

أساسيات علم الوراثة



PRINCIPLES OF GENETICS (3303-205)

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Definition and Subdivisions of Genetics

Adenine (A): A nitrogenous base, one member of the *base pair* A- T (*adenine-thymine*).

Alleles: Alternative forms of a genetic *locus*; a single allele for each locus is inherited separately from each parent (e.g., at a locus for eye color the allele might result in blue or brown eyes).

Amino acid: Any of a class of 20 molecules that are combined to form *proteins* in living things. The sequence of amino acids in a protein and hence protein function are determined by the *genetic code*.

Autosome: A *chromosome* not involved in sex determination. The *diploid* human *genome* consists of 46 chromosomes, 22 pairs of autosomes, and 1 pair of *sex chromosomes* (the X and Y chromosomes).

Back Cross: A cross between a Hybrid breed and an original breed.

Base pair (bp): Two nitrogenous bases (*adenine* and *thymine* or *guanine* and *cytosine*) held together by weak bonds. Two strands of DNA are held together in the shape of a double helix by the bonds between base pairs.

Base sequence: The order of *nucleotide* bases in a DNA molecule.

Centromere: A specialized *chromosome* region to which spindle fibers attach during cell division.

Chromosomes: The self-replicating genetic structures of cells containing the cellular DNA that bears in its *nucleotide* sequence the linear array of *genes*. In *prokaryotes*, chromosomal DNA is circular, and the entire genome is carried on one chromosome. *Eukaryotic* genomes consist of a number of chromosomes whose DNA is associated with different kinds of *proteins*.

Cloning: The process of asexually producing a group of cells (clones), all genetically identical, from a single ancestor.

Crossing over: The breaking during *meiosis* of one maternal and one paternal *chromosome*, the exchange of corresponding sections of DNA, and the rejoining of the chromosomes. This process can result in an exchange of alleles between chromosomes. Compare *recombination*.

Cytosine (C): A *nitrogenous base*, one member of the *base pair* G- C (*guanine* and *cytosine*).

Diploid: A full set of genetic material, consisting of paired *chromosomes* one chromosome from each parental set. Most animal cells except the *gametes* have a diploid set of chromosomes. The diploid human *genome* has 46 chromosomes. Compare *haploid*.

DNA (deoxyribonucleic acid): The molecule that encodes genetic information. DNA is a double-stranded molecule held together by weak bonds between *base pairs* of *nucleotides*. The four nucleotides in DNA contain the bases: *adenine* (A), *guanine* (G), *cytosine* (C), and *thymine* (T). In nature, *base pairs* form only between A and T and between G and C; thus the *base sequence* of each single strand can be deduced from that of its partner.

DNA replication: The use of existing DNA as a template for the synthesis of new DNA strands. In humans replication occurs in the cell *nucleus*.

DNA sequence: The relative order of *base pairs*, whether in a fragment of DNA, a *gene*, a *chromosome*, or an entire *genome*. See *base sequence analysis*.

Dominant: A gene which is always expressed when present.

Double helix: The shape that two linear strands of DNA assume when bonded together.

F1 (Cross) Hybrids: A cross between two pure bred lines producing offspring with desirable characteristics and hybrid vigour

Gamete: Mature male or female reproductive cell (sperm or ovum) with a *haploid* set of chromosomes (23 for humans).

Gene: The fundamental physical and functional unit of heredity. A *gene* is an ordered sequence of *nucleotides* located in a particular position on a particular *chromosome* that encodes a specific functional product (i.e., a *protein* or *RNA molecule*). See *gene expression*.

Genetics: The study of the patterns of inheritance of specific traits.

Genetic Modification: The altering of the genetic make-up of an organism to produce esirale traits

Genome: All the genetic material in the *chromosomes* of a particular organism; its size is generally given as its total number of *base pairs*.

Genome projects: Research and technology development efforts aimed at *mapping* and *sequencing* some or all of the *genome* of human beings and other organisms.

Genotype: The actual genes present for a characteristic (compare phenotype)

Guanine (G): A nitrogenous base, one member of the *base pair* G- C (guanine and *cytosine*).

Haploid: A single set of *chromosomes* (half the full set of genetic material), present in the egg and sperm cells of animals and in the egg and pollen cells of plants. Human beings have 23 chromosomes in their reproductive cells. Compare *diploid*.

Heterozygous: When the genes for a particular gene are different.

Homozygous: When the genes for a particular trait are the same

Homologous chromosomes: A pair of *chromosomes* containing the same linear *gene* sequences, each derived from one parent.

Human gene therapy: Insertion of normal DNA directly into cells to correct a genetic defect.

Interphase: The period in the cell cycle when DNA is replicated in the nucleus; followed by *mitosis*.

Incomplete Dominance: Occurs when neither allele is dominant over the other and the resultant phenotype is a mix of the two gene traits.

Linkage: The proximity of two or more *genes* on a *chromosome*; the closer together the markers are, the lower the probability that they will be separated during DNA repair or replication processes (binary fission in *prokaryotes*, *mitosis* or *meiosis* in *eukaryotes*), and hence the greater the probability that they will be inherited together.

Locus (pl. loci): The position on a *chromosome* of a *gene* or other chromosome *marker*; also, the DNA at that position. The use of *locus* is sometimes restricted to mean regions of DNA that are *expressed*. See *gene expression*.

Meiosis: The process of two consecutive cell divisions in the *diploid* progenitors of sex cells. Meiosis results in four rather than two daughter cells, each with a *haploid* set of *chromosomes*.

Messenger RNA (mRNA): RNA that serves as a template for protein synthesis.

Metaphase: A stage in *mitosis* or *meiosis* during which the *chromosomes* are aligned along the equatorial plane of the cell.

Mitosis: The process of nuclear division in cells that produces daughter cells that are genetically identical to each other and to the parent cell.

Mutation: Any heritable change in DNA *sequence*.

Multiple Alleles: Many different forms of the same gene e.g. Eye colour

Nucleic acid: A large molecule composed of *nucleotide* subunits.

Nucleotide: A subunit of DNA or RNA consisting of a nitrogenous base (*adenine*, *guanine*, *thymine*, or *cytosine* in DNA; adenine, guanine, *uracil*, or cytosine in RNA), a phosphate molecule, and a sugar molecule (deoxyribose in DNA and ribose in RNA). Thousands of *nucleotides* are linked to form a DNA or RNA molecule. See *DNA*, *base pair*, *RNA*.

Nucleus: The cellular organelle in *eukaryotes* that contains the genetic material.

Performance testing: A comparison of growth rates of animals under similar conditions

Phenotype: The physical expression of the genotype (i.e. Bb gives brown)

Polypliody: Having three or more sets of chromosomes which generally leads to infertility

Progeny Testing: Testing of the performance of offspring relative to their parents

Prokaryote: Cell or organism lacking a membrane-bound, structurally discrete *nucleus*. Bacteria are prokaryotes. Compare *eukaryote*. See *chromosomes*.

Recessive: A gene that is not expressed in the presence of a dominant gene

Ribosomes: Small cellular components composed of specialized ribosomal RNA and protein; site of protein synthesis. See *ribonucleic acid (RNA)*.

Sex chromosomes: The X and Y *chromosomes* in human beings that determine the sex of an individual. Females have two X chromosomes in diploid cells; males have an X and a Y chromosome. The sex chromosomes comprise the 23rd chromosome pair in a *karyotype*. Compare *autosome*.

Sex Linkage: The inheritance of genes which are located on the X chromosome.

Somatic cells: Any cell in the body except *gametes* and their precursors.

Thymine (T): A nitrogenous base, one member of the *base pair* A-T (*adenine*- thymine).

Transcription: The synthesis of an *RNA* copy from a *sequence* of DNA (a *gene*); the first step in *gene expression*. Compare *translation*.

Transfer RNA (tRNA): A class of *RNA* having structures with triplet *nucleotide* sequences that are *complementary* to the triplet nucleotide coding sequences of *mRNA*. The role of tRNAs in protein synthesis is to bond with *amino acids* and transfer them to the ribosomes, where proteins are assembled according to the genetic code carried by mRNA.

Transformation: A process by which the genetic material carried by an individual cell is altered by incorporation of exogenous DNA into its *genome*.

Translation: The process in which the genetic code carried by mRNA directs the synthesis of *proteins* from amino acids. Compare *transcription*.

Uracil: A nitrogenous base normally found in RNA but not DNA; uracil is capable of forming a *base pair* with *adenine*.

Variation: Differences amongst individuals of the same species.

PRINCIPLES OF GENETICS

Introduction: History and Development of Genetics.

Definition:

The branch of Biology that studies the transmission of characteristics in Living from parents to offspring generation after generation.

Gregor Mendel:

- 1) He was the author of the foundation stone of genetics.
- 2) He was the first to reach significant results in this science.
- 3) He was a teacher of physics, biology and natural history at the High School in Brunn, (Chico Slovakia),
- 4) He grew pea plants in the garden of the monastery where he lives, to explore how the genetic traits transmitting from parents to children.
- 5) In **1866**, he clarified the results collected in previous years.
- 6) The results were neglected until the beginning of **1900**, when scientists discovered the importance of these tests after his death.
- 7) Mendel has worked at the time were not chromosomes or cell division had yet known.

Branches of genetics:

- **Classical genetics (Mendelian genetics):** the branch of genetics which study the techniques and methodologies used in genetics before the presence of molecular biology.
- **Molecular genetics:** the branch of genetics which study the structure and function of genes at a molecular level.

- **Quantitative genetics:** the branch of genetics which study the continuous traits (such as height, weight, skin color) and their underlying mechanisms.
- **Population genetics:** the branch of genetics which study the allele frequency distribution and change under the influence of natural selection, genetic drift, mutation and gene flow.
- **Ecological genetics:** the branch of genetics which study the traits of ecological significance that effect on organism's survival and reproduction.
- **Behavioral genetics:** the branch of genetics which study the inheritance of behavioral traits in animals (including humans).

Applications:

1- In agriculture:

**** Improvement of important traits of economic plants and animals by**

- increasing crop production such as rice, maize
- Improvement of taste, increasing size and production of species without seeds in fruits.
- Increasing meat production in cattle and sheep.
- Increasing the resistance of plants to diseases.

2- In medicine by:

- The recognition of genetic basis of many genetic disorders such as **hemophilia**, **diabetes**, **deafness** and **blindness** for the development of treatment and preventive measures.
- **EX. Genetic counselling:** provides parents with objective information's enable them to take rational decisions.

3- Legal applications: By identifying blood groups,

- a- The court can govern in fact issues.
- b- Take decisions in mixing between new born in hospitals.

Mendel's Principles

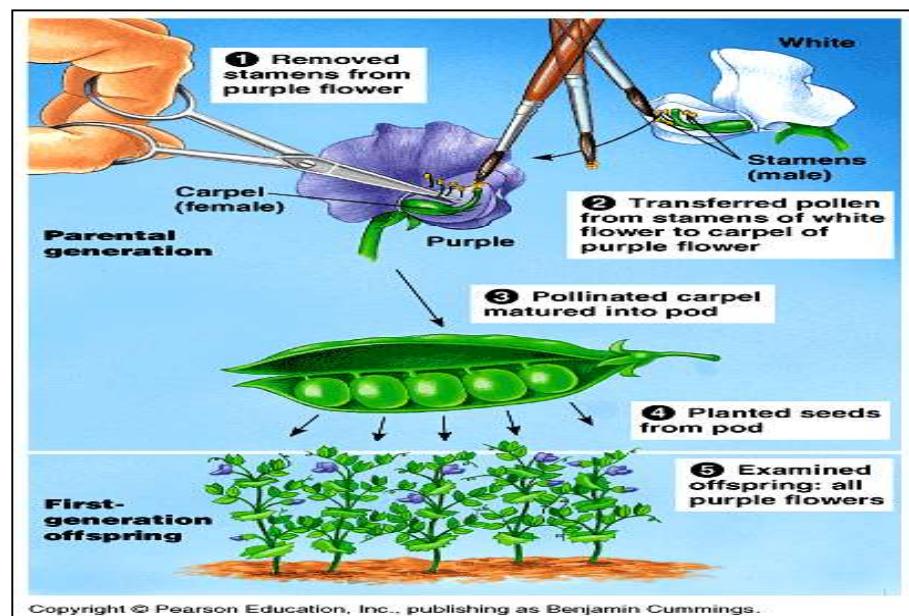
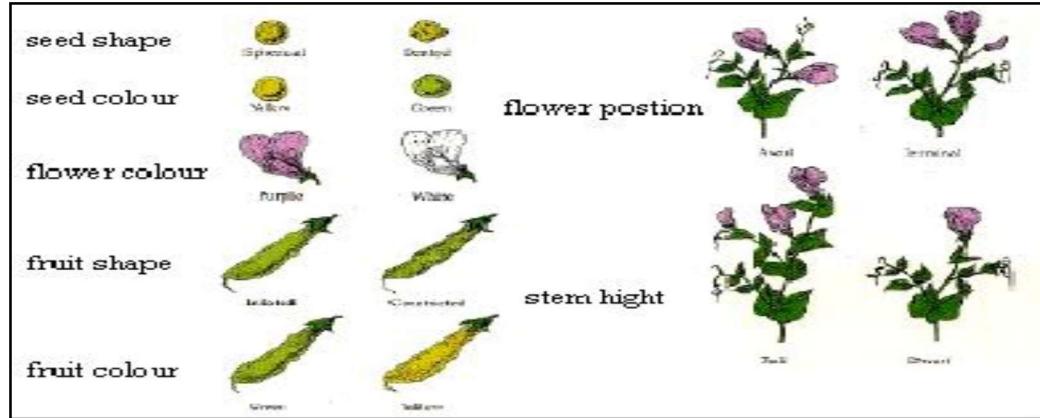
Mendelian genetics

Mendel's Studies:

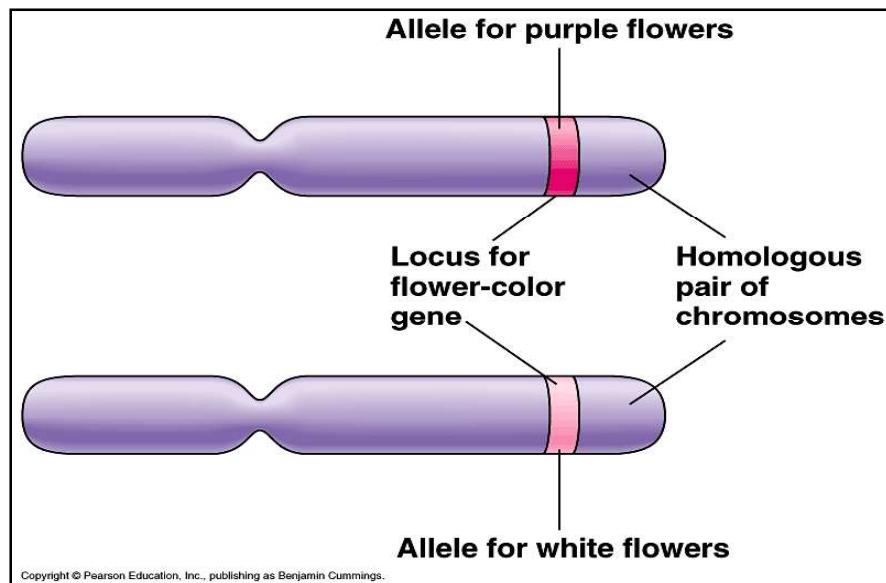
- Mendel studied 30,000 plants in 7 years

- Pea plants were an ideal choice for study because:

- 1- It displayed seven traits in one of two contrasting forms (Seed shape, seed color, seed coat color, pod shape, pod color, flower position, stem length)
- 2- Most abundant plant.
- 3- Self (fertilization) pollination.
- 4- Short life time and give more crop production.



- **Chromosomes** in living organisms occur in pairs (**homologous chromosome pairs**).
- Also, **genes** occur in pairs each pair responsible for a particular trait.
- **Locus:** specific position of gene on a chromosome.
- **Alleles:** alternate forms of the same gene at the same locus.
- **Each individual carries one copy (allele) of a gene on the chromosome from their mother, and a second copy on the homologous chromosome from their father.**



- **Homozygous individual:** Have two identical alleles at a gene locus.

- **Heterozygous individual:** Have two different alleles at a gene locus.
- **The dominant allele:** masks the expression of the other allele. and represents by **Capital letter**
- **The recessive allele:** not expressed in heterozygote. But, expressed in a ratio of 100% in homozygote. it represents by **small letter**
- **Genotype:** refers to the alleles an individual receives at fertilization.

Or, the genetic structure of an individual.

- **Phenotype** - the physical appearance of the individual.

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TABLE 9.4 Genotype Versus Phenotype		
Genotype	Genotype	Phenotype
TT	Homozygous dominant	Tall plant
Tt	Heterozygous	Tall plant
tt	Homozygous recessive	Short plant

Symbols:

X : cross

P₁: parents.

G₁: gametes of parents.

F₁: first filial generation.

G₂: gametes of 1st generation.

F₂: second filial generation.

First Mendel's law (Law of Segregation)

monohybrids cross:

- Mendel's first law deals with the inheritance of one allelomorphic characteristic.

The law of segregation states:

- Each individual has two factors (genes) for each trait. $TT \times tt$
- The factors segregate (separate) during the formation of gametes.
- Each gamete contains only one factor from each pair of factors.
- Fertilization gives each new individual two factors for each trait. Tt



Using Punnett square:

- 1- This square resembles the chess square. On its top, the female gametes are put, while the male gametes are put on the left of the square.
- 2- it is used to determine the possible combinations of male and female gametes

Example:

If crossing takes place between a pure tall-stemmed pea plant and another short-stemmed pea plant, the F₁ plants of this cross will be all tall-stemmed pea plants, when the individuals of F₁ are left for self-pollination, fertilization takes place, and F₂ plants are obtained. They are tall-stemmed pea plants, and short-stemmed pea plants in the ratio 3 tall-stemmed : 1 short stemmed as follows in the following 2 figures.

Tall -stemmed pea plant
 P_1 TT

Short -stemmed pea plant

G₁

T

x

tt

F₁

plants

Tt

100%

		T	T
t	Tt	Tt	Tt
t	Tt	Tt	Tt

P₂

Tt

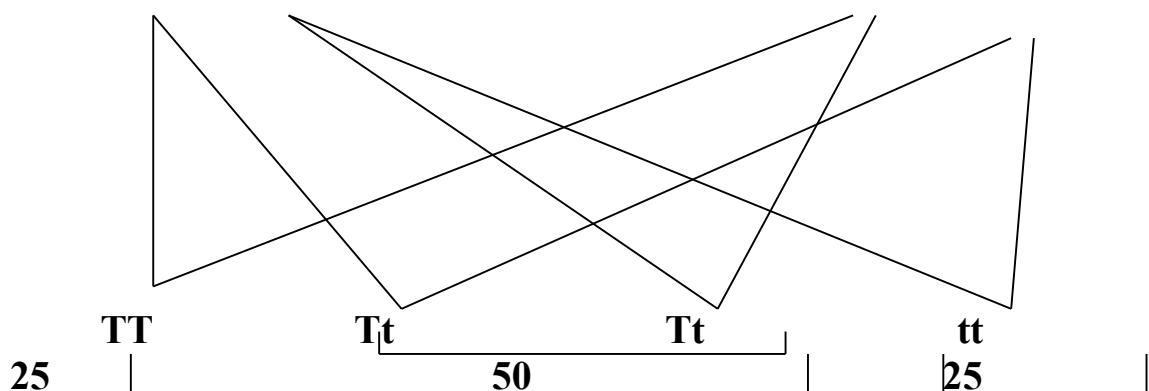
×

Tt

G₂

T t

T



F₂

Tall

Short

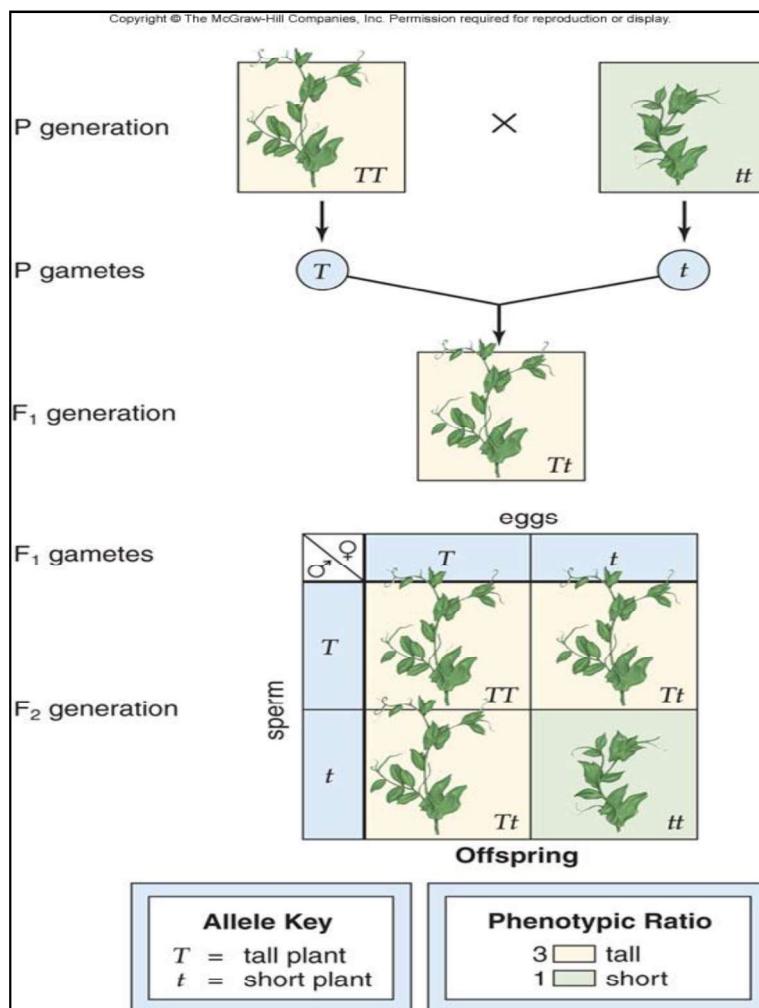
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By using Punnet square

♀	T	t
T	TT	Tt
T	Tt	tt

NOTE:

- The genotypes of the parents: TT and tt.
- The phenotypes of the parents tall -stemmed pea plant (TT)
- The genotype of F₁ Tt.
- The phenotype of F₁ tall-stemmed pea plant (hybrid).



Second Mendel's law of independent assortment (dihybrid cross):

The law of independent assortment states the following:

- Two pairs of factors separates (assorts) independently (without regard to how the others separate) during gamete formation.
- All possible combinations of factors can occur in the gametes.

NOTE:

- Mendel in its second law **studies the inheritance of two allelomorphic characteristics in the same time.**

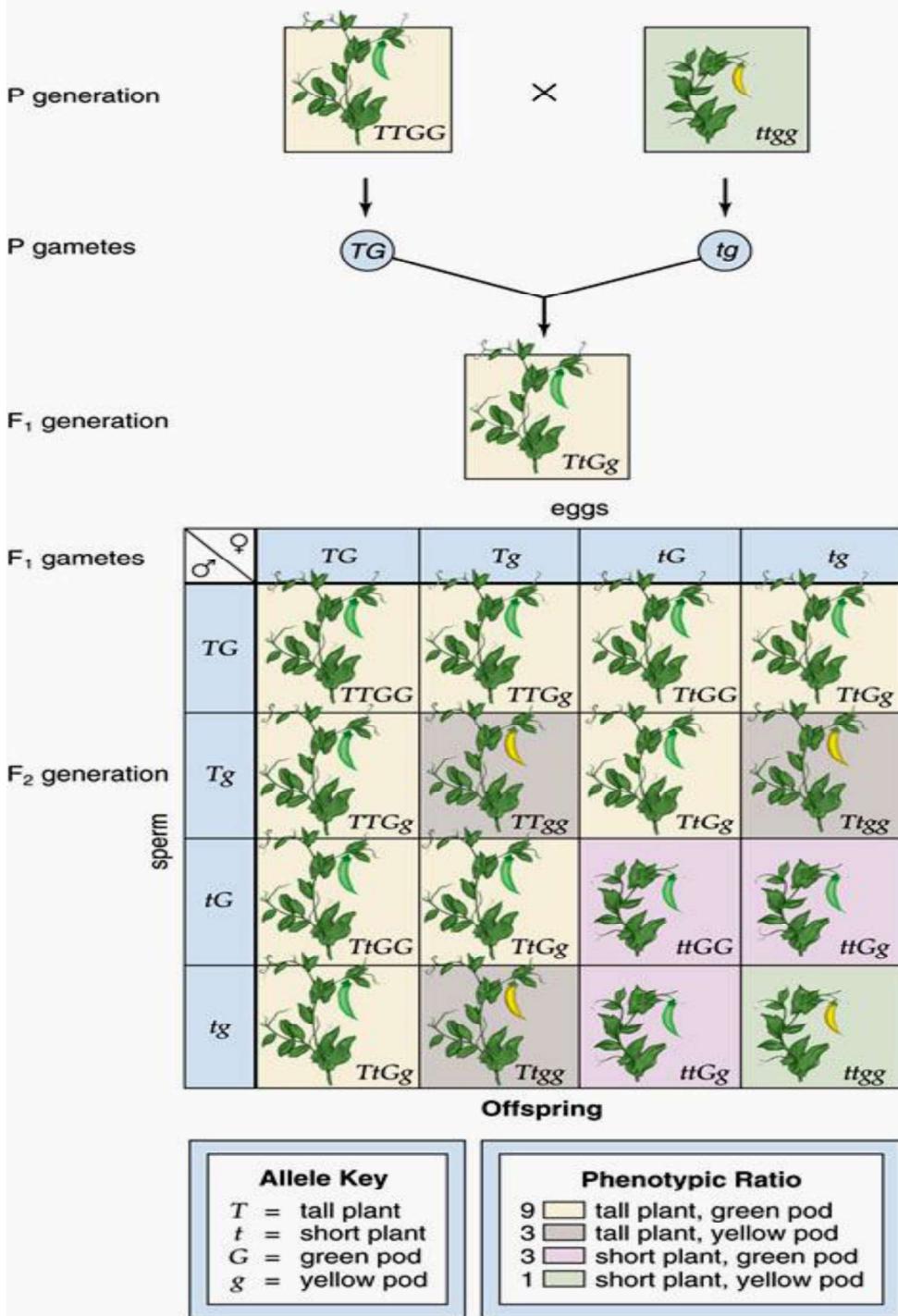
EX: - Mendel chose two homozygous pea plants one with tall plant and green seeds (two dominant characteristics), whereas the other with short plant and yellow seeds (two recessive characteristics). When he crossed these two plants, he found that:

F₁ generation: All the produced pea plants were tall plant and green seeds. When he left the F₁ generation to be self-pollinated, he obtained:

F₂ generation:

- 9 Tall plant and green pod.
- 3 Tall plant and yellow pod.
- 3 Short plant and green pod.
- 1 Short plant and yellow pod.

The ratio of the above mentioned individuals of F₂ is: **9: 3: 3: 1**



Trihybrid crosses:

- It obeys second Mendel's law in that three pairs of traits were segregate independently of one another during gamete formation.

P₁ **AABBCC**

\times

aabbcc

G₁

AB

abc

F₁

AaBbCc

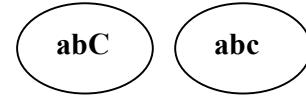
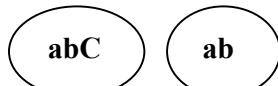
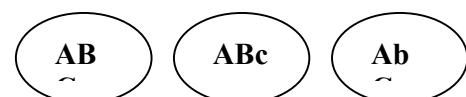
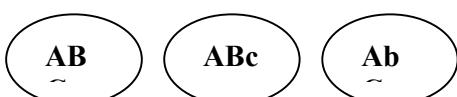
100%

P₂

AaBbCc

\times

AaBbCc



Results = 64 gamete combinations.

The test crosses:

Testcross: intentional breeding in order to determine underlying genotypes.

One-trait Test crosses:

- 1- When a **homozygous dominant** individual is crossed with one that is **homozygous recessive**, the results are always 100% phenotypic ratio. (**TT × tt**).
- 2- When a **heterozygous** individual is crossed with one that is **homozygous recessive**, the results are always a 1:1 phenotypic ratio. (**Tt × tt**)

Two-trait Test crosses:

1-When an individual is **heterozygous for the first trait** is crossed with one that is **recessive** for the traits; the offspring have a 1:1 phenotypic ratio.

Ex: (TtGG × ttgg)

2-When an individual is **heterozygous for the second trait** is crossed with one that is **recessive** for the traits; the offspring have a 1: 1 phenotypic ratio.

Ex: (TTGg × ttgg)

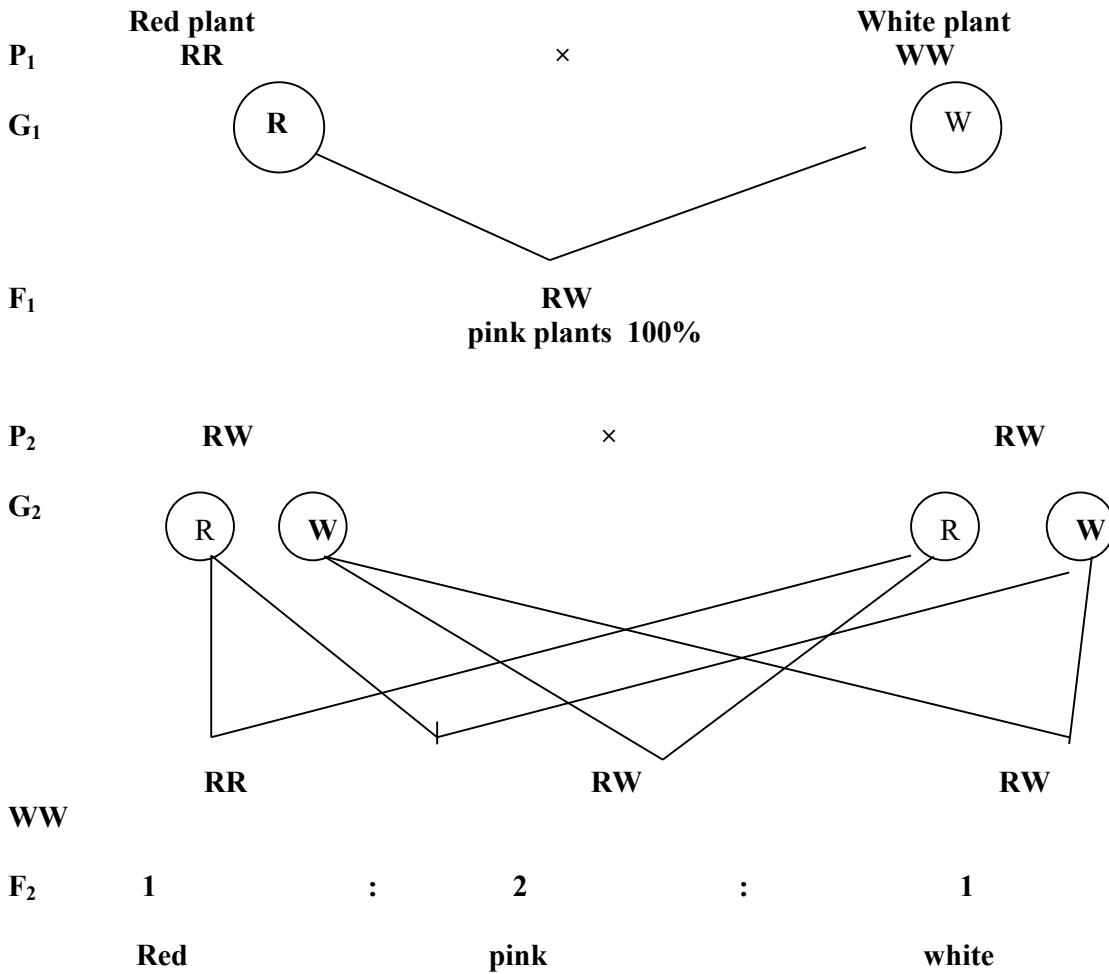
3- When an individual is **heterozygous for two traits** is crossed with one that is **recessive** for the traits, the offspring have a 1:1:1:1 phenotypic ratio.

Ex: (TtGg × ttgg)

Non-Mendelian Inheritance

Modifications in Mendelian ratios

In complete dominance: In heterozygotes both alleles of the same gene participate to produce intermediate phenotype between parents. (Neither of both alleles dominates on the other allele). **EX: 4' (Oclocks plant)**



***By using Punnet square:

♂	♀		
		R	R
	W	RW	RW
	W	RW	RW

Co-dominance

Definition: in heterozygotes both alleles of the gene express about themselves in an equivalent manner(both dominant).

EX: the antigens (blood group) represent co-dominance example.

- If **N**, **M** genes represent two co-dominant alleles.

1- **M** gene produce **M** antigen on the surface of red blood cells.

2- **N** gene produce **N** antigen on the surface of red blood cells.

In **heterozygotes (MN)** produces **M** and **N** antigens on the surface of red blood cells.

So, there are three phenotypes **M**, **N** and **MN**.

Expected Parental phenotypes	offspring phenotypes
M × M	all M
N × N	all N
M × N	all MN
M × MN	50% M : 50% MN
N × MN	50% M : 50% MN
MN × MN	1 M : 2 MN : 1

Multiple alleles

Definition: Some traits are the result of 3 or more alleles for any particular gene at a locus on the chromosome.

1-The ABO blood types: there are 3 possible alleles:

- Allele represented by **I**

****I^A** allele produces **A antigens** on the surface of blood cells and **anti-B antibodies** in blood serum.

****I^B** allele produces **B antigens** on the surface of blood cells and **anti-A antibodies** in blood serum.

****I^A I^B** allele produces **A, B antigens** on the surface of blood cells and no **antibodies** in blood serum.

****I^O** allele produces **no antigens** on the surface of blood cells and **anti-A & anti-B antibodies** in blood serum.

****I^A & I^B** are co-dominant alleles.

****I^O or (i)** is a recessive allele

****I^A & I^B** alleles dominate on **I^O**.

** **I** → isoagglutinogen

Table 14.2 Determination of ABO Blood Group by Multiple Alleles

Genotype	Phenotype (Blood Group)	Red Blood Cells
$I^A I^A$ or $I^A i$	A	
$I^B I^B$ or $I^B i$	B	
$I^A I^B$	AB	
ii	O	

(a) Phenotype (blood group)	(b) Genotypes (see p.258)	(c) Antibodies present in blood serum	(d) Results from adding red blood cells from groups below to serum from groups at left			
			A	B	AB	O
A	$I^A I^A$ or $I^A i$	Anti-B				
B	$I^B I^B$ or $I^B i$	Anti-A				
AB	$I^A I^B$	—				
O	ii	Anti-A Anti-B				

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- **A group** gives to **A**, receives from **A** and **O**.
- **B group** gives to **B**, receives from **B** and **O**.
- **AB group** gives to **AB**, receives from **A**, **B**, and **O** (because there were no antibodies in blood serum). **AB** called universal recipient.
- **O group** gives to all blood types, receives only from **O** (because A,B antibodies can react with antigens of blood of other groups). **O** called **universal donner**
- There are **six genotypes** of blood groups **AA, AO, BB, BO, AB, OO**.
- While, there are **four phenotypes** of blood groups **A, B, AB, O**.

2- The Rh antigens:

There are other antigens in blood called **Rhesus antigens**.

- Production of Rhesus antigens is controlled by **three pairs of genes**.

These genes are very close in their effect, and they are close to each other on the pair of chromosomes that carries them.

- The presence of any pair of these pairs of genes in the dominant state leads to an Rh^+ person. Thus, Rh^+ persons may be homozygous, or heterozygous, where some of the three pairs of genes are dominant, while the rest are recessive.

- In the Rh^- persons, all his genes in recessive state.

If an Rh^- woman is married to Rh^+ man, their children will be:

. 100% Rh^+ children(heterozygous), if the father was homozygous.

. 50% Rh^+ children, and 50% Rh^- children, if the father was heterozygous.

- **If the fetus is Rh^+ and the mother is Rh^- ,** some of the blood leaks from the fetus to the mother's blood stimulates it to produce antibodies against the Rhesus factor, these antibodies move to the fetus through the placenta and causes disintegration of the fetal red blood cells, infecting the fetus with severe anemia.

- The first baby is not usually affected.

- The second baby receives large amount of the antibodies that may lead to his death, unless his blood is changed, or the mother is injected with a protective serum after the birth of the first baby (anti Rh antisera that destroys any Rh^+ cells that entered the mother circulation so, she does not produce her own anti Rh antibodies).

Lethal alleles

Lethal alleles: Alleles of mutated essential gene can result in a lethal phenotype and cause an organism to die.

1- Dominant lethal allele, the homozygote and heterozygote for the allele will show the lethal phenotype.

- The individuals carry these genes die during the formation of zygote

Ex- dominant lethal allele: yellow rats

If the allele present in the individual in homozygote form, the individual dies

Y= yellow color

y= grey color

YY= yellow (die)

Yy=yellow (live)

yy= grey rat

P₁

YY \times **yy**

G₁

Y **y**

F₁

Yy 100% yellow

P₂

Yy \times **Yy**

G₂

Y **y** **Y** **y**

F₂

YY **Yy** **Yy** **yy**

0(die) 2 yellow 1 grey

***The ratios modified in second generation in to 2: 1

2- recessive lethal allele, the **homozygote** for the allele will have the lethal phenotype and **die**. Recessive lethal alleles **don't cause death** in the **heterozygous**.

ex- recessive lethal alleles: caused a [cystic fibrosis](#), [Tay-Sachs disease](#), [sickle-cell anemia](#), and [brachydactylic](#) diseases. Most lethal genes are recessive.

Ex: Sickle-cell Anemia in Man: Is a genetic disease arises from genetic disorder in the gene responsible for Hemoglobin synthesis in the red blood cells. - It causes the red blood cells become sickle-shaped.

- These abnormal red blood cells are unable to pick up Oxygen used in respiration. This leads in many cases to malfunctioning of the body, and finally to the death of the sick person.

(S) —————→ normal Hemoglobin.

(s) —————→ deformed Hemoglobin.

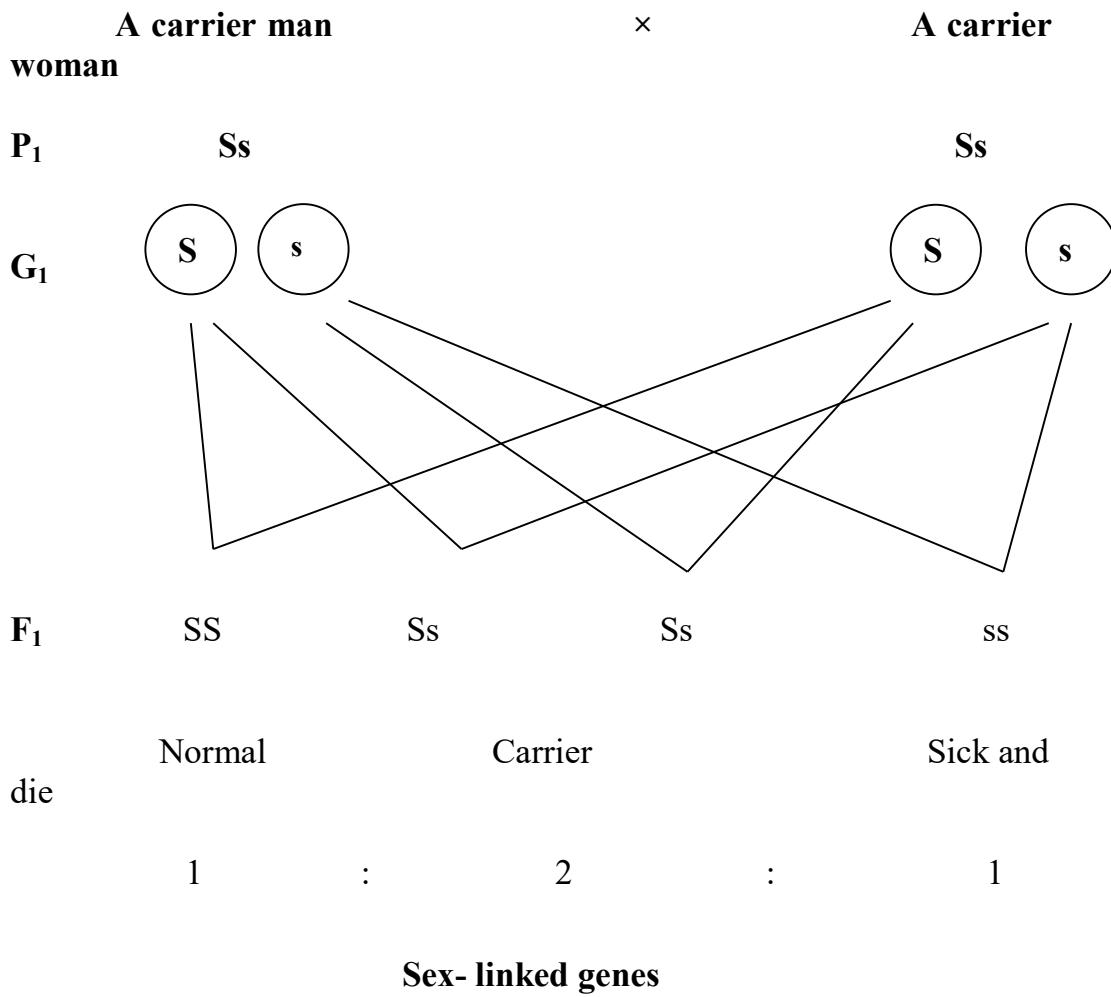
There are three possible genotypes for Human individuals:

SS : Normal persons. They are homozygous, and have normal Hemoglobin.

Ss : Carrier persons. They are heterozygous, and the symptoms of the disease appear on them after physical exertion, or if present in places where

Oxygen is scarce.

ss : Sick persons that die before maturity. They are homozygous recessive.



definition: the genes on the X or Y chromosome are called sex linked genes.

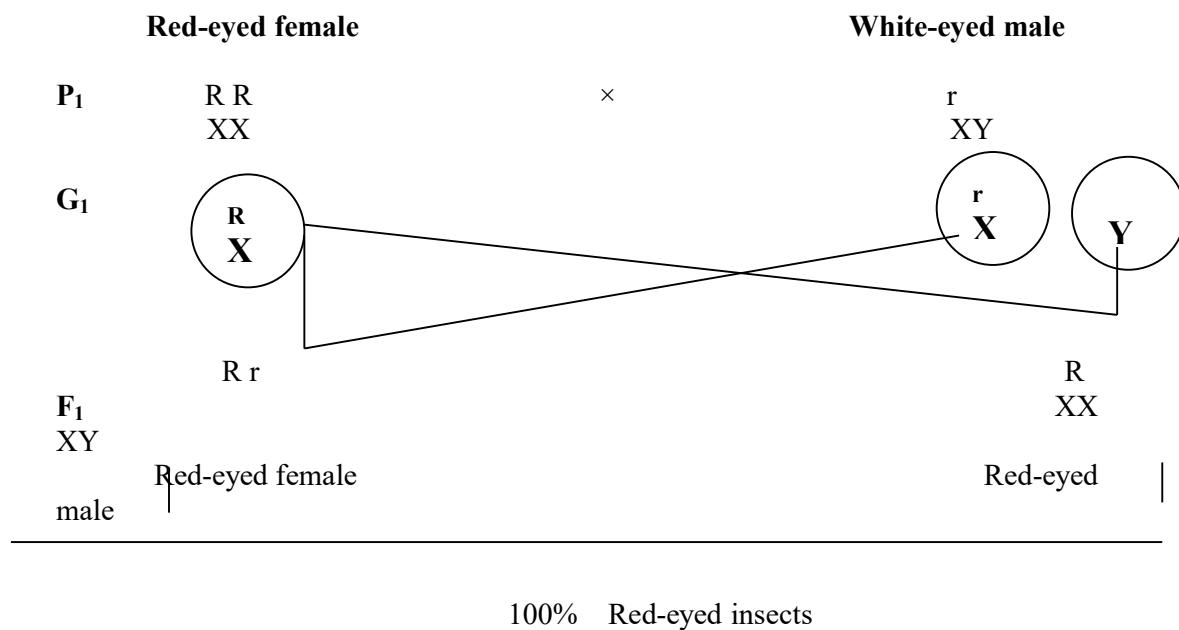
- 1- Morgan studied the inheritance of **Drosophila eye color**.
 - 2- He found that some white-eyed male insects appeared in his culture of the wild red-eyed insects.
 - 3- When he crossed a white-eyed male with a red-eyed female, the F_1 generation was all red-eyed indicating that:
 - The red color of eyes is dominant over the white color of eyes.
 - The F_2 individuals got red-eyed and white-eyed insects in the ratio 3:1.

However, the white-eyed insects were all males.

Morgan explained the appearance of white-eyed males in the F1 generation by assuming that **the gene for the white color of the eye is recessive and carried on the sex chromosome X**. Due to the shortness of the chromosome Y; it doesn't carry the other allele of the gene. Thus, the presence of one gene of the white color of eyes is sufficient for males to be white-eyed.

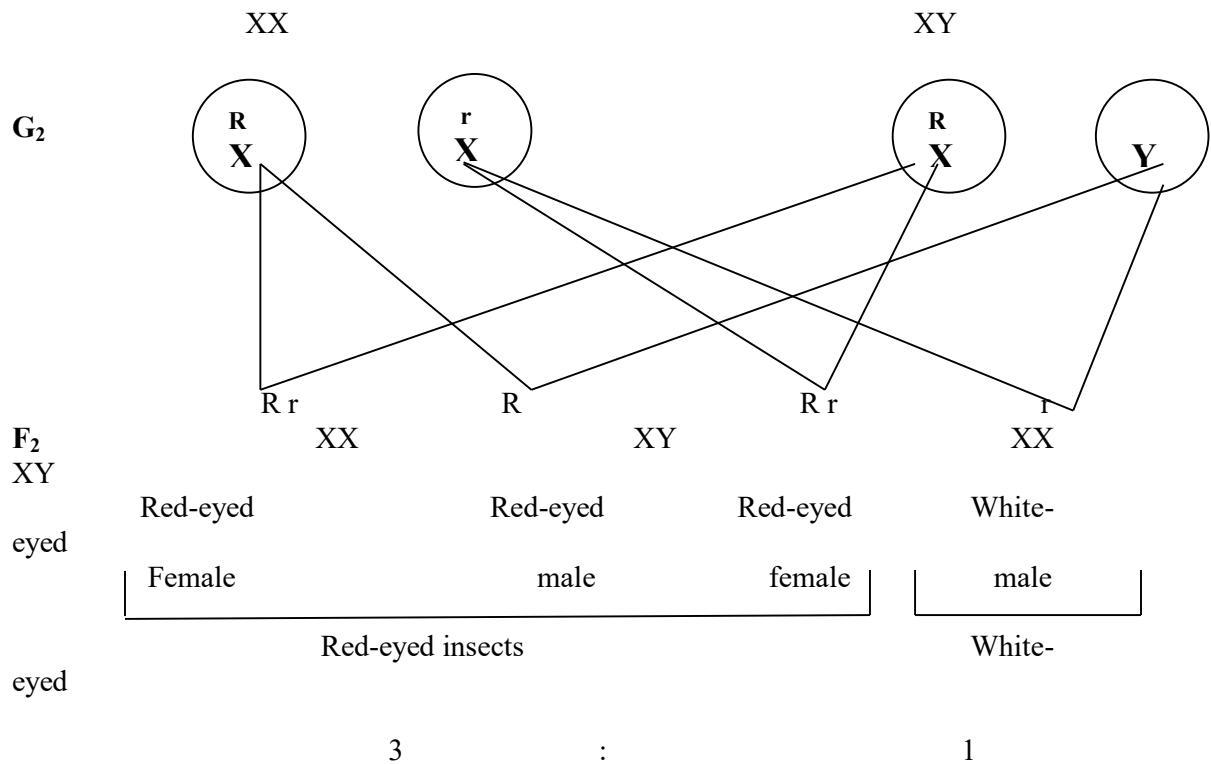
Morgan called this case **sex-linked inheritance** to refer to traits that are determined by the genes located on the sex chromosome X. The white color of eyes rarely appears in female insects because they have two X chromosomes. Even if the white-eyed gene is found on one of the two X chromosomes, it will be masked by the dominant red-eyed gene found on the other X chromosome. Thus this female will be red-eyed.

EX: if

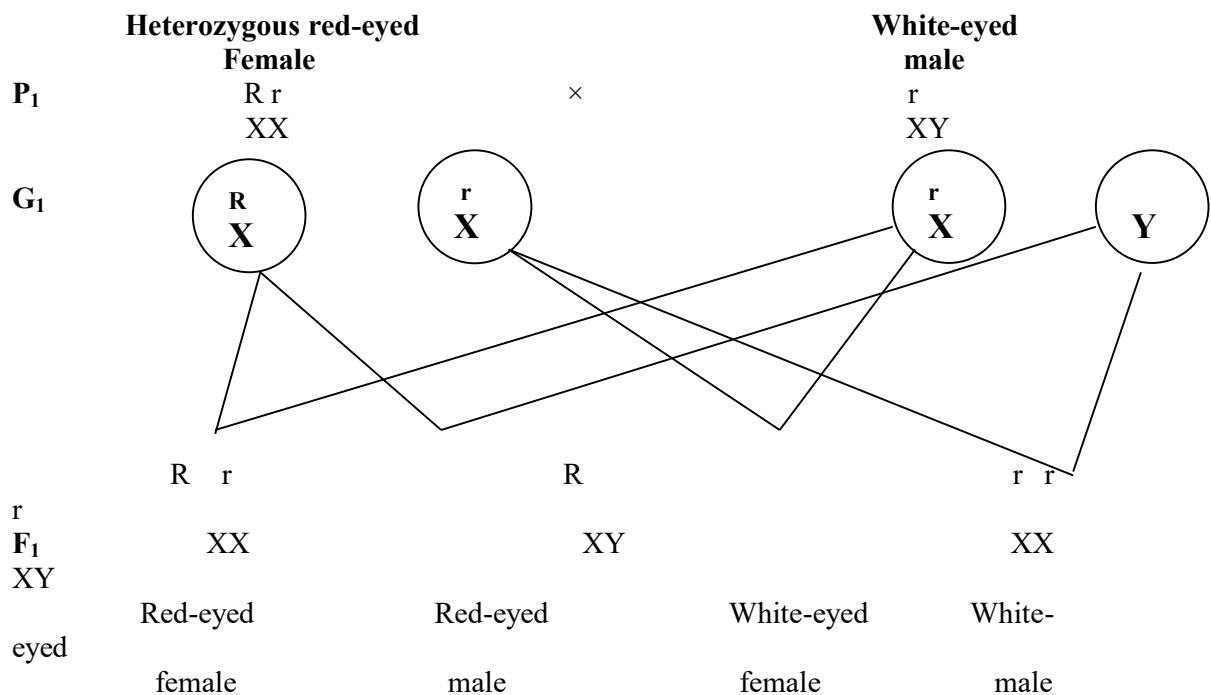


By inbreeding F1 individuals, red-eyed insects and white-eyed insects appear in the ratio 3:1, where the white color of eyes appears in males only as follows:



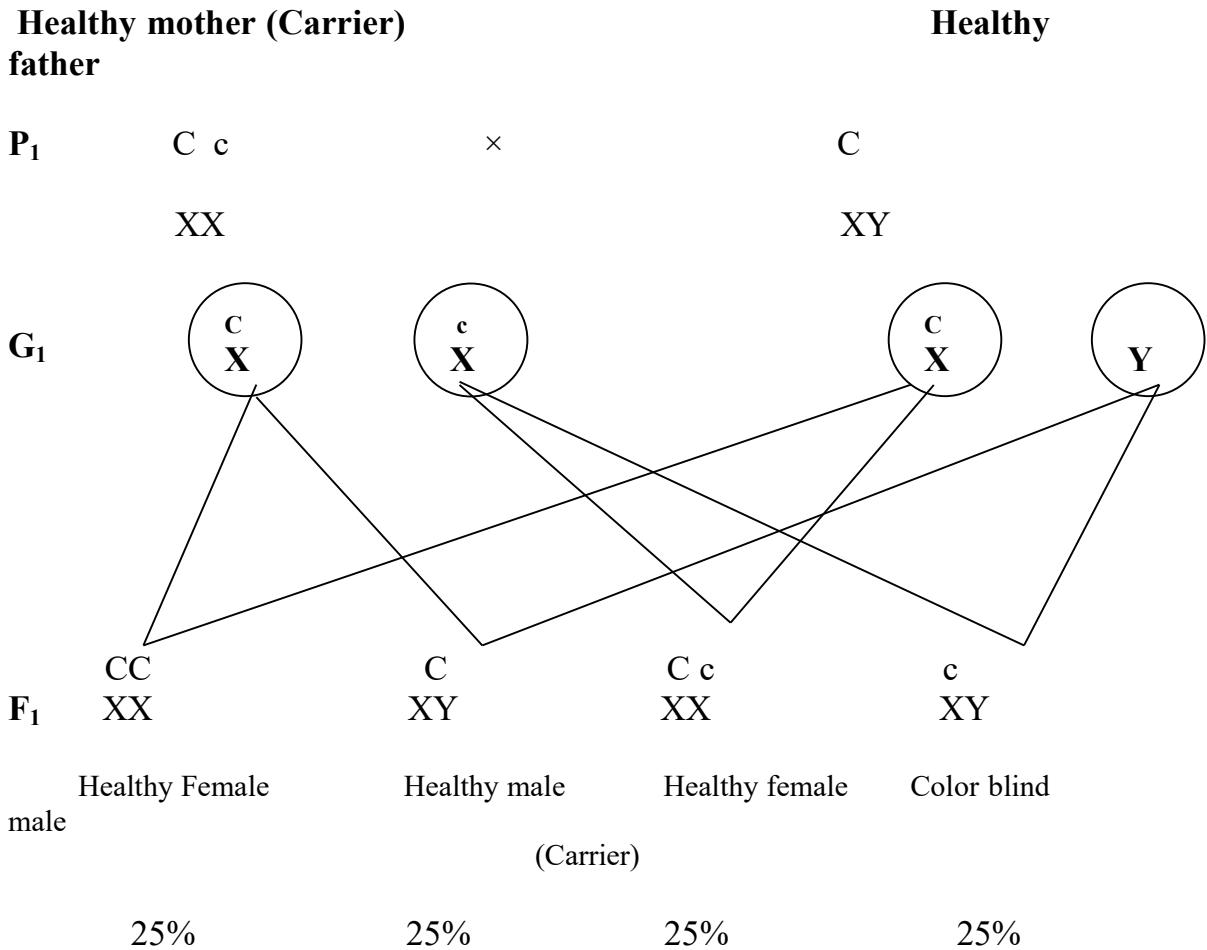


- if both sex chromosomes of the female carry the gene for white-eyed color, it will be white-eyed.
- Morgan obtaining white-eyed females by crossing red-eyed females (heterozygous) with white-eyed males.



EX : in human the color blindness trait (**recessive trait**), hemophilia, night blindness.

- The female passes these traits to her sons.
- The sick male passes these traits to his grandsons through his daughters.
- Sons inherit the sex linked gene from their mothers.



Combinations of two gene pairs:

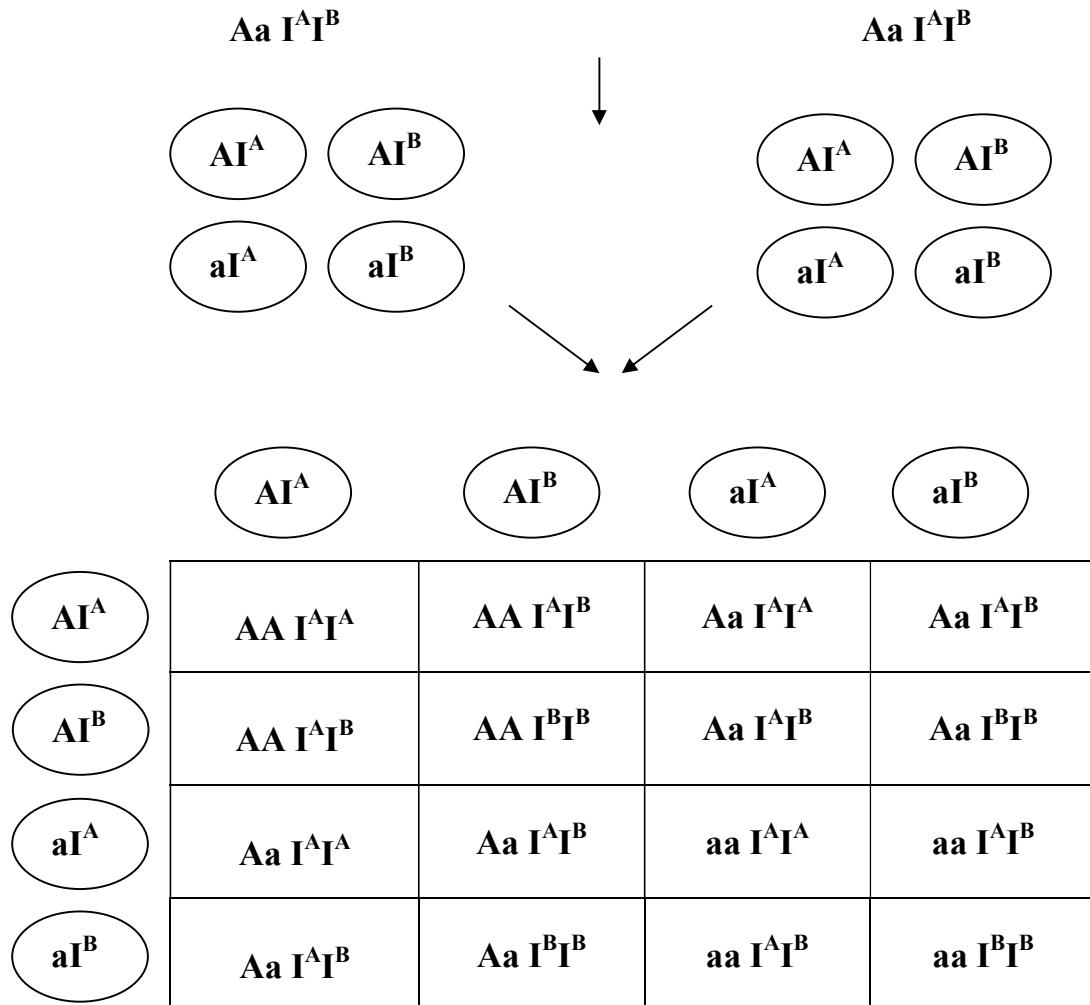
In this case Mendel's law of independent assortment was applied, provided that the genes controlling each character are not located on the same chromosome.

For example:

When mating occur between two humans are heterozygous for albinism (autosomal recessive gene) and both with blood group AB

- The possible combinations occur in a 3: 6: 3: 1: 2: 1 ratio

Normal pigment, blood type AB X Normal pigment, blood type AB



Gene interaction

- Non-Mendelian patterns of Inheritance

-these are deviations from Mendelian Ratios (first law (3:1), second law(9:3:3:1)).

- There are 2 types: **Allelic** and **Non-allelic** gene interactions.

1-Allelic Gene Interactions: No complete dominance-recessive relationship

between alleles of a gene pair.

- In Heterozygous condition (Aa), they interact together and produce new phenotypes.

Examples: Incomplete Dominance, Co-Dominance

2- Non-allelic gene interaction:

- One Character influenced by 2 or more pairs of **non-allelic gene pairs** (Aa, Bb, Cc...).

- Phenotypes decided by interaction between the alleles of these non-allelic genes.

- Mendelian ratios are modified.

Examples: Epistasis.

Epistasis:

One non-allelic gene masking or suppressing the action of another gene at another locus.

1- Suppressor gene called **Epistatic gene**.

2- Affected or inactivated gene called **Hypostatic gene**.

Ex: Coat color in mice (recessive epistasis) depends on 2 genes:

- **First** gene determines **pigment color** (A = agouti, a = black)

- **Second** gene responsible for **pigment synthesis in hair** (C = color, c = no color)

If the gene C found in dominant state CC, Cc → the color appear.

If the gene C found in recessive state cc → the color disappear

1-if the gene responsible for agouti color A is (dominant) and the gene responsible for color synthesis C also dominant the produced color will be **agouti**.

2-If the gene responsible for agouti color is (a) and the gene responsible for color C synthesis is dominant the produced color will be **black** .

3- If the gene responsible for color c is recessive the produced color will be **white**.

So, CCAA, CCAa, CcAa agouti

CCaa black

ccAA, ccAa, ccaa white(albino)

EX: if mating occur between black mice and albino mice the result will be

P1	CCaa	x	ccAA	
G1	Ca		cA	
F1	CcAa			
P2	CcAa	x	CcAa	
	CA	Ca	cA	ca
CA	CCAA	CCAa	CcAA	CcAa
Ca	CCAa	CCaa	CcAa	Ccaa
cA	CcAA	CcAa	ccAA	ccAa
Ca	CcAa	Ccaa	ccAa	ccaa

9 agouti : 3 black : 4 albinos

Quantitative Inheritance (polygenic inheritance)

- When a trait is governed by two or more genes having different alleles.
- Each dominant allele has a quantitative effect on the phenotype
- These effects are additive and result in continuous variation of phenotypes
 - The amount and degree of the trait increased with increasing the number of the dominant alleles.

EX: - eye color in humans: (Black, Brown, Hazel, Green, Blue)

- the height of the human person: (a giant, long, medium, short, dwarf)
- skin color in humans: (black, brown, wheaten, light, white)
- Fruit color in some plants.

EX: 1

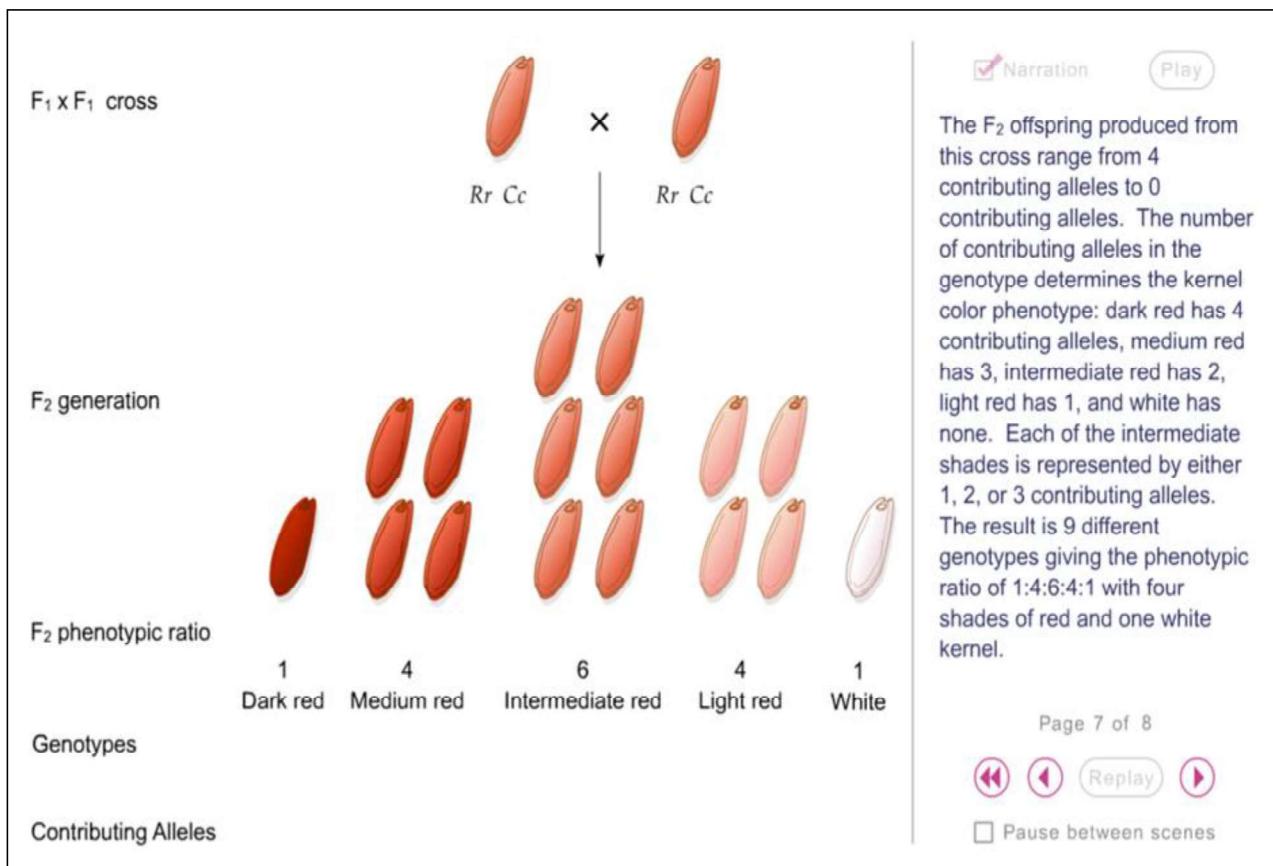
In wheat when mating occurred between a dark red beans and another white beans, the F₁ generation all the beans are median red, the F₂ generation resulting from crossing F1 individuals, from the obtained results the sum of produced phenotypes were 16 which indicate that the wheat bean, color trait controlled by 2 pairs of factors (2 genes) 2 genes .

If the symbols of the two genes R, C

P ₁	RRCC	×	rrcc
G ₁	R C		r c
F ₁	RrCc		
P ₂	RrCc	×	RrCc
G ₂	RC Rc rC rc		RC Rc rC rc
F ₂			
RRCC	dark red	(4 dominant alleles)	
RRCc, RrCC, rRCC, RRcC	median red	(3 dominant alleles)	

RrCc, RRcc, rrCC, rRcC, rRCc, RrcC **intermediate red** (2 dominant alleles)

Rrcc, rRcc, rrCc, rrcC	light red	(1 dominant allele)
rrcc	white	(no dominant alleles)



EX:2

- Skin color in man controlled by 2 or more genes.
- We assume that A, B are the genes for color.
- As the number of dominant alleles increase as the amount and the degree of skin color increase.

AABB	black	(4 dominant alleles)
AABb, AAbB, AaBB, aABB	brown	(3 dominant alleles)

AAbb, aaBB, AaBb, aAbB, aABb, AabB wheaten (2 dominant alleles)

Aabb, aAbb, aaBb, aabB	light	(1 dominant allele)
aabb	white	(no dominant alleles)

EX: If mating occurred between a dark male with white female they produced offspring will be

P₁	AABB	×	aabb
G₁	(AB)		(ab)
F₁		(AaBb)	

P₁ AaBb × AaBb

	AB	Ab	aB	Ab
AB	AABB	AABb	AaBB	Aa Bb
Ab	AABb	AAbb	AaBb	Aabb
aB	AaBB	AaBb	aaBB	aaBb
ab	AaBb	Aabb	aaBb	aabb

Polygenic inheritance of skin colour

Example (2 genes, 2 alleles each)

Assume genes are not linked (they are on separate chromosomes)

Gene A: A = add melanin
a = don't add melanin

Gene B: B = add melanin
b = don't add melanin

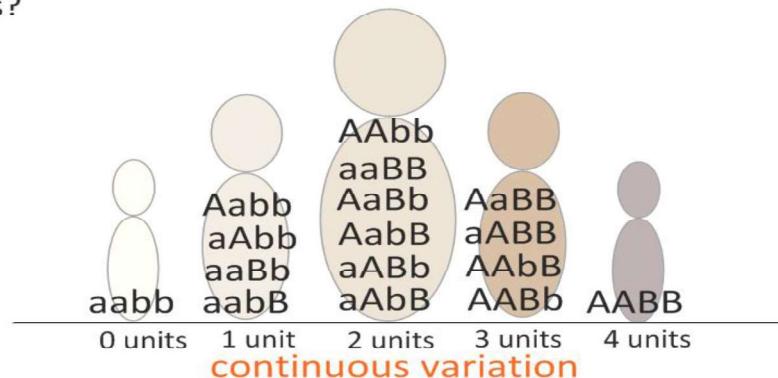
} For every dominant allele present in the genotype, one 'unit' of melanin is added to the skin. More contributing alleles leads to darker skin.



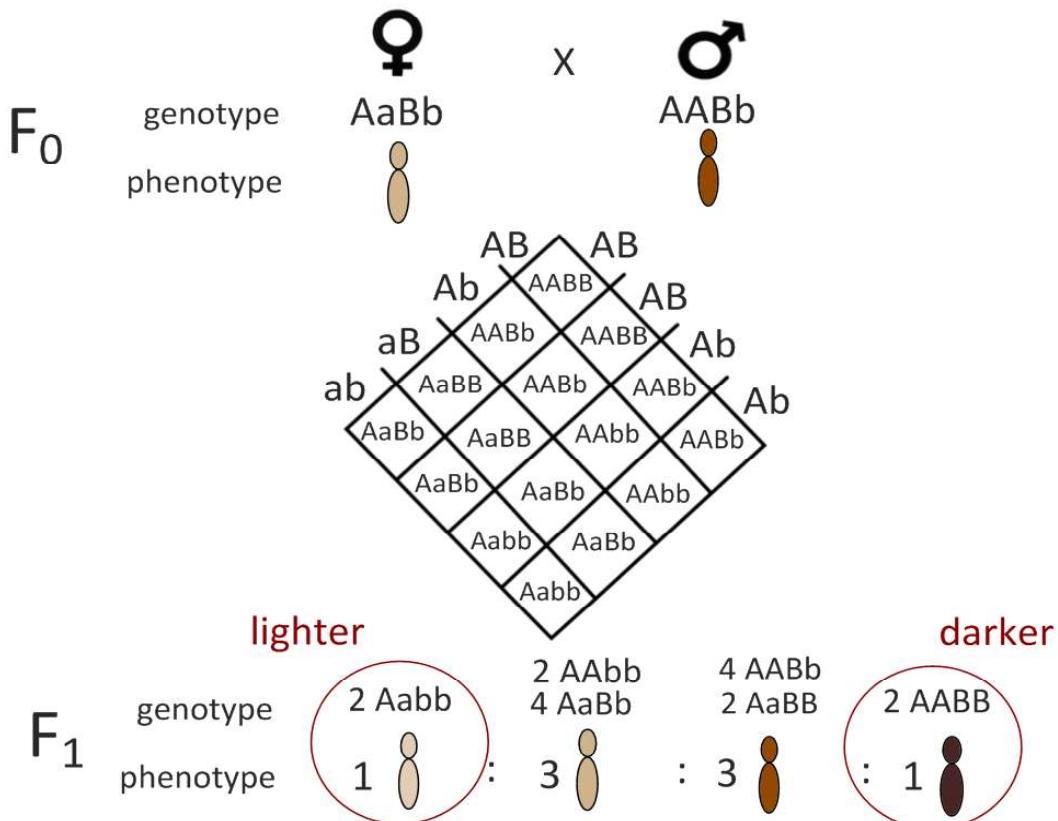
What are the possible genotypes?

Arrange them in order of phenotypes: lightest - darkest.

Notice that a **normal distribution** of phenotypes is produced.



Is it possible for children to be darker (or lighter) than both parents?



Definitions of the Gene



An albino giraffe with three normally pigmented companions.

The gene: has been defined as the unit of genetic information that controls a specific aspect of the phenotype.

Such a description, though accurate, does not provide a precise, unambiguous definition that can be used to identify a gene at the molecular level. At a more fundamental level, the gene has been defined as the unit of genetic information that specifies the synthesis of one polypeptide.

Linkage and Mapping in Eukaryotes

Gene linkage and chromosomal maps

- Each chromosome carries a great number of genes.
- The number of genes is greater than the number of chromosomes.
- These chromosomes are transferred from generation to generation through the gametes.
- The genes that are carried on the chromosomes may be **inherited independently** from each other, or **inherited together** as one unit.

There are two types of genes, according to their distribution on chromosomes:

1. Free or independent genes:

These genes are carried on different chromosomes and are distributed independently on the gametes during meiosis. Thus the traits of the progeny follow Mendel's second law of the independent assortment of the genetic factors.

2. Linked genes:

These are different genes carried on the same chromosome and carried together during meiosis and gamete formation and don't follow the rule of independent assortment but produces other genetic ratios.

LINKAGE: The transfer of these genes carried on the same chromosome from parents to offspring together as one unit.

..... There are two kinds of linkage:

a) Complete linkage:

If the distance between the linked genes is too small, so, no chance for crossing over to take place between them.

But this kind of linkage is not the normal case in all the genes.

The linked genes do not stay always like this unless they are very close to each other on the chromosome.

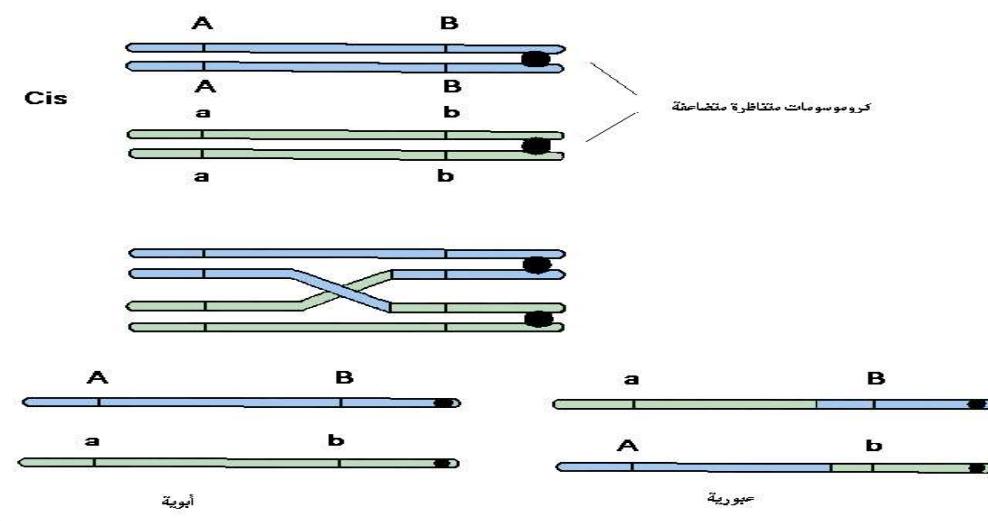
b) Incomplete linkage:

- If the distance between the linked genes (that are carried on the same chromosomes) is large enough for crossing over to take place between them.

.....When two pairs of genes on the same homologous chromosomes they arranged as follow:

1- Cis arrangement:

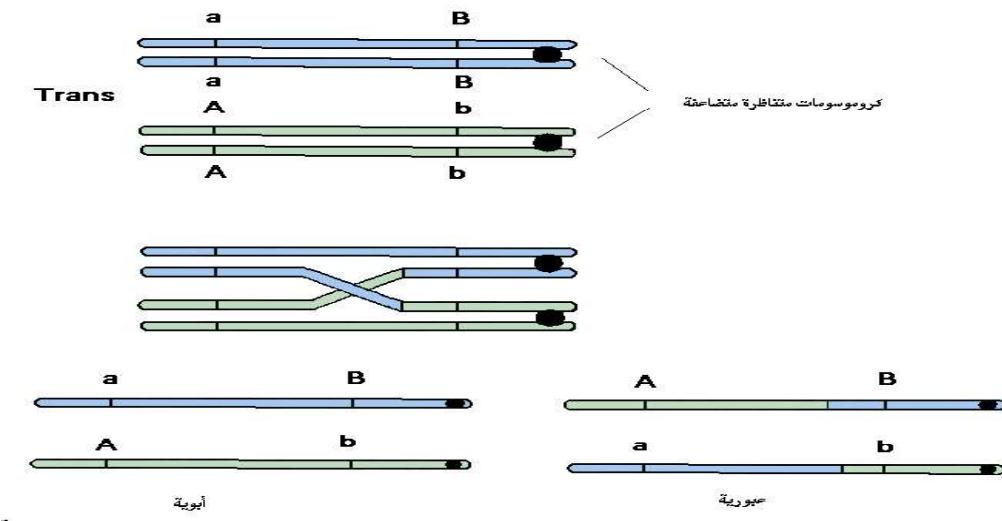
The two dominant alleles found on one chromosome and the two recessive alleles of the same gene on the other chromosome.



2- Trans arrangement:

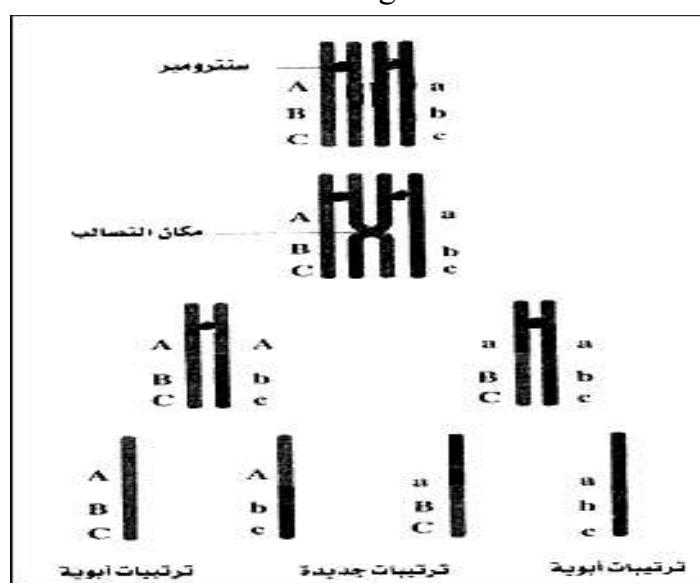
The dominant allele and the recessive allele found on the same chromosome.

And so, the type of produced gametes and new recombinants were determined according to the arrangement of genes on chromosomes.



Crossing over steps:

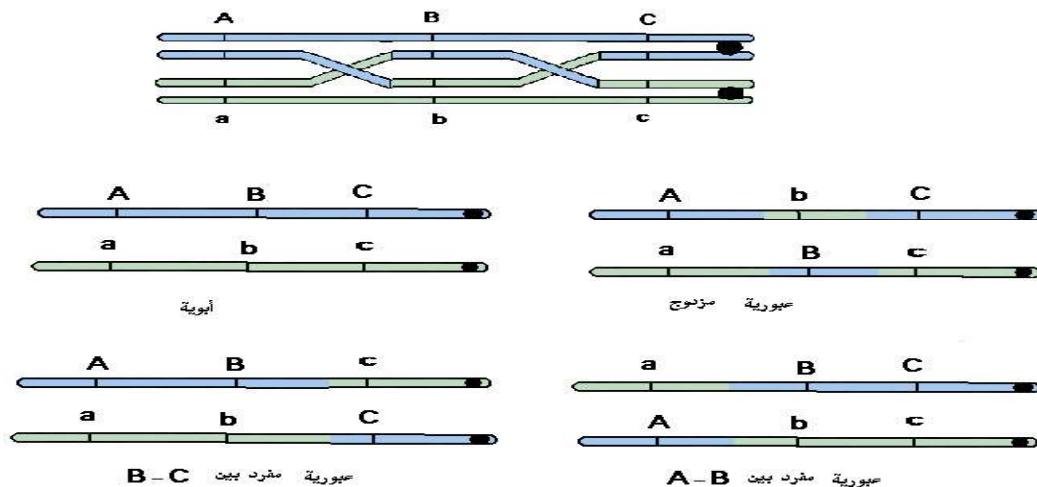
1. Pairing of the homologous chromosomes in the prophase of the first meiotic division.
2. Crossing over and exchange of segments between two non-sister chromatids. **Each point of turning between the internal chromatids is known as chiasma**
3. Separation of the chromosomes in the first anaphase of the meiotic division.
4. Separation of the chromatids into chromosomes in the second anaphase and its distribution in the gametes.



Note:

- 1)- The internal chromatids, where exchange of genes occurs are called the new recombinant chromosomes.
- 2)- The external chromatids where crossing did occur are called the parental chromosomes
- 3)- Crossing over leads to incomplete linkages that result in a change in the genetic characteristics but in a limited ratio that depends on the distance between the genes on the chromosome.
- 4)- Sometimes, more than one crossing over occurs in the same chromosome this is called doubled crossing over.

Doubled crossing over:



- 5)- the new recombinant types are little than 50% but the parental types are more than 50%.
- 6)- If crossing over occurs between two chromatids having the same alleles as in the case of homozygous dominant or homozygous recessive genes, no change will occur in the resulting ratio.

The importance of crossing over:

- 1- Crossing over increases the chances of diversity in the traits among members of the same species, which helps in their survival, and evolution.
- 2- Crossing over is used in drawing maps that illustrate the distribution of the genes that known as **chromosomal maps**.

The chromosomal maps:

The American geneticist Morgan introduced a method to explain the results of linkage and crossing over to draw maps that determine the location of genes on the chromosomes of some plants, and animals, and for some chromosomes in Man.

The distance unit between genes:

The crossing over percentage could be considered as a measure to the distance between genes that called centimorgan and equals 1% of crossing over.

Example: if the genetic type **Ab / aB** gave gametes after crossing over having the genetic structure **AB, ab** in a percentage **8%**.

-----**This means that** the distance between the two genes equals 8 units on the genetic map.

Ex.: if the percentage of crossing over between the black color gene, and the vestigial wing gene was 17%. If another ratio of crossing over of 5% appeared between the black color gene and the gene for purple color of the eye, and both are located on the chromosome no. 2. Then the percentage of crossing over between the gene for the purple color of eye, and the gene for the vestigial wing is 12%, and then it is possible to draw a map for its chromosome as follows:

* ----- 12 وحدة ----- * 5 وحدات ----- *



Sex Linkage and Pedigree Analysis

Sex- linked genes

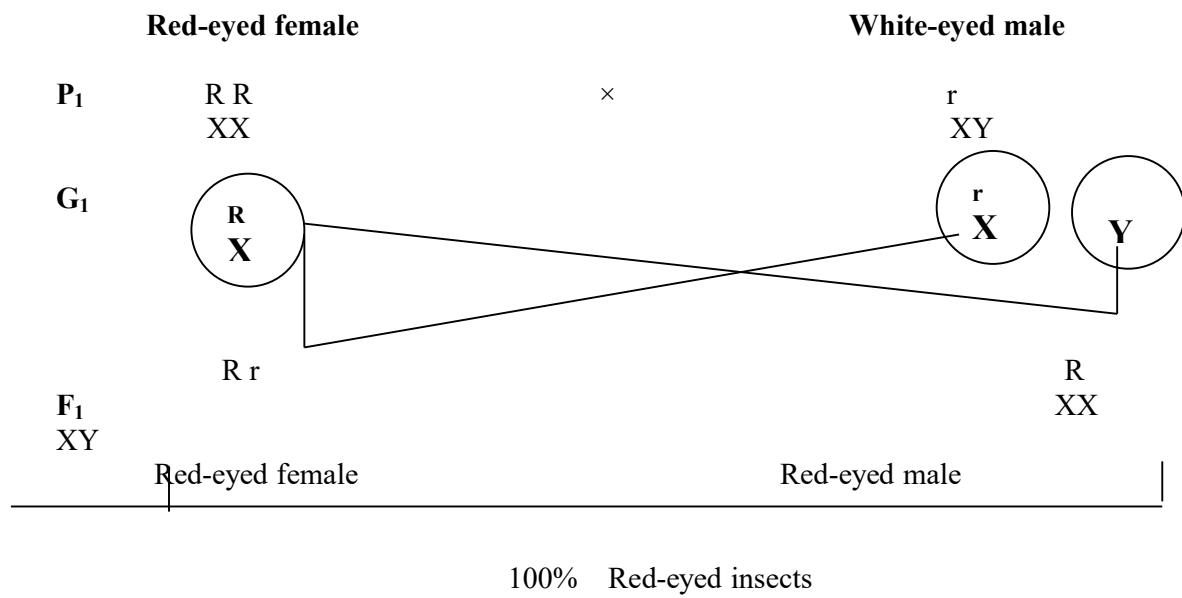
Definition: the genes on the X or Y chromosome are called sex linked genes.

- 1- Morgan studied the inheritance of **Drosophila eye color**.
- 2- He found that some white-eyed male insects appeared in his culture of the wild red-eyed insects.
- 3- When he crossed a white-eyed male with a red-eyed female, the F₁ generation was all red-eyed indicating that:
 - The red color of eyes is dominant over the white color of eyes.
 - The F₂ individuals got red-eyed and white-eyed insects in the ratio 3:1.However, the white-eyed insects were all males.

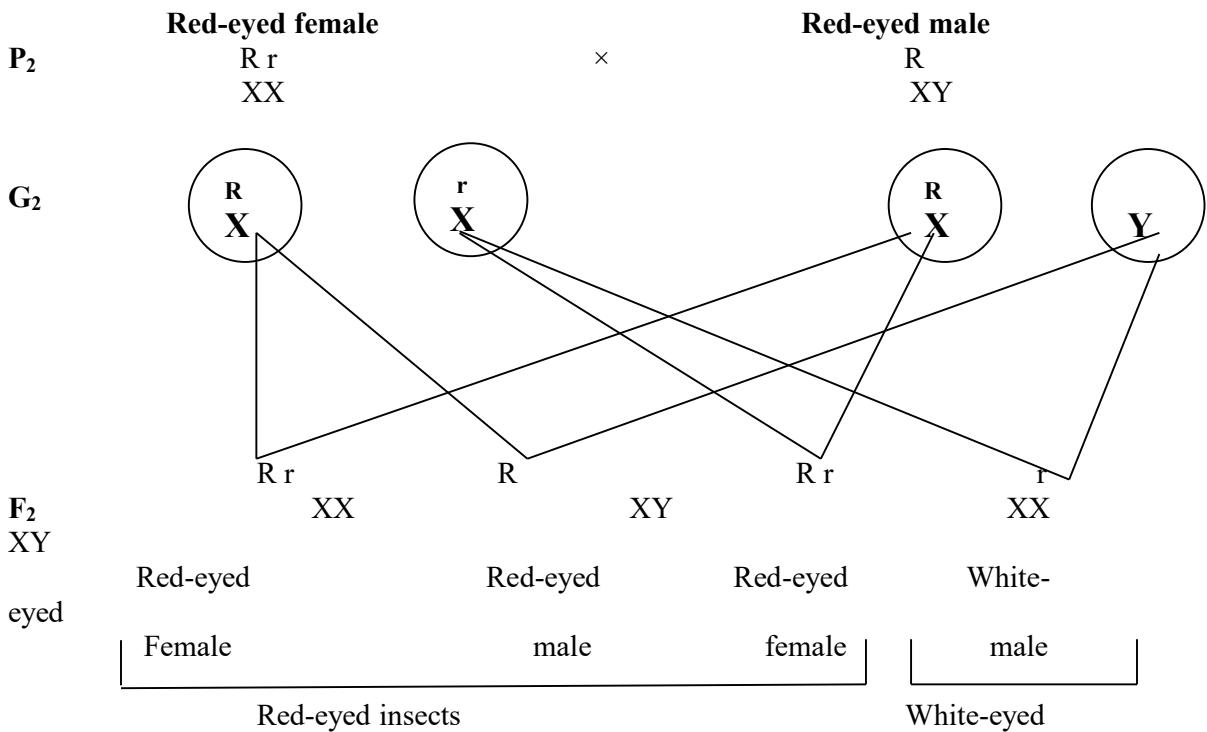
Morgan explained the appearance of white-eyed males in the F₁ generation by assuming that **the gene for the white color of the eye is recessive and carried on the sex chromosome X**. Due to the shortness of the chromosome Y; it doesn't carry the other allele of the gene. Thus, the presence of one gene of the white color of eyes is sufficient for males to be white-eyed.

Morgan called this case **sex-linked inheritance** to refer to traits that are determined by the genes located on the sex chromosome X. The white color of eyes rarely appears in female insects because they have two X chromosomes. Even if the white-eyed gene is found on one of the two X chromosomes, it will be masked by the dominant red-eyed gene found on the other X chromosome. Thus this female will be red-eyed.

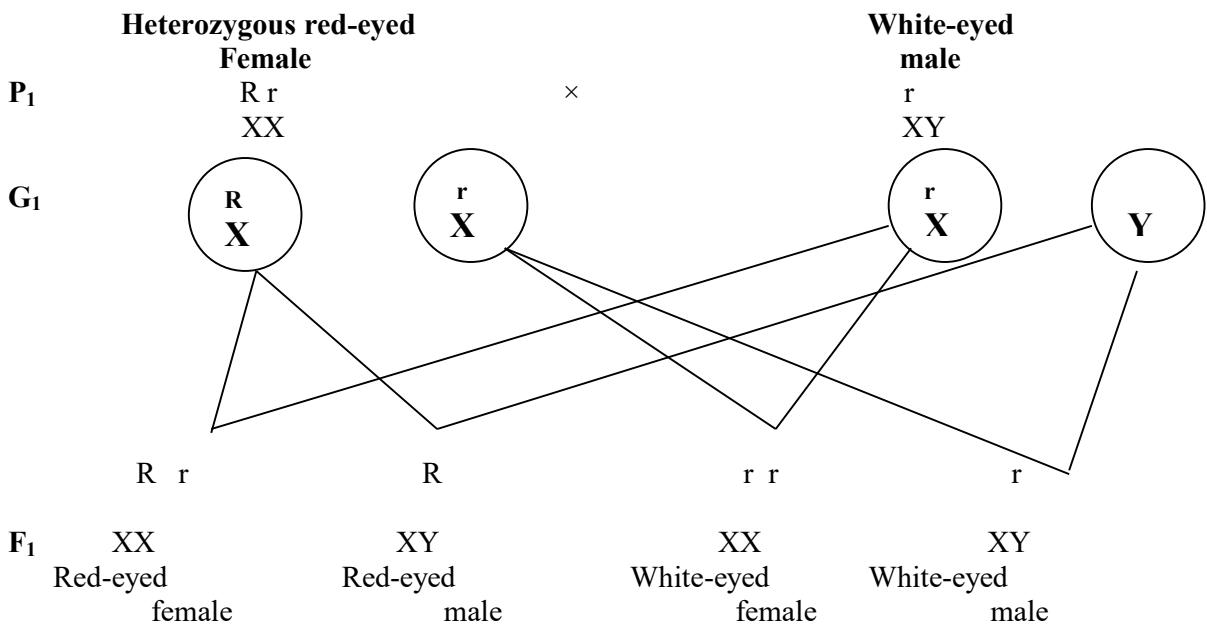
EX:



By inbreeding F₁ individuals, red-eyed insects and white-eyed insects appear in the ratio 3:1, where the white color of eyes appears in males only as follows:

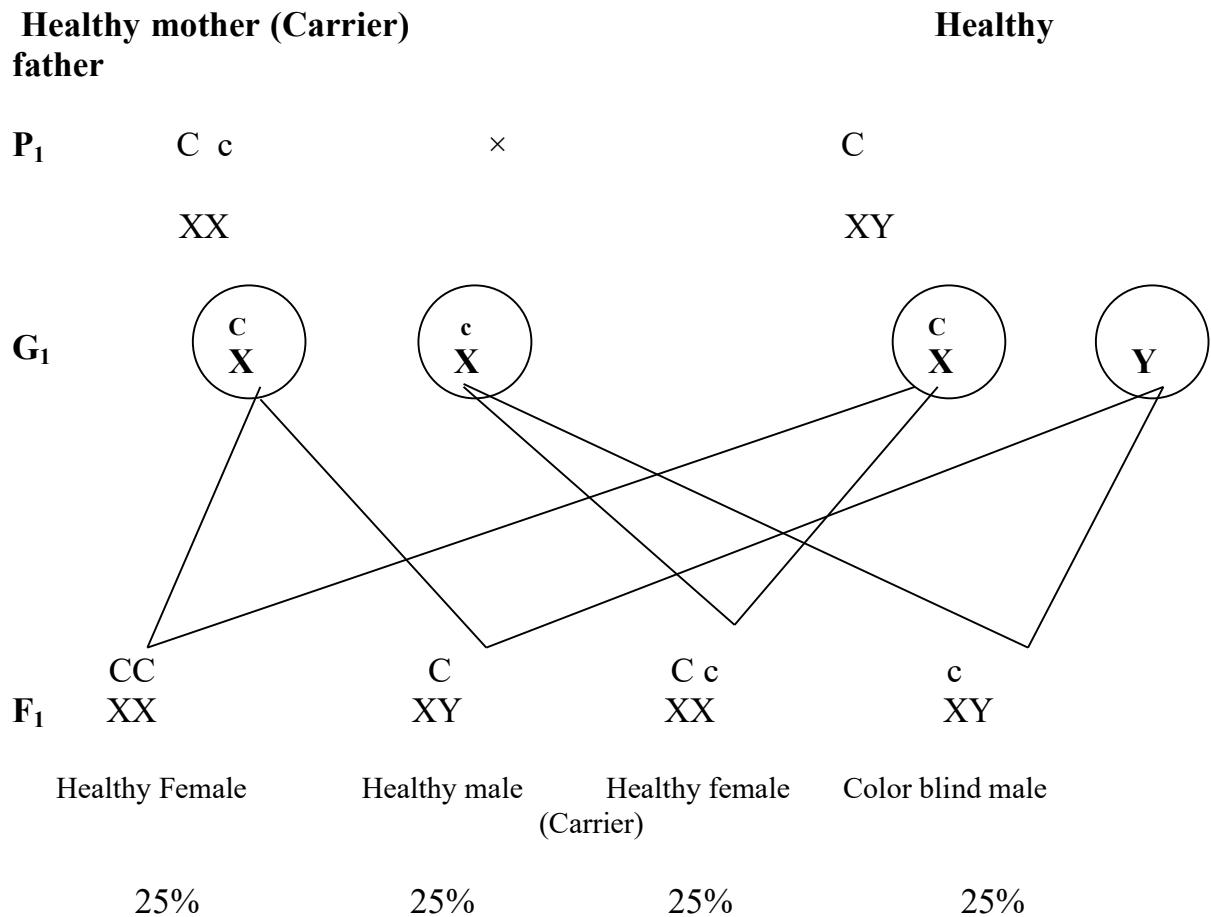


- If both sex chromosomes of the female carry the gene for white-eyed color, it will be white-eyed.
- Morgan obtaining white-eyed females by crossing red-eyed females (heterozygous) with white-eyed males.



EX : In human the color blindness trait (**recessive trait**), hemophilia, night blindness.

- The female passes these traits to her sons.
- The sick male passes these traits to his grandsons through his daughters.
- Sons inherit the sex linked gene from their mothers.



Pedigrees can reveal the patterns of inheritance:

- Pedigree: a family tree describing the interrelationships of parents & children across generations
- The pedigree or family tree: used to determine how the gene controlling a trait is inherited.

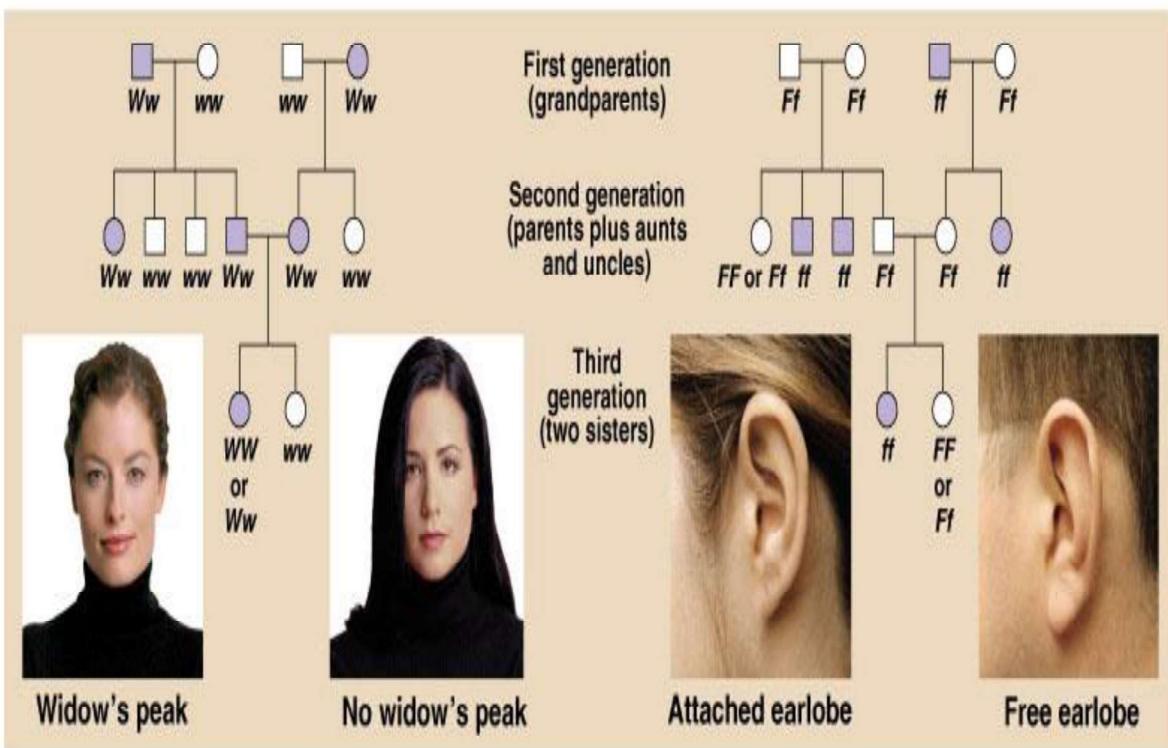
Symbols:

Female

shaded = affected

Male

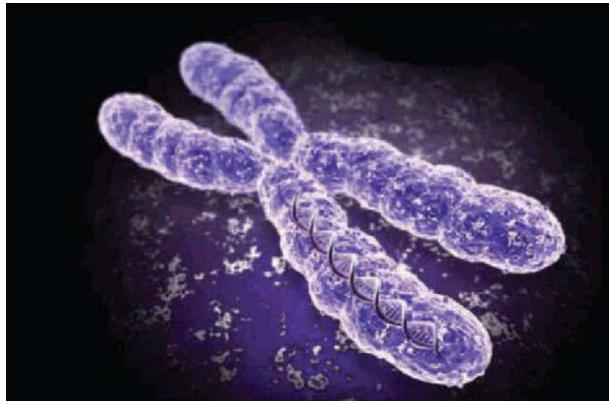
partial shading = carrier



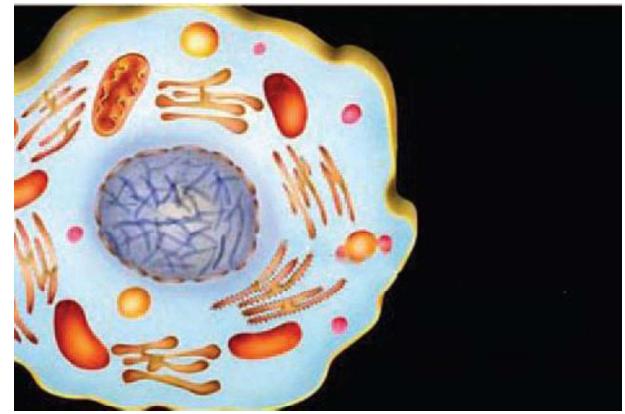
Cytogenetics: The Cell Cycle, Mitosis and Meiosis

Cell division

- The cell nucleus contains the genetic material of the living organism. This genetic material consists of a number of chromosomes. Chromosomes have the main role in cell division.



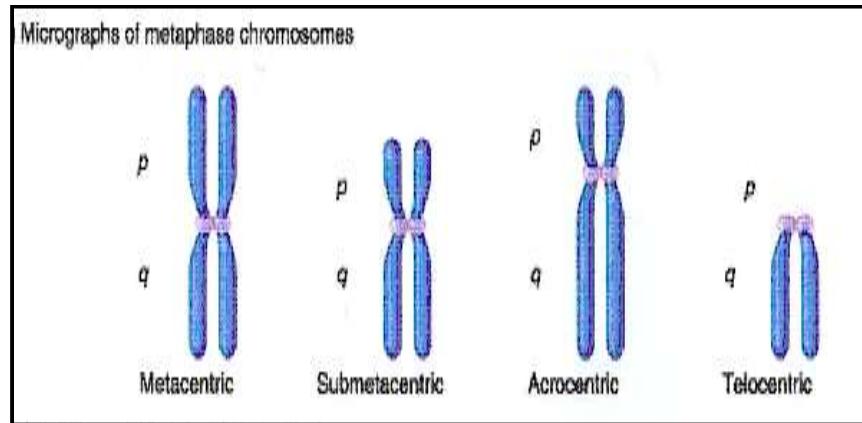
A chromosome



The cell

Chromosome:

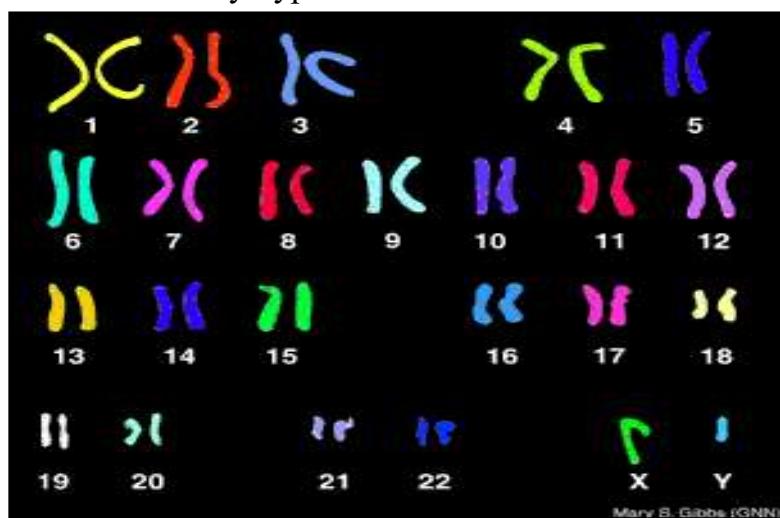
- It consists of two connected threads at the Point of attachment called centromere. Each thread is called **a chromatid**.
- The chromosome chemically consists of nuclear acid called **D.N.A** and **protein**. (DNA carries the genetic traits of the organism).
- **Chromosomes classified in to four types according to the position of centromere:**
 - 1- **Metacentric** Chromosomes (centromere at the middle).
 - 2- **Sub-metacentric** Chromosomes (centromere between the middle and the end).
 - 3- **Acrocentric** Chromosomes (centromere close to the end).
 - 4- **Telocentric** Chromosomes (centromere at the end).



Karyotype:

The whole characteristics that allow the identification of a particular chromosomal set **as** the number of chromosomes, relative length, position of centromere, length of arms, secondary constrictions and satellites.

- **It prepared by** cutting out individual chromosomes from a photograph and arranging them in a series of descending size (metacentric, sub-metacentric, acrocentric, telocentric).
- **Karyotype importance:** in genetic disorders associated with abnormalities of karyotype and sex determination.



Male karyotype

Mitosis

- Mitosis occurs in the somatic cells of organisms.
- It is important in growth and compensation of the damaged cells.
- Before starting division the cell passes through a phase called

1- Interphase:

- The genetic material in the form of chromatin
- DNA and chromosomal proteins are replicated to prepare the cell for division.
- This phase lasts a few hours.

2- Prophase:

- Chromatin condenses into distinct "rods", called chromosomes.
- Chromosomes appear thin and long.
- Spindle fibers forms extending between the two poles of the cell.
- At the end of this phase, chromosomes thickened and consists of two sister chromatids.
- The nucleolus and nuclear membrane starts to disappear.

3- Metaphase:

- Chromosomes arranged along the cell equator.

4- Anaphase:

- Centromeres splits dividing Chromosomes into two Chromatids that separate from each other.
- Spindle fibers shrink and each chromatid group migrate towards each pole of the cell.

5- Telophase:

- Cleavage furrow start to form.
- Nuclear envelop and nucleolus reformed around each group.

Cytokinesis: in which the cytoplasm divides forming two cells.

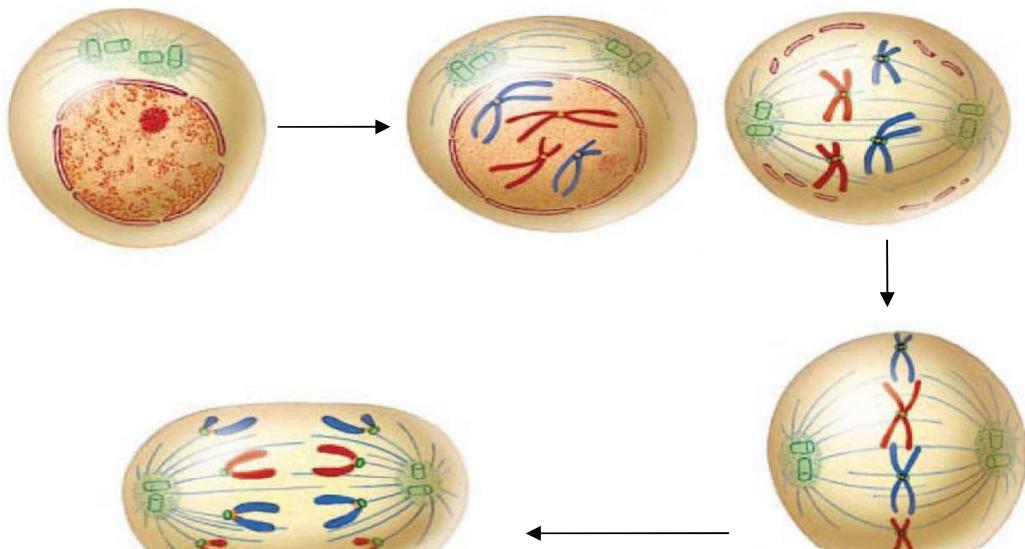
- Each has the same number of the mother cell's chromosomes ($2n$)
- In **animal** cells this starts from the **outside**.

In **plants**, a **cell plate** first forms to split the cell in to **two** cells.

Interphase

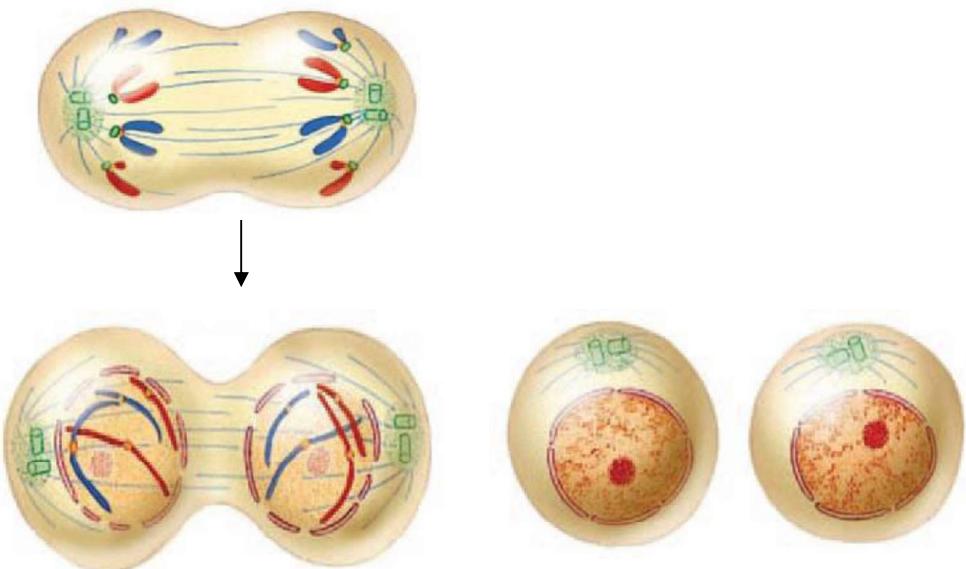
early prophase

late prophase



Anaphase

Metaphase



Cytokinesis

2 daughter cells ($2n$)

Meiosis

- Meiosis occurs in living organisms that reproduce by gametes.
- In humans and animals, this division occurs in the testis to produce the male gametes (sperms) and in the ovary to form the female gametes (ova).
- In flowering plants this division occurs **in the anther** to produce the **pollen grains** and in the **flower ovary** to form eggs.
- Meiosis produced cells contain half the number of chromosomes of the parent cell.
- Meiosis occurs in two stages meiosis1 and meiosis2.

- First meiotic division:

Meiosis I

1- Interphase: DNA is doubled for preparing the cell to divide.

2- Prophase I:

- 1 - The first and longest stage of meiosis I
 - 2- There are 5 stages of it leading to the formation of **tetrads** in which Chromosomes arranged in homologous pairs, each pair consists of 4 chromatids.
 - 3- At the end of prophase I, **the crossing over phenomenon** occurs by exchanging segments between non-sister chromatids to produce new genetic arrangements.
 - 4- Finally, nuclear membrane and nucleolus disappears, the spindle appears and the chromosomes connected with spindle fibers.
- 3- Metaphase I:** Homologous Chromosome pairs arrange on the Cell's equator

4- Anaphase I:

- Every two homologous chromosomes start to move away from each other.
- Each pole contains half the number of chromosomes of the parent cell.

5- Telophase I:

- The spindle fibers shrink, nuclear membrane and nucleolus reformed

Cytokinesis: the cytoplasm divides and the division finished forming two cells each have half the number of chromosomes of the mother cell (n).

- Each cell enters into the second meiotic division.

Second meiotic division:

Metaphase II: Chromosomes (2 chromatids) arrange on the cell's equator.

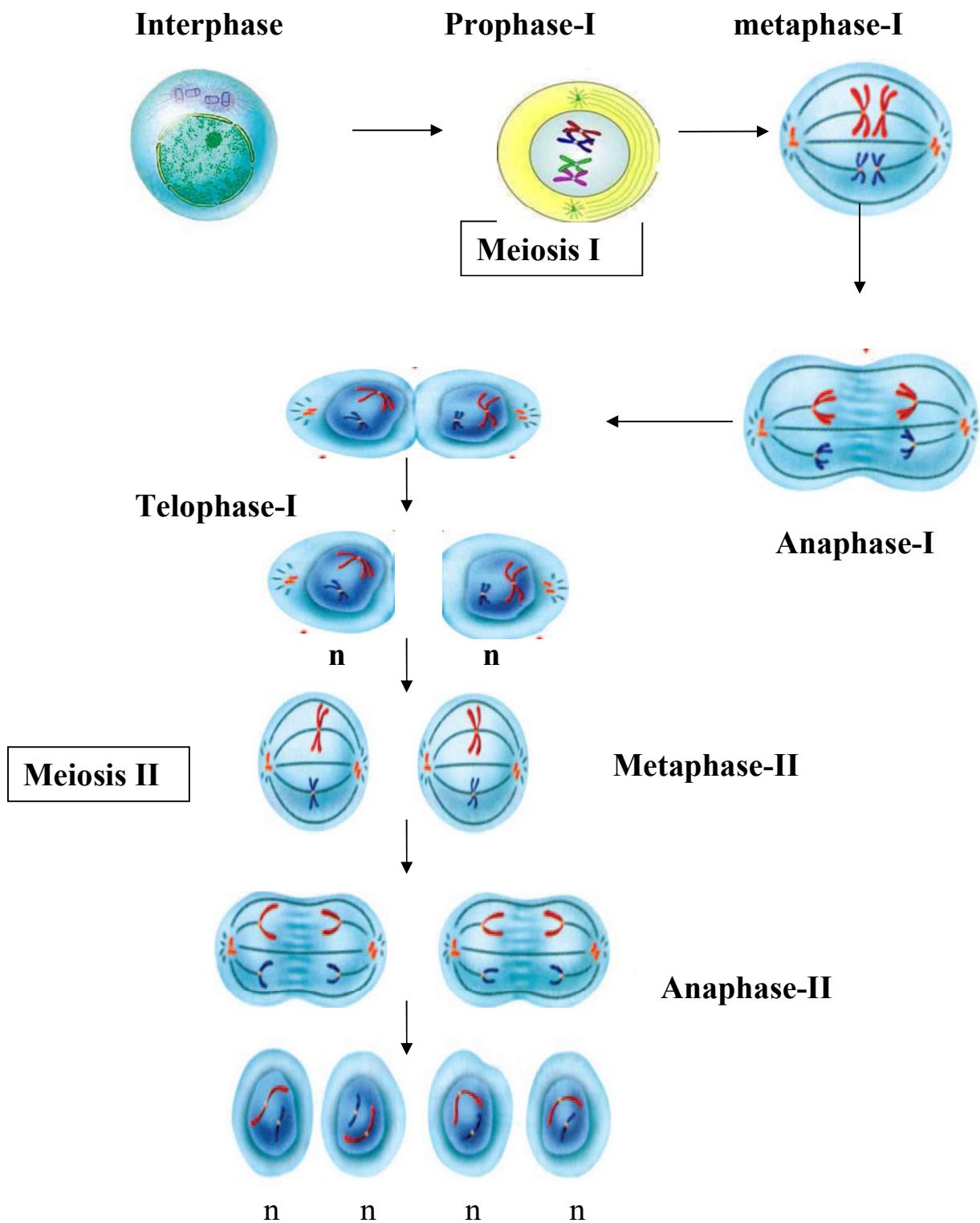
Anaphase II: centromeres split, Sister chromatids separate and move to opposite poles.

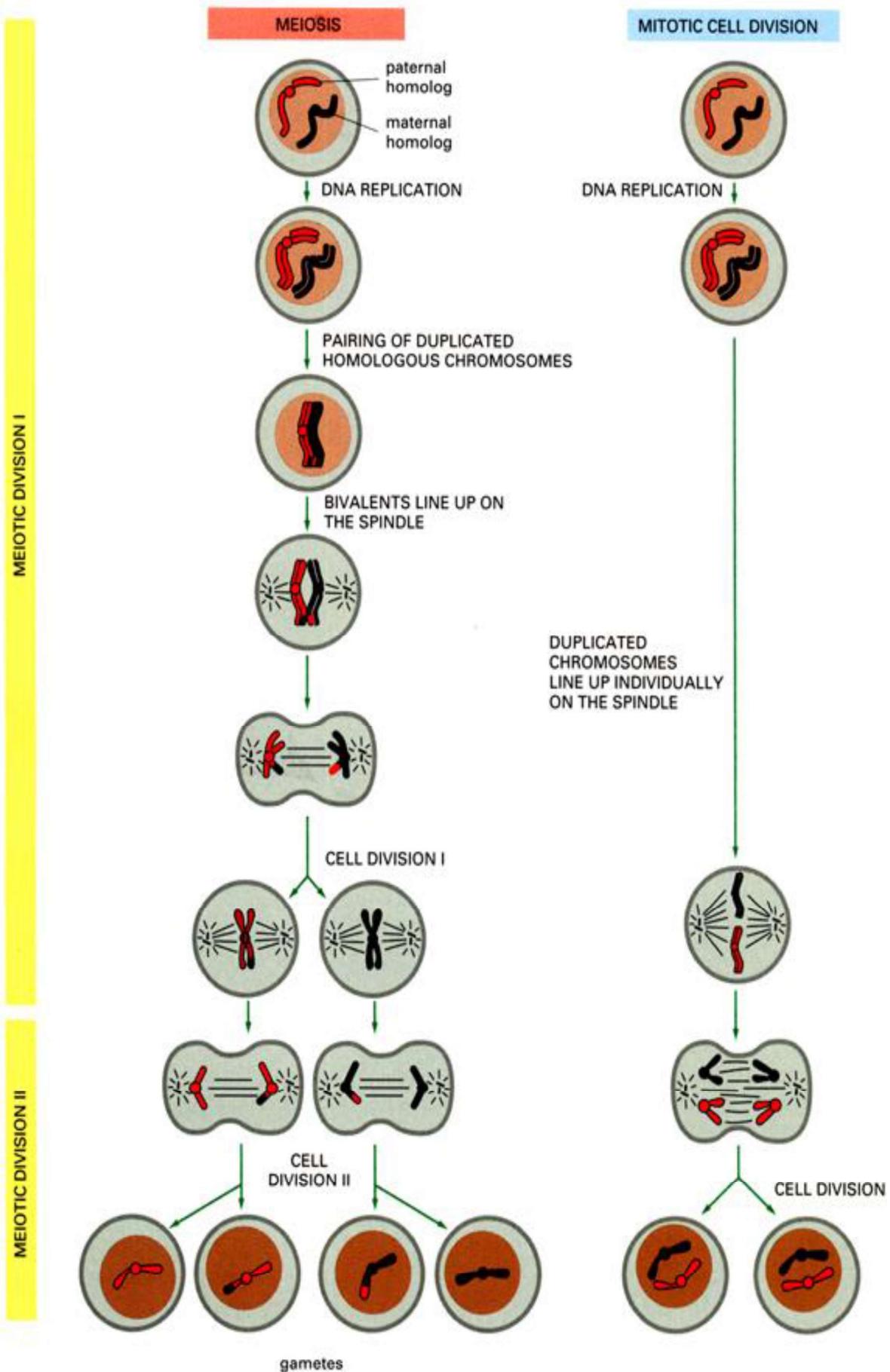
Telophase II: spindle shrinks, nuclear envelope reformed around each group of the chromosomes at each pole of the cell.

Cytokinesis: the cytoplasm divides forming four cells each of them contains half the number of chromosomes of the parent cell.

- The meiosis division aims to increase the number of produced cells (gametes), containing half the number of species chromosomes.

- When the male gamete (n) combines with the female gamete (n), the Zygote is formed ($2n$).





Differences between Mitosis and Meiosis:

	Mitosis	Meiosis
Number of divisions	one	two
Number of daughter cells	two	four
Genetically identical?	Yes	No
Chromosomes	Same as parent	Half of parent
Where?	Somatic cells	Sex cells
When?	Throughout life	At sexual maturity
Role	Growth and repair	Sexual reproduction

Cytoplasmic inheritance

There are many exceptions to the rule in genetics.

1- not all inherited characters are determined by genes located in the nucleus.

2- A small minority are controlled by genes located in cell organelles in the cytoplasm i.e. **cytoplasmic genes**, and these of course are exceptions to the chromosome theory of inheritance.

3-These genes are **extrachromosomal** (i.e. outside the chromosomes) and not subject to the normal rules of Mendelian heredity.

Plastid inheritance in *Mirabilis*:

1-The cytoplasm of plants contains small particles called **plastids**.

2- Plastids are of two types, **green** are **chloroplasts** and the **colorless** are **leucoplasts**.

In ***Mirabilis Jalapa, three types of branches occur.

They are **green**, **variegated** and **colourless**.

1) **Green branches** contain green plastids in their leaves,

2) **Variegated branches** contain green plastids and colorless plastids. So the leaves have white spots.

3) **Colorless branches** are due to the presence of colorless plastids.

a. **Seeds collected from green branches** produce only green plants.

b. **Seeds collected from white branches** produce only white plants

(Which cannot survive because of the absence of chlorophyll).

c. **Seeds collected from variegated branches** produce three kinds of plants, namely green, variegated and colorless

Green branches → Seeds → All green plants

Colorless branches → Seeds → All colorless plants

Variegated branches → Seeds → Three types of plants

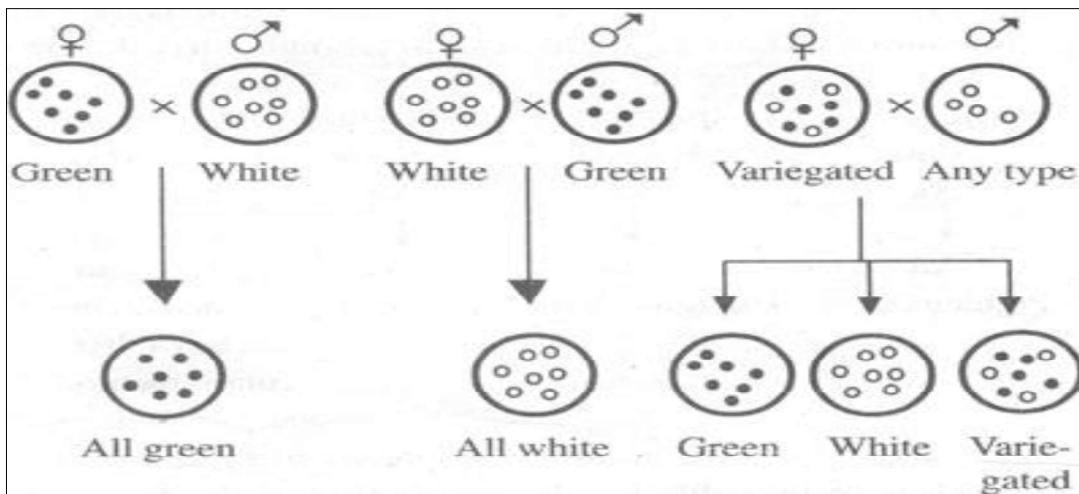
1- When **flowers on a green branch** are **pollinated with pollen from a colorless branch**.....all the resulting offspring are **green**.

2- When **flowers on a colorless branch** are **pollinated by pollen from a green branch**..... all the resulting offspring are **colorless**.

3- When **flowers on variegated branch** are **pollinated by pollens from any branch**..... all the **three types** of offspring are produced.

****These experiments show **that the phenotype of the off-springs is determined by the parent who contributed the egg**. This is because the **zygote** receives cytoplasm with plastids only from the egg.

***In eukaryote organisms **the zygote normally receives the bulk of its cytoplasm from the egg cell** and the male gamete contributes only little more than a nucleus.

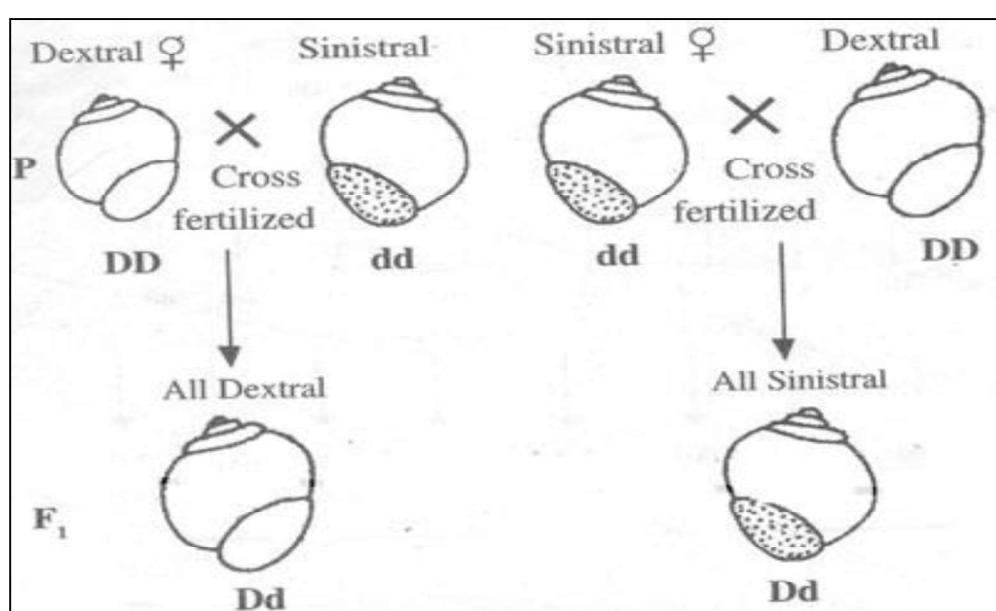


Shell Coiling in Snail

- In the snail **Limnaea**, the nature of shell coiling is a **cytoplasmic inheritance**.
- The phenotype of the offspring is determined by the genotype of the female parent. This phenomenon is called **maternal inheritance**.
- There are two types of shell coiling, namely **dextral** and **sinistral**.
 - In **dextral**, the coiling is in the **clockwise** direction when viewed from the apex.
 - In **sinistral**, the coiling is in the **anticlockwise** direction.
- The **dextral** shell is **dominant** and is controlled by dominant genes **DD**.
 - The **sinistral** shell is **recessive** and is controlled by recessive genes **dd**.
- When a female dextral snail (**DD**) is crossed with a male sinistral snail

(**dd**), all the F_1 snails (**Dd**) are **dextral** like the female parent.

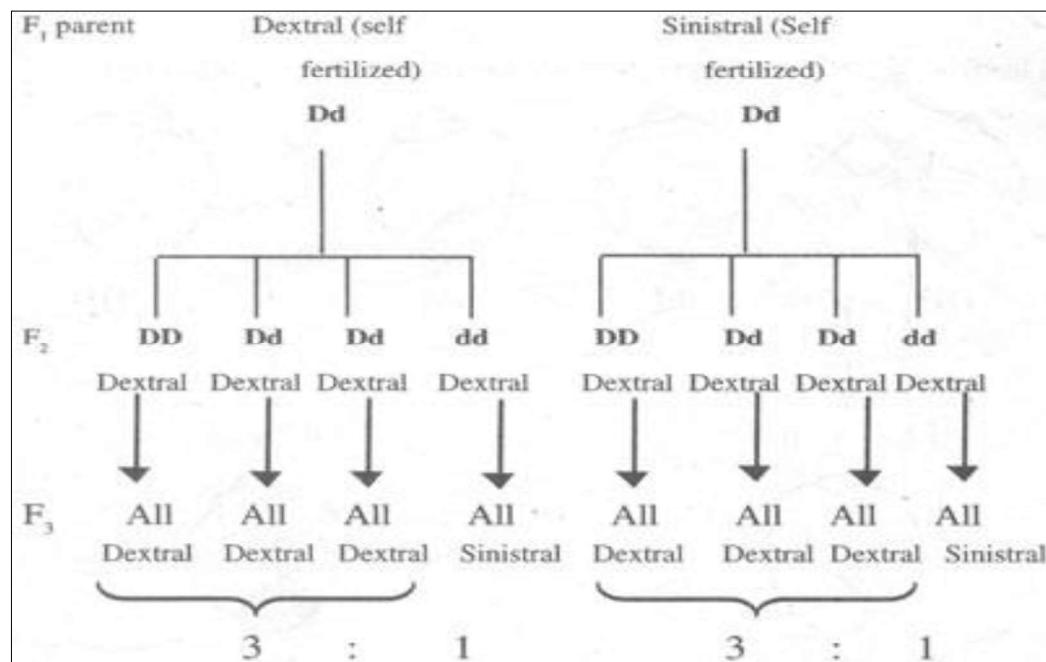
- When a female sinistral snail (**dd**) is crossed with a male dextral snail (**DD**), all the F_1 snails (**Dd**) are sinistral like the female parent.
- In the above two crosses, the F_1 snails have the **same genotypes**, but they have **different phenotypes**. Here, the **phenotype of the offspring is determined by the genotype of the mother**.
- In the first cross, **the offspring has dextral shell because the mother's genotype is DD**.
- In the second cross, **the offspring has sinistral shell because the mother's genotype is dd**. Thus in reciprocal crosses, the results are different.



The **F_2 generation** is obtained by self-fertilization of a single snail as the snail is **hermaphrodite**.

- 1- When a **dextrally coiled** F_1 snail (**Dd**) is self-fertilized, the F_2 's offsprings appear in the genotypic ratio **1DD: 2Dd: 1dd**. But phenotypically, all the F_1 individuals are **dextral** because the parents genotype (**Dd**) has a dominant gene **D**.
- 2- When a **sinistral** F_1 snail (**Dd**) is self-fertilized, all the F_2 offspring are **dextral** because the parent's genotype (**Dd**) has a dominant gene **D**.

- The inheritance of shell coiling follows **a simple Mendelian character**. In the F_2 generation, the genotypes appear in the ratio **1DD: 2Dd: 1dd**. However the phenotypic ratio **3:1** of F_2 generations appears only in the F_3 's generation. This is due to delayed inheritance. Inheritance of shell coiling in F_2 and F_3 generations



Karyotype and Chromosomal Aberrations

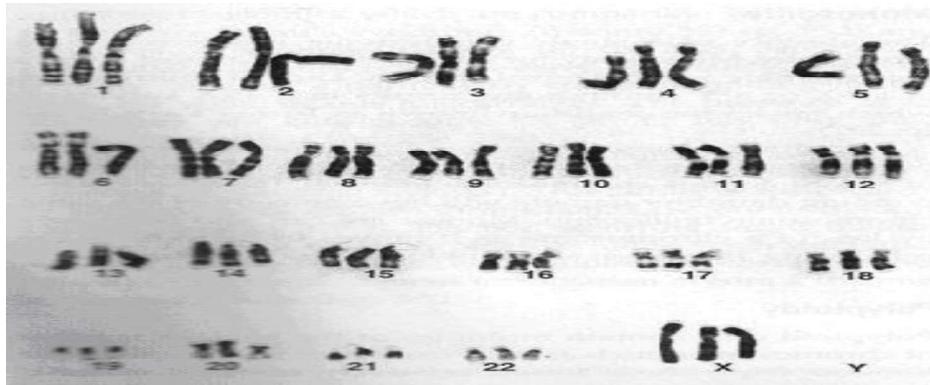
Chromosomal abnormalities

There are two types of abnormalities:

- 1- Numerical changes (changes in chromosome number).
- 2- Structural changes (changes in the internal structure or rearrangement of the genetic material within or between individual chromosomes).

1- Numerical changes in chromosomes:

- a- **Euploidy:** changes which involve the addition or loss of complete sets of chromosomes.
- the individuals may be:
 - **Haploid (n)** carry one entire chromosomal set.
 - **Diploid (2n)** two entire chromosomal sets.
 - **Triploid (3n)** three entire chromosomal sets.
 - **tetraploid(4n)** four entire chromosomal sets.



The normal that the individuals are diploid (2n), while the others will be abnormally.

The organisms have more than two sets of chromosomes (2n) are referred to as polyploidy (rarely found).

b- **Aneuploidy:** in which changes involve the addition or loss of individual chromosomes.

There are several types:

trisomic ($2n+1$) → in which one chromosome added to the two entire chromosomal sets.

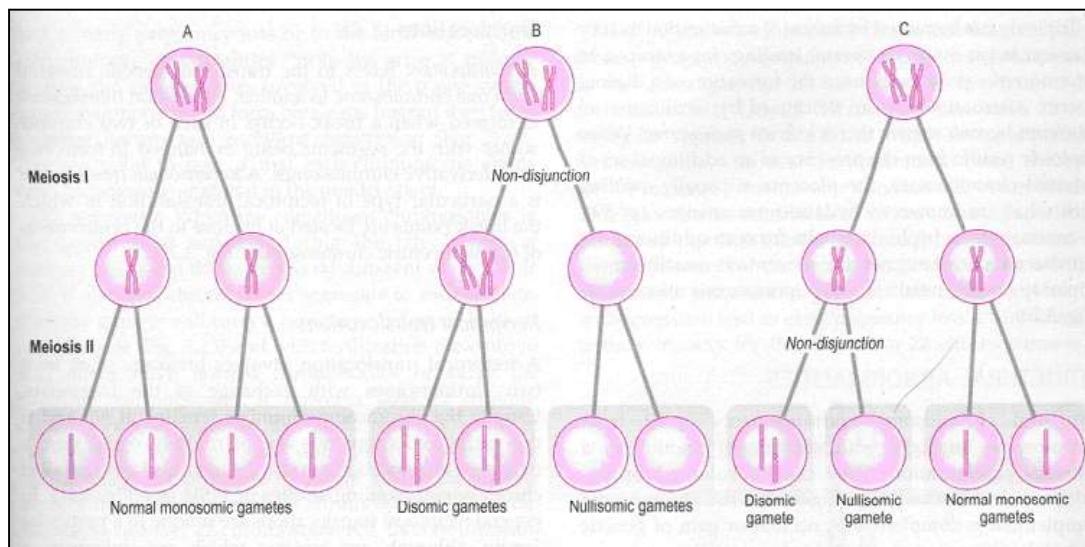
tetrasomic ($2n+2$) → in which two chromosomes added to the two entire chromosomal sets.

Monosomic ($2n-1$) → in which one chromosome lossed from the two entire chromosomal sets.

nullisomic ($2n-2$) → in which a pair of chromosomes lossed from the two entire chromosomal sets.

Aneuploidy can arise during mitosis and meiosis due to:

- 1- Non disjunction of one or more chromosomes at anaphase.
- 2- Delayed movement of chromosome at anaphase.



**** Trisomy in man ex: Trisomy 21 (Downs Syndrome)**

- Occurance I ---- 600 birth

Affected children have:

- mengolian eyes(epicanthal fold) –mentally retarded
- a characteristic facial appearance
- may have associated congenital heart disease
- Risk of acute leukaemia.



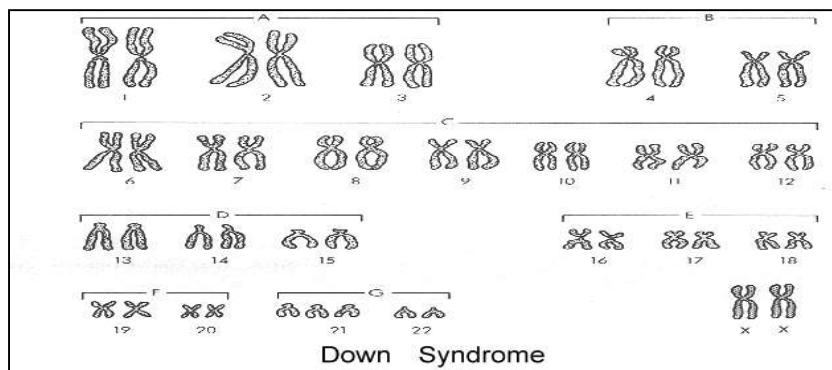
Down syndrome frequency correlates with the age of mother.

The cause of non-disjunction is

- Advancing maternal age.

- Environmental agents, such as ionizing radiation

- Delayed fertilization after ovulation.



Aberrations in sex chromosomes:

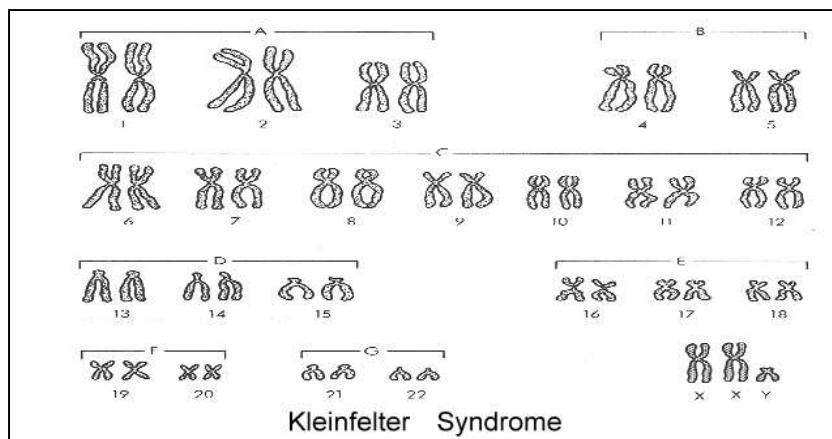
Klinefelters Syndrome (47 chromosome)

- External appearance are males (44+xxY)

- 1 in each 500 birth
- mentally retarded
- long arms and legs
- sterile

- small testes so, produce very little testosterone hormone.

- Enlargement of the breast
- increase incidence to breast cancer



Causes:

- Fertilization of non disjunctioned ovum (xx) by normal sperm (y) giving (xxy).
- Fertilization of normal ovum (x) by non disjunctioned sperm (xy) giving (xxY).

Turner syndrome (45 chromosomes) (44+X)

- 1 or 3 in each 10000 births
- external features female
- sterile
- Very small ovaries
- two small immature breasts
- a broad chest

Causes:

Due to fertilization of gamete (x) by an empty gamete (0) giving (x0).

2- Structural changes in chromosomes:

Which involve changes in chromosome structure through the loss, gain or rearrangement of particular segments.

- The structural changes are caused by breaks in the chromosome; the broken segments may follow the following:
 - 1- They may remain un united.
 - 2- Immediate reunion of the same broken ends may occurred.
 - 3- Exchange between different breaks.
- The structural changes may be **balanced** such as **inversion**, **reciprocal translocation**.

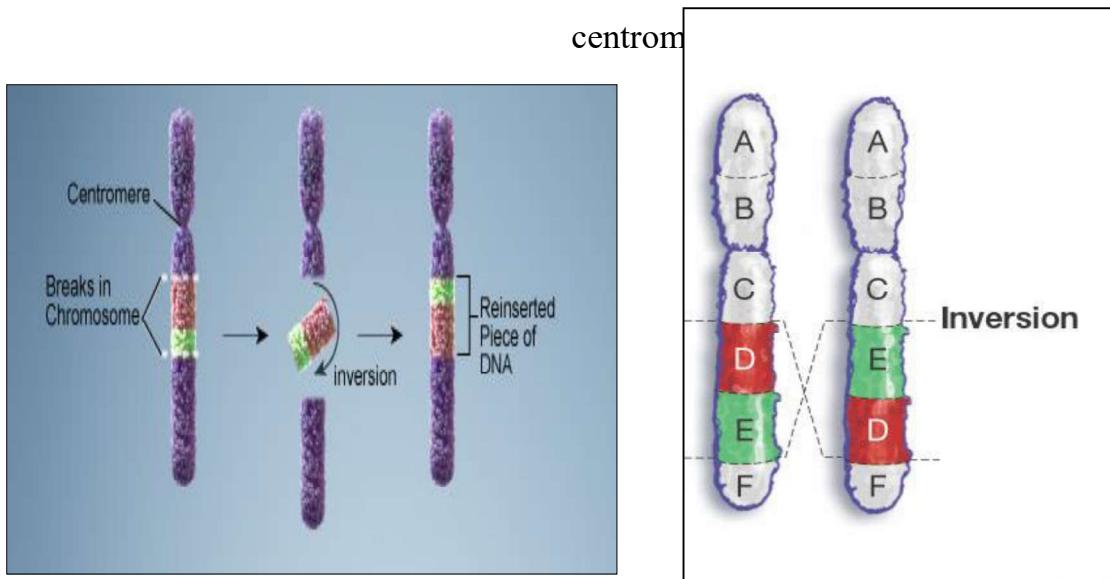
Or **imbalanced** such as **deletion**, **duplication** and **nonreciprocal translocation**.

Balanced structural changes:**1- Inversion:**

A portion of the chromosome has broken off, turned upside down (inverted 180°) and reattached, therefore the genetic material is inverted.

There are two types of inversion:

- a) **pericentric inversion:** the inversion includes the centromere.
- b) **Paracentric inversion:** the inversion does not include the centromere

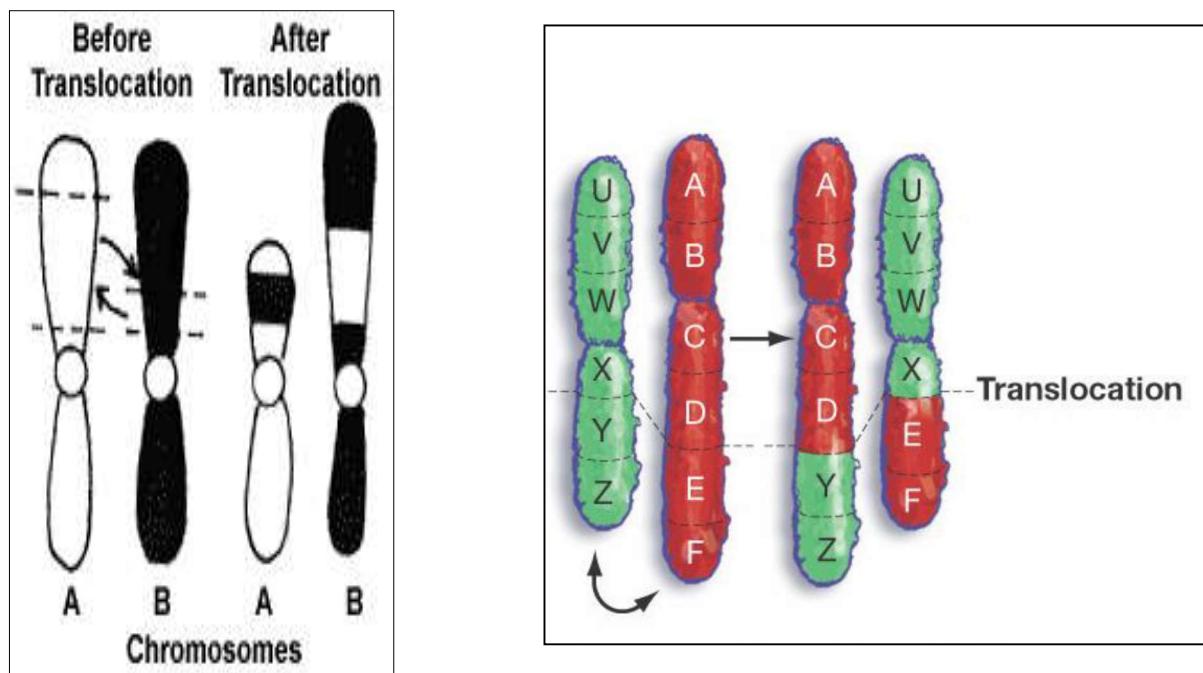


2- Translocation: in which a segment of a chromosome changes position.

There are two types: reciprocal and non-reciprocal translocations.

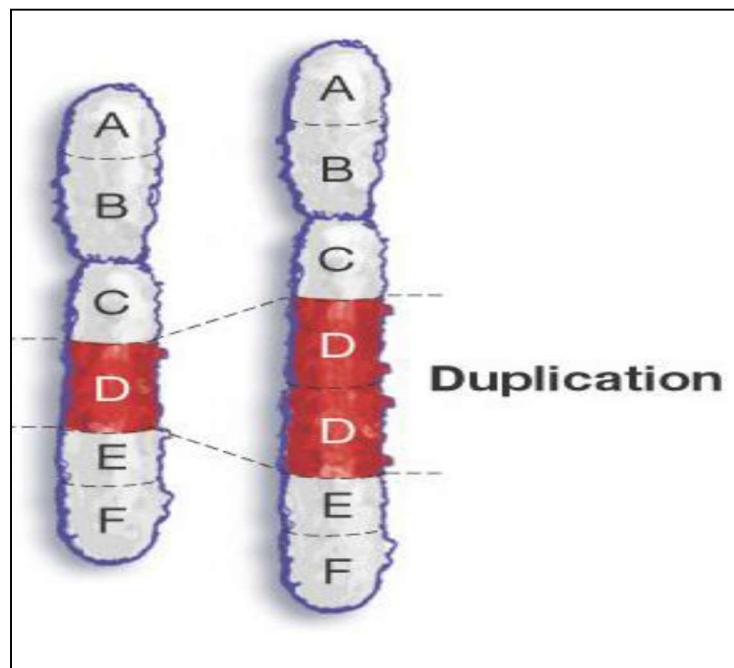
- a) **Reciprocal interchromosomal translocations:** occur between two chromosomes.
- b) **Non reciprocal interchromosomal translocations:** occur on the same chromosome.
- c) **Non reciprocal interchromosomal translocations:** occur between two chromosomes.
 - The change in location of a segment may alter the regulation of a gene in the segment.
 - The **unregulated gene can cause cancer**

EX: Translocation between chromosomes 9 and 22, Creating the Philadelphia chromosome which causes about 90% of the cases of chronic myeloleukemia.



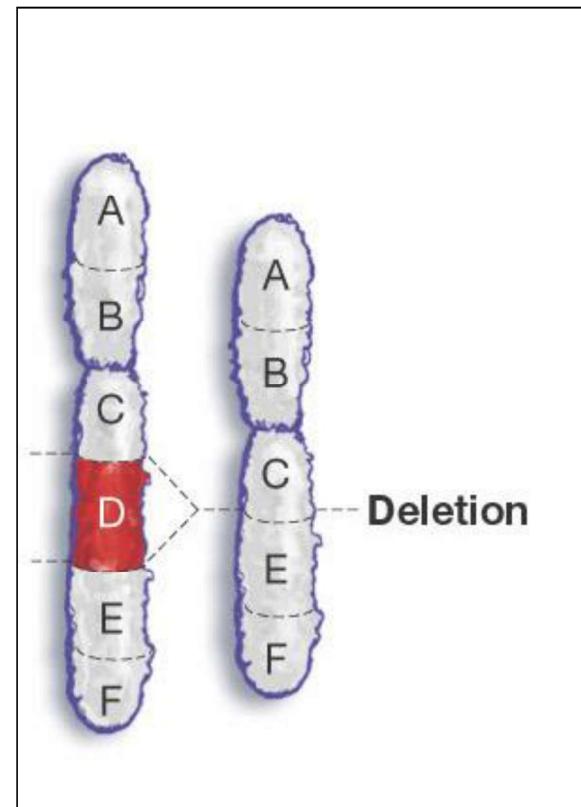
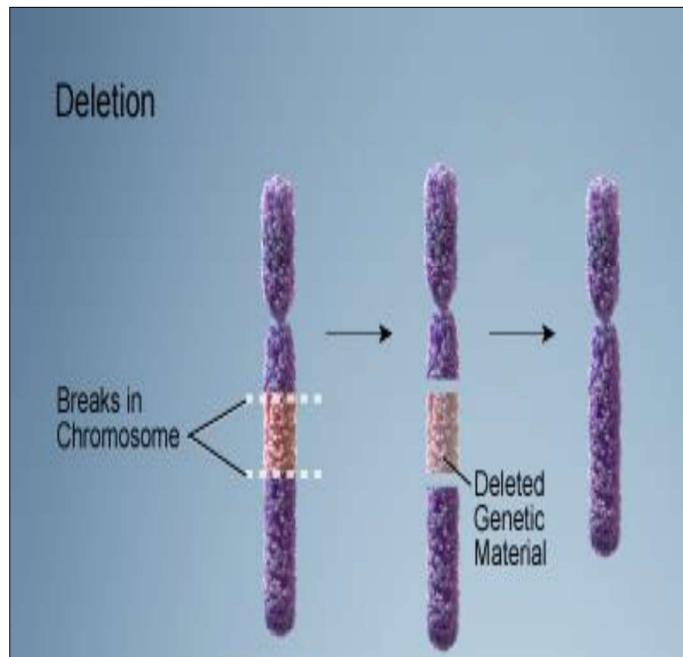
3- Duplication: a segment of chromosome is doubled probably due to unequal crossing over resulting in extra genetic material.

A B C D E ----- A B C DD E



4- Deletion: A portion of the chromosome is missing or deleted.

Causing Known disorders in humans like **Jacobsen syndrome**,
also called the terminal 11q deletion disorder.



Mutations

Definition: is a Change in the nucleotide sequence of DNA .

The mutations may be:

Somatic mutations: - that occur in somatic cells of an individual.

- Not inherited to the offspring.

Germline (gamete) mutations: - occur in gametes (sperm, ovum).

- Can be inherited to the offspring.

Origin of mutations:

- 1- **Spontaneous mutations:** which happen spontaneously in nature without man interference under the effect of chemicals, radiation, viruses.
- 2- **Induced mutations:** which induced by man to make desirable changes in characteristics of some plants, animals and man using chemicals **such as** Colchicine's, X- ray, Ultraviolet radiation and Gamma radiation.

Types of mutations:

Gene mutations: a change in nucleotide sequence of a gene.

It includes **point mutations** and **frame shift mutations**.

- **Point mutations:** Change of a single nucleotide
- Includes, the deletion, insertion, or substitution of ONE nucleotide in a gene.

Substitution when a base is substituted

Guanine for Cytosine	CGG <u>CCC</u> AAT
	CGG <u>CGC</u> AAT

Insertion - when a base is added

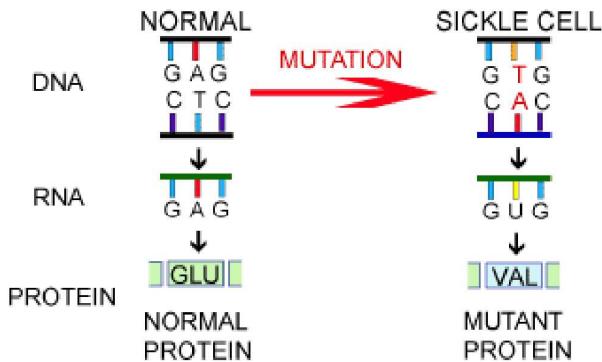
Guanine is added	CGG <u>CCC</u> AAT
	CGG <u>CGC</u> CAA T

Deletion - the loss of a base

loss of Cytosine

CGG CCC AAT
CGG CCA A T

EX: sickle cell anemia is an example of **point mutation**



Frame shift Mutation:

- Inserting or deleting one or more nucleotides
- Changes the “reading frame” like changing a sentence
- Proteins built incorrectly

Frame Shift insertion (“A” added):

Original THE FAT CAT ATE THE WEE RAT.

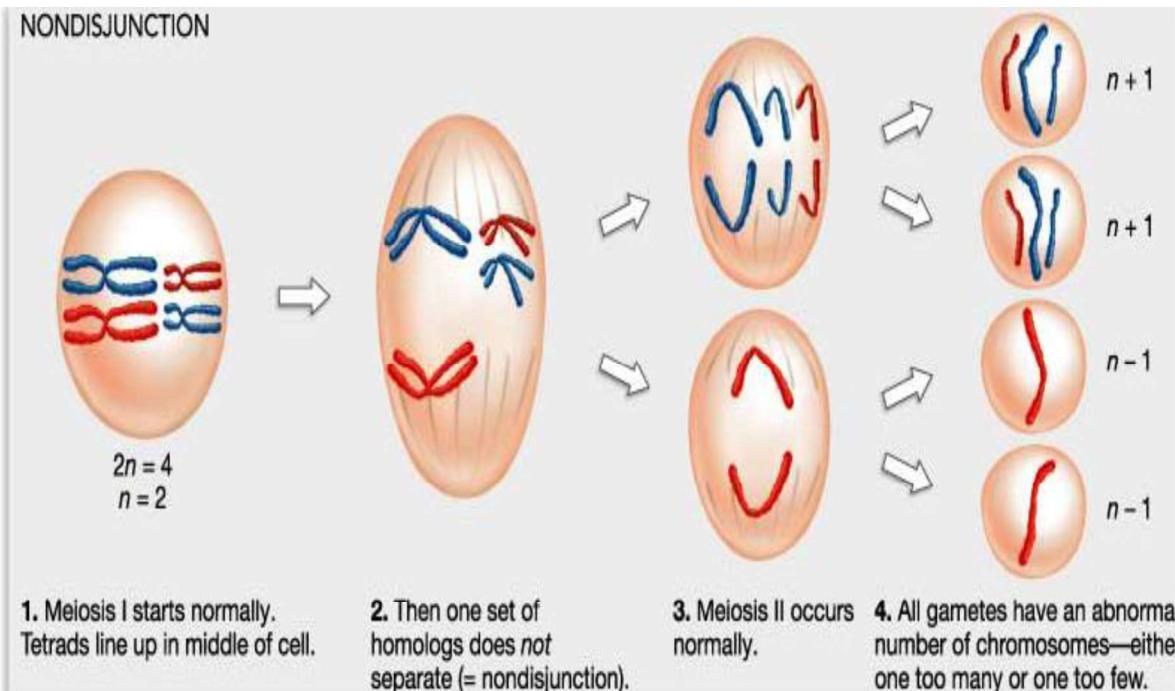
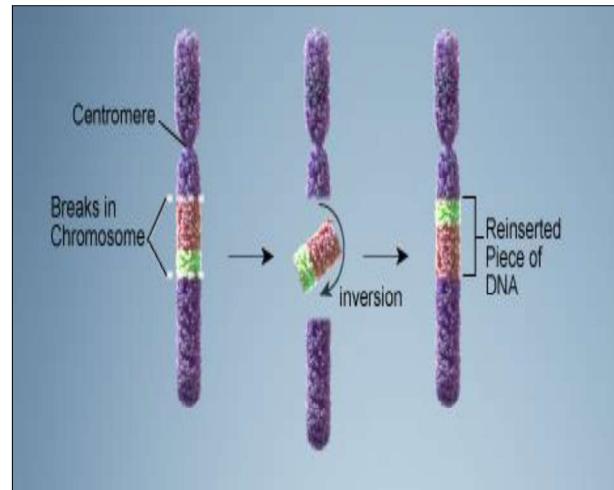
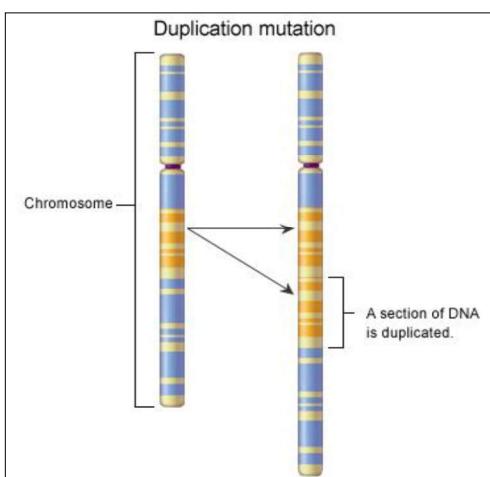
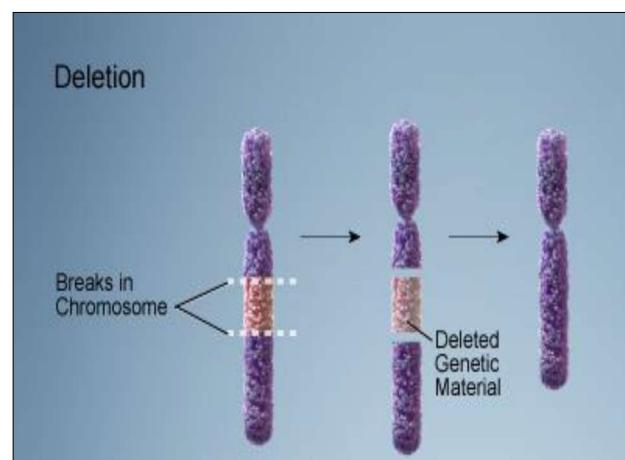
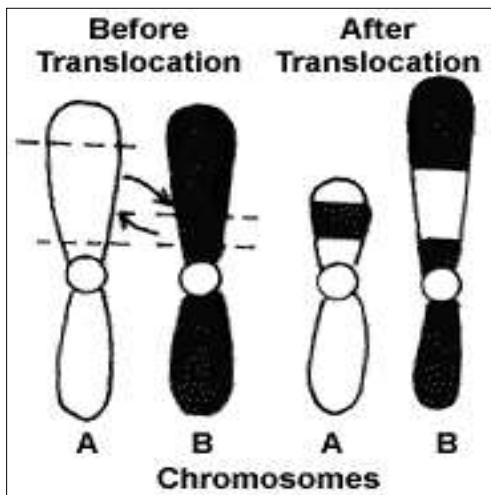
Frame Shift THE FAT CAA TET HEW EER AT.

Frame Shift deletion (“H” deleted):

Original THE FAT CAT ATE THE WEE RAT.

Frame Shift TEF ATC ATA TET HEW EER AT.

Chromosomal mutations: a change in the structure of chromosome through loss, gain, translocation, duplication and nondisjunction.



Original Chromosome



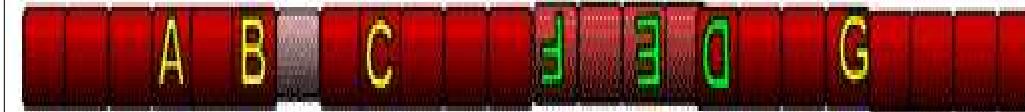
Duplication



Deletion



Inversion



Inversion



Molecular Genetics

DNA

In 1953: Watson & Crick introduced a model for the double helix structure of DNA and obtained Nobel prize in 1962.

- The previous studies on different microorganisms proved that the material that transmit the genetic characteristics from generation to another generation is the nucleic acid DNA (Deoxy ribo Nucleic Acid)

- Nucleic acids are polymers (Long chains of monomers, called

Nucleotides), **each nucleotide consists of :**

1-pentose Sugar (deoxy-ribose in DNA , ribose in RNA)

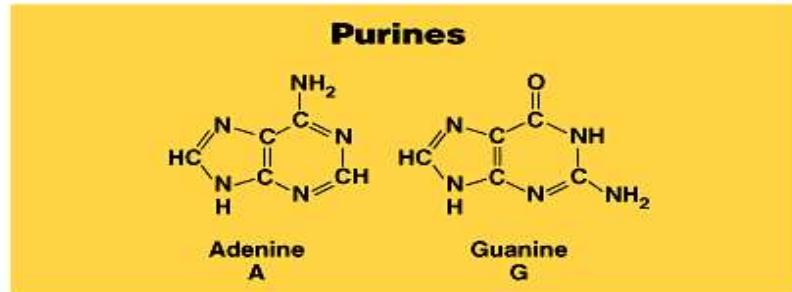
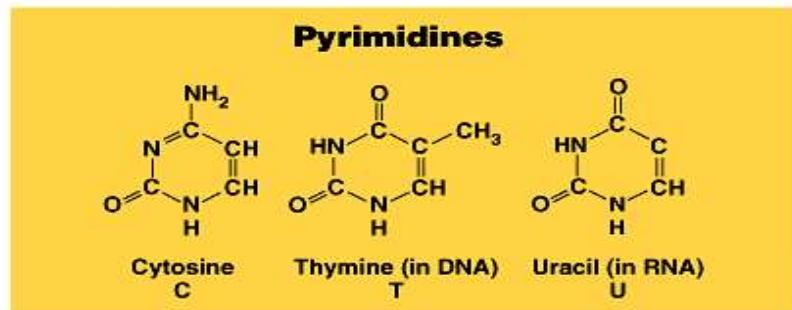
2- Phosphate group (PO₄)

3- Nitrogenous Bases which divided in to purines and pyrimidines

purines : consists of double rings Adenine (A) Guanine (G)

pyrimidines : consists of single ring Cytosine (C) Thymine (T)

OR Uracil (U) in RNA

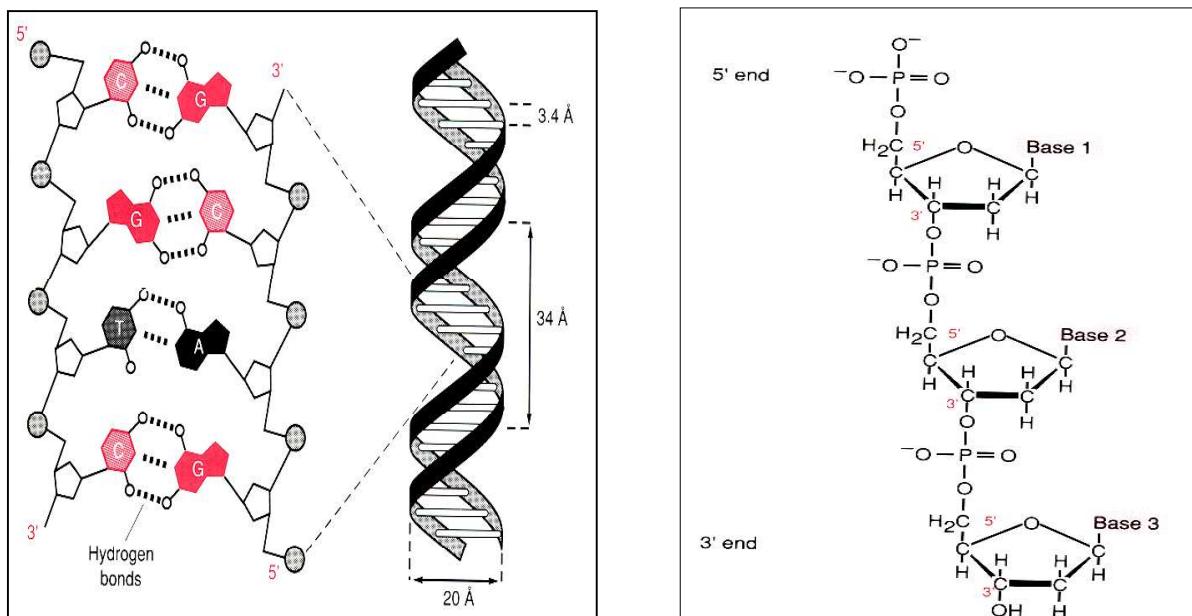


Characters of DNA:

- Copy itself
- Repair itself
- Pass from Generation to another generation
- Store the Genetic information

Structure of DNA double helix:

- 1- The DNA molecule is composed of 2 chains (strands) of nucleotides arranged in a double helix.
- 2- The backbone of each chain is formed by phosphodiester bonds between the 3' and 5' carbons of adjacent sugars.
- 3- The 2 chains are held together by hydrogen bonds which are two in case of (A , T) and three in case of (G , C) via Nitrogenous bases forming base pairs.
- 4- DNA has a polarity, i.e. DNA is -very charged.



- 5- If we know the sequence of bases on one strand, we know the sequence on the opposite strand.

6- The two strands are **complementary**.

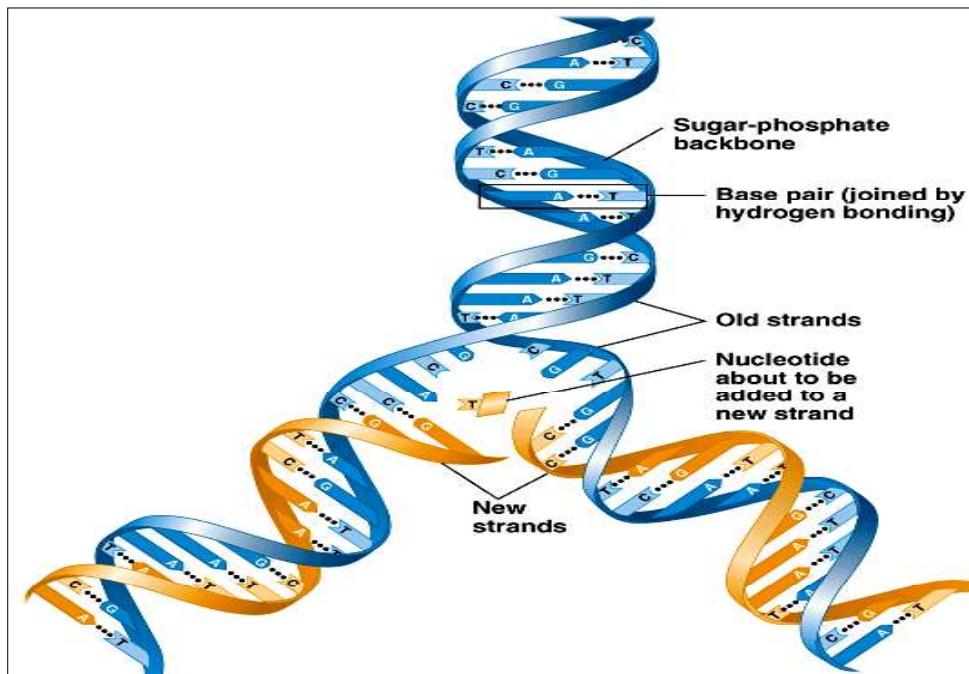
e.g. If a segment of one strand has the base sequence: **AGGTCCG**

the other strand must have the sequence: **TCCAGGC**

How genetic information is maintained from one generation to the next?

1- Complete **Replication of DNA** is essential to maintain genetic continuity from cell to cell.

- This happens during interphase.
- The helix of DNA unwinds by **Helicase enzyme** splitting the DNA molecule into two strands, each strand can serve as a template for the synthesis of a new strand.
- Replication of DNA is semi-conservative since one strand is new ‘daughter’ and the other is old ‘parent.



Structure of RNA

RNA (Ribonucleic acid) contains ribose sugar (5 carbons).

RNA contains Uracil (U) base instead of T in DNA.

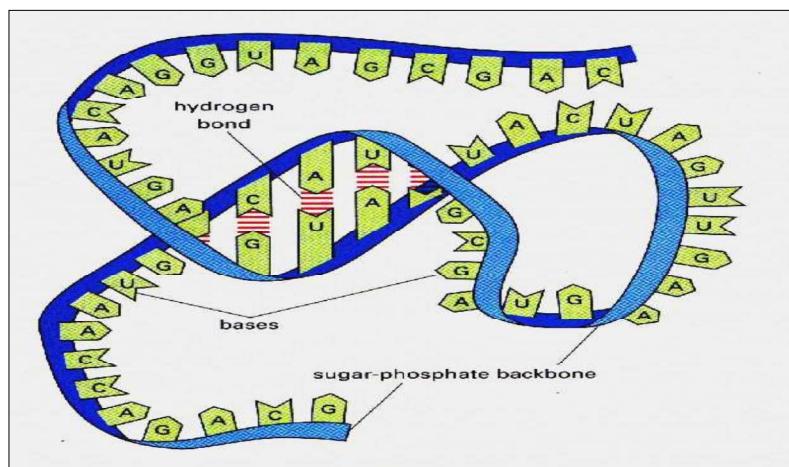
RNA is present in the cytoplasm and in high concentrations in the nucleolus.

Types of RNA: rRNA, tRNA, mRNA

rRNA: the main component of ribosomes(the main site of protein synthesis in the cytoplasm).

tRNA: which bring the correct amino acid to ribosome site.

mRNA: carry the genetic information from DNA to the cytoplasm.



	DNA	RNA
Structure	Double strand	single strand
Length	Long	short
Bases	A, G, C, T	A, G, C, U
Sugar	Deoxyribose	Ribose
Found	Mainly in Nucleus and Mitochondria.	Cytoplasm and in high concentration in nucleolus

Protein synthesis

We must know that:

Each three bases form a codon

Each codon represents an amino acid.

several codons represent the same amino acid (e.g. triplet bases CUC,

CUU, CUA, CUG represent **Leu.**(Leucin amino acid).

- Each mRNA strand has:

1- **Start codon**: ‘**AUG**’ represent Methionine (Met).

2- **Stop codons**: **UAA, UAG or UGA** that does not encode amino acid, but terminates translation.

		Second base of codon									
		U	C	A	G						
First base of codon	U	UUU UUC UUA UUG	Phenylalanine phe	UCU UCC UCA UCG	Serine ser	UAU UAC UAA UAG	Tyrosine tyr	UGU UGC UGA UGG	Cysteine cys	U C A G	U
	C	CUU CUC CUA CUG	Leucine leu	CCU CCC CCA CCG	Proline pro	CAU CAC CAA CAG	Histidine his	CGU CGC CGA CGG	Arginine arg	C A G	U
	A	AUU AUC AUA AUG	Isoleucine ile	ACU ACC ACA ACG	Threonine thr	AAU AAC AAA AAG	Asparagine asn	AGU AGC AGA AGG	Serine ser	U C A G	U
	G	GUU GUC GUA GUG	Methionine met (start codon)	GCU GCC GCA GCG	Alanine ala	GAU GAC GAA GAG	Lysine lys	GGU GGC GGA GGG	Arginine arg	C A G	C
			Valine val				Aspartic acid asp		Glycine gly		A

The protein synthesis process occur in the cytoplasm by several steps:

- 1- **Transcription:** mRNA firstly transcribed from one template strand of DNA (3` and 5` DNA strand)
 - mRNA is synthesized in the 5` to 3` direction (has the same sequence of 5`-3` DNA strand) in the nucleus.

2- the single mRNA strand experts from nucleus to the cytoplasm at ribosome(consists two sub units small and large).

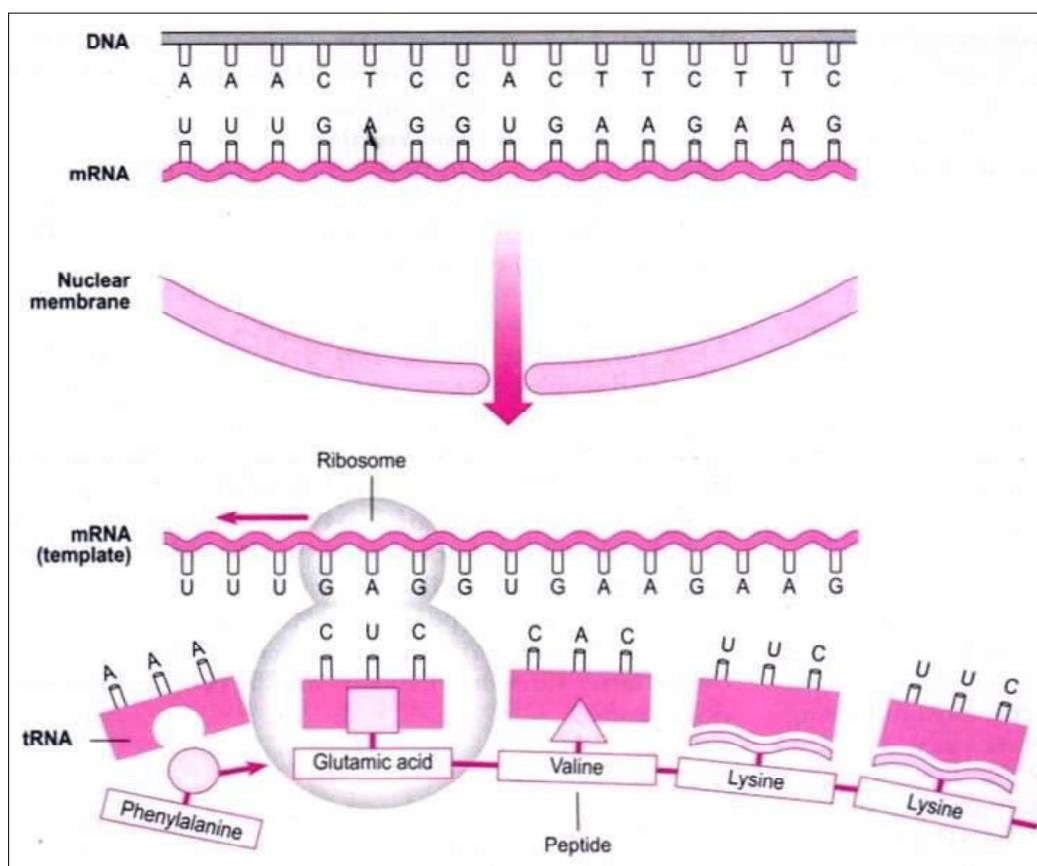
3- Small ribosomal subunit covalently binds to a tRNA carrying AUG (met) at 5' end of the mRNA.

4- Large ribosomal subunit binds to the small subunit.

5- Ribosome moves to the next codon and tRNA brings the complementary (anti) codon (amino acid) and attach to the growing protein chain.

6- The ribosome moves again to the next codon, and the process is repeated till “stop codon” comes up.

The polypeptide chain (protein) is formed and the two ribosomal sub units separated.



Population genetics

Population genetics: is the study of [allele frequency](#) under the influence of the four main evolutionary processes: [natural selection](#), [genetic drift](#), [mutation](#) and migration ([gene flow](#)).

A population: is a set of organisms of the same species in which any pair of members can breed together.

For example, the moths of the same species living in an isolated forest are a population.

- A gene in this population may have several alternate forms, which account for variations between the phenotypes of the organisms.
- **An example:** a gene for coloration in moths that has two alleles: black and white.

A gene pool: is the complete set of alleles for a gene in a single population.

Allele frequency: the fraction of the genes in the pool that is composed of that allele.

The Hardy-Weinberg principle:

States that the frequencies of alleles (variations in a gene) in a sufficiently large population will remain constant if the only forces acting on that population are the random reshuffling of alleles during the formation of the sperm or egg, and random combination of the alleles in these sex cells during fertilization. Such a population is said to be in ***Hardy-Weinberg equilibrium***.

Terms of equilibrium:

- Infinitely large population size
- No migration (Isolation) in to or from the population.
- No net mutations.
- Random mating.
- No natural selection

If there are two alleles: the dominant allele is denoted **A** and the recessive is **a** and their frequencies are denoted by p and q ; freq (**A**) = p ; freq (**a**) = q ; $p + q = 1$.

- If the population is in equilibrium, then we will have
 - freq(**AA**) = p^2 for the **AA** homozygotes in the population
 - freq(**aa**) = q^2 for the **aa** homozygotes
 - freq(**Aa**) = $2pq$ for the heterozygotes
- **This example is the simplest case:**
 - If there are 2 alleles, one is dominant and the other is recessive

if **p** = frequency of one allele (dominant)

q = frequency of the other (recessive)

Then: $p + q = 1$

probability of AA(homozygote dominant) = p^2

probability of aa(homozygote recessive) = q^2

probability of Aa (heterozygote) = $2pq$

• **Therefore:** $p^2 + 2pq + q^2 = 1$

- **Uses of Hardy-Weinberg**

- 1- We can calculate the frequency of a gene in a population if you know the frequency of the genotypes.
- 2- important in genetic disease counseling.

The four processes that change the genetic equilibrium:

Natural selection: is the process by which some individuals in a population of organisms will survive more successfully than others in their current environment.

- Natural selection acts on the phenotype, or the observable characteristics of an organism, but the genetic (heritable) basis of any phenotype which gives a reproductive advantage will become more common in a population.

Natural selection remains the primary explanation for evolution.

Genetic drift

the change in the gene frequency of a very small population due to probability and chance.

That is, the alleles in the offspring in the population are a random sample of those in the parents. And chance has a role in determining whether a given individual survives and reproduces.

- A population's allele frequency is the fraction or percentage of its gene copies compared to the total number of gene alleles that share a particular form.
- Genetic drift is an important evolutionary process which leads to changes in allele frequencies over time.
- It may cause gene variants to disappear completely, and thereby reduce genetic variability.

- In contrast to natural selection, which makes gene variants more common or less common depending on their reproductive success,
- The effect of genetic drift is larger in small populations, and smaller in large populations.

Mutation

Mutations are changes in the DNA sequence and are caused by radiation, viruses, transposons and mutagenic chemicals, as well as errors that occur during meiosis or DNA replication.

Migration: some individuals of a population migrate in to or out of the population which lead to gain or loss of some genes and thus lead to change in allele frequencies and then lead to gene flow.

(Gene flow):

Gene flow is the exchange of genes between populations, which are usually of the same species.

- Examples of gene flow within a species include the migration and then breeding of organisms, or the exchange of pollen.
- Migration into or out of a population can change allele frequencies, as well as introducing genetic variation into a population.
- Gene flow is hindered by mountain ranges, oceans and deserts or even man-made structures such as the Great Wall of China, which has hindered the flow of plant genes.

For example, if a species of grass grows on both sides of a highway, pollen is likely to be transported from one side to the other and vice versa. If this pollen is able to fertilize the plant where it ends up and produce viable offspring, then the alleles in the pollen have effectively been able to move from the population on one side of the highway to the other.

Basics of Carcinogenesis

Cell Biology and Cancer

What Is Cancer?

Cancer results from a series of molecular events that fundamentally alter the normal properties of cells. In cancer cells the normal control systems that prevent cell overgrowth and the invasion of other tissues are disabled. These altered cells divide and grow in the presence of signals that normally inhibit cell growth; therefore, they no longer require special signals to induce cell growth and division. As these cells grow they develop new characteristics, including changes in cell structure, decreased cell adhesion, and production of new enzymes.

Genetics of Cancer

Only a small number of the approximately 35,000 genes in the human genome have been associated with cancer. Alterations in the same gene often are associated with different forms of cancer. These malfunctioning genes can be broadly classified into three groups. The first group, called proto-oncogenes, produces protein products that normally enhance cell division or inhibit normal cell death. The mutated forms of these genes are called oncogenes. The second group, called tumor suppressors, makes proteins that normally prevent cell division or cause cell death. The third group contains DNA repair genes, which help prevent mutations that lead to cancer.

Tumor Suppressor Genes

The proteins made by tumor suppressor genes normally inhibit cell growth, preventing tumor formation. Mutations in these genes result in cells that no longer show normal inhibition of cell growth and division. The products of tumor suppressor genes may act at the cell membrane, in the cytoplasm, or in the nucleus. Mutations in these genes result in a loss of function (that is, the ability to inhibit cell growth) so they are usually recessive. This means that the trait is not expressed unless both copies of the normal gene are mutated. Using the analogy to a car, a mutation in a tumor suppressor gene acts much like a defective brake: if your car had two brakes and only one was defective, you could still stop the car.

Table 1. Some Genes Associated with Cancer

NAME	FUNCTION	EXAMPLES of Cancer / Diseases	TYPE of Cancer Gene
APC	regulates transcription of target genes	Familial Adenomatous Polyposis	tumor suppressor
BCL2	involved in apoptosis; stimulates angiogenesis	Leukemia; Lymphoma	oncogene
BLM	DNA repair	Bloom Syndrome	DNA repair
BRCA1	may be involved in cell cycle control	Breast, Ovarian, Prostatic, & Colonic Neoplasms	tumor suppressor
BRCA2	DNA repair	Breast & Pancreatic Neoplasms; Leukemia	tumor suppressor
HER2	tyrosine kinase; growth factor receptor	Breast, Ovarian Neoplasms	oncogene
MYC	involved in protein-protein interactions with various cellular factors	Burkitt's Lymphoma	oncogene
p16	cyclin-dependent kinase inhibitor	Leukemia; Melanoma; Multiple Myeloma; Pancreatic Neoplasms	tumor suppressor
p21	cyclin-dependent kinase inhibitor		tumor suppressor
p53	apoptosis; transcription factor	Colorectal Neoplasms; Li-Fraumeni Syndrome	tumor suppressor
RAS	GTP-binding protein; important in signal transduction cascade	Pancreatic, Colorectal, Bladder, Breast, Kidney, & Lung Neoplasms; Leukemia; Melanoma	oncogene
RB	regulation of cell cycle	Retinoblastoma	tumor suppressor
SIS	growth factor	Dermatofibrosarcoma; Meningioma; Skin Neoplasms	oncogene
XP	DNA repair	Xeroderma pigmentosum	DNA repair

What Causes Cancer?

The prevailing model for cancer development is that mutations in genes for tumor suppressors and oncogenes lead to cancer. However, some scientists challenge this view as too simple, arguing that it fails to explain the genetic diversity among cells within a single tumor and does not adequately explain many chromosomal aberrations typical of cancer cells. An alternate model suggests that there are “master genes” controlling cell division. A mutation in a master gene leads to abnormal replication of chromosomes, causing whole sections of chromosomes to be missing or duplicated.

Tumor Biology

Cancer cells behave as independent cells, growing without control to form tumors. Tumors grow in a series of steps. The first step is hyperplasia, meaning that there are too many cells resulting from uncontrolled cell division. These cells appear normal, but changes have occurred that result in some loss of control of growth. The second step is dysplasia, resulting from further growth, accompanied by abnormal changes to the cells. The third step requires additional changes, which result in cells that are even more abnormal and can now spread over a wider area of tissue.

Environmental Factors

Several environmental factors affect one's probability of acquiring cancer. These factors are considered carcinogenic agents when there is a consistent correlation between exposure to an agent and the occurrence of a specific type of cancer. Some of these carcinogenic agents include X-rays, UV light, viruses, tobacco products, pollutants, and many other chemicals. X-rays and other sources of radiation, such as radon, are carcinogens because they are potent mutagens.

Screening, Genetic Tests and Counseling

Early diagnosis of cancer greatly increases survival; therefore, regular exams for cancer can help to prevent deaths from cancer. These include mammograms and Pap tests for women, prostate cancer tests for men, colonoscopy exams for colon cancer, and regular physical exams for other types of cancer. Individuals with a strong family history of cancer should consider genetic tests for cancer and cancer risk counseling.

Anaplastic: A term used to describe cancer cells that divide rapidly and have little or no resemblance to normal cells.

Angiogenesis: Blood vessel formation. Tumor angiogenesis is the growth of blood vessels from surrounding tissue to a solid tumor. This is caused by the release of chemicals by the tumor.

Apoptosis: A normal series of events in a cell that leads to its death. Also called "programmed cell death."

Cyclins: Proteins that form complexes with cyclin-dependent kinases to control various steps in the cell cycle.

Dysplasia: Cells that look abnormal under a microscope but are not cancerous.

Hyperplasia: An abnormal increase in the number of cells in an organ or tissue.

Kinase: An enzyme that catalyzes the transfer of a phosphate group from ATP to another molecule, often a protein.

Oncogene: An altered form of a gene that normally directs cell growth. Oncogenes can promote or allow the uncontrolled growth of cancer.

Phytochemicals: Chemicals found in plants. Many of these chemicals are thought to reduce a person's risk of getting cancer.

Radioimmune therapy: Treatment with a radioactive substance that is linked to an antibody that will attach to the tumor when injected into the body.

Telomerase: An enzyme that replaces the repeat sequences at the ends of chromosomes that are lost during chromosome replication.

Transcription factor: A protein that influences transcription of another gene by binding to DNA.

Tumor suppressor gene: Genes that can suppress or block the development of cancer.

Types of Immunity

Innate immunity

The natural defense mechanism of all organisms is known as innate immunity.

Acquired immunity

The resistance developed by man during his life time is known as acquired

immunity. Acquired immunity is of two types namely active and passive.

Active immunity is the resistance developed by an individual in response to an antigenic stimulus. It involves production of immunologically active cells.

Natural active immunity is developed by the host in response to the antigen

that enters by natural infections. E.g.: A person attacked by measles or small

pox develops natural immunity as he recovers from the disease.

Artificial active immunity is attained by the host in response to the antigen

got by vaccination.

The immunity that non immune individuals acquires by receiving antibodies or sensitized white blood cells from another immune individual is known as

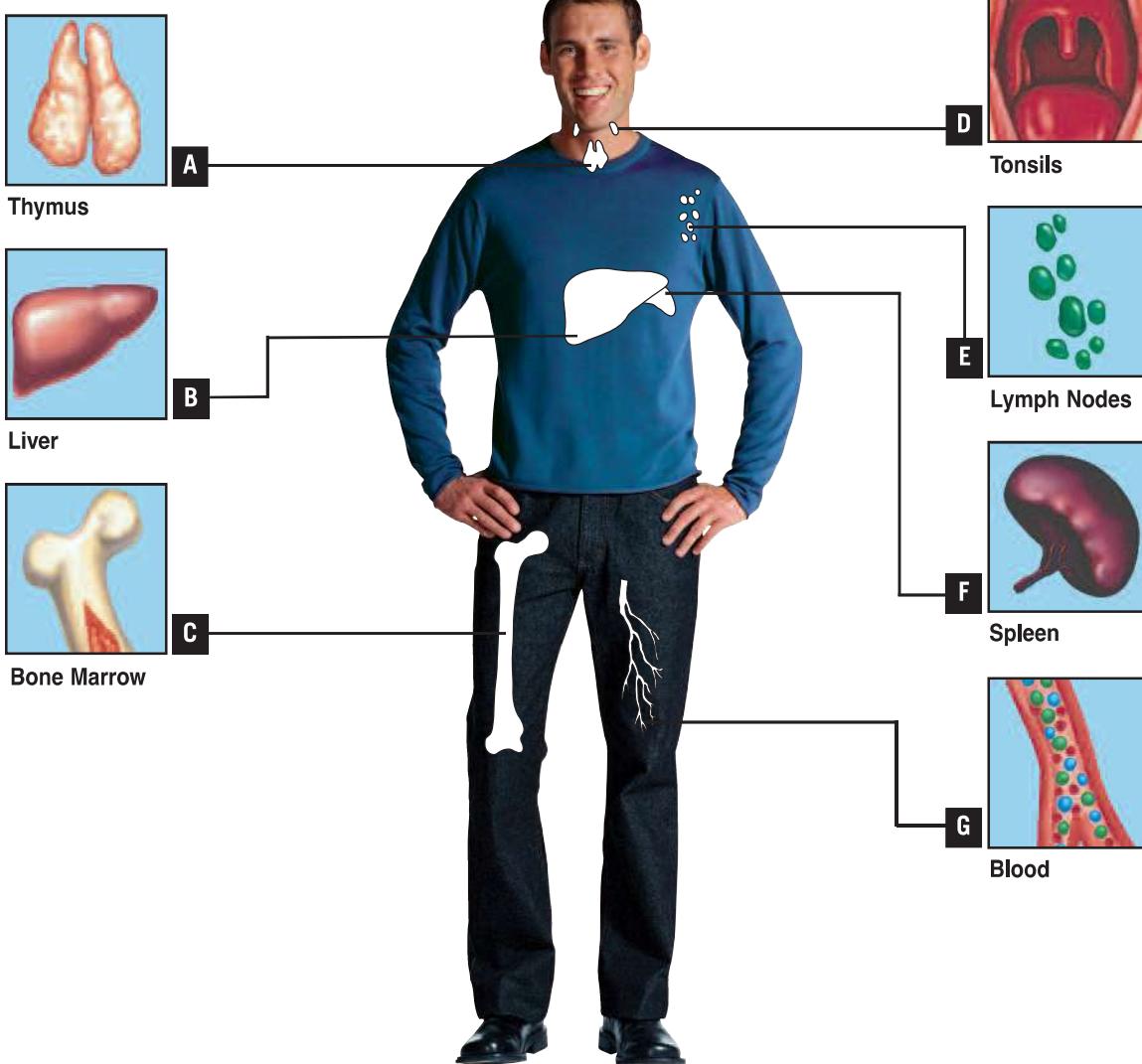
passive immunity. The immunity caused by passive immunization is less effective and inferior than that caused by active immunization. The main advantage of this is that it is immediate in its action.

The immunity transferred from the mother to the child passively is known as natural passive immunity.

Adaptive immunity: This is a type of passive immunity produced by injecting immunologically competent lymphocytes and not by injecting antibodies. This method is adopted in the treatment of tuberculosis and leprosy.

Major Organs of the Immune System

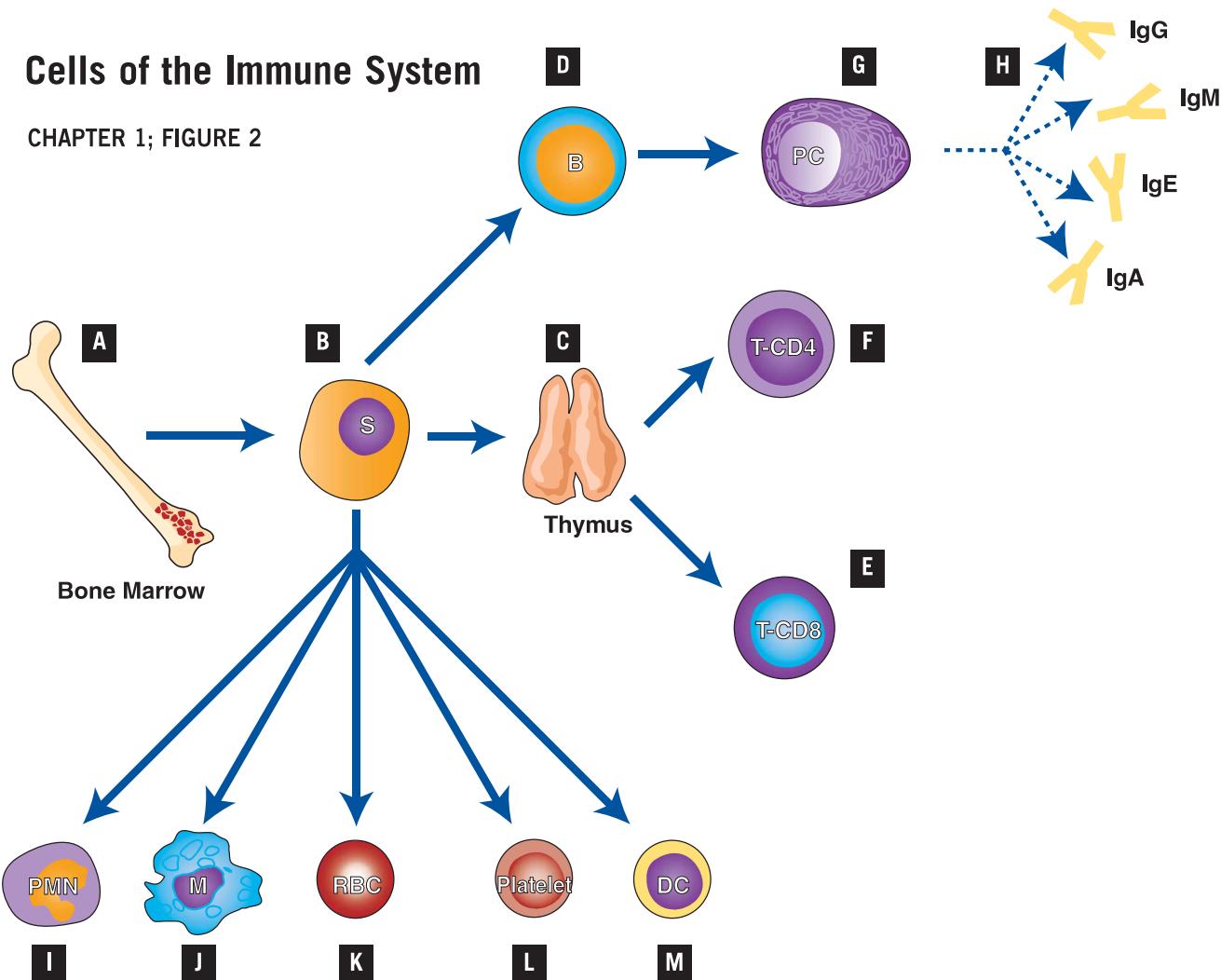
CHAPTER 1; FIGURE 1



- A. Thymus:** The thymus is an organ located in the upper chest. Immature lymphocytes leave the bone marrow and find their way to the thymus where they are “educated” to become mature T-lymphocytes.
- B. Liver:** The liver is the major organ responsible for synthesizing proteins of the complement system. In addition, it contains large numbers of phagocytic cells which ingest bacteria in the blood as it passes through the liver.
- C. Bone Marrow:** The bone marrow is the location where all cells of the immune system begin their development from primitive stem cells.
- D. Tonsils:** Tonsils are collections of lymphocytes in the throat.
- E. Lymph Nodes:** Lymph nodes are collections of B-lymphocytes and T-lymphocytes throughout the body. Cells congregate in lymph nodes to communicate with each other.
- F. Spleen:** The spleen is a collection of T-lymphocytes, B-lymphocytes and monocytes. It serves to filter the blood and provides a site for organisms and cells of the immune system to interact.
- G. Blood:** Blood is the circulatory system that carries cells and proteins of the immune system from one part of the body to another.

Cells of the Immune System

CHAPTER 1; FIGURE 2



- A. **Bone marrow:** The site in the body where most of the cells of the immune system are produced as immature or stem cells.
- B. **Stem cells:** These cells have the potential to differentiate and mature into the different cells of the immune system.
- C. **Thymus:** An organ located in the chest which instructs immature lymphocytes to become mature T-lymphocytes.
- D. **B-Cells:** These lymphocytes arise in the bone marrow and differentiate into plasma cells which in turn produce immunoglobulins (antibodies).
- E. **Cytotoxic T-cells:** These lymphocytes mature in the thymus and are responsible for killing infected cells.
- F. **Helper T-cells:** These specialized lymphocytes "help" other T-cells and B-cells to perform their functions.
- G. **Plasma Cells:** These cells develop from B-cells and are the cells that make immunoglobulin for the serum and the secretions.
- H. **Immunoglobulins:** These highly specialized protein molecules, also known as antibodies, fit foreign antigens, such as polio, like a lock and key. Their variety is so extensive that they can be produced to match all possible microorganisms in our environment.
- I. **Neutrophils (Polymorphonuclear PMN Cell):** A type of cell found in the blood stream that rapidly ingests microorganisms and kills them.
- J. **Monocytes:** A type of phagocytic cell found in the blood stream which develops into a macrophage when it migrates to tissues.
- K. **Red Blood Cells:** The cells in the blood stream which carry oxygen from the lungs to the tissues.
- L. **Platelets:** Small cells in the blood stream which are important in blood clotting.
- M. **Dendritic Cells:** Important cells in presenting antigen to immune system cells.

Table of Genetic Disorders

Disease	Gene/Defect	Inheritance	Clinical Features
Achondroplasia	Fibroblast growth factor receptor 3 (<i>FGR3</i>) – constitutively active (gain of function)	Autosomal dominant (normal parents can have an affected child due to new mutation, and risk of recurrence in subsequent children is low)	Short limbs relative to trunk, prominent forehead, low nasal root, redundant skin folds on arms and legs
Cystic Fibrosis	Cystic fibrosis transmembrane regulator (<i>CFTR</i>) – impaired chloride ion channel function	Autosomal Recessive (most common genetic disorder among Caucasians in North America)	Pancreatic insufficiency due to fibrotic lesions, obstruction of lungs due to thick mucus, lung infections (<i>Staph. aureus</i> , <i>Pseud. aeruginosa</i>)
Duchenne Muscular Dystrophy	Dystrophin (<i>DMD</i>) - deletions	X-linked recessive	Gradual degeneration of skeletal muscle, impaired heart and respiratory musculature
Hypercholesterolemia	LDL receptor (commonly)	Autosomal dominant (haploinsufficiency)	Impaired uptake of LDL, elevated levels of LDL cholesterol, cardiovascular disease and stroke. Symptoms more severe in homozygous individuals
Fragile X Syndrome	(<i>FMR1</i>) – CGG trinucleotide repeat expansion in 5' untranslated region of the gene (expansion occurs exclusively in the mother)	X-linked dominant (females less severely affected) Inheritance characterized by anticipation	Disorder shows anticipation (female transmitters in succeeding generations produce increasing numbers of affected males) Boys with syndrome have long faces, prominent jaws, large ears, and are likely to be mentally retarded.
Gaucher's Disease	B-Glucosidase	Autosomal recessive	Lysosomal storage disease characterized by splenomegaly, hepatomegaly, and bone marrow infiltration. Neurological symptoms are not common
Glucose 6-phosphate dehydrogenase deficiency	Glucose 6-phosphate dehydrogenase	X-linked recessive (prominent among individuals of Mediterranean and African descent)	Anemia (due to increased hemolysis) induced by oxidizing drugs, sulfonamide antibiotics, sulfones (e.g. dapsone), and certain foods (e.g. fava beans)
Hemochromatosis	Unknown gene on the short arm of chromosome 6	Autosomal recessive (Incidence ~0.3% in Caucasoid population. Women less affected due to increased iron loss through menstruation)	Enhanced absorption of dietary iron with accumulation of abnormal, pigmented, iron-protein aggregates (hemosiderin) in visceral organs. Cirrhosis, cardiomyopathy, diabetes, skin pigmentation, and arthritis.
Holoprosencephaly	Sonic Hedgehog (<i>SHH</i>)	Autosomal dominant (haploinsufficiency?)	Malformation of the brain (no or reduced evidence of an interhemispheric fissure), dysmorphic facial features, mental retardation
Huntington Disease (Also Huntington Chorea)	Huntingtin (<i>HD</i>) – CAG repeat expansion within exon 1 (expansion occurs in father)	Autosomal dominant (gain-of-function mutation) Shows anticipation	Disorder is characterized by progressive motor, cognitive and psychiatric abnormalities. Chorea – nonrepetitive involuntary jerks – is observed in 90% of patients

Klinefelter Syndrome	47,XXY males	50% of cases due to errors in paternal meiosis I	Sterile males with long limbs, small genitalia, breast development, and feminine body contours, and learning disabilities
Marfan Syndrome	Fibrillin-1 gene (<i>FBN1</i>) encodes a microfibril-forming connective tissue protein	Autosomal dominant (dominant negative effect)	Abnormalities of the skeleton (disproportionate tall stature, scoliosis), heart (mitral valve prolapse, aortic dilatation, dissection of the ascending aorta), pulmonary system, skin (excessive elasticity), and joints (hypermobility). A frequent cause of death is congestive heart failure.
Myoclonic Epilepsy with Ragged Red Fibers (MERRF)	Mitochondrial DNA mutation in the <i>tRNA^{lys}</i> gene	Maternal transmission, heteroplasmy	Age of onset varies depending on fraction of mutant mitochondrial DNA inherited. Symptoms include myopathy (disease takes its name from abnormal histological appearance of skeletal muscle biopsies), dementia, myoclonic seizures, ataxia, and deafness
Myotonic Dystrophy	A protein kinase gene (<i>DMPK</i>) – CTG repeat expansion in 3' untranslated region of the gene	Autosomal dominant Shows anticipation	Disorder shows anticipation. Muscle weakness, cardiac arrhythmias, cataracts and testicular atrophy in males. Children born with congenital form have a characteristic open triangle-shaped mouth
Neurofibromatosis I	Microdeletion at 17q11.2 involving the <i>NF1</i> gene	Autosomal dominant	The disorder is characterized by numerous benign tumors (neurofibromas) of the peripheral nervous system, but a minority of patients also show increased incidence of malignancy (neurofibrosarcoma, astrocytoma, Schwann cell cancers and childhood CML – chronic myelogenous leukemia)
Osteogenesis Imperfecta	Either of the genes encoding the α1 or α2 chains of type I collagen	Usually autosomal dominant (null mutations result in haploinsufficiency, missense mutations often produce a dominant negative effect)	Null mutations produce a milder form of the disease. Missense mutations that act in a dominant negative manner are often perinatal lethal. The disorders are associated with deformed, undermineralized bones that are subject to frequent fracture.
Phenylketonuria	Usually due to a mutation in Phenylalanine hydroxylase (<i>PAH</i>)	Autosomal recessive	Mental retardation, if untreated, possibly due to inhibition of myelination and disruption of neurotransmitter synthesis. Detectable by newborn screening and treatable
Polycystic Kidney Disease	Mutations in either polycystin-1 (<i>PKD1</i>) or polycystin-2 (<i>PKD2</i>) gene	Autosomal dominant (disease appears to follow a "two-hit model", requiring the loss of both alleles of <i>PKD1</i> or <i>PKD2</i> for the disease to be evident.)	Heterozygous individuals are predisposed to polycystic kidney disease because they are likely to lose the second good copy of the gene during their lifetime. Multiple renal cysts, blood in urine, end-stage renal disease and kidney failure.

Prader Willi/Angelman (PWS/AS)	Deletion of the PWS region and AS gene located at 15q11-q13. Can also be caused by uniparental disomy involving chromosome 15	Complex Parent of origin effects due to genomic imprinting.	Inheriting the deletion through the mother gives rise to Angelman syndrome, which is characterized by short stature, severe mental retardation, spasticity, seizures, and a characteristic stance. Inheriting the deletion from the father produces the more common Prader-Willi syndrome, which is characterized by obesity, excessive and indiscriminate gorging, small hands, feet, hypogonadism and mental retardation. In rare cases, uniparental disomy involving chromosome 15 produces PWS when both copies are inherited from the mother and AS when both copies are inherited from the father.
Sex Reversal	Variety of causes	Various	See Thompson & Thompson, Medical Genetics, 6 th ed.
Tay-Sachs Disease	B-Hexosaminidase (A isoenzyme (<i>HEXA</i>))	Autosomal recessive (common among Jews of Eastern European ancestry and French Canadians).	Hypotonia, spasticity, seizures, blindness, death by age 2. An early indication is a cherry red spot on the retina. (Incidence greatly reduced by screening)
Thalassemias		Autosomal Recessive	Severe anemia
Turner Syndrome	45,X females	Usually due to a paternal error in sex chromosome transmission	Although usually lethal in utero, the defect poses little risk to survival in infants that do come to term. Short stature, webbed necks, broad chest with widely spaced nipples, and sterility. Infants show evidence of lymphedema in fetal life. Intelligence is normal.
Xeroderma pigmentosum	Anyone of nine genes involved in nucleotide excision repair (locus heterogeneity)	Autosomal recessive characterized by variable expressivity, and genetic heterogeneity	Acute photosensitivity, premature skin aging, premalignant actinic keratoses, and benign and malignant neoplasms of the skin, including basal cell carcinoma, squamous cell carcinoma, or both. 5% of patients develop melanomas. Patients also exhibit ocular problems due to UV damage and have a 10- to 20-fold increased incidence of internal neoplasms due to an inability to repair DNA damage by endogenously generated and environmental genotoxic agents.

Behavior genetics

Introduction

- 1- The animal behavior is due to heredity and environmental factors
- 2- Cow bird called this name because it spend long time on cattle for capturing insects around the feet and on their back.
- 3- In mating season some birds put their eggs in other bird species nest EX. Ahwaz birds feed other small birds that spend their first life between these birds.

Later, small birds behavior does not reflect just little in the environment where caring.

So, the inheritance is the most important influence

Test the effects of genetics on behavior:-

(A) Hybridization: intermarried mutually different biological species to identify genetic factors that is passed from one generation to another with maintaining the stability of the environment.

Used as a test for the effect of biological inheritance on animal behavior
The best animals for these tests are dogs.

(B) Animal rearing in strange environment or the so-called modified environment:

- 1- The European animal scientist Conrad Lawrence used this way with many types of birds.
- 2- Taking the young Black Crow directly after hatching from their and rear them on his hands away completely from other birds.
- 3- The wild black Crow living in ruins in small flocks, noisy and very intelligent.
- 4- The reared black Crow become extremely hung up but continued to display many images of behavior of wild species as attacking wearing a black glove on his hands as attack wild birds.

5- Reared species do not appear scared of cats and other predators, so they have little chance to survive if left in the terrestrial environment.

6-While, the matured wild bird do a high sharp voice when a cat approach so, the small birds can make links between predators and escape.

7- It is clear that part of the behavior is shaped through learning and the other part from its biological inheritance and both parts form the bird behavior.

(C) genetic factors Change by selection

1- Selection tests showed in rats that: genetics changes the external behavior and both internal physiological and emotional interactions.

2- The selection modifies behavior by changing heredity, so, dogs are species that selection modifies clearly their behavior.

(D) Mutual experiences adopter:

1- Mutual adoption where two strains exchange their young's (babies).

2- The results showed that biological genetics controlled behavior while the animal behavior resulting from training and education of young by parents came in second place.

3- C strain is peaceful rats, while C57 are stiff rats

4- Mothers of C57strain while sons of other parents stay calm not affected by parents according to genetics

5- Mothers of C strain and young of other stiff stain by acted by genetics and tried to take food from her parents the peaceful parents begins in the stiff competition of adopted children this shows that the behavior controlled by inheritance of children affected the behavior of the parents.

Genetic influences and how they happen?

- 1- Genetics play an important role in animal behavior and differences in behavior moves from parents to children in the same way that genetic factors travels.
- 2- each chromosome carry one or more genes that produce chemical changes in Physiology and in turn influence the behavior.
- 3- Sex is one of the most important natural characteristics
- 4- Sex affects animal anatomy and behavior and differences between male and female is due to the differences in the specific sex chromosomes

** In honey bee insects there is another mechanism to determine sex.

- 1- Honey bee queen laid two types of eggs: first type is unfertilized hatching males, the second type is fertilized and hatching females whether fertilized females (Queens) or atrophic females in which egg machine modified to sting machine (workers)
- 2- Queen fertilized once in her life and rarely fertilized twice during their lives (5-7 years).

In some insects, the Hermaphroditism phenomenon exists and these individuals are sterile.

****Intersexes: which appear between male and female forms as a result of the disturbance in the natural balance between male and female specific genes during growth due to hybridization between related species or after exposure to high thermal temperatures.

Physiological genetic influences on behavior:

- 1- Sex in vertebrates is specific and fully separated.
 - 2- Genital organs in male produce male hormones and in females produce female hormones.
 - 3- Sexual behavior could be changed in animals with a Castration process.
 - 4- Castration in male sheep, cattle and chicken improve their meat characteristics and increase obesity.
 - 5- In Birds left ovary grow well but the right one is atrophied, at castration both ovaries must be eradicated because if the right one left, it swells and produces male and female hormones and the characteristics of hen and behavior become compromise between both sexes,
But if the two ovaries removed, the hen turns into quite castrated rooster
- 3- In old aged hen it stop laying eggs and the ovary wiped out then the right one starts in the activity and show characteristics of male behavior.
 - 4- The male and female behavior depending on the level of male or female hormones in the blood and whichever is higher.

Chemical influences of heredity to behavior dynamic:

- 1- The heredity has a direct effect on the normal physiology of animal.
- 2- Genetic factors have a great relation with the nervous system and its operations and its control over the rest of the body parts.
- 3- In humans the genetic factors may cause a genetic disease called **Phenylpyruvic oligophernia** and its symptoms are patients lose large quantities of phenyl pyruvic acid with urine and lack of intelligence.
...The processes of mutation that occurs in the nervous system as a result of learning and acquire are of the chemical and biological effects of heredity

Genetics and human

- Biological genetics play a big and important role in human behavior, but less than its role in animal behavior as a result of learning, gaining experience and cultural inheritance in humans.

Examples:

- crow birds learn his fears from older individuals(parents)
- the sheep Learn follow each other by tracking.
- In human, the Cultural inheritance is more important than Biological inheritance in behavior
- Social conditions play a big role in the acceptance of diversity in human behavior, the genetic difference may be simple but has important role in human behavior

EX: in high jumping sports, someone may increase than another one by one inch to become a global sport man.

EXERCISE 11 – MENDELIAN GENETICS PROBLEMS

These problems are divided into subdivisions composed of problems that require application of a specific genetic principle. These problems are intended to complement the lecture portion of this course; specifically, the material described in lecture is to be applied to solve these problems. The answers are provided in Appendix A. You are strongly advised against consulting this appendix before you have made a serious attempt to answer a problem.

A. Monohybrid Crosses

1. In *Coleus*, some plants have shallowly crenated edges and others have deeply incised leaves. A cross is made between homozygous deep and shallow individuals. The shallow trait is dominant.
 - a. Using S and s to symbolize the genes for this trait, give the phenotypic and genotypic ratios for the F_1 generation.
 - b. If self pollination is allowed, what is the phenotypic ratio for the F_2 generation?
2. a. In a pea plant that breeds true for tall, what possible gametes can be produced? Use the symbol *D* for tall, *d* for dwarf.
b. In a pea plant that breeds true for dwarf, what possible gametes will be produced?
c. What will be the genotype of F_1 offspring from a cross between these two types?
d. Assuming that the allele for tall is dominant, what will be the phenotype of F_1 offspring from a cross between these two types?
e. What will be the probable distribution of traits in the F_2 generation? (Illustrate with a Punnett square).
3. The ability to taste a bitter chemical, phenylthiocarbamide (PTC), is due to a dominant gene. Use *T* and *t* to symbolize the two alleles of this gene.
 - a. What is the genotype of a nontaster? What are the possible genotypes of a taster?
 - b. Could a person with two tasters as parents be a non-taster? How?
4. A woman heterozygous for polydactyly (extra fingers and toes), a dominant trait, is married to a normal man. What is the probability of producing an offspring that has extra fingers or toes?
5. Parents who do not have Tay Sachs disease produce a child who has this terrible affliction. What are the chances that each child born of this union will be affected?
6. In human beings, ability to curl the tongue into a U-shaped trough is a heritable trait. "Curlers" always have at least one curler parent, but "noncurlers" may occur in families where one or both parents are curlers. Using *C* and *c* to symbolize this trait, what is the genotype of a noncurler?

7. Albinism, the total lack of pigment, is due to a recessive gene. A man and woman plan to marry and wish to know the probability of their having any albino children. What are the probabilities if:
 - a. both are normally pigmented, but each has one albino parent.
 - b. the man is an albino, the girl is normal, but her father is an albino.
 - c. the man is an albino and the girl's family includes no albinos for at least three generations.

8. In a certain plant, both purple x purple and purple x blue yield purple and blue colored progeny, but blue x blue gives rise only to blue.
 - a. What does this tell you about the genotypes of blue- and purple-flowered plants?
 - b. Which gene is dominant?

9. Two short-haired female cats are mated to the same long-haired male. Several litters are produced. Female No. 1 produced eight short-haired and six long-haired kittens. Female No. 2 produced 24 short-haired ones and no long-haired. From these observations, what deductions can be made concerning hair-length inheritance in these animals? Assuming the allelic pair S and s, give the likely genotypes of the two female cats and the male.

10. In human beings, a downward pointed frontal hairline ("widow's peak") is a heritable trait. A person with a widow's peak always has at least one parent who also has this trait, whereas persons with a straight frontal hairline may occur in families in which one or even both parents have widow's peak. When both parents have a straight frontal hairline, all children also have a straight hairline. Using W and w to symbolize genes for this trait, what is the genotype of an individual without widow's peak?

11. Rh negative children (those not producing rhesus antigen D) may be born to either Rh positive or Rh negative parents, but Rh positive children always have at least one Rh positive parent. Which phenotype is due to a dominant gene?

B. Dihybrid Crosses

1. In the fruit fly *Drosophila melanogaster*, vestigial wings and hairy body are produced by two recessive genes located on different chromosomes. The normal alleles, long wings and hairless body, are dominant. Give the genotype and phenotype of F_1 progeny obtained from a cross between a vestigial-winged, hairy male and a normal, homozygous female. If the F_1 from this cross are permitted to mate randomly among themselves, what phenotypic ratio would be expected in the F_2 generation?

2. In peas, a gene for tall plants (T) is dominant over its allele for short plants (t). The gene for smooth peas (S) is dominant over its allele for wrinkled peas (s). The genes are not linked. Calculate both phenotypic and genotypic ratios for the results of each of the following crosses:
 - a. $TtSs \times TtSs$
 - b. $Ttss \times ttss$
 - c. $ttSs \times Ttss$
 - d. $TtsSs \times ss$

3. In a particular species of flower, tall is dominant to short, and orange petals are dominant to the recessive white color. Use T and t to symbolize the alleles for height, and F and f

to symbolize the alleles for flower color. A homozygous tall white flower is crossed with a flower heterozygous for both traits. List the genotypes of the parents. What are the F_1 genotypic and phenotypic ratios?

4. How many phenotypic classes are produced by a dihybrid test-cross where one parent is heterozygous for both pairs of genes?
5. In hogs, an allele that produces a white belt around the animal's body (W) is dominant over its allele for a uniformly colored body (w). The dominant allele of another gene (F) produces a fusion of the two hoofs on each foot. Suppose a uniformly-colored hog homozygous for fused hoofs is mated with a normal-footed hog homozygous for the belted character.
 - a. What are the genotypes of the parents?
 - b. What are the genotypic and phenotypic ratios of the F_1 ?
 - c. If the F_1 were allowed to interbreed, what are the genotypic and phenotypic ratios of the F_2 ?
6. In watermelons, the genes for green color and for short length are dominant over their alleles for striped color and for long length. Suppose a plant with long striped fruit is crossed with a plant heterozygous for both of these characters. What phenotypes would this cross produce and in what ratios?

C. Modifications of Complete Dominance

Incomplete Dominance

1. The so-called "blue" (really gray) Andalusian variety of chicken is produced by a cross between the black and white varieties, both of which breed true (i.e., both are homozygous). What color chickens (and in what proportions) would you expect if you crossed two blues? a blue and a black?
2. In four o'clock, red color exhibits incomplete dominance over white; when both exist together, the flowers are pink.
 - a. In a cross between a red flower and a white one, what is the genotype of the offspring?
 - b. What is the genotypic ratio of the F_2 generation if two of the F_1 from (a) are crossed?
 - c. List the genotypes of offspring produced by a cross between the F_1 generation and red parent.
3. It has long been known in the field of human genetics that wavy hair is the expression of a heterozygous genotype in which the allele for straight hair is paired with the allele for curly hair. Lucinda Lovelee married Larry Legg. Both of these charmers have wavy hair. What is the probability that their offspring, the littlest Legg, will have:
 - a. wavy hair?
 - b. curly hair?
 - c. straight hair?

4. If pale colored horses are crossed with chestnut-colored horses to produce "palomino", an intermediate coat color:
 - a. What type of expression is suggested?
 - b. A number of matings between palominos produced 19 pale, 21 chestnut, and 44 palominos. Does this evidence support or contradict your answer to (a)? Why?

Codominance

1. For each of the following pairs of parental genotypes, calculate the phenotypic ratios for the F_1 generation.
 - a. $I^A I A \times ii$
 - b. $I^A I A \times I^A I B$
 - c. $I^A I A \times I^B i$
 - d. $I^A I A \times I^A i$
 - e. $I^A i \times I^A i$
 - f. $I^A i \times I^A I B$
 - g. $I^A i \times ii$
2. If Mr. and Mrs. Fecundity, both having blood type B, have 12 children, 3/4 of whom are type B and 1/4 of whom are O, what are the genotypes of the parents?
3. A family of six includes four children, each of whom has a different blood type: A, B, AB and O. What are the genotypes of parents for this trait?
4. A man with blood type B, with one parent of blood type O, marries a woman with blood type AB. What will be the theoretical percentage of their children with blood type B?
5. Mrs. Smith and Mrs. Doe were roommates at Harris Hospital and both had daughters at about the same time. After Mrs. Smith took Susie home, she became convinced that the babies had been switched. Blood tests were performed with the following results:
 Mr. and Mrs. Smith were both type AB;
 Mr. and Mrs. Doe were both type A;
 Susie Smith was type A and Debbie Doe was type O.

Had a switch occurred?

6. Mortimer has type B blood. His wife Murgatroyd is unsure of her blood type. If their first child, Magnifica, is type B, their second offspring, Maximum, is AB and the twins, Maud and Lyn, are A, can you determine the genotypes of Mort and Murg?
7. In a well-publicized paternity case, the following facts were unearthed; the mother, a strikingly beautiful, twice-convicted axe murderer, is blood type A, her child, Lizzie, is type O, and the alleged father, a mild-mannered felon, is type B. Could he be the father? Explain. Is there any chance that little Lizzie, the "Bad Seed", will grow up to be a missionary lady?

D. Lethal Alleles

1. Cystic fibrosis is caused by a recessive lethal gene and can be detected by an excess concentration of chloride in sweat. If a sweat test reveals a man to be heterozygous and his wife to be homozygous normal, what are the chances that their children will have the disease? Could any of their grandchildren have the disease?

2. In humans, sickle-cell anemia is caused by a recessive lethal allele Hb^S; individuals who are Hb^AHb^S have sickle-cell trait, but are healthy.
 - a. What is the probability of two heterozygous individuals giving birth to a child with sickle-cell trait?
 - b. What is the probability of two heterozygous individuals giving birth to a child with sickle-cell anemia?
 - c. If a normal Hb^AHb^A individual receives a blood transfusion from a Hb^AHb^S individual (heterozygous for sickle cell) what are the chances that the Hb^AHb^A man and his Hb^AHb^A wife will have Hb^AHb^S children?
3. Albinism in corn plants is caused by a recessive lethal gene that results in death before maturity. What will the adult phenotypic ratio be for the F₁ generation of heterozygous parents?
4. Huntington's chorea is a dominant lethal in humans. The disease does not appear until later in life, so that afflicted individuals may already have produced children. What are the F₁ genotypic and phenotypic ratios of parents who are homozygous dominant and heterozygous?

E. Sex-linked Genes

1. Red-green color blindness is inherited as a sex-linked recessive. If a color-blind woman marries a man who has normal vision, what would be the expected phenotypes of their children with reference to this character?
2. Suppose that gene b is sex-linked, recessive, and embryonic lethal. A man marries a woman who is heterozygous for this gene. If this couple had many normal children, what would be the predicted sex ratio of these children?
3. A man and his wife both have normal color vision, but a daughter has red-green color blindness, a sex-linked recessive trait. The man sues his wife for divorce on grounds of infidelity. Can genetics provide evidence supporting his case?
4. In the mouse, the dominant sex-linked gene B results in a short, crooked tail. Its recessive allele b produces a normal tail. If a normal-tailed female is mated with a bent-tailed male, what phenotypic ratio should occur in the F₁ generation?
5. In cats, a gene for coat color is sex-linked. Cats homozygous for allele A have yellow coats; those homozygous for allele a have black coats; and heterozygotes have tortoise-shell coats. What type(s) of offspring would result from a mating of a black male and a tortoise-shell female? Is it possible to obtain a tortoise-shell male?
6. On the X chromosome of *Drosophila* there may occur a recessive gene l, which is lethal in the larval stage. A heterozygous female is crossed to a normal male; what F₁ adult sex phenotypic ratio results?

F. Recombination

1. In *Drosophila melanogaster*, there is a dominant gene for gray body color and another dominant gene for normal wings. The recessive alleles of those two genes result in black body color and vestigial wings, respectively. Flies homozygous for gray body and normal wings were crossed with flies that had black bodies and vestigial wings. The F₁ progeny were then test-crossed, with the following results:

Gray body, normal wings	236
Black body, vestigial wings	253
Gray body, vestigial wings	50
Black body, normal wings	61

Would you say that these two genes are linked? If so, how many units apart are they on the chromosome?

2. A series of dihybrid test crosses gives the following crossover frequencies: A-B, 3%, A-C, 13%; B-C, 10%
 - a) What is the gene sequence?
 - b) Another cross gives a frequency of 19% for A-D. Can you locate the position of D in the sequence?
 - c) If the crossover for C-D is found to equal 6%, where would gene D be located?
3. In the nematode *Caenorhabditis elegans*, *dpy-18* and *unc-32* are recessive alleles which confer the phenotypes of a dumpy body and uncoordinated movement, respectively. A test cross is performed, and yields the following progeny:

Phenotype	# Progeny
Dpy Unc	409
Wild type	391
Dpy	106
Unc	93

Are the genes linked? If so, how many units apart are they on the chromosome?

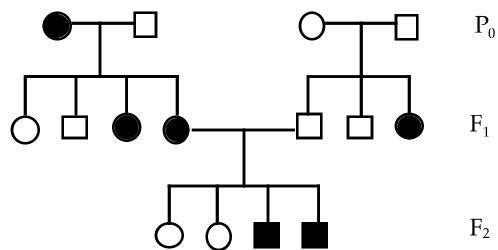
4. In the same organism, *dpy-5* and *unc-4* are another set of recessive alleles which confer the same properties. A similar test cross is performed.

Phenotype	# Progeny
Dpy Unc	243
Wild Type	251
Unc	247
Dpy	249

Are the genes linked? If so, how many units apart are they on the chromosome?

G. Pedigree Analyses

1. The diagram shows three generations of the pedigree of deafness in a family. Black circles and squares indicate deaf persons. ● and ○ indicate a female; ■ and □ indicate a male. Is the condition of deafness in this pedigree inherited as (1) a dominant autosomal characteristic, (2) a recessive autosomal characteristic, (3) a sex-linked dominant characteristic, or (4) a sex-linked recessive characteristic?

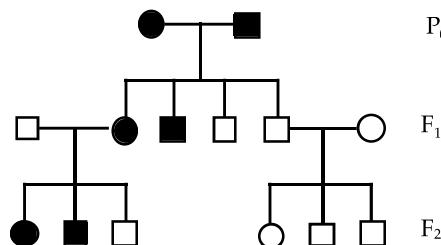


2. In the following pedigree charts,

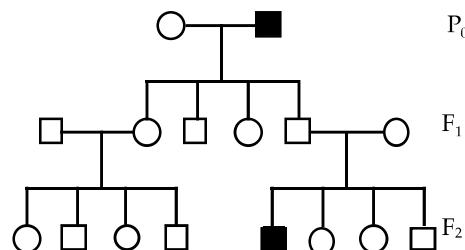
- = afflicted female
- = afflicted male
- = normal female
- = normal male

Indicate the pattern of inheritance.

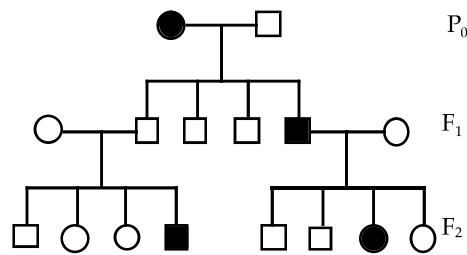
A.



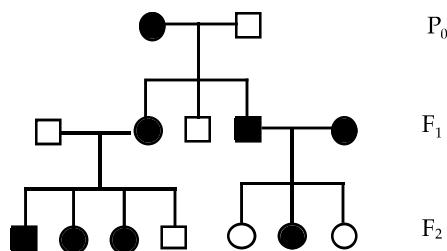
B.



C.



D.



APPENDIX -----Answers to Genetics Problems

A. Monohybrid Crosses

1. a. $SS \times ss$
Shallow deep

genotypic = all Ss
phenotypic = all shallow

- b. F_2 Genotypic = 1 : 2 : 1 or 1/4 SS : 1/2 Ss : 1/4 ss

Phenotypic = 3 : 1 or 3/4 shallow; 1/4 deep

2. a. D b. d c. Dd d. All tall e. F_2

	D	d
D	DD	Dd
d	Dd	dd

3. a. tt; TT or Tt
b. Yes, if both his or her parents were heterozygous.
4. 50%
5. 25%
6. cc
7. a. 25% b. 50%
c. Probably zero: the girl's family history suggests that she is homozygous normal.
8. a. Purple is heterozygous; blue is homozygous b. Purple
9. Short hair is the dominant trait. Genotypes: Female No. 1 is Ss; Female No. 2 is SS; the male is ss.
10. ww - homozygous recessive
11. Rh^+ is dominant.

B. Dihybrid Crosses

1. The genes may be symbolized as:

v = vestigial h = hairy body
V = long wing H = hairless body

The genotypes of the parents are: Male vvhh, Female VVHH.

One hundred percent of the F₁ will be VvHh (normal long wing, hairless body).

The F₂ phenotypic ratio is 9 normal long wing, hairless body; 3 vestigial wing, hairless body; 3 normal long wing, hairy body; 1 vestigial wing, hairy body. This can be obtained by multiplying the two phenotypic ratios times one another.

The phenotypic ratio for wings is 3 normal long : 1 vestigial. The phenotypic ratio for hair is 3 hairless : 1 hairy. Since the two traits segregate independently -

$$\begin{array}{r} 3 : 1 \\ 3 : 1 \\ \hline 9 : 3 : 3 : 1 \end{array}$$

2. The two ratios can again be multiplied, since the genes (S+T) are not linked.

<u>Genotypic Ratio</u>	<u>Phenotypic Ratio</u>
a) 1TT : 2Tt : 1tt <u>1SS : 2Ss : 1ss</u> 1TTSS : 2TtSS : 1ttSS 2TTSs : 4TtSs : 2 ttSs short, smooth 1TTss : 2Ttss : 1 ttss	3 tall : 1 short <u>3 smooth : 1 wrinkled</u> 9 tall, smooth : 3 short, smooth: 3 tall, wrinkled : 1 short, wrinkled
b) 1Tt : 1tt <u>1ss</u> 1Ttss : 1ttss	1 tall : 1 short <u>all wrinkled</u> 1 tall, wrinkled : 1 short, wrinkled
c) 1tt : 1Tt <u>1Ss : 1ss</u> 1ttSs : 1TtSs 1ttss : 1Ttss	1 tall : 1 short <u>1 smooth : 1 wrinkled</u> 1 tall, smooth : 1 short, smooth : 1 tall, wrinkled:1 short, wrinkled
d) 1Tt <u>1Ss</u> 1TtSs	All tall <u>All smooth</u> All tall, smooth
3. The parental genotypes are: TTff x TtFf The F ₁ genotypic ratio is: 1 : 1 : 1 : 1 The F ₁ phenotypic ratio is: 1 : 1	
4. Four. For example: CcBb x ccbb ---Cc Bb Cc bb cc Bb cc bb	
5. a) The parental genotypes are: ww FF x WW ff	

- b) All the F₁'s are WwFf (white belted with fused hoofs).
 - c) The genotypic ratio is: 1:2:1:2:4:2:1:2:1
The phenotypic ratio is: 9:3:3:1
6. 1 green short: 1 green long: 1 striped short: 1 striped long

C. Modifications of Complete Dominance

Incomplete Dominance

- 1. The genotypes of the black and white may be represented as BB and bb, respectively. A "blue" chicken has the genotype Bb. Crossing two blues would produce 1/4 black, 1/2 blue, and 1/4 white. Crossing a blue and a black would produce 1/2 blue and 1/2 black.
- 2. a. If the parental genotypes are RR and rr, the offspring would be Rr.
 - b. 1 RR : 2 Rr : 1 rr
 - c. 1 RR : 1 Rr
- 3. The genotypes may be symbolized as follows: AA = straight hair, aa = curly hair, Aa = wavy hair.
 - a. 50%
 - b. 25%
 - c. 25%
- 4. a. incomplete dominance
 - b. We suspect palominos to be heterozygous. If they are crossed, a 1:2:1 ratio should result. It does, which supports our answer.

Codominance

- 1. a. 100% A
 - b. 50% A, 50% AB
 - c. 50% AB, 50% A
 - d. 100% A
 - e. 75% A, 25% O
 - f. 50% A, 25% AB, 25% B
 - g. 50% A, 50% O
- 2. I^Bi x I^Bi
- 3. Parents must be I^Ai and I^Bi
- 4. 50%. The parental genotypes are: I^Bi x I^AI^B
- 5. Mr. and Mrs. Smith must both have genotypes I^AI^B. Mr. and Mrs. Smith could not have given birth to Debbie Doe - Type O. A switch had not occurred.
- 6. Mortimer is I^Bi. Murgatroyd is either I^Ai or I^AI^B.

7. The mother may be $I^A i$, while the father is $I^B i$. Consequently, there would be a 25% chance of the child being type O. Criminal behavior has never been found to be correlated with chromosomal inheritance. With the proper environment, Little Lizzie could turn out to be an angel.

D. Lethal Alleles

1. None of their children will have cystic fibrosis. Their grandchildren could have the disease if the heterozygous children marry other heterozygotes.
2. a) $Hb^A Hb^S$ 50%
b) $Hb^S Hb^S$ 25%
c) 0: the genotype is not affected by the blood transfusion.
3. All adult F_1 will be green, albinos die.
4. Genotypic ratio: 1 homozygous dominant: 1 heterozygote
Phenotypic ratio: All F_1 will have Huntington's chorea.

E. Sex-Linked Genes

1. All girls are normal, but carriers.
All boys are color-blind.
2. Two-thirds female: one-third male.
3. A color-blind girl could only be the result of a union of (a) a mother with normal vision but a carrier ($X^O X$), with a colorblind male ($X^o Y$); or (b) a spontaneous mutation of the X chromosome handed down by the father. The smart money goes for (a).
4. One normal male: one bent female.
5. 1/4 tortoise female; 1/4 black female; 1/4 yellow male; 1/4 black male. No.
6. Two normal females: 1 normal male (male with lethal dies).

F. Recombination

1. The P_0 cross is BBVV x bbvv.
The F_1 test cross is: BbVv x bbvv.
If unlinked, the F_2 phenotypic ratio should be 1:1:1:1. It is not, so the two genes are on the same chromosome.

The two smallest F₂ phenotypic classes are recombinants. Since map distance is defined as
#Recombinants/total X 100, 111/600 x 100 = 18%.

2. a) A B C b) not with this information alone c) furthest away from A (*i.e.*, A B C D)
3. The genes are linked; otherwise the phenotypic ratio would be 1:1:1:1. Dpy and Unc are the smallest, and hence recombinant, classes. Therefore, 200/1000 x 100 = 20% or 20 map units.
4. The genes are not linked.

G. Pedigree Analyses

1. This condition is not autosomal dominant or sex-linked dominant because F₁ #7 is afflicted and her parents are normal.

This condition is not sex-linked recessive because a cross between parents 1 and 2 would give all normal heterozygous daughters and all afflicted sons. (Note: F₁ #2 is not deaf).

Deafness appears to be passed on in accordance with expectations for inheritance of a recessive autosomal allele.

2. a. dominant
b. recessive, probably sex-linked (male afflicted, female carrier)
c. recessive
d. dominant

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