EXTENSION OF MENDELIAN INHERITANCE: BEYOND MENDELIAN GENETICS (part 3)

II. Sex related gene: Sex-linked, sex influenced and sex limited

Many organisms have homologous pairs of all chromosomes except for those that determine sex. The chromosomes that occur as homologous pairs in all organisms of a species are called **autosomes**. Chromosome pairings that can vary depending on the sex of an organism are called **sex chromosomes**. In most vertebrates, including humans, females with XX have two copies for X-linked genes; On the other hand, XY males are one copy (hemizygous) with respect to the genes present on the different X and Y chromosome. In humans, there are hundreds of genes located on the X chromosome that have no counterpart on the Y chromosome. X-linked inheritance diseases are single gene disorders that reflect the presence of defective genes on the X chromosome.

There are three categories of genes that may have different effects depending on an individual's gender. These are referred to as:

1.sex-linked genes 2. sex-limited genes 3. Sex-influenced

I. Sex-linked inheritance:

Gene located on the sex chromosomes are said to be sex-linked and have different patterns of inheritance.

a) The eye color in *Drosophila* is X-linked with the gene for wild red-eyes (w+) being dominant over the white-eyed gene (w).

By crossing white-eyed females and red-wild eyed males (genotypes X^{w} X^{w} and $X^{w+}Y$). Since the wild red-eye gene is dominant, the result of this cross was all wild eyed are females and white eyed are males (F_1).

F1 Cross: $X^{w}X^{w} \times X^{w+}Y$

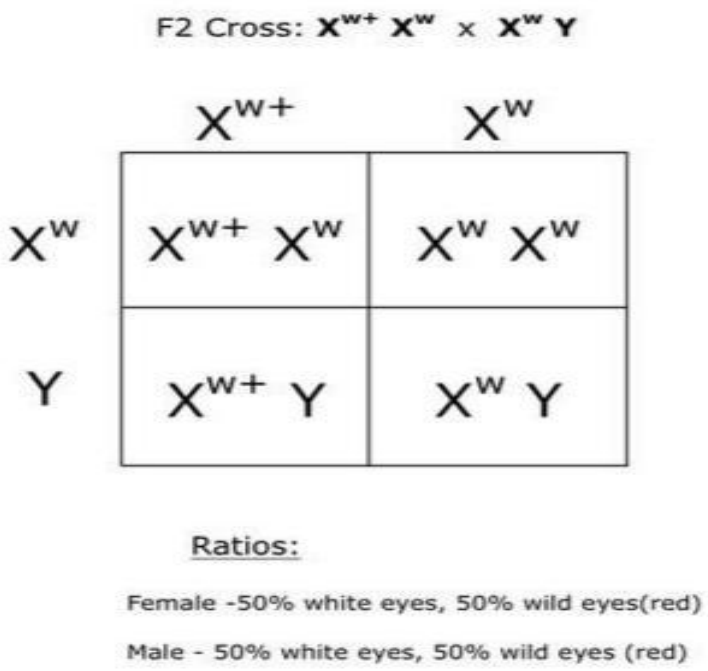
	X^{w}	X^{w}
X^{w+}	X^{w+} X^{w}	X^{w+} X^{w}
Y	X^{w} Y	X^{w} Y

Ratios:

Female -100% wild eyes (red)

Male - 100% white eyes

By crossing, the wild-red eyed females and white-eyed males from the F_1 generation. The expected result would be a 1:1 ratio of wild red-eyes to white eyes for both male and female flies.



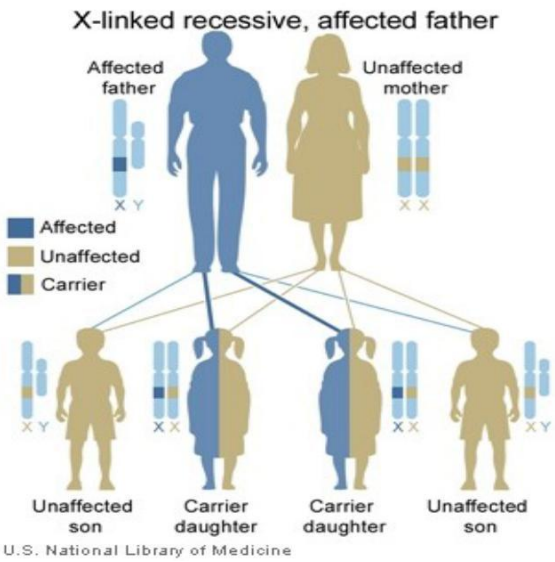
The inheritance patterns of X-linked diseases in family pedigrees (cross) are complicated and can be either recessive or dominant. The X-linked dominant diseases are very uncommon, but X-linked recessive diseases are much more frequent and include Duchenne and Becker forms of muscular dystrophy and hemophilia, as well as red-green color blindness.

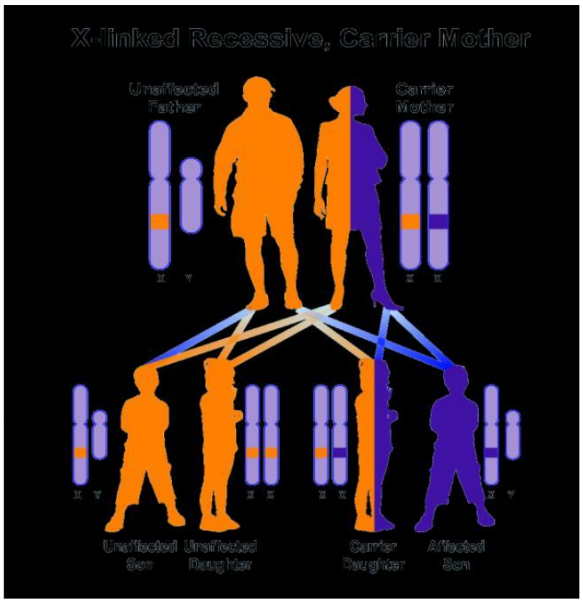
These diseases are much more common in males than females because two copies of the mutant allele are required for the disease to occur in females, while only one copy is required in males so, they express the genes it contains whether they are dominant or recessive.

The inheritance pattern of an X-linked recessive disease has the following unique characteristics:

1. Males always pass their X chromosome to their daughters but never to their sons (no father-to-son transmission) since sons will inherit the Y rather than the X chromosome. Affected males pass the defective X chromosome to all of their daughters, who are described as obligate carriers. This means they carry the disease-causing allele but generally show no disease symptoms since a functional copy of the gene is present on the other chromosome.

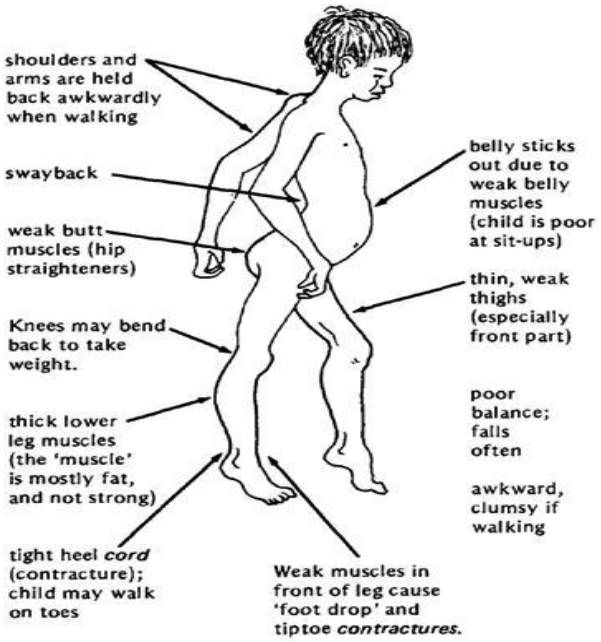
2. The carrier females (heterozygote) have a 50 percent chance of passing the mutant gene to each of her children (daughters and sons). Female carriers pass the defective X chromosome (mutant X gene) to half their sons (who are affected by the disease, known as **hemizygotes**) which express the trait and half their daughters (who are therefore also carriers). The other children inherit the normal copy of the chromosome.





Eg (1): Duchenne and Becker forms of muscular dystrophy

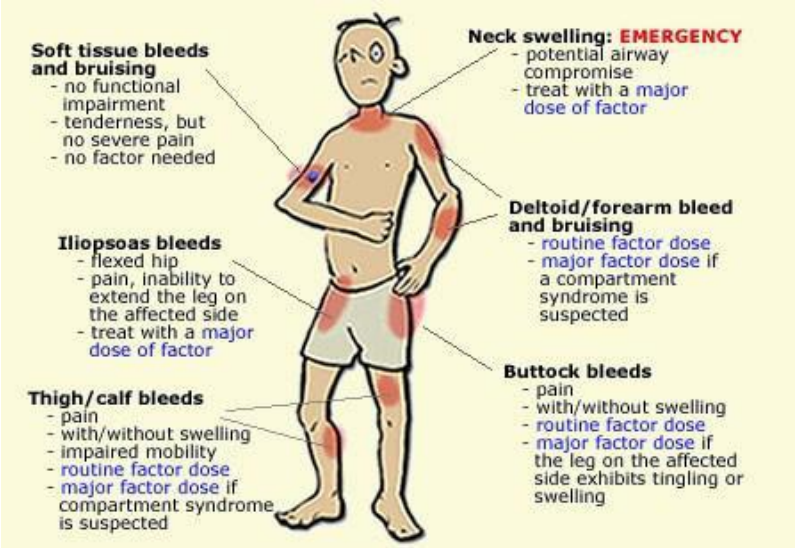
It is a type of dystrophinopathy, which includes a spectrum of muscle diseases in which there is insufficient dystrophin produced in the muscle cells, resulting in instability in the structure of muscle cell membrane. This is caused by mutations in the dystrophin gene, which encodes the protein dystrophin. Becker muscular dystrophy (BMD) is related to Duchenne muscular dystrophy (DMD) in that both result from a mutation in the *dystrophin* gene, but in Duchenne muscular dystrophy no functional dystrophin is produced making DMD much more severe than BMD.



Muscular dystrophy

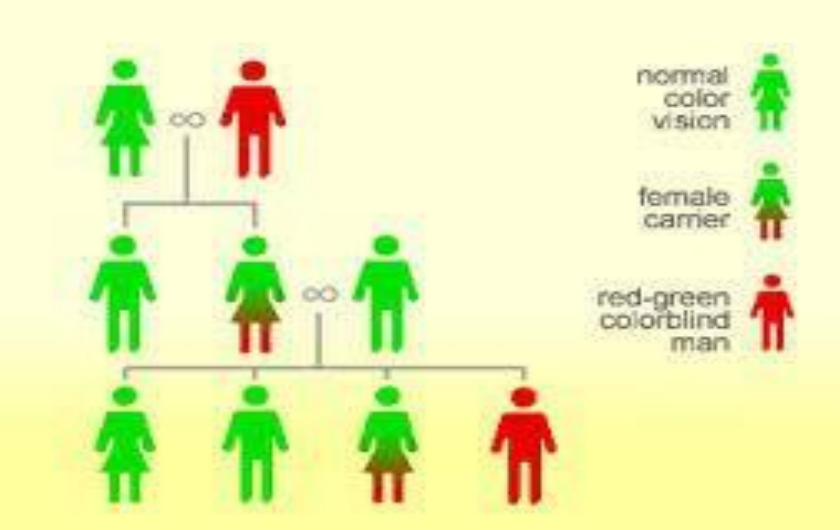
Eg (2): Hemophilia

It is a group of hereditary genetic disorders that impair the body's ability to control blood clotting or coagulation, which is used to stop bleeding when a blood vessel is broken. Haemophilia A (clotting factor VIII deficiency) is the most common form of the disorder, present in about 1 every 5,000–10,000 male births. Haemophilia B (factor IX deficiency) occurs in around 1 every 20,000–34,000 male births.

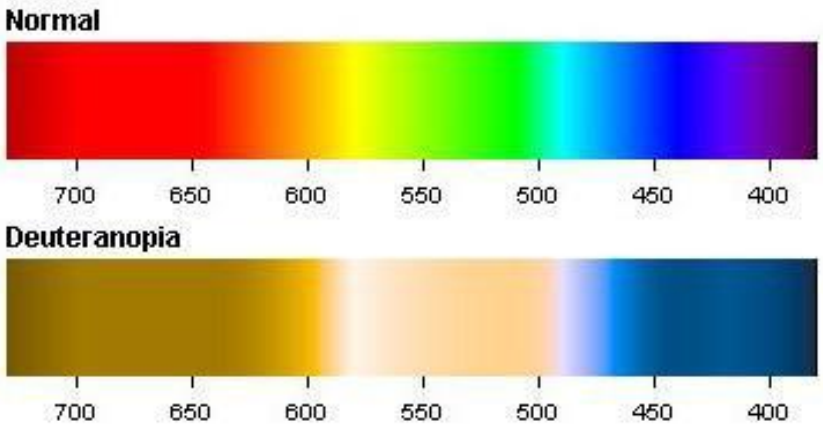


Eg (3): Red-green color blindness:

Color blindness, or **color vision deficiency (**deuteranopia) is the inability or decreased ability to see color, or perceive color differences, under normal lighting conditions as red and green are the main *problem* colors. Color blindness affects a significant percentage of the population. There is no actual blindness but there is a deficiency of color vision. The most usual cause is a fault in the development of one or more sets of retinal cones that perceive color in light and transmit that information to the optic nerve. The genes that produce photopigments are carried on the X chromosome; if some of these genes are missing or damaged, color blindness will be expressed in males with a higher probability than in females because males only have one X chromosome (in females, a functional gene on only one of the two X chromosomes is sufficient to yield the needed photopigments).



The English chemist John Dalton published the first scientific paper on this subject in 1798, "Extraordinary facts relating to the vision of colours", after the realization of his own color blindness.



Normal and color blindness Spectrum

Pedigree (cross) for all X-linked recessive disease:

P XX X^cY

Normal **Diseased**

↓

F1 XX^c XY

50% ♀ carrier : 50% ♂normal

P XX^c XY
Carrier **Normal**
↓
F1 XX XX^c XY X^cY
25% ♀ normal : 25% ♀carrier : 25% ♂ normal : 25% ♂ diseased

P XX^c X^cY
Carrier **Diseased**
↓
F1 XX^c X^cX^c XY X^cY
25% ♀ carrier : 25% ♀ Diseased : 25% ♂ normal : 25% ♂ Diseased

P X^cX^c X^cY
Diseased **Diseased**
↓
F1 X^cX^c X^cY
50% ♀ Diseased : 50% ♂ Diseased
(so, 100% diseased)

The difference between the 3 diseases will be the superscript sign: **d** for Duchenne and Becker forms of muscular dystrophy, **h** for Hemophilia and **c** for color blindness.

II. Sex-limited inheritance: They are autosomal genes (genes located on autosome chromosomes, i.e. not located on the sex chromosomes) that are expressed only in males or females, but not both (i.e. expressed in only one sex and 'turned off' in the other).

1. Sex organs production **in Human**: Sperm in testes for males (♂) and egg in ovary for females (♀).

2. **In Chicken**, the production of egg is performed by Hen not by Rooster. Feathering way of Rooster differs from Hen (Males of most chicken breeds distinguish from their females in having longer, sharp and more scalloped feathers in neck, hackle, saddle and wing bows).

3. The genes that control milk yield and quality **in mammalians**; for example it is present in both bulls (♂) and cows (♀), but their effects are expressed only in the female cattle.

III. Sex-influenced inheritance: Traits are autosomal, meaning that their genes are not carried on the sex chromosomes but are inherited by males and females and appear in both, but normally differ in how the phenotypes are expressed as the trait is dominant in men while at the same time it is recessive in women.

Eg **Patterned baldness** is controlled by the same allele pair in both sexes, but the allele is dominant in males and recessive in females. Obviously other factors (genes) are involved in the expression of this trait.

Pedegree (cross):

P XX X^RY
Normal **Baldness**
↓
F1 X^RX XY
50% ♀ carrier : 50% ♂normal

P XX^R XY

Carrier **Normal**

↓

XX XX^R XY X^RY

25% ♀ normal : 25% ♀ carrier : 25% ♂ normal : 25% ♂ Baldness

P XX^R X^RY

Carrier **Baldness**

↓

F1 XX^R X^RX^R XY X^RY

25% ♀ carrier : 25% ♀ Baldness : 25% ♂ normal : 25% ♂ Baldness

P X^RX^R X^RY

Baldness **Baldness**

↓

F1 X^RX^R X^RY

50% ♀ Baldness : 50% ♂ Baldness

(so, 100% Balness)

P X^RX^R XY

Baldness **Normal**

↓

F1 X^RX X^RY

50% ♀ Carrier : 50% ♂ Baldness

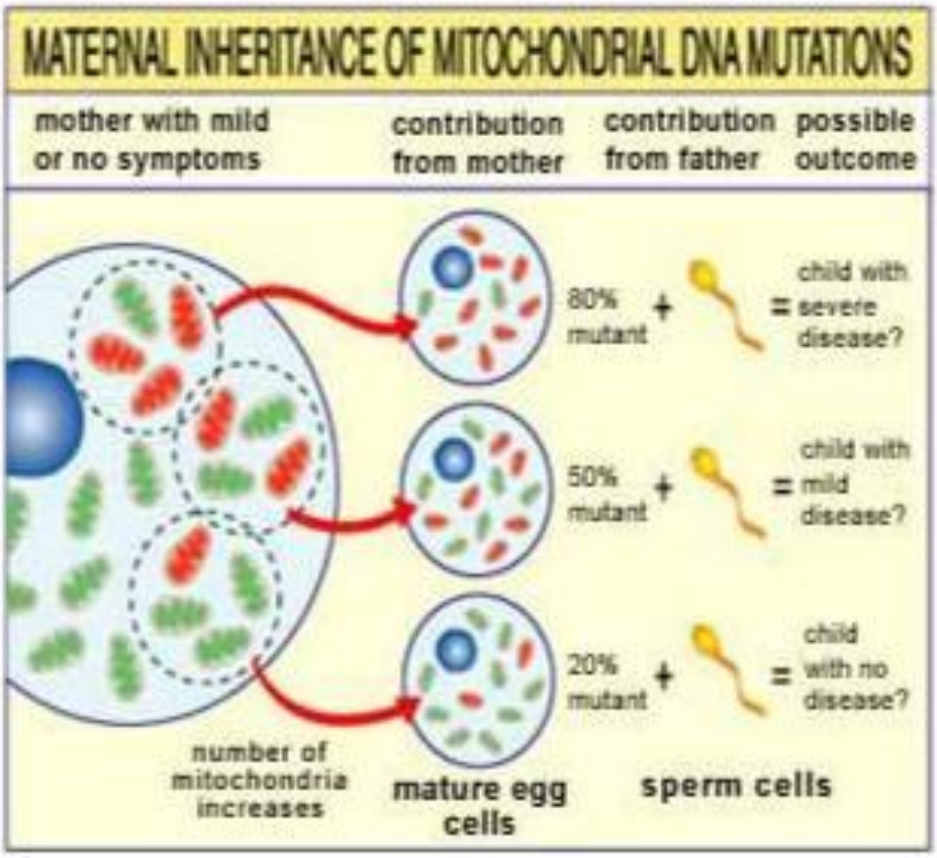
V. Cytoplasmic inheritance

Extranuclear inheritance or **cytoplasmic inheritance** is the transmission of genes that occur outside the nuclear chromosomes i.e. from mitochondrial DNA or chloroplast DNA. It is found in most eukaryotes and is commonly known to occur in cytoplasmic organelles such as mitochondria and chloroplasts.

Extranuclear Inheritance of Organelles

Mitochondria are organelles which function to produce energy as a result of cellular respiration of human, plants, …. Chloroplasts are organelles which function to produce sugars via photosynthesis in plants and algae. The genes located in mitochondria and chloroplasts are very important for proper cellular function. The extranuclear genomes of mitochondria (mt DNA) and chloroplasts (ct DNA or cp DNA) however replicate independently of cell division. They replicate in response to a cells increasing energy needs which adjust during that cells lifespan.

Both chloroplasts and mitochondria are present in the cytoplasm of maternal gametes only (egg). Paternal gametes (sperm) do not have cytoplasmic mitochondria and plastids. This **inheritance** is known as **uniparental** when extranuclear genes from only one parent contribute organellar DNA to the offspring. Thus, the phenotype of traits linked to genes found in either chloroplasts or mitochondria are determined exclusively by the maternal parent, so their diseases are received from the mother to their offspring during sexual reproduction. Progeny of an affected female will all show the disease, but if an affected male is crossed to a normal female, all the progeny will be normal.



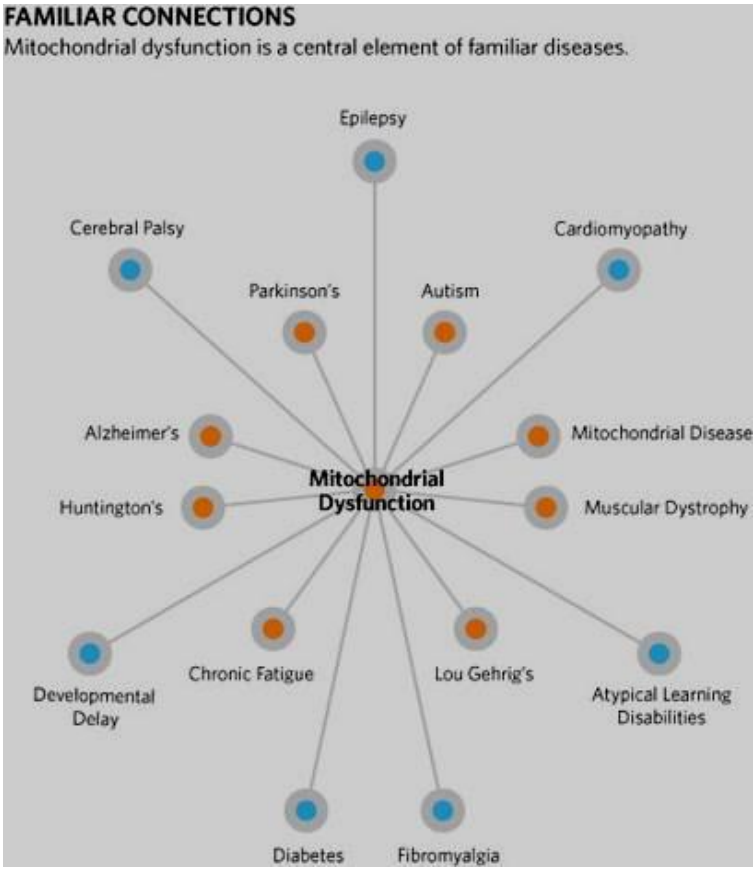
Cytoplasmic inheritance plays a role in several disease processes:

1. Mitochondrial Diseases

One cell contains numerous mitochondria, and each mitochondrion contains dozens of copies of the mitochondrial genome. Moreover, the mitochondrial genome has a higher mutation rate (about 100-fold higher) than the nuclear genome. This leads to a heterogeneous population of mitochondrial DNA within the same cell, and even within the same mitochondrion; as a result, mitochondria are considered heteroplasmic. When a cell divides, its mitochondria are partitioned between the two daughter cells. However, the process of mitochondrial segregation occurs in a random manner and is much less organized than the highly accurate process of nuclear chromosome segregation during mitosis. As a result, daughter cells receive similar, but not

identical, copies of their mitochondrial DNA. So, we can say that mitochondrial disease refers to any illness resulting from mutation of any genes on mt DNA, which is involved in energy metabolism.

In humans, mutations in mtDNA causes malfunctions in mitochondria lead to multi-systemic defects in the brain, heart, muscles, kidney and endocrine and respiratory systems. The many possible clinical symptoms and diseases include loss of motor control, muscle weakness, heart disease and strock, diabetes (type 2), respiratory problems, Alzheimer's and Parkinson's disease, vision and hearing problems, different types of cancers and developmental delays.



In plants, cytoplasmic male sterility (CMS) in maize (in Texas USA, 1970) arises spontaneously via mutations in nuclear and/or mt genes causing the failure of plants to produce functional anthers, pollen, or male gametes (i.e fertility loss of flowers).

2. Plastids Diseases

The **plastid** is a major organelle found in the cells of plants and algae. Plastids often contain pigments used in photosynthesis. They are the site of manufacture and storage of important chemical compounds (as sugar and starch) used by the cell for producing energy and as raw material for the synthesis of other molecules (amino acids, fatty acids, and diverse isoprenoids).

In plant, Mutant genes that disrupt aspects of chloroplast function can result in abnormal growth, male sterility of flowers, and abnormal photosynthesis. **Examples:**

b) Reduced rates of chlorophyll synthesis cause the **chlorophyll loss in leaves and the delay of fruit ripening** (eg strawberry, tomato,..).

b) Variegation (patched) in *Mirabilis jalapa*

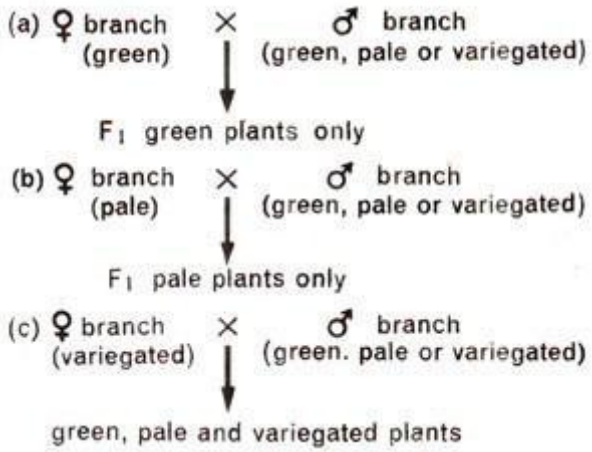
It is believed that variation in color of leaves, branches or whole plants (*Mirabilis* and maize) is due to two kinds of plastids (normal and mutant albino). Three kinds of branches according to occurrence of plastids may be found: (i) completely green, (ii) completely pale green or (iii) variegated (as patches). In such cases, phenotype of offspring will depend upon phenotype of branch on which flowers are pollinated i.e. depend on the plastids of the egg.

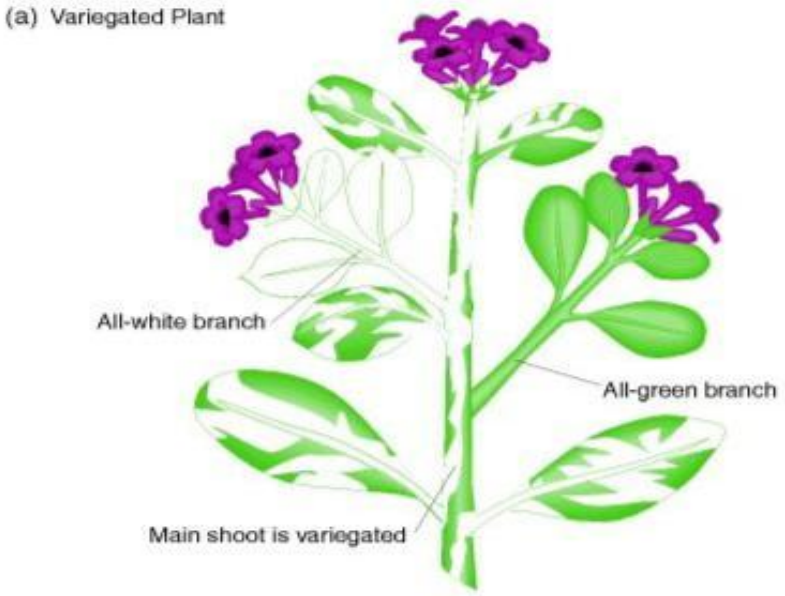
These two types of plastids will faithfully multiply due to cell division, but may not equally distribute themselves to daughter cells. An egg having both kinds of plastids may give rise to three types of offspring namely

(i) those with mainly normal green plastids;

(ii) those with mainly mutant albino plastids and

(iii) those with both kinds of plastids.





(b) Results of crosses between branches

Egg cell of female *(n)*	Pollen cell of male *(n)*	Zygote constitution *(2n)*
White ♀	Any ♂	White
Green ♀	Any ♂	Green
Variegated ♀	Any ♂	
Egg type 1		White
Egg type 2		Green
Egg type 3		Cell division → Variegated

VI. Environmental influenceson gene expression

(Gene expression–environment interaction or G×E)

The phenotype of an individual is not only the result of inheriting a particular set of parental genes but from the interactions between genes and the environment.

Phenotype = Genotype + Environment

The phenotypes differ in their degree of dependence on environment:

IV. Some may **never** be affected

V. Others may be **completely** affected

VI. Most of them are **temporary** affected (influenced)

Some environment factors (external and internal) that may **affect** the gene expression (phenotypic appearance):

VII. By inducing a phenotype that matches a phenotype of known genotype in the organism **(Phenocopies).**

Eg (1): The Vanessa (butterfly) genus of butterflies have spectrum of phenotypic plasticity to appear similar to the genetical one as they can change the phenotype of their wing color patterns based on the local temperature. A long-term low-temperature treatment or heat-shock treatment produced various modification types, characterized by the expanded or reduced black spots on the proximal forewing, the reduced white band on the dorsal forewing, and unique hindwing patterns.

Eg (2): In Himalayan rabbits. When raised in moderate temperatures, Himalayan rabbits are white in colour with black tail, nose, and ears, making them phenotypically distinguishable from genetically Black rabbits. However, when raised in cold temperatures, Himalayan rabbits show black colouration of their coats, resembling the genetically black rabbits. Hence this Himalayan rabbit is a phenocopy of the genetically black rabbit.

II. By inducing a different phenotype that doesn't match the original phenotype of known genotype in the organism.

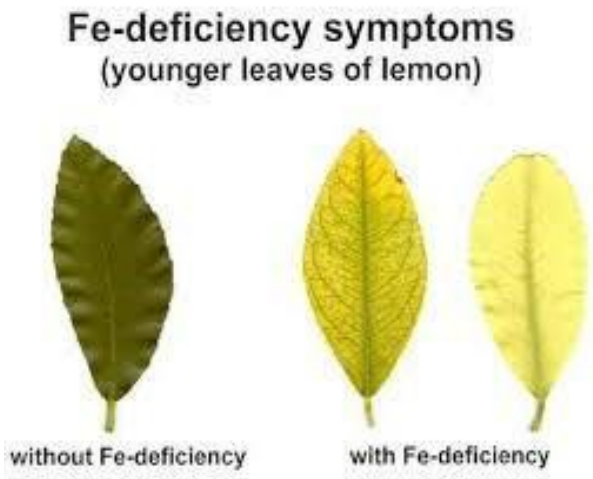
1. Light/Dark

Eg: Albinism in seedlings and plants growing in dark. Plants are green

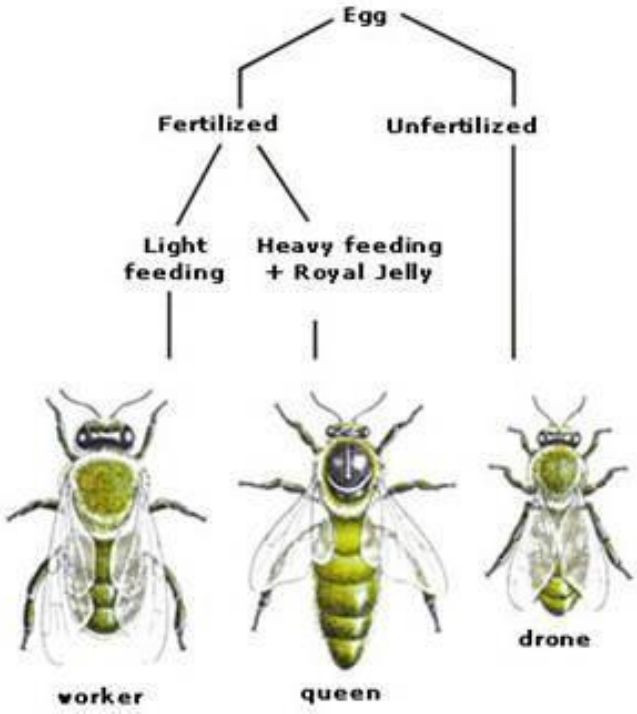
because they contain chloroplasts with chlorophyll that absorbs blue and red light and reflects light in the green wavelength; that is why it looks green. Therefore, absence of light affects the concentration of chlorophyll in the leaf, in turn, affect gene expression of the color of that leaf.

2. Nutrition

Eg (1): Chlorosis (yellow color) in plants grown in iron lacking soil (Fe-deficiency). Iron Fe is most important for the respiration and photosynthesis processes. Iron is also implied in many enzymatic systems like chlorophyll synthesis. So, its deficiency causes chlorotic yellow of blade but the veins remaining green. At severe deficiency, the leaves may become very pale yellow, and the veins become chlorotic, too.



Eg (2): Quality and quantity of food where determine whether the diploid larvae (fertilized) of **honey bees** may be a female worker or a fertile queen.



3. Temperature

Eg (1): In the **Chinese primrose**, the color of the flowers varies from white, at a temperature of 30°C or over and to pink, at 10-20°C.

Eg(2): The white borderon the wings of mourning **cloak butterflies** that develop in summer, at high temperatures, is sharply delineated; when members of the same species develop in spring, at low temperatures, the outline of the border is diffuse.

Eg (3): After mating at sea, adult female **sea turtles** return to land to nest at night. After the hole is dug, the female then starts filling the nest around 50 to 200 eggs, depending on the species. After laying, she re-fills the nest with sand, then returns to the ocean, leaving the eggs untended. The hatchling's gender depends on the sand temperature: higher temperatures (30°C) results in more female hatchlings, but lower temperature (10-20°C) results male hatchlings.

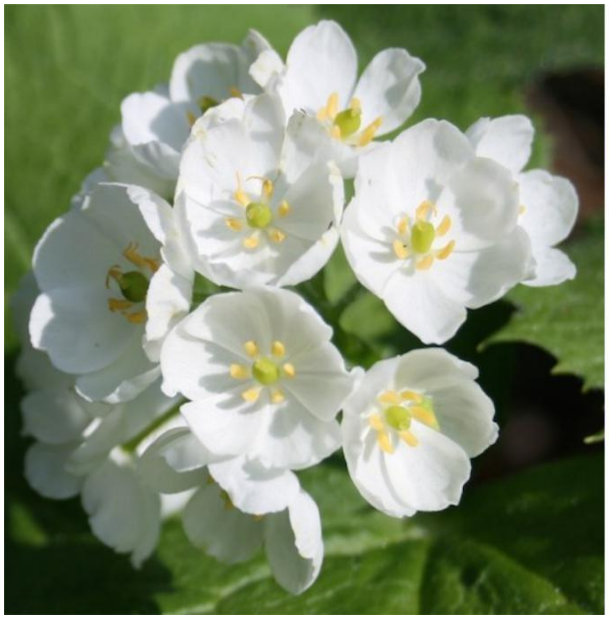
4. Humidity (or Rain)

The body color of ***Drosophila*** is mainly either black or white, but in humid conditions, the body became striped.

Eg Skeleton flower

The *Diphylleia grayi* is a beautiful white flower that turns transparent upon contact with water. When it rains, the clusters of lovely blooms magically transform into glistening, crystal-like blossoms. Because of this amazing phenomenon, the *Diphylleia grayi* is commonly known as the 'skeleton flower'.

The plant generally grows on moist, wooded mountainsides in the colder regions of Japan and China. It is recognizable by its large, umbrella-shaped leaves that are topped with small clusters of pearly white flowers. While the plant is perennial, and can grow up to a height of 0.4 meters, the flowers bloom from mid-spring to early-summer in shady conditions. As the petals of these flowers are soaked in water, they slowly begin to lose their white pigmentation, turning completely transparent over time. When dry, they return to their original white version.




Another skeleton flower is that of a White Lady (*Thunbergia fragrans*) grow in windward moderately wet coastal areas in Hawaii.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