Allele Concept: Multiple Alleles, Pseudo-allele and Lethal Allele

Multiple alleles refer to the existence of more than two forms of an allele in a species, which can give rise to a number of variations for a particular phenotype. Multiple alleles exist within a population and an individual possesses only two of its forms. Multiple alleles have been found in most populations including humans and have significant role in genetic stability of the population. Different allelic forms of a gene differ very minutely in their nucleotide sequence and thereby exhibit different levels of activity of their respective gene products. The phenotypes produced by multiple alleles may thus range from wild type (normal) to mutant. Most of the genes in populations of most organisms have multiple alleles. The 'normal' or 'wild-type' allele is thus not characterized by a single nucleotide sequence; rather it is a set of different nucleotide sequences, each of which is capable of carrying out the normal function of the gene.

A classic example of multiple alleles is coat colours in rabits (Fig. 2.4). This phenotype is determined by a gene that has four alleles denoted differently i.e. allele *C* is for wild-type i.e. full colour, c^h is for Himalayan characterized by white coat with black tips, c^{ch} is for chinchilla having mixed coat colour and white hair, and *c* stands for albino. The range of coat colours also exhibits a kind of gradation in the order of dominance of the concerned genes, as shown below-

$C > c^{ch} > c^h > c$

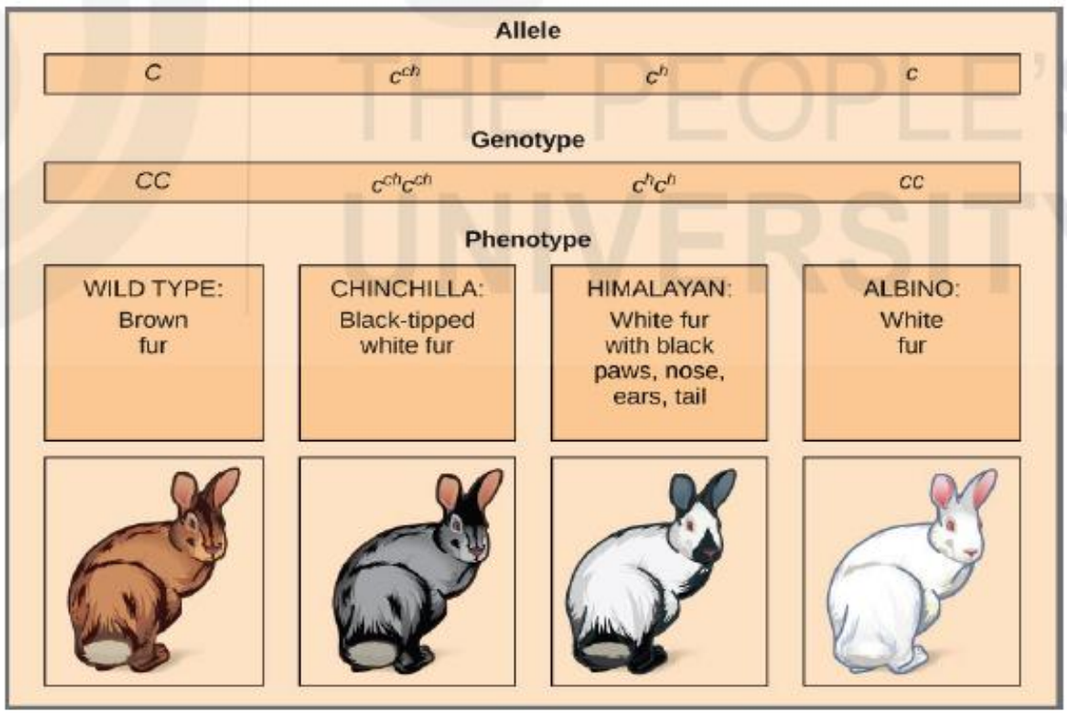


Fig. 2.4: Expression of multiple alleles in coat colour of rabbits.

According to this phenomenon, full colour C is dominant to all other coat colour alleles, chinchilla is dominant to Himalayan and albino, and Himalayan is dominant only to albino. This gradation has profound effect on the phenotypic and genotypic ratios of successive generations. The occurrence of homozygous dominant individuals (CC) is highest and this allele is called 'wild type'. Rest other alleles (*cch*, *ch* and *c)* are called mutants (Table 2.2).

Table 2.2: Different Genotypes and their respective Phenotypes for coat colour in rabbit.

Genotypes	Phenotypes
CC, Cc^{ch}, Cc^{h}, Cc	Full Colour (Wild type)
$c^{ch}c^{ch}$, $c^{ch}c^{h}$, $c^{ch}c$	Chinchilla
$c^{h}c^{h}$, $c^{h}c$	Himalayan
cc	Albino

The inheritance pattern of multiple alleles of coat colour in rabbit is explained on the basis of two crosses between individuals of different phenotypes. When wild type homozygous full colour (*CC*) rabbit is crossed with homozygous recessive albino (*cc*), the phenotype of F_1 heterozygous offspring (*Cc*) resembles dominant parent because allele C is dominant over c. The cross between two heterozygous (*Cc*) individuals yields coloured phenotype in 3:1 ratio in F_2 generation. In another cross, when Himalayan (c^hc^h) individual is crossed with albino type (*cc*), the F_1 heterozygous offspring (c^hc) show Himalayan phenotype. The cross between individuals of F_1 generation again yields 3:1 phenotypic ratio in F_2 generation (Fig. 2.5).

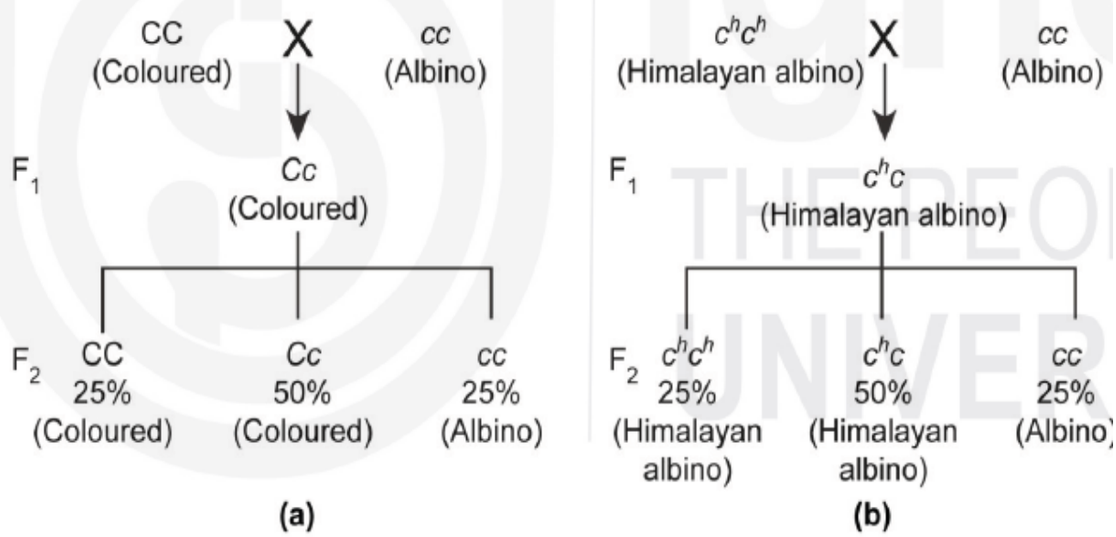


Fig. 2.5: Cross showing inheritance of coat colour phenotype in rabbits. (a) Cross between coloured and albino, (b) Cross between Himalayan and albino.

ABO Blood Type Alleles in Humans:

Another common example of multiple alleles is ABO blood types in humans (Table 2.3). The blood groups in humans are classified as A, B, O, or AB, depending upon the three types of alleles I^A, I^B, and I^O. Here, 'I' denotes an antigen 'isoagglutinogen' which is present on the surface of red blood cells. There are two types of oligosaccharides, either of which are attached to the common acceptor isoagglutinogen by the action of enzyme glycosyltransferase. This enzyme is the product of ABO gene having three alleles. Allele 'I^A' encodes for A-glycosyltransferase which converts isoagglutinogen into A antigen, and allele 'I^B' encodes for B-glycosyltransferase which converts isoagglutinogen into B antigen. Allele 'I^O'does not encode any of these enzyme, instead produces a different protein, therefore no oligosaccharide component is attached to its corresponding isoagglutinogen and it is left unaltered.

The blood group of an individual is determined by the type of allelic pair present. Both the alleles of blood types i.e. A and B, are codominant and express completely. Individuals having the genotype I^AI^A or I^AI^O have type A blood group and the ones having the genotype I^BI^B or I^BI^O have type B blood group. Heterozygous individuals I^AI^B have both A and B types of antigens therefore their blood group is designated as AB. People having homozygous allele combination I^OI^O lack either of the two antigens and their blood group is designated as O.

Table 2.3: Genotypes and blood groups arising from different allelic combinations

Genotype		Blood Type	Antigen on red blood cells	Antibodies in plasma	Can receive blood from	Can donate blood to
AO, AA	I^AI^O, I^AI^A	A	A	anti-B	O and A	A and AB
BO, BB	I^BI^O, I^BI^B	B	B	anti-A	O and B	B and AB
AB	I^AI^B	AB	A and B	neither	O, A, B, and AB	AB only
OO	I^OI^O	O	neither	anti-A and anti-B	O only	O, A, B, and AB

Pseudoalleles:

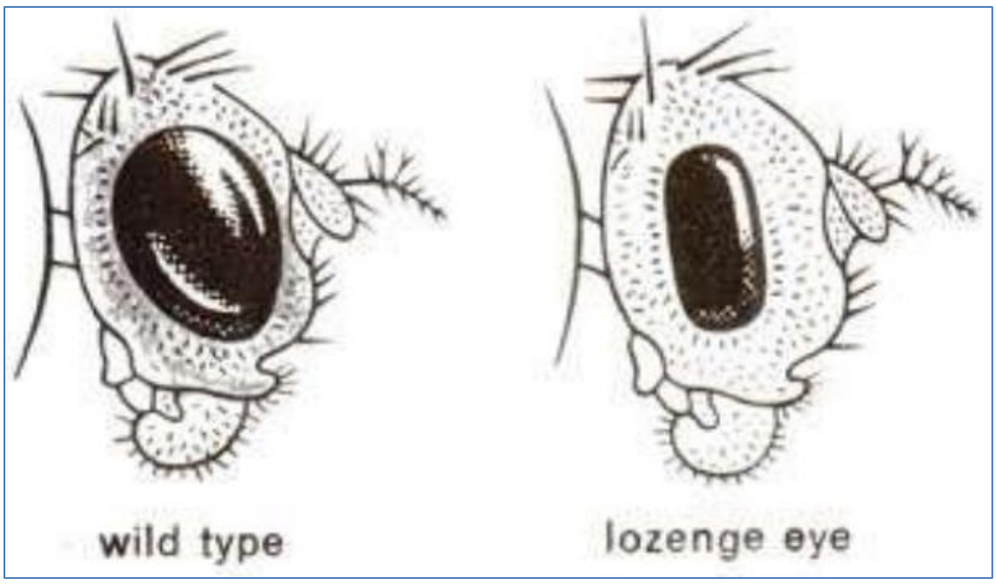
- Pseudoallelism is a state in which two genes with similar functions are located so close to one another on a chromosome that they are genetically linked.
- Term given by Morgan 1928 and Lewis 1948.
- This means that the two genes (pseudoalleles) are nearly always inherited together. Since the two genes have related functions, they may appear to act as a single gene.
- In rare cases, the two linked pseudoalleles can be separated, or recombined. One hypothesis is that pseudoalleles are formed as a result of gene duplication events, and the duplicated genes can undergo gene evolution to develop new functions.

Characteristic of pseudoalleles:

- These are closely linked allele within which crossing over occur.
- They affect the same character.

Examples:

- Red eye colour of Drosophila has different mutants like white and apricot.
- They affect pigmentation i.e., affect the same character. So, they are allelic.
- They can undergo recombination, i.e., they are non-allelic.



LETHAL ALLELES:

Genes may affect viability as well as visible traits of an organism. The living beings carrying certain genes are disadvantaged as they have impaired structural as well as, biochemical functioning. For example, *Drosophila* flies having white eyes and' vestigial wings have lower viability than their wild types. The detrimental physiological effects are apparently associated with the genes involved, that is, **w** and **vg** respectively. Some other genes have no effect on the appearance of a fly but do influence viability in some ways. Other genes have such serious effects that the organism is unable to live. These are called **lethal genes** and the alleles involved in the situation are termed as **lethal alleles.**

If the lethal effect is dominant and immediate in expression, all individuals carrying the gene will die and the gene will be lost. Some **dominant lethals,** however, have a delayed effect so that the organism lives for some time. **Recessive lethals** present in the heterozygous condition have no effect but may come to expression when mating between carriers occurs.

We shall now take up an example for discussion, that clearly illustrates the functioning of these genes. In 1904, shortly after the rediscovery of Mendel's principles, a French geneticist, Lucien Cuénot, while carrying out experimental crosses on coat colour in mice, found that a gene was not consistent with the mendelian predictions. He observed from his experiments that the yellow body colour allele (Y) was dominant and agouti allele (*y*) was recessive. The crosses between two yellow mice (see Fig. 2.13) yielded approximately a 2:1 ratio of yellow to agouti mice rather than the expected ratio of 3: 1. Further, when the yellow individuals (Yy) are crossed to the agouti (*yy*) Cuénot found that some agouti progeny are produced. He, therefore, concluded that yellow mice were heterozygous (*Yy*) and there were no yellow homozygotes (*YY*) in the progeny. Later, it was suggested that the yellow homozygotes were actually lethal, and they died while still in the uterus. It was found that approximately $\frac{1}{4}$ of the embryos from yellow by yellow crosses failed to develop. Therefore, the observed ratio of phenotypes differs from the expected ratio, as they die very young - much before reaching the reproductive age.

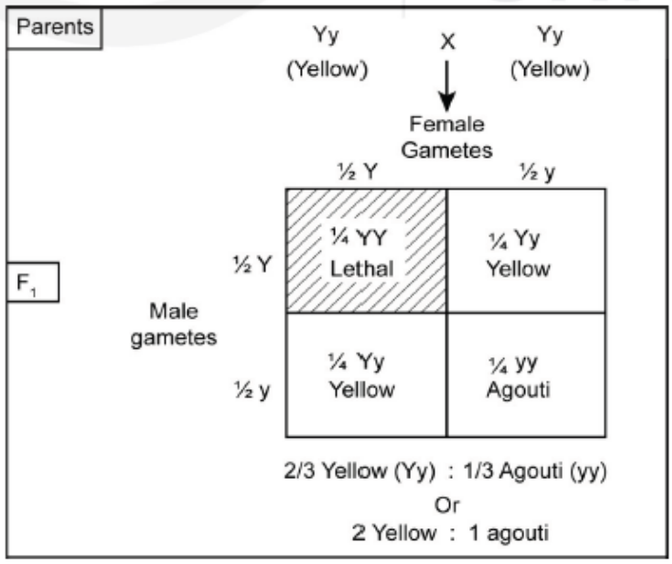


Fig. 2.13: A cross between two yellow mice, yielding a 2:1 ratio in the offspring.

Such lethals are by no means exceptional and must always be considered in populations of plants and animals. Many lethals produce no pronounced effect at all on the phenotype, but they may make their presence known by a decrease in the life span or the very elimination of the carrier. It has been estimated that each human carries, on the average, about six lethal alleles.

Different lethals eliminate individuals at different stages of the life cycle. The **complete lethal** removes the carrier before the reproductive age so that those affected have no offspring, e.g., the allele for yellow coat colour in mice; in humans the recessive factor for **Tay-Sachs disease** which kills in infancy, In humans, the dominant factor for **Huntington's disease,** a fatal, deterioration of the nervous system, does not usually express itself before the age of **30.** Such genetic determinants which can result in death but permit the carrier to live to reproductive age, are often grouped as **sublethals**. There is actually no sharp boundary during the life cycle at which lethals act.