Human Genotypes

An estimated 25 000 genes determine all human **traits**. While most traits are determined by more than one gene, a number are determined by a single gene system, with dominant/recessive, codominant, or multiple allele inheritance. Single gene traits (below) show **discontinuous variation** in a population, with individuals showing only one of a limited number of phenotypes (usually two or three). Single gene traits may, however, show variable **penetrance**. Penetrance describes the extent to which the properties controlled by a gene will be expressed. Highly penetrant genes will be expressed regardless of the effects of the environment, whereas a gene with low penetrance will only sometimes produce the trait with which it is associated.

Trait: Handedness

Dominant

Phenotype: Right-handed
Allele: R

Recessive

Phenotype: Left-handed
Allele: r

The trait of left or right handedness is genetically determined. Right-handed people have the dominant allele, while left handedness is recessive. People that consider themselves ambidextrous can assume they have the dominant allele for this trait.

Trait: Hand clasp

Dominant

Phenotype: Left thumb on top
Allele: C

Recessive

Phenotype: Right thumb on top
Allele: c

Like handedness, hand clasping shows dominance/recessiveness. When the hands are clasped together, either the left or the right thumb will naturally come to rest on top. The left thumb on top is the dominant trait (C), while the right thumb on top is recessive (c).

Trait: Dimpled chin

Dominant

Phenotype: Chin cleft
Allele: D

Recessive

Phenotype: No chin cleft
Allele: d

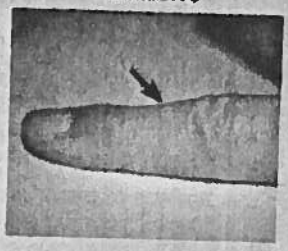
A cleft or dimple on the chin is inherited. A cleft is dominant (D), while the absence of a cleft is recessive (d), although this gene shows **variable penetrance**, probably as a result of modifier genes.

Trait: Middle digit hair

Dominant

Phenotype: Hair on middle segment
Allele: M

Recessive

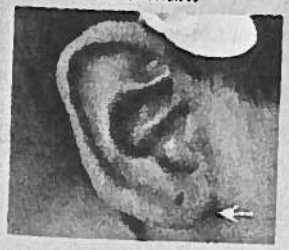


Phenotype: No hair on mid segment
Allele: m

Some people have a dominant allele that causes hair to grow on the middle segment of their fingers. It may not be present on all fingers, and in some cases may be very fine and hard to see.

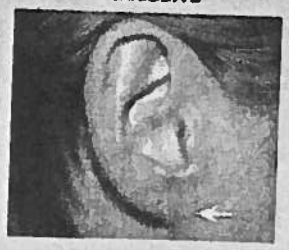
Trait: Ear lobe shape

Dominant



Phenotype: Lobes free
Allele: F

Recessive



Phenotype: Lobes attached
Allele: f

In people with only the recessive allele (homozygous recessive), ear lobes are attached to the side of the face. The presence of a dominant allele causes the ear lobe to hang freely.

Trait: Thumb hyperextension

Dominant

Phenotype: 'Hitchhiker's thumb'
Allele: H

Recessive

Phenotype: Normal thumb
Allele: h

There is a gene that controls the trait known as 'hitchhiker's thumb' which is technically termed distal hyperextensibility. People with the dominant phenotype are able to curve their thumb backwards without assistance, so that it [illegible]

Your Genotype Profile

Use the descriptions and the symbols on the previous page to determine your own genotype. In situations where you exhibit the dominant form of the trait, it may be helpful to study the features of your family to determine whether you are homozygous dominant or heterozygous. If you do not know whether you are heterozygous for a given trait, assume you are.

Your traits:	Thumb	Ear lobes	Chin cleft	Middle digit hair	Handedness	Hand clasp
Phenotype:						
Genotype:						

1. Enter the details of your own genotype in the table above. The row: 'Phenotype' requires that you write down the version of the trait that is expressed in you (e.g. chin cleft). Each genotype should contain two alleles.
2. Use a piece of paper and cut out 12 squares. Write the symbols for your alleles listed in the table above (each of the two alleles on two separate squares for the six traits) and write your initials on the back.
3. Move about the class, shaking hands with other class members to simulate mating (this interaction does not have to be with a member of the opposite sex).
4. Proceed to determine the possible genotypes and phenotypes for your offspring with this other person by:
   (a) Selecting each of the six characters in turn
   (b) Where a genotype for a person is known to be homozygous (dominant or recessive) that person will simply place down one of the pieces of paper with their allele for that gene. If they are heterozygous for this trait, toss a coin to determine which gets 'donated' with heads being the dominant allele and tails being the recessive.
   (c) The partner places their allele using the same method as in (b) above to determine their contribution to this trait.
   (d) Write down the resulting genotype in the table below and determine the phenotype for that trait.
   (e) Proceed on to the next trait.
5. Try another mating with a different partner or the same partner and see if you end up with a child of the same phenotype.

Child 1	Thumb	Ear lobes	Chin cleft	Middle digit hair	Handedness	Hand clasp
Phenotype:						
Genotype:						

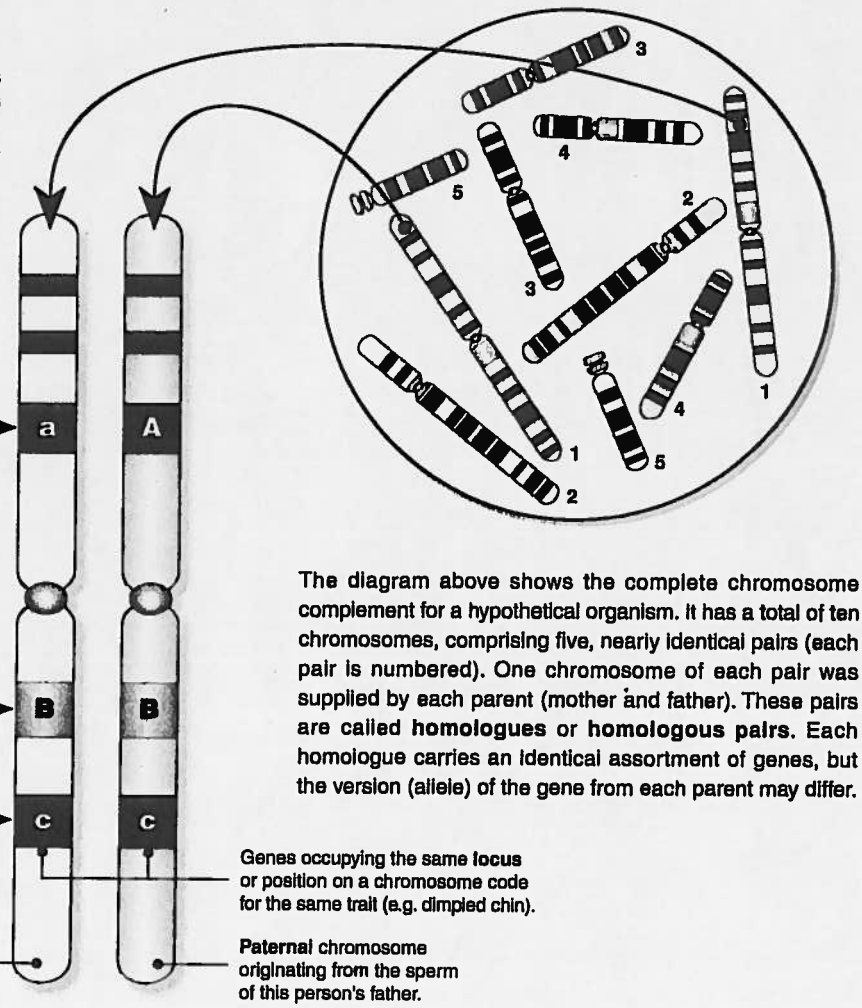
Child 2	Thumb	Ear lobes	Chin cleft	Middle digit hair	Handedness	Hand clasp
Phenotype:						
Genotype:						

Alleles

Sexually reproducing organisms in nearly all cases have paired sets of chromosomes, one set coming from each parent. The equivalent chromosomes that form a pair are termed **homologues**. They contain equivalent sets of genes on them. But there is the potential for different versions of a gene to exist in a population and these are termed **alleles**.

Homologous Chromosomes

In sexually reproducing organisms, most cells have a homologous pair of chromosomes (one coming from each parent). This diagram shows the position of three different genes on the same chromosome that control three different traits (A, B and C).



The diagram above shows the complete chromosome complement for a hypothetical organism. It has a total of ten chromosomes, comprising five, nearly identical pairs (each pair is numbered). One chromosome of each pair was supplied by each parent (mother and father). These pairs are called **homologues** or **homologous pairs**. Each homologue carries an identical assortment of genes, but the version (allele) of the gene from each parent may differ.

1. Define the following terms used to describe the allele combinations in the genotype for a given gene:

   (a) Heterozygous: _____

   (b) Homozygous dominant: _____

   (c) Homozygous recessive: _____

2. For a gene given the symbol 'A', name the alleles present in an organism that is identified as:

   (a) Heterozygous: _____ (b) Homozygous dominant: _____ (c) Homozygous recessive: _____

3. Explain what a homologous pair of chromosomes is: _____

   _____

   _____

4. Discuss the significance of genes existing as **alleles**: _____

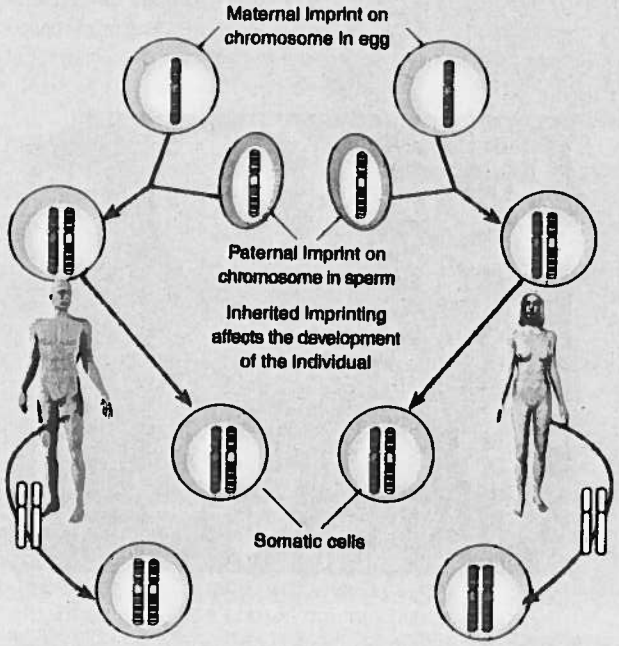
   _____

Genomic Imprinting

The phenotypic effects of some mammalian genes depend on whether they were inherited from the mother or the father. This phenomenon, called **genomic imprinting** (or parental imprinting), is part of **epigenetics**, the study of the heritable changes in gene function that occur without involving changes in the DNA sequence. Just as cells inherit genes, they also inherit the instructions that communicate to the genes when to become active, in which tissue, and to what extent. Epigenetic phenomena are important because they regulate when and at what level genes are expressed.

Genomic Imprinting

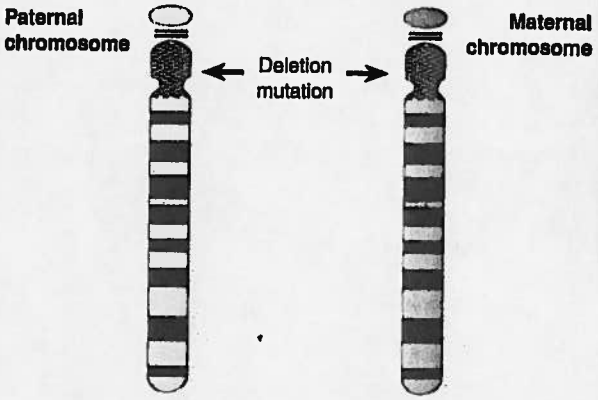
Genomic imprinting describes how a small subset of the genes in the genome are expressed according to their parent of origin. 'Imprints' can act as silencers or activators for imprinted genes. A mammal inherits two sets of chromosomes, one from the mother and one from the father. In this way the imprinted gene expression is balanced; a prerequisite for a viable offspring in mammals.



Maternal and paternal chromosomes are differently imprinted. Chromosomes are newly imprinted (reprogrammed) each generation.

Imprinted Genes Are Different

Some imprinted genes are expressed from a maternally inherited chromosome and **silenced** on the paternal chromosome, while other imprinted genes show the opposite expression pattern and are only expressed from a paternally inherited chromosome. Evidence of this is seen in two human genetic disorders. Both are caused by the same mutation; a specific deletion on chromosome 15. The disorder expressed depends on whether the mutation is inherited from the father or the mother.



Inherited from the father:
Prader-Willi syndrome

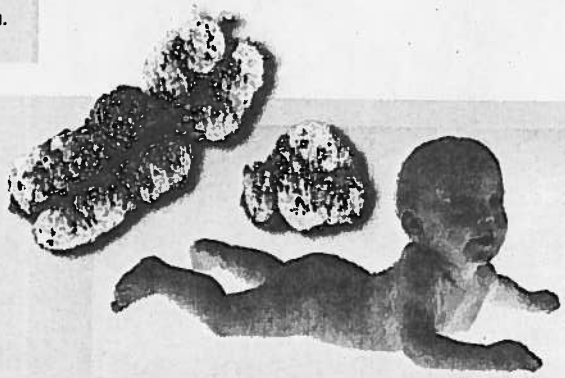
Phenotype:
Mental retardation, obesity, short stature, unusually small hands and feet

Inherited from the mother
Angelman syndrome

Phenotype
Uncontrollable laughter, jerky movements, motor and mental abnormalities

How Are Genes Silenced?

- In many instances, **gene silencing** achieved through **methylation** of the DNA of genes or regulatory sequences, which results in the gene not being expressed.
- **Methylation** turns off gene expression by adding a methyl group to cytosines in the DNA. This changes the state of the chromatin so that the expression of any genes in the methylated region is inhibited. Methylation is also important in X-inactivation.
- In other instances, phosphorylation or other chemical modification of histone proteins appears to lead to silencing.



Which genes did you inherit from your mother and which from your father? For some genes, imprinting will affect phenotypic expression.

1. (a) Explain what is meant by genomic imprinting: _____

   _____

   (b) Describe one of the mechanisms by which imprinting is achieved: _____

   _____

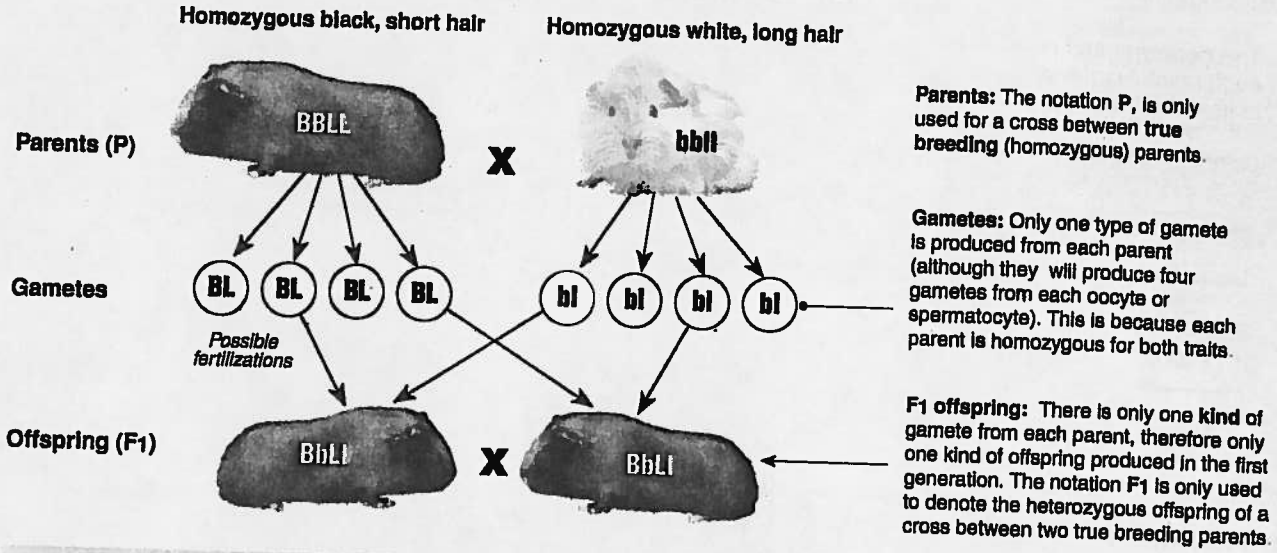
2. Explain the significance of imprinting to the inheritance of genes: _____

   _____

   _____

Dihybrid Cross

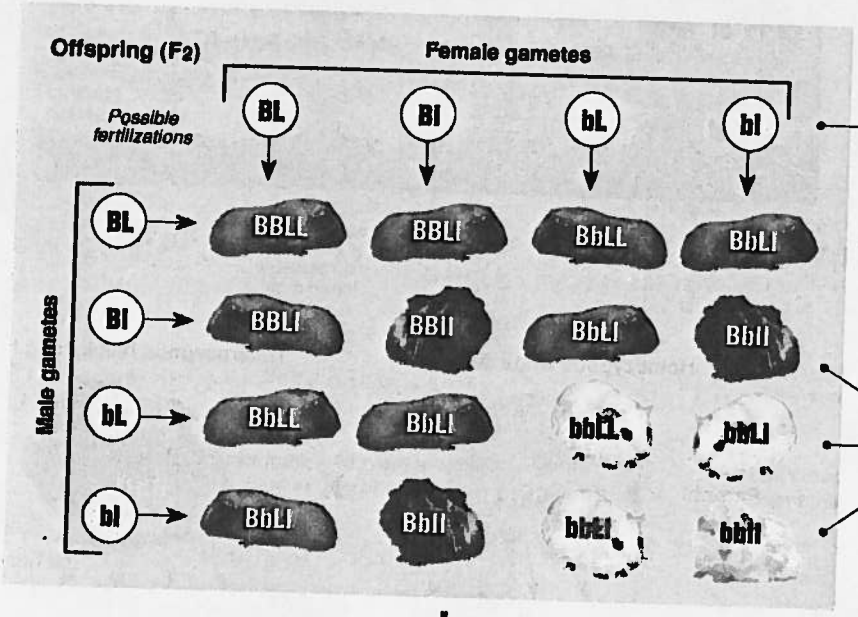
A cross (or mating) between two organisms where the inheritance patterns of **two genes** are studied is called a **dihybrid cross** (compared with the study of one gene in a monohybrid cross). There are a greater number of gamete types (four) produced when two genes are considered. Remember that the genes described are being carried by separate chromosomes and are sorted independently of each other during meiosis (that is why you get four kinds of gamete). The two genes below control two unrelated characteristics **hair color** and **coat length**. Black and short are dominant.



Parents: The notation **P**, is only used for a cross between **true breeding** (homozygous) parents.

Gametes: Only one type of gamete is produced from each parent (although they will produce four gametes from each oocyte or spermatocyte). This is because each parent is homozygous for both traits.

F1 offspring: There is only one **kind** of gamete from each parent, therefore only one kind of offspring produced in the first generation. The notation **F1** is only used to denote the heterozygous offspring of a cross between two true breeding parents.



F2 offspring: The F1 were mated with each other (**selfed**). Each individual from the F1 is able to produce four different kinds of gamete. Using a grid called a **Punnett square** (left), it is possible to determine the expected genotype and phenotype ratios in the F2 offspring. The notation **F2** is only used to denote the offspring produced by crossing F1 heterozygotes.

Each of the 16 animals shown here represents the possible zygotes formed by different combinations of gametes coming together at fertilization.

Heredity

The offspring can be arranged in groups with similar phenotypes:

Genotype	Phenotype
1 BBLL 2 BbLL 2 BBLl 4 BbLl	9 black, short hair
1 BBll 2 Bbll	3 black, long hair
1 bbLL 2 bbLl	3 white, short hair
1 bbll	1 white, long hair

A total of 9 offspring with one of 4 different genotypes can produce black, short hair

A total of 3 offspring with one of 2 different genotypes can produce black, long hair

A total of 3 offspring with one of 2 different genotypes can produce white, short hair

Only 1 offspring of a given genotype can produce white, long hair

Cross N°. 1

The dihybrid cross on the right has been partly worked out for you. You must determine:

1. The genotype and phenotype for each animal (write your answers in its dotted outline).
2. Genotype **ratio** of the offspring:

   _____

   _____

   _____

   _____

   _____

   _____

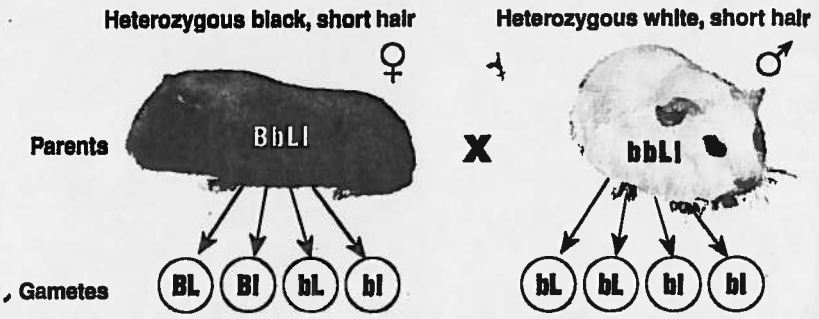
3. Phenotype **ratio** of the offspring:

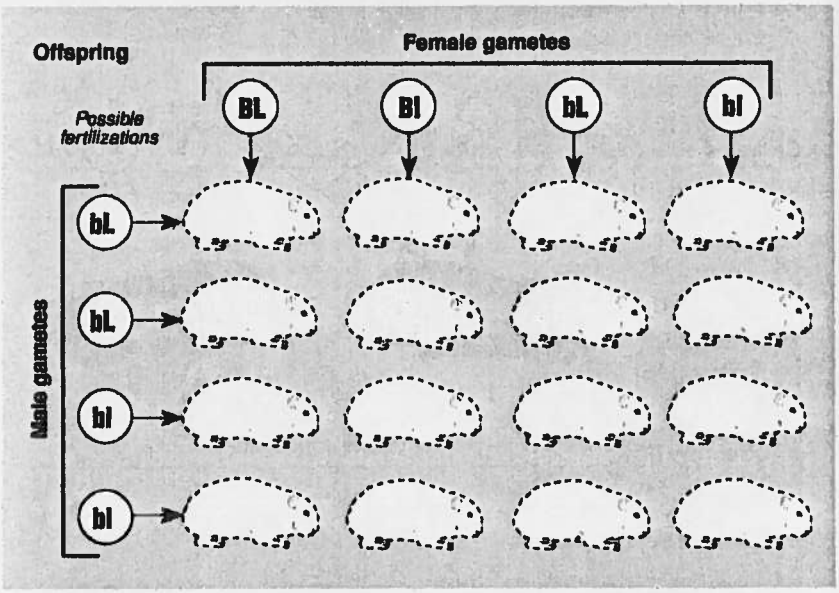
   _____

   _____

   _____

   _____





Cross N°. 2

For the dihybrid cross on the right, determine:

1. Gametes produced by each parent (write these in the circles).
2. The genotype and phenotype for each animal (write your answers in its dotted outline).
3. Genotype **ratio** of the offspring:

   _____

   _____

   _____

   _____

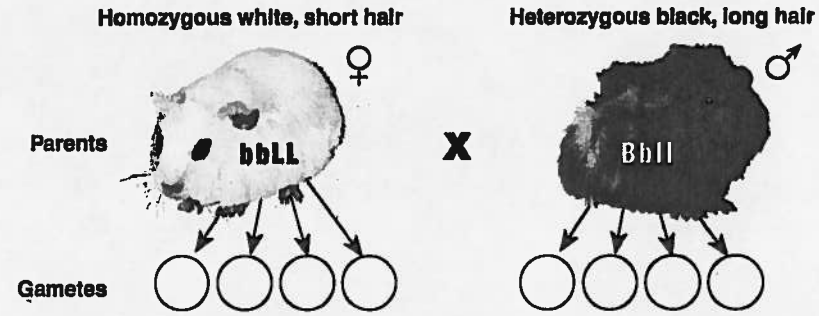
4. Phenotype **ratio** of the offspring:

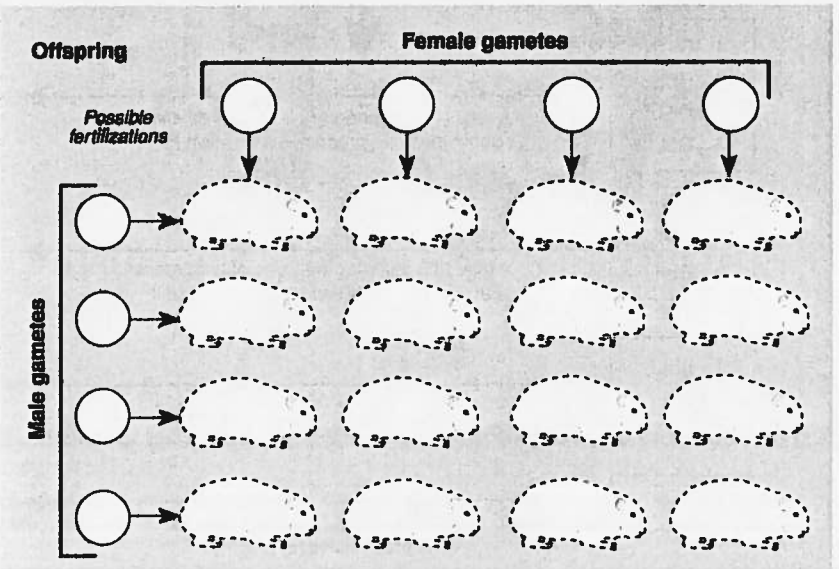
   _____

   _____

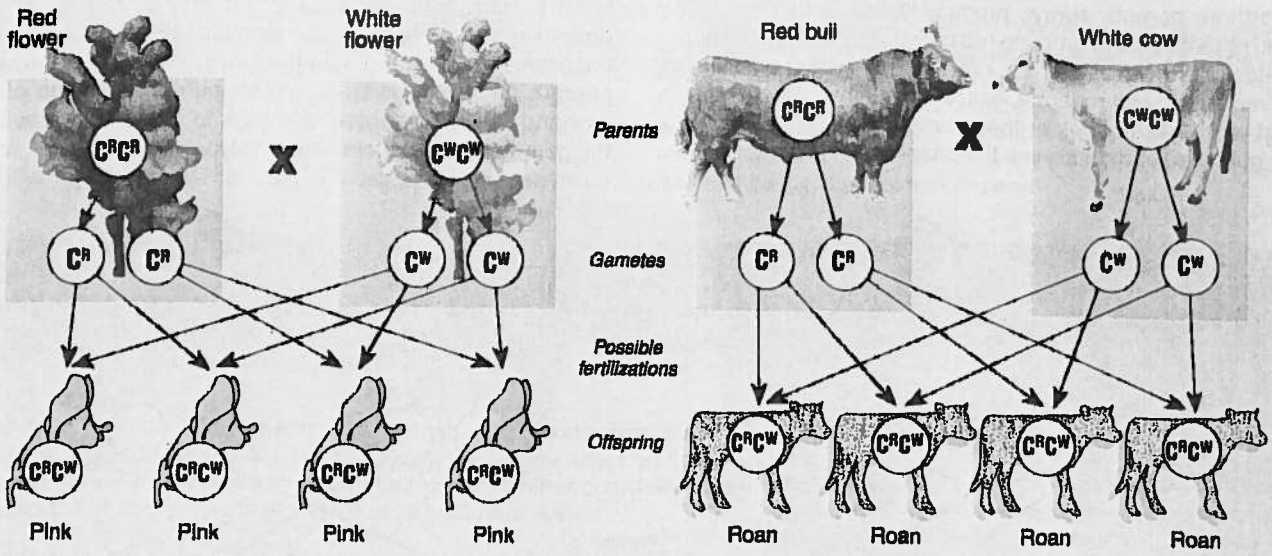
   _____

   _____





Dominance of Alleles



Incomplete Dominance

Incomplete dominance refers to the situation where the action of one allele does not completely mask the action of the other and neither allele has dominant control over the trait. The heterozygous offspring is **intermediate** in phenotype between the contrasting homozygous parental phenotypes. In crosses involving incomplete dominance the phenotype and genotype ratios are identical. Examples include snapdragons (*Antirrhinum*), where red and white-flowered parent plants are crossed to produce pink-flowered offspring. In this type of inheritance the phenotype of the offspring results from the partial influence of both alleles.

Codominance

Codominance refers to inheritance patterns when both alleles in a heterozygous organism contribute to the phenotype. Both alleles are **independently** and **equally expressed**. One example includes the human blood group AB which is the result of two alleles: A and B, both being equally expressed. Other examples include certain coat colors in horses and cattle. Reddish coat color is not completely dominant to white. Animals that have both alleles have coats that are **roan**-colored (coats with a mix of red and white hairs). The red hairs and white hairs are expressed equally and independently (not blended to produce pink).

1. In incomplete and codominance, two parents of differing phenotype produce offspring different from either parent. Explain the mechanism by which this occurs in:

   (a) Incomplete dominance: _____

   _____

   (b) Codominance: _____

   _____

2. For each situation below, explain how the heterozygous individuals differ in their phenotype from homozygous ones:

   (a) Incomplete dominance: _____

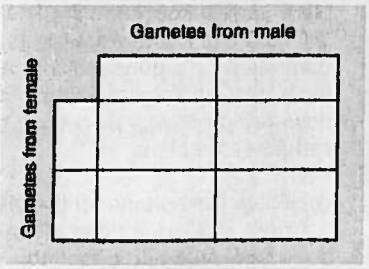
   (b) Codominance: _____

3. Describe the classical phenotypic ratio for a codominant gene resulting from the cross of two heterozygous parents (in the case of the cattle described above, this would be a cross between two roan cattle). Use the Punnett square (provided right) to help you:

   _____

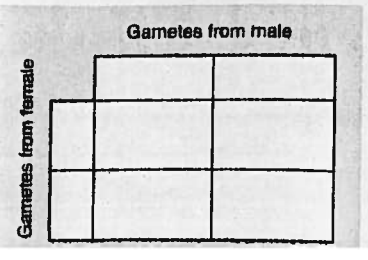
   _____

   _____

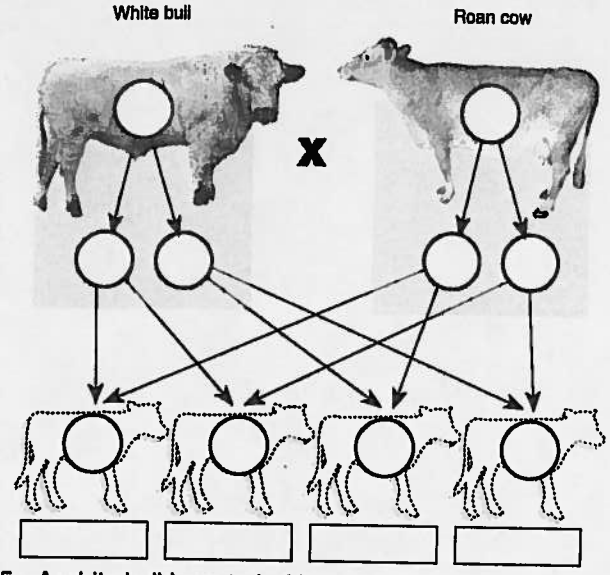


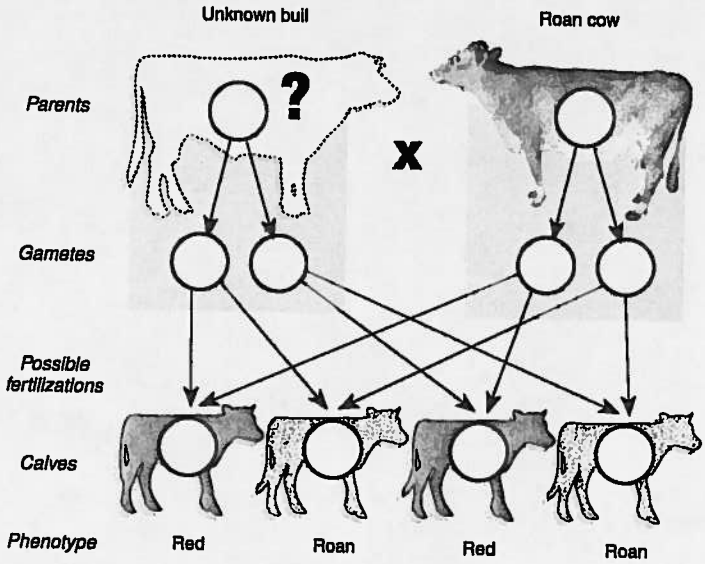
4. A plant breeder wanted to produce flowers for sale that were only pink or white (i.e. no red). Determine the phenotypes of the two parents necessary to produce these desired offspring. Use the Punnett square (provided right) to help you:

   _____



In the shorthorn cattle breed coat color is inherited. White shorthorn parents always produce calves with white coats. Red parents always produce red calves. But when a red parent mates with a white one the calves have a coat color that is different from either parent, called roan (a mixture of red hairs and white hairs). Look at the example on the previous page for guidance and determine the offspring for the following two crosses. In the cross on the left, you are given the phenotype of the parents. From this information, their genotypes can be determined, and therefore the gametes and genotypes and phenotypes of the calves. In the cross on the right, only one parent's phenotype is known. Work out the genotype of the cow and calves first, then trace back to the unknown bull via the gametes, to determine its genotype.





5. A white bull is mated with a roan cow (above, left).

   (a) Fill in the spaces on the diagram (above, left) to show the genotype and phenotype for parents and calves.

   (b) State the phenotype ratio for this cross: _____

   (c) Suggest how the farmer who owns these cattle could control the breeding so that the herd ultimately consisted of red colored cattle only:

   _____

   _____

   _____

6. A unknown bull is mated with a roan cow (above, right). A farmer has only roan shorthorn cows on his farm. He suspects that one of the bulls from his next door neighbors may have jumped the fence to mate with his cows earlier in the year. All the calves born were either red or roan. One neighbor has a red bull, the other has a roan bull.

   (a) Fill in the spaces on the diagram (above, right) to show the genotype and phenotype for parents and calves.

   (b) State which of the neighbor's bulls must have mated with the cows: **red** or **white** (*delete one*)

7. A plant breeder crossed two plants of the plant variety known as Japanese four o'clock. This plant is known to have its flower color controlled by a gene which possesses incomplete dominant alleles. Pollen from a pink flowered plant was placed on the stigma of a red flowered plant.

   (a) Fill in the spaces on the diagram on the right to show the genotype and phenotype for parents and offspring.

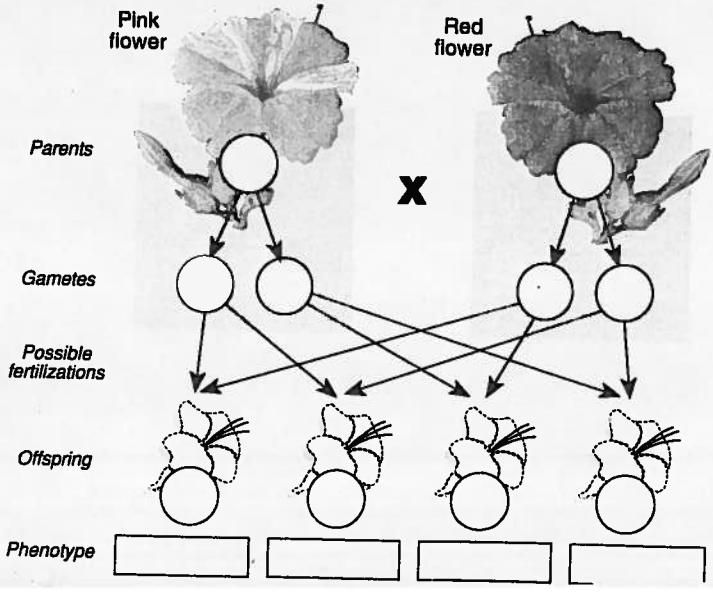
   (b) State the phenotype ratio:

   _____

   _____

   _____

   _____



Multiple Alleles in Blood Groups

The four common blood groups of the human 'ABO blood group system' are determined by three alleles: ***A***, ***B***, and ***O*** (also represented in some textbooks as: I^A, I^B, and I^O or just I). This is an example of a **multiple allele** system for a gene. The ABO antigens consist of sugars attached to the surface of red blood cells. The alleles code for enzymes (proteins) that join together these sugars. The allele ***O*** produces a non-functioning enzyme that is unable to make any changes to the basic antigen (sugar) molecule. The other two alleles ***(A, B)*** are **codominant** and are expressed equally. They each produce a different functional enzyme that adds a different, specific sugar to the basic sugar molecule. The blood group A and B antigens are able to react with antibodies present in the blood from other people and must be matched for transfusion.

Recessive allele: ***O*** produces a non-functioning protein
Dominant allele: ***A*** produces an enzyme which forms **A antigen**
Dominant allele: ***B*** produces an enzyme which forms **B antigen**

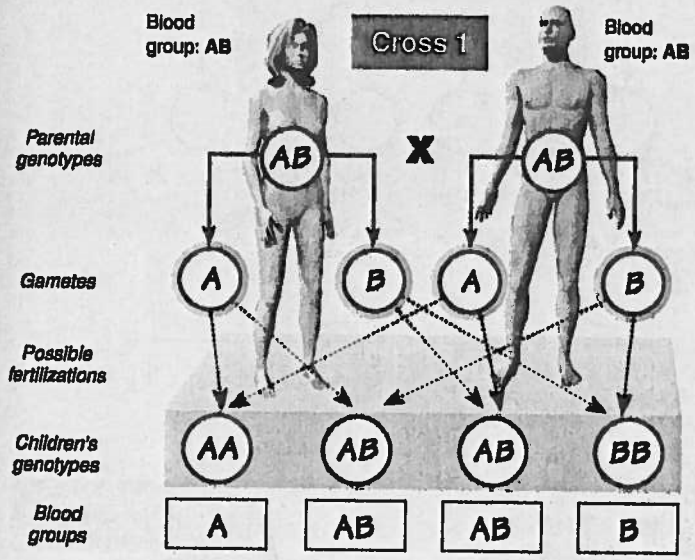
If a person has the ***AO*** allele combination then their blood group will be group **A**. The presence of the recessive allele has no effect on the blood group in the presence of a dominant allele. Another possible allele combination that can create the same blood group is ***AA***.

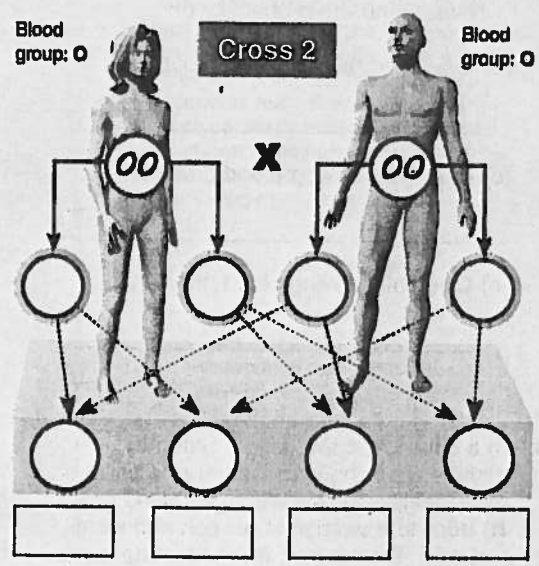
Blood group (phenotype)	Possible genotypes	Frequency*		
		White	Black	Native American
O	*OO*	45%	49%	79%
A	*AA AO*	40%	27%	16%
B		11%	20%	4%
AB		4%	4%	1%

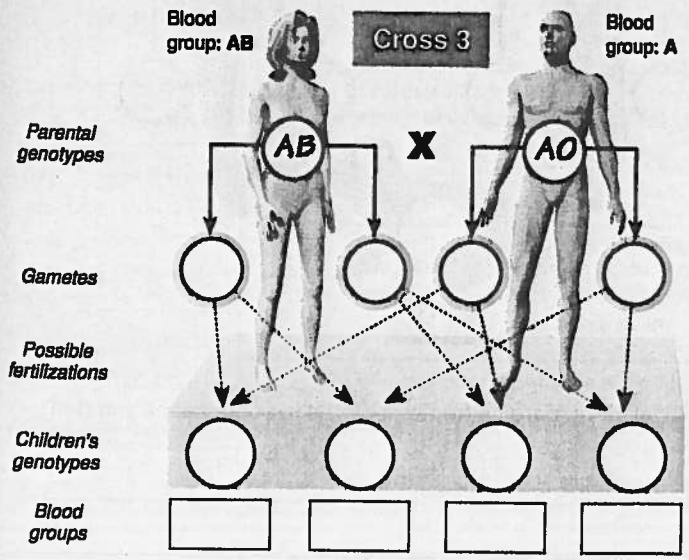
* Frequency is based on North American population
Source: www.kcom.edu/faculty/chamberlain/Website/MBTUART/Lect18.htm

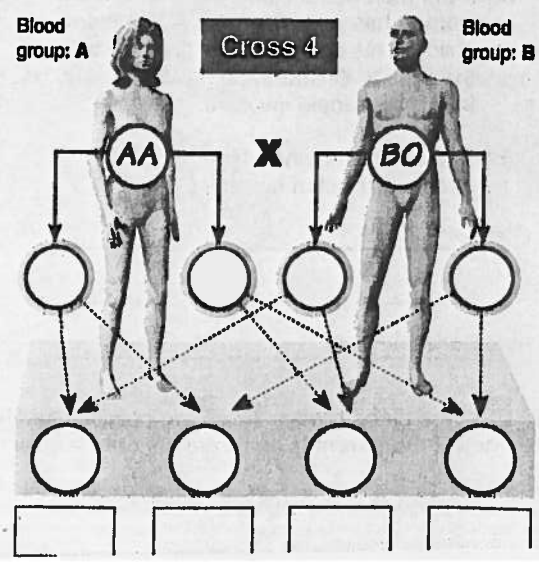
1. Use the information above to complete the table for the possible genotypes for blood group B and group AB.

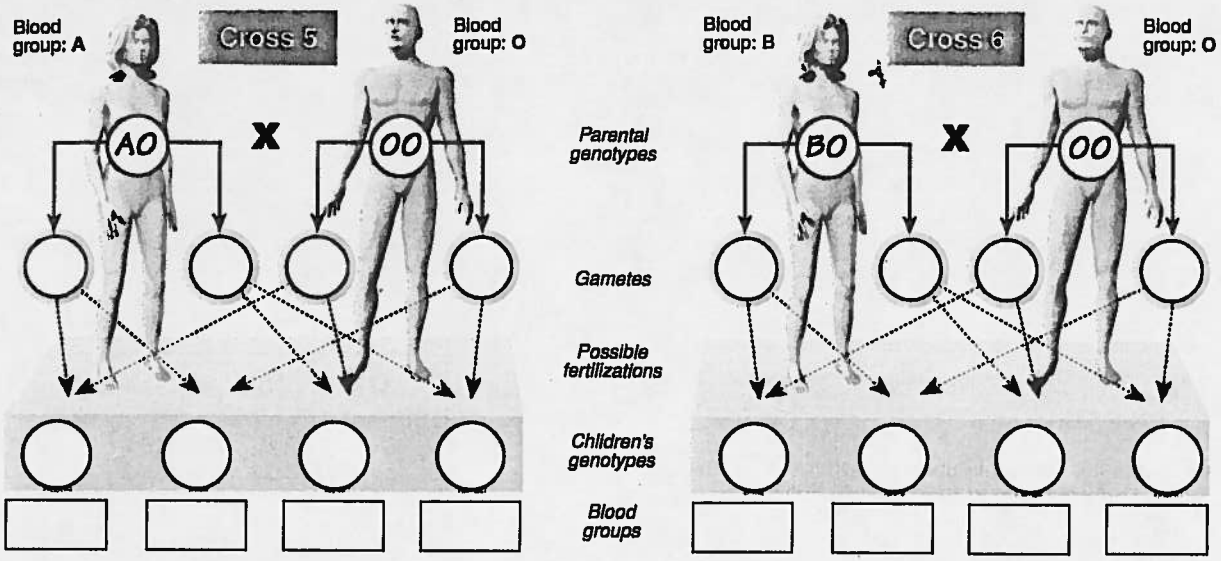
2. Below are six crosses possible between couples of various blood group types. The first example has been completed for you. Complete the genotype and phenotype for the other five crosses shown:



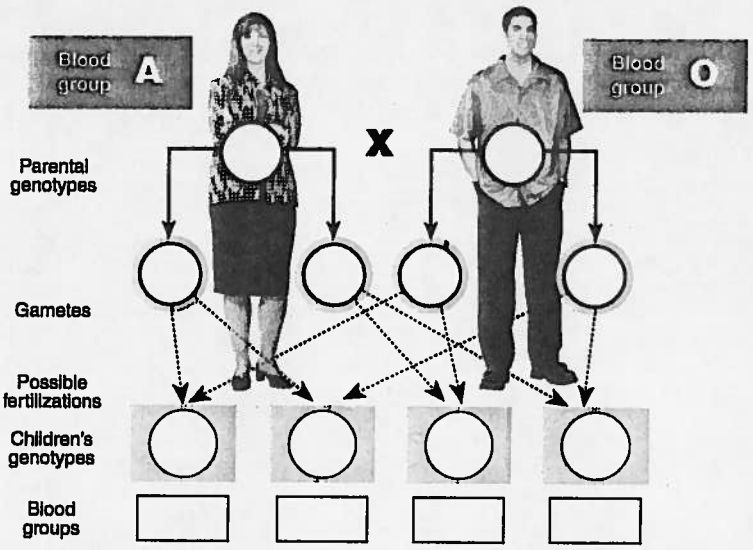








3. A wife is heterozygous for blood group **A** and the husband has blood group **O**.



(a) Give the genotypes of each parent (fill in spaces on the diagram on the right).

Determine the probability of:

(b) One child having blood group **O**:

_____

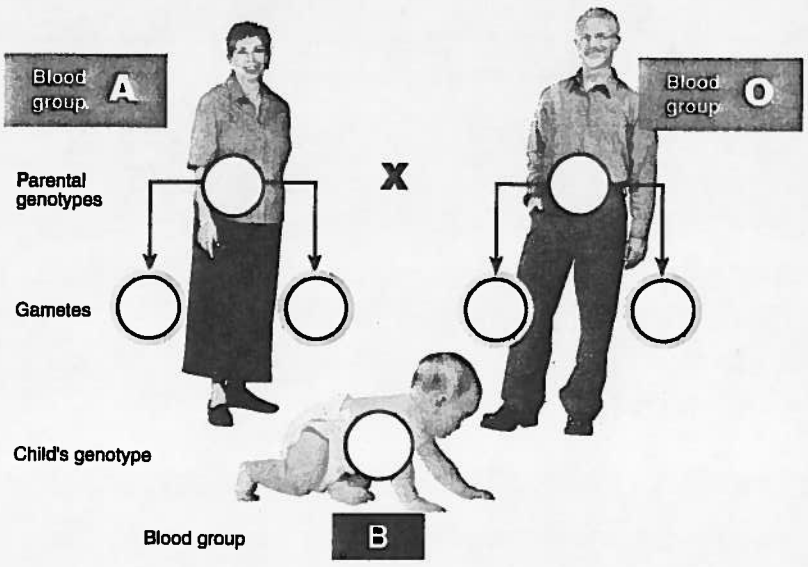
(c) One child having blood group **A**:

_____

(d) One child having blood group **AB**:

_____

4. In a court case involving a paternity dispute (i.e. who is the father of a child) a man claims that a male child (blood group **B**) born to a woman is his son and wants custody. The woman claims that he is not the father.



(a) If the man has a blood group **O** and the woman has a blood group **A**, could the child be his son? Use the diagram on the right to illustrate the genotypes of the three people involved.

(b) State with reasons whether the man can be correct in his claim:

_____

_____

_____

5. Give the blood groups which are possible for children of the following parents (remember that in some cases you don't know if the parent is homozygous or heterozygous).

(a) Mother is group **AB** and father is group **O**: _____

(b) Father is group **B** and mother is group **A**