- The genetic systems proposed so far have been limited to a single pair of alleles.

- The maximum number of alleles at a gene locus that an individual possesses is **two**, with one on each of the homologous chromosomes.

- Since genes can change to alternative forms by the process of mutation, a large number of alleles is theoretically possible in a population of individuals.

- ❖ Though we typically teach about genetics using the simplest possible genetic situations, more complicated relationships exist.

- ❖ In fact, the more complicated gene interactions are probably much more common than the simple ones which are so easy to figure out.

- In most cases we teach with genes for which only two alleles are known, ***but many genes have more than two different alleles.***

- ***Thus, whenever more than two alleles are identified at a gene locus in a population, they are referred to as multiple alleles.***

- One such gene which is of great interest to humans is the **ABO blood group gene**.
- This particular gene has **three alleles**, rather than two.
- Each of us has only two sets of chromosomes, so any one individual has only two of these alleles at once.

- The presence of three different alleles means that there are **six possible genotypes**, rather than the three possible for the more familiar two-allele situation.

- It must be noted that, with the multiple alleles, the number of different genotypes possible among diploid organisms is a function of the number of alleles that exist for any given gene.

- **If n is the number of alleles of a gene, then, the number of different genotypes possible is n(n+1)/2.**

- Thus, with 2, 3, 4, or 5 alleles, there are **3, 6**, **10**, and **15** possible genotypes.

- It must also be noted that, although a large number of different alleles of a given gene may be present in a population or a species, **only two of those alleles can be present in any one diploid organism**.

Symbols for Multiple Alleles

- The dominance hierarchy should be defined at the beginning of each problem involving multiple alleles.
- A capital letter is commonly used to designate the allele which is dominant to all others in the series.
- The corresponding lower case letter designates the allele which is recessive to all others in the series.

- Other alleles, intermediate in their degree of dominance between these two extremes, are usually assigned the lower case with some suitable superscript.

Examples:

- A classic example of multiple alleles involves coat color in rabbits.

- Four alleles of the rabbit coat color (c) gene have been studied:

- C (**wild-type** or **full color**), c^{ch} ("chinchilla,"i.e. mixed colored), c^{h} ("himalayan," i.e. white with black tips on the extremities), and c ("albino" which fails to produce pigment).

- The above alleles show a gradation in dominance of **$C > c^{ch} > c^{h} > c$**

- That is, C is dominant to each of the three mutant alleles, while c^{h} is recessive to c^{ch} and so on.

ABO Blood Type Alleles in Humans

- One of the most firmly established series of multiple alleles in humans involves the genetic locus controlling the blood types, A, B and O.

- All humans can be typed for the ABO blood group.

- There are **four principal types**: A, B, AB, and O.

- There are **two antigens** and **two antibodies** that are mostly responsible for the ABO types.

- The specific combination of these four components determines an individual's type in most cases.

- An **antigen** is a substance or molecule that, when introduced into the body, triggers the production of an **antibody** by the **immune system**, which will then kill or neutralize the antigen that is recognized as a foreign and potentially harmful invader.

- An **antibody**, also known as an **immunoglobulin,** is used by the immune system to identify and neutralize foreign objects such as bacteria and viruses.

- For the ABO gene, the three alleles are the **I^A**, **I^B** and **i** alleles. We typically call these alleles "A," "B," and "O,"

- The rules for assigning symbols to alleles demand that all three be represented by some version of the same symbol.

- In this case, that common symbol is the letter "**I**" which stands for "**immunoglobin.**"

- Things get a bit more complicated when there are three alleles instead of just two.

- As the symbols above should suggest, the i allele (OR the "O" allele) is recessive to both the I^A and I^B alleles (the "A" and "B" alleles).

- The I^A and I^B show **co-dominance.**

- This means that in an individual who is heterozygous for these two alleles, the phenotypes of **both** alleles are completely expressed, thus producing blood type **AB**.

- (i.e. I^AI^B heterozygous have **both** A and B antigens on their red blood cells) and I^A and I^B are said to be codominant.

- I^O is recessive (i.e. I^OI^O homozygotes have **no** ABO antigens on their red blood cells)

- I^AI^O and I^BI^O heterozygotes have A and B antigens respectively on their red blood cells.

- The ABO locus controls the type of glycolipids found on the surface of erythrocytes, apparently by specifying the type of glycosyl-transferases synthesized in the red blood cells.

- The specific types of glycolipids on the red cell surface provide the antigenic determinants that react with specific antibodies present in the blood serum.

- Humans, like all other mammals, produce antibodies and circulate them in the blood serum as a defense mechanism.

- No antibodies are synthesized (in normal individuals) that react with antigens present on the individual’s own cells.

- The table below summarizes the cell surface antigenic determinants and the serum antibodies present in the four major ABO blood types.

- Individuals with blood type AB have both A and B antigens on their erythrocytes, but no anti-A and anti-B antibodies in their blood serum.

Blood Transfusion Compatibility for the ABO Blood Groups

Blood Group	Terminal Sugar of Antigens Present	Antibodies Present	Red Cell Type Agglutinated	Transfusions Accepted From
A	A (galactosamine)	Anti-B	B, AB	A or O
B	B (galactose)	Anti-A	A, AB	B or O
AB	A (galactosamine) & B (galactose)	None	None	A, B, AB or O
O	None	Anti-A & Anti-B	A, B, and AB	O

- Type O individuals lack both antigens, but carry both anti-A and anti-B antibodies in their blood serum.

- Type O individuals are referred to as **universal donors.**

- Type O blood can be used in transfusion for individuals of any blood type if the blood is introduced slowly to permit sufficient dilution of the anti-A and anti-B antibodies present in the serum of the donor.

Blood Transfusion Compatibility for the ABO Blood Groups

Blood Group	Terminal Sugar of Antigens Present	Antibodies Present	Red Cell Type Agglutinated	Transfusions Accepted From
A	A (galactosamine)	Anti-B	B, AB	A or O
B	B (galactose)	Anti-A	A, AB	B or O
AB	A (galactosamine) & B (galactose)	None	None	A, B, AB or O
O	None	Anti-A & Anti-B	A, B, and AB	O

- For example, people with type A blood will have the A antigen on the surface of their red cells (as shown in the table above).

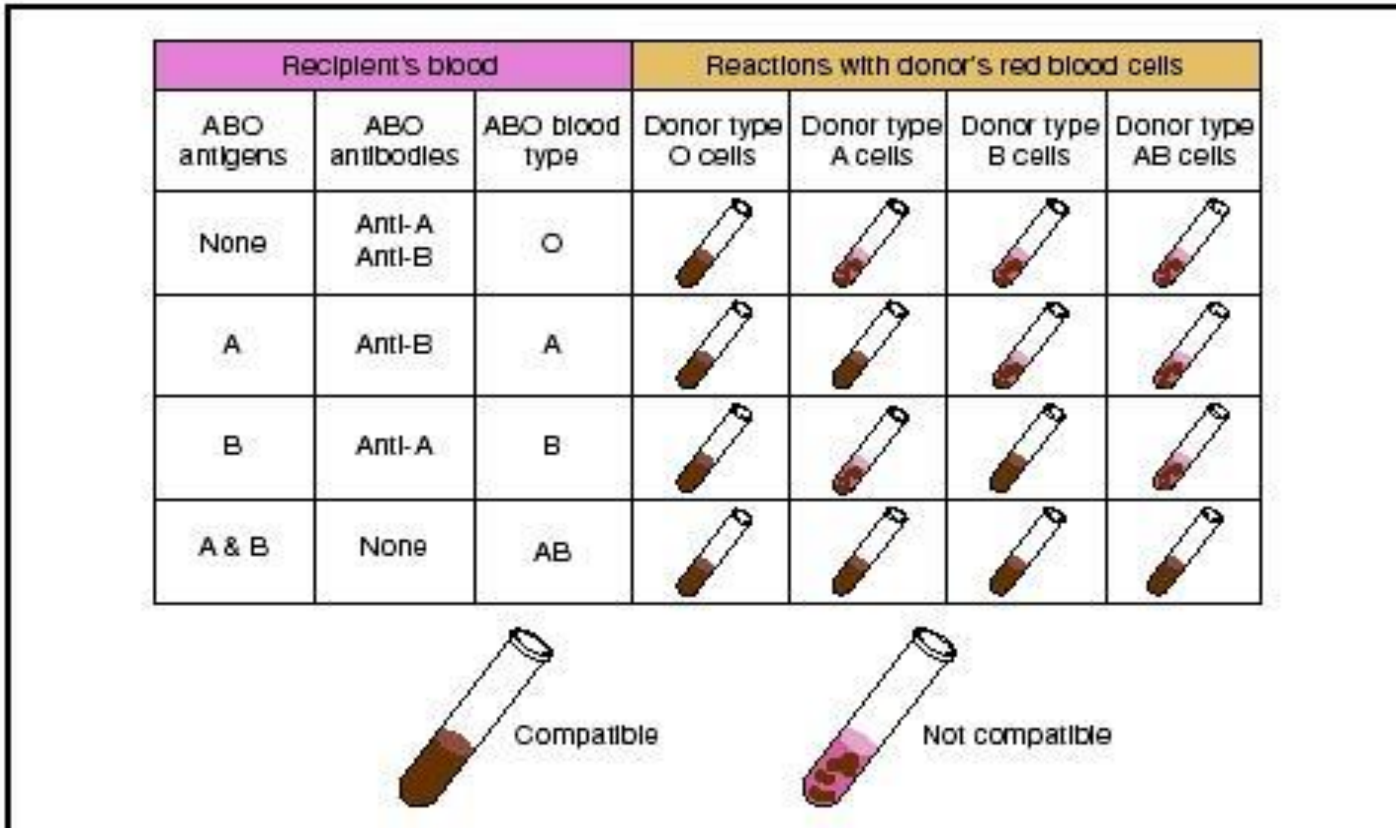
- As a result, anti-A antibodies will not be produced by them because they would cause the destruction of their own blood.

- However, if B type blood is injected into their systems (people with type A blood), anti-B antibodies in their plasma will recognize it as alien and burst or agglutinate the introduced red cells in order to cleanse the blood of alien protein

- However, when type A and B blood are mixed, the anti-A antibodies in the type B blood serum react with the antigens on the type A blood cells, and vice versa, and produces agglutination or clumping of cells (see the table below).

- Cross-matching blood types to determine compatibility is thus essential in blood transfusions.

- In this process, blood donors and recipients are tested for the presence of antigens and antibodies that are incompatible (see the table below).



Recipient's blood			Reactions with donor's red blood cells			
ABO antigens	ABO antibodies	ABO blood type	Donor type O cells	Donor type A cells	Donor type B cells	Donor type AB cells
None	Anti-A Anti-B	O				
A	Anti-B	A				
B	Anti-A	B				
A & B	None	AB				

- We can test the hypothesis that three alleles control ABO blood types by examining potential offspring from all possible matings.
- If we assume heterozygosity wherever possible, we can then predict which phenotypes can occur.

Potential phenotypes in the offspring of parents with all the possible ABO blood type combinations

P_1 Generation		F_1 Phenotype			
Phenotypes	Heterozygous Genotypes	A	B	AB	O
A x A	$I^A I^O$ x $I^A I^O$	X	...	...	X
B x B	$I^B I^O$ x $I^B I^O$	...	X	...	X
O x O	$I^O I^O$ x $I^O I^O$	...	...	...	X
A x B	$I^A I^O$ x $I^B I^O$	X	X	X	X
A x AB	$I^A I^O$ x $I^A I^B$	X	X	X	...
A x O	$I^A I^O$ x $I^O I^O$	X	...	...	X
B x AB	$I^B I^O$ x $I^A I^B$	X	X	X	...
B x O	$I^B I^O$ x $I^O I^O$	...	X	...	X
AB x O	$I^A I^B$ x $I^O I^O$	X	X	...	...
AB x AB	$I^A I^B$ x $I^A I^B$	X	X	X	...

- Our knowledge of human blood types has several practical applications.

- Compatible blood transfusions can be achieved and decisions of disputed parentage more accurately made.

- In the latter case, newborns have been inadvertently mixed up in hospitals, but more commonly, an adult male is accused of fathering an illegitimate child.

- In both cases, an examination of the ABO phenotypes of the possible parents and the child may help to resolve the situation.

- **The only mating which can result in offspring of all four phenotypes is between two heterozygous individuals, one showing the A phenotype and the other showing the B phenotype.**

Questions

1. *A case was brought before a certain judge in which a woman of blood group A presented a baby of blood group O, which she claimed as her child, and brought suit against a man of group AB whom she claimed was the father of the child. What bearing might the blood-type information have on the case?*

2. *In another case, a woman of blood group AB presented a baby of group O, which she claimed as her baby. What bearing might the blood-type information have on the case?*