatibility marriages for giving healthy child births.

Legal applications:

1. Criminal investigations;
2. Disputed parentage settlements;
3. Identification of disaster victims;
4. Description of human populations and races etc.

Suggested reading:

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Wikipedia: www.wikipedia.com
ইসলাম, ম.সা., খান, হা.সা. ও রানা, ম.হা.তা. ২০১৭। *জেনেটিক্স: মিল ও অমিলের বিজ্ঞান*। অন্যপ্রকাশ, ঢাকা।