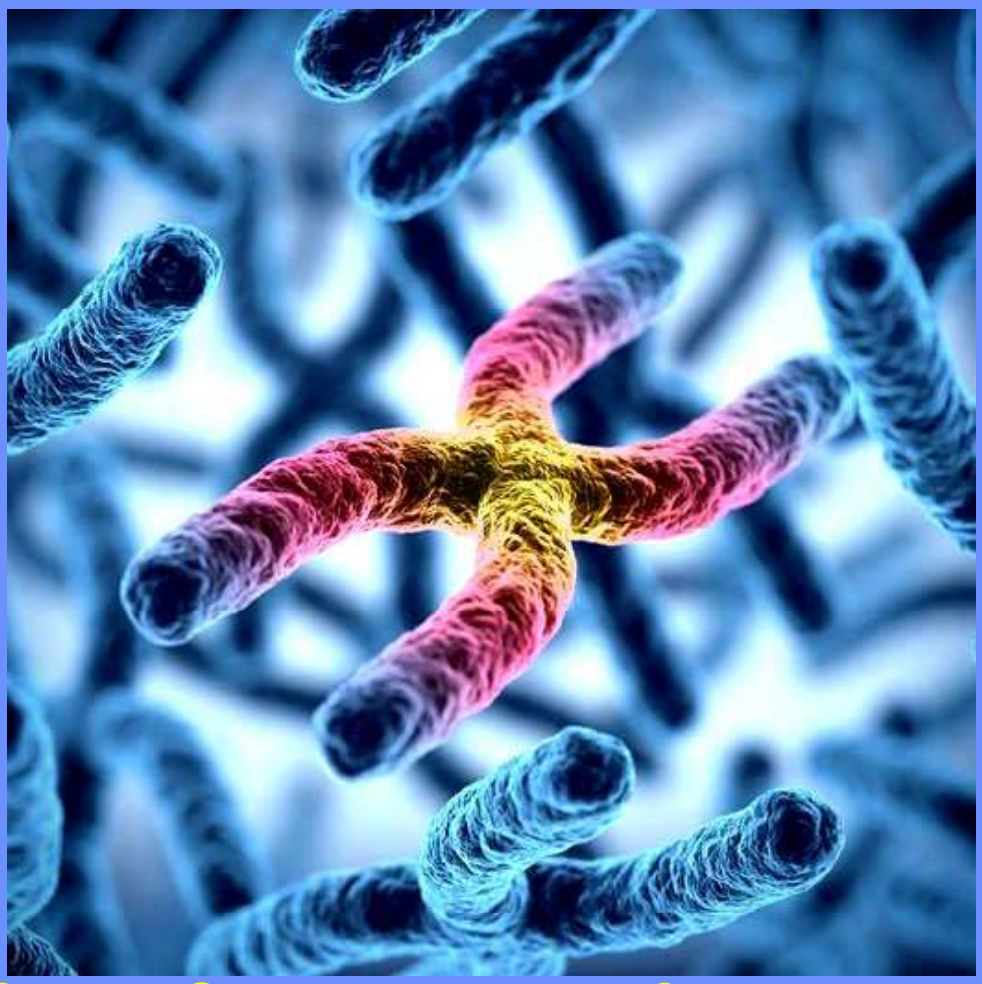
EduBull

BIOLOGY

for NEET & BOARD



PRINCIPLE OF INHERITANCE & VARIATION

Key Features

1. All-In One Study Material (For Boards/Medical/Olympiads).
2. Concise, Conceptual & Trick – Based Theory.
3. NTA Based Solved Multiple Choice Questions With Answers.

Principle Of Inheritance & Variation

Chapter – 5

India's First Trick Based Study Material

1 INTRODUCTION

The study of transmission of characters from one generation to the other in human population is called **human genetics**. The principles of inheritance are applicable to man in the same way as in other animals and plants. Only during the past several decades human genetics became a flourishing discipline with increasingly sophisticated techniques for the diagnosis and treatment of many inherited conditions. The experimental study of inheritance of characters in human is not so easy as it has been in case of guinea pig, Drosophila etc. however, more than two hundred traits are reported to be inherited in human.

2 INHERITANCE: HEREDITY AND VARIATIONS

HEREDITY :

- It is the transmission of genetic characters from parents to the offsprings.
- It deals with the phenomenon of "like begets like", *e.g.,* human babies are like human beings in overall characteristics.
- About **200** characters are found to be hereditary in man.
- **Variations** are common in sexually reproducing organisms.
- Asexually reproducing organisms are mono-parental, hence exhibit no genetic variations.
- Variations are of following two types:

(1) Somatogenic Variations: These are acquired variations and are non-inheritable in nature. The ability of an organism to alter its phenotype in response to environment is called **phenotypic plasticity**.

(2) Blastogenic Variations: These are germinal variations and are hereditary in nature. They are again of two types :

(a) Continuous Variations: These are the fluctuating variations and can not give rise to new species. These are further of two types :

(i) Substantive: Variation in size, shape and colour of organism.

(ii) Meristic: Variation in number of parts, *e.g.,* number of grains in an ear of wheat.

(b) Discontinuous Variations: Also known as **mutations, sports or saltations.** These variations are responsible for formation of new species and the organism thus formed, is called' a **mutant**.

- Types of discontinuous variations :
  - (i) **Substantive variations:** These influence shape, colour, size etc., *e.g.,* hairless cat, short legged ancon sheep.
  - (ii) **Meristic variations:** These affect number of parts, *e.g.,* polydactyly in humans. Variations are of great significance in evolution as they make the organism better suited to modifying environmental conditions, produce new trait in organism and provide raw material for evolution.

Branches Of Genetics

(i) **Transmission genetics or Classical genetics,** *e.g.*, It is the study of Mendelian genetics and non-Mendelian genetics.

(ii) **Forward genetics** : It is the identification of mutated gene using the mutated phenotype.

(iii) **Reverse genetics :** It is the study of genes whose protein products are unknown.

(iv) **Cytogenetics:** It is the study of various aspects of chromosomes.

(v) **Molecular/biochemical genetics** : It is the study of structure and functions of genes.

(vi) **Population or biometrical genetics** : It is the study of the behaviour and effects of gene in population using mathematical models.

(vii) **Behavioural Genetics:** It is the study of interaction of genes with the environment to produce a particular pattern of behaviour.

Pre-Mendelian Ideas About Inheritance or Theories of Blending Inheritance

- The science of genetics arose with the rediscovery of Mendelism in 1900. Early philosophers, thinkers and workers have presented various theories to explain the phenomenon of inheritance.
- These are called theories of blending inheritance. Some of these theories are:

(a) **Moist Vapour Theory** (Pythagoras : 500 B.C.) : Various body parts emit certain vapours, which get aggregated to form new individual.

(b) **Reproductive Blood Theory** (Aristotle: 384-322 B.C.) : According to him, menstrual fluid and semen are kinds of highly purified blood. Menstrual fluid provide inert substance for embryo formation and semen provide form and shape to embryo.

(c) **Preformation Theory or Homunculus theory** (J. Swammerdam) : According to this theory miniature form of individual is already present in sperm or egg called **"homunculus".** Fertilization is required to stimulate its growth.

(d) Theory of **Pangenesis** (Darwin 1868) : According to him, each part of body produces minute particle called **gemmules or pangenes,** which aggregate into gamete. On fusion they give rise to new individual.

(e) **Theory of Epigenesis** (K.F. Wolff) : According to this idea,· neither egg nor sperm had a structural homunculus but the gametes contained undifferentiated living substance capable of forming the organized body after fertilization. This suggested that many new organs and tissue which were originally absent, develop structurally *de novo* due to mysterious vital force.

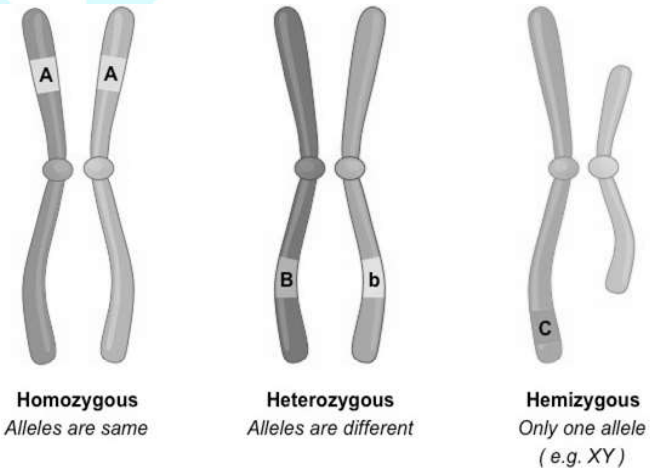
- Theory of pangenes was disproved by Weismann.
- **A.Weismann** proposed his **theory of germplasm,** according to which the changes which affect the **germplasm** are heritable and the changes which affect **somatoplasm** are non heritable.

- *Objections to blending inheritance:*

1. Unisexual traits
2. Skin colour in humans
3. Atavistic character

GENETIC TERMS AND SYMBOLS

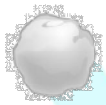
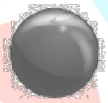
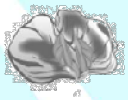
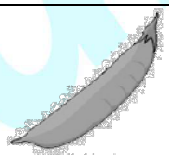
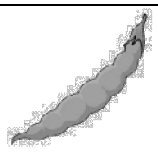
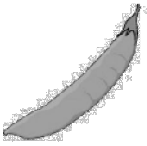
Terms	Meaning	Examples
Character	It is the feature of the individual.	Flower colour
Trait	An inherited character and its detectable variant.	Violet or white
Unitfactor	A unit of inheritance called gene by modern geneticists. Each gene or factor controls a character.	R or r
Allele	Genes which code for a pair of contrasting traits are known as alleles. It represents atleast two alternative forms of a gene or unit factor.	RR, Rr, rr
Phenotype	It is observable morphological appearance. The phenotypes of an individual is determined by different combinations of alleles.	Tallness or dwarfness
Genotype	It is representation of an individual's genetic constitution with respect to a single character or a set of characters.	TT, Tt, tt
Homozygous	When the two alleles of a gene are similar they are said to be in homozygous combination.	TT or tt
Heterozygous	When the two alleles in a pair are different they are in heterozygous state.	Tt
Dominant	An allele that influences the appearance of the phenotype even in the presence of an alternative Complete / unmodified product.	T
Recessive	An allele that influences the appearance of the phenotype only in the presence of another identical allele. Its product is either incomplete or less efficient or it has no product at all.	t

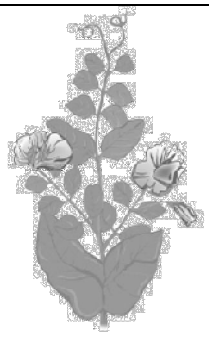
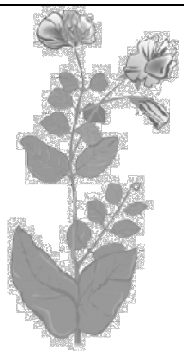
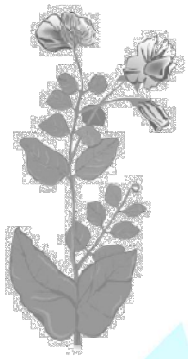
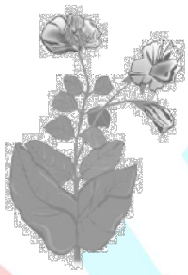


2 MENDELIAN INHERITANCE

- Mendel was born on July 22, 1822. He worked on *Pisum sativum* (Garden pea or Edible pea) for 7 years by taking 7 pairs of contrasting traits.
- The results were read out in two meeting of Natural History Society of Brunn in 1865.
- His paper **"Experiments on plant Hybridisation"** was published in 4th volume of *"Proceedings of Natural Science Society of Brunn" in 1866.*
- Mendel was first to apply statistical analysis and mathematical logic.
- He selected 14 true breeding pea plant varieties. He died due to kidney disorder in 1884.

Mendel selected following characters in pea plant for carrying out hybridisation experiments:

S.No.	Character	Contrasting traits		Location of trait (on chromosome number)
		Dominant trait	Recessive trait	
1.	Seed shape	 Round	 Wrinkled	7
2.	Seed colour	 Yellow	 Green	1
3.	Flower colour	 Violet	 White	1
4.	Pod shape	 Full/Inflated	 Constricted	4
5.	Pod colour	 Green	 Yellow	5

6.	Flower position	 Axial	 Terminal	4
7.	Stem height	 Tall	 Dwarf	4

- Mendel failed to produce same results in **Hawkweed** *(Hieracium)* and **Beans** *(Lablab).* Detailed investigation by **S. Blixt** on pea plant led to locate Mendel's seven characters on 4 different chromosomes, *i.e.,* 1, 4, 5 and 7.
- However, Mendel's work did not receive any recognition, it deserved, till 1900.
- Mendel's work remained unnoticed and unappreciated for several years due to following reasons:
  (1) Communication was not easy in those days and his work could not be widely publicised.
  (2) His concept of stable, unblending, discrete units or factors for various traits did not find acceptance from the contemporaries.
  (3) His approach of using mathematical and statistical analysis to explain biological phenomena was totally new and unacceptable to many of the biologists of that time.
  (4) He could not provide any physical proof for the existence of factors. It was rediscovery of his work by a Dutch -**Hugo de Vries**, a German -**Carl Correns** and an Austrian botanist -**Erich von Tschermak**, independently in 1900, that brought Mendel to limelight. Correns raised status of Mendel's generalisations to laws.
- **Selection of pea plant :** The main reasons for adopting garden pea *(Pisum sativum)* for experiments by Mendel were as follows :
  (1) Pea has many distinct alternative traits (clear contrasting characters).
  (2) Life span of pea plant is short.
  (3) Flowers show self (bud) pollination, so are true breeding.
  (4) It is easy to artificially cross-pollinate the pea flowers. The hybrids thus produced were fertile.

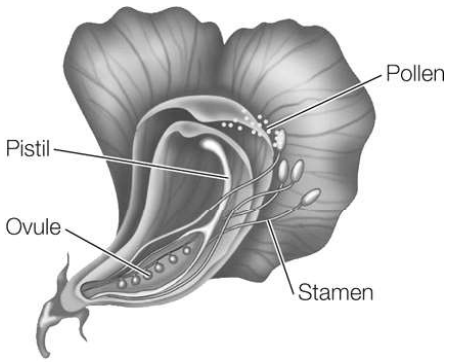


Fig: Pea flowers normally self-fertilize. However, the male organs can be removed from a flower so that it can be manually fertilized with pollen from a different flower.

Memories

- Term allele was given by Bateson, term homozygous and heterozygous were given by Bateson and Saunders; genotype, phenotype, gene and pureline by Johannsen.
- Father of genetics -Mendel; Father of Modem genetics -Bateson
- **Isoalleles** : Alleles that produce similar phenotypes but are distinguishable amongst themselves through changed optima, *e.g.*, I^{A1} , I^{A2} ,I^{A3} .
- **Pseudoalleles** : Genes are present together side by side and they produce related phenotypes.
- These are distinguished from true alleles through rare crossing over, *e.g.*, star (dominant) and asteroid (recessive) traits in Drosophila.
- **Pure lines (pure breeding line)** : A population obtained by continuous inbreeding over many generations, such that each individual has essentially the same genome as every other member of the inbred line and that all (or most) loci are homozygous.

Mendel's Work and Results

- Mendel has made cross between parents having contrasting traits.
- Firstly he made **monohybrid cross** (cross between parents, differ from each other in one character) followed by **dihybrid cross** (cross between parents, differ from each other in two characters) and then trihybrid.
- The F_1 hybrids were self crossed to give rise to F_2 generation.
- Mendel also carried out the reciprocal crosses and found that reciprocal crosses gave the same result.
- **(Reciprocal cross** means opposite cross, *i.e.,* the parent which provides male gamete in one cross, in second experiment it provides the female gamete and vice versa).
- The result of reciprocal cross proves that both gametes produce the same effect and it does not matter which parent provides male and which one provides female gamete.
- According to the law of independent assortment, pairs of alleles are inherited independently of one another if their gene loci are on separate chromosomes – these genes are said to be *unlinked*
  - This is due to the random orientation of homologous pairs during metaphase I of meiosis
  - The independent segregation of unlinked genes results in a greater number of potential gamete combinations, as well as a greater variety of possible phenotypes
  - This also results in more complex inheritance patterns (e.g. monohybrid versus dihybrid crosses)

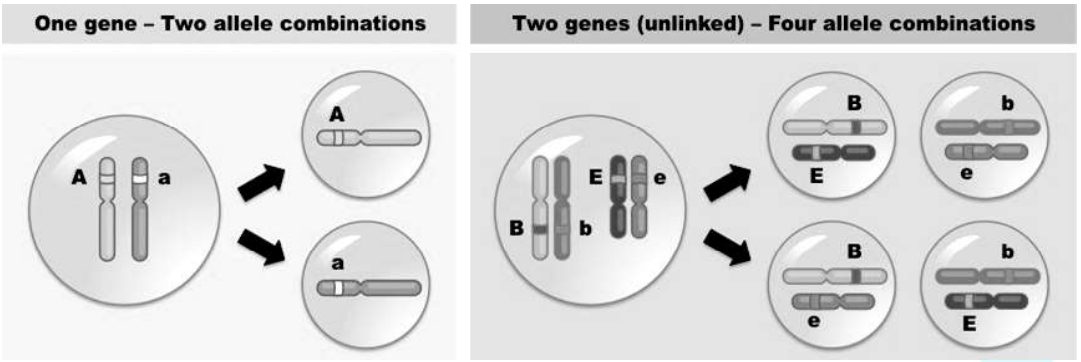


Fig: Inheritance of a Single Gene versus Two Unlinked Genes

- On the basis of his experimental crosses, he formulated four postulates.

Postulate I:

According to this postulate characters are controlled by a pair of **unit factors.** The two factors are now called **alleles** or allelomorphic pair.

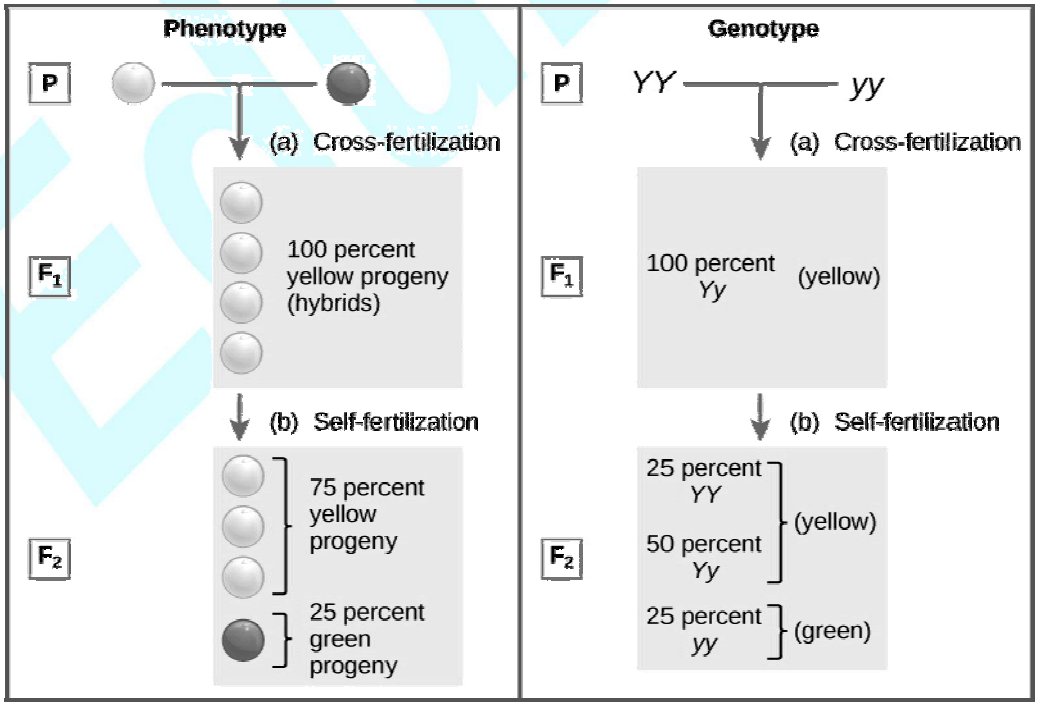
Postulate II :

If two dissimilar unit factors are present in an individual, only one expresses itself. The one which expresses itself is known as **dominant factor,** while the second which does not express at all is known as **recessive factor.**

Postulate III :

According to this postulate, two contrasting alleles responsible for contrasting traits present in an individual do not get mixed and get separated from each other at the time of gamete formation by F_1 hybrid and due to their recombination, four combinations can be obtained in equal frequency.

- All the above three postulates are based upon Mendel's **monohybrid cross or one gene interaction.**
- **Law of dominance** and **law of segregation** can be explained on the basis of monohybrid cross or one gene interaction.



(1) Law of dominance :

- This law states that when two contrasting alleles for a character come together in an organism, only one is expressed completely and shows visible effect.
- It is called **dominant** and the other allele of the pair which does not express and remains hidden is called **recessive.**
- *This law is not universally applicable.*
- *Plant height is controlled by two alleles -Dominant allele (T) and Recessive allele (t) These two alleles can be present in three forms*

  TT - Dominant allele expressed - HOMOZYGOUS

  tt - Recessive allele expressed - HOMOZYGOUS

  Tt -Dominant allele expressed] Heterozygous (Hybrid for character)
- Mendel crossed two pea plants, one homozygous tall (TT) and another homozygous dwarf (tt).
- He observed that all the F_1 progeny plants were tall, like one of the parents, none were dwarf.
- He made similar observations for the other pair of traits and found that F_1 always resembled only one of the parents, and that the trait of other parent was not seen in them.

(2) Law of segregation or Law of purity of gametes:

- This law states that both parental alleles (recessive and dominant) of F_1 separate and are expressed phenotypically in F_2 generation. **This law is universally applicable.**
- The F_2 generation was produced by allowing F_1 hybrid to self pollinate, to find out segregation or separation.
- It was observed that both dominant and recessive plants appeared in 3 : 1 ratio. Thus, F_2 progeny shows both parental forms.
- On the basis of F_2 generation, following observations can be made:
  (i) An organism generally has two alleles for each character. These alleles may either be similar or dissimilar. Organism with similar alleles of a pair is called **pure** or **true breeding** for that character. If the organism contains dissimilar alleles of a pair, the organism is **impure** or hybrid.
  (ii) An organism receives one of the two alleles from the male gamete and the other from the female gamete. The gametes fuse during fertilization and form a zygote. Zygote develops into an organism.
  (iii) Each gamete (male or female) has only one allele of the pair. Thus, each gamete is pure for a trait. That is why this law is often called as Law of purity of gametes.
  (iv) The fusion between male and female gametes to produce zygote is a random process.
- The plants obtained in F_2 generation show 3 (tall) : 1 (dwarf) phenotypic ratio. Of these three tall plants, one is pure or homozygous dominant and the remaining two are heterozygous (tall in this case). There is only one plant that shows recessive character (dwarf in this case). Dwarf is pure or true breeding, being homozygous recessive

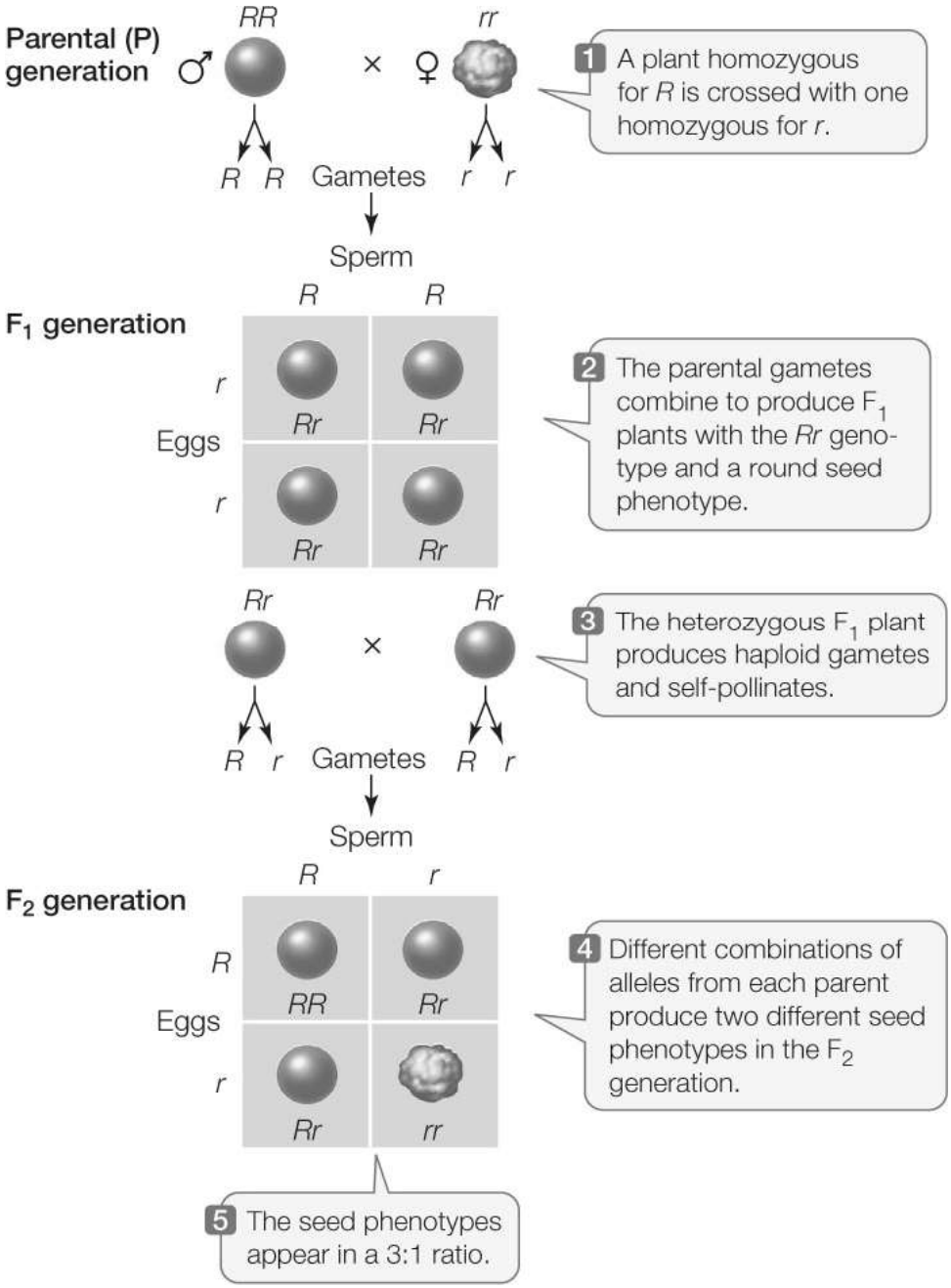


Fig: Mendel's Explanation of Inheritance Mendel concluded that inheritance depends on discrete factors from each parent that do not blend in the offspring.
(R = Round; r = Wrinkled)

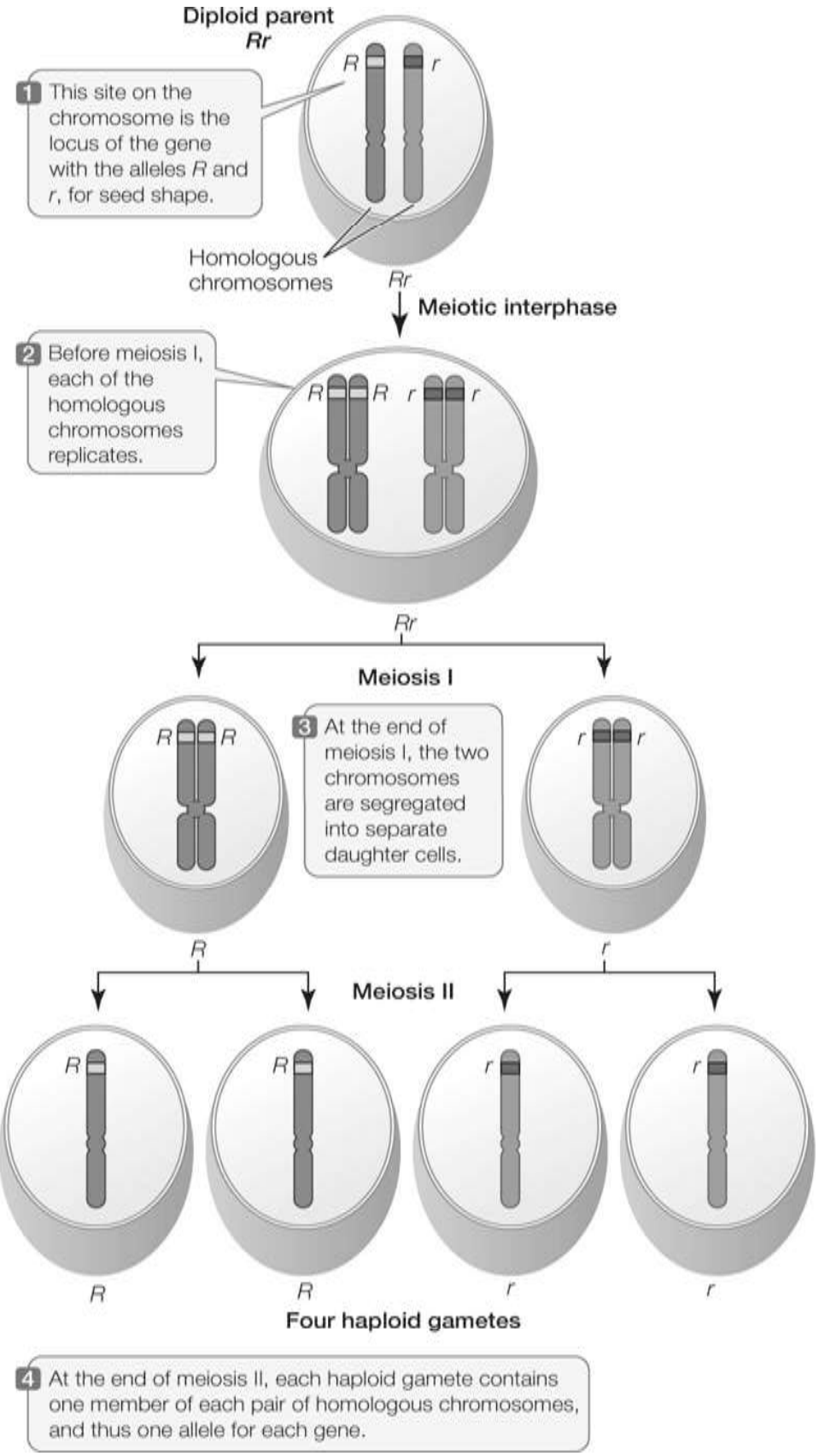


Fig: Meiosis Accounts for the Segregation of Alleles Although Mendel had no knowledge of chromosomes or meiosis, we now know that a pair of alleles resides on homologous chromosomes, and that those alleles segregate during meiosis. (R = Round; r = Wrinkled)

- This postulate was made on the basis of **dihybrid cross** or **two genes interaction**.
- He postulated that inheritance of one character is independent of the inheritance of another character.
- On the basis of this postulate, Mendel proposed the **"Law of independent assortment"**.

(3) Law of independent assortment :

- The law of independent assortment states that when a cross is made between two individuals different from each other in two or more characters, then the inheritance of one character is independent of the inheritance of another character.
- Because of their independent assortment, besides the parental types, recombinants are also obtained.
- In dihybrid cross, these combinations are obtained in the ratio of 9 : 3 : 3 : 1. *e.g.,* He crossed homozygous dominant round and yellow seeded plant (RRYY) with homozygous recessive wrinkled and green seeded (rryy) plant
- The F_1 hybrids were all heterozygous, showing yellow and round seeded plants. This law is not universally applicable.

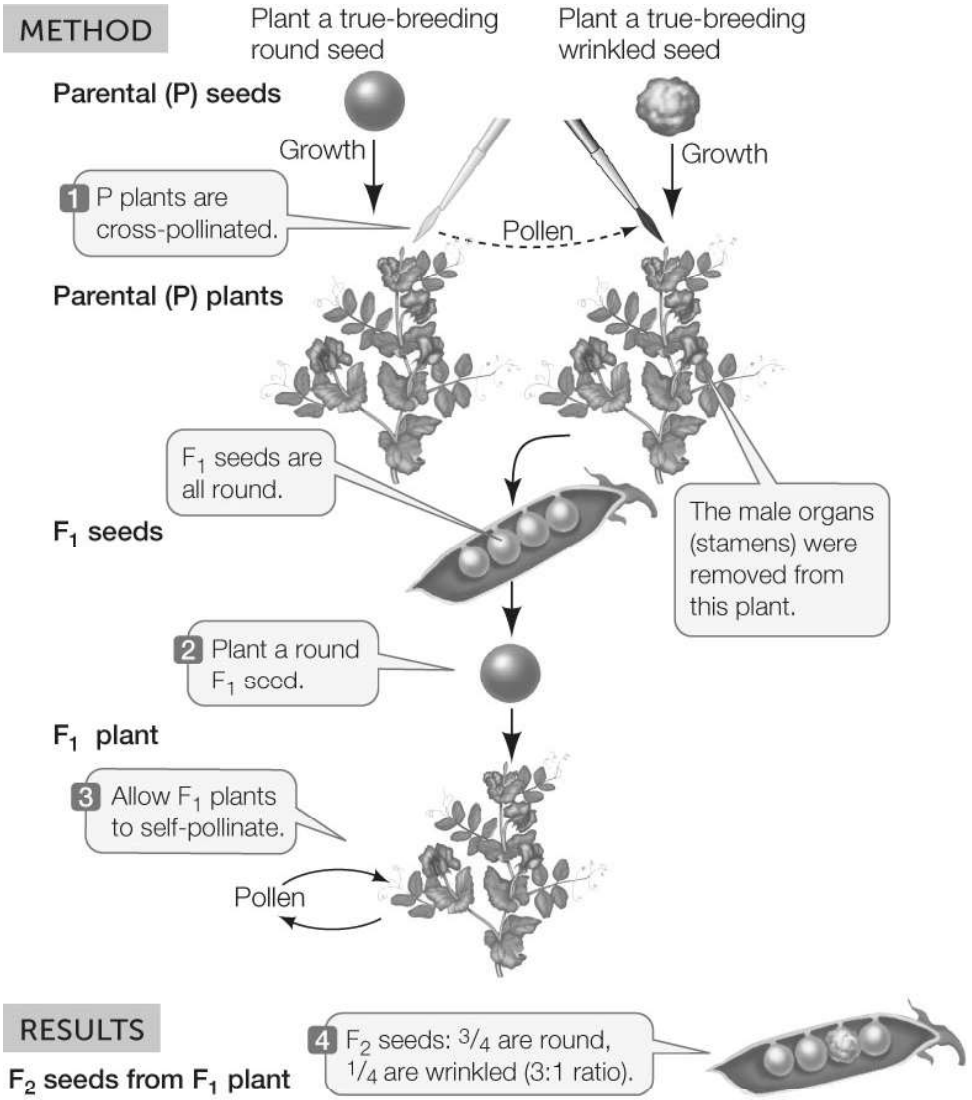


Fig: Mendel's Monohybrid Experiments: Mendel performed crosses with pea plants and

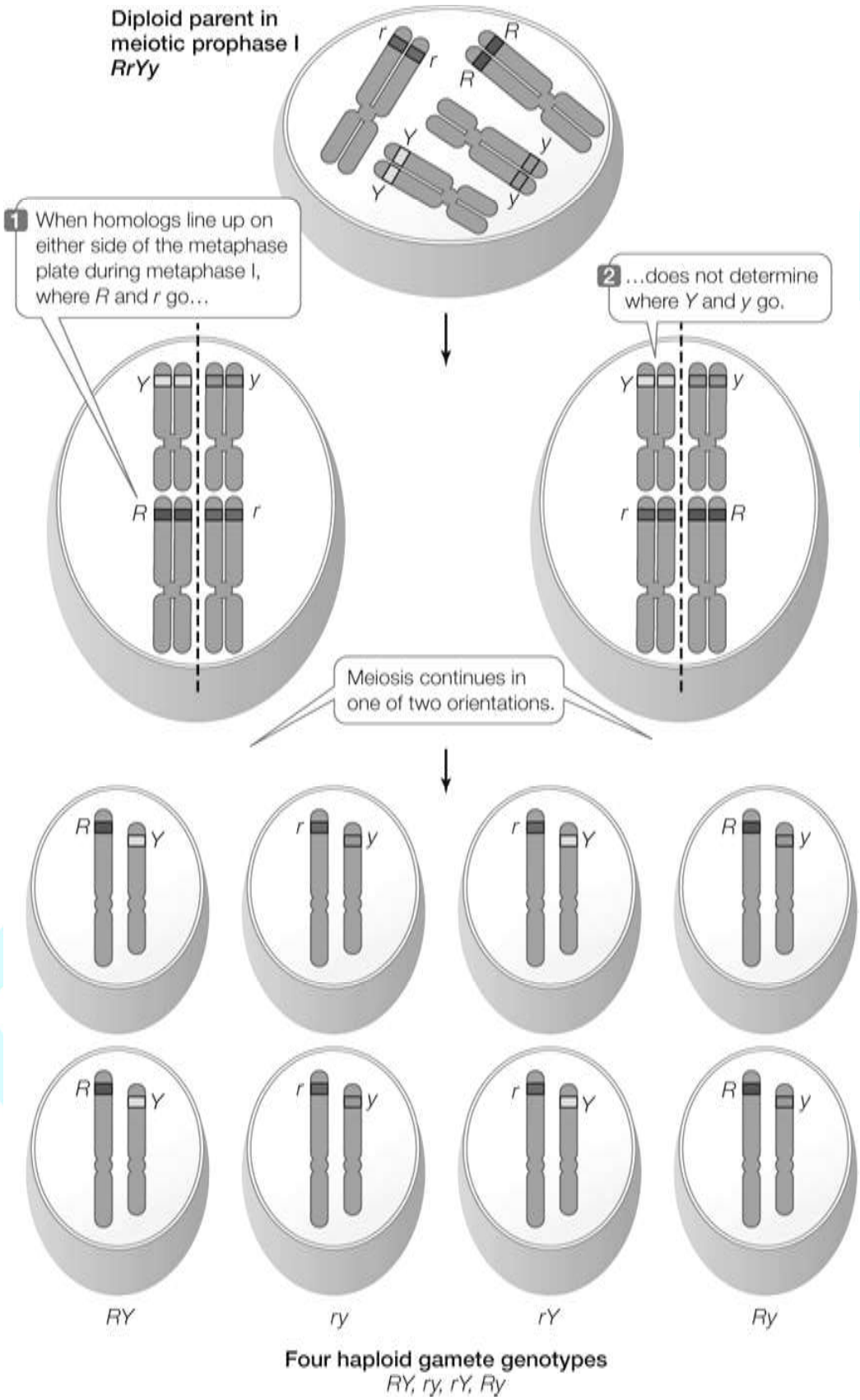


Fig: Meiosis Accounts for Independent Assortment of Alleles : We now know that copies of genes on different

chromosomes are segregated independently during metaphase I of meiosis. Thus a parent of genotype *RrYy* can form gametes with four different genotypes. *R* (round) *Y* (yellow) *r* (wrinkled) *y (green).*

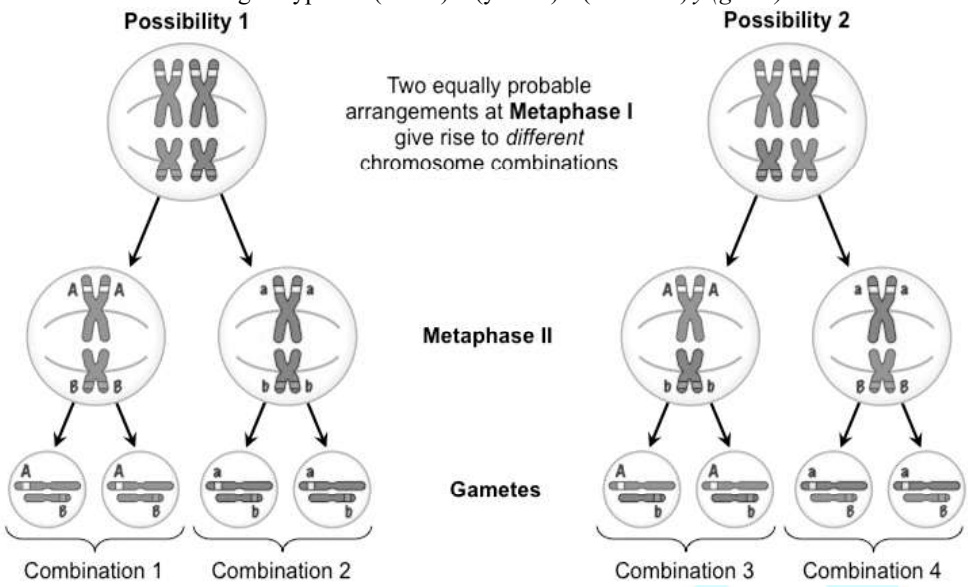


Fig: Independent Assortment of Genes via the Random Separation of Homologous Chromosomes

- If the phenotypic ratio of each pair of alleles *(e.g.,* yellow and green colour of seed) is considered, it shows 12(9 + 3) yellow seeded plants and 4(3 +1) green seeded plants.
- This comes to 3 : 1 ratio; similar to one obtained in F_2 generation of monohybrid cross showing segregation.
- The same is true for another pair of alleles involved, *i.e.,* round and wrinkled seeded plants. So, the results of each character are similar to the monohybrid ratio.

SUMMARISED ACCOUNT OF MENDEL'S EXPERIMENTS:

Trait	Dominant vs recessive	F_2 generations		Ratio
		Dominant	Recessive	
Flower colour		705	224	3.15 : 1
Seed colour		6022	2001	3.01 : 1
Seed shape		5474	1850	2.96 : 1
Pod colour		428	152	2.82 : 1
Pod shape		882	299	2.95 : 1
Flower position		651	207	3.14 : 1
Plant height		787	227	2.84 : 1

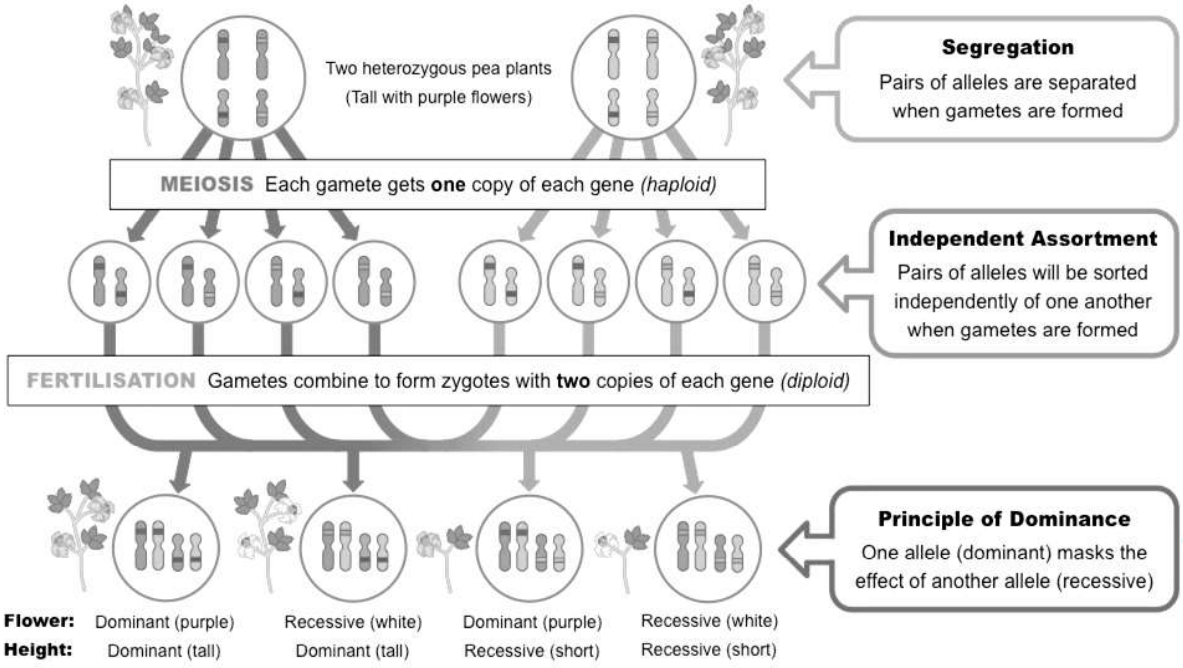


Fig: The Role of Meiosis in Mendelian Inheritance

BACK CROSS AND TEST CROSS:

- F_1 hybrids are obtained by crossing two plants of parental generation.
- Mendel devised a cross where F_1 hybrid is crossed with anyone of the two parents, *i.e.,* homozygous dominant and homozygous recessive.
- Thus, there would be two possibilities:

  (a) F_1 hybrid (Tt) is crossed with homozygous dominant (TT)

  (b) F_1 hybrid (Tt) is crossed with homozygous recessive (tt)
- Both these crosses collectively are called as **back cross.** If F_1 is crossed with dominant parent, it is called **out cross.**

Test Cross:

- Out of the two types of back crosses, a **cross between F_1 hybrid (Tt) and its homozygous recessive parent (tt) is called test cross.**
- This cross is called test cross because it helps to find out whether the given dominant F_1 phenotype is homozygous or heterozygous.

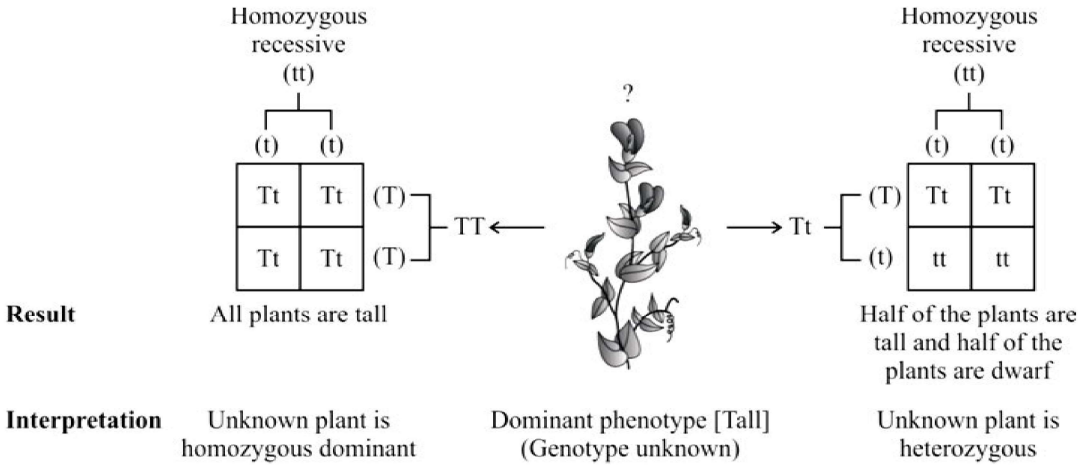
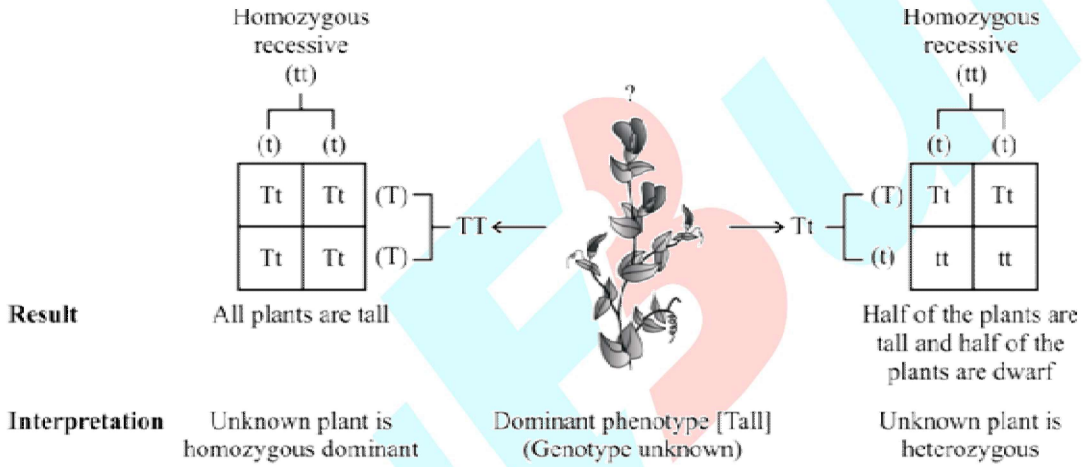


Fig: Diagrammatic representation of monohybrid test cross



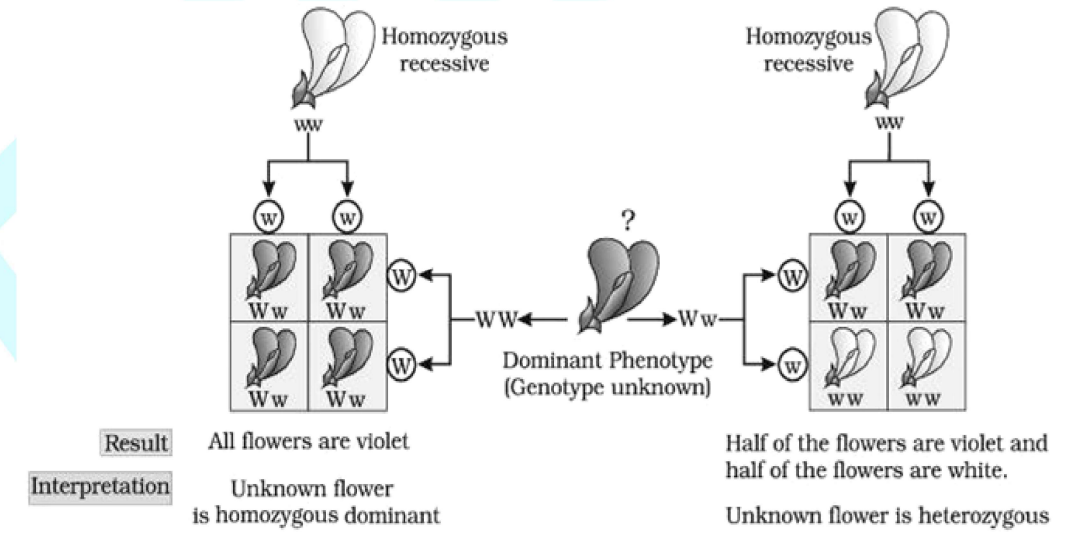


Fig. : Diagrammatic representation of monohybrid test cross

METHOD

- A monohybrid test cross between F_1 tall plant (Tt) and its homozygous recessive parent (tt) will produce 50% heterozygous tall (Tt) and 50% homozygous recessive (tt), *i.e.,* 1 : 1 ratio, for both phenotype and genotype.
- If a test cross with two characters, *i.e.,* dihybrid test cross is made, it gives four types of plants in 1 : 1 : 1 : 1 ratio
- The phenotypes obtained are similar to those found in F_2 generation of dihybrid cross.
- Thus, a dihybrid test cross between F_1 yellow and round seeded plant (YyRr) and its homozygous recessive parent green and wrinkled (yyrr) would give following combinations:
  - 1 yellow, round (YyRr) Parental combination 25%
  - 1 yellow, wrinkled (Yyrr) Recombinants 25%
  - 1 green, round (yyRr) Recombinants 25%
  - 1 green, wrinkled (yyrr) Parental combination 25%
- If this ratio is obtained, it would be confirmed that F_1 hybrid with dominant phenotype is infact heterozygous.
- The parental combinations (50%) are equal to the frequency of recombinants (50%).

Trihybrid cross.

- Mendel crossed two pea plants which differed in 3 characters and observed independent assortment of genes in them.
- He crossed two pea plants pure in three traits viz., height of stem, form of seed and colour of cotyledon of seed.
- He crossed homozygous tall, round and yellow (TT RR YY) plant with dwarf, wrinkled and green (tt rr yy).
- All the F_1 individuals produced were tall, round and yellow (Tt Rr Yy) and are called trihybrids.
- On selfing trihybrids, F_2 phenotypic ratio is 27 : 9 : 9 : 9 : 3 : 3 : 3 : 1. The ratio for a trihybrid test cross is 1 : 1 : 1 : 1 : 1 : 1 : 1 : 1 .

Probability Is Used To Predict Inheritance

One key to Mendel's success was his use of large sample sizes. By counting many progeny from each cross, he observed clear patterns that allowed him to formulate his theories. After his work became widely recognized, geneticists began using simple probability calculations to predict the ratios of genotypes and phenotypes in the progeny of a given cross or mating. They use statistics to determine whether the actual results match the prediction.

You can think of probabilities by considering a coin toss. The basic conventions of probability are simple:

- If an event is absolutely certain to happen, its probability is 1.
- If it cannot possibly happen, its probability is 0.
- All other events have a probability between 0 and 1.

There are two possible outcomes of a coin toss, and both are equally likely, so the probability of heads is ½—as is the probability of tails.

If two coins (say a penny and a dime) are tossed, each acts independently of the other. What is the probability of both coins coming up heads? In half of the tosses, the penny comes up heads, and in half of that fraction, the dime comes up heads. The probability of both coins coming up heads is ½ × ½ = ¼. In general, *the probability of two independent outcomes occurring together is found by multiplying the two individual probabilities*. This can be applied to a monohybrid cross. After the self-pollination of an *Rr* F_1 plant, the probability that an F_2 plant will have the genotype *RR* is ½ × ½ = ¼, because the chance that the sperm will have the genotype *R* is ½, and the chance that the egg will have the genotype *R* is also ½. Similarly, the probability of *rr* offspring is also ¼.

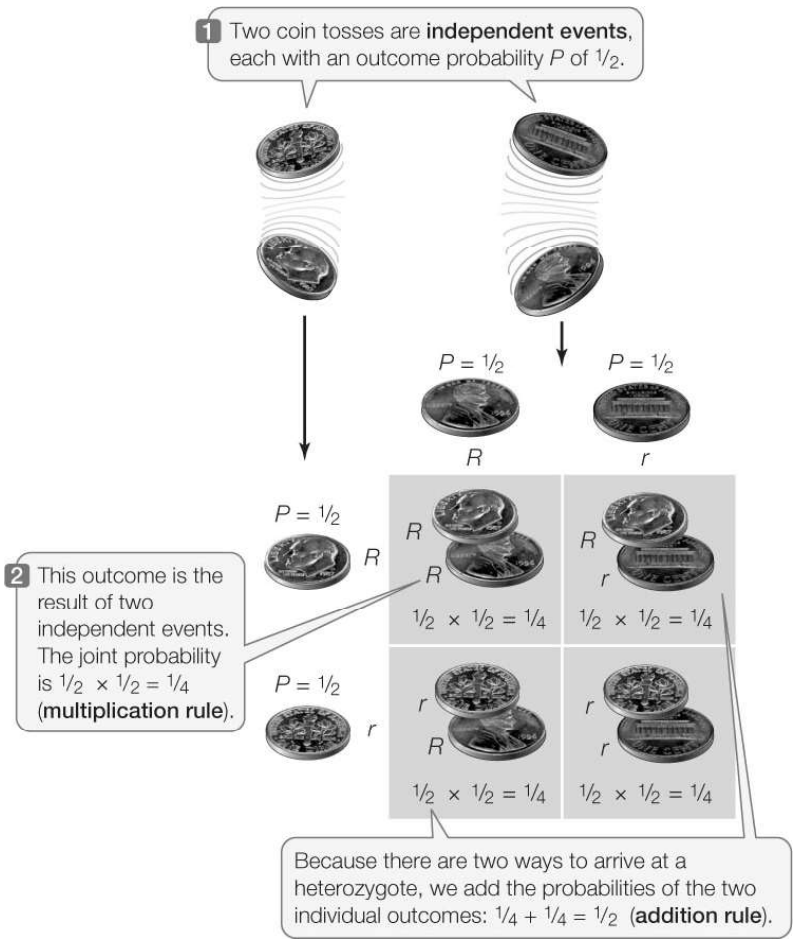


Fig: Using Probability Calculations in Genetics : Like the results of a coin toss, the probability of any given combination of alleles appearing in the offspring of a cross can be obtained by multiplying the probabilities of each event. Since a heterozygote can be formed in two ways, these two probabilities are added together.

What about the probability of getting a heterozygote? As you can see in Figures **8.2** and **8.7**, there are *two* ways to get an *Rr* plant or a head and a tail in a coin toss. In the case of the seed shape gene, the *R* allele can come from a sperm and the *r* from an egg (probability ¼). Or the *R* allele could come from the egg and the *r* from the sperm (probability ¼). *The probability of an event that can occur in two or more different ways is the sum of the individual probabilities of those ways*. Thus the probability that an F_2 plant will be a heterozygote is equal to the sum of the probabilities of the two ways of forming a heterozygote: ¼ + ¼ = ½.

3 ONE GENE INTERACTION (W.R.T. POST-MENDELIAN INHERITANCE)

(1) Incomplete dominance:

- After Mendelism a few cases were observed where F_1 phenotype is intermediate between dominant and recessive phenotypes.
- The most common example of incomplete dominance is that of flower colour in *Mirabilis jalapa* (Gulbansi or 4'O clock plant), studied by **Carl Correns**.
- Homozygous red (R^1R^1) flowered variety was crossed with white (r^1r^1) flowered variety.
- F_1 offspring had pink flowers.
- Thus, here one allele is incompletely dominant over the other so that intermediate phenotype is produced by F_1 hybrid with respect to the parents.
- This is called **incomplete dominance**.
- Incomplete dominance for flower colour [Red(R^1R^1), Pink(R^1r^1), White (r^1r^1)] is also known to occur in *Antirrhinum majus* (Snapdragon or Dog flower).
- The phenotypic ratio and genotypic ratio in F_2 generation is identical in case of incomplete dominance *i.e.,* 1 : 2 : 1.

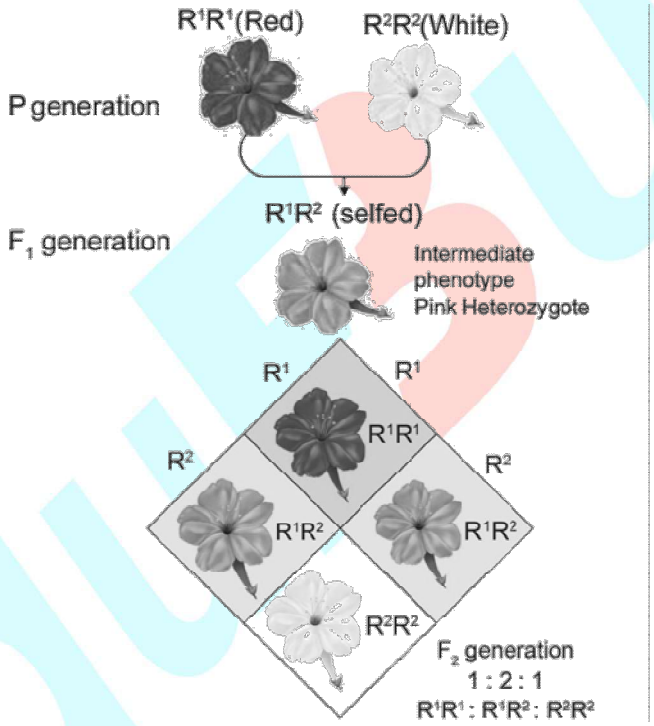


Fig. : Incomplete dominance in flower colour in *Mirabilis*

Explanation of the concept of dominance:

- Every gene contains information to express a particular trait.
- Diploid organisms have two copies of each gene, they are called **alleles**.
- These two alleles may be identical or non-identical.
- One of them may be different due to some changes that it has undergone which modifies the information that particular allele contains.
- Theoretically, the modified allele could be responsible for production of
  (i) The normal/less efficient enzyme, or
  (ii) a non-functional enzyme, or
  (iii) no enzyme at all
- In case (i), the modified allele is equivalent to the unmodified allele, *i.e.,* it will

produce the same phenotype/trait.

- But, if the allele produces a non-functional enzyme or no enzyme [case (ii) &(iii)], the phenotype may be effected.
- The unmodified (functioning) allele, which represents the original phenotype is the dominant allele and the modified allele is generally the recessive allele.
- Hence, the recessive trait is due to nonfunctional enzyme or because no enzyme is produced.
- If the mutated allele forms an altered but functional product, it behaves as incompletely or codominant allele.

(2) Multiple allelism:

- Mendel proposed that each gene has two contrasting forms, *i.e.,* alleles.
- But there are some genes which are having more than two alternative forms (allele).
- Presence of more than two alleles for a gene is known as **multiple allelism**.
- Multiple alleles are present on the same locus of homologous chromosome.
- Multiple alleles can be detected only in a population.
- A well known example to explain multiple alleles in human beings is ABO blood type.
- Landsteiner discovered ABO system of blood groups. The fourth group AB was discovered by **de Castello** and **Steini**.
- **Bernstein** showed that these groups are controlled by 3 alleles -I^A, I^B and I^O/i.
- These alleles are autosomal and follow Mendelian pattern of inheritance.
- The alleles I^A and I^B produce a slightly different form of the sugar while I^O doesn't produce any sugar. Because humans are diploid organism, each person possesses any two of the three I gene alleles.
- I^A and I^B are completely dominant over I^O, but when I^A and I^B are present together they both express their own types of sugar thus, behaving as codominant alleles.

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

- Possible blood types of children from parents of various blood types.

S.No.	Blood groups of parents	Possibilities of Children's blood group
1.	A × A	A and O
2.	A × B	A, B, AB and O
3.	A × AB	A, B and AB
4.	B × B	B and O
5.	A × O	A and O
6.	B × O	B and O
7.	B × AB	A, B and AB
8.	AB × O	A and B

9.	AB × AB	A, B and AB
10.	O × O	O

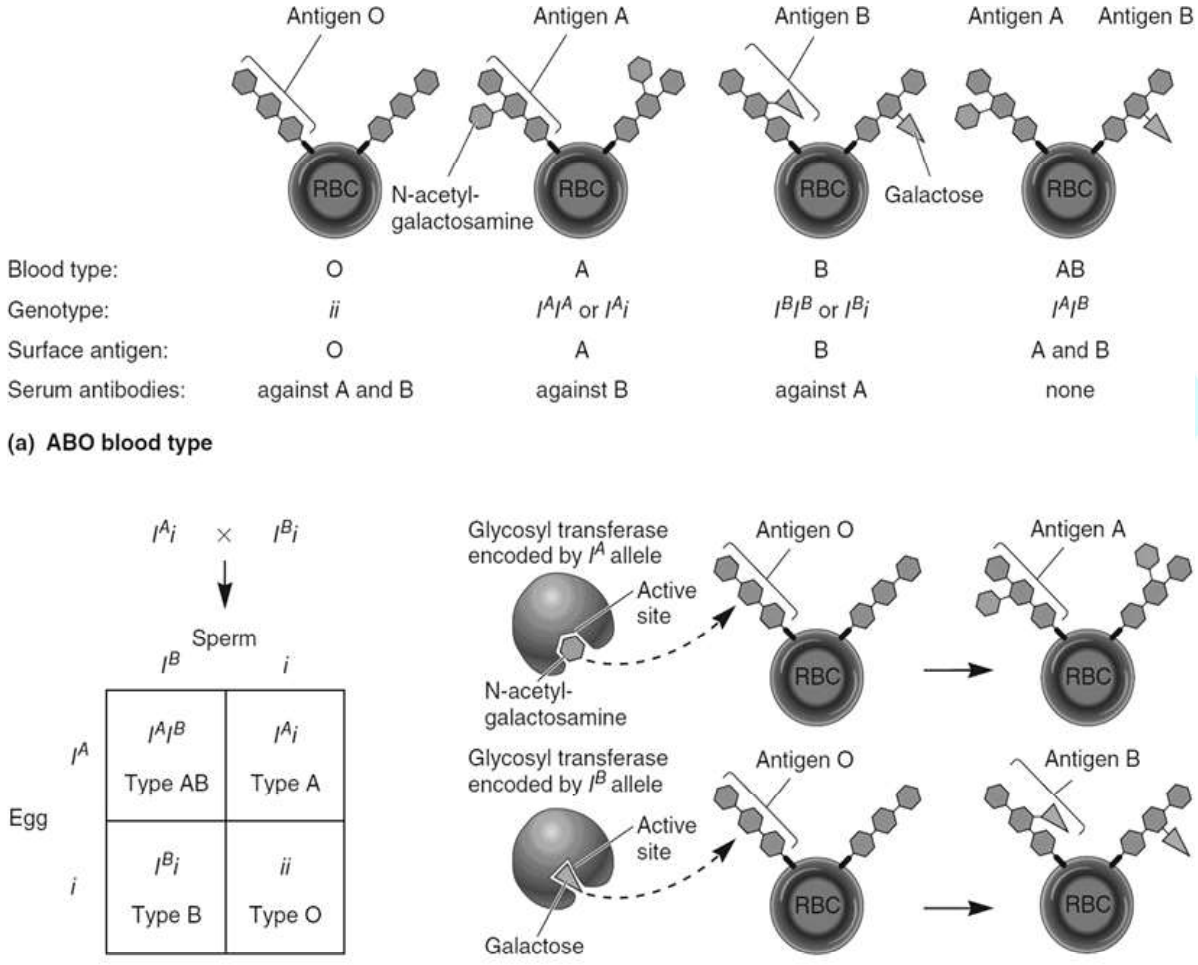


Fig: ABO blood type is due to a surface antigen and the complementary serum antibodies.
(a) Antigens on the RBC surfaces and the associated antibodies in the blood serum.
(b) To predict offspring genotypes and phenotypes, one must relax the assumption that only two alleles are segregating in a mating.
(c) Glycosyl transferase alleles encoded by the I gene recognize and bind different sugars to the carbohydrate tree.

- **Other examples of multiple alleles are -** coat colour in rabbit, eye colour in *Drosophila* and self incompatibility in tobacco. Formula to find out number of genotypes for multiple allelism is n/2(n +1) , where 'n' is number of alleles.

(3) Co-dominance.

- In co-dominance, the genes of an allelomorphic pair are not related as dominant and recessive but both of them express themselves equally in F_1 hybrids.

- These follow the law of segregation and F_2 progeny exhibits 1 : 2 : 1 ratio. Heterozygous for sickle cell anaemia (Hb^AHb^S), AB and MN blood groups are examples of co-dominance of alleles.

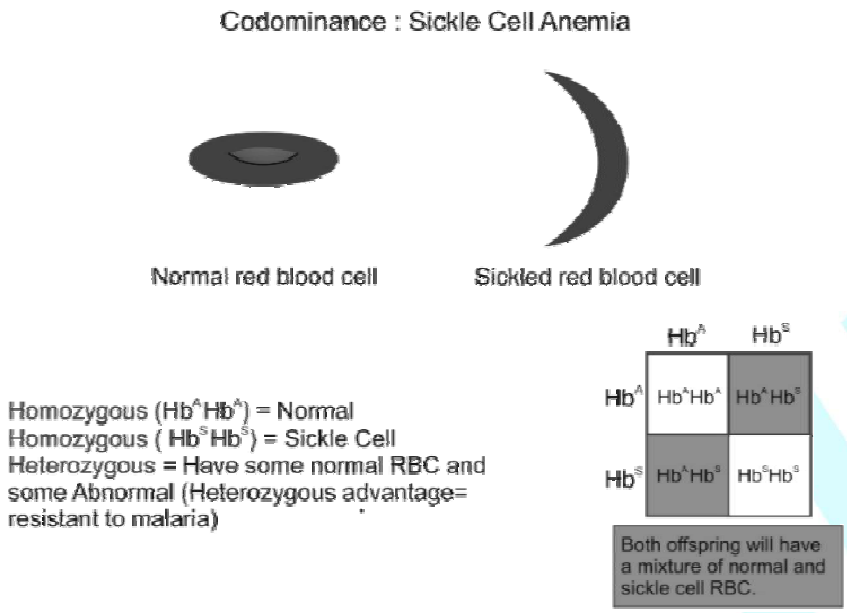


Fig: Co-dominance: sickle cell anaemia shows 1 : 2 : 1 ratio

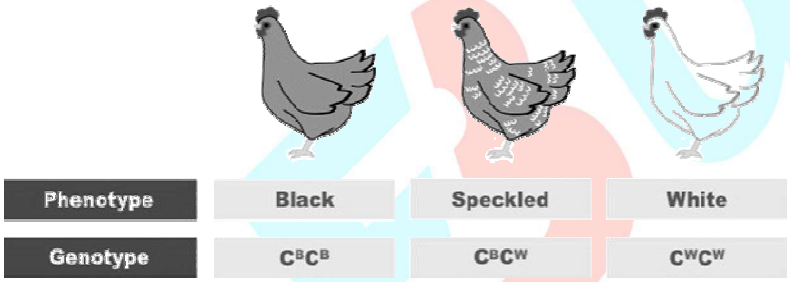


Fig: An example of co-dominance is feathering in chickens – black (C^B) and white (C^W) feathers create a speckled coat (C^BC^W)

(4) Lethal genes or lethality.

- A lethal gene usually results in the death of an individual when present in homozygous condition. Most striking example to explain lethal gene is sickle cell anaemia (Hb^SHb^S).
- **Cuenot** (1905) first reported that inheritance in mouse body colour did not agree with Mendelian inheritance, because the dominant allele for yellow body colour is lethal in homozygous condition.
- The homozygous dominant gene carrying mouse died, proving dominant gene is lethal in homozygous form.
- This is called **absolute lethality**. In plants, it was first reported in *Antirrhinum majus* by **E. Baur**, where yellow leaved or golden leaved or Aurea plant never breed true. Thus, the ratio comes out to be 2 : 1.

Fig: An allele which has the potential to cause the death of an organism is called a "Lethal Allele". In 1907, E. Baur reported a lethal gene in snapdragon (Antirrhinum sp.). It is an example for recessive lethality. In snapdragon there are three kinds of plants

1. Green plants with chlorophyll. (CC)
2. Yellowish green plants with carotenoids are referred to as pale green, golden or aurea plants (Cc).
3. White plants without any chlorophyll. (cc) T he genotype of the homozygous green plants is CC. The genotype of the homozygous white plant is cc.

The aurea plants have the genotype Cc because they are heterozygous of green and white plants. When two such aurea plants are crossed the F1 progeny has identical phenotypic and genotypic ratio of 1 : 2 : 1 (viz. 1 Green (CC) : 2 Aurea (Cc) : 1 White (cc)) Since the white plants lack chlorophyll pigment, they will not survive. So the F2 ratio is modified into 1 : 2. In this case the homozygous recessive genotype (cc) is lethal.

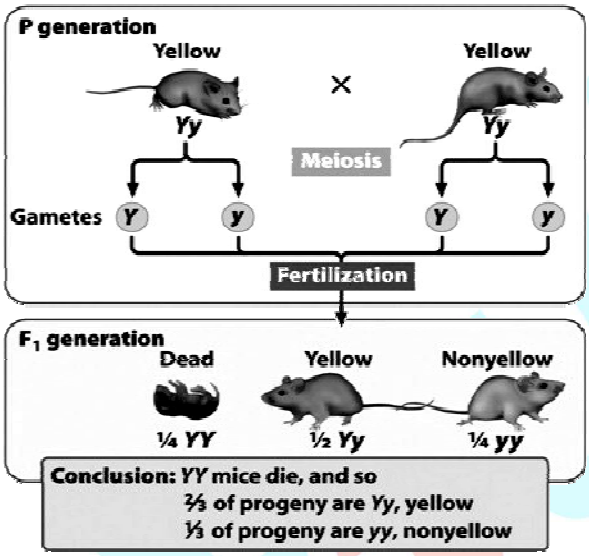


Fig: Lethality in mice

(5) Pleiotropic genes:

- The ability of a gene to have multiple phenotypic effects (as it influences a number of characters simultaneously) is known as **pleiotropy**.
- The gene having multiple phenotypic effects is called **pleiotropic gene**.
- It is not essential that the traits are equally influenced. Sometimes, the effect of the gene is more evident in case of one trait (major effect) and less evident in case of others (secondary effect).
- Occasionally, a number of related changes are caused by a gene.
- They are together called **syndrome**.
- Some common examples in humans are -Cystic fibrosis, Marfan syndrome and Phenylketonuria, while in *Drosophila,* a single gene influences the size of wings, character of balancers, position of dorsal bristles, eye colour, shape of spermathecae, fertility and longevity.
- In human beings pleiotropy is exhibited by sickle cell anaemia in heterozygous condition (Hb^AHb^S).
- In case of pea, the gene which controls the starch synthesis also controls the shape of the seed.

For starch synthesis, gene 'B' shows incomplete dominance	For shape of seed, gene shows dominant recessive relationship
BB × bb Large starch grain — Small starch grain ↓ Bb	BB × bb Round — Wrinkled ↓ Bb

Intermediate grain size	Round

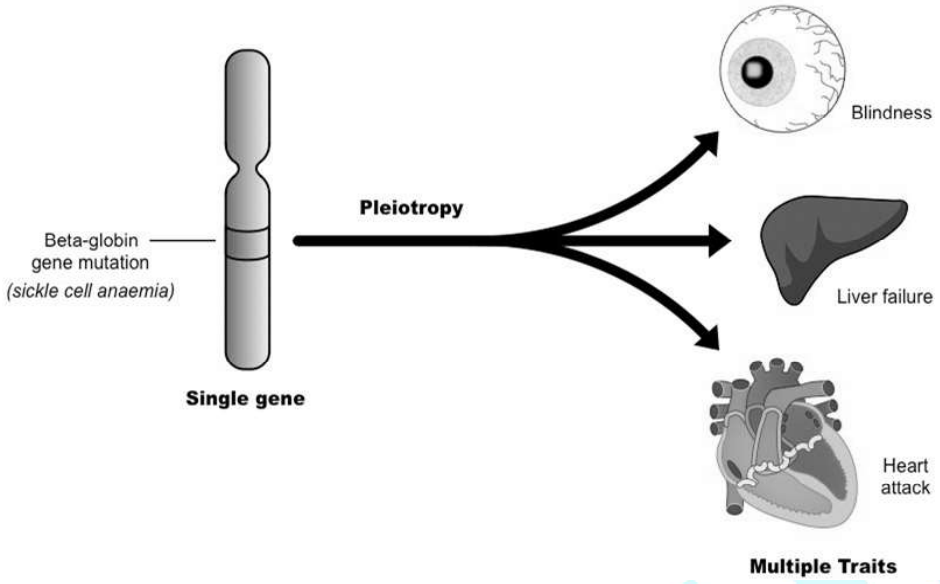


Fig: Pleiotropy observed in the multiple health issues arising from sickle cell anaemia (mutation to the beta-globin gene)

- The rapid breakdown of red blood cells causes *anaemia*, leading to increased *lethargy* and higher risks of infection
- The clotting of sickle cells in vessels can cause *heart attacks* and *brain damage* (*strokes* and *paralysis*)
- The accumulation of blood cells in specific organs can lead to loss of function (e.g. *liver* or *splenic failure*, *kidney damage*, etc.)

ROLE OF ENVIRONMENT

- ✍ The **phenotype** is the observable characteristics or traits of an organism
- ✍ It is predominantly determined by the organism's *genotype* (allele combination) for each particular feature
  However *environmental factors* may also influence the expression of characteristics
- ✍ Hydrangeas change colour depending on the pH of the soil (acidic soil = blue flower ; alkaline soil = pink flower)
- ✍ Human skin colour is determined by the expression of melanin pigment, but levels can change depending on sun exposure

Fig: The Role of Soil pH in the Determination of Hydrangea Flower Colour

4 TWO GENES INTERACTION (W.R.T POST-MENDELISM)

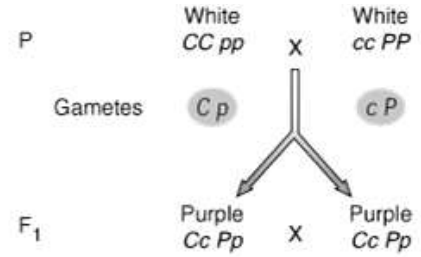
- ➔ Genes usually function or express themselves singly or individually.
- ➔ But, many cases are known where two genes of the same allelic pair or genes of two or more different allelic pairs influence one another.
- ➔ This is called **gene interaction**. **Non-allelic genetic interactions.**
- ➔ These are interactions between genes located on the same chromosome or on different but non-homologous chromosomes controlling a single phenotype to produce a

different expression.

- ➔ Each interaction is typical in itself and ratios obtained are different from those of the Mendelian dihybrid ratios.
- ➔ Some of these interactions of genes are explained here which fall under this category and deviate from Mendel's ratios.

1. Complementary genes :

- ➔ The complementary genes are two genes present on separate loci that interact together to produce dominant phenotypic character, neither of them if present alone, can express itself. It means that these genes are complementary to each other.



Male gametes

Female gametes	C P	C p	c P	c p
C P	CC PP Purple	CC Pp Purple	Cc PP Purple	Cc Pp Purple
C p	CC Pp Purple	CC pp White	Cc Pp Purple	Cc pp White
c P	Cc PP Purple	Cc Pp Purple	cc PP White	cc Pp White
c p	Cc Pp Purple	Cc pp White	cc Pp White	cc pp White

F2 phenotypic ratio -9 (Purple) : 7 (White)

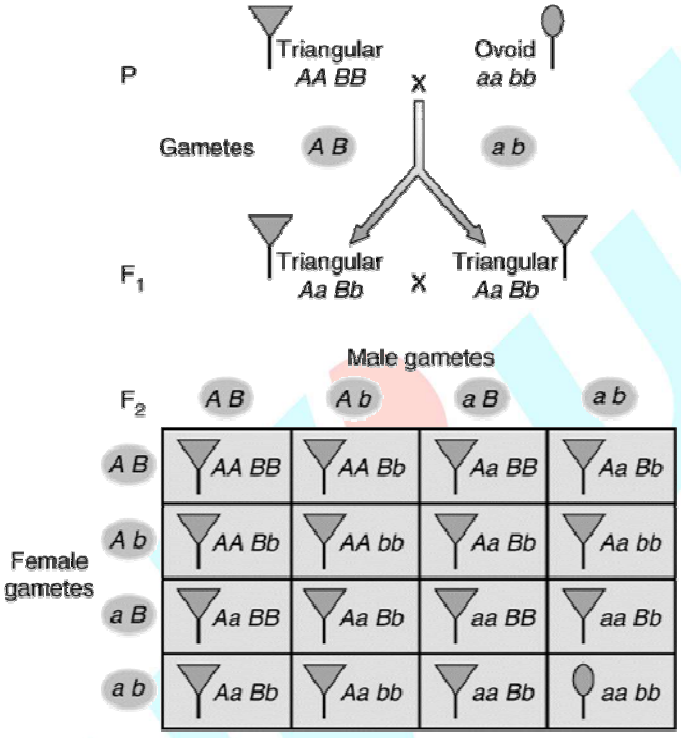
Fig. : Results of an experiment showing inheritance of flower colour in Lathyrus odoratus controlled by complementary genes

- ➔ **Bateson and Punnet** have demonstrated that in sweet pea *(Lathyrus odoratus)* purple colour of flowers develop as a result of interaction of two dominant genes C and P.
- ➔ In the absence of dominant gene C or P or both, the flowers are white
- ➔ It is believed that gene C produces an enzyme that catalyzes the formation of necessary raw material for the synthesis of pigment anthocyanin and gene P produces an enzyme which transforms the raw material into the pigment.
- ➔ It means the pigment anthocyanin is the product of two biochemical reactions, the end product of one reaction forms the substrate for the other
- Therefore, if a plant has ccPP, ccPp, CCpp or Ccpp genotypes, it bears only white flowers. Purple flowers are formed in plants having genotype CCPP or CCPp or CcPP or CcPp.
- From checker board, it is clear that 9 : **7 ratio** between purple and white is a modification of 9 : 3 : 3 : 1 ratio.

2. Duplicate genes.

- If the dominant alleles of two gene loci produce the same phenotype, whether inherited together or separately, the 9 : 3 : 3 : 1 ratio is modified into a **15 : 1 ratio**.

Example: The capsules of shepherd's purse *(Capsella)* occur in two different shapes, *i.e.,* triangular and top-shaped. When a plant with triangular capsule is crossed with one having top-shaped capsule, in F_1 only triangular character appears. The F_1 offspring by self crossing produced the F_2 generation with the triangular and top-shaped capsules in the ratio of 15 : 1. Two independently segregating dominant genes (A and B) have been found to influence the shape of capsule in the same way. All genotypes having dominant alleles of both or either of these genes (A and B) would produce plants with triangular-shaped capsules. Only those with the genotype aabb would produce plants with ovoid shaped capsules. The results of this example are given below.



Summary: 15/16 triangular, 1/16 ovoid

Fig. : Duplicate genes interaction

3. Epistasis

- A gene which masks (hides) the action of another gene (non allelic) is termed as epistatic gene. The process is called epistasis. The gene whose effects are masked is called hypostatic gene.
- Epistasis is of two types :

(a) Recessive epistasis :

- Here the recessive allele in homozygous condition masks the effect of dominant allele,
- The ratio 9 : 3 : 3 : 1 is modified to 9 : 3 : 4.

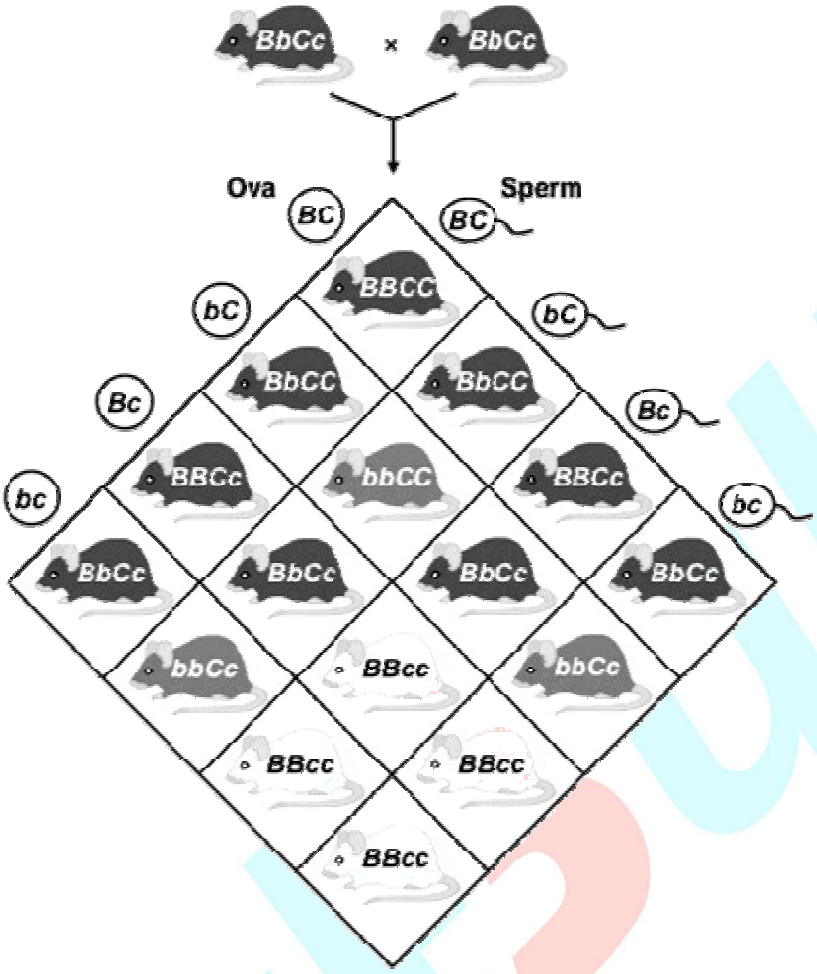


Fig: In mice, the expression of a specific fur colour by one gene is dependent upon the production of hair pigment by another gene. Black fur (B) is dominant to brown fur (b), but in the absence of hair pigment (cc) mice will appear albino

(b) Dominant epistasis :

- In summer squash or *Cucurbita pepo,* there are three types of fruit colour -yellow, green and white.
- White colour is dominant over other colours, while yellow is dominant over green
- Gene for white colour (W) masks the effects of yellow colour gene (Y).
- So, yellow colour is formed only when the dominant epistatic gene is represented by its recessive allele (w). When the hypostatic gene is also recessive (y) , the colour of the fruit is green.

White Fruit	–	W – Y –, W – y –
Yellow Fruit	–	wwY –
Green Fruit	–	wwyy

- A cross between a pure breeding white summer squash, (WWYY) with a pure breeding green summer squash, (wwyy) yields white fruits in the F_1 generation. Upon selling of F_1, the F_2 generation comes to have **12 white fruit : 3 yellow fruit : 1 green fruit.**

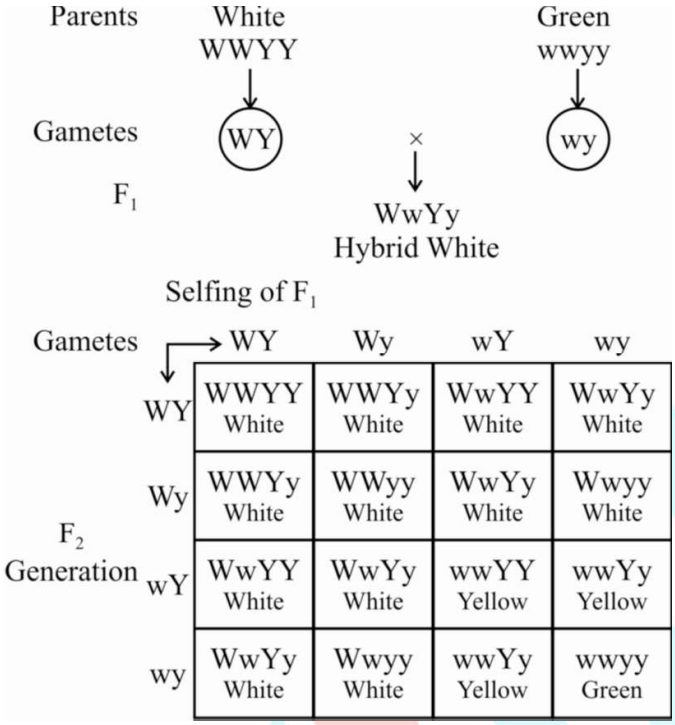


Fig. : Dominant epistasis: F_2 Phenotype ratio -12 White: 3 Yellow: 1 Green or 12 : 3 : 1

S.No.	Types of non-allelic genetic interactions	Dihybrid phenotypic ratio in F_2 generation
1.	Complementary genes	9 : 7
2.	Duplicate genes	15 : 1
3.	Recessive epistasis	9 : 3 : 4
4.	Dominant epistasis	12 : 3 : 1
5.	Polymeric/Additive genes	9 : 6 : 1
6.	Inhibitory genes	13 : 3
7.	Supplementary genes	9 : 3 : 4
8.	Collaborative gene action	9 : 3 : 3 : 1

Polygenic Inheritance Or Quantitative Inheritance

- Quantitative inheritance is controlled by two or more genes in which the dominant alleles have cumulative effect, with each dominant allele expressing a part of functional polypeptide and full trait is shown when all the dominant alleles are present.
- Genes involved in quantitative inheritance are called **polygenes**.
- **H. Nilsson-Ehle (1908) and East (1910)** demonstrated segregation and assortment of genes controlling quantitative traits, *e.g.,* **Kernel colour in wheat and corolla length in tobacco**.
- Kernel colour in wheat. Swedish geneticist, H. Nilsson-Ehle (1908) crossed red kerneled variety with white kerneled variety of wheat.
- Grains of F_1 were uniformly red but intermediate between the red and white of parental generation.
- When members of F_1 were self-crossed among themselves, five different phenotypic classes appeared in F_2 showing the ratio of 1 : 4 : 6 : 4 : 1.

(i) The extreme red -1/16 (as red as to the parent of F_1)
(ii) Deep red (Dark red) -4/16
(iii) Intermediate red -6/16 (similar to F_1)
(iv) Light red -4/16
(v) White -1/16 (as white as to the parent of F_1)

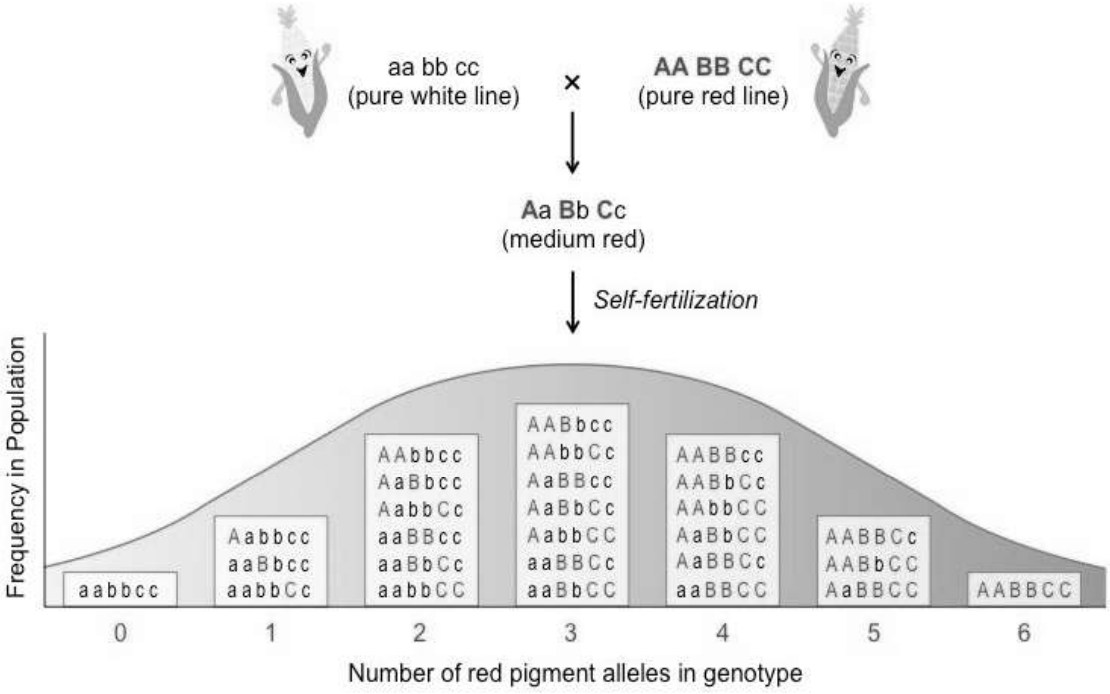


Fig: Continuous Variation in Maize Grain Colour

- Nilsson Ehle found that the kernel colour in wheat is determined by two pairs of genes AA and BB.
- Gene A and B determine the red colour of kernel and are dominant over their recessive alleles. Each gene pair shows Mendelian segregation.
- Heterozygotes for two pairs of genes (AaBb) segregate into 15 red and one white kerneled plants.
- But all the red kernels do not exhibit the same shade of redness.
- The degree of redness was found to correspond with the number of dominant alleles.

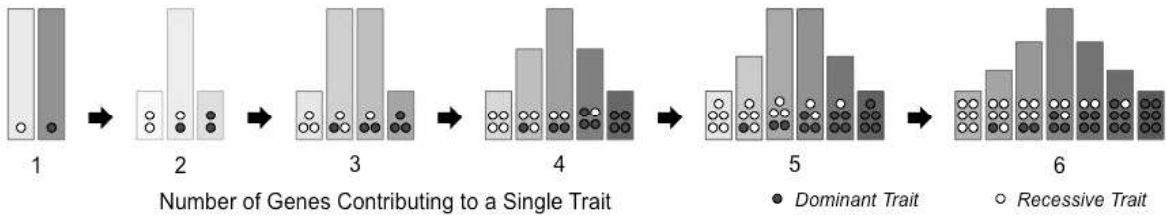
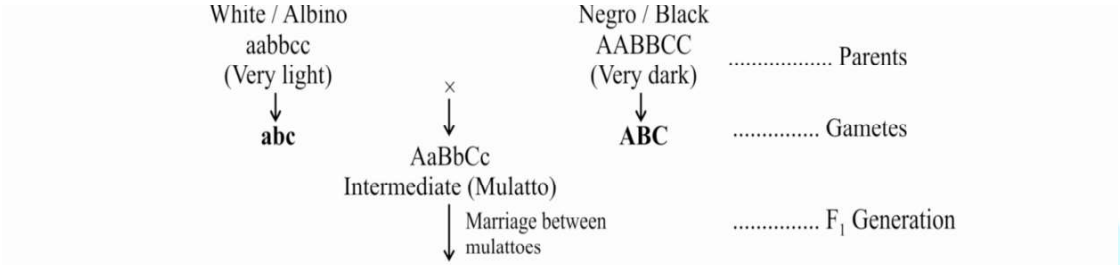


Fig: Monogenic → Polygenic Inheritance

Skin Colour in Man

- The presence of melanin pigment in the skin determines the skin colour.
- The amount of melanin developing in the individual is determined by three (two also) pairs of genes.
- These genes are present at three different loci and each dominant gene is responsible for the synthesis of fixed amount of melanin.

- The effect of all the genes is additive and the amount of melanin produced is always proportional to the number of dominant genes.
- Subsequent studies after Davenport have shown that as many as six genes may be involved in controlling the skin colour in human beings.
- As shown in table, the effect of all the genes is additive (The character is assumed to be fixed by three pairs of polygenes).

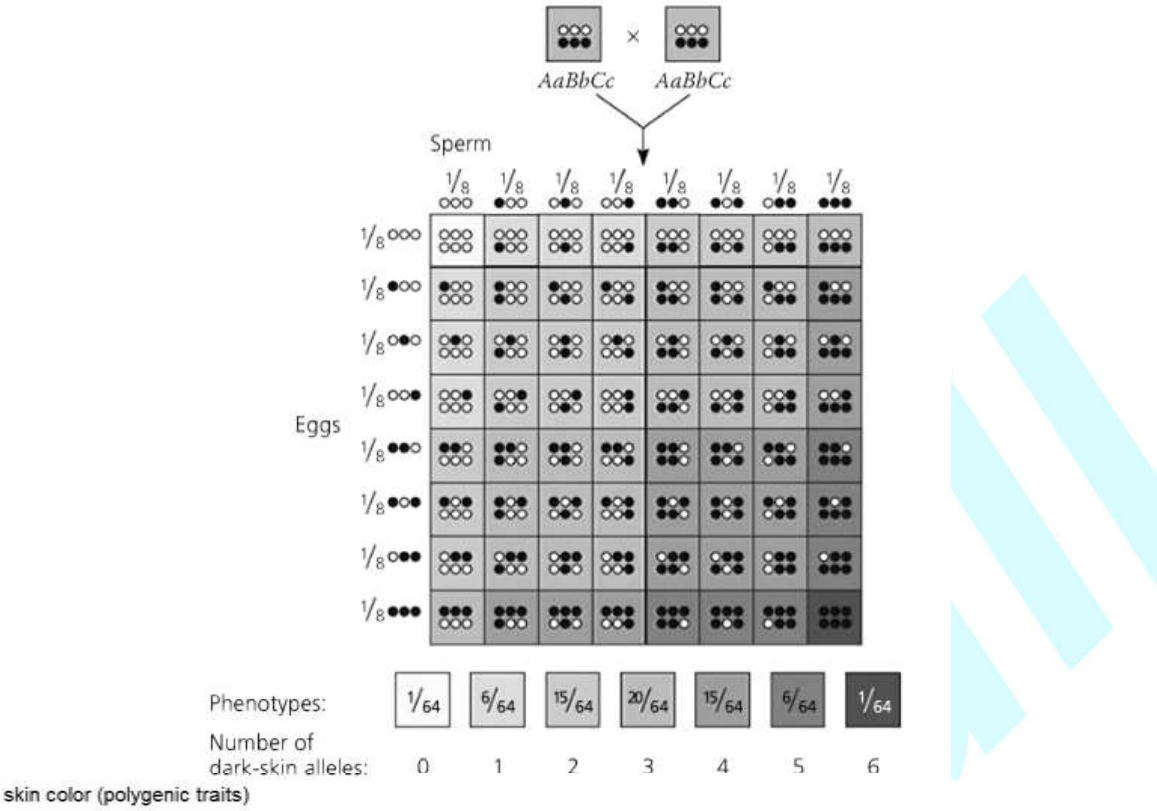


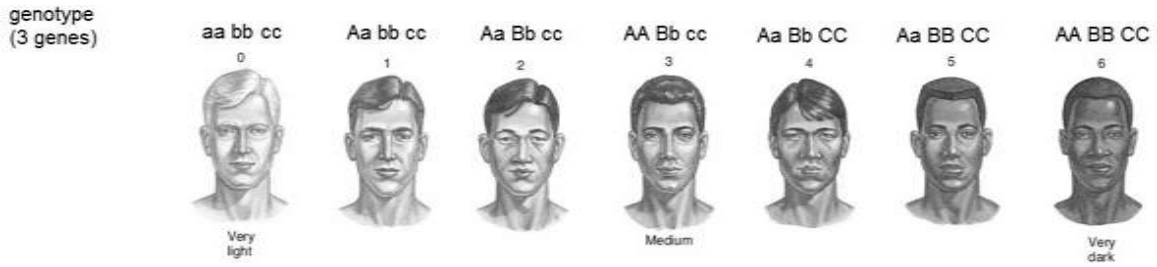
Gametes → / ↓	ABC	aBC	AbC	abC	ABc	Abc	aBc	abc
ABC	AABBCC Very dark	AaBBCC Dark	AABbCC Dark	AaBbCC Fairly dark	AABBCc Dark	AABbCc Fairly dark	AaBBCc Fairly dark	AaBbCc Intermediate
aBC	AaBBCC Dark	aaBbCC Fairly dark	AaBbCC Fairly dark	aaBbCC Intermediate	AaBBCc Fairly dark	AaBbCc Intermediate	aaBBCc Intermediate	aaBbCc Fairly light
AbC	AABbCC Dark	AaBbCC Fairly dark	AabbCC Fairly dark	aaBbCC Intermediate	AABbCc Fairly dark	AabbCc Intermediate	AaBbCc Intermediate	AabbCc Fairly light
abC	AaBbCC Fairly dark	aaBbCC Intermediate	AabbCc Intermediate	aabbCC Fairly dark	AaBbCc Intermediate	AabbCc Fairly light	aaBbCc Fairly light	aabbCc Light
ABc	AABBCc Dark	AaBBCc Fairly dark	AABbCc Fairly dark	AaBbCc Intermediate	AABBcc Fairly dark	AABbcc Intermediate	AaBBcc Intermediate	AaBbcc Fairly light
Abc	AABbCc Fairly dark	AaBbCc Intermediate	AAbbCc Intermediate	AabbCc Fairly light	AABbcc Intermediate	AAbbcc Fairly light	AaBbcc Fairly light	Aabbcc Light
aBc	AaBBCc Fairly dark	aaBBCc Intermediate	AaBbCc Intermediate	aaBbCc Fairly light	AaBBcc Intermediate	AaBbcc Fairly light	aaBBcc Fairly light	aaBbcc Light
abc	AaBbCc Intermediate	aaBbCc Fairly light	AabbCc Fairly light	aabbCc Light	AaBbcc Fairly light	Aabbcc Light	aaBbcc Light	aabbcc Light

Phenotypes: 1 (Very dark) : 6 (Dark) : 15 (Fairly dark) : 20 (Intermediate) : 15 (Fairly light) : 6 (Light) : 1 (Very light)

Fig. : Results of polygenic inheritance of skin colour in man

- The F_1 progeny between an albino and a negro individual called mulatto produces intermediate skin colour.
- In F_2 generation, the coloured offsprings exhibit different shades in the ratio 1 : 6 : 15 : 20 : 15: 6 : 1.
- The frequency distribution for skin colour can be represented either as a histogram or in the form of a bell-shaped normal distribution curve.





- Looking at the histogram, it can be concluded that in polygenic inheritance, the extreme phenotypes are rare and the intermediate ones are more frequent.
- Some other example of quantitative traits are cob length in maize, human intelligence, milk and meat production, height in human and size, shape and number of seeds and fruits in plants.
  - Number of phenotype for polygenes = 2n + 1
  - Number of genotype for polygenes = 3^n, where n represent pair of polygenes

5 CHROMOSOMAL THEORY OF INHERITANCE/PARALLELISM BETWEEN CHROMOSOMES AND MENDELLIAN FACTORS

- Chromosomal theory of inheritance was proposed independently by **Sutton and Boveri.**
- The two workers found a close similarity between the transmission of hereditary traits and behaviour of chromosomes while passing from one generation to the next through the agency of gametes.
- Sutton and Boveri noted that the behaviour of chromosomes is parallel to the behaviour of Mendelian factors (Genes).

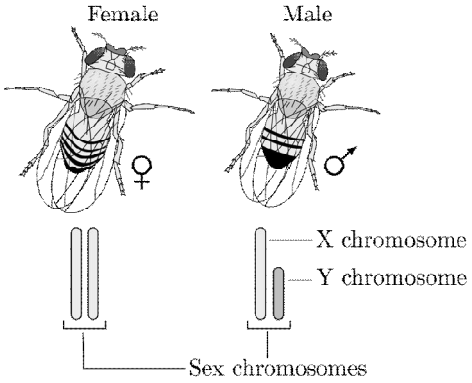
- *The salient features of chromosomal theory of inheritance are as follows :*

individuality throughout the life of an organism and from generation to generation. The two neither get lost nor mixed up. They behave as units.

2. Both chromosomes as well as genes occur in pairs in the somatic or diploid cells. The two alleles of a gene pair are located on homologous sites on homologous chromosomes.
3. A gamete contains only one chromosome of a type and only one of the two alleles of a trait.
4. The paired condition of both chromosomes as well as Mendelian factors is restored during fertilization
   - *Homologous chromosomes synapse during meiosis and then separate or segregate independently into different cells which establishes the quantitative basis for segregation and independent assortment of hereditary factors.*
   - Sutton united the knowledge of chromosomal segregation with Mendelian principles and called it the **chromosomal theory of inheritance.**
   - **Johannsen** (1909) coined the term gene, for mendelian factor.
   - Following the synthesis of ideas, **experimental verification of the chromosomal theory of inheritance by T.H. Morgan** and his colleagues, led to discovery of the basis for the variations, that sexual reproduction produced.
   - **Thomas Hunt Morgan** (1866-1945) is known as **father of experimental genetics.** He was awarded Nobel Prize of physiology in 1933 for his pioneer work in experimental genetics.

***Drosophila melanogaster* as material for experimental Genetics**

- Fruit fly *Drosophila* is a tiny fly of about 2 mm size which is found over ripe fruits like mango and banana.
- The fly is actually attracted to yeast cells present on the surface of the ripe fruits. ***Drosophila* is more suitable than pea as experimental material because** of following reasons :



Sex chromosome of Drosophila

(i) It can be easily reared and bred under laboratory conditions.

(ii) The fly has a short **life span of about two weeks.** The fruit fly can be bred throughout the year so that numerous generations can be obtained in a single year instead of one as in case of Pea.

(iii) A single mating produces hundreds of offsprings.

(iv) Females are easily distinguishable from the males by the larger body size and presence of ovipositor (egg laying structure).

(v) The animal shows a number of **externally visible** and easily identifiable contrasting traits.

(vi) It has a **smaller number** (4 pairs) of morphologically distinct chromosomes.

(vii) **Polytene chromosomes** occur in the salivary glands of larva. Polytene chromosomes can be used to study different types of chromosome aberrations.

(viii) It has heteromorphic (XY) sex chromosomes in the male. The transmission of heteromorphic chromosomes can be easily studied from one generation to another

6 LINKAGE (EXCEPTION TO LAW OF INDEPENDENT ASSORTMENT)

- According to Mendel's law of independent assortment, the gene controlling different characters get assorted independent to each other.
- It is correct if the genes are present on two different chromosomes, but if these genes are present on same chromosome they may or may not show independent assortment.
- If crossing over takes place between these two genes then the genes get segregated and they will assort independent to each other. But if there is no crossing over between these two genes there is no segregation, hence only parental combination will be found in gametes.

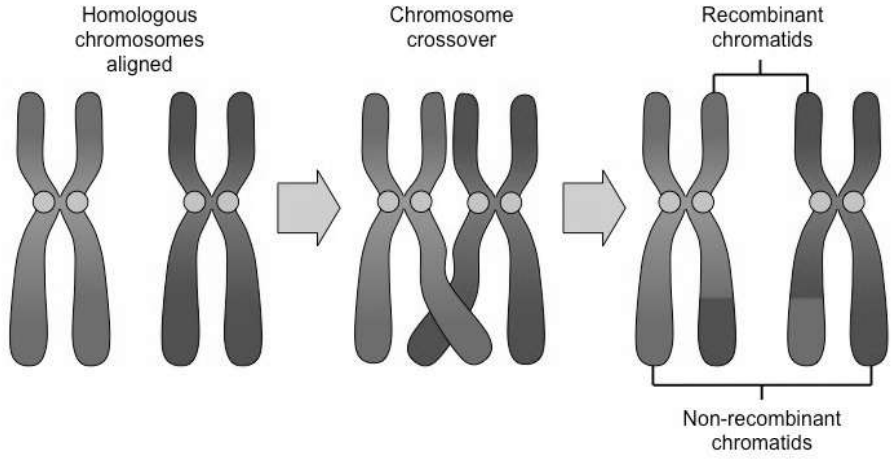


Fig: Forming Recombinant Chromosomes via Crossing Over

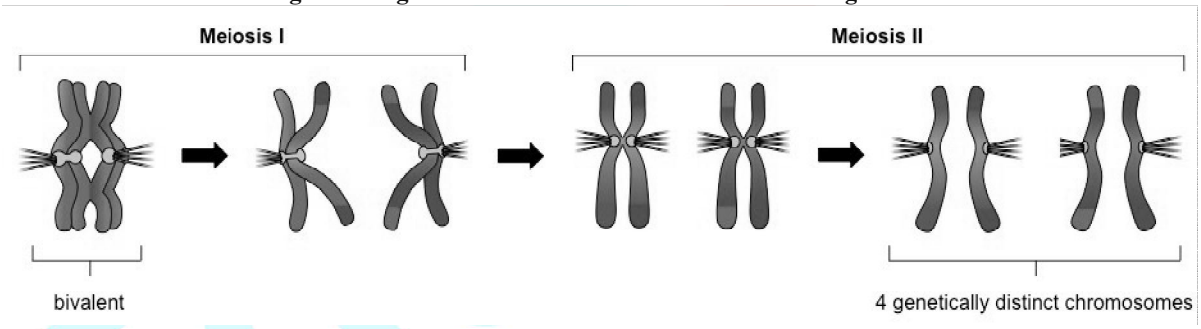


Fig: Overview of Meiotic Recombination

- The tendency of some of the genes to inherit together (en block) is known as **linkage**.
- In 1906, Bateson and Punnet crossed two varieties of *Lathyrus odoratus* (sweet pea) and observed that the results do not agree with the Mendel's law of independent assortment.

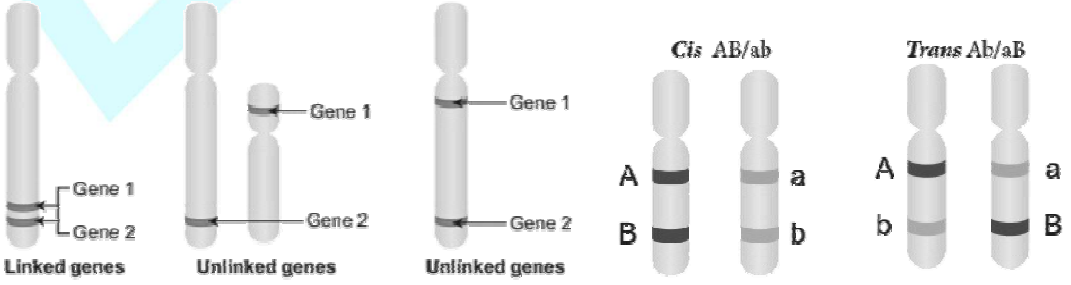


Fig: Arrangement of linked and unlinked genes on chromosome and Cis-Trans arrangement of genes

- They formulated the hypothesis of coupling and repulsion to explain the unexpected

F_2 results of dihybrid cross between a homozygous sweet pea having dominant alleles for blue flowers (BB) and long pollen grains (LL) with another homozygous double recessive plant with red flowers and round pollen grains (bbll).

- Test cross ratio of 7 : 1 : 1 : 7 indicated that there was a tendency of the dominant alleles to remain together. Similar was the case with recessive alleles.
- It was called **gametic coupling** by **Bateson** and **Punnet**.
- Two dominant genes from one parent entered the same zygote more frequently than expected.
- The tendency of two dominant genes to remain together in the process of inheritance was called as coupling.
- In another cross, they took a sweet pea plant with blue flowers and round pollens (BBII) and other plant with red flowers and long pollens (bbLL) and obtained the ratio of 1 : 7 : 7 : 1 by test crossing F_1 generation.
- When two dominant or recessive genes come from different parents, they tend to remain separate hence, this ratio was called **repulsion ratio**.
- **T.H. Morgan** in 1910 showed that coupling and repulsion are two aspects of the same phenomenon called **linkage**
- He suggested that the two genes present on the same chromosome, are in coupling phase and when present on two different homologous chromosomes are in repulsion phase.

The two dominant alleles or recessive alleles occur in the same homologous chromosomes, tend to inherit together into same gamete are called **coupling or *cis* configuration**. If dominant or recessive alleles are present on two different, but homologous chromosomes they inherit apart into different gamete are called **repulsion or *trans* configuration.**

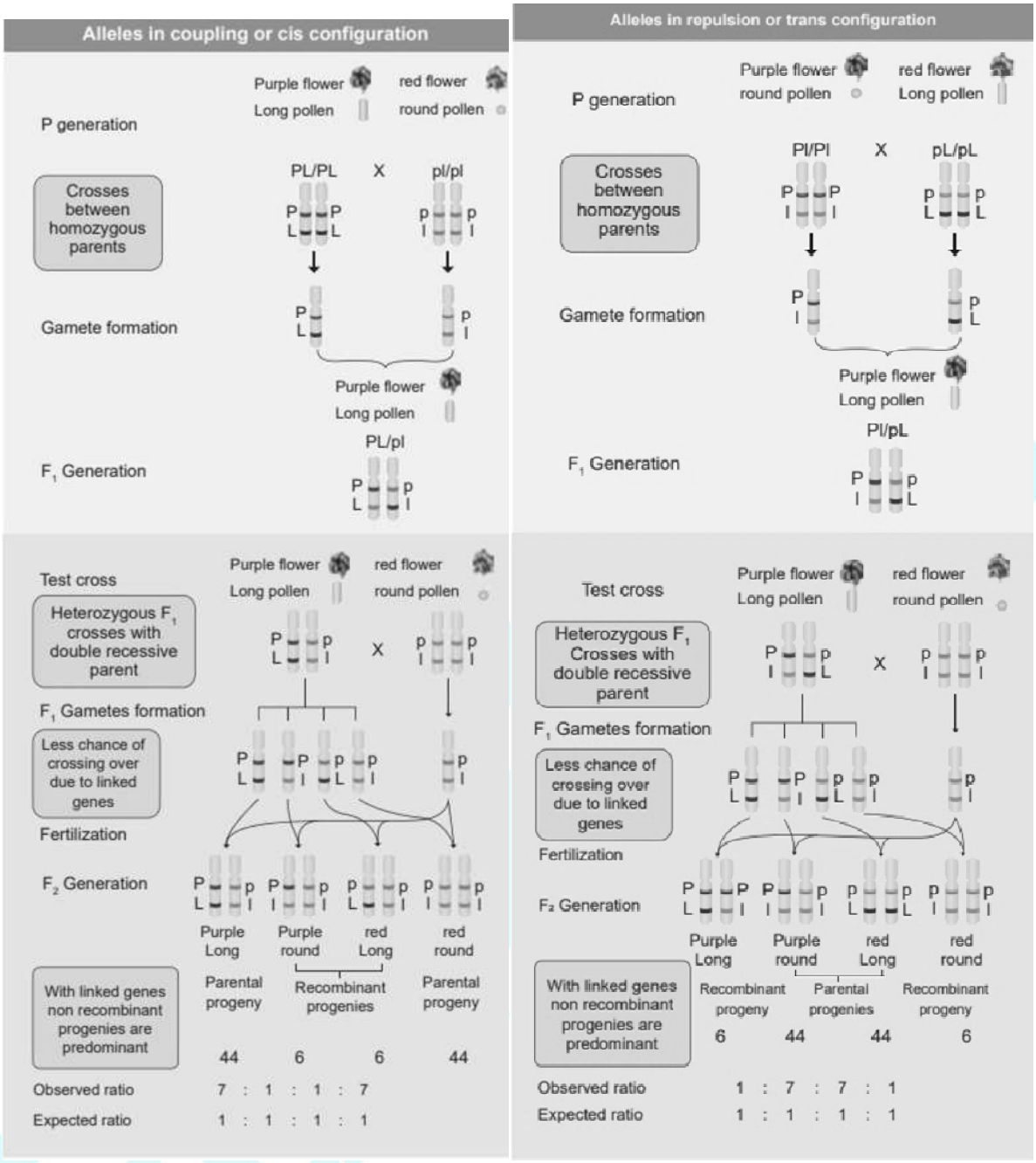


Fig: (a) Alleles in coupling or cis configuration; (b) Alleles in repulsion or trans configuration

- Morgan carried out several dihybrid crosses in *Drosophila* to study genes that were sex-linked.

(A) At first, he crossed yellow bodied (y) and white eyed (w) female with brown bodied (y^+) red eyed (w^+) male which produced F_1 with brown bodied red eyed female and yellow bodied white eyed male. In F_2 generation, obtained by intercrossing of F_1 hybrids, the ratio deviated significantly from expected. He found 98.7% to be parental and 1.3% as recombinants.

(B) In a second cross between white eyed and miniature winged female (wwmm) with wild red eyed (w^+) normal winged male (m^+), the F_1 generation included red eyed normal winged female and white eyed miniature winged male. After intercrossing the F_1 progeny, he found 62.8% parental and 37.2% recombinants.

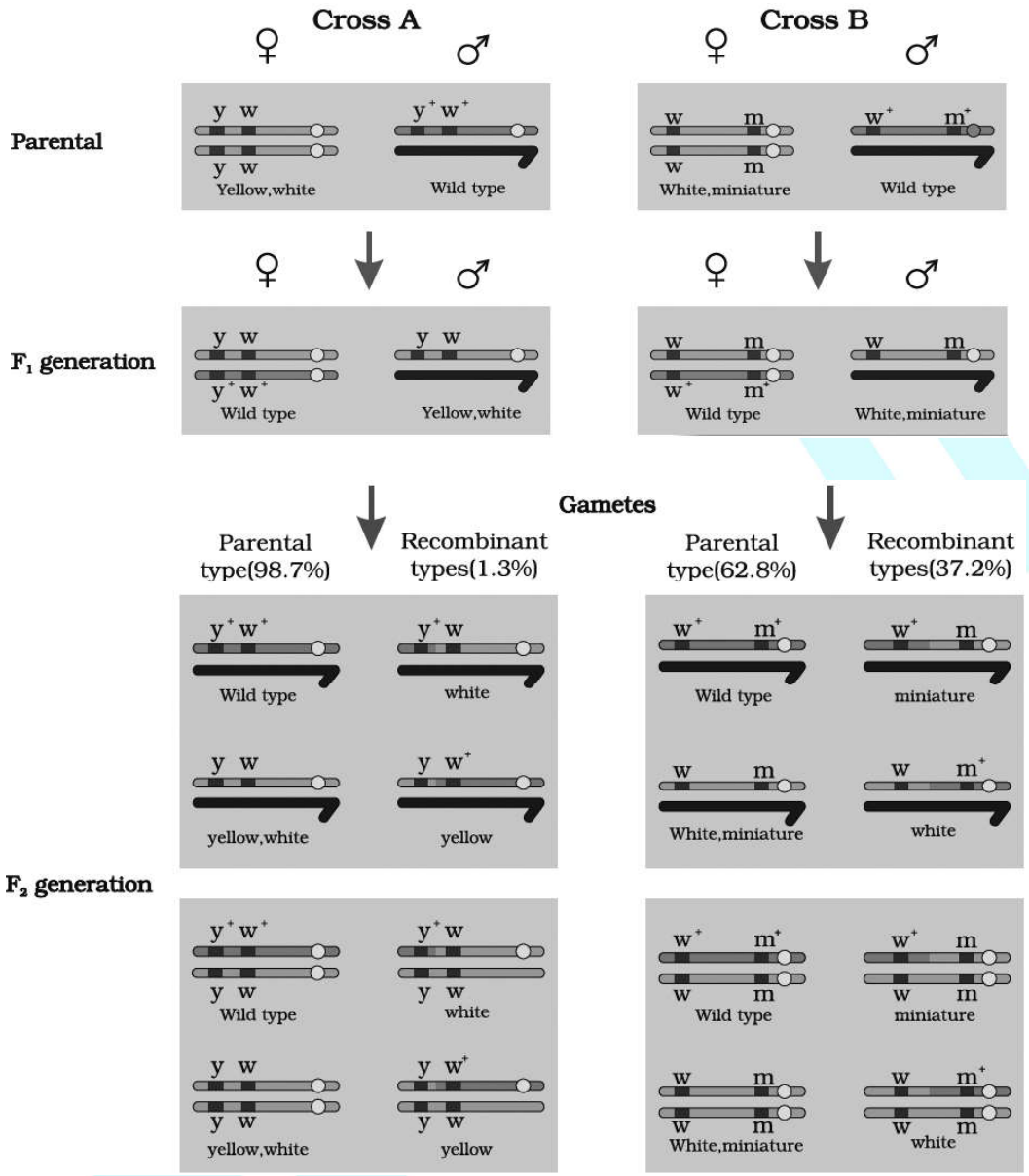


Fig. : Results of two dihybrid crosses conducted by Morgan on the basis of results we can say that strength of linkage between y and w is higher than w and m

- According to Morgan, the degree or the strength of linkage depends upon the distance between the linked genes in the chromosome.
- Linkage, therefore, may be defined as "**The tendency of two genes of the same chromosome to remain together in the process of inheritance**".

Kinds of Linkage

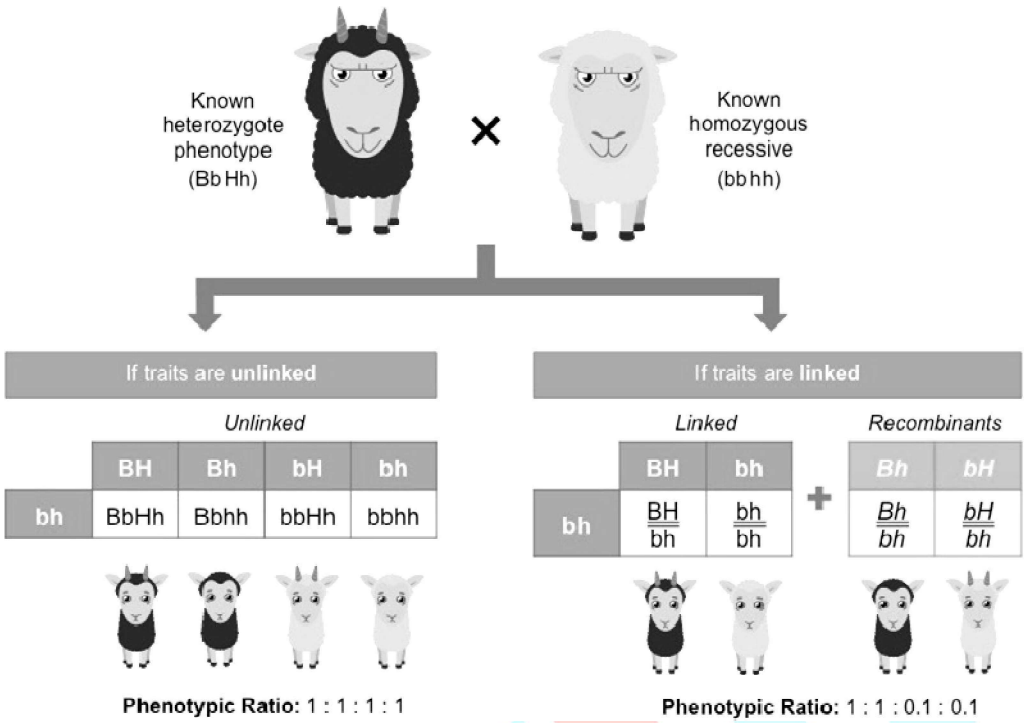
- T.H. Morgan and his coworkers found two types of linkage :

(1) Complete linkage.

- Linkage of genes on a chromosome which is not altered and is inherited as such from generation to generation without any cross over.
- In this type of linkage, genes are closely associated and tend to remain together.
  Example: Male *Drosophila* and female silk worm *(Bombax mort)*.

Fig. Cross showing complete linkage in male Drosophila

Testing For Gene Linkage



(2) Incomplete linkage.

- The linked genes do not always stay together because homologous non sister chromatids may exchange segments of varying length with one another during meiosis.
- This is known as crossing over.
- The linked genes may have chances of separation by crossing over, are called **incompletely linked genes** and the phenomenon of their inheritance is called **incomplete linkage**.
- It produces both parental and recombinant types in variable ratio.
- Bateson and Punnet studied *Lathyrus odoratus* and defined coupling and repulsion of dominant and recessive gene
- In cis arrangement or coupling condition, the incomplete linkage ratio was 7 : 1 : 1 : 7 (14-parental 2-recombinants).
- In trans arrangement or repulsion case, the ratio was 1:7:7:1 (parental 14, recombinants = 2). **Example:** In maize, incomplete linkage was observed by **Hutchinson** w.r.t seed coat colour and seed shape. The results show that parental combination of alleles (CS/CS and cs/cs) appear in about 96% cases. The other two are new combinations (Cs/cs and cS/cs) wh ich appear in about 4% cases. Thus, in about 4% cases, crossing over has occurred between linked genes.

Parents	Coloured & full CS/CS	×	Colourless & shrunken cs/cs
Gametes	(CS)	×	(cs)
F_1	CS/cs (Coloured & full)		
Test cross	CS/cs	×	cs/cs
Gametes	cs		
Result : CS	CS/cs	– Coloured & full 48.2%	
Cs	Cs/cs	– Coloured & shrunken 1.8%	
cS	cS/cs	– Colourless & full 1.8%	
cs	cs/cs	– Colourless & shrunken 48.2%	

Fig. : Cross showing incomplete linkage

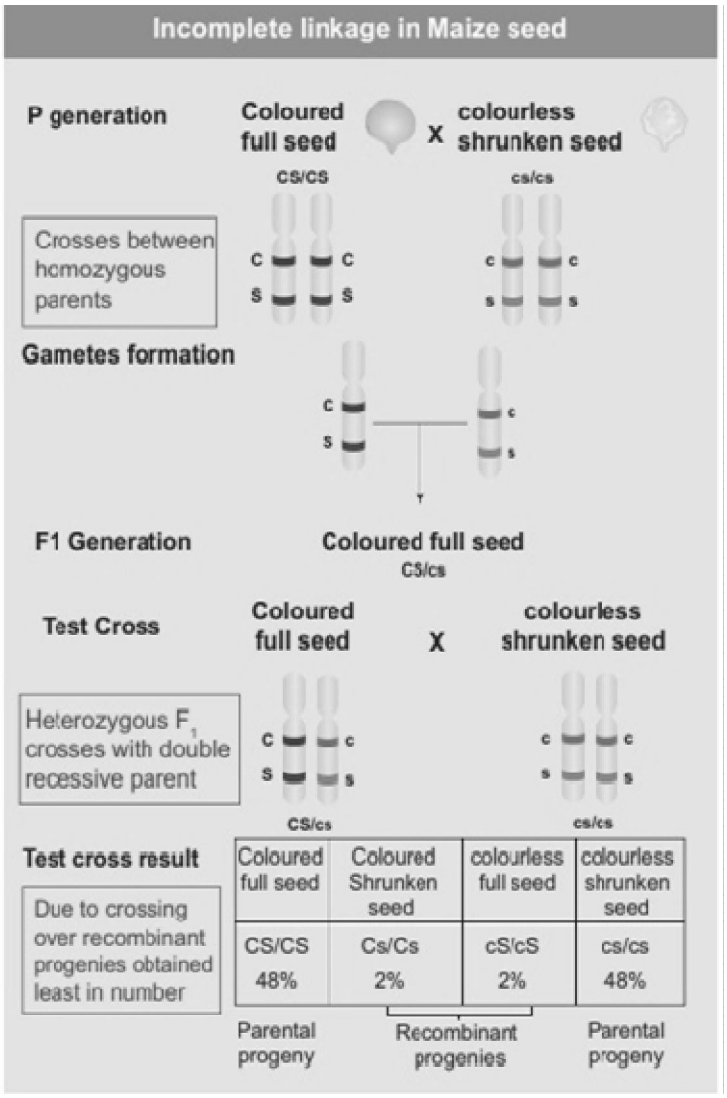
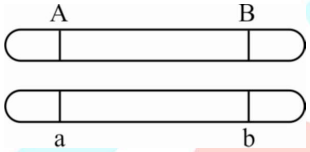


Fig: Incomplete Linkage in Maize

DO YOU KNOW ?

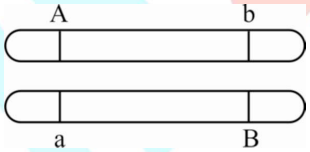
7 CROSSING OVER AND RECOMBINATION

- Crossing over is a process that produces new combination of genes by interchanging of segments between nonsister chromatids of homologous chromosomes.
- The crossing over occurs in between the homologous chromosomes at four stranded or tetrad stage during pachytene of prophase I of Meiosis I.
- A condition where an individual heterozygous for two pairs of linked genes (AaBb) possesses the two dominant genes on one member of the chromosome pair and the two recessive on the other, is said to be **cis arrangement.**



C is arrangement

- If an individual heterozygous for two pairs of linked genes (AaBb) possesses one dominant and one recessive allele of each pair of genes on each member of the homologous pair of chromosome, the arrangement is said to be **Trans arrangement.**



Trans arrangement

- When two genes are located very close to each other in chromosomes, hardly any crossing over can be detected.
- The linkage is broken down due to crossing over.
- Crossing over will be relatively more frequent if the distance between two genes is more.
- *Frequency of crossing over can be determined cytologically by counting the number of* ***chiasmata***.
- The details of the crossing over for two genes A and B and their alleles a and b on the homologous chromosomes are shown in figure.

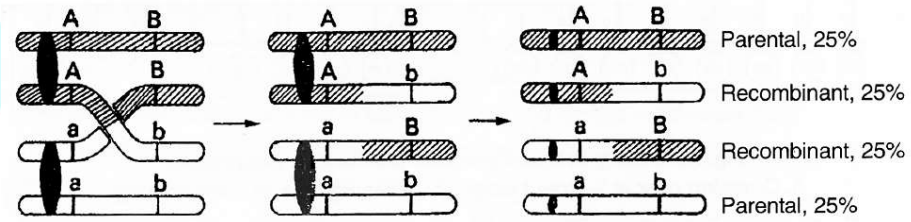


Fig. : Crossing over showing 50 per cent parental and 50 percent

Depending upon the number of chiasmata formed crossing over may be classified into three types:

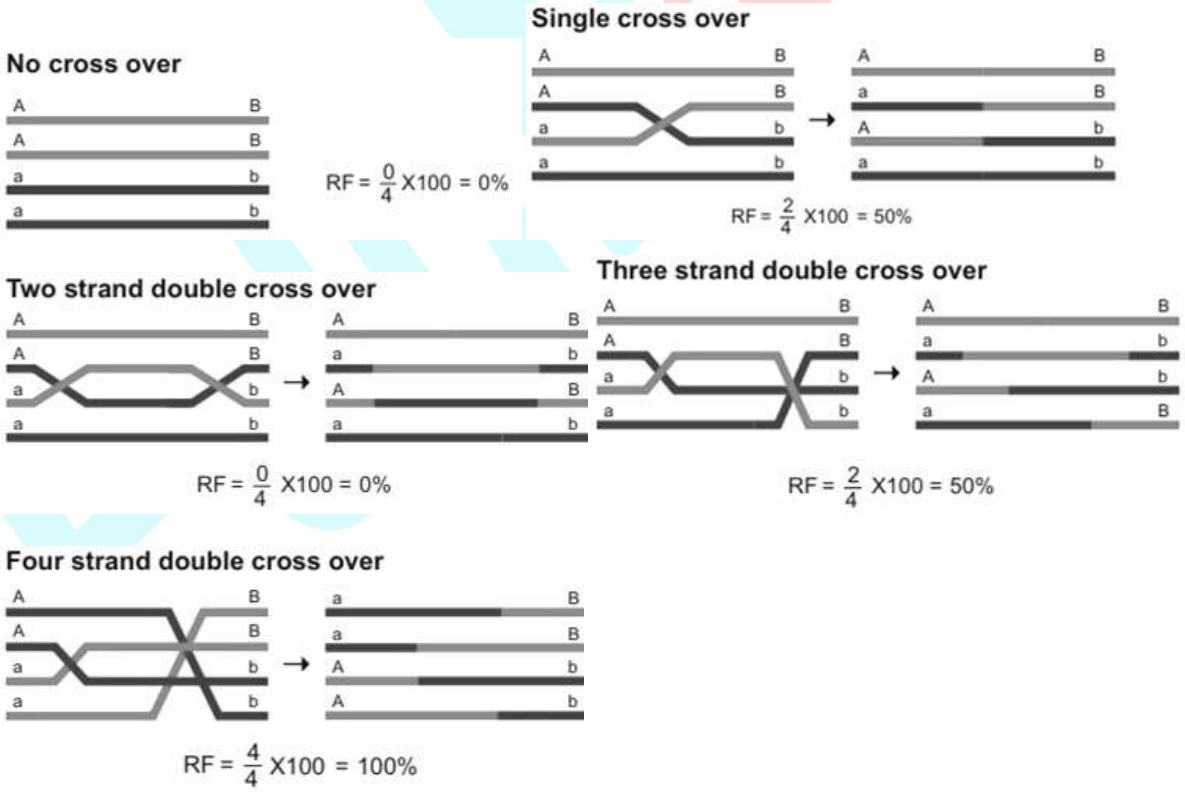


Fig: types of crossing over and its recombination frequency (RF)

Crossing Over Occurs at Four Stranded Stage

- *Neurospora* (pink mould), an ascomycetous fungus is used to demonstrate that crossing over takes place at 4-stranded stage.
- It has following advantages as experimental organism :

(1) It is haploid and there is only one allele at each locus. Hence, dominant-recessive relationship does not interfere with observations and analysis.
(2) The products of single meiosis can be easily analysed.
(3) The products of meiosis occur in the form of 'ordered tetrads', *i.e.,* the eight ascospores formed, are linearly arranged in a sac-like structure called **ascus**

- If genes A and B are located on same chromosome and undergo independent assortment, the genotype of linearly arranged ascospores can be studied. If crossing over takes place at 2-strand stage, the ascospores would show Ab, Ab, Ab, Ab, aB, aB, aB, aB, (4 Ab + 4 aB) arrangement.
- If crossing over takes place at 4-stranded stage, the ascospores would show AB, AB, Ab, Ab, aB aB, ab, ab, (2AB + 2 Ab + 2 aB + 2 ab) arrangement or 2: 4 : 2 arrangement.
- Tetrad analysis has demonstrated the presence of such an arrangement and thus, it is now confirmed that crossing over occurs at 4-stranded stage.

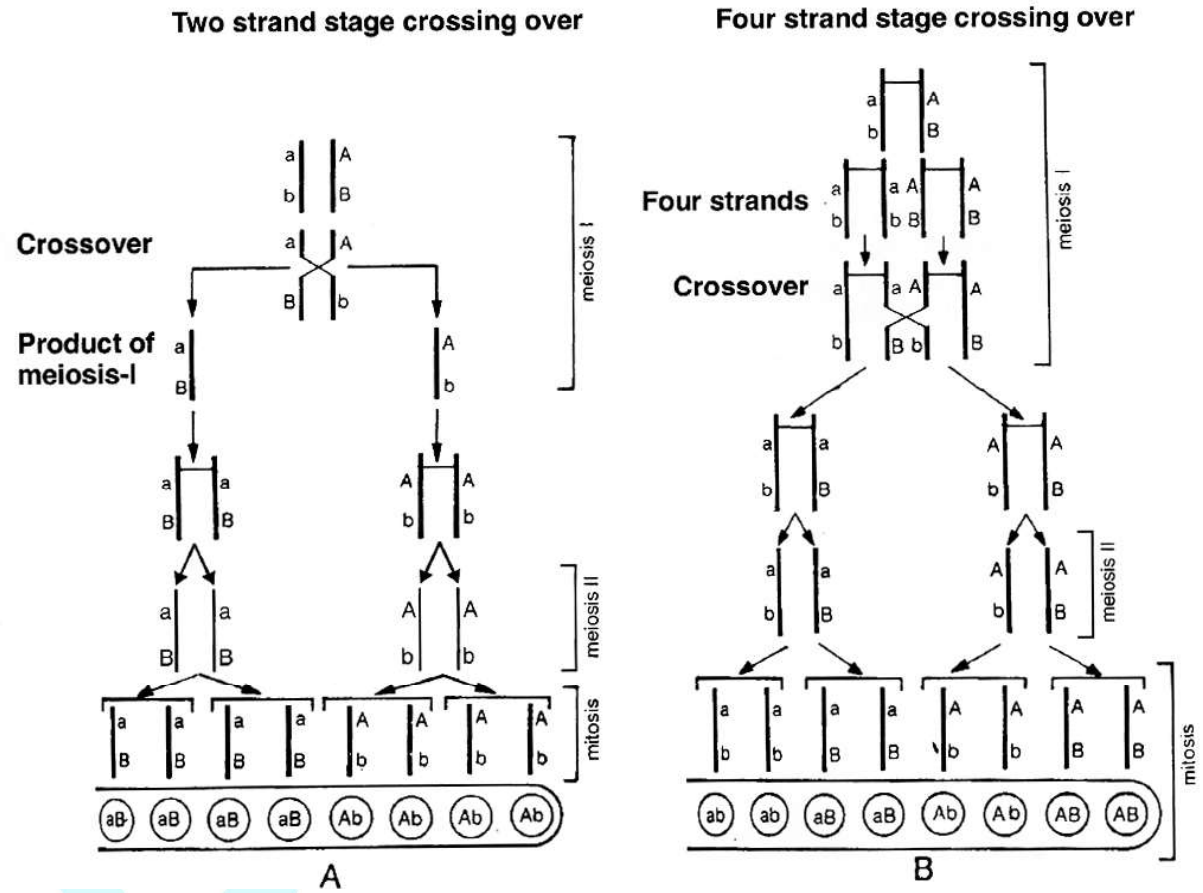


Fig. : Crossing over and possible products in Neurospora
A. Crossing over at 2-strand stage; B. Crossing over at 4-strand stage

Factors affecting crossing over:

(i) Distance between the genes is directly proportional to crossing over.
(ii) Cross over decreases with age.
(iii) X-rays and temperature increases crossing over.
(iv) Centromere and heterochromatin positions decrease crossing over.
(v) One cross over reduces the frequency of other crossover in its vicinity which is called as interference.

RECOMBINATION: Crossing over results in the formation of new combination of characters in an organism called recombinants. In this, segments of DNA are broken and recombined to produce new combinations of alleles. This process is called **Recombination**

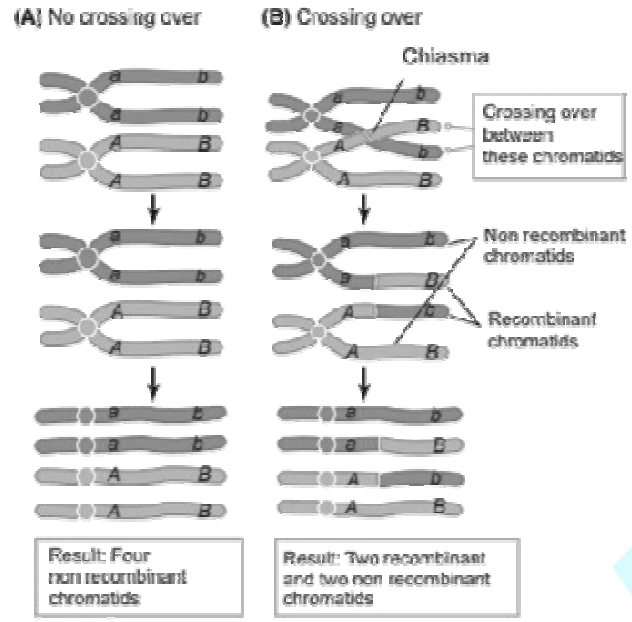


Fig: Recombination

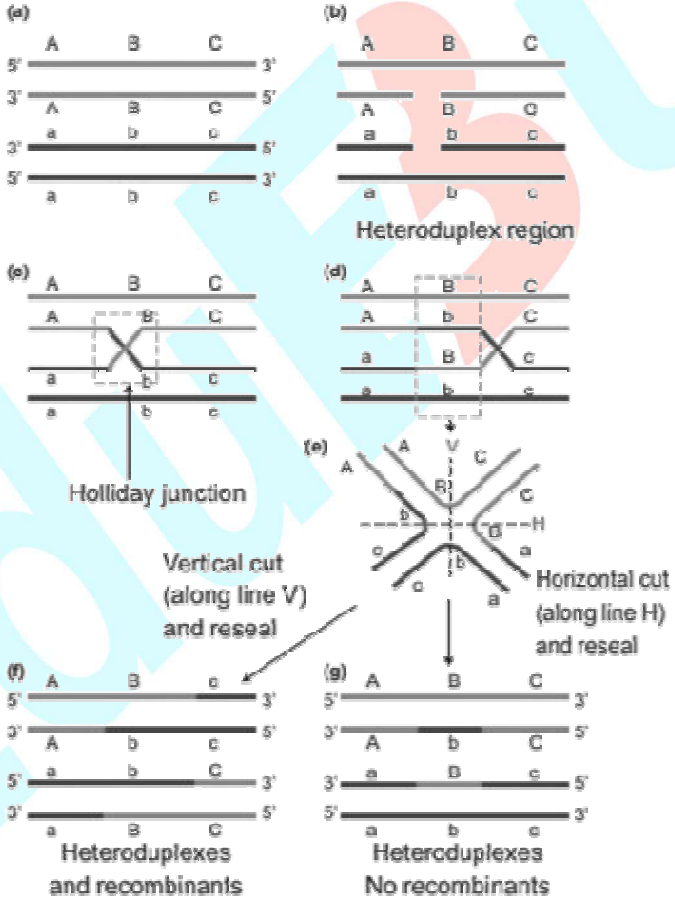
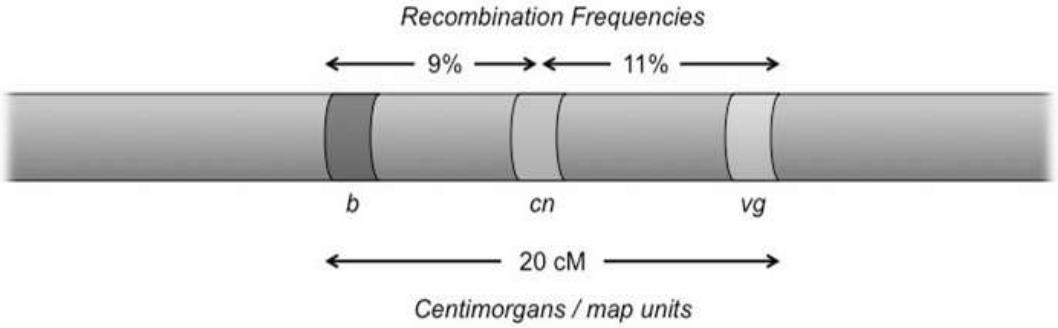


Fig: Holiday Model of Recombination

8 CHROMOSOMAL MAPPING

- Crossing over is important in locating the genes on chromosome.
- The genes are arranged linearly on the chromosome.
- This sequence and the relative distances between various genes is graphically represented in terms of **recombination frequencies** or cross over values (COV).

- This is known as linkage map of chromosome.
- Distance or cross over units are called **centimorgan (cM)** or map unit.



- Term **centimorgan** is used in eukaryotic genetics and **map unit** in prokaryotic genetics
- The recombination frequency depends upon the distance between the genes.
- If the distance between the genes is lesser the chances of crossing over is less and hence recombination frequency is also lesser and vice versa.
- So, recombination frequency is directly proportional to the distance between genes.
- In any cross, if recombination frequency is 5%.
- It means the distance between the genes is 5 map unit.
- **A.H. Sturtevant** suggested that these recombination frequencies can be utilized in predicting the sequence of genes on the chromosome.
- On the basis of recombination frequency, he prepared first chromosomal map or genetic map for *Drosophila.*

Memories

- **T.H. Morgan** (1910) developed the theory of the gene as a **locus or discrete unit** on the chromosomes from his studies on Drosophila melanogaster.
- **Stern** .(193 1) showed that genetic crossing over was accompanied with actual exchange of chromosome segments. He, therefore, gave the **cytological proof ofcrossing over.**
- Map unit is related with frequency of crossing over and not with linkage.
- **C.D. Darlington** -Precocity theory of crossing over.
- **J. Belling** -Belling's hypothesis and copy choice mechanism of crossing over.
- **Creighton and McClintock** -Cytological evidence of crossing over using corn as the material.
- **Pontecarvo** (1952) -Defined genes as the ultimate unit of recombination.
- **Janssen** -Discovered Chiasmata formation

9 CHROMOSOMES

The chromosomes are capable of self-reproduction and maintaining morphological and physiological properties through successive generations. They are capable of transmitting the contained hereditary material to the next generation. Hence these are known as '**hereditary vehicles**'. The eukaryotic chromosomes occurs in the nucleus and in certain other organelles, and are respectively called nuclear and extranuclear chromosomes. Nuclear chromosomes are long,

double stranded DNA molecules of linear form and associated with proteins, separated from the cytoplasm by nuclear envelope and replicated during S phase of cell cycle, while extranuclear chromosomes are present in the mitochondria and plastid. They are short, double stranded DNA molecules of circular form and are not associated with proteins and also called prochromosomes.

(i) Discovery of chromosomes

Hofmeister (1848) : First observed chromosomes in microsporocytes (microspore mother cells) of *Tradescantia*.

Flemming (1879) : Observed splitting of chromosomes during cell division and coined the term, 'chromatin'.

Roux (1883) : He believed the chromosomes take part in inheritance.

W.Waldeyer (1888) : He coined the term 'chromosome'.

Benden and Boveri (1887) : They found a fixed number of chromosomes in each species.

(ii) Kinds of chromosomes

(a) **Viral chromosomes :** In viruses and bacteriophages a single molecule of DNA or RNA represents the viral chromosome.

(b) **Bacterial chromosomes :** In bacteria and cyanobacteria, the hereditary matter is organized into a single large, circular molecule of double stranded DNA**,** which is loosely packed in the nuclear zone. It is known as bacterial chromosome or *nucleoid*.

(c) **Eukaryotic chromosomes :** Chromosomes of eukaryotic cells are specific individualized bodies, formed of deoxyribonucleo proteins (DNA + Proteins).

(iii) Number of chromosomes : The number of chromosomes varies from two, the least number an organism can have, to a few hundred in different species. The number of chromosomes a species possesses has no basic significance, nor it necessarily shows relationship between two different species that have the same number.

Both dog and fowl have 78 chromosomes. Thus, it is not the number of chromosomes, but the genes in them which differentiate species. Their number also does not indicate the size or complexity of the organism. *Amoeba proteus* has 250 chromosomes and man has 46. The related species tend to have similar chromosome. Man and his nearest relatives, the apes, have chromosomes similar in size, shape and banding pattern. The least number of chromosomes are found in *Ascaris megalocephala i.e.* 2 while in a radiolarian protist (*Aulocantha*) has maximum number of chromosomes is 1600. The male of some roundworms and insects have one chromosome less than the females. For instance, the male and female roundworm *Coenorhabditis* have 11 and 12 chromosomes respectively and the male and female cockroach (*Blatta*) have 23 and 24 chromosomes respectively.

Diploid number of chromosomes in some animals

Common name	Zoological name	Chromosomes
(1) Man	Homo sapiens	46
(2) Gorilla	Maccaca mulatta	48
(3) Pig	Sas scrofa	40
(4) Sheep	Ovis aries	54
(5) Cat	Felis maniculata	38
(6) Dog	Canis familiaris	78
(7) Rat	Rattus rattus	42

(8) Rabbit	Oryctolagus cuniculus	44
(9) Honey bee	Apis mellifera	32, 16
(10) Mosquito	Culex sp	6
(11) Grasshopper	Gryllus	23(male), 24(female)

(iv) Chromosome structure : Different regions or structure recognized in chromosomes are as under

(a) **Pellicle :** It is the outer thin but doubtful covering or sheath of the chromosome.

(b) **Matrix :** Matrix or ground substance of the chromosome is made up of proteins, small quantities of RNA and lipid. It has one or two chromonemata (singular-chromonema) depending upon the state of chromosome.

(c) **Chromonemata :** They are coiled threads which form the bulk of chromosomes. A chromosome may have one (anaphase) or two (prophase and metaphase) chromonemata. The coiled filament was called chromonema by Vejdovsky in 1912. The coils may be of the following 2 types:

(1) **Paranemic coils :** When the chromonemal threads are easily separable from their coils then such coils are known as paranemic coils.

(2) **Plectonemic coils :** When the chromosomal threads remain inter-twined so intimately that they cannot be separated easily are known as plectonemic coils.

(d) **A primary Constriction and Centromere (kinetochore) :** A part of the chromosome is marked by a constriction. It is comparatively narrow than the remaining chromosome. It is known as primary constriction. The primary constriction divides the chromosome into two arms. It shows a faintly positive Feulgen reaction, indicating presence of DNA or repetitive type. This DNA is called centromeric heterochromatin.

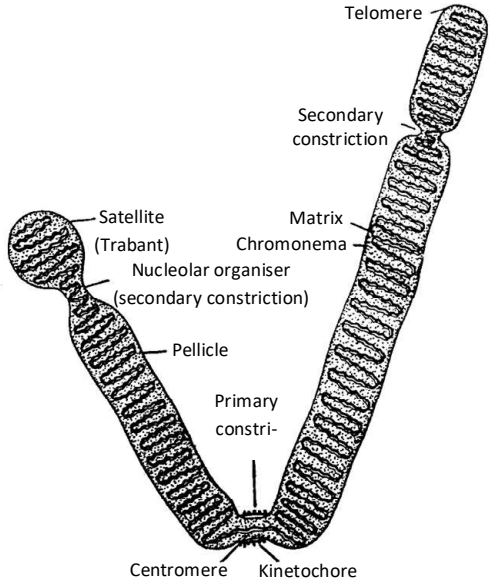


Fig : Structure of chromosome

Centromere or kinetochore lies in the region of primary constriction. The microtubules of the chromosomal spindle fibres are attached to the centromere. Therefore, centromere is associated with the chromosomal movement during cell division. Kinetochore is the outermost covering of centromere.

Type of chromosomes based on number of centromeres : Depending upon the number of centromeres, the chromosomes may be :

(1) Monocentric with one centromere.

(2) Dicentric with two centromeres, one in each chromatid.

(3) Polycentric with more than two centromeres.

(4) Acentric without centromere. Such chromosomes represent freshly broken segments of chromosomes, which do not survive for long.

(5) Diffused or non-located with indistinct throughout the length of chromosome. The microtubules of spindle fibres are attached to chromosome arms at many points. The diffused centromeres are found in insects, some algae and some groups of plants.

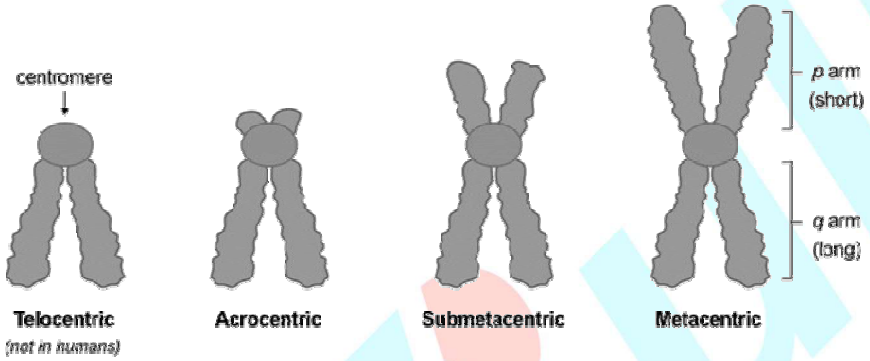
Types of chromosomes based on position of centromere : Based on the location of centromere the chromosomes are categorised as follows :

(1) **Telocentric :** These are rod-shaped chromosomes with centromere occupying a terminal position. One arm is very long and the other is absent.

(2) **Acrocentric :** These are rod-shaped chromosomes having subterminal centromere. One arm is very long and the other is very small.

(3) **Submetacentric :** These are J or L shaped chromosomes with centromere slightly away from the mid-point so that the two arms are unequal.

(4) **Metacentric :** These are V-shaped chromosomes in which centromere lies in the middle of chromosomes so that the two arms are almost equal.

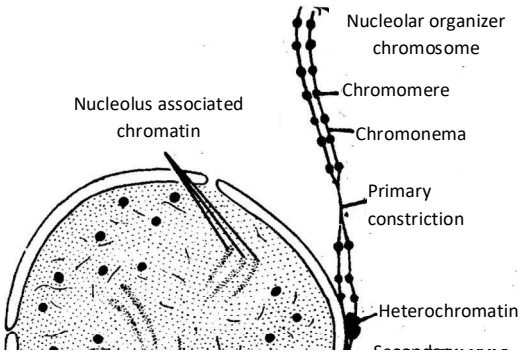


(e) **Chromomeres :** Chromomeres are linearly arranged bead-like and compact segments described by J. Bellings. They are identified by their characteristic size and linear arrangement along a chromosome.

(f) **Secondary constriction or nucleolar organizer :** Sometimes one or both the arms of a chromosome are marked by a constriction other than the primary constriction. During interphase this area is associated with the nucleolus and is found to participate in the formation of nucleolus. It is, therefore, known as nucleolar organizer region or the secondary constriction. In certain chromosomes, the secondary constriction is (In human beings 13, 14, 15, 20 and 21 chromosome are nucleolar organizer) intimately associated with the nucleolus during interphase. It contains genes coding for 18S and 28S ribosomal RNA and is responsible for the formation of nucleolus. Therefore, it is known as nucleolar organizer region (*NOR*).

(g) **Telomeres :** The tips of the chromosomes are rounded and sealed and are called telomeres which play role in Biological clock. The terminal part of a chromosome beyond secondary constriction is called *satellite*. The chromosome with satellite is known as *sat chromosome*, which have repeated base sequence.

(h) **Chromatids :** At metaphase stage a chromosome consists of two chromatids joined at the common centromere. In the beginning of anaphase when centromere divides, the two chromatids acquire independent centromere and each one changes into a chromosome.



SYNAPSIS

- ✍ During prophase I of meiosis, homologous chromosomes become connected in a process known as **synapsis.**
- ✍ The connected homologues are known as a *bivalent* (bi = two chromosomes) or a *tetrad* (tetra = four chromatids)
- ✍ The chromosomes are connected by a protein-RNA complex called the synaptonemal complex
- ✍ While autosomes always undergo synapsis during meiosis, sex chromosomes often remain unpaired

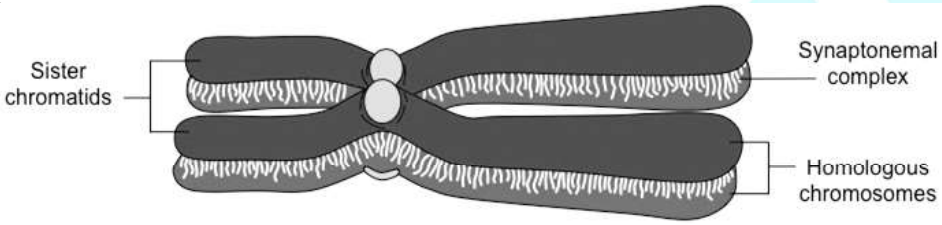


Fig: Pairing of Homologous Chromosomes via Synapsis

Species	*Parascaris equorum*	*Oryza sativa*	*Homo sapiens*	*Pan troglodytes*	*Canis familiaris*
Chromosome #	4	24	46	48	78
Common Name	 Roundworm	 Rice	 Human	 Chimpanzee	 Dog

Fig: Diploid Chromosome Number Comparisons

(v) Molecular organisation of chromosome : Broadly speaking there are two types of models stating the relative position of DNA and proteins in the chromosomes.

(a) **Multiple strand models :** According to several workers (Steffensen 1952, Ris 1960) a chromosome is thought to be composed of several DNA protein fibrils and atleast two chromatids form the chromosome.

(b) **Single strand models :** According to Taylor, Duprow etc. The chromosome is made up of a single DNA protein fibril. There are some popular single strand models.

(1) **Folded fibre model :** Chromosomes are made up of very fine fibrils 2 *nm* - 4 *nm* in thickness. As the diameter of DNA molecule is also 2 *nm* (20*Å*). So it is considered that a single fibril is a DNA molecule. It is also seen that chromosome is about a hundred times thicker than DNA whereas the length of DNA in chromosome is several hundred times that of the length of chromosome. So it is considered that long DNA molecule is present in folding manner which forms a famous model of chromosome called folded fibre model which given by *E.J. Dupraw* (1965).

(2) **Nucleosome model :** The most accepted model of chromosome or chromatin structure is the 'nucleosome model' proposed by Kornberg and Thomas (1974). Nucleosomes are also called *core particles or Nu-bodies*. The name nucleosome was given by *P. Outdet* et al. The nucleosome is a oblate particle of 55$\mathring{A}$ height and 110$\mathring{A}$ diameter. Woodcock (1973) observed the structure of chromatin under electron microscope. He termed each beaded structure on chromosome as nucleosome. Nucleosome is quasicylindrical structure made up of histones and DNA.

Histone are mainly of two types :

(a) **Nucleosomal histone :** These are small proteins responsible for coiling DNA into nucleosome. These are H_2A, H_2B, H_3 and H_4. Each histone protein consist of two molecule, thus the four histone proteins form a octamer. These form the inner core of nucleosome.

(b) **Linker histone :** H_1 proteins is known as linker histone that connect one core particle with another. These are present once per 200 base pairs. These are loosely associated with DNA. H_1 histone are responsible for packing of nucleosome into 30 *nm* fibre.

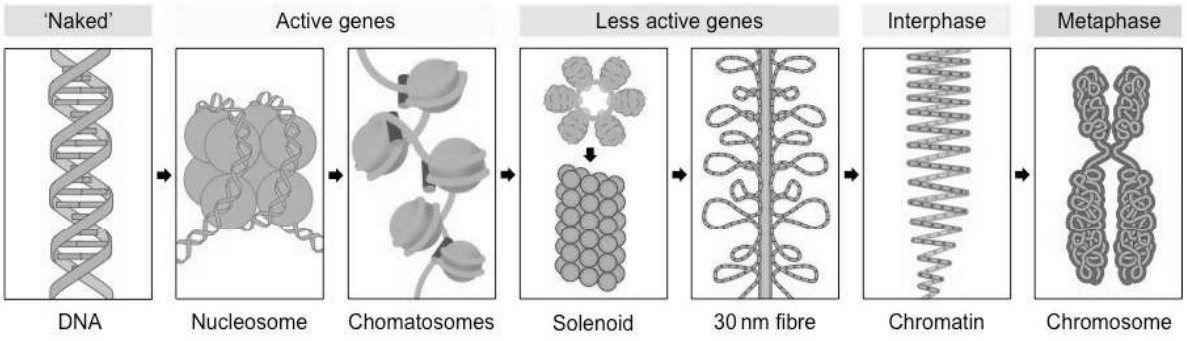


Fig: Organisation of DNA in Eukaryotic Chromosomes

Functions of histones : Histones in eukaryotic chromosomes serve some functions.

- These either serve as structural elements and help in coiling and packing of long DNA molecules.
- Transcription is possible only by dissolution of histones in response to certain molecular signals.

DNA in nucleosome : Nucleosome is made of core of eight molecules of histones wrapped by double helical DNA with $1\frac{3}{4}$ turns making a repeating unit. Every $1\frac{3}{4}$ turn of DNA have 146 base pairs. When H_1 protein is added the nucleotide number becomes 200. DNA which joins two nucleosome is called linker DNA or spacer DNA.

(3) **Solenoid model :** In this model the nucleosomal bead represents the first degree of coiling of DNA. It is further coiled to form a structure called solenoid (having six nucleosome per turn). It represents the second degree of coiling. The diameter of solenoid is 300$\mathring{A}$. The solenoid is further coiled to form a supersolenoid of 2000-4000$\mathring{A}$ diameter. This represent the third degree of coiling. The supersolenoid is perhaps the unit fibre or chromonema identified under light microscopy. The solenoid model was given by Fincy and Klug 1976. Klug was awarded by nobel prize in 1982 for his work on chromosome.

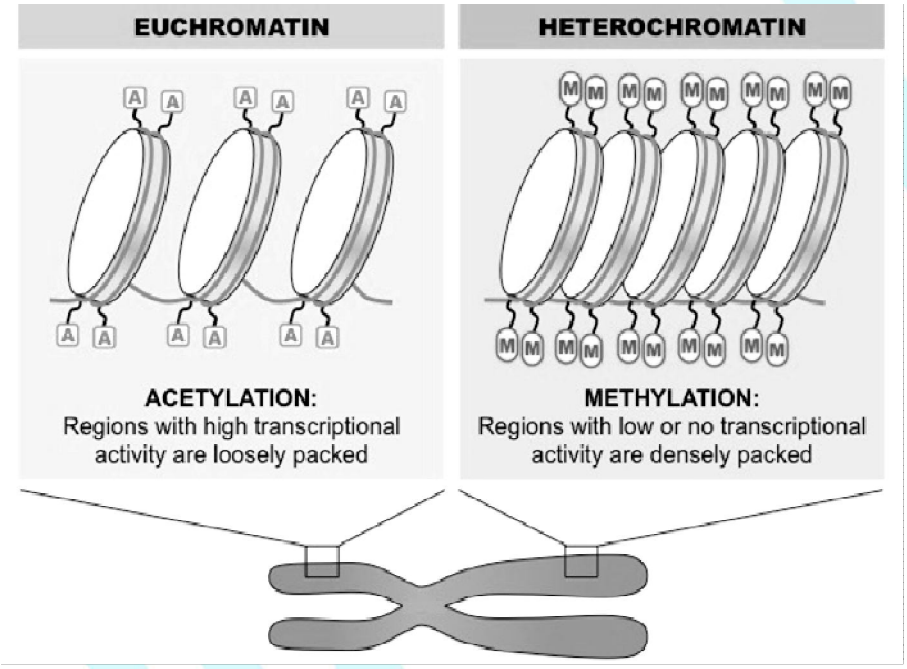
(4) **Dangier-String or Radial Loop Model :** (Laemmli, 1977). Each chromosome has one or two interconnected scaffolds made of nonhistone chromosomal proteins. The scaffold bears a large number of lateral loops all over it. Both exit and entry of a lateral loop lie near each other. Each lateral loop is 30 *nm* thick fibre similar to chromatin fibre. It develops through solenoid coiling of nucleosome chain with about six nucleosomes per turn. The loops undergo folding during compaction of chromatin to form chromosome.

(vi) Heterochromatin and Euchromatin : Flemming (1880) named the readily stainable material in nuclei as chromatin. It is present both during *interphase* and *cell division* (as the chromosomal material). It consists of about equal parts by weight of *DNA and histones.* There are two classes of chromatin structure, heterochromatin and euchromatin.

(a) **Heterochromatin** or static chromatin is highly condensed and is usually transcriptionally inactive and found in the centromeres of chromosomes.

Heterochromatin is of two types, (i) genetically inactive *constitutive heterochromatin* which is a permanent part of the genome, and (ii) *facultative heterochromatin* which varies in its state in different cell types and development stages.

(b) **Euchromatin** or dynamic chromatin is relatively extended and open. It at least has the potential of being actively transcribed. It makes up the major part of the genome, and is visible only during mitosis.



Comparison of heterochromatin and euchromatin

Heterochromatin	Euchromatin
Remains condensed throughout interphase (positive heteropycnosis) giving rise to chromocentres.	Shows normal cycle of condensation during cell division and extension during interphase.
Because of the condensed state, it stains more heavily giving rise to banding patterns or chromosomes.	Because it is less condensed, it stains less heavily (normal staining properties). Only slightly basophilic.
Found in condensed regions of the chromosome and in association with tight folding or coiling of the chromosomal fibre.	Found diffuse or less tightly coiled regions. Undergoes typical condensation-decondensation cycle.
May contain highly repetitive (satellite) *DNA* or single copy (unique) *DNA*.	Almost free of repetitive *DNA*. Contains predominantly single copy *DNA*.
Relatively inert metabolically, but does not contain a few genes.	Genetically active : Almost all the genes are located on euchromatin.
DNA is genetically inert and *does not*	Genetically active, dispersed part of

transcribe mRNA for protein synthesis in the condensed state.	chromatin in interphase nuclei. Its DNA synthesizes *mRNA* for protein synthesis.
Late replication of DNA at the S phase of the cell cycle. Under-replication in polytene chromosomes.	Comparatively early replication of DNA during the early stage of the S phase of cell cycle.
Crossover frequency is less, because condensed regions of the chromosomal fibre cannot come close together for frequent crossover. This may help protect vital genes from the effects of crossover.	Crossover frequency is more because of the decondensed (extended) state of euchromatin.

(vii) Chromosome banding : It was the technique demonstrated by **Casperson** (1968) using a fluorescent dye quinacrine mustard for the study of finer chromosomal aberrations. The development of banding techniques has made the identification of individual chromosomes easier. Each chromosome can be identified by its characteristic banding pattern. In X chromosomes the bands are large, each containing ~$10^7 bp$ of DNA, and could include several hundreds of genes. The different banding techniques are identified by the letters Q, G, C, R and T.

Differentiation of chromosomes by banding

Type of banding	Staining technique	Nature of bands
Q (quinacrine) banding	Chromosomes exposed to quinacrine mustard (acridine dye) which preferentially binds to AT-rich DNA. Other fluorescent dyes used are *DAPI or Hoeschst* 33258.	UV fluorescence reveals fluorescencing *Q* bands which correspond to G-bands. DNA of Q/G bands contains more closely spaced SARs, giving tighter loops (Q loops).
G (Giemsa) banding	Chromosomes treated with alkaline solution and subjected to controlled trypsin digestion before staining with Geimsa, a DNA banding chemical dye. Relatively permanent stain.	Dark bands are called G bands and pale bands are G-negative. G bands are presumed to be *AT-rich*. They are late replicating and contain highly condensed chromatin.
R (reverse) banding	Chromosomes treated with heated saline or restrictase to denature AT-rich DNA and stained with *Giemsa*. GC-specific chromomycin dyes, *e.g,* chromomycin A, olivomycin or mithracin give the same pattern.	R-banding pattern is essentially the reverse of the *G*-banding pattern. R bands are Q negative. They generally replicate in the S-phase and have less condensed chromatin.
T (telomaric) banding	Prolonged heat treatment of chromosomes before staining with Giemsa or combination of dyes and fluorochromes.	T bands are a subset of R bands which are the most inetnsely staining. They are especially concentrated at the telomeres.
C (centromere)	Chromosomes pre-treated with sodium hydroxide or barium	Preferred darkening of constitutive centromeric heterochromatin. Rest

banding	hydroxide and stained with Giemsa.	of the chromosome show Q banding pattern.

(viii) Human karyotype and idiogram : **Tjio** and **Levan** (1956) of Sweden found that human cells have 23 pairs or 46 chromosomes. 22 pairs or 44 chromosomes are autosome and the last or 23rd pairs is that of sex chromosomes, XX in females and XY in males. A set of chromosomes of an individual or species is called a karyotype. In human the 23 pairs of chromosomes in somatic cells form the karyotype. It is possible to identify individual chromosomes on the basis of the following characteristics.

(1) The total length of the chromosomes.

(2) Arm ratio.

(3) The position of the secondary constrictions and nucleolar organizers.

(4) Subdivision of the chromosome into euchromatic and heterochromatic regions.

Homologous pairs of identified chromosomes can be arranged in a series of decreasing lengths. Such an arrangement is called an idiogram. Idiogram not possible in symmetrical karyotype.

(a) **Karyotyping of human chromosomes :** Chromosomes are clearly visible only in rapidly dividing cells. Human chromosomes are studied in blood cells (WBCs), cells in bone marrow, amniotic fluid and cancerous tissues. The WBCs divide when added with phytohaemagglutinin (PHA). The division stops when colchicine is added at metaphase stage. These dividing WBCs are then treated with hypotonic saline solution. Chromosomes are now stained with stains like orcein, Giemsa dye or recent quinacrine dye. When viewed with special miscroscope in ultraviolet light the stain produces fluorescent bands on chromosomes. The chromosomes are then arranged on photographic plate for making diagram and their study. The pictorial representation of a person's chromosomes is called Karyotype.

(b) **Classification of chromosomes :** The human metaphase chromosomes were first of all classified by a conference of cytogeneticists at Denver, Colorado in 1960 and is known as the 23 pairs (46) chromosomes in human has been numbered from 1 to 23 according to their decreasing size. Patau (1960) divided the human chromosome into the following seven groups designated A to G.

Characteristics of the Chromosomes in the Human Karyotype

Group	Size	Shape	Number in set	Number in a cell
A	Large	Metacentric Submetacentric	1-3	6
B	Large	Submetacentric	4-5	4
C	Medium	Submetacentric	6-12 and X	15 male 16 female
D	Medium	Acrocentric	13-15	6
E	Small	Submetacentric	16-18	6
F	Small	Metacentric	19-20	4
G	Smallest	Acrocentric	21-22 and Y	5 male 4 female
				46

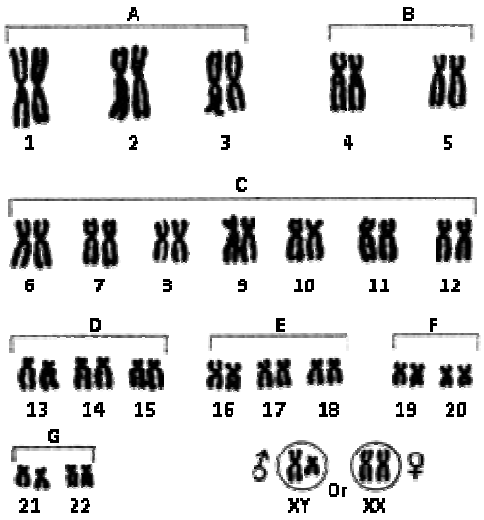


Fig : Human karyotype

- The group A consist of longest metacentric chromosomes.
- The group G consist of the shortest acrocentric chromosomes. These chromosomes have satellites that correspond to nucleolar organizers. In males, group G includes a variable Y chromosome which lacks the satellite.
- Chromsomes of group D also contains satellite.
- The X chromosomes is the member of group C and can be identified by special banding or staning methods.

(ix) Special types of chromosomes

(a) **Supernumerary, Accessory or B chromosomes or Satellite chromosomes or Giant lines plasmid :** In some species, chromosomes have been found that are in addition to the normal autosomes and heterosomes. These chromosomes have been called supernumerary chromosomes, accessory chromosomes or B-chromosomes, and differ from normal or A-chromosomes in the following respects.

(1) They are usually smaller than A-chromosomes.
(2) They are frequently heterochromatic and telocentric.
(3) They are genetically unnecessary, and normally do not strongly influence viability and phenotype.
(4) Their number may vary in different cells, tissues, individuals and populations.
(5) They are not homologous with any of the A-chromosomes and do not synapses with them.
(6) They are found more commonly in plants than in animals.

Among animals they have been reported mostly in insects and a few species of flatworms. Of the 50 species of insect in which B-chromosomes have been reported, 29 are short horned grasshoppers belonging to the family Acridiae. Usually each nucleus has one or two B-chromosomes. In *Tradescantia edwardsiana* there are 50 B-chromosomes in addition to the 12 somatic A-chromosomes.

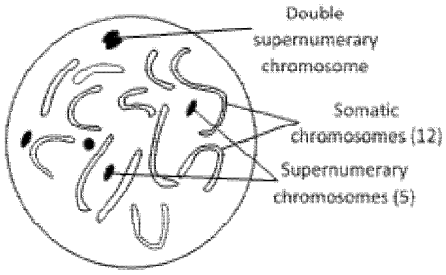


Fig : Diagram of supernumerary chromosomes of *Tradescantia edwardsiana*

(b) **Limited or L-chromosomes :** Limited or L-chromosomes are so called because they are limited to the germ line. They have been found in the family Sciaridae (Diptera: Insecta). The germ line cells in females have 10 chromosomes: three pairs of autosomes, a pair of X-chromosomes and a pair of L-chromosomes. Those of males have 9 chromosomes, there being only one X-chromosome. Somatic cells have 8 chromosomes in females and 7 in males, the L-chromosomes being absent. During the fifth and sixth cleavages, L-chromosomes are eliminated from nuclei destined to form somatic tissue, but retained in germ line cells. L-chromosomes differ from B-chromosomes in that they are constant in all individuals of the species having them. B-chromosomes are found only in some individuals of the species.

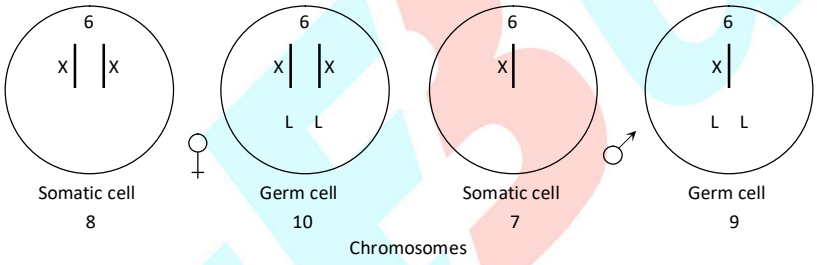


Fig : Schematic representation of the L-chromosomes in the *Sciaridae*

(c) **Minute or m-chromosomes :** Minute or m-chromosomes are so called because of their extremely small size (0.5 micron or less). They have been found in a variety of species of bryophytes, higher plants, insects of the family Coreidae (Heteroptera) and birds. They have been seen mainly during meiosis, and only occasionally during mitosis. Usually one or two chromosomes are seen, but four to five may also be present. In the moss, *Sphagnum* there are 19 large bivalents and 2 *m*- chromosomes.

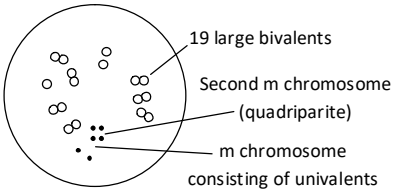


Fig : Minute or m-chromosomes

(d) **S and E-chromosomes :** S and E-chromosomes have been reported in insects in the family Cecidomyiidae (gall insects) and family Chironomidae (Diptera). In the gall insect *Miastor*, both males and females have 48 chromosomes in germ line cells. In somatic cells, however, there are only 12 chromosomes in females and 6 in males. Chromosomes which are present in both germ and somatic cells are called *S*-chromosomes. Those which are eliminated from somatic cells but are present in germ cells are called *E*-chromosomes. Thus in females the germ line cells have 12 S-chromosomes and 36 E-chromosomes. In male germ line cells there are

6 S-chromosomes and 42 E-chromosomes. The zygote receives half its S-chromosomes from each parent, while all the E-chromosomes are received from the female parent.

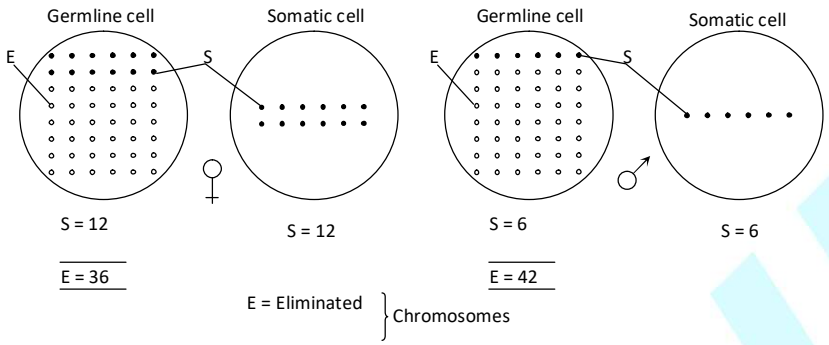


Fig : Schematic representation of the S and E chromosomes of the gall insect *Miastor*

(e) **Polytene chromosome :** Polytene chromosome was described by **Kollar** (1882) and first reported by **Balbiani** (1881) in the salivary gland cells of chironomus larva. They are found in salivary glands of insects (*Drosophila*) and called as salivary gland chromosomes. These are reported in endosperm cells of embryosac by **Malik** and **Singh** (1979). Length of this chromosome may be upto 2000μm. The chromosome is formed by somatic pairs between homologous chromosomes and repeated replication or endomitosis of chromonemata. These are attached to chromocentre. It has pericentromeric heterochromatin. Polytene chromosomes show a large number of various sized intensity bands when stained. The lighter area between dark bands are called interbands. They have puffs bearing *Balbiani rings*. Balbani rings produce a number of *m*-RNA, which may remain stored temporarily in the puffs, are temporary structures. These are also occur in Malpighian tubules, rectum, gut, foot pads, fat bodies, ovarian nurse cells etc.

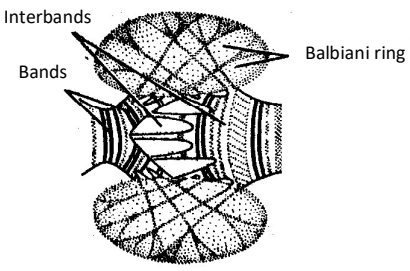


Fig : Polytene chromosome showing balbiani ring

(f) **Lampbrush chromosomes :** They are very much elongated special type of synapsed or diplotene chromosome bivalents already undergone crossing over and first observed by **Flemming** (1882). The structure of lampbrush chromosome was described by **Ruckert** (1892). The lampbrush chromosomes occur at the diplotene stage of meiotic prophase in the primary oocytes of all animal species, both vertebrates and invertebrates as in sagitta (chaetognatha), sepia (mollusca), Echinaster (Echinodermata) and in several species of insect, sharks, amphibians, reptiles, birds and mammals. Lampbrush chromosomes are also found in spermatocytes of several species, giant nucleus of acetabularia and even in plants. In urodele oocyte the length of lampbrush chromosome is upto 5900μm. These are found in pairs consisting of

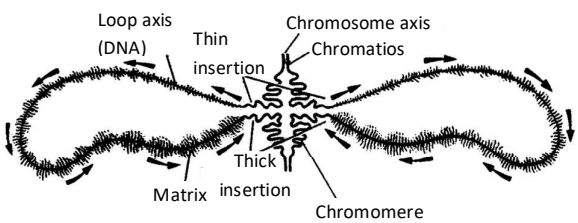


Fig : A part of main axis with a pair of lateral loops of a lampbrush chromosome showing synthesis of RNA

homologous chromosomes jointed at chiasmata (meiotic prophase-I). The chromosome has double main axis due to two elongated chromatids. Each chromosome has rows of large number of chromatid giving out lateral loops, which are uncoiled parts of chromomere with one-many transcriptional units and are involved in rapid transcription of *m*RNA meant for synthesis of yolk and other substances required for growth and development of meiocytes. Some *m*RNA produced by lampbrush chromosome is also stored as informosomes *i.e.*, *m*RNA coated by protein for producing biochemicals during the early development of embryo. Length of loop may vary between 5-100μm.

Memories

- *H_1, H_2A and H_2B proteins are lysine rich (H_1 is very lysine rich) while H_3 and H_4 are arginine rich polypeptide chains.*
- *Chromosomes are stained by acetocarmine or acid fushsin.*
- *Morgan is called father of experimental genetics.*
- *Bateson is called father of modern genetics.*
- *Netil stevens (1902) discovered Y chromosomes.*
- *One gene one enzyme theory was given by Beadle and Tautum.*
- *Strasburger was first of all described chromosome in nucleus.*
- *Sum of genes in a population is called gene pool.*
- *One pair of genes can completely mask the expression of another pair of gene is called epistasis.*

10 MULTIPLE ALLELISM

(i) **Mode of origin :** Genes having only two distinct alleles. If mutation occurs in the same gene but in different directions in different individuals, the population as a whole will have many different alleles of that gene. Each allele may produce a different phenotype, and various combinations of alleles produce several genotypes and phenotypes in the population.

(ii) **Characteristics**

(a) There are more than two alleles of the same genes.

(b) All multiple alleles occupy the corresponding loci in the homologous chromosomes.

(c) A chromosome or a gamete has only one allele of the group.

(d) Any one individual contains only two of the different alleles of a gene, one on each chromosome of the homologous pair carrying that gene.

(e) Multiple alleles express different alternative of a single trait.

(f) Different alleles may show codominance, dominance-recessive behaviour or incomplete dominance among themselves.

(g) Multiple alleles confirm to the Mendelian pattern of inheritance.

(iii) **Definition :** More than two alternative forms (alleles) of a gene in a population occupying the same locus on a chromosome or its homologue are known as multiple alleles.

(iv) **Examples of multiple allelism :** A well known example of a trait determined by multiple alleles is the blood groups in man and skin colour.

BLOOD GROUPS IN MAN

(a) **Blood proteins :** According to **Karl landsteiner** (1900) a Nobel prize winner, blood contains two types of proteinous substances due to which agglutinations occurs.

(1) **Agglutinogen or antigen :** It is a protein found on the cell membrane of RBC's.

(2) **Agglutinin or antibody :** This the other proteinous substance, found in the plasma of the blood.

Whenever the blood of a person receives the foreign proteins (antigen) his blood plasma starts forming the antibodies in order to neutralize the foreign antigens.

(b) **Agglutinations :** Two types of antigens are found on the surface of red blood corpuscles of man, antigen A and B. To react against these antigens two types of antibodies are found in the blood plasma which are accordingly known as antibody – *anti-A or a* and *anti-B or b*. Agglutination takes place only when *antigen A* and *antibody a* occur together or *antigen B* and *antibody b* are present in the blood. Under such condition *antibody a* reacts with *antigen A* and makes it highly sticky. Similarly *antigen B* in presence of *antibody b* become highly sticky with the result RBC's containing these antigens clump to form a bunch causing blockage of the capillaries. Agglutination in blood is therefore antigen-antibody reaction.

(c) **Types of blood groups**

(1) **ABO blood group : Landsteiner** divided human population into four groups based on the presence of antigens found in their red blood corpuscles. Each group represented a blood group. Thus there are four types of blood groups viz. A, B, AB and O. He observed that there was a reciprocal relationship between antigen and antibody according to which a person has antibodies for those antigens which he does not possess. For example a person of blood group B does not possess *antigen A* but his blood plasma has *antibody 'a'* due to which agglutination with the blood of a person with blood group A occurs. Similarly persons with blood group AB possess both the *antigens A* and *B* but their blood plasma does not possess any of the antibodies. In the same way person having blood group A does not possess *antigen B* but *antibody 'b'* is found in his blood plasma. Persons with blood group O possess none of the antigens and that is why their blood possesses both the *antibodies 'a'* and *'b'*.

Blood groups of man with antigen and antibodies

Antigen	Antibody	Type of blood group	% in society
(1) A	*Anti-B* or '*b*'	A	23.5
(2) B	*Anti-A* or '*a*'	B	34.5
(3) A, B	Absent	AB	7.5
(4) None	'a' and 'b'	O	34.5

(2) **M, N blood group : K. Landsteiner** and **A.S. Wiener** discovered that antigen M,N or both MN are also found on the surface of red blood corpuscles of human beings. No antibodies are however formed in the blood plasma for these antigens. If however, these antigens are injected

into rabbit's blood, they produced such antibodies which are not found in human beings. Inheritance of such kind of blood groups is also brought about like that of A, B and AB.
In this way when blood with M group is injected in rabbit it will produce antibodies in the blood serum which will bring about agglutination with blood group M and MN but not with blood of N group. In the same way on injecting blood of N group into the rabbit it will bring about agglutination with blood group N and MN and not with blood having blood group M.

(d) **Blood transfusion :** Blood transfusion is best done in the persons of same blood group. At the same time it is possible to know in which different blood groups the blood transfusion can be made possible.

Persons with blood group AB are called **universal recipients** because both antigens A and B are found in their blood and the two antibodies 'a' and 'b' are absent. Therefore, such persons can receive blood of all the blood groups. In the same way persons who have blood group O^- are **universal donors** as they lack both the antigens and Rh^- person can donate to Rh^+ person as well as Rh^- person but Rh^+ person cannot donate blood to Rh^- person. But at the same time such persons can not be given the blood of any other blood group except blood group O because their blood possesses both the antibodies 'a' and 'b'. Persons belonging to blood group A and B contain only one antigen and one antibody against it, in their blood. Such persons can therefore receive blood either of the blood group of their own or the blood group O.

Possibilities of blood transfusion

Blood group	Can accept from	Can donate to	Agglutination				Specific mention
			A	B	AB	O	
(1) A	A, O	A, AB	No	Yes	No	Yes	
(2) B	B, O	B, AB	Yes	No	No	Yes	
(3) AB	A, B, AB, O	AB only	Yes	Yes	No	Yes	Universal recipient
(4) O	O only	A, B, AB, O	No	No	No	No	Universal donor

(e) **Blood bank :** A place where blood of different blood groups is safely stored in bottles for emergency use, is called blood bank. Blood after proper testing is stored in a sealed bottle at a definite temperature (4°-6°c) to be preserved for a definite time period.
Artificial anticoagulants are used to prevent blood clotting in the blood banks. These anticoagulants are added to the blood preserved in bottle. Such anticoagulants include sodium citrate, double oxalates (sodium and ammonium), dicumarol and EDTA (ethylene diamine tetra acetic acid). The whole blood in this way can be stored for a maximum period of 21 days.

(f) **Inheritance of blood groups :** Blood groups in human are **inheritable trait** and are inherited from parents to offsprings on the basis of Mendel's Laws. Blood group inheritance depends on genes received from parents. Genes controlling blood group in man are three instead of two and are called multiple alleles. All these three genes or alleles are located on the same locus on homologous chromosomes. A person can have only two of these three genes at a time which may be either similar or dissimilar in nature. These genes control the production of blood group/antigens in the offspring. The gene which produces antigen A is denoted by I^a, gene for antigen B by I^b and the gene for the absence of both antigens by I^o. it is customary to use the letter I (Isohaemagglutinogen) as a basic symbol for the gene at a locus. Based on this, six genotypes are possible for four blood groups in human population.

Genotype of blood groups in man.

	Genotype	Nature of gene	Type of blood group
(1)	$I^a I^a$	Homozygous Dominant	A
(2)	$I^a I^o$	Heterozygous	A
(3)	$I^b I^b$	Homozygous Dominant	B
(4)	$I^b I^o$	Heterozygous	B
(5)	$I^a I^b$	Codominant	AB
(6)	$I^o I^o$	Homozygous Recessive	O

The alleles I^a and I^b of human blood group are said to be codominant because both are expressed in the phenotype AB. Each produces its antigen and neither checks the expression of the other. There is codominance as well as dominant recessive inheritance in the case of the alleles for the blood groups in human beings. The alleles I^a and I^b are codominant and are dominant over the allele I^o ($I^a = I^b > I^o$). The human blood groups illustrate both multiple allelism and codominance. This blood group are inherited in the simple Mendelian fashion. Thus offsprings with all four kinds of blood groups are possible. If the parents are heterozygous for blood groups A and B which is shown below.

Cross between parents heterozygous for blood group A and B

Male
(Heterozygous for blood group A)

Female (Heterozygous for blood group B)	Gametes	I^a	I^o
I^b I^o	I^b	$I^a I^b$	$I^b I^o$
		Group AB	Group B
	I^o	$I^a I^o$	$I^o I^o$
		Group A	Group O

If we know the blood groups of a couple the blood groups of their children can easily be predicted as shown below.

Possible blood groups of children for known blood groups of parents.

	Blood groups of parents (known)	Genotype of parents (known)	Blood groups of children	
			Possible	Not possible
(1)	O and O	$I^o I^o \times I^o I^o$	O	A, B, AB
(2)	O and A	$I^o I^o \times I^a I^o$	O, A	B, AB
(3)	A and A	$I^a I^o \times I^a I^o$	O, A	B, AB
(4)	O and B	$I^o I^o \times I^b I^o$	O, B	A, AB
(5)	B and B	$I^b I^o \times I^b I^o$	O, B	A, AB

(6)	A and B	$I^aI^a \times I^bI^b$ $I^aI^a \times I^bI^o$ $I^aI^o \times I^bI^o$	O, A, B, AB	None
(7)	O and AB	$I^oI^o \times I^aI^b$	A, B	O, AB
(8)	A and AB	$I^aI^o \times I^aI^b$	A, B, AB	O
(9)	B and AB	$I^bI^o \times I^aI^b$	A, B, AB	O
(10)	AB and AB	$I^aI^b \times I^aI^b$	A, B, AB	O

(g) **Significance of blood groups :** The study of blood groups is important in settling the medico-legal cases of disputed parentage because with the help of blood group of a child it can be decided as to who can be his or her genuine father, if the blood group of mother is known. It means that blood groups of the mother and a child being known, the possibilities of blood group in the father can be worked out or if blood group of child and that of father is known then that of mother can be known with the help of the table given below. Blood groups can also save an innocent from being hanged in the case of murder and can help in hanging the real culprit.

Possibilities of blood groups of other parent on the basis of blood group of child and one parent being known.

S.No.	Blood group of child (known)	Genotype of child (known)	Blood group of father or mother (known)	Blood group of other parent	
				Possible	Not possible
(1)	O	I^oI^o	O A B	A, B O, B O, A	AB
(2)	A	I^aI^o, I^aI^a	O, B	A, AB	O, B
(3)	B	I^bI^o , I^bI^b	O, A A	B, AB B, AB	O, A O, A
(4)	AB	I^aI^b	B AB	A, AB A, B, AB	O, B O

(h) **Rhesus or Rh factor**

(1) **Rh factor : Landsteiner** and **Weiner** (1940) discovered a different type of protein in the blood of Rhesus monkey. They called it Rh antigen or Rh factor after Rhesus monkey. When injected the blood of these monkeys into the blood of guinea pigs they noticed the formation of antibodies against the Rh antigen in the blood of guinea pigs. Formation of Rh antigen is controlled by dominant gene (R) and its absence by recipient gene (r). People having this antigen with genotype (RR or Rr) are called Rh positive (Rh^+) and those whose blood is devoid of it with genotype (rr) are Rh negative (Rh^-). About 85% human beings in Europe and 97% in India are Rh^+.

(2) **Importance of Rh factor :** Generally human blood is devoid of Rh antibodies. But it has been noticed that on transfusion of blood of a Rh^+ person to Rh^- person, the recepient develops Rh antibodies in its blood plasma. If Rh^+ blood is transfused for the second times it causes agglutination and leads to the death of Rh^- person.

(3) **Erythroblastosis foetalis :** This disease is related to the birth of a child related with Rh factor. It causes the death of the foetus within the womb or just after birth. It was studies by **Levine** together with **Landsteiner** and **Wiener**. The father of Rh affected foetus is Rh^+ and the mother is Rh^-. The child inherits the Rh^+ trait from the father. A few Rh^+ red blood corpuscles of foetus in the womb enter in the blood of the mother where they develop Rh antibodies. As

mother's blood is Rh^- *i.e.* devoid of Rh antigen, it causes no harm to her. These Rh antibodies alongwith the mother's blood on reaching the foetal circulation cause clamping of foetal RBCs or agglutination reaction. The first child is some how born normal because by that time the number of antibodies in mother's blood remain lesser but they increase with successive pregnancies. Thus the foetus following the first child dies either within the womb or just after its birth. This condition is known as erythroblastosis foetalis. So a marriage between Rh^+ boy and Rh^- girl is considered biologically incompatible.

Type of biological marriage on the basis of Rh factor

Boy	Girl	Type of biological marriage
Rh^+	Rh^+	Compatible marriage
Rh^-	Rh^-	Compatible marriage
Rh^-	Rh^+	Compatible marriage
Rh^+	Rh^-	Incompatible marriage

However, there is no danger if both parents are Rh^- or mother is Rh^+ and father is Rh^-. Rh factor serum has been developed which when given to the Rh^- mother after each child birth saves the next child. This serum contains Rh antibodies which destroy the Rh antigens of foetus before they can initiate formation of Rh antibodies in the mother.

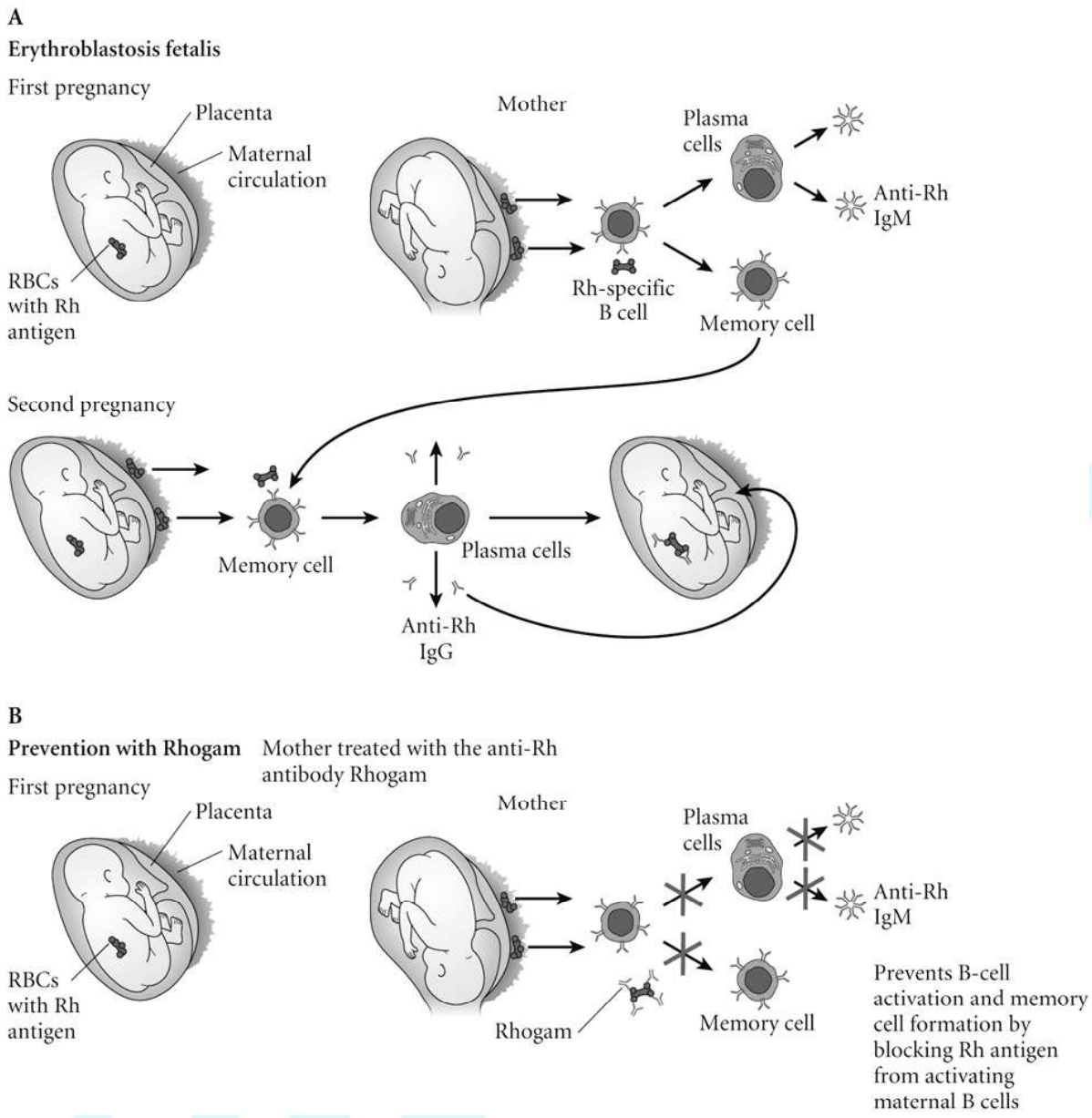
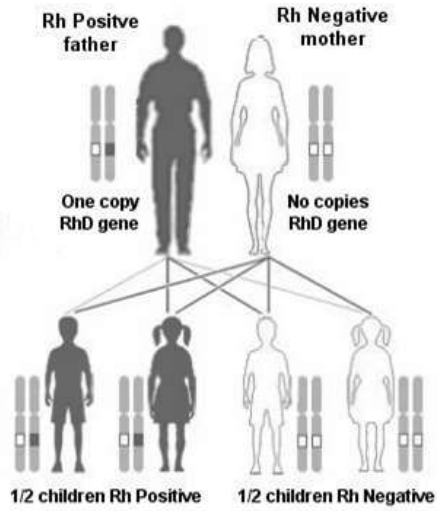


Fig : Foetal death in the womb due to erythroblastosis foetalis

(4) **Rhogam method :** It is a method of preventing erythroblastosis foetalis. In this method the Rh^- mother is given a special blood test after delivery of her Rh^+ child. If foetal Rh^+ cells are present in mother's blood. She is given injections of rhogam. Rhogam is a preparation of anti-Rh antibodies. It is obtained from immunized donors. The rhogam forms a coat around foetal RBCs in mother's blood. As a result no Rh^+ antigens are available to stimulate mother's circulation and no antibodies are formed.

(5) **Inheritance of Rh factor :** Rh factor or Rh antigen is determined by a series of four pair of multiple alleles. They are denoted as R^1, R^2, R^0, R^z, r', r", r^y and r. The alleles denoted by capital letter give rise to Rh^+ condition while those denoted by small letter to Rh^- condition. Rh^+ condition is dominant over Rh^- condition. Thus Rh^+ person may be homozygous (RR) or heterozygous (Rr) while Rh^- persons are always homozygous(rr). Hereditary trait for Rh^- factor is inherited according to Mendelian principle.



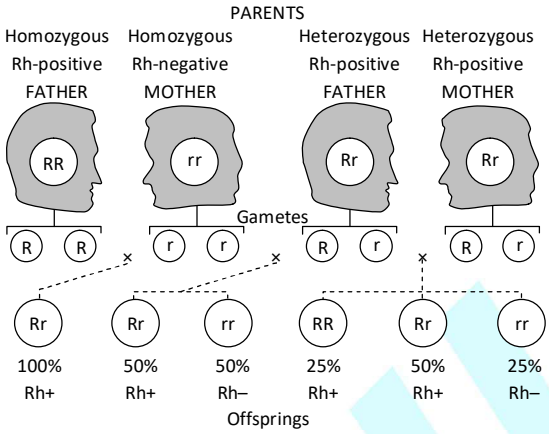


Fig : Inheritance of Rh antigen

11 GENETIC VARIATIONS

The idea of mutation first originated from the observations of a Dutch botanist **Hugo de Vries** (1880) on variations in plants of *Oenothera lamarckiana*. The mutation can be defined as sudden, stable discontinuous and inheritable variations which appear in organism due to permanent change in their genotype.

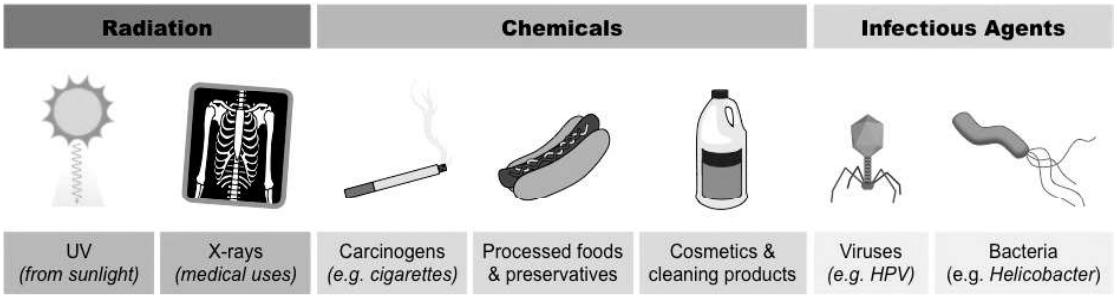


Fig: Types of Mutagens

Mutation is mainly of two types :

- **Spontaneous mutations :** Mutation have been occurring in nature without a known cause is called spontaneous mutation.
- **Induced mutation :** When numerous physical and chemical agents are used to increase the frequency of mutations, they are called induced mutations.

(i) Gene mutations : Gene or point mutations are stable changes in genes *i.e.* DNA chain. Many times a change in a gene or nucleotide pair does not produce detectable mutation. Thus the point or gene mutation mean the process by which new alleles of a gene are produced. The gene mutation are of following types

(a) **Tautomerism :** The changed pairing qualities of the bases (pairing of purine with purine and pyrimidine with pyrimidine) are due to phenomenon called tautomerism.

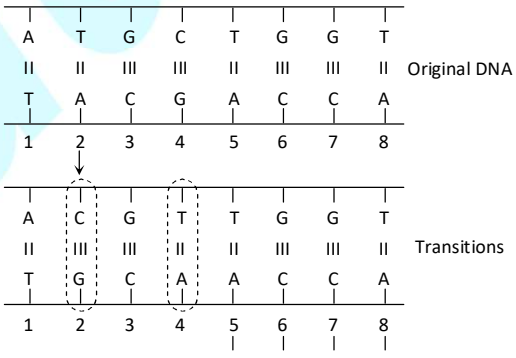
Tautomeres are the alternate forms of bases and are produced by rearrangements of electrons and proton in the molecules.

Uncommon Tautomer

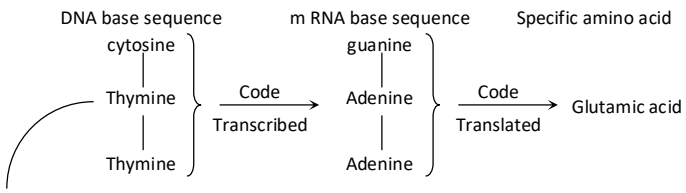
Tautomerism is caused by certain chemical mutagens. In the next replication purines pair with pyrimidines and the base pair is altered at a particular locus. The uncommon forms are unstable and at the next replication, cycle revert back to their normal forms.

(b) **Substitutions (Replacements) :** These are gene mutations where one or more nitrogenous base pair are changed with others. It may be further of three sub types.

(1) **Transition :** In transition, a purine (adenine or guanine) or a pyrimidine (cytosine or thymine or uracil) in triplet code of DNA or *m*RNA is replaced by its type *i.e.* a purine replaces purine and pyrimidine replaces pyrimidine.



(2) **Transversion :** Transversion are substitution gene mutation in which a purine (adenine or guanine) is replaced by pyrimidine (thymine or cytosine) or vice versa.



(3) **Frame shift mutations :** In this type of mutations addition or deletion of single nitrogenous base takes place. None of the codon remains in the same original position and the reading of genetic code is shifted laterally either in the forward or backward direction.

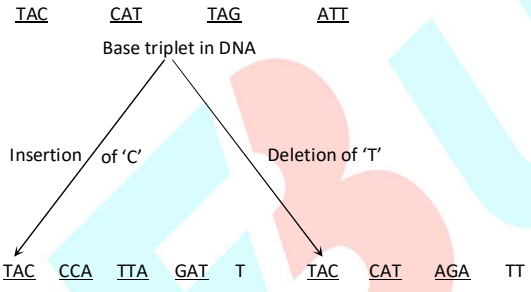


Fig : Frame shift mutations

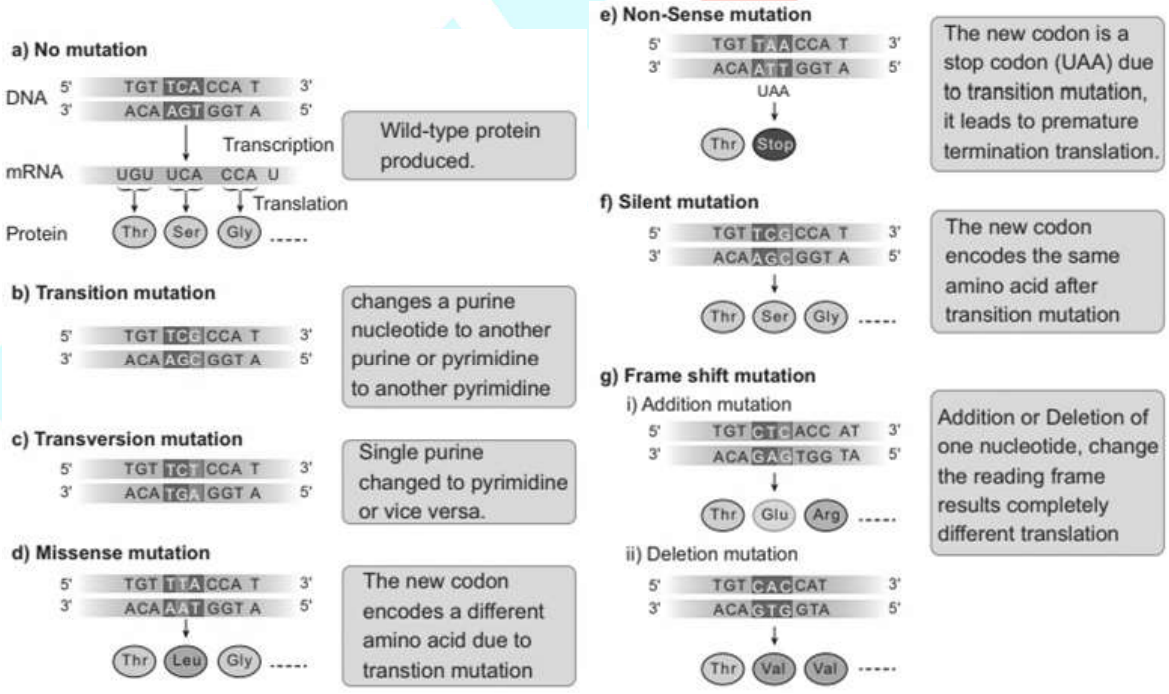


Fig: Types of mutation (point mutation)

(ii) Chromosomal mutation or aberrations : A gene mutation normally alters the information conveyed by a gene, it alters the message. On the other hand, chromosomal mutation only alters the number or position of existing genes. They may involve a modification in the morphology of chromosome or a change in number of chromosomes.

Morphological aberrations of chromosomes :

(a) **Deletion or deficiency :** Sometimes a segment of chromosome break off and get lost. Deficiency generally proves lethal or semilethal.

- **Deficiency :** If a terminal segment of a chromosome is lost, it is called deficiency.
- **Deletion :** If intercalary segment is lost it is termed deletion.

Deletions in human beings

- A missing chromosome segment is referred to either as deletion or deficiency.
- In a dilpoid organism, the deletion of a chromosome segment makes the part of genome hypoploid.
- Deletion may be associated with phenotypic effect, especially if the it is large.

(1) **Cri-du-chat Syndrome**

- A classical example of deletion is the Cri-du-chat syndrome (from the french words for "cry of the cat") in human beings discovered by **Lejeune** in 1963.
- This condition is caused by a conspicuous deletion in the short arm of one of the 5^{th} autosomes.
- These individuals are severely impaired, mentally as well as physically; their plaintive catlike crying gives the syndrome its name.

(2) **Wolf-Hirschhorn's Syndrome**

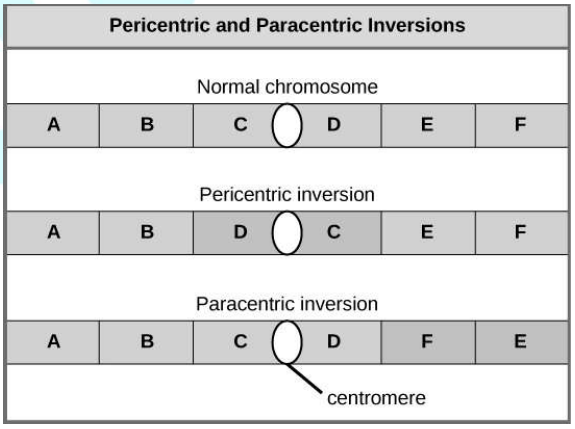
- Wolf-Hirschhorn's syndrome is another well characterized deletion syndrome in human beings caused by a deletion of short arm of chromosome 4 (4p-).
- The phenotypic effect includes wide-spaced eyes and cleft lip.

(b) **Duplication :** In this mutation deleted chromosomal segment is attached to its normal homologous chromosome. Here a gene or many genes are repeated twice or more times in the same chromosome.

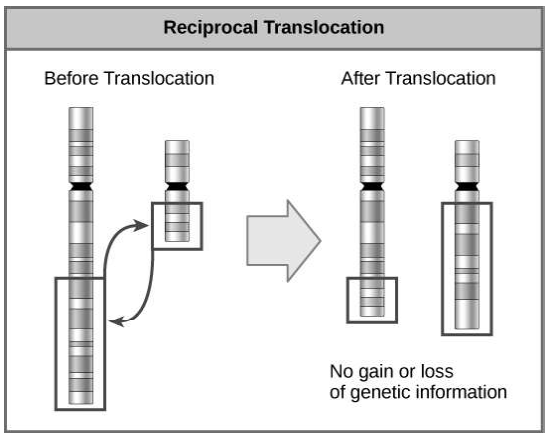
(c) **Inversion :** A piece of chromosome is removed and rejoined in reverse order. For example a chromosome with the gene order A, B, C, D, E, F, G, H is broken between B,C,D and between f and g and the centre portion turned through 180°, the resulting gene order is A, D, C, B, E, F, G, H it is of two types.

(1) **Pericentric inversion :** The centromere lies within the inverse order.

(2) **Paracentric inversion :** The centromere lies outside the inverted segment.



(d) **Translocation :** Mutual exchange (reciprocal) of the chromosome segments between non homologous chromosome. An exchange of parts between two non homologous chromosomes is called reciprocal translocation. In simple translocation a segment of one chromosome breaks and is transferred to another non-homologous chromosome.



Translocations in human beings

- Certain types of cancer are associated with chromosome rearrangements.
- Two examples of tumours associated with consistent chromosome translocations are Chronic Myelogenous Leukaemia (CML) and burkitt's lymphoma.

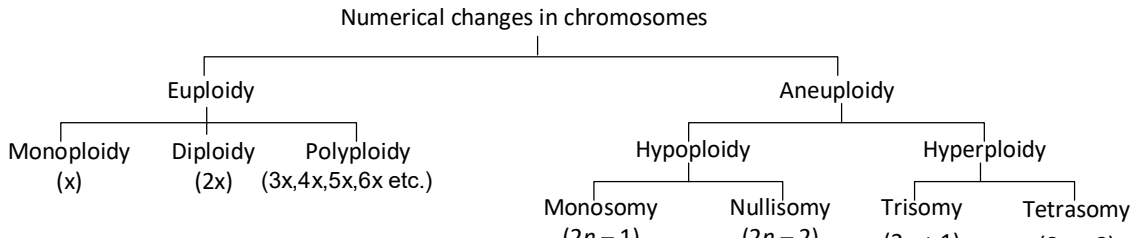
(1) **Chronic Myelogenous Leukaemia (CML)**

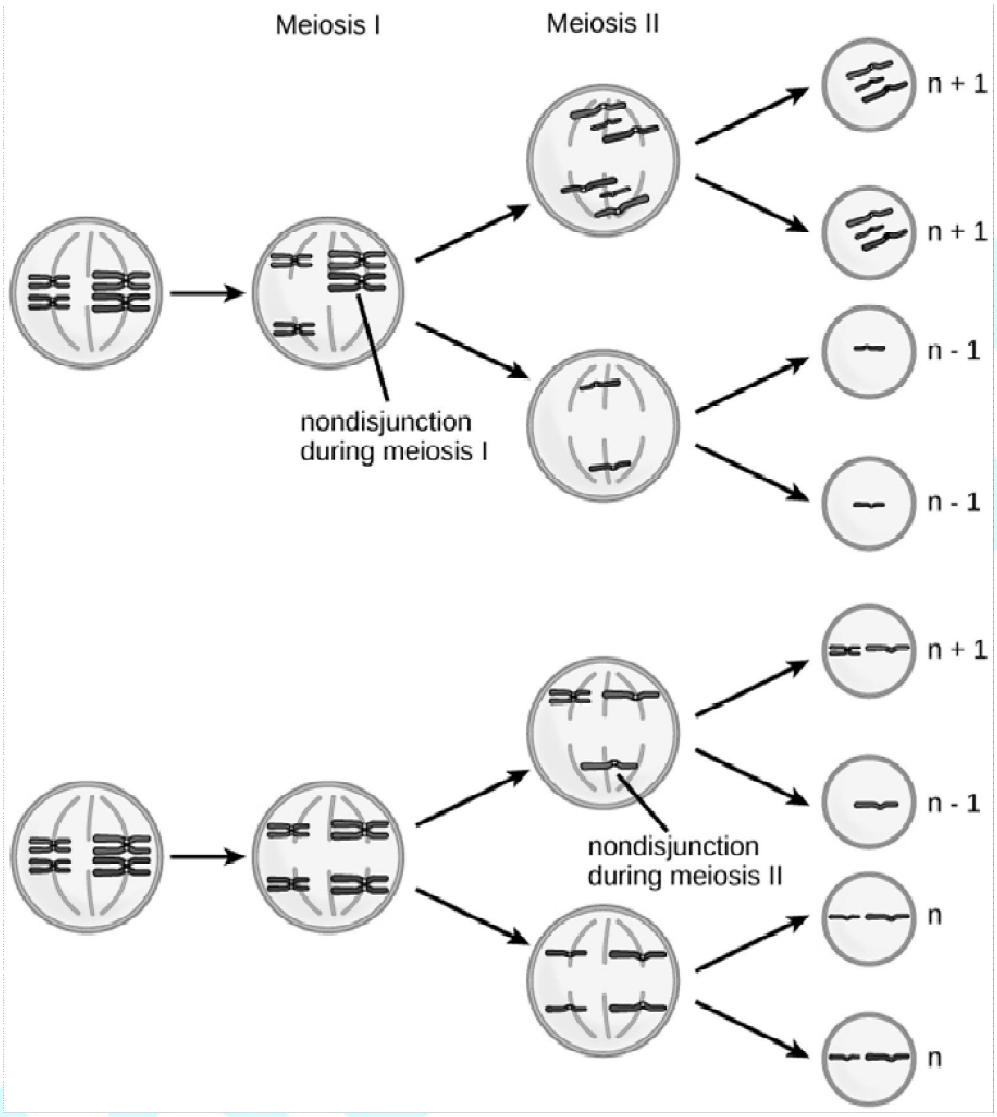
- Chronic myelogenous leukaemia in human beings is a fatal cancer involving uncontrolled replication of myeloblasts (stem cells of white blood cells).
- Ninety percent of CML is associated with an aberration of chromosome 22.
- This abnormal chromosome was originally discovered in the city of Philadelphia in 1959 and thus is called the 'Philadelphia chromosome'.
- Initially it was though to have a simple deletion in its long arm, however, subsequent analysis using molecular techniques has shown that the Philadelphia chromosome is actually the result of a reciprocal translocation between chromosomes 9 and 22.
- In the Philadelphia translocation, the tip of the long arm of chromosome 9 has been joined to the body of chromosome 22 and the distal portion of the long arm of chromosome 22 has been joined to the body of chromosome 9.
- CML is characterized by an excess of granular leucocytes in the blood.
- With the increase in the number of leucocytes, there is a reduction in the number of RBCs resulting in severe anaemia.

(2) **Burkitt's Lymphoma**

- Burkitt's lymphoma, a particularly common disease in Africa, is another example of a white blood cell cancer associated with reciprocal translocations.
- These translocations invariably involve chromosome 8 and one of the three chromosomes (2, 14 and 22) that carry genes encoding the polypeptides that form immunoglobulins or antibodies.
- Translocations involving chromosomes 8 and 14 are the most common.

Numerical aberrations of chromosomes : Each species has a characteristic number of chromosome. Variations or numerical changes in chromosomes (Heteroploidy) can be mainly of two types:





ALLOPOLYPLOIDY

- Normally different species cannot interbreed because they have different chromosome numbers and cannot form diploid pairs
- Offsprings produced by such unions are typically sterile due to this uneven chromosome pairing
- If cytokinesis fails to occur in one of the gametes, the hybrid offspring will have paired chromosomes from that parent species
- If the hybrid interbreeds with a member of the other parent species, all chromosomes from both parent species will be paired
- The resulting offspring will now be fertile and have the combined chromosome composition of both parental species
- Allopolyploids are more prevalent than autopolyploids as they do not show polysomic inheritance and have better fertility rates

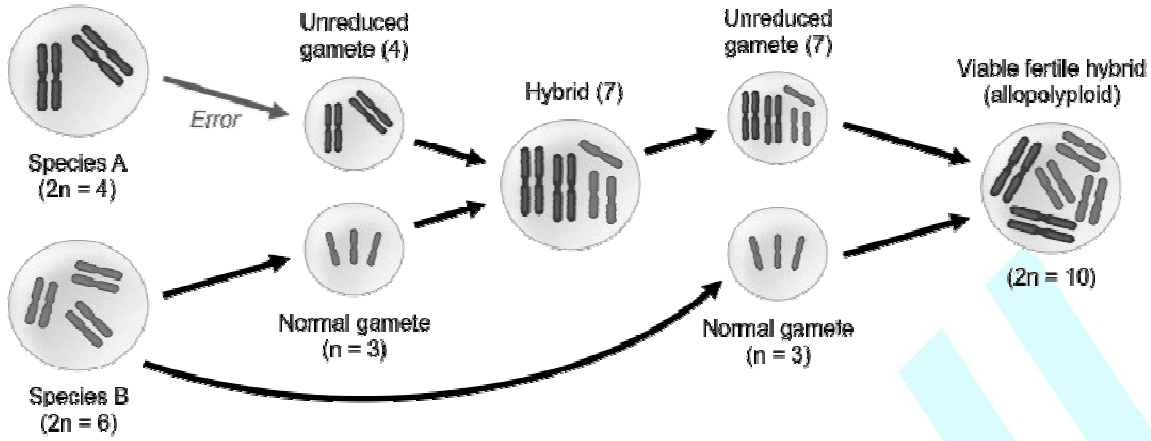


Fig: Allopolyploidy

(a) **Euploidy :** The somatic chromosome number in euploids is the exact multiple of basic haploid number. In euploidy an organism acquires an additional set of chromosomes over and above the diploid complement.

(1) **Monoploidy or haploidy :** Monoploids possess only one set or single basic set of chromosomes. Haploids on the other hand have half the somatic chromosome number. In diploid organisms monoploids and haploids are identical while in a tetra-or hexaploid with 4*n* or 6*n* chromosomes the haploids will possess 2*n* or 3*n* chromosome whereas its monoploid will possess only one set (*n*) of chromosome.

(2) **Diploidy :** The common chromosome number in the somatic cells of plants and animals.

(3) **Polyploidy :** Organism with more than two sets of chromosomes are known as polyploids. It may be triploid with three sets of chromosomes (3*n*) or tetraploid with four sets of chromosome (4*n*) and so on.

(b) **Aneuploidy :** Aneuploidy is the term applied for the chromosomal mutations involving only a part of a set, *i.e.*, loss (hypoploidy) or addition (hyperploidy) of one or more chromosomes. Aneuploidy may result from non disjunction of chromosome during cell division.

(1) **Monosomy :** Diploid organism that are missing one chromosome of a single pair with genomic formula $2n - 1$. Monosomics can form two kind of gametes, (n) and ($n - 1$).

(2) **Nullisomy :** An organism that has lost a chromsome pair is nullisomic. The result is usually lethal to diploids ($2n - 2$).

(3) **Trisomy :** Diploids which have extra chromosome represented by the chromosomal formula $2n + 1$. One of the pairs of chromosomes has an extra member, so that a trivalent may be formed during meiotic prophase.

(4) **Tetrasomy :** In tetrasomic individual particular chromosome of the haploid set is represented four times in a diploid chromosomal complement. The general chromosomal formula for tetrasomics is $2n + 2$ rather than $2n + 1 + 1$. The formula $2n + 1 + 1$ represents a double trisomic.

Types of aneuploidy : Aneuploidy may be of following types on the basis of chromosomes involved in non disjunction.

(a) **Aneuploidy involving non-disjunction in sex chromosomes :** This kind of aneuploidy is brought about due to non-disjunction in sex chromosomes. It may lead to following types of syndromes :

(1) **Turner's syndrome :** Such persons are monosomic for sex chromosomes *i.e.* possess only one X and no Y chromosome (XO). In other words they have chromosome number $2n - 1 = 45$. They are phenotypic females but are sterile because they have under developed reproductive organs. They are dwarf about 4 feet 10 inches and are flat chested with wide spread nipples of mammary glands which never enlarge like those in normal woman. They develop as normal female in childhood but at adolescence their ovaries remain under developed. They lack female hormone estrogen. About one out of every 5,000 female births results in Turner's syndrome.

(2) **Klinefelter's syndrome :** Since 1942, this abnormality of sex is known to geneticists and physicians. It occurs due to Trisomy of sex chromosomes which results in (XXY) sex chromosomes. Total chromosomes in such persons are $2n + 1 = 47$ in place of 46. **Klinefelter** (1942) found that testes in such male remain under developed in adulthood. They develop secondary sex characters of female like large breasts and loss of facial hair. Characters of male develop due to Y chromosome and those like female due to XX chromosomes. About one male child out of every 5,000 born, develops **Klinefelter's syndrome**.

Such children are born as a result of fertilization of abnormal eggs (XX) by normal sperms with (X) or (Y) chromosomes or by fertilization of normal eggs with (X) chromosomes by abnormal sperms with (XY) chromosome. They are sterile males mentally retarded and are **eunuchs**.

(3) **Super females and metasuper females :** Presence of extra (X) chromosomes in females shows such condition leading to (XXX, XXXX, XXXXX), having total 47, 48 or 49 chromosomes in each cell. Females with this type of aneuploidy show abnormal sexual development and mental retardation. Severeness of abnormality increases with the increase in number of (X) chromosomes.

(4) **Criminal's syndrome (super males) :** Presence of an extra (Y) chromosome in males causes such a condition (XYY) resulting in individuals with $2n + 1 = 47$ chromosomes. They have unusual height, mentally retarded and criminal bent of mind since birth. Their genital organs are under developed. Their frequency is one in every 300 males.

(b) **Aneuploidy involving non-disjunction in autosomes :** This type of aneuploidy occurs due to trisomy of autosomes. In any particular autosomal pair, having 3 instead of normal 2 chromosomes. Such persons may be males $45 + XY = 47(2n + 1)$ or females $45 + XX = 47(2n + 1)$. On the basis of the number of the autosome pair affected by trisomy, they can be of following types.

(1) **Down's syndrome :** This autosomal abnormality is also known as Mongolian idiocy or mongolism. In Langdon Down of England (1866) studied the Mongolian idiocy and described the trisomic condition of their chromosomes. Down's syndrome, a very common congenital abnormality arises due to the failure of separation of 21^{st} pair of autosomes during meiosis. Thus an egg is produced with 24 chromosomes instead of 23. A Down's syndrome has 3 autosomes in 21st pair instead of 2. Total number of chromosomes in this case is $2n + 1 (21^{st}) = 47$.

The affected children have a very broad fore head, short neck, flat palms without crease, stubby fingers, permanently open mouth, projecting lower jaw and a long thick extending tongue. They have low intelligence and are short heighted. They have defective heart and other organs. They are born to mothers aged 40 year and above during first pregnancy. They may survive upto 20 years under medical care.

They are called mongolian idiots because of their round, dull face and upper eyelids stretched downwards similar to mongolian race.

(2) **Edward's syndrome :** This autosomal abnormality occurs due to trisomy of eighteenth pair of autosomes in which the number of chromosomes are $2n + 1 = 47$. The child with this defect survives only about 6 months. Such children have defective nervous system, malformed ears and a receding chin.

(3) **Patau's syndrome :** This is trisomy of thirteenth pair of autosomal chromosome. This trisomic condition involves numerous malformations such as harelip, clefted palate and cerebral, ocular and cardiovascular defects. Such children usually survive for about 3 months only.

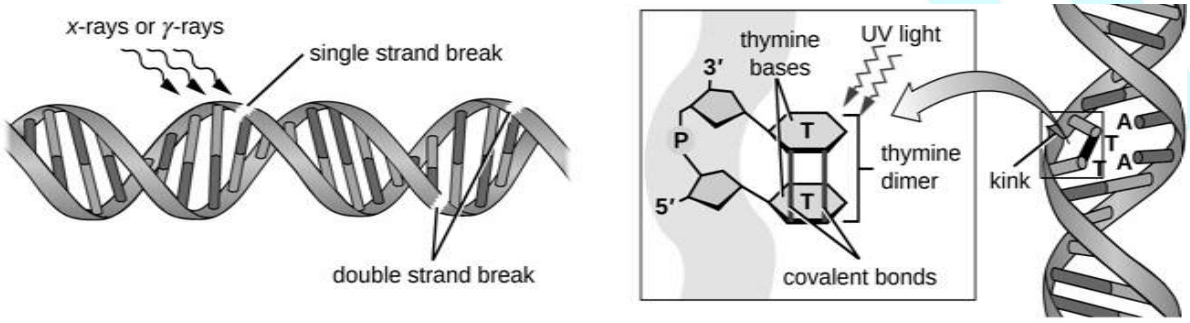
(iii) Mutagens : Any substance or agent inducing mutation is called a mutagen. The mutagens may be broadly grouped into two classes.

(a) **Physical mutagens :** It comprise mainly radiations. Radiation has been used to induce mutations for the first time by **H.J. Muller** (1927) on animals and **L.J. Stadler** (1928) on plants. Radiation that can produce mutation is known as effective radiations which are as follows.

(1) **Ionizing (Particulate) :** α-particles, β-rays, protons and neutrons.

(2) **Ionizing (non particulate) :** X-rays, r-rays and cosmic rays.

(3) **Nonionizing :** Ultraviolet rays



(a) Ionizing radiation (b) Non-ionizing radiation

(b) **Chemical mutagen :** A large number of chemicals react with the four nucleotides and modify their base-pairing capabilities. These are as follows.

(1) **Base analogues :** 5-bromodeoxyuridine (Brdu), 2-amino purine.

(2) **Chemicals modifying base-pairing**

- Hydroxylamine**;** Nitrous acid
- **Alkylating agent :** Nitrogen mustard, ethyl methane sulfonate (EMS), methyl methane sulfonate (MMS) and N-methyl-N'-nitro-nitroso-guanidine (NTG).

(3) **Intercalating agents :** Proflavin and acridine orange

(iv) Genetic diseases in man : There are many diseases in man due to gene mutations. It is either dominant or recessive. The mutated person may become incapable to produce specified enzyme, so result in inborn errors of metabolism.

(a) **Chondrodystrophic dwarfism**

(1) Chondrodystrophic dwarfism is a dominant autosomal mutation, most people are homozygous for recessive allele (c/c).

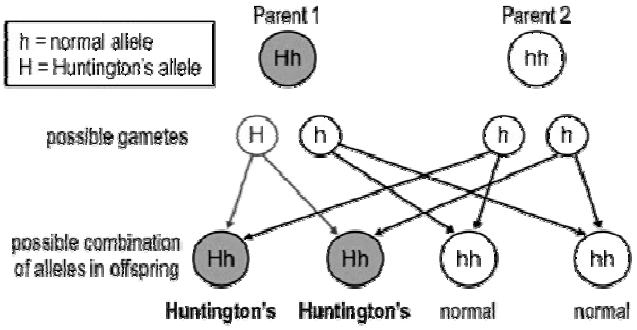
(2) The presence of one dominant C results in the premature closure of the growth areas of long bones of arms and legs, resulting in shortened and bowed arms and legs.

(b) **Huntington disease**

(1) Huntington disease is caused by a dominant gene on chromosome 4.

(2) The mutated gene causes abnormality by producing a substance that interferes with normal metabolism in the brain that leads to progressive degeneration of brain cells.

(3) The death comes ten to fifteen years after the onset of symptoms.



Inheritance of an Autosomal Dominant Disease

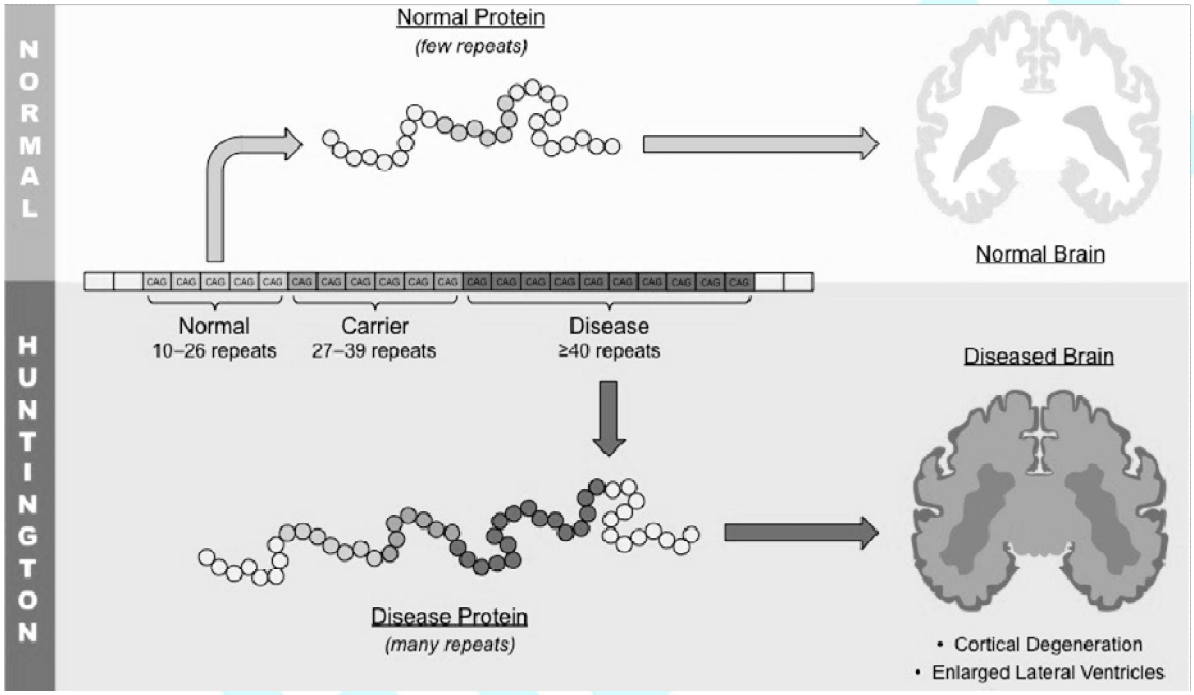


Fig: Huntington disease

(c) **Neuro-fibromatosis**

(1) Also called "von Recklinghausen disease" caused by a dominant gene on chromosome 17.

(2) The affected individual may have ten spots on the skin which later may increase in size and number.

(3) Small benign tumours called neurofibromas may occur under the skin or in various organs.

(d) **Tay-Sachs disease**

(1) Tay-Sachs disease results from the lack of the dominant gene on chromosome 15 for the production of hexosaminidase and subsequent storage of its substrate, a fatty substance known as glycosphingolipid, in lysosomes.

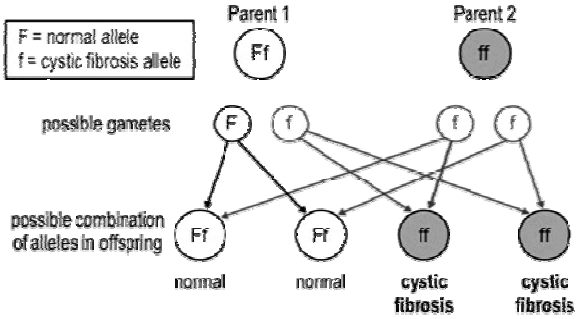
(2) The patient suffers from defective vision, muscular weakness and gradual loss of all mental and physical control, death occurs by the age of three or four years.

(e) **Cystic fibrosis**

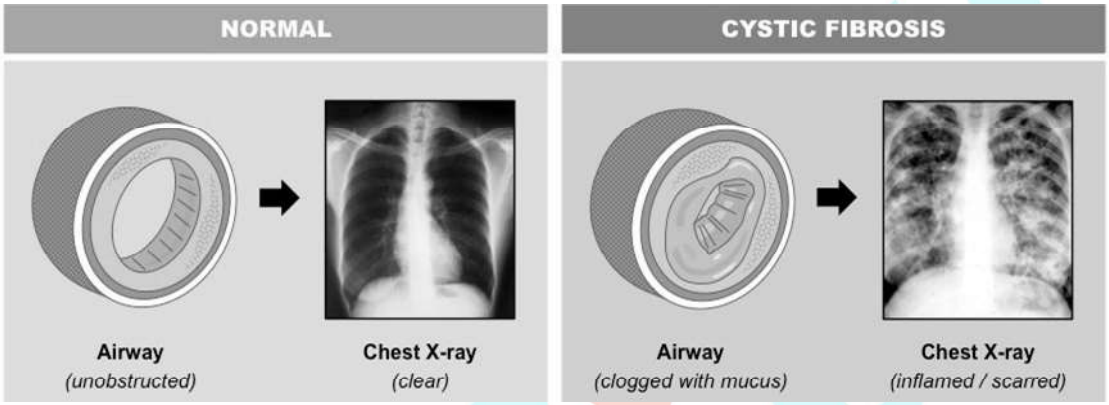
(1) The most common lethal genetic disease due to a recessive mutation on the chromosome 7.

(2) The body produces abnormal glycoprotein which interferes with salt metabolism.

(3) The mucus secreted by body becomes abnormally viscid and blocks passages in the lungs, liver and pancreas.



Inheritance of an Autosomal Recessive Disease



(f) **Alzheimer's disease**

(1) Alzheimer's disease, named after the German neurologist Alzheimer, is a degenerative brain disease characterized by memory loss, confusion, restlessness, speech disturbances, erosion of personality, judgement, and inability to perform the functions of daily living.

(2) Alzheimer's disease, a form of dementia, occurs in karyotypically normal individuals.

(3) About 5 percent of karyotypically normal individuals over age of 65 develop Alzheimer disease, and nearly 25 percent of those over age 80 do so.

(4) The brain of Alzheimer's patients show a marked loss of neurons.

(5) These patients also show an accumulation of senile plaques, which are thickened nerve cell processes (axons and dendrites) surrounding a deposit of particular type of polypeptide called amyloid β protein.

(6) In the brain of normal persons, amyloid β protein is produced and processed in a number of ways from a large number of amyloid precursor protein.

(7) The occurrence of Alzheimer's disease in people with Down's syndrome suggests that a gene or genes on chromosome 21 is involved.

(8) Genetic mapping has demonstrated that the gene for amyloid β protein is located on chromosome 21; this gene encodes an Amyloid Precursor Protein (APP) that is enzymatically cleaved to produce amyloid β proteins.

(9) According to **Bush** (2003) Alzheimer's disease is caused by a copper and zinc build up in the brain.

(g) **Marfan's syndrome**

(1) Marfan's syndrome is due to dominant mutation resulting in the production of abnormal form of connective tissues and characteristic extreme looseness of joints.

(2) The long bones of body grow longer; fingers are very long called 'spider fingers' or arachnodactyly.

(3) The lenses in eyes become displaced.

(h) **Albinism**

(1) Albinism is an autosomal recessive mutation.
(2) An albino cannot synthesize melanin which provides black colouration to skin and hair.
(3) Albinism is due to tyrosinase deficiency.
(4) The enzyme tyrosinase normally converts the amino acid tyrosine to melanin through an intermediate product **DOPA** (dihydro phenyl alanine).

(i) **Sickle-cell disease**

(1) Sickle-cell disease is a genetic disease reported from negroes due to a molecular mutation of gene Hb^A on chromosome 11 which produces the β chain of adult haemoglobin.
(2) The mutated gene Hb^S produces sickle-cell haemoglobin.
(3) The sixth amino acid in β chain of normal haemoglobin is glutamic acid.
(4) In sickle-cell haemoglobin this amino acid is replaced by valine.
(5) The children homozygous (Hb^SHb^S) produce rigid chains.
(6) When oxygen level of the blood drops below certain level, RBCs undergo sickling.
(7) Such cells do not transport oxygen efficiently; they are removed by spleen causing severe anaemia.
(8) Individuals with the Hb^AHb^A genotype are normal, those with the Hb^SHb^S genotype have sickle-cell disease, and those with the Hb^AHb^S genotypes have the sickle-cell trait.
(9) Two individuals with sickle-cell trait can produce children with all three phenotypes.
(10) Individuals of sickle-cell trait are immune to malaria.

(j) **Thalassemia**

(1) Thalassemia is a human anaemia due to an autosomal mutant gene and when this gene is present in double dose, the disease is severe thalassemia major with death occurring in childhood.
(2) Heterozygous persons show a milder disease, thalassemia minor or also called **Cooley's anaemia**.
(3) The persons suffering from thalassemia major are unable to produce β chain.
(4) Their haemoglobin contains δ chains like that of foetus which is unable to carry out normal oxygen transporting function.

(k) **Alkaptonuria**

(1) Alkaptonuria was the first of the recessive human trait discovered in 1902 by **Archibald Garrod**, 'father of physiological genetics' or 'father of biochemical genetics'.
(2) Patients of alkaptonuria excrete large amounts of homogentistic acid in urine.
(3) Such urine turns black upon exposure to light.
(4) In normal person, homogentistic acid (alkapton) is oxidized by a liver enzyme homogentistic acid oxidase to maleyl acetoacetic acid.

(l) **Phenylketonuria (PKU)**

(1) Phenylketonuria was discovered by the Norwegian physician **A. Folling** in 1934; an autosomal recessive mutation of gene on chromosome 12.
(2) PKU results when there is a deficiency of liver enzyme phenylalanine hydroxylase that converts phenylalanine into tyrosine.
(3) There is a high level phenylalanine in their blood and tissue fluids.
(4) Increased phenylalanine in the blood interferes with brain development; muscles and cartilages of the legs may be defective and the patients cannot walk properly.

(m) **Gaucher's disease**

(1) Gaucher's disease is a genetic disease associated with abnormal fat metabolism, caused by the absence of the enzyme **glucocerebrosidase** required for proper processing of lipids.
(2) Non processing of lipids results in accumulation of fatty material in spleen, liver, bone marrow and brain.
(3) The swelling of these organs occurs and patients usually die by the age of 15 years.

(n) **Galactosemia**

(1) Galactosemia is inherited as an autosomal recessive, and the affected person is unable to convert galactose to glucose.
(2) Galactosemia is due to the deficiency of the enzyme Galactose Phosphate uridyl Transferase (GPT).
(3) Milk is toxic to galactosemic infants; child usually dies at three years of age.

12 SEX DETERMINATION

Fixing the sex of an individual as it begins life is called sex determination.

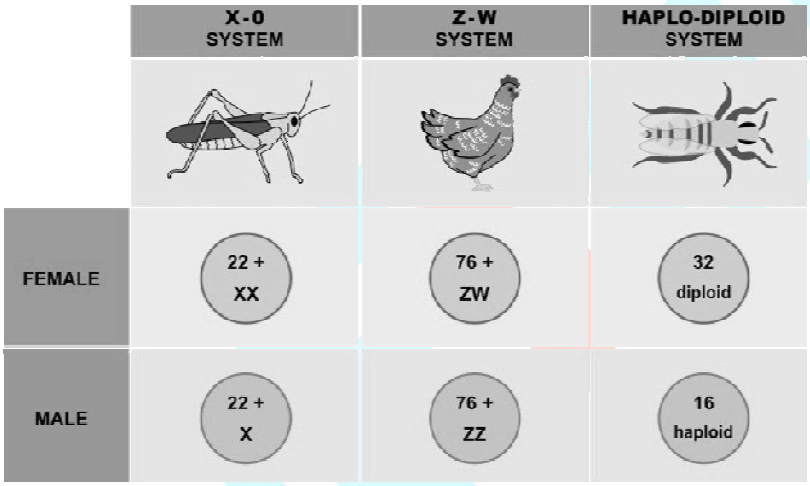


Fig: Sex Determination Systems

The various genetically controlled sex-determination mechanisms have been classified into following categories:

(i) Chromosomal theory of sex determination : The X-chromosome was first observed by German biologist, **Henking** in 1891 during the spermatogenesis in male bug and was described as X-body. The chromosome theory of sex determination was worked out by **E.B. Wilson** and **Stevens** (1902-1905). They named the X and Y chromosomes as sex-chromosomes or allosomes and other chromosomes of the cell as autosomes.

Sex chromosomes carry genes for sex. X-chromosomes carries female determining genes and Y-chromosomes has male determining genes. The number of X and Y chromosomes determines the female or male sex of the individual, Autosomes carry genes for the somatic characters. These do not have any relation with the sex.

(a) **XX-XY type or Lygaeus type :** This type of sex-determining mechanism was first studied in the milk weed bug, Lygaeus turcicus by **Wilson** and **Stevens**. Therefore, it is called Lygaeus type. These are two different patterns of sex determination in Lygaeus type.

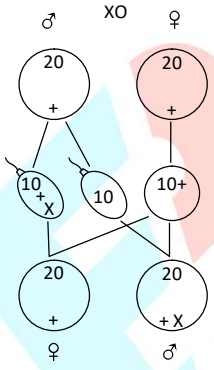
(1) **Female homogametic XX and male heterogametic XY :** The homogametic sex (XX) is female and produces ova all of one type, *i.e.* having X-chromosome. The male is heterogametic-XY and produces sperm of two types. 50% of which possess X-chromosome and other 50% Y-chromosome. This is simple XX-XY type and is found in man, *Drosophila* and certain insects.

Example : In *Drosophila* total number of chromosomes is eight, of which six are autosomes, common to both male and female. The fourth pair is of sex chromosomes. In male this is

represented by XY *i.e.* Karyotype of male *Drosophila* 6+XY and in female XX *i.e.* 6+XX. Ova produced by female are all similar possessing 3+X chromosomes, whereas the sperm produced by male are 3+X and 3+Y in equal numbers.

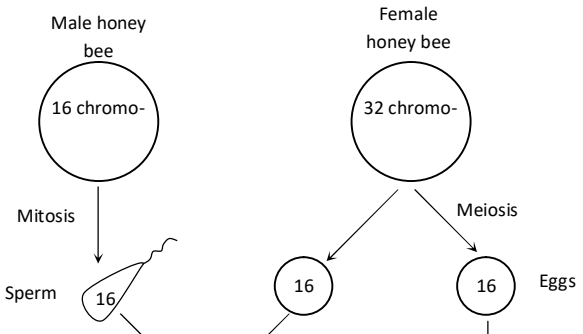
(2) **Female heterogametic and male homogametic :** In fowl, other birds and some fishes, certain moths and butterflies, the female sex is heterogametic, with X and Y chromosome often represented by Z and W and laying two types of eggs, one half with X or Z chromosome and the other half with Y or W chromosome. The male sex is homogametic having XX or ZZ chromosomes. It produces sperm all of one type.

(b) **XX-XO type or Protenor type : Mc clung** in male squash bug (*Anasa*) observed 10 pairs of chromosomes and an unpaired chromosome. Their females have eleven pairs of chromosomes (22). Thus all the eggs carry a set of eleven chromosomes but the sperm are of the two types: fifty percent with eleven chromosomes and the other fifty percent with ten chromosomes. The accessory chromosome was X-chromosomes. Fertilization of an egg by a sperm carrying eleven chromosomes results in a female, while its fertilization by a sperm with ten chromosomes produces male. It is said to be evolved by the loss of Y-chromosome.



(c) **Haploid-diploid mechanism of sex determination :** Hymenopterous insects, such as bees, wasps, saw flies, and ants, show a unique phenomenon in which an unfertilized egg develops into a male and a fertilized egg develops into a female. Therefore, the female is diploid (2N), and the male is haploid (N). eggs are formed by meiosis and sperms by mitosis. Fertilization restores the diploid number of chromosomes in the zygote which gives rise to the female. If the egg is not fertilized, it will still develop but into a male. Thus, the sex is determined by the number of chromosomes.

In honeybee, the quality of food determines whether a diploid larva will become a fertile queen or a sterile worker female. A larva fed on royal jelly, a secretion from the mouth of nursing workers, grows into a queen, whereas a larva fed on pollen and nectar grows into a worker bee. Thus, the environment determines fertility or sterility of the bee but it does not alter the genetically determined sex. The sex ratio of the offspring in the hive is controlled by the queen. She lays more fertilized eggs that produce worker females and fewer unfertilized eggs which produce haploid males. The queen mates only once in her life time, keeps a store of sperms in the seminal receptacle, and can control fertilization of eggs by releasing or not releasing sperms.



Different types of chromosomal mechanisms of sex-determination in animals

S. No.	Organisms	Heteroga-metic sex	Gamete		Zygotes	
			Sperms	Eggs	Females	Males
(1)	*Drosophila*, man etc.	Male	X and Y	All X	XX	XY
(2)	Protenor(Bug, Grasshopper)	Male	X and O	XX	XX	XO
(3)	Birds, moths	Female	All X	X and Y	XY	XX
(4)	Fumea (a moth)	Female	All X	X and O	X	XX

(ii) Quantitative or ratio theory of sex determination : **C.B Bridges** worked out ratio theory of sex determination in *Drosophila*. According to this theory the ratio of chromosomes to autosomes is the determining factor for the sex. Single dose of X-chromosome in a diploid organism produces male, whereas 2X-chromosomes produce a female. If a complete haploid set of autosomes is designated by A then 2A : X will give rise to male and 2A : 2X to female.

(a) **Intersexes in *Drosophila* and ratio theory of sex determination :** Bridges hypothesis was supported by studies of flies arising after abnormal distribution of chromosomes on account of non-disjunction. Due to abnormal meiosis during oogenesis both the X-chromosomes fail to separate and move to one pole of meiotic spindle. Thus few eggs are formed with single autosomal genome but with 2X chromosomes, *i.e.* (AXX) and other with single autosomal genome but no sex chromosome (A). when such abnormal eggs are fertilized with normal sperm, the following result are obtained.

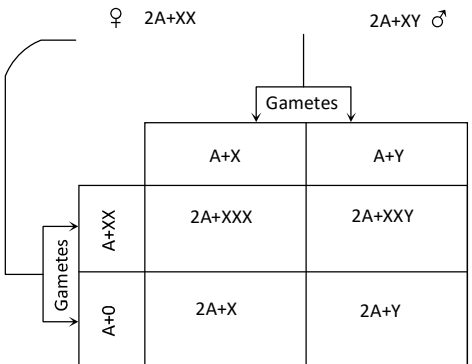
Results of fertilization of abnormal female gametes

AAXXY – Female

AAXXX – Super female

AAX – Sterile male

AAY – Nonviable



Out of this progeny 1/4th males with no X are nonviable; the other 1/4 are without Y-chromosome and sterile. 1/4th females have an extra Y-chromosome while rest 1/4th females with 3X are super females. These are sterile with under developed sexual characteristics.

(iii) Triploid intersexes and balance theory : The triploid flies with (3A + 3X) are much like the normal diploid females both in appearance as well as in fertility. On mating to diploid males their progeny consisted of following types.

(1) AAAXXX – Triploid females
(2) AAXX – Dilpoid females
(3) AAXXY – Diploid females
(4) AAAXX – Intersexes
(5) AAAXXY – Intersexes
(6) AAXY – Normal males
(7) AAXXX – Super females
(8) AAAXY – Super males

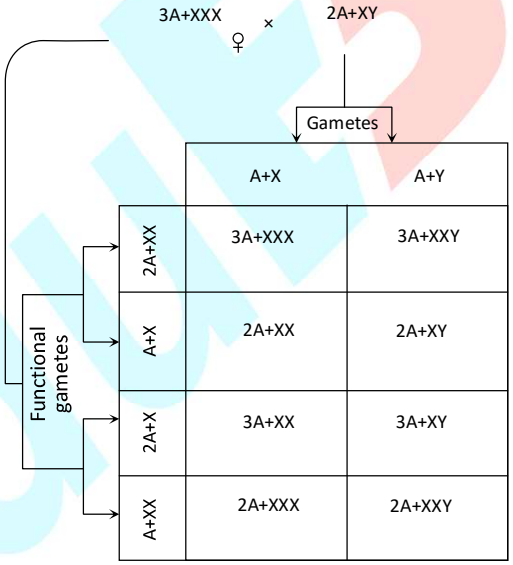


Fig : Results of a cross between triploid female and diploid male

The intersexes are sterile and intermediate between females and male, because the sex balance ratio in the intersexes comes to 2 : 3.

(2) **Gyandromorphs in Dorsophila and ratio theory of sex determination :** In *Drosophila* occasionally flies are obtained in which a part of the body exhibits female characters and the other part exhibits male characters. Such flies are known as **gynandromorphs**. These are formed due to misdivision of chromosomes and start as female with 2A+2X-chromosomes. One of the X-chromosomes is lost during the division of the cell with the result that one of the daughter cells possesses 2A+2X chromosomes and the other 2A+X. If this event happens during first zygotic division, two blastomeres with unequal number of X-chromosomes are formed. The blastomere with 2A+2X-chromosomes develops into female half, while the second blastomere

with 2A+X chromosomes produces male half and the resultant fly is a bilateral gynandromorph. The occurrence of gynandromorphs clearly indicates that the number of X-chromosomes determines the sex of the individual.

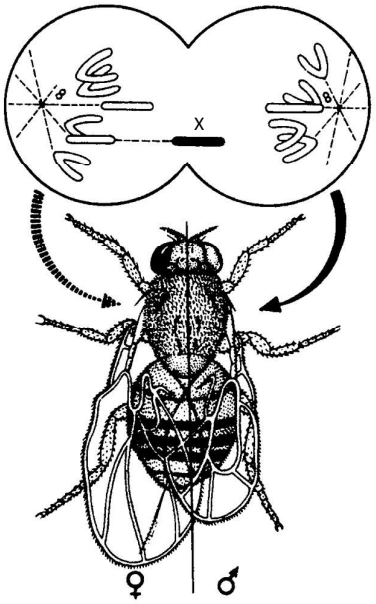


Fig : Gynandromorph of Drosophila in which right half is male and left half is female

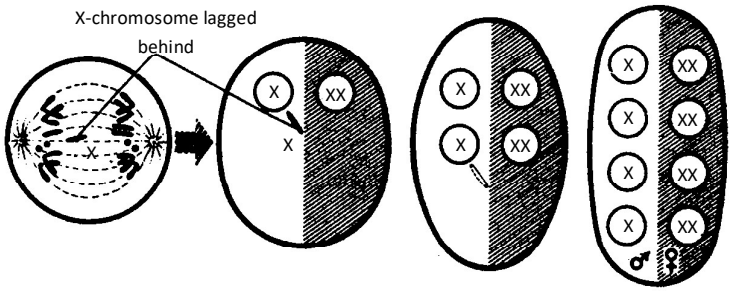


Fig : Diagram to show origin of gynandromorphs

(iv) Genic balance theory : Based upon the observations of ratio theory **Bridges** put forward genic balance theory in which he suggested that every individual whether male or female possesses in its genotype genes for both male and female characteristics. Which sex will actually develop is decided by the preponderance of that type of genes.

According to the genic balance theory of Bridges in *Drosophila melanogaster*, sex is determined by the ratio of the X-chromosomes and the set of autosomes. The *Y*-chromosomes play no part in sex determination it only governs male fertility. The XO flies are male, but sterile. Sex is governed by the ratio of the number of X chromosomes to sets of autosomes. The table given below indicates how the ratio of X/A help to determine the sex.

Ratio of X-chromosome to autosomes and the corresponding phenotype in *Drosophila*

S. No.	Sex	Number of X-chromosomes	Number of autosomal set	Sex index X/A ratio
(1)	Super female	XXX (3)	AA (2)	3/2 = 1.5
(2)	Normal female Tetraploid Triploid Diploid Haploid	 XXXX (4) XXX (3) XX (2) X (1)	 AAAA (4) AAA (3) AA (2) A (1)	 4/4 = 1.0 3/3 = 1.0 2/2 = 1.0 1/1 = 1.0
(3)	Intersex	XX (2)	AAA (3)	2/3 = 0.66
(4)	Normal male	X (1)	AA (2)	1/2 = 0.50
(5)	Super male	X (1)	AAA (3)	1/3 = 0.33

Genes for maleness are carried on the autosomes, those for femaleness on the X-chromosomes. The sex index ratio of female is 1.0 while in males is 0.50. If X/A ratio is greater than 1.0 produces super females (meta females) and less than 0.50 produces super males. The X/A ratio lesser than 1.0 but greater than 0.5 (for example 0.66) result in intersexes. The degree of femaleness is greater where the X/A ratio is closer to 1.0 and the degree of maleness is greater where that ratio is closer to 0.5.

Human sex determination : The genic balance theory of sex determination is not universally accepted. Unlike *Drosophila* X : A does not influence sex determination. The key to sex determination in humans is the SRY (for sex region on the Y) gene located on the short arm of the Y-chromosome. In the male, the testis-determining factor (TDF) is produced by SRY on the Y-chromosome. TDF induces the medulla of the embryonic gonads to develop into testes. In the absence of SRY on Y, no TDF is produced. The lack of TDF allows the cortex of the embryonic gonads to develop into ovaries.

(v) Hormonal theory of sex determination : The sex determination theories of chromosomes and genic balance successfully apply to the lower animals but in higher vertebrates and under certain conditions in invertebrates, the embryo develops some characters of the opposite sex together with the characters of its own sex-chromosome. It means, the sex changes under specific circumstances. This is due to the hormones secreted by the gonads of that animal.

(a) **Free martinism :** The influence of hormones on sex determination comes from free-martins often found in cattles. LILLIE and others found that where twins of opposite sex (one male and other female) are born, the male is normal but female is sterile with many male characteristics. Such sterile females are known as free martins.

The scientific explanation for the formation of free martins is the effect of hormones of the male sex on the female. In cattle the foetal membranes of the twins are fused in such a manner that they have a common circulation of blood. The female hormone is produced at a slightly later stage in the development and guides its development towards female side. But since the twins have a common circulation and blood passes from one twin into the body of other twin, the male hormone which is produced slightly in advance of female hormone, enters the body of female twin and before the female hormone onsets the development of female characteristics it is already differentiated in the guidance of male hormone. As a result the developing female is sterile.

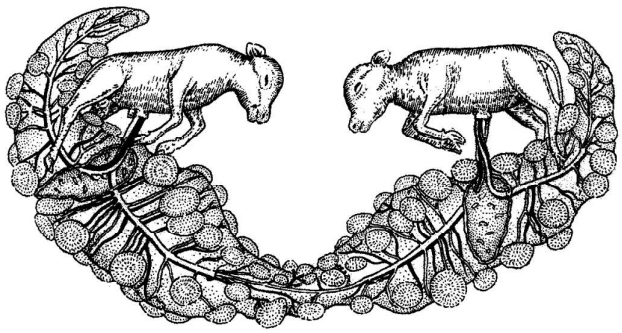


Fig : Free martins in cattle

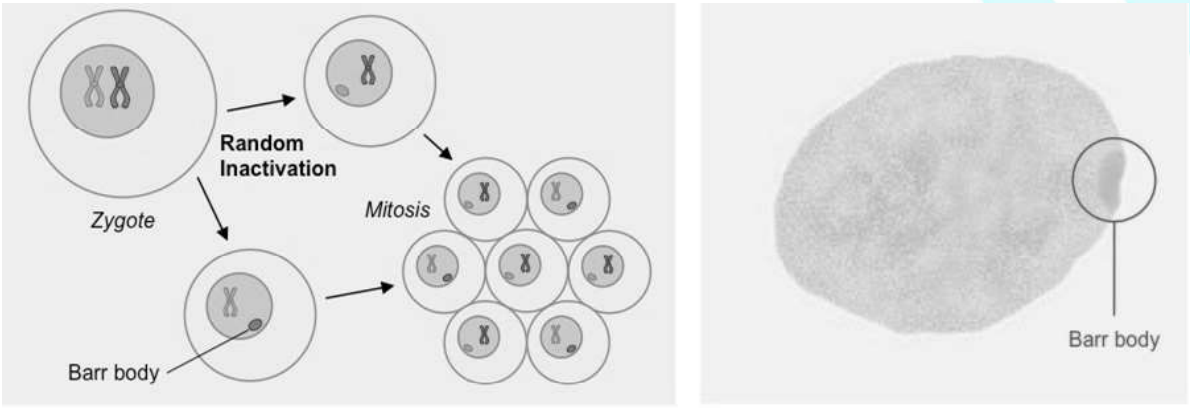
(vi) Environmental theory of sex determination : In some animals, there is environmental determination of sex.

(a) In *Bonellia*, a marine worm, the swimming larva has no sex. If it settles down alone, it develops into a large (2.5 *cm*) female. If it lands on or near an existing female proboscis, a

chemical secreted from her proboscis causes the larva to develop into a tiny (1.3 *mm*) male. Male lives as a parasite in the uterus of the female.

(b) In turtles, a temperature below 28°C produces more males, above 33°C produces more females, and between 28°C to 33°C produces males and females in equal proportion, while in crocodile male sex is predominant at high temperature.

(vii) Barr body in sex determination : **Murray Barr** (1949), a geneticist noticed a small body in the nucleus of the nerve cells of female cats which stained heavily with nuclear stains. Further investigations showed that not only nerve cells, but many other cells from female cats only, had these bodies, now known as sex chromatin or Barr bodies. It was soon learnt that such bodies can be found in females of many mammals including human. In women the Barr body lies against the nuclear membrane like a round disc in the neutrophil blood cells, skin cells, nerve cells, cells of mucous membrane, cells of lining in vagina and urethra. They are absent in man. These bodies are thus named after the discover **Barr**.



Summary of the Process of X-Inactivation Barr Body in a Human Nucleus

Fig : Chromosome variations and Barr body (X-Inactivation)

Barr bodies are used to determine the sex of unborn human embryos. In this technique called **amniocentesis** sample of the amniotic fluid is examined for Barr bodies. The sex is determined by the presence or absence of Barr bodies in epithelial cells of embryo present in the amniotic fluid sample. Studies from the cells of aborted embryos show that Barr bodies can be distinguished at about 15 or 16th day after conception that means several weeks before the formation of gonads. Whereas sex of embryo is determined soon after fertilization, sex differentiation can be noticed in third week stage of pregnancy.

Mary Lyon hypothesis : According to the British geneticist **Mary Lyon** (1961), one of the two X-chromosomes of a normal female becomes heterochromatic and appears as Barr body. This inactivation of one of the two X-chromosomes of a normal female is the dosage compensation or Lyon's hypothesis.

It is estimated that number of Barr bodies is one less from the total number of X chromosomes present in embryo. Therefore, Barr bodies are also used to decide the genic constitution of such persons who have irregular number of sex chromosomes. More than one X chromosome in such persons is transformed into Barr bodies.

S. No.	Individual	No. of X chromosome	No. of Barr body (X – 1)
(1)	Normal woman	XX	2–1 = 1 (one barr body)
(2)	Women with Turner's syndrome	XO	1–1 = 0 (no barr body)
(3)	Super female	XXX	3–1 = 2 (two barr bodies)
(4)	Man	XY	1–1 = 0 (no barr body)

(5)	Man with Klinefelter's syndrome	XXY	2–1 = 1 (one barr body)

Sex can also be distinguished by studies of simple blood smears. The neutrophils, the most common of the white blood corpuscles, have a nucleus divided into two or three lobes. Female neutrophils showing a small drumstick extending out from one of the nuclear lobes, is a definite indication of the female chromosome component in the cells.

Mosaicism describes the presence of two populations of cells with distinct genotypes within a single organism

- ➔ It is caused when either mutation or division error creates two distinct cell types which divide into separate cell lines
- ➔ Mosaicism is more pronounced when errors occur in early embryo development and thus affects a greater proportion of cells
- ➔ X-inactivation in mammals creates a mosaic of genotypes linked to the *X chromosome only*, and hence is **not** true mosaicism.

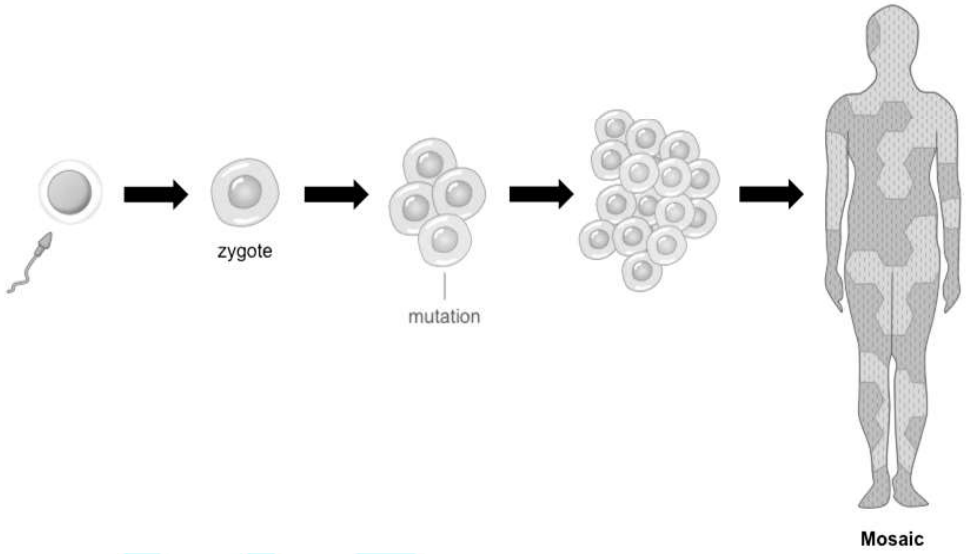


Fig: Mosaicism

13 SEX LINKED INHERITANCE

Sex chromosomes of some animals and man besides having genes for sex character also possess gene for non sexual (somatic) characters. These genes for non sexual characters being linked with sex chromosomes are carried with them from one generation to the other. Such non-sexual (somatic) characters linked with sex chromosomes are called **sex linked characters** or traits, genes for such characters are called **sex linked genes** and the inheritance of such characters is called **sex linked inheritance**. The concept of sex-linked inheritance was introduced by **THOMAS H. MORGAN** in 1910, while working on *Drosophila melanogaster*.

The sex chromosomes in man and *Drosophila* are almost same in structure. The X and Y chromosomes, although different (non-homologous) in shape, size and structure, have atleast some similar (homologous) part which is known as homologous segment and the remaining part as non-homologous or differential segment. Genes for sex linked characters occur in both segments of X and Y chromosomes. Many sex linked characters (About 120) are found in man. Such characters are mostly recessive.

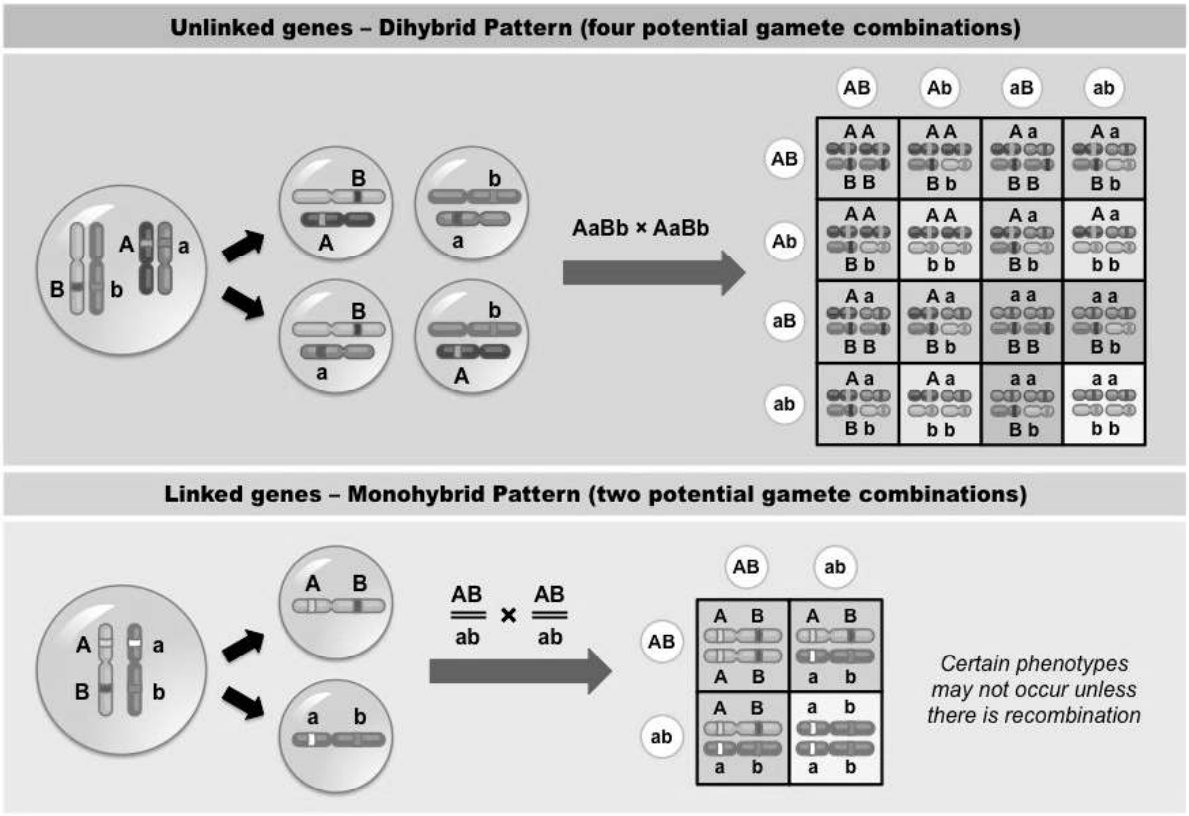


Fig: Unlinked versus Linked Inheritance Patterns

(i) Types of sex linked inheritance

(a) **Diandric sex linked or X linked traits :** Genes for these characters are located on non-homologous segment of X chromosome. Alleles of these genes do not occur on Y chromosome. Genes of such characters are transferred from father to his daughter and from his daughter to her sons in F_2 generation. This is known as Cris-cross inheritance. As the genes for most sex linked characters are located in X chromosome, they are called X-linked characters *e.g.* colour blindness and haemophilia in man and eye colour in *Drosophila*.

(1) **Sex linked inheritance in Drosophila :** *Drosophila melanogaster* has XX and XY sex chromosomes in the female and male respectively. Its eye colour is sex linked.

Allele of the eye colour gene is located in the X chromosome, and there is no corresponding allele in the Y chromosome. The male expresses a sex-linked recessive trait even if it has a single gene for it, whereas the female expresses such a trait only if it has two genes for it. The normal eye colour is red and is dominant over the mutant white eye colour. The following crosses illustrate the inheritance of X-linked eye colour in *Drosophila*.

Red-eyed female × White-eyed male : If a homozygous red-eyed female fly is mated with a **hemizygous** (having a single allele for a trait) white-eyed male fly, all the F_1 flies, irrespective of their sex, are red eyed. When the red-eyed male and female flies of F_1 are intercrossed (equivalent to self pollination in peas), the F_2 flies are in the ratio of 2 red-eyed females to 1 red-eyed male to 1 white-eyed male. Thus, the red-eyed and white-eyed flies are in the ratio of 3 : 1 in F_2 generation (Mendelian monohybrid ratio).

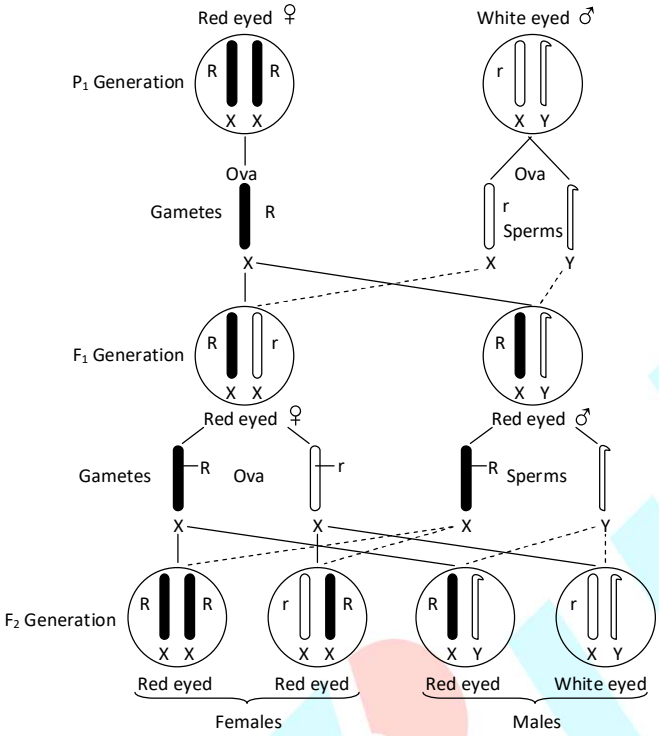


Fig : Sex-linked inheritance in *Drosophila melanogaster*. Note the transmission of sex chromosomes carrying eye colour gene R and r in a cross between red-eyed female and white-eyed male

If X^R represents a gene for red eye and X^r that for white eye colour, the above cross may be diagramed as follows. The above cross shows that a recessive X-linked trait follows criss-cross inheritance, *i.e.*, transmission from the father to the grandsons through the daughters. The latter are called carriers because they have a trait but do not express it.

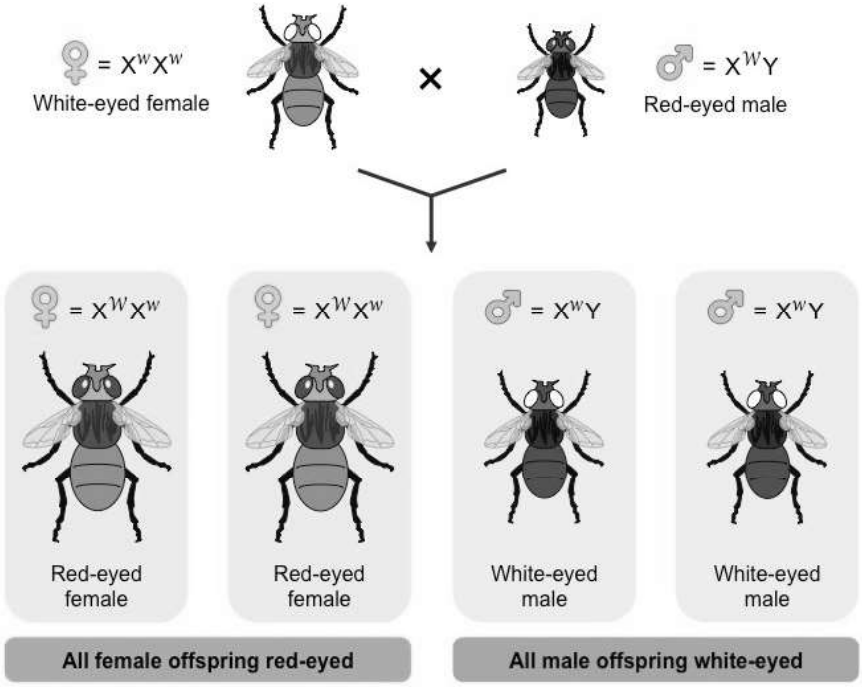


Fig: Morgan's Discovery of Sex Linkage in *Drosophila*

Gene Linkage

Morgan went on to identify a number of different traits in fruit flies that did not conform to Mendelian ratios

➔ Certain phenotypic combinations occurred in much lower frequencies than was to be expected

Based on this data, Morgan made two key proposals:

➔ The alleles for these traits were located on a shared chromosome *(gene linkage)* and hence did not independently assort
➔ Linked alleles could be uncoupled via recombination *(crossing over)* to create alternative phenotypic combinations, but these new phenotypes would occur at a much lower frequency

Morgan also observed that the amount of crossing over between linked genes differed depending on the combination of traits

➔ This led to the idea that crossover frequency may be a product of the distance between two genes on a chromosome – genes with a higher crossover frequency are further apart, whereas genes with a lower crossover frequency are closer together
➔ Morgan used this concept to develop the first gene linkage maps that showed the relative positions of genes on a chromosome.

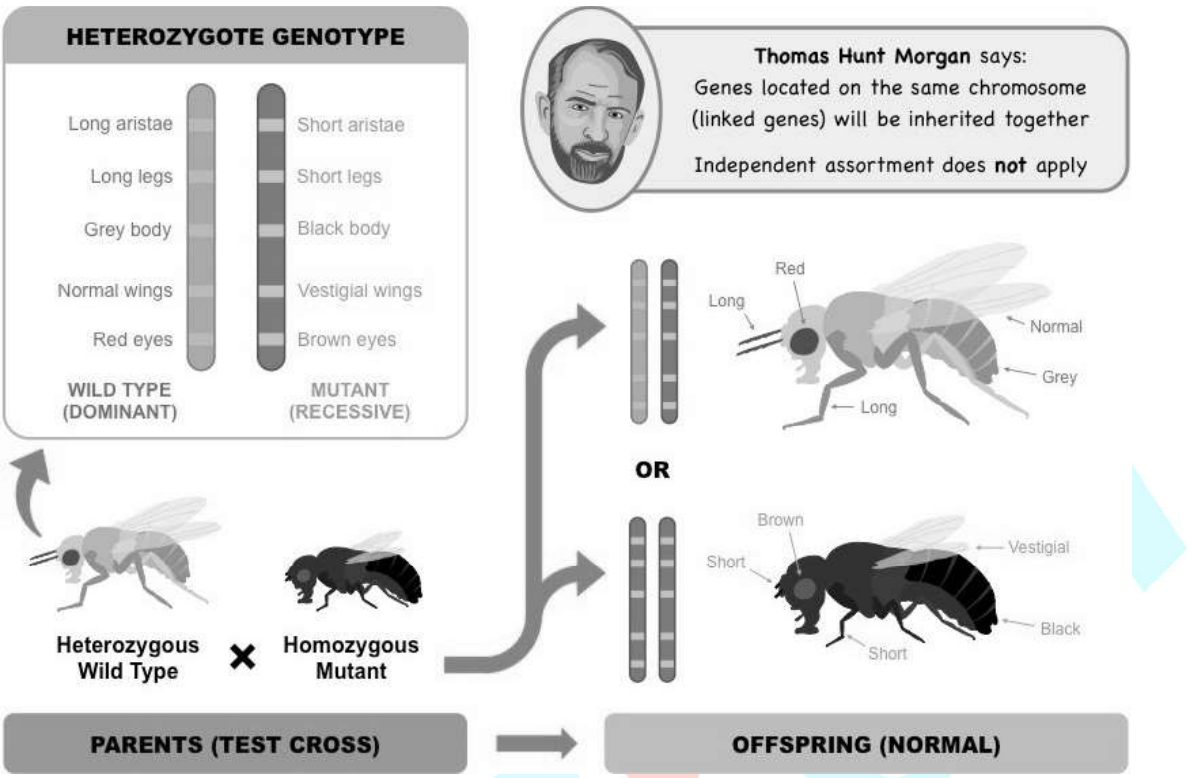


Fig: Gene Linkage and Recombination Frequencies

From the above diagrams it can be seen that:

- Long aristae and red eyes are *more likely* to be separated via recombination (high crossover frequency)
- Long aristae and long legs are *less likely* to be separated via recombination (low crossover frequency). This indicates that the aristae and leg genes are located closer together, whereas the eye gene is more distant

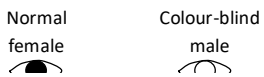
(2) **Sex linked inheritance in man**. Colour blindness and Haemophila are the two main sex linked or X-linked disease are found in man.

(I) **Colour blindness :** Person unable to distinguish certain colours are called colour blind. Several types of colour blindness are known but the most common one is 'red-green colour blindness'. It has been described by **HORNER** (1876).

The red blindness is called protanopia and the green blindness deutoranopia. X-chromosome possesses a normal gene which control the formation of colour sensitive cells in the retina. Its recessive allele fails to do its job properly and results in colour blindness.

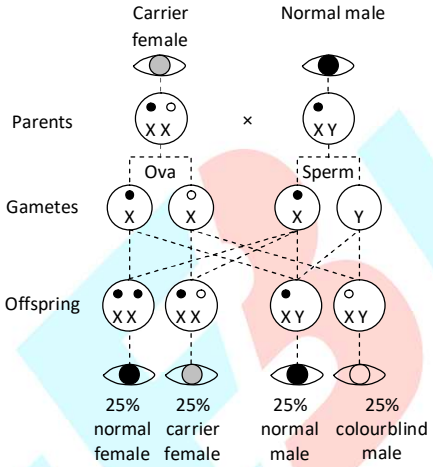
These alleles are present in X chromosome is evidenced by the following results.

(1) If a normal female is married to a colour blind man.



Results : All her sons and daughter have normal colour vision, but all daughters are carrier.

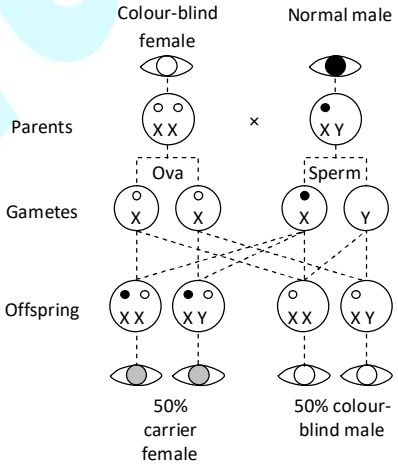
(2) But when her daughter (carrier) are married to man with normal colour vision man.



Result : Some colour blind sons are formed.

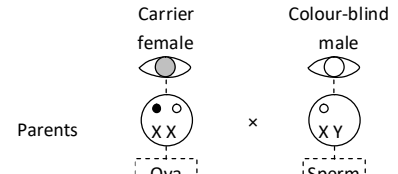
Conclusion : It means that a woman with normal colour vision whose father is colour blind gives birth to children, of which about half of the sons are colour blind and other half are normal.

(3) If a colour blind woman is married to a normal man.



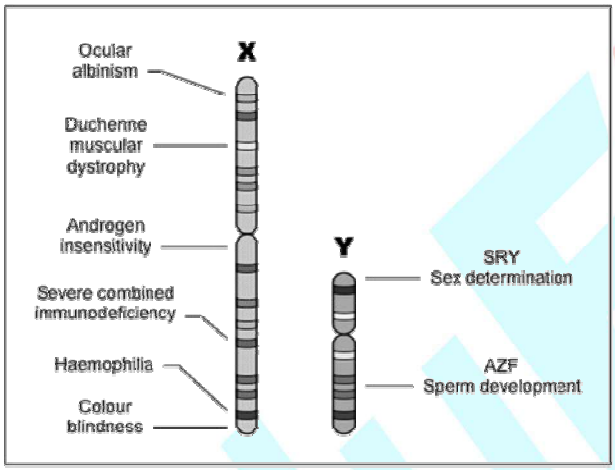
Result : All her sons are colour blind whereas all the daughter have normal colour vision.

(4) But when these daughters having normal colour vision (Heterozygous) are married to colour blind man.

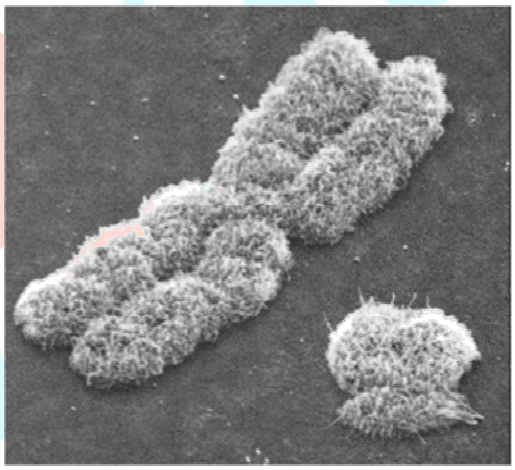


Result : The colourblind grandsons and grand daughters are produced with almost equal number of normal grandsons and grand daughters.

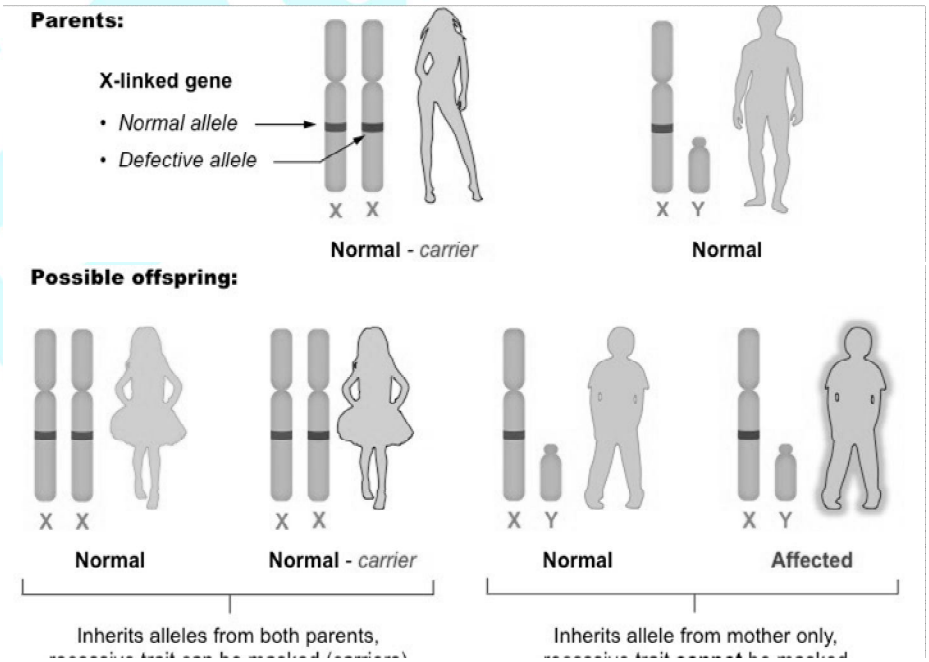
Conclusion : It means that a colour blind woman has sons all colour blind and daughters all with normal vision and a colour blind woman always has a colour blind father and her mother is a carrier.



Genetic Comparison of X and Y Chromosomes



Micrograph of X and Y Chromosomes



S.No.	Sex limited traits	Sex Influenced traits	Holandric traits
1.	The genes of these traits are **autosomal** and found in both sexes but **express in one sex only.**	These are those **autosomal genes** which are influenced by the sex of the bearer. These traits appear **more frequently in one sex** than in the other.	These are **Y-linked traits** those inherit from **male to male only.**
2.	**Examples:** (i) Milk glands in female (ii) Beard in man (iii) Deep male voice (iv) Antlers in male deer (v) Brilliant plumage in peacock (iv) Female or male musculature	(i) Pattern baldness (affected by male sex hormone/testosterone) (ii) Short index finger in male	(i) Porcupine skin (ii) TDF (Testes determining factor) (iii) Hypertrichosis

Inheritance of colourblindness

PARENTS				OFFSPRINGS			
Female		Male		Daughters		Sons	
Genotype	**Phenotype**	**Geno-type**	**Pheno-type**	**Geno-type**	**Pheno-type**	**Geno-type**	**Pheno-type**
XX	Normal	X^cY	Colourblind	XX^c	Carrier	XY	Normal
XX^c	Carrier	XY	Normal	(i) XX (ii) XX^c	Normal Carrier	XY X^cY	Normal Colourblind
XX^c	Carrier	X^cY	Colourblind	(i) XX^c (ii) X^cX^c	Carrier Colourblind	XY X^cY	Normal Colourblind
X^cX^c	Colourblind	XY	Normal	X^cX	Carrier	X^cY	Colourblind

The above results could easily be explained with the assumption that colour vision is sex linked character and its gene is present on X-chromosome, Y-chromosome lacks its allele. Always male receives its X-chromosome from mother (through ovum) and Y-chromosome from father (through sperm), whereas the female receives one X-chromosome from each parent (through ovum and sperm). From the above result following conclusions may be drawn.

(1) Colour blindness is more common in males than in females.

(2) Two recessive genes are needed for the expression of colour blindness in female, whereas only one gene gains expression in male.

(3) Males are never carriers.

(4) Colour blind women always have colour blind fathers and always produce colour blind sons.

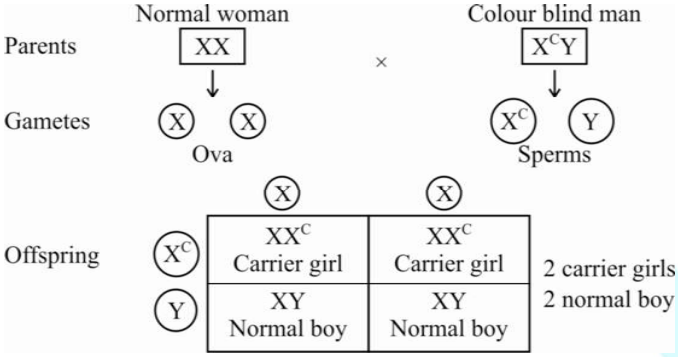
(5) Colourblind women produce colour blind daughters only when their husbands are colour blind.

(6) Women with normal colour vision, whose fathers are colour blind, produce normal and colour blind sons in approximately equal proportion.

- If a colour blind man (XcY) marries a girl with normal vision (XX), the daughters would have normal vision but would be carrier, while sons would also be normal

(shown in cross(a)).

Cross (a)



- If the carrier girl (heterozygous for colour blindness, X^CX) now marries a colour blind man X^CY, the offspring would show 50% females and 50% males
- Of the females, 50% would be carrier for colour blindness and the rest 50% would be colour blind.
- Of the males, 50% would have normal vision and the 50% would be colour blind **(shown in cross** (b).

Cross (b)

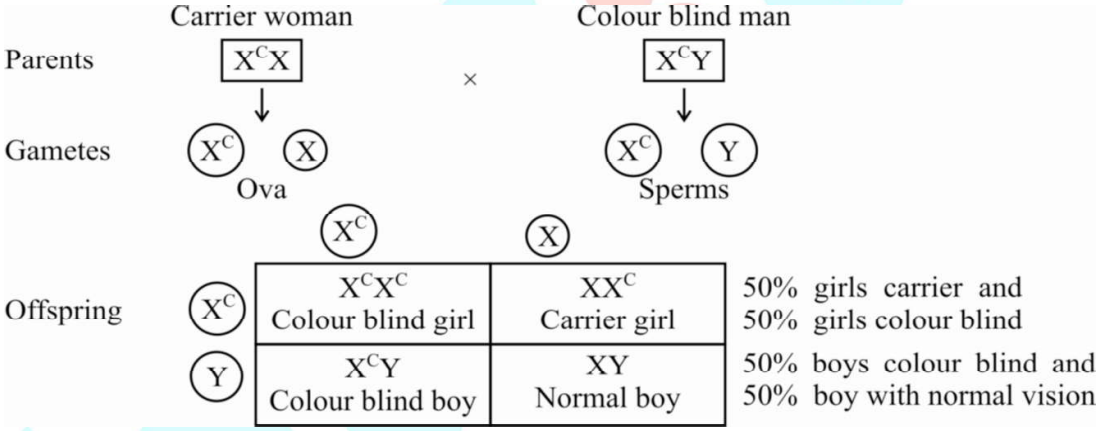


Fig. : Sex-linked inheritance of colour blindness -cross (a) and cross (b)

(ii) **Haemophilia :** In haemophilia the blood fails to clot when exposed to air and even a small skin injury results in continuous bleeding and can lead to death from loss of blood.

It is also called bleeder's disease, first studied by **John Cotto** in 1803. The most famous pedigree of haemophilia was discovered by **Haldane** in the royal families of Europe. The pedigree started from Queen Victoria in the last century. In a patient of haemophilia blood is deficient due to lack necessary substrate, thromboplastin. It is of two types.

(a) **Haemophilia-A :** Characterized by lack of antihaemophilic globulin (Factor VIII). About four-fifths of the cases of haemophilia are of this type.

(b) **Haemophilia-B :** 'Christmas disease' (after the family in which it was first described in detail) results from a defect in Plasma Thromboplastic Component (PTC or Factor IX).

Like colour blindness, haemophilia is a well known disorder which is sex-linked recessive condition. The recessive X-linked gene for haemophilia shows characteristic Criss-cross inheritance like the gene for colour blindness. Its single gene in man results in disease haemophilia, whereas a woman needs two such genes for the same.

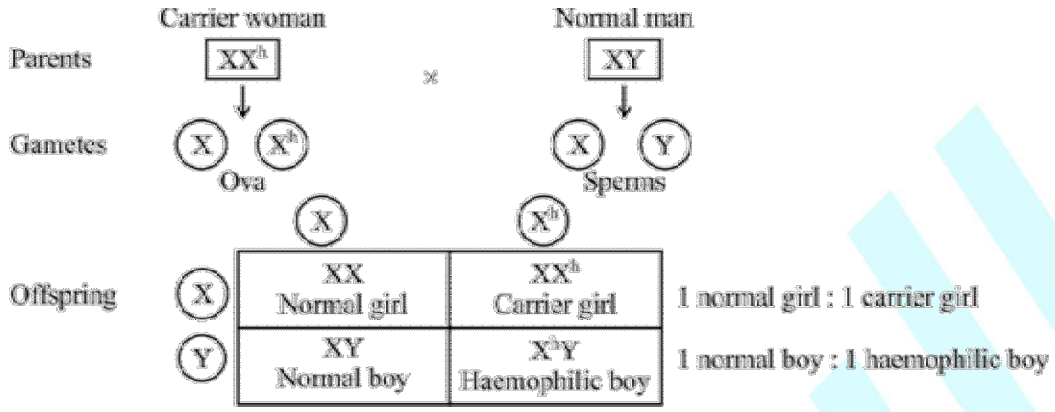


Fig.: Inheritance of haemophilia when the mother is carrier and the father is normal

- If a normal man marries a girl who is carrier for haemophilia, the progeny would consist of 50% females and 50% males.
- Of the females, 50% would be normal and the rest 50% would be hemophilia carrier.
- Of the males, 50% would be normal and the rest would be haemophiliacs
- **Haemophilia**-B (christmas disease) -plasma thromboplastin is absent, Inheritance is just like Haemophilia A.
- Red-green colour blindness and haemophilia are both examples of X-linked recessive conditions
- Consequently, they are both far more common in males than in females (males cannot mask the trait as a carrier)
- When assigning alleles for a sex-linked trait, the convention is to write the allele as a superscript to the sex chromosome (X)
- *Haemophilia:* $\mathbf{X^H}$ = unaffected (normal blood clotting) ; $\mathbf{X^h}$ = affected (haemophilia)
- *Colour blindness:* $\mathbf{X^A}$ = unaffected (normal vision) ; $\mathbf{X^a}$ = affected (colour blindness)

(iii) **Defective enamel :** It is a dominant X-linked trait and is inherited through a dominant X-linked gene. As X-chromosome is present in both man and woman, it is expressed in both the sexes. However, such persons have defective enamel on teeth like grey or brown unlike pure white enamel in a normal man.

Another example of dominant X-linked gene is the dimpled cheeks. Dimple may occur on one or both the cheeks.

(b) Holandric or Y-linked traits : Genes for these characters are located on non-homologous segment of Y chromosome. Alleles of these genes do not occur on X chromosome. Such characters are inherited straight from father to son or male to male *e.g.* hypertrichosis of ears in man.

Hypertrichosis of ears : This is a condition in which excessive amount of large hair grow on the pinna in man. It is sex-linked trait controlled by a gene present on the non-homologous segment of the Y-chromosome. Hence its inheritrance is called **holandric inheritance** and it appears only in man. It passes directly from father to son.

(c) XY-linked inheritance : The genes which occur in homologous sections of X and Y-chromosomes are called XY-linked genes and they have inheritance like the autosomal genes. Example of XY-linked genes are those of the inheritance of following

(1) **Xeroderma pigmentosa**, a skin disease characterized by the pigment patches and cancerous growth on the body.

(2) **Nephritis**, a kidney disease.

(d) Sex-influenced traits : The autosomal traits in which the dominant expression depends on the sex hormones of the individual are called sex-influenced traits. These traits differ from the sex limited traits which are expressed in only one sex. It has following examples.

(1) **Baldness in man :** Baldness in humans is the best example of sex-influenced traits. This trait is due to a single mutant gene but the expression of the heterozygous is different in man and woman. This is a hereditary character controlled by sex-influenced gene which is dominant in men and recessive in women. The difference in expressions may be caused by varying amounts of male and female sex hormones. If autosome dominant gene 'B' is regarded to inherit the baldness, the homozygous (BB) dominant condition will cause baldness in man as well as women. This gene for baldness acts recessively in woman when present in heterozygous (Bb) condition, the baldness develops in males only because under such condition the phenotype expression (baldness) is influenced by androgen hormone secreted by man. A heterozygous female is normal. A homozygous recessive condition (bb) does not allow baldness to develop either in male or female.

Phenotypic expression of genotype for baldness

Genotype	Phenotype	
	Men	Women
B/B	Bald	Bald
B/b	Bald	Non-bald
b/b	Non-bald	Non-bald

The different phenotypes in men and women shown in above table are sex-influenced characters and also called sex-controlled traits.

The progeny that would be obtained from the marriage of heterozygous (B/b) man and woman for baldness have been shown below.

Progeny resulting from the marriage of bald men and non-bald women both heterozygous

P_1 Male gametes Female gametes	Women (B/b) (non-bald) B and b	Man (B/b) Bald B and b
	B	b
B	B/B bald male Bald female	B/b bald male Non-bald female
b	B/b bald male Non-bald female	b/b non-bald male Non-bald female

(2) **Length of index finger :** It is another example of sex-influenced trait in man. It is controlled by a gene which is dominant in male and recessive in the female. When the hand is placed on white board the tip of the fourth finger or ring finger just touches a horizontal line, it is seen that index or second finger does not reach this line in many cases. In some persons index finger extends beyond this horizontal line as shown in figure. The short index finger is inherited as a dominant trait in men and as a recessive condition in women.

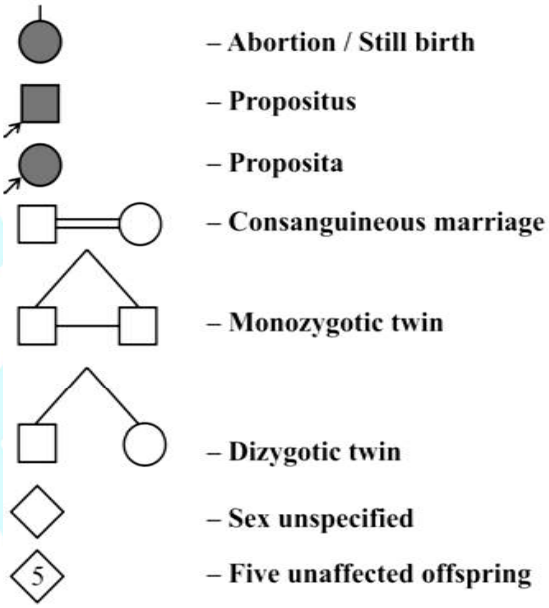
(e) Sex limited traits : Traits or characters which develop only in one sex are called sex-limited characters. They are produced and controlled by the genes which may be located on autosomes in only one sex. Such genes are responsible for secondary sexual characters as well as primary sexual characters. They are inherited according to Mendel's laws.

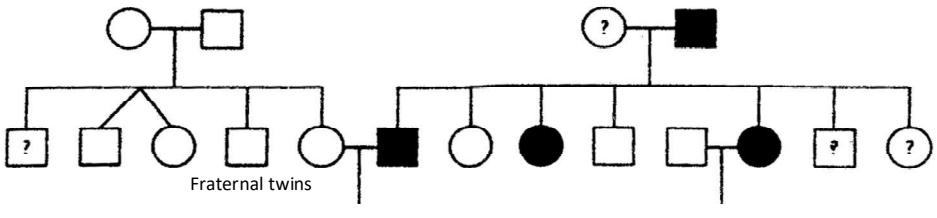
Sex-limited traits in man : Beard is produced by sex-limited genes in man, which does not develop in woman. Breast development is normally limited to woman. In case of abnormalities of hormonal secretions facial hair may develop in woman and a faminine breast development may occur in man. It means that expression of sex-limited characteristics in vertebrates depend upon the secretion of sex hormones. For example genes for deep masculine voice, masculine body, masculature in man will express themselves only in the presence of male hormone. Genes for faminine voice and faminine musculature on the other hand express themselves in the absence of male hormone and will not require the secretion of female hormone. Similarly, breast development in woman requires the presence of female hormone rather than mere absence of the male hormone. It can be concluded that certain sex-limited characteristics are expressed in the absence of certain hormones and other express only in the presence of sex-hormones.

14 PEDIGREE ANALYSIS

Inheritance of hundreds of characteristics such as polydactyly, haemophilia, colour blindness, attached ear lobes and tongue rolling, generation after generation in particular families of man have been studied. In order to conduct such study, a standard method has been used to represent the family pedigree in a concise, easily understood form so that one can visualize the entire pedigree (family history) at a glance of the chart.

Pedigree chart and symbols : It is customary to represent men by squares and women by circles in a chart for study of pedigree analysis. Marriage is indicated by a connecting horizontal line and the children by attachment to a vertical line extending downward from the horizontal line. Individuals having particular characters to be studied are denoted by solid squares or circles while those not having them are indicated by outlines only. Twins are denoted by bifurcating vertical lines.





In such a pedigree analysis a person who is the beginner of the family history is called proband. It is called propositus, if male and poposita, if female. The children of such parents are known as sibs or siblings. So a family is constituted by such parents and their siblings. Sometimes, a very large family is formed as a result of interconnected marriages. Such a circle of large persons interconnected is called Kindred.

In order to study pedigree analysis we have taken some of the important case histories as follows :

(a) **Polydactyly :** The pedigree of this trait has become standard usage among the geneticists and it helps us to understand the process of transmission of this trait.

This inheritable trait was discovered when a woman brought her young daughter to a doctor for examination as she had an extra finger on one hand and an extra toe on one foot.

On investigation it was found that child's father had this characters (though his extra finger had been removed surgically) and that her brother also had the character. The other two children of this family had normal number of fingers and toes. This type of inheritance is typical of characters which are known as dominant.

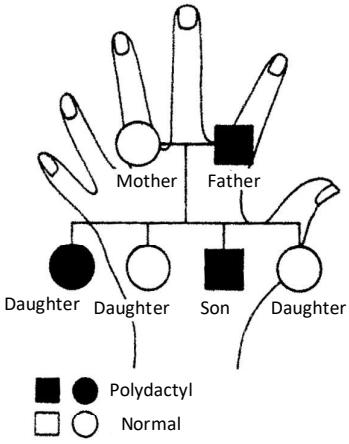


Fig : Pedigree of polydactyly

(b) **Attached ear lobes :** This is a recessive type of inheritance and is inherited in a different way.

(1) Two parents with free ear lobes produced two children with attached ear lobe in a family of five children.

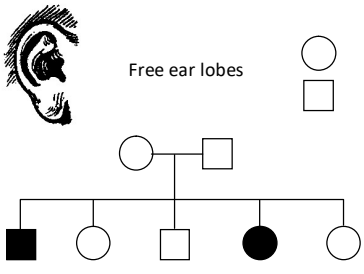


Fig : Pedigree of free ear lobes

(2) In another family both parents had attached ear lobes but all the four of their children had this trait of attached ear lobes.

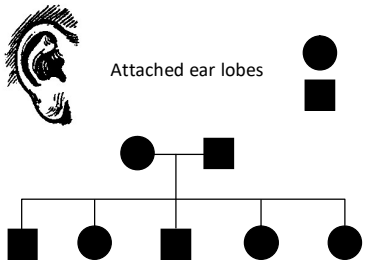


Fig : Pedigree of attached ear lobes

(c) **Tongue rolling :** Some persons are capable of rolling their tongue while others are not gifted with this power. A couple both of whom are tongue roller have two out of these children as tongue rollers.

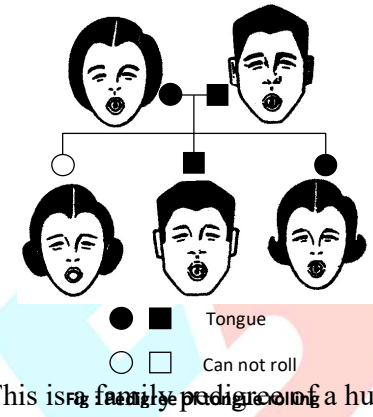


Fig : Pedigree of tongue rolling

(d) **Crooked little fingers :** This is a family pedigree of a human family where crooked little fingers are inherited through a simple dominant gene. In this pedigree a woman had two sons one of which had crooked little finger. Her husband also had same type of defective fingers. On further survey of her husbands, family it was found that her husband's sister and mother both had crooked little fingers, as well as his grandfather also possesses this trait. The characteristic also appeared in more distant relatives.

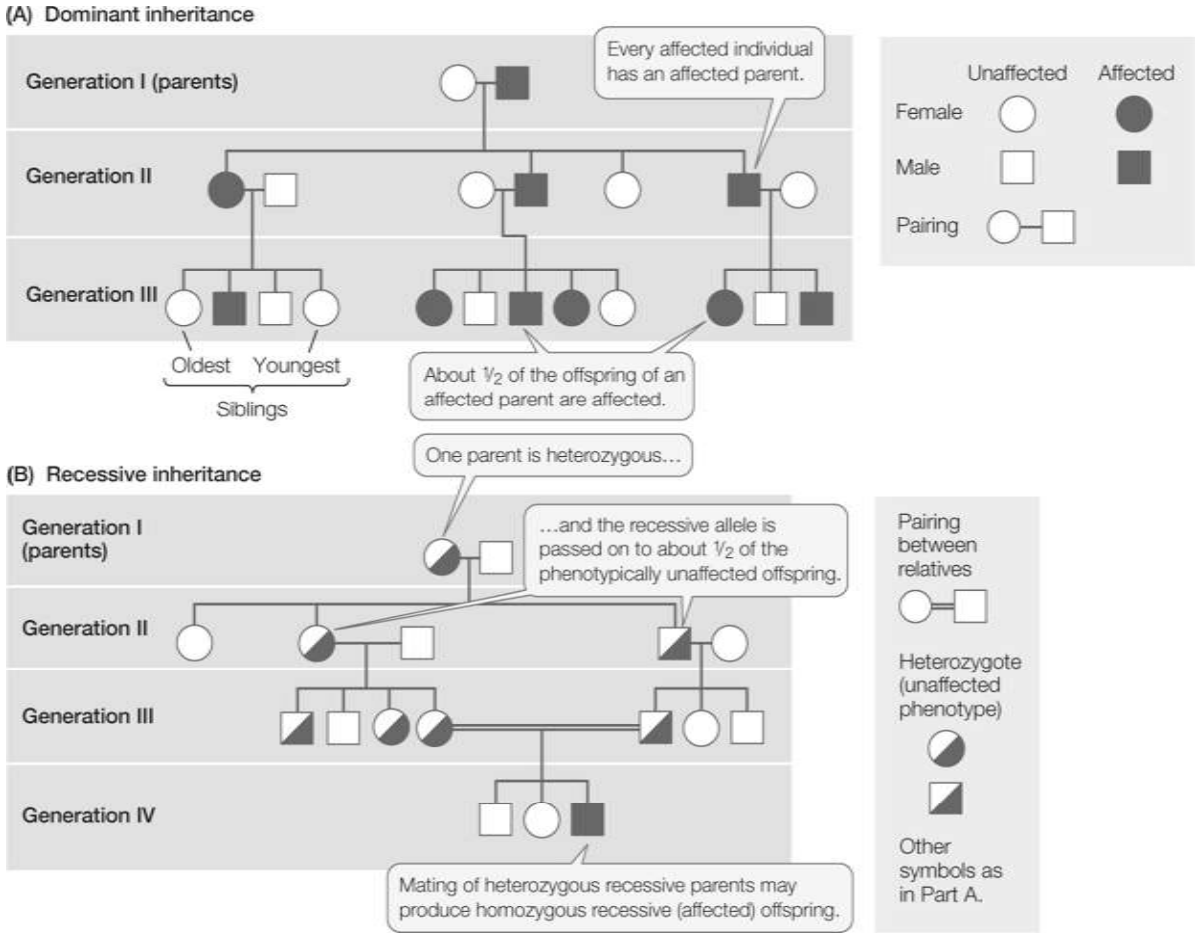


Fig: Pedigree Analysis and Inheritance (A) This pedigree represents a family affected by Huntington's disease, which results from a rare dominant allele. Everyone who inherits this allele is potentially affected. (B) The family in this pedigree carries the allele for albinism, a recessive trait. Because the trait is recessive, heterozygotes do not have the albino phenotype, but they can pass the allele on to their offspring. Affected persons must inherit the allele from two heterozygous parents, or (rarely) from one homozygous recessive and one heterozygous parent, or (very rarely) two homozygous recessive parents. In this family, the heterozygous parents in generation III are cousins, however, the same result would occur if the parents were unrelated

15 TWINS

Twins : Two birth occurring at the same time in human are called twins, they are of peculiar genetic interest. The hereditary basis of a number of human traits has been established by the study of twins. There are 3 kinds of twins.

(i) Identical or monozygotic twins : Identical twins are formed when one sperm fertilizes one egg to form a single zygote. As a result of separation of two daughter cells or blastomeres after the first cleavage, each of the cell develops into a separate individual. Such individuals are called **identical twins**. Since they develop from a single zygote, they are called **monozygotic twins**. They have the same genotype and phenotype and are of same sex. Differences if any, may be due to different environmental conditions.

***(ii) Siamese twins or conjoint twins* :** Like monozygotic twins, siamese twins also originate from one zygote but the daughter cells formed as a result of first cleavage fail to separate completely and they remain joined at some point. They grow into two individuals joined together. Thus the two individuals called **conjoint twins** remain attached at one or more parts of the body. They were first studied in the country Siam, hence called Siamese twins. Siamese twins

usually do not survive after birth although a few cases of their survival are well known. They are always of the same sex, same genotype and phenotype.

(iii) Fraternal twins : They are dizygotic twins formed from the two eggs fertilized by two sperms separately but at the same time. They may be both males, both females or one male and one female. They may have different genotypic constitution and different phenotype. Thus fraternal twins develop in same environment with different constitution but are the members of same age. They resemble each other just like any two brothers and sisters. Although they may be of same sex but due to different hereditary traits, they may carry congenital variations. Among the twins fraternal twins are most common and Siamese twins are most rare.

16 EUGENICS, EUTHENICS AND EUPHENICS

(i) Eugenics : The term eugenics (Gr. Eugenes, well born) was coined by British scientist **Sir Francis Galton** in 1883. Galton is called 'Father of eugenics' as this branch has been started by him.

Eugenics is the branch of science which deals with improvement of human race genetically. This aspect of human betterment aims to improve the human germplasm by encouraging the inheritance of best characteristics so that defective characters may be eliminated. Eugenics attempts to attain its objective bilaterally by suggesting a number of 'do's and 'don'ts' to improve the human gene pool. The 'don'ts' are meant to check inheritance of the poor or undesirable germplasm, while the do's aim at perpetuating desirable germplasm to be inherited. By this method aim of improvement of human race may be achieved by two ways :

(a) **Positive eugenics :** In this approach of eugenics the future generations are improved by encouraging the inheritance of better traits. Following methods may be adopted to achieve this.

(1) **Planned marriages :** The selection of mate for marriage should be made on the basis of better traits rather than on the basis of dowry, caste or religion etc. will give rise to the progeny with better traits.

(2) **Perevention of loss of good germplasm :** Many intelligent, specialists, educationists and politicians with better traits should be encouraged getting marriage at early stage and practice polygamy may contribute for more and more utilization of good germplasm.

(3) **Medical engineering :** To destroy the unwanted germplasm or such genes before their expression **Liederberg** (1963) put forth a novel idea of medical engineering.

(4) **Germinal choice or eutelegenesis :** In human beings artificial fertilization or insemination is a biological process. **Muller** (1963) put forward the idea of production of children of high mental qualities and good traits by artificial fertilization of a woman of high quality traits with the sperms of desired best man.

(5) **Genetic counselling :** Production of healthy progeny should be the endeavour of man to ensure a better future for humanity. Genetic counselling can make a significant contribution in this direction. It can provide much needed relief for families with history of genetic diseases. Genetic counselling is even useful after marriage. A Rh^- woman with Rh^+ partner when aware of the implications in the second child, can go for suitable medical aid well in advance.

(b) **Negative eugenics :** This is a negative aspect of improving mankind by restricting the transmission of poor and defective germplasm. This restriction can be brought about in the following ways.

(1) **Segregation :** Persons with serious abnormal hereditary defects like feeble mindedness, epilepsy, leucoderma, criminals, immorals and stupid people, should be isolated *i.e.* should not be permitted to mingle and marry with normal, intelligent persons.

(2) **Restriction on blood marriages :** Marriage between close relative like cousins tend to bring together the recessive alleles in homozygous condition and can be expressed in haemophilia, albinism and colour blindness.

(3) **Sterilization :** The most effective method to stop the persons with defective germplasm to produce offsprings is the sterilization. This prevents the transmission of undesirable traits in man and woman by vasectomy and tubectomy respectively.

(ii) Euthenics : Euthenics is the improvement of human race by improving the environmental conditions, *i.e.*, by subjecting them to better nutrition better unpolluted ecological conditions, better education and sufficient amount of medical facilities.

(a) **Better education :** Education is one of the surest agents which can provide better humanity. The conditions of surroundings *i.e.* the immediate environment of an individual has a great bearing upon personality of the person. The society which an individual chooses determines to some extent, his character. Medical facilities are largely responsible for maintenance of sound health. Employment conditions determine the degree of fulfillment of the individual's basic requirements and hence it influences his entire outlook. Euthenics attempts to provide the best of education, the healthiest of surroundings, the finest of societies, full medical facilities and rewarding employment conditions.

(b) **Subsidization of superior students :** Euthenics requires that a best student be selected and be provided opportunities for his multifaceted development. Students of no definite class and group may be equally intelligent. A few are most intelligent, some are average, still others are below average and some are dull or feeble minded or idiots. A definite scale to measure the mental ability has been prescribed which is known as intelligence quotient.

Intelligence quotient (IQ) : The ratio between actual (chronological) age and mental age multiplied with 100 is known as I.Q. Intelligence quotient is the mental competence in relation to chronological age in man. It can be denoted by following formula.

$$\text{I.Q.} = \frac{\text{Mental age}}{\text{Actual age}} \times 100$$

By applying this formula we can easily calculate the IQ, such as if a 10 year child has mental age 14, his IQ will be

$$\text{I.Q.} = \frac{14}{10} \times 100 = 140$$

On the basis of different levels of I.Q. persons are classified as follows.

S. No.	I.Q.	Person
(1)	0 – 24	Idiot
(2)	25 – 49	Imbecile
(3)	50 – 69	Moron
(4)	70 – 79	Dull
(5)	80 – 89	Ordinary
(6)	90 – 109	Average
(7)	110 – 119	Superior
(8)	120 – 139	Most superior
(9)	140 or more	Genius

(iii) Euphenics : The study of born defectives and their treatment is called euphenics. The term euphenics was given by **A.C. Pai** (1974) for symptomatic treatment of human genetic disease especially in born errors of metabolism. Following methods can be employed as euphenic measures.

(a) **Amniocentesis :** It is a test to detect genetic diseases as well as the sex of embryo during development in mother's womb. Amniotic fluid is tested and if embryo has genetic disease the embryo can be aborted.

(b) **Infusion of missing enzyme :** Genetic physiological diseases occur due to lack of particular enzymes. Infusion of such missing enzyme may help in treatment of such disease.

(c) **Genetic engineering :** Treatment of the gene controlling genetic disease by genetic surgery and genetic engineering is also helpful in euthenics.

17 GENETIC ENGINEERING

(I) RECOMBINANT DNA TECHNOLOGY

(a) **Definition :** Genetic engineering, a kind of biotechnology, is the latest branch in applied genetics dealing the alteration of the genetic make up of cells by deliberate and artificial means. Genetic engineering involves transfer or replacement of genes, so also known as recombination DNA technology or gene splicing.

(b) **Tools of genetic engineering :** Two enzymes used in genetic engineering are restriction endonuclease and ligases. R.E. is used to cut the plasmid as well as the foreign DNA molecules of specific points while ligase is used to seal gaps or to join bits of DNA.

The ability to clone and sequence essentially any gene or other DNA sequence of interest from any species depends on a special class of enzymes called restriction endonucleases. Restriction endonucleases are also called as molecular scissors or 'chemical scalpels'. Restriction endonucleases cleave DNA molecules only at specific nucleotide sequence called restriction sites. The first restriction enzyme identified from a bacterial strain is designated I, the second II and so on, thus, restriction endonuclease EcoRI is produced by Escherichia coli strain RY 13. Restriction enzyme called EcoRI recognizes the sequence $\begin{matrix} G\downarrow A\,A\,T\,T\,C \\ C\,T\,T\,A\,A\uparrow G \end{matrix}$ and cleaves the DNA between G and A on both strands. Restriction nucleases make staggered cuts; that is, they cleave the two strands of a double helix at different joints and blunt ended fragments; that is, they cut both strands at same place.

Characteristics of some restriction endonucleases

Enzyme name	Pronunciation	Organism in which enzyme is found	Recognition sequence and position of cut
Bam HI	"bam-H-one"	*Bacillus amyloliquefaciens* H	5′ G↓GAT C C 3′ 3′ C CTAG↑ G 5′
Bgl II	"bagel-two"	*Bacillus globigi*	A↓G A T C T T C T A G↑A
Eco RI	"echo-R-one"	*E. coli* RY13	G↓ A A T T C C T T A A↑G
Hae II	"hay-two"	*Haemophilus aegyptius*	R G C G C↓Y Y↑C G C G R
Hind III	"hin-D-three"	*Haemophilus influenzae* Rd	A↓ A G C T T T T C G A↑ A
Pst I	"P-S-T-one"	*Providencia stuartii*	C T G C A↓G G↑ A C G T C

(c) **Steps of recombinant DNA technology**

(1) Isolating a useful DNA segment from the donor organism.

(2) Splicing it into a suitable vector under conditions to ensure that each vector receives no more than one DNA fragment.

(3) Producing of multiple copies of his recombinant DNA.

(4) Inserting this altered DNA into a recipient organism.

(5) Screening of the transformed cells.

(d) **Vectors :** Vector in genetic engineering is usually a DNA segment used as a carrier for transferring selected DNA into living cells. Which are as follows

(1) **Plasmid :** Plasmid are extrachromosomal, closed circular double stranded molecules of DNA present in most eukaryotes. All plasmid carry replicons pieces of DNA that have the genetic information required to replicate. Plasmid pBR 322 was one of the first widely used cloning vectors, it contain both ampicillin and tetracycline resistance genes.

(2) **Phage :** It is constructed from the phage λ chromosomes and acts as bacteriophage cloning vectors.

(3) **Cosmid :** The hybrids between plasmid and the phage λ chromosome give rise to cosmid vectors.

Beside all these there are artificial chromosomes like

BACs (Bacterial Artificial chromosomes)

YACs (Yeast Artificial chromosomes)

MACs (Mammalian Artificial chromosomes) are very efficient vectors for eukaryotic gene transfers.

(e) **Application of recombinant DNA technology :** The technique of recombinant DNA can be employed in the following ways.

(1) It can be used to elucidate molecular events in the biological process such as cellular differentiation and ageing. The same can be used for making gene maps with precision.

(2) In biochemical and pharmaceutical industry, by engineering genes, useful chemical compounds can be produced cheaply and efficiently which is shown in table.

Applications of recombinant DNA products

Medically useful recombinant products	Applications
Human insulin	Treatment of insulin-dependent diabetes
Human growth hormone	Replacement of missing hormone in short stature people
Calcitonin	Treatment of rickets
Blood clotting factor VIII/IX	Replacement of clotting factor missing in patients with Haemophilia A/B
Interferon	Treatment of pathogenic viral infections, cancer
Interleukins	Enhancement of action of immune system
Vaccines	Prevention of infectious diseases such as hepatitis B, herpes, influenza, pertussis, meningitis, etc.

(II) CLONING : Cloning is the process of producing many identical organisms or clones. In this process nucleus of ovum (n) is removed and replaced by nucleus of diploid cell of same organism. Now the egg with $2n$ nucleus is transferred to the uterus of mother to have normal pregnancy and delivers clone of itself.

Examples of organism cloning

(1) Cloning of sheep was done by **Dr. Ian Wilmut** (1995) of Roslin Institute, Edinberg U.K. and normal healthy lamb (DOLLY) was born in Feb, 1996. This lamb was exactly similar to her mother.

(2) The first cloned calves George and Charlie were born in January 1998.

(3) ANDI was the world's first genetically altered primate produced by inserting a jelly fish gene into the embryo of a rhesus monkey.

(4) Scientist at Scotland cloned POLLY and MOLLY. Unlike Dolly, polly and molly were transgenic (they carried human protein gene) polly and molly were born in july 1997.

(5) **Brigitte Boissliar**, a 46-year old french chemist announced the creation of the world's first cloned human boby nicknamed "Eve" (December 2002).

(III) POLYMERASE CHAIN REACTION (PCR) : It was developed by **Kary Mullis** in 1983 and won Nobel prize in 1993. PCR is a method for amplifying a specific piece of DNA molecule without the requirement for time-consuming cloning procedure. This process require Target DNA, a heat stable DNA polymerase, which work at optimum temperature of 70°C usually Taq DNA and four types of nucleotides with small single stranded strands of DNA of about 20 nucleotide called primers, produce multiple copy of desired DNA.

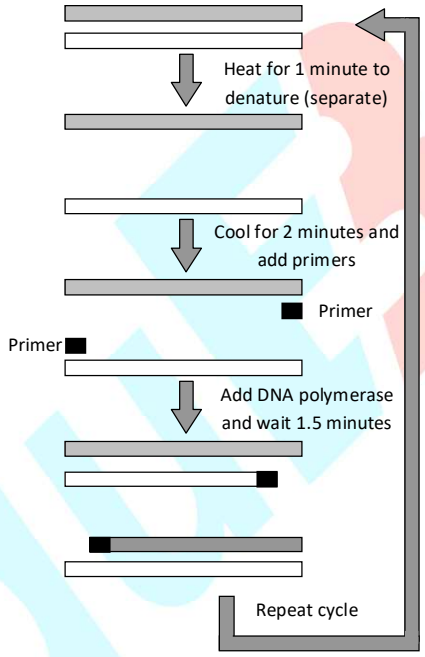


Fig : DNA amplification by PCR

(IV) GENE LIBRARIES AND GENE BANKS

(a) **Gene libraries :** A gene library is a collection of gene clones that contains all the DNA present in some source. If the original source of the DNA was original DNA from a living organism, then the library seek to include clones of all that DNA, it is called a genomic gene library. Gene libraries can also be created by using RNA.

(b) **cDNA :** If a gene library is created by enzymatic copying of RNA by reverse transcriptase (RNA-dependent DNA polymerase), it would be called c-DNA library. c-DNA stands for complimentary DNA or copy DNA. c-DNA is made to use PCR to amplify an RNA. PCR does not work on RNA, so one can copy it to DNA using reverse transcriptase and then PCR amplify the c-DNA; this is called RT-PCR (reverse transcriptase PCR).

(c) **Gene bank :** A gene bank is repository of clones of known DNA fragments, genes, gene maps, seeds, spores, frozen sperms or eggs or embryos. These are stored for possible use in genetic engineering and breeding experiment where species have become extinct.

(V) DNA FINGER PRINTING :

Alec Jeffreys et al (1985) developed the procedure of genetic analysis and forensic medicine, called DNA finger printing. It is individual specific DNA identification which is made possible by the finding that no two people are likely to have the same number of copies of repetitive DNA sequences of the regions. It is also known as DNA profiling. The chromosomes of every human cell contain scattered through their DNA short, highly repeated 15 nucleotide segments called "mini-satellites" or variable-number Tandem Repeat (VNTR).

(a) **Technique for DNA fingerprinting**

- Only a small amount tissues like blood or semen or skin cells or the hair root follicle is needed for DNA fingerprinting.
- Typically DNA content of about 100,000 cells or about 1 microgram is sufficient.
- The procedure of DNA fingerprinting involves the following major steps :

(i) DNA is isolated from the cells in a high-speed refrigerated centrifuge.

(ii) If the sample of DNA is very small, DNA can be amplified by Polymerase Chain Reaction (PCR).

(iii) DNA is then cut up into fragments of different length using restriction enzymes.

(iv) The fragments are separated according to size using gel electrophoresis through an agarose gel. The smaller fragments move faster down the gel than the larger ones.

(v) Double stranded DNA is then split into single stranded DNA using alkaline chemicals.

(vi) These separated DNA sequences are transferred to a nylon or nitrocellulose sheet placed over the gel. This is called 'Southern Blotting' (after **Edward Southern**, who first developed this method in 1975).

(vii) The nylon sheet is then immersed in a bath and probes or makers that are radioactive synthetic DNA segments of known sequences are added. The probes target a specific nucleotide sequence which is complementary to VNTR sequences and hybridizes them.

(viii) Finally, X-ray film is exposed to the nylon sheet containing radioactive probes. Dark bands develop at the probe sites which resemble the bar codes used by grocery store scanners to identify items.

(b) **Applications of DNA fingerprinting**

This technique is now used to :

(i) Identify criminals in forensic laboratories.

(ii) Settle paternity disputes.

(iii) Verify whether a hopeful immigrant is, as he or she claims, really a close relative of already an established resident.

(iv) Identify racial groups to rewrite biological evolution.

(VI) GENE THERAPY :

The use of bioengineered cells or other biotechnology techniques to treat human genetic disorders is known as gene therapy. Gene therapy is the transfer of normal genes into body cells to correct a genetic defect. It can be used to treat genetic diseases like sickle-cell anaemia and Severe Combined Immuno Deficiency (SCID). It (SCID) is caused by a defect in the gene for the enzyme adenosine deaminase (ADA). SCID patients have no functioning T lymphocytes and one treated with the injections of their white blood cells that have been engineered to carry the normal ADA alleles.

(VII) TRANSGENICS :

A gene that has been introduced into a cell or organism is called a transgene (for transferred gene) to distinguish it from endogenous genes. The animal carrying the introduced foreign gene is said to be transgenic animal and the possessor called Genetically Modified Organisms (GMOs). Most of the transgenic animals studied to date were produced by

microinjection of DNA into fertilized eggs. Prior to microinjection, the eggs are surgically removed from female parent and fertilized *in vitro* then DNA is microinjected into the male pronucleus of the fertilized egg through a very fine-tipped glass needle. The integration of injected DNA molecules appears to occur at random sites in the genome.

The first transgenic animal produced was the 'supermouse' by the incorporation of the gene for human growth hormone by **Richard Palmiter** and **Ralph Brinster** in 1981.

(VIII) GENOMICS AND HUMAN GENOME PROJECT :

The term genome has been introduced by **Winkler** in 1920 and the genomics is relatively new, coined by **Thomas Rodericks** in 1986. Genomics is the subdiscipline of genetics devoted to the mapping, sequencing and functional analysis of genomes. Genomics is subdivided into following types:

(a) **Structural genomics :** It is the study of genome structure deals with the complete nucleotide sequences of the organisms.

(b) **Functional genomics :** It is the study of genome function which includes transcriptome and proteome. Transcriptome is a complete set of RNAs transcribed from a genome while proteome is a complete set of proteins encoded by a genome and aims the determination of the structure and function of all the proteins in living organisms. The human genome project, sometimes called "biology's moon shot", was launched on october 1, 1990 for sequencing the entire human genome of 2.75 billion (2.75×10^9 or 2750000 bp or 2750000 kilobase pairs or 2750 megabase pairs) nucleotide pairs.

Two important scientist associated with human genome are **Francis Collins**, director of the Human Genome Project and **J. Craig Venter**, founding president of Celera genomics. The complete sequencing of the first human chromosome, small chromosome 22, was published in December 1999.

Genome of Model organisms

S. No.	Organism	No. of base pair	No. of genes
(1)	Bacteriophage	10 thousand	–
(2)	E. coli	4.7 million	4000
(3)	*Saccharomyces cerevisiae*	12 million	6000

Prospects and implications of human genome :

(1) The genome project is being compared to the discovery of antibiotics.

(2) Efforts are in progress to determine genes that will revert cancerous cells to normal.

(3) The human genome sequencing not only holds promise for a healthier living. It also holds the prospects of vast database of knowledge about designer drugs, genetically modified diets and finally our genetic identity.

18 MENDELIAN DISORDERS

Sickle-Cell Anaemia

- It is an **autosomal recessive disorder.** In this disorder, the RBCs become sickle shaped under low O_2 concentration.
- The affected persons die young.
- Other heterozygous for this trait are having normal phenotype and long lived.
- The disease is due to base substitution of sixth codon in the gene coding for chain of haemoglobin.
- The middle base of a DNA triplet coding for the amino acid **glutamic acid** is mutated so that the triplet now codes for valine instead.

The mutant haemoglobin molecule undergoes polymerisation under low O_2 tension causing the change in the shape of RBC from biconcave disc to elongated sickle like structure

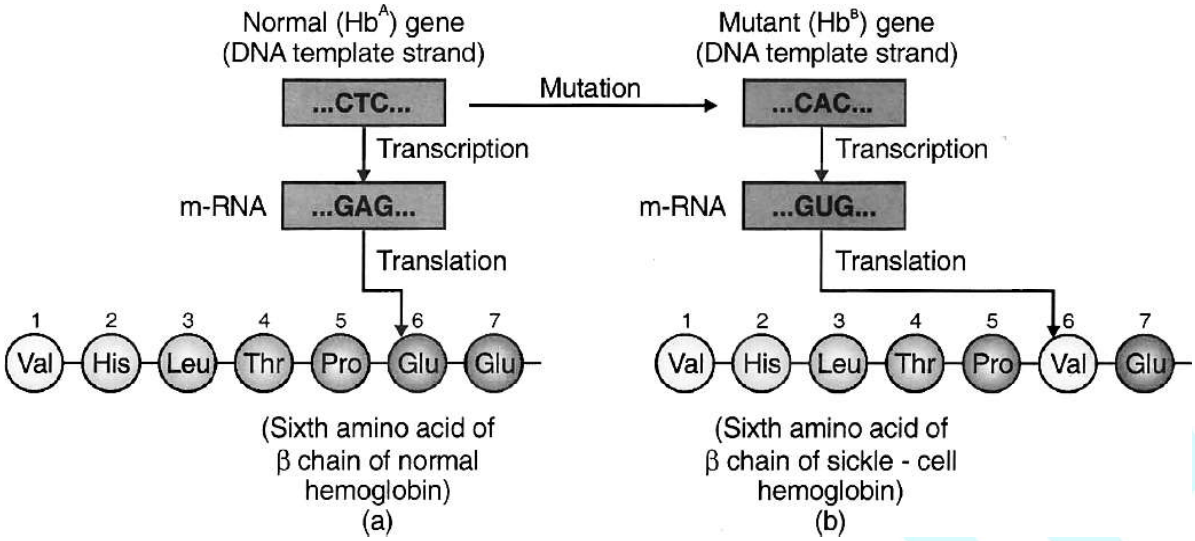


Fig.: Amino acid composition of the relevant portion of l3-chain haemoglobin: (a) from a normal individual; (b) from an individual with sickle-cell anaemia.

Phenylketonuria

Recessive autosomal disorder (Chromosome 12) related to **phenylalanine metabolism** to tyrosine. This disorder is due to absence of a liver enzyme called **phenylalanine hydroxylase.** Due to lack of this enzyme, phenylalanine follows another pathway and gets converted into phenylpyruvic acid. This phenyl pyruvic acid upon accumulation in joints causes arthritis and if it hits the brain, then it causes mental retardation known as **phenyl pyruvic idiocy.** These are also excreted through urine because of poor absorption by kidney.

Cystic Fibrosis

It is an **autosomal recessive disorder** common among Caucasian Northern Europeans. Persons suffering from this disease are having extremely salty sweat. It is due to decreased Na^+ and Cl^- reabsorption in the ducts. Disease is due to a gene present on chromosome 7. Due to a defective glycoprotein, thick mucus develops in pancreas and lungs and formation of fibrous cyst occurs in pancreas.

Huntington's Chorea

It is an **autosomal dominant disorder.** The gene responsible for this disorder is present on chromosome 4. Disease is characterised by gradual degradation of brain tissue in the middle age and consequent shrinkage of brain.

Myotonic dystrophy is due to a dominant autosomal mutant gene located on the long arm of chromosome 19. Mild myotonia -atrophy and weakness of the musculature of the face and extremities, is most common.

Other Mendelian disorders :

(i) Alkaptonuria (Garrod, 1908)	- Due to deficiency of oxidase enzyme.
(ii) Albinism (Chromosome 11)	- Absence of tyrosinase
(iii) Tay-Sach's disease (Chromosome 15)	- Absence of hexosaminidase B.
(iv) Gaucher's disease (Chromosomes 1) glucocerebrosidase	- Due to the inhibition of enzyme action which leads to accumulation of cerebroside.

Other abnormalities due to autosomal dominant gene mutation

(i) Polydactyly - Presence of extra fingers and toes
(ii) Brachydactyly - Abnormal short fingers and toes

Abnormalities due to sex linked (X-linked) recessive gene mutation

(i) Haemophilia A - Due to lack of antihaemophilic-globulin.
Haemophilia B - Due to lack of plasma thromboplastin
(ii) Red-green colour blindness - Daltonism
Protanopia - Red colour blindness
Tritanopia - Blue colour blindness
Deuteranopia - Green colour blindness
(iii) Muscular dystrophy - Due to non-synthesis of protein

CHROMOSOMAL DISORDERS

A. *Autosomal abnormalities (Due to mutation in body chromosome)*

(i) Down's Syndrome -It occurs due to trisomy of 21^{st} chromosome. The affected individual is short statured with small round head, furrowed tongue and partially open mouth. Palm is broad with characteristic palm crease and mental retardation. Physical and psychomotor development is retarded.
(ii) Edward's syndrome - Trisomy of 18^{th} chromosome
(iii) Patau's syndrome - Trisomy of 13^{th} chromosome
(iv) Cri du chat syndrome - Due to deletion in short arm of 5^{th} chromosome.

B. Allosomal or Sex Chromosomal Disorder

(i) Klinefelter's Syndrome - It occurs due to the trisomy of X-chromosome in male, resulting into a karyotype of 47, (44 + XXY). Individuals have long legs, sparse body hair, small prostrate gland, small testes, reduced mental intelligence and enlarged breasts (Gynaecomastia). Such individuals are sterile.
(ii) Turner's Syndrome - It is caused due to absence of one of the X-chromosome in female *i.e.* 45 with chromosome complement 44 + XO. Such females are sterile with undeveloped breast, short stature, reduced ovaries & absence of menstrual cycle.
(iii) Super female -AA + XXX, AA + XXXX
(iv) Jacob's syndrome or Super male syndrome. -AA + XYY, also called as criminal

Representative Recessive and Dominant Human Traits	
Recessive Traits	**Dominant Traits**
Albinism	Achondroplasia