L1 Extensions and Exceptions to Mendel's Laws

Mendel studied were not observed any exceptions because of:

1- All the traits he examined showed dominant or recessive.

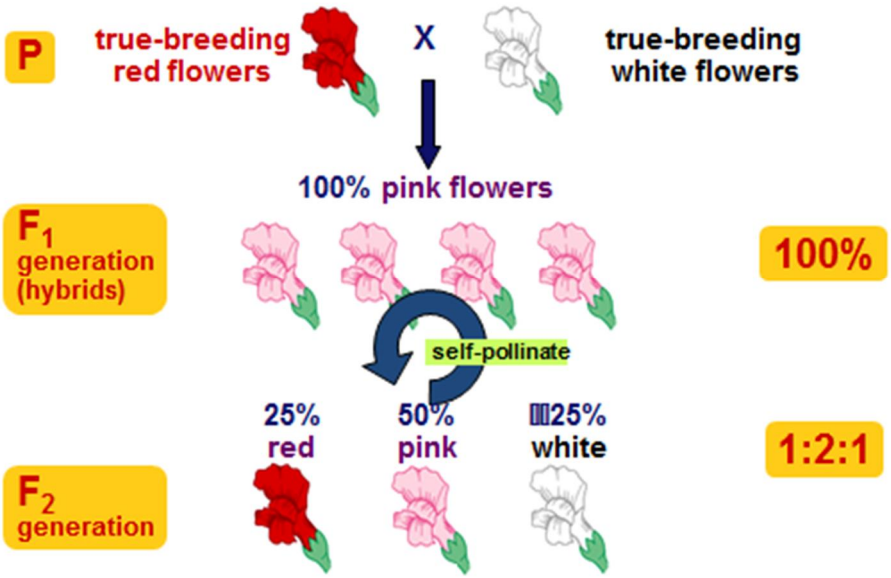
2- Each trait was determined by single gene or two alleles.

3- These alleles assorted independently.

We shall see, not all traits are controlled by single gene nor are all genes represented by two alleles. Furthermore, the presence of two different alleles in a hybrid does not always result in simple dominant; these exceptions to the patterns Mendel observed do not invalidate his laws of inheritance. These exceptions can be summarized as the following:

Incomplete dominance (Intermediate inheritance)

The dominant allele cannot completely mask expression of the other allele. So the phenotype of heterozygous is intermediate to those homozygous. A more obvious example of incomplete dominance occurs in the snapdragon plant. The crosses between red (RR) and white (rr) flower plants give pink flowers in ratio (1red: 2 pink: 1white) .

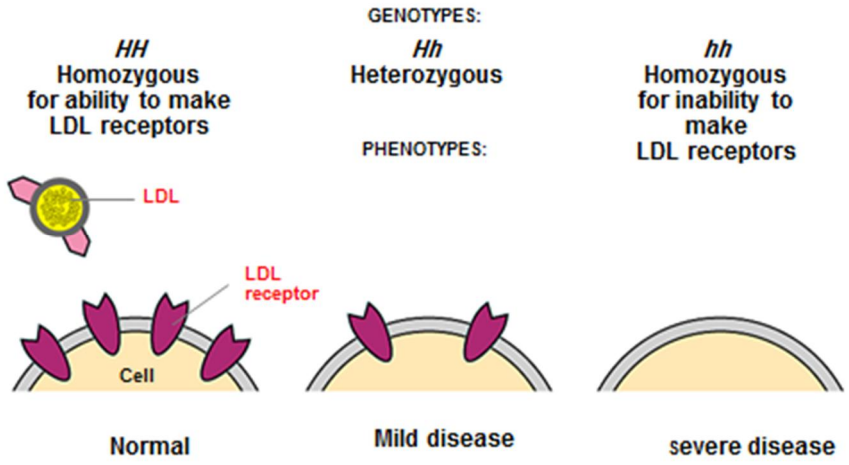


Familial hypercholesterolemia is an example of incomplete dominance in humans.

Hypercholesterolemia

Refer to dangerously high levels of cholesterol in the blood .Normal individuals are (HH). Heterozygote's (Hh) have blood cholesterol levels about twice normal, and they may have heart attacks from blocked heart arteries by their mid-thirties. Hypercholesterolemia is even more serious in homozygous individuals (hh), has about 5 times the normal amount of blood cholesterol and may have heart attacks as early as age two.

The normal individuals with dominant allele (HH) have specifies a cell surface protein called LDL receptor (low density lipoproteins).The LDL receptors pick up LDL particles from the blood and break down the cholesterol. This process helps prevent the accumulation of the cholesterol in arteries. Without the receptors, lethal levels of LDL build up in the blood. Heterozygote (Hh) have only half the normal number of LDL receptors, and homozygote(hh) have none .



Codominant

Different alleles that are both expressed in heterozygous are codominant. The ABO blood group and MN blood group are based on the expression of codominant alleles.

MN blood group:

The MN blood group in humans is under the control of a pair of co-dominant alleles, L^M and L^N. in an autosomal locus found on chromosome number 4. MN locus codes for surface glycoprotein on red blood cells; can detect

immunochemically. $L^M L^M$ gives M phenotype $L^M L^N$ gives MN phenotype ,$L^N L^N$ gives N phenotype . $L^M L^N$ X $L^M L^N$ crosses produces 1/4 $L^M L^M$, 1/2 $L^M L^N$, 1/4 $L^N L^N$

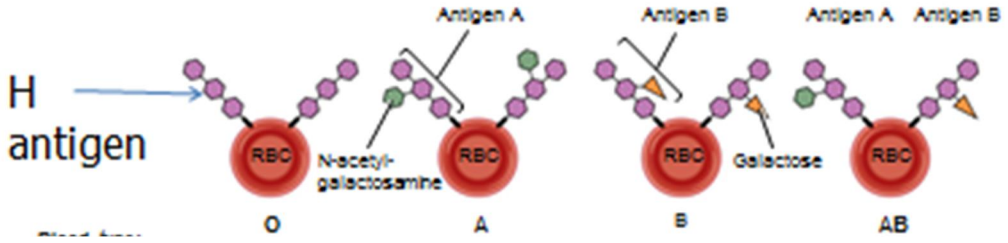
genotypes	Antigen on surface	Phenotypes
$L^M L^M$	M	M
$L^M L^N$	M and N	MN
$L^N L^N$	N	N

Multiple alleles

Many genes possess multiple alleles, several of which may be common within population. For example; ABO blood group and Rh blood group.

ABO blood group:

Three alleles, I^A,$I^B$and i for the same gene control the inheritance of ABO blood groups. The three alleles of the ABO system have six genotypic combinations contributing to four phenotypes . Each allele responsible for encoding an enzyme that adds sugar molecules to lipid on the surface of red blood cells, these sugars act as recognition markers for cells in immune system called cell surface antigen .Allele I^B adds the sugar galactose, allele I^A adds the galactosamine and O codes for protein that does not add a sugar .Allele A codominant to B allele, and both of them are dominant over O.



Rh blood group system:

Genetically, the Rh groups are complex, but can be described simply as follows: A pair of alleles D &d produced 3 genotypes DD, Dd, dd. DD and Dd are phenotypically Rh+ and dd is Rh-.

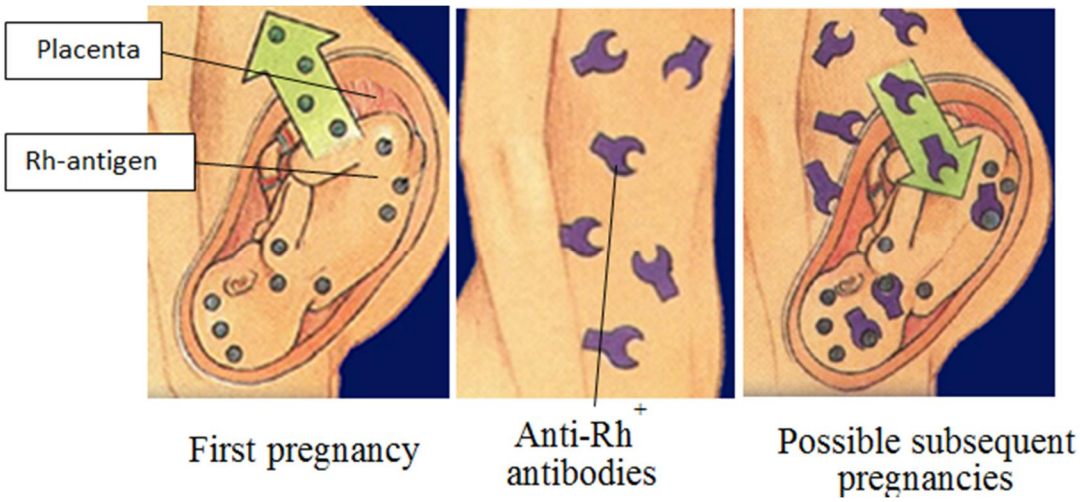
According to the Fisher-Race hypothesis, Rh blood groups are determined by a series of three linked genes C,D ,E with allelic forms c, d, e. The *D* gene is dominant to the *d* gene, but *Cc* and *Ee* are co-dominant. There are eight different combinations of these six genes.

Wiener suggest, Rh blood groups are determined by 8 genes: R^0, R^1, R^2, R^z ,r, r′, r″, r^y .

Fisher-Race	Antigens	(Weiner Gene)
Dce	D, c, e	R^0
DCe	D, C, e	R^1
DcE	D, c, E	R^2
DCE	D, C, E	R^z
dce	c,e	*r*
dCe	C,e	*r′*
dcE	c,E	*r″*
dCE	C,E	r^y

Fisher-Race and Wiener Nomenclature

***Rh incompatibilities:** caused hemolytic disease of new born (H DN) this disorder takes place in Rh- women bearing Rh+ fetus.



Gene interaction:

Pairs of alleles often interact to produce the phenotype. Sometimes a recessive pair of alleles at one locus prevents the expression of a dominant allele at another locus called **Epistasis** (covering up).For example in plants the purple of flower peas had the genotype CCPP, the genotypes Ccpp or ccPP , were white –flowers instead. The homozygous recessive (pp) prevents the expression of the dominant allele C, and the homozygous recessive (cc) prevents the expression of the dominant P. So the phenotypic ratio:

p1 *CCPP* *X* ccpp

purple plant White

G1 *CP* *cp*

F1 *CcPp*

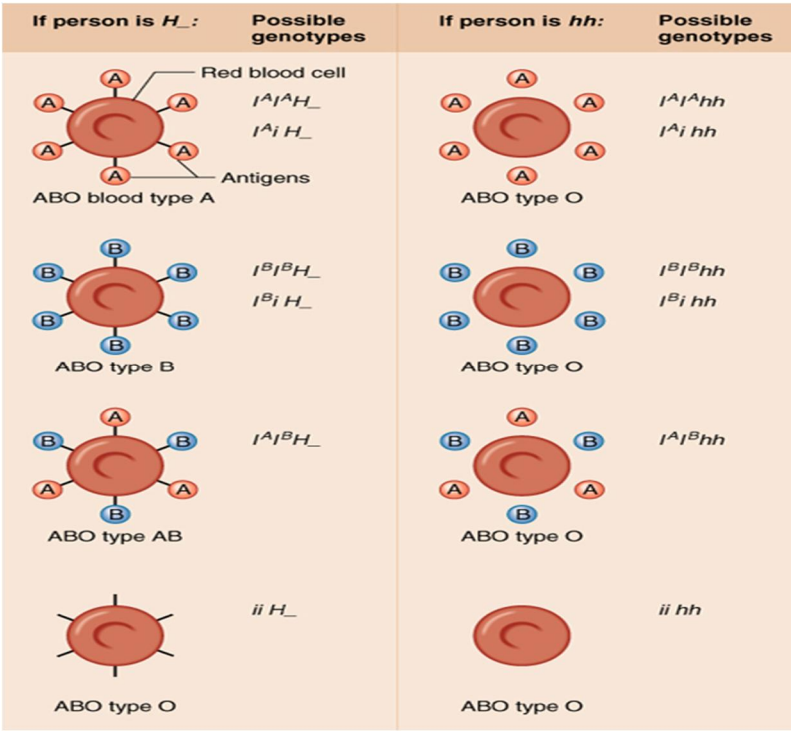
Colored flowers

		Female Gametes			
		CP	*Cp*	*cP*	*cp*
Male Gametes	*CP*	*CCPP*	*CCPp*	*CcPP*	*CcPp*
	Cp	*CCPp*	*CCpp*	*CcPp*	*Ccpp*
	cP	*CcPP*	*CcPp*	*ccPP*	*ccPp*
	cp	*CcPp*	*Ccpp*	*ccPp*	*ccpp*

Albinism and Bombay phenotype are examples of epistasis in human.

Bombay phenotype:

Is the mutant recessive allele (hh) masks phenotype of ABO. The normal H allele encodes an enzyme that inserts a sugar molecule, called antigen H protein on the surface of an immature red blood cell in which the A or B antigens are attached. The recessive h allele produces an inactive form of the enzyme that cannot insert the sugar. As long as at least one H allele is present, the ABO genotype dictates the ABO blood type (figure 3.). However, in a person with genotypes hh, no H antigen bind to the A and B antigens , and they fall away. The person has blood type O, although the ABO blood group can be anything (A, B, AB, or O).



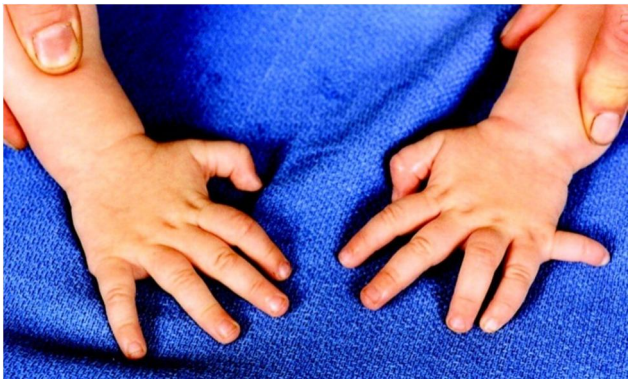
Variable expressivity & Incomplete Penetrance

Penetrance refers to the all-or-none expression of a genotype

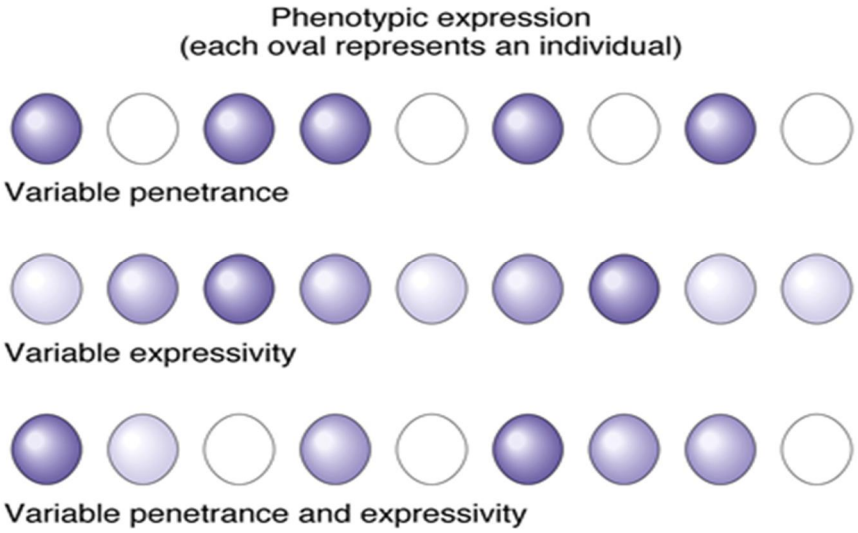
Incomplete penetrant: The phenotype is not always observed among individuals carrying the genotype .

Polydactyly: Is incompletely penetrant in which a person has more than five fingers per hand or five toes per foot. Polydactyl occurs in the womb; instead of developing only one thumb and four fingers an extra finger is added. That is caused by a mutation.

When it is inherited, it is known as an autosomal dominant gene. The disorder is located on one of the short arms of chromosome 7.Some people who inherit the dominant allele have more than five digits on a hand of foot, yet others who must have the allele have the normal number of fingers and toes.



Expressivity refers to the range of phenotypic variation that is present. In other words, for a given genotype the degree to which the phenotype is expressed. For example, one person with polydactyly might have an extra digit on both hands and a foot, but another might have just one extra fingertip. Therefore, polydactyly is both incompletely penetrant and variably expressive . Other example, Individuals with the same genotype for deafness have varying levels of symptoms FF or Ff all show mild or profound deafness.



Modifier or dominance modification

Sometimes, alleles at one locus seem to modify the expression of dominant allele at another locus, for example in human:

There are 2 alleles for eye color , B for brown eyes and b for blue eyes. The presence of modifying genes however, could explain why there are also shades of gray and green in addition to blue eyes .

Lethal gene

A mutation of a gene that produces a product that is nonfunctional. In some the homozygous dominant is lethal – it dies as an embryo so get a ratio of 2:1 instead of 1:2:1. For instance, achondroplasia, the most common form of dwarfism, with a normal length body trunk but shortened limbs determined by recessive genes, homozygosity for some such rare genes is known to be lethal and cause death during embryonic development or the first few months of life .

Huntington's disease is a fatal genetic disorder in which the nervous system gradually wastes away. People heterozygous for the dominant Huntington allele always develops the disease, but may not show any symptoms until age 40 and can thus unknowingly pass the allele on to their children.

Pleiotropy:

Refer to the multiple phenotypic effects produced by a single mutant gene or gene pair. For examples in human: sickle cell anemia, albinism and phenylketonuria (pku).

Sickle cell disease:

A disorder characterized by divers symptoms, all of these possible phenotypic effects result from the action of a single kind of allele when it is present on both homologous chromosomes. The direct effect of the sickle cell allele is to make red blood cell produce abnormal hemoglobin molecules. These molecules tend to link together and crystallize, when the O2 content of the blood is lower than usual ,the normally disk shaped red blood cells deform to a sickle shape with jagged edges,

sickled cells are destroyed rapidly by the body ,and the destruction causing anemia and general weakening of the body .Also because their angular shape, sickled cells do not flow smoothly in the blood and tend to accumulate and clog the tiny blood vessels resulting in fever, sever pain, and damage to various organs, sickle cells accumulate in the spleen, damaging .