B.Sc. ZOOLOGY
SEMESTER V
CORE PAPER V - GENETICS

UNIT I

Introduction – Mendalism – Gene interaction (Complementary genes, Lethal genes and Epitasis. **Multiple alleles -** Blood group in man and Coat colour in Rabbit.

UNIT II

Linkage and crossing over –Types, theories and significance – Chromosomal Map.
Sex linked inheritance (Haemophilia, Colour blindness and Drosophila eye colour). Sex limited and sex
influenced genes.

UNIT III

Sex determination in man and Drosophila, Chromosomal Theory and Gynandromophs
Mutations: Types, Chromosomal aberrations, Aneuploidy and Euploidy.

UNIT IV

Inbreeding and out breeding – significance, merits and demerits.
Syndromes (Down syndrome and Turners syndrome, Twins in man).

UNIT V

Human genome project – Pedigree analysis - Gene structure and functions – Genetic Engineering Recombinant DNA technology.

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MULTIPLE ALLELES

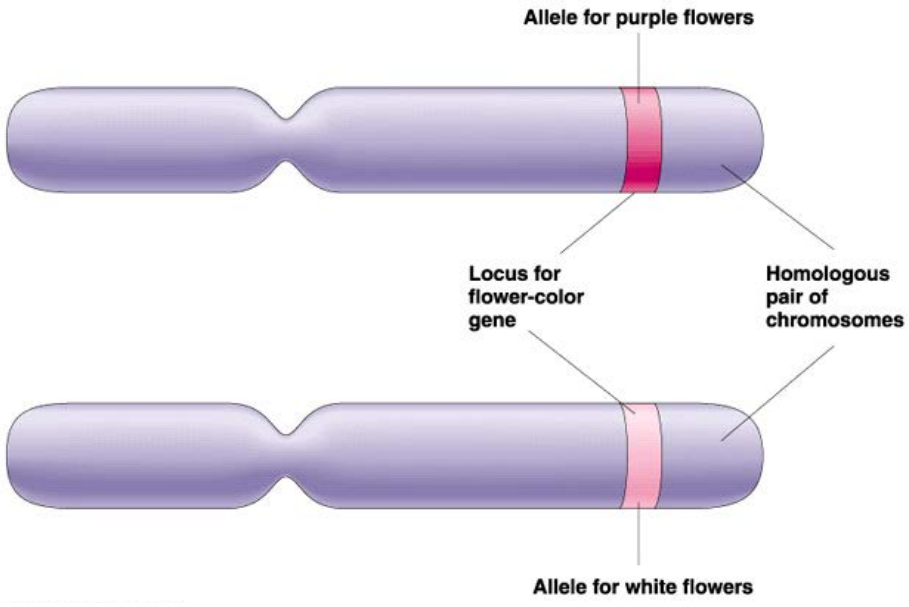
Allele is a shorter term than allelomorph (another form) is the alternate form of gene. Many genes have two alternate forms but several other have more than two alternate forms. More than two alleles at the same locus give rise to a multiple allelic series. Multiple alleles can be defined as a series of forms of a gene situated at the same locus of homologous chromosomes. According to Mendel, each gene had two alternate forms or allele morphs are being dominant and the other being recessive. Dominant being the wild type from which recessive mutant was evolved through mutation. Likewise, a wild type can mutate in many ways and produce many mutant forms and a mutant can again undergo another mutation and give rise to a new mutant. Hence, a gene can exist in more than two allelomorphs. Usually wild type allele is dominant over its recessive allele. wild allele is represented as + .

Multiple alleles can be defined as a

- series of forms of a gene
- situated at the same locus of homologous chromosomes
- affecting same character.

Multiple alleles are

- different forms of the same gene
- that is the sequence of the bases is slightly different in the genes located on the same place of the chromosome.



Multiple alleles are alternative states at the same locus. Remember: each individual will only have two alleles for a trait but there are several alleles to choose from.) The classical example for multiple alleles is human blood group self incompatibility in tobacco, coat colour in rabbit, self incompatability genes in brassica.

The number of possible genotypes in a series of multiple alleles is ½ n (n+1)

n = no of alleles

- Di-allelic genes can generate 3 genotypes.
- Genes with 3 alleles can generate 6 genotypes.
- Genes with 4 alleles can generate 10 genotypes.
- Genes with 8 alleles can generate 36 genotypes

Important features of multiple alleles

1) Multiple alleles always belong to the same locus and one allele is present at a locus at a time in a chromosome

2) Multiple alleles always control the same character of an individual

3) Wild type allele is dominant over other alleles

4) There is no crossing over in the multiple alleles

5) In a series of mutiple alleles wild type is always dominant

6) When two mutant types are crossed wild form cannot be recovered

7) The cross between two mutant alleles will always produce mutant phenotype. Examples of multiple alleles are 1) fur colour in a rabbit, 2) ABO blood group in man 3) Wing type in drosophila 4) Eye colour in drosophila etc. Fur colour in Rabbit. In rabbit, three alternate forms of genes, which controls coat colour. C causes wild type and its alleles.

Skin colour in rabbit

In rabbits, four kinds of skin colour are known.

Possible genotypes	CC, Cc^{ch}, Cc^{h}, Cc	$c^{ch}c^{ch}$	$c^{ch}c^{h}$, $c^{ch}c$	$c^{h}c^{h}$, $c^{h}c$	cc
Phenotype	Dark gray	Chinchilla	Light gray	Himalayan	Albino

CC, Cc^{ch}, Cc^{h}, Cc^{a} - Agouti (wild type)

c^{ch}, c^{ch}, $c^{ch}c^{h}$, $c^{ch}c$ - Chinchilla (salivary grey hair)

c^h c^h, c^h c - Himalayan (white except black feet nose ear tail)

cc - Albino (complete white).

Agouti

This has full colour and is also known as wild type. This colour is dominant over all the remaining colour and produces agouti colour in F1 and 3:1 ratio in F2 when crossed with any of the other three colours in rabbits. C represents this colour.

Chinchilla

This is lighter than agouti. This colour is dominant over Himalayan and albino and produces chinchilla in F1 and 3:1 ratio in F2 when crossed either Himalayan or albino. This is represented by c^{ch}.

Himalayan

The main body is white while the tips of ear, feet, tail and snout are coloured. This colour is dominant over albino and produces 3:1 ratio in F2 when crossed with albino. This is represented by c^h **.**

Albino

This has pure white fur colour and is recessive to all other types. This is represented by c. Thus the order of dominance for fur colour in rabbits can be represented as follows.

Agouti	Chinchilla	Himalayan	Albino
(C)	(cch)	(ch)	(c)

ABO Blood group in man.

Antibody

Antibody is a type of protein, which is commonly referred to as immunoglobin. It is usually found in the serum or plasma. The presence of antibody can be demonstrated by its specific reaction with an antigen.

Antigen

An antigen refers to an substance or agent, which when introduced into the system of vertebrate animal like cow, goat, man etc induces the production of specific antibody, which binds specifically to this (Antigen) substance Antigen are located in the red blood corpuscles (RBC). If a person has a particular antigen in his RBCs, his serum has usually antibodies against the other antigen. In human RBC two types of antigens viz A and B are present. Depending upon the presence or absence of antigen A and B the blood group in man is of four types viz A, B, AB and O. A person with blood group A has antigen A on the surface of RBCs: protein with blood group B will have antigen B those with blood group AB have antigens A and B; and those with blood group O have no antigen on the surface of their RBCs.

Blood Group	Genotype	Antigen found	Antibody present	Compatible blood group
A	I^AI^A, I^Ai^A	A	B	A and O
B	I^BI^B, I^bI^b	B	A	B and O
AB	I^AI^B	AB	None	A,B, AB,O
O	ii	None	AB	O

Recent studies shows that antigen is galactosamine and B is galactose Antibodies A, B, AB and None and are naturally present in the serum of individuals having A,B,AB, and O blood group respectively. The agglutination or coagulation of RBCs leads to clotting of blood due to interaction between antigen antibody. The blood group B cannot be transferred to an individual having blood group A because the recipient has antibody against antigen B which is present on the RBCs of blood group B. Similarly the reverse transfusion is not possible. The blood group AB does not have antibody A and B. Hence individuals with AB blood group can accept all types of blood, viz., A, B, AB and O. Such individuals are known as **universal acceptors** or recipients. The O blood group does not have any antigen and has antibody against antigen A and B, It cannot accept blood group other than O. Individuals with blood group O are known as **universal donors**, because transfusion of blood group O is possible with all the four blood types. The consideration of Rh (rhesus) type is important in blood transfusion. Each blood group has generally two types of Rh group, viz positive and negative. The same type of Rh is compatible for blood transfusion Opposite type lead to reaction resulting in death of the recipient. These are few examples of multiple alleles Now it is believed that multiple alleles are present almost for all genes.

Multiple alleles in plants

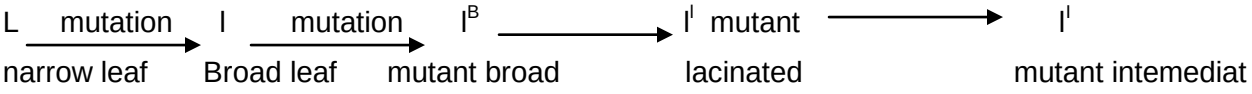
The classical example of multiple alleles in plants is ‘self incompatability alleles’ which prevents self fertilization**.**

Multiple alleles in Maize

Multiple allelic series affecting seed color is seen in Maize.

A $\xrightarrow[\text{(purple)}]{\text{Mutation}}$ a $\xrightarrow[\text{(white)}]{\text{Mutation}}$ a’ light purple

Multiple allele in cotton



For information

- About 30% of the genes in humans are di-allelic, that is they exist in two forms.
- About 70% are mono-allelic, they only exist in one form and they show no variation.
- A very few are poly-allelic having more than two forms.

Pleiotropism

In general one gene affects a single character. But many genes are known to affect more than one character such genes are known as pleiotropic genes and the condition is termed as pleiotrophy. An example of a pleiotropic gene in human beingsis the recessive gene s which produces sickle cell anemia in the ss homozygotes. These gene causes changes in two or more parts of characters, which are not related, then the gene is said to be pleiotropic gene. E.g. In cotton the Punjab hairy lintless gene lic produces seeds without lint. This gene also causes incomplete lancinations of the leaf, reduction in boll size and fertility. In a plant a gene may produce red pigment in several organs, such as flowers stem, leaves but still it is not correct to say that the gene is pleiotropic because the gene has only one general effect, the production of pigment. A gene for wing may be vestigial gene can be called as bristle gene or a fecundity gene. A number of other recessive genes produce marked and often detrimental effect in human beings. They are referred as syndromes.

Penetrance

Most genes produce identical phenotypes in all the individuals in which they are present in the appropriate genotype. For example, all the seeds having the w gene governing the seed shape in pea, in the homozygous state (ww) have uniformly wrinkled shape. Similarly, those seeds that have either WW or Ww genotype are uniformly round. The ability of a gene to produce identical phenotypes in all the individuals carrying it in the appropriate genotype is known as complete expressivity. As opposed to this, many genes have incomplete expressivity in that they produce variable phenotypes in the individuals that have this gene in the appropriate genotype.

Expressivity

In general, genes express themselves in all the individuals in which theya re present in the appropriate genotype, this is known as complete penetrance. But many genes do not

produce the concerned phenotype in all the individuals which carry them in the appropriate genotype. Such a situation is known as incomplete prenetrance. When a gene is present in the appropriate genotype, the per cent of individuals in which it is able to express itself is a measure of its penetrance. Thus the chlorophyll deficiency gene in lima beans has a penetrance of 10 %. Almost all the genes showing incomplete penetrance exhibit incomplete expressivity as well. Thus incomplete penetrance is in fact an expression of incomplete expressivity in that some individuals show such a small expression of the gene that the trait is not detectable.

Isoalleles

These alleles, which are similar but on testing it proves to be a different one. Blood group A person have three slightly different types such as IA1, IA2, IA3 which are similar but found to be different after testing.

Pseudoalleles

The genes that are so closely linked can be separatable only by rare crossing over. Such genes are called pseudoalleles.

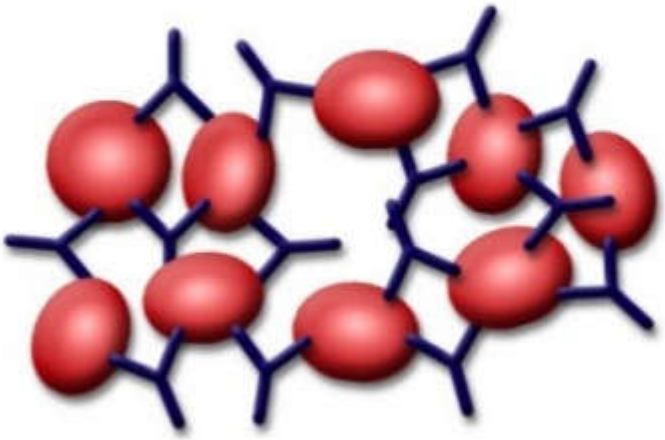
MULTIPLE ALLELES

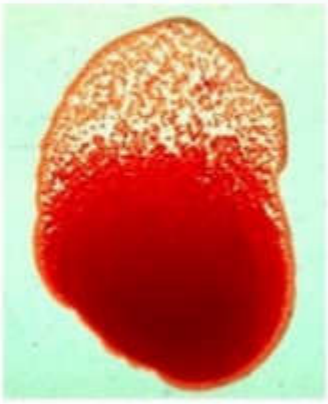
Genes which have more than two alleles

Blood types and transfusions

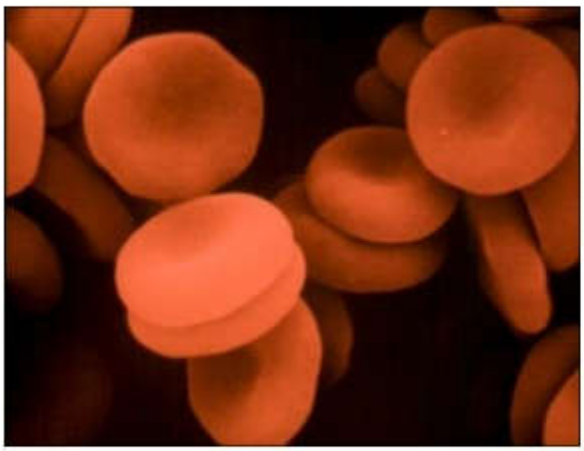
- People who are Type A blood produce antibodies to agglutinate cells which carry Type B antigens
  They recognise them as **non-self**
- The opposite is true for people who are Type B
- Neither of these people will agglutinate blood cells which are Type O
  Type O cells do not carry any antigens for the ABO system
  Type O cells pass incognito
- What about type AB people?

Agglutination





Antigens



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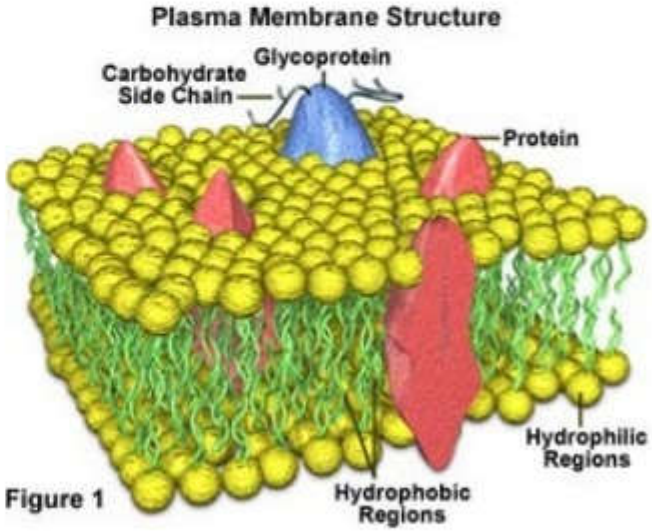

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Blood types and transfusions

- Blood types vary and your immune system recognises your own blood type as being **self**
- Other blood types are recognised as **non-self**
- If a blood which is incompatible with your body is transfused it will result in the **agglutination** of the foreign red blood cells

The ABO blood system

Genotypes	Phenotypes (Blood types)
$I^A I^A$	A
$I^A I^B$	AB
$I^A i$	A
$I^B I^B$	B
$I^B i$	B
ii	O

Note:

- Blood types A and B have two possible genotypes – homozygous and heterozygous.
- Blood types AB and O only have one genotype each.

The ABO blood system

- This is a controlled by a **tri-allelic gene**
- It can generate **6 genotypes**

- The alleles control the production of **antigens** on the surface of the red blood cells
- Two of the alleles are **codominant** to one another and both are dominant over the third

- Allele $\mathbf{I^A}$ produces antigen **A**
- Allele $\mathbf{I^B}$ produces antigen **B**
- Allele **i** produces **no** antigen

Genes and the immune system

- Poly-allelic alleles are usually associated with tissue types
- These genes are so varied that they provide us with our genetic finger print
- This is very important to our immune system which must tell the difference between our own cells (**self**) and invading disease causing microbes (**non-self**)

Genes and their alleles

- About 30% of the genes in humans are **di-allelic**, that is they exist in two forms, (they have two alleles)
- About 70% are **mono-allelic**, they only exist in one form and they show no variation
- A very few are **poly-allelic** having more than two forms

Donor-recipient compatibility

Recipient

Donor Type	A	B	AB	O
A				
B				
AB				
O				

= Agglutination

= Safe transfusion

Note:

- **Type O blood** may be transfused into all the other types = the **universal donor**.
- **Type AB blood** can receive blood from all the other blood types = the **universal recipient**.

Principle of Multiple Allele

The genes of a particular trait are located in specific loci in the chromosomes. Through the help of the modern technology, geneticists discovered that there are some traits that are not controlled only by two alleles but by multiple alleles.

Human blood groups

- one example of the traits controlled by multiple alleles is the human blood groups: A, B, AB and O. These 3 letters refer to 2 types of carbohydrates designated as A and B that are incorporated in the membranes of red blood cells.
- Although an individual can only have 2 alleles per gene, 3 alleles control this characteristic, which in various combination, produce the 4 human blood groups: A, AB, B and O.

the human blood relationship

Table 2.6: The Human Blood Relationship

Blood Group (Genotypes)	Phenotypes	Antigen (Type of Carbohydrates)	Antibodies (Plasma of the Blo
$I^A I^A$ or $I^A i$	Type A	Antigen A	Anti – b
$I^B I^B$ or $I^B i$	Type B	Antigen B	Anti – a
$I^A I^B$	Type AB	Antigen A and B	None
ii	Type O	None	Anti a and b

- It shows that the alleles for A (I^A) and B (I^B) are dominant over the O (i) allele.
- Persons with type O carry the homozygous alleles for O (ii). This means that they lack the A and B alleles in their blood. A person heterozygous for blood type AB carries the Alleles for A and B and since both alleles are expressed these alleles codominant with each other.

Coat Color in Rabbits

- Another example of a trait controlled by multiple genes is coat color in rabbits. There are 4 types of coat color in rabbits and each type denots specific alleles.
- Agouti coat is pure black or yellow and sometimes with patches.
- Chinchilla coat - silvery gray
- Himalayan - white coats with black color in the extremities.
- Albino coat- pure white due to absence of pigmentation.

Table 2.8: Genetic Table for Coat Color in Rabbit

Phenotypes	Symbols	Allelic Genotypes
Agouti	A	C^AC^A; C^AC^{Ch}; C^AC^H; C^AC^a;
Chinchilla	Ch	$C^{Ch}C^{Ch}$; $C^{Ch}C^H$; $C^{Ch}C^a$
Himalayan	H	C^HC^H; C^HC^a;
Albino	O	C^aC^a;

This shows the genotypes of the different coat colors of in rabbit. Take not that Agouti is the most dominant among the coat colors, followed by Chinchilla

Table 2.9: Multiple Allele Cross for Coat Color

G1	Agouti $C^A C^a$	x	Chinchilla $C^{Ch} C^a$
Gametes (P1)	C^A C^a		C^{Ch} C^a

G2

	C^A	C^a
C^{Ch}	$C^A C^{Ch}$ (Agouti)	$C^{Ch} C^a$ (Chinchilla)
C^a	$C^A C^a$ (Agouti)	$C^a C^a$ (Albino)

Ratio	Genotypic Ratio = 1: 1: 1: 1 or 25% $C^A C^{Ch}$
	$C^A C^{Ch}$ 25%
	$C^{Ch} C^a$ 25%
	$C^A C^a$ 25%
	$C^a C^a$ 25%
	Phenotypic Ratio = 2:1:1 or 50% Agouti 25% Chinchilla 25% Albino

Cross between Agouti and Chinchilla coat color

3. Genic Interaction (Factor Hypothesis)

The expression of a single character by the interaction of more than one pair of genes is called ***genic interaction*** or ***interaction of genes.*** It includes several deviations from the usual mendelian inheritance.

Bateson and ***Punnet*** proposed ***factor hypothesis*** to explain genic interaction. According to this hypothesis, *some characters are produced by the interaction of two or more pairs of factors (genes).*

The genic interaction is of two types, namely

1. *Non-allelic gene interaction.*
2. *Allelic gene interaction.*

The genic interaction occurring between genes located in different locus of the same chromosome or different chromosomes is known as ***non-allelic gene interactions.***

The genic interaction between the two alleles of a single locus is known as ***allelic gene interaction.***

Some of the important forms of genic interactions are as follows:-

- *1. Complementary genes*
- *2. Supplementary genes*
- *3. Duplicate genes*
- *4. Epistasis*
- *5. Lethal genes*

} Non-allelic gene interaction

- *6. Complete dominance*
- *7. Incomplete dominance (Blending inheritance)*
- *8. Co-dominance*
- *9. Pleiotropism*
- *10. Penetrance*
- *11. Expressivity*
- *12. Cumulative genes or Multiple genes or polygenes* (Refer chapter .5)

} Allelic gene interaction

1. Complementary Genes

Complementary genes may be defined as, *"two or more non-allelic dominant genes interact with one another to produce a character; but one gene cannot produce that character in the absence of the other"*. The action of these independent genes are complementary. It is a ***non-allelic gene interaction***.

1. Flower Colour in Sweet Pea

Bateson and ***Punnet*** studied the inheritance of flower colour in sweet pea, *Lathyrus odoratus*. There are two varieties of pea plants, one producing ***red flower*** and the other ***white flower.***

The red colour of the flower is due to the presence of a pigment called ***anthocyanin.*** *The anthocyanin is produced from a colourless substance* called ***chromogen*** by the action of an ***enzyme.*** The chromogen cannot be converted into anthocyanin in the absence of the enzyme. Thus for the production of red colour both chromogen and enzyme should be present in the plant. In the absence of anyone, the red colour cannot be produced.

A dominant gene ***C*** is responsible for the production of ***chromogen.*** When this gene is recessive ***c,*** the chromogen cannot be produced.

Similarly, another dominant gene ***A*** is responsible for the production of the ***enzyme*** which converts the chromogen into anthocyanin. When this gene is recessive ***a,*** the enzyme cannot be produced and thus chromogen cannot be converted into anthocyanin.

Parents : White **CCaa** x White **ccAA**

Gametes : **Ca** **cA**

F_1 : Red **CcAa**

F_1 Plants are crossed : Red **CcAa** x Red **CcAa**

Gametes : **CA** **Ca** **cA** **ca** **CA** **Ca** **cA** **ca**

Gametes	CA	Ca	cA	ca
CA	CCAA Red	CCAa Red	CcAA Red	CcAa Red
Ca	CCAa Red	CCaa White	CcAa Red	Ccaa White
cA	CcAA Red	CcAa Red	ccAA White	ccAa White
ca	CcAa Red	Ccaa White	ccAa White	ccaa White

Fig.3.1: Inheritance of flower colour in sweet pea Ratio 9:7.

Gene C ⟶ Chromogen

Gene A ⟶ Enzyme

Chromogen + Enzyme ⟶ Anthocyanin (Red)

Red flower is produced by the interaction of both dominant genes *C* and ***A***. *C* or *A* cannot give red colour independently.

A homozygous white flowered sweet pea plant ***(CCaa)*** is crossed with another white flowered sweet pea plant ***(ccAA)***. The F_1 plants have red coloured flowers.

When the F_1 red hybrid plants ***(CcAa)*** are crossed, in F_2 red and white are produced in the ratio 9:7.

Both the non-allelic genes *C* and *A* are complementary in nature. In the absence of either one or both of the complementary genes, white flowers are produced.

2. Pericarp Colour in Barley

In barley, red pericarp colour in grains is due to the accumulation of a red colour pigment called ***anthocyanin***. This anthocyanin is synthesized from a colourless substance called ***chromogen*** by the activity of an ***enzyme***. If the enzyme is absent, anthocyanin cannot be synthesized in cells. Thus the synthesis of anthocyanin needs both the chromogen and enzyme. In the absence of any one, the red colour cannot be produced.

The dominant gene ***Re*** is responsible for the production of chromogen . If this gene is recessive (***re***), there would be no chromogen formation. Another dominant gene ***J*** is responsible for the enzyme that converts chromogen into anthocyanin. If this gene is recessive ***j***, there is no enzyme synthesis for the conversion of chromogen. Hence, the grains are colourless.

L.Smith made studies on the inheritance of grain colour in some strains of barley. A true breeding homozygous strain bearing colourless grains (***ReRejj***) was crossed with another strain bearing colourless grains (***rereJJ***). The F_1 plants produced red coloured grains (***RereJj***).

Parents : White grain x White grain

ReRejj **rereJJ**

Gametes : **Rej** **reJ**

F1 : **RereJj**

Red grain

F1 Selfed : **RereJj** Red grain x **RereJj** Red grain

Gametes : **ReJ** **Rej** **reJ** **rej** **ReJ** **Rej** **reJ** **rej**

♀ / ♂	**ReJ**	**Rej**	**reJ**	**rej**
ReJ	ReReJJ Red grain	ReReJj Red grain	RereJJ Red grain	RereJj Red grain
Rej	ReReJj Red grain	ReRejj White grain	RereJj Red grain	Rerejj White grain
reJ	RereJJ Red grain	RereJj Red grain	rereJJ White grain	rereJj White grain
rej	RereJj Red grain	Rerejj White grain	rereJj White grain	rerejj White grain

coloured grains. In the absence of any one of the [illegible], the plants produce colourless grains.

2. Supplementary Genes

Supplementary genes may be defined as *two independent pairs of dominant genes, which interact in such a way that each dominant gene produces its effect whether the other is present or not, but when the second dominant gene is added to the first, a new character is expressed. It is a* ***non-allelic gene interaction.***

1. Inheritance of Combs in Fowls (9:3:3:1)

The interaction of two dominant genes, to control the same character was discovered by ***Bateson*** and ***Punnet*** (1908) in fowls. In fowls, there are four types of combs. They are ***rose*** comb, ***pea*** comb, ***walnut*** comb and ***single*** comb.

Rose comb is controlled by a dominant gene ***R*** and pea is controlled by another dominant gene ***P.*** The recessive alleles of the above genes in the homozygous condition ***(rrpp)*** produce single comb. But when the two dominant genes ***R*** and ***P*** are brought together they interact and produce a new comb called ***walnut.***

Fig.3.3: Types of combs in fowls.

Walnut comb is due to the interaction of two non-allelic dominant genes ***R*** and ***P*** and the single comb is due to the interaction of two recessive genes ***r*** and ***p.***

A pure rose combed ***(RRpp)*** chicken is crossed with pure pea combed ***(rrPP)*** chicken. The F_1 progeny [illegible]

two types of seed cases, a ***triangular*** seed case and ***oval*** seed case. The triangular seed case is controlled by two dominant genes *T* and ***D*** independently. Any one dominant gene can produce triangular seed case. The recessive genes ***t*** and ***d*** produce oval seed case.

When these two types of plants are crossed, the resulting F_1 plants produce triangular seed case. When the F_1 hybrids are selfed, in F_2 plants, triangular seed and oval seed cases are produced in the ratio 15:1.

4. Epistasis

Epistasis is *the prevention of the expression of one gene by another* non-allelic gene. Epistasis means ***stopping*** or ***inhibiting***.

The inhibiting gene is called ***epistatic gene.*** The inhibited gene is called ***hypostatic gene.***

Epistasis is of two types, namely ***dominant epistasis*** and ***recessive epistasis.***

Dominant Epistasis

The prevention of the expression of a gene by a dominant non-allelic gene is called ***dominant epistasis.*** Eg. *White and colour feather in fowls*.

Epistasis is a ***non-allelic gene interaction.*** In epistasis, a single character is controlled by the interaction of two or more non-allelic genes.

Here gene located on one locus interacts with another gene located in another locus. So it is a ***non-allelic gene interaction.***

1. Inheritance of Colour Pattern in Poultry

Inheritance of ***colour pattern*** in poultry is a case of ***dominant epistasis.***

In ***white Leghorn,*** there are ***white birds*** and ***coloured birds.*** The coloured birds are due to a dominant gene ***C*** which produces colour pigment. When this gene is recessive ***c,*** the bird cannot produce colour pigment and the bird is white.

Further, the dominant gene ***C*** is inhibited by another dominant gene ***I*** located in another locus. When ***I*** is present along with C, the bird cannot produce colour pigment and hence the bird is white. The recessive gene ***i*** cannot inhibit ***C***. Thus the colour pattern in white leghorn occurs as follows:

CCII - White
CCIi - White
ccII - White

CCii - Colour cCIi - White
Ccii - Colour CCIi - White
ccii - White CcIi - White

Parents: White leghorns (Genetically coloured) x Plymouth rock (white)

CCII x **ccii**

CcIi
White

F_1 :
F_1 individuals are inbred

CcIi White x **CcIi** White

Gametes: CI Ci cI ci CI Ci cI ci

Gametes	CI	Ci	cI	ci
CI	**CCII** White	**CCIi** White	**CcII** White	**CcIi** White
Ci	**CCIi** White	**CCii** Colour	**CcIi** White	**Ccii** Colour
cI	**CcII** White	**CcIi** White	**ccII** White	**ccIi** White
ci	**CcIi** White	**Ccii** Colour	**ccIi** White	**ccii** White

F_2 generation: 13 White: 3 Colour

Fig.3.7: Inheritance of colour pattern in poultry.

In ***plymouth rock,*** the coloured bird is due to a dominant gene ***C*** and white bird is due to a recessive gene ***c.*** Here also the ***I*** gene inhibits the ***C.***

When white leghorn and plymouth rock are crossed, the F_1 birds are all white. When the F_1 birds are crossed, in the F_2 generation,

fruit colour. Since one dominant gene masks the expressi
r dominant gene, it is said to be a ***dominant epistasis***.
summer squash plant producing white fruits (***WWyy***) is cr
nother variety with yellow fruit colour (***wwYY***) to get F1 p
plants are all white fruit producing plants (***WwYy***). Whe
nts are crossed together, the F2 plants with fruits colour w
and ***green*** in the ratio of 12:3:1.

nts : White fruit x Yellow fruit

WWyy **wwYY**

etes: Wy wY

WwYy

: White fruit

etes: WY Wy wY wy WY Wy wY wy

♀ / ♂	WY	Wy	wY	wy
WY	WWYY White	WWYy White	WwYY White	WwYy White
Wy	WWYy White	WWyy White	WwYy White	Wwyy White
wY	WwYY White	WwYy White	wwYY Yellow	wwYy Yellow
wy	WwYy White	Wwyy White	wwYy Yellow	wwyy Green

3/16 individuals, the gene W is absent but Y is present and hence they produce yellow fruits. In the remaining 1/16 individuals, neither W nor Y is present so that they produce ***green fruits***.

Recessive Epistatis

The prevention of the expression of a gene by a recessive non-allelic gene is called ***recessive epistasis.*** Eg. *Coat colour in mice.*

1. Inheritance of Coat Colour in Mice

Inheritance of ***coat colour in mice*** is an example of ***recessive epistasis.***

Parents : Black male **MMaa** x Albino female **mmAA**

Gametes : Ma, A

F_1 generation : **MmAa** Agouti

F_1 individuals crossed : Agouti male **MmAa** x Agouti female **MmAa**

Gametes: MA, Ma, mA, ma, MA, Ma, mA, ma

Gametes	MA	Ma	mA	ma
MA	**MMAA** Agouti	**MMAa** Agouti	**MmAA** Agouti	**MmAa** Agouti
Ma	**MMAa** Agouti	**MMaa** Black	**MmAa** Agouti	**Mmaa** Black
mA	**MmAA** Agouti	**MmAa** Agouti	**mmAA** Albino	**mmAa** Albino
ma	**MmAa** Agouti	**Mmaa** Black	**mmAa** Albino	**mmaa** Albino

F_2 Generation : Agouti 9: Black 3: Albino 4.

Fig 3.9: Inheritance of coat colour in mice

5. Lethal Genes

A lethal gene kills its possessor. Thus the victims of lethal genes do not live to reproduce.

Lethal Genes in Man

There is a mutant recessive gene in man, which causes internal adhesions of the lungs.

A child homozygous for the lethal gene might be able to survive at embryonic development, but at birth, when it suddenly becomes dependent upon its lungs for its oxygen supply, it would die because its lungs could not expand properly. Being recessive, it could be carried by normal parents in the heterozygous condition without any ill effects.

The defects of the kidneys, lungs and digestive organs probably would not be lethal until birth, because these organs do not begin functioning until this time. So genes causing some types of these defects would not be lethal early in embryonic life.

But genes causing heart defects would be lethal even early in embryonic life, since the heart begins to function even early in embryonic life.

The infants with ***juvenile amaurotic idiocy*** disease lose eyesight between the ages of 4 and 7. Mental and physical powers deteriorate and they die before adolescence. This disease is due to a recessive gene in homozygous condition.

Infantile amaurotic idiocy is another dangerous disease in infants. It is also due to the presence of a particular recessive gene in homozygous condition.

Sickle cell anaemia is another disease caused by a recessive lethal gene in homozygous condition.

Sickle Cell Anaemia in Man

Sickle cell anaemia is a ***hereditary blood disease***. The disease is characterised by sickle shaped RBC. The patient dies before reaching sexual maturity.

Sickle cell anaemia is due to recessive genes Hb^SHb^S. They produce sickle cell haemoglobin. The normal dominant genes Hb^AHb^A produce normal ***adult*** haemoglobin. The heterozygotes Hb^AHb^S are normal.

When two heterozygotes Hb^AHb^S marry, they produce offspring in the ratio of $1\ Hb^A\ Hb^A : 2Hb^AHb^S : 1Hb^S\ Hb^S$. The Hb^SHb^S homozygous recessive individual dies before reaching sexual maturity. Hb^SHb^S genotype is ***lethal***.

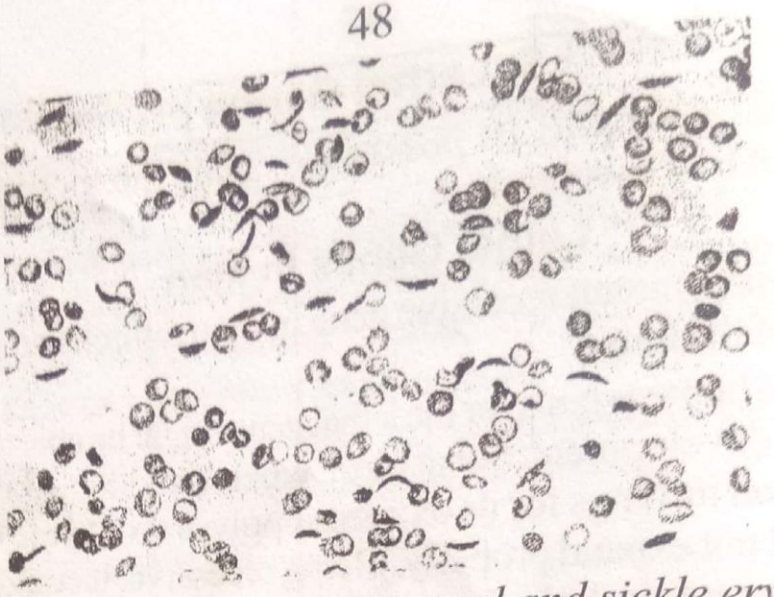


Fig.3.13: Blood smear showing normal and sickle erythrocytes.

This lethal gene modifies the Mendelian ratio of 3:1 into 1:2.

It is an ***allelic interaction.***

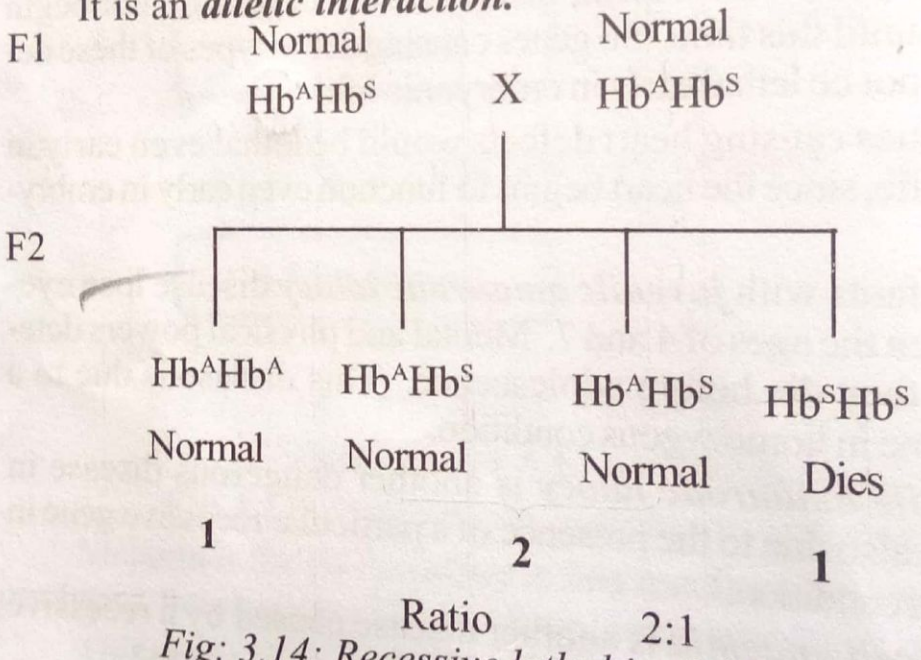


Fig: 3.14: Recessive lethal in sickle cell anaemia.

Lethal Genes in Mice

In the house mouse, ***yellow coat colour*** is due to a dominant gene ***Y.*** The dominant ***Y*** produces lethal effect when two ***YY*** are present. Hence in an individual all yellow individuals are heterozygous ***(Yy).***

When two yellow individuals are bred together, they always produce offspring in the ratio of 2 heterozygous yellow and 1 non-yellow. But the expected ratio is 1 pure yellow; 2 heterozygous yellow and 1 non-yellow.

The actual ratio 2:1 is an unusual ratio and is due to the fact that the homozygous yellow individuals ***(YY)*** died in the embryonic stages.

What is **haemophilia A**?

Haemophilia is an inherited, **serious bleeding disorder** where a person's **blood does not clot properly**, leading to uncontrolled bleeding which can occur spontaneously or after minor trauma.

It can **dramatically reduce the quality of life** of people affected, as well as their family, friends and caregivers[1].

Haemophilia A is the most common form – affecting

~320,000 people worldwide[2,3]

50–60% of whom have severe haemophilia[4].

What happens in the blood of a person with **haemophilia A**?

In a healthy person, proteins called **clotting factors** work together to form a blood clot and help stop bleeding.

People with haemophilia A either **lack or do not have enough** of a clotting factor called

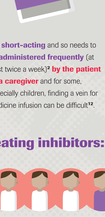
factor VIII

which leads to their blood not being able to clot properly.

Without treatment, people with **haemophilia** can suffer:

Bruising

Repeated bleeding into muscles and joints, which can lead to **long term disability** or **joint disease**[5,6]



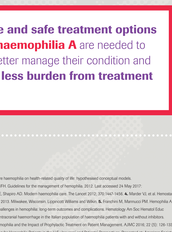
Spontaneous bleeding, which can be life threatening if it occurs in **vital organs**, such as the brain[7]

Prolonged and uncontrolled bleeding following injury or surgery[8]

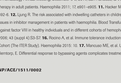
Life with **haemophilia** – the **burden of treatment**:

Life for people with haemophilia and their caregivers is often **centred on treatment infusions**, taking up a large amount of time and having a **significant impact on their lives**[9].

People with haemophilia A report difficulty **balancing treatment with daily life**, so compliance can be a challenge[10,11] leaving them **vulnerable to potentially dangerous bleeds**.



Factor VIII replacement



The mainstay of current treatment for haemophilia A **is factor VIII replacement therapy**, which is taken **on-demand** (as needed to treat bleeds), or on an **ongoing basis** (to prevent bleeds).

It is **short-acting** and so needs to be **administered frequently** (at least twice a week)[3] **by the patient or a caregiver** and for some, especially children, finding a vein for medicine infusion can be difficult[12].

Treating inhibitors: ITI and bypassing agents

One in four (25–30%) people with severe **haemophilia A develop 'inhibitors' to factor VIII replacement therapies**[13].

People with haemophilia A with inhibitors may need **more frequent treatment infusions**, as well as '**immune tolerance induction**' (ITI), where the patient is given very high doses of factor VIII over a long period of time.

Inhibitors are **antibodies that attack and destroy the replaced factor VIII**, because it is recognised as foreign[14]. As a **serious complication** of treatment[14], many people with haemophilia A **live in fear** of developing inhibitors.

However, ITI can take many years, is very costly and is **ineffective in ~30%** of people[15,17].

'**Bypassing agents**' are another treatment for people with inhibitors, often used after ITI fails. However, these are **short-acting, needing to be taken often and give variable bleeding control**[16].

Further effective and safe treatment options for people with **haemophilia A** are needed to enable them to better manage their condition and live their lives with **less burden from treatment**

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NP/ACE/1511/0002

UNDERSTANDING LINKAGE, AND GENETIC MAPPING

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INTRODUCTION

- Each species of organism must contain hundreds to thousands of genes
  - Yet most species have at most a few dozen chromosomes
- Therefore, each chromosome is likely to carry many hundred or even thousands of different genes
  - The transmission of such genes will violate Mendel's law of independent assortment

5.1 LINKAGE AND CROSSING OVER

- In eukaryotic species, each linear chromosome contains a long piece of DNA
  - A typical chromosome contains many hundred or even a few thousand different genes
- The term linkage has two related meanings
  - 1. Two or more genes can be located on the same chromosome
  - 2. Genes that are close together tend to be transmitted as a unit

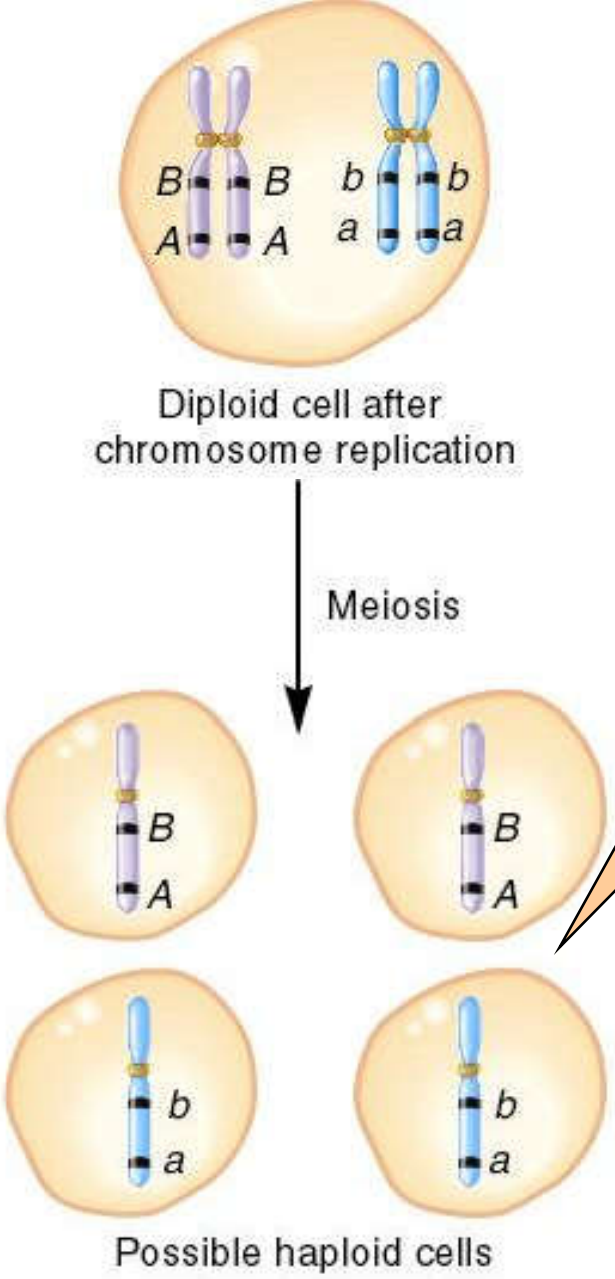
- Chromosomes are called linkage groups
  - They contain a group of genes that are linked together
- The number of linkage groups is the number of types of chromosomes of the species
  - For example, in humans
    - 22 autosomal linkage groups
    - An X chromosome linkage group
    - A Y chromosome linkage group
- Genes that are far apart on the same chromosome may independently assort from each other
  - This is due to crossing-over

Crossing Over May Produce Recombinant Phenotypes

- In diploid eukaryotic species, linkage can be altered during meiosis as a result of crossing over

- Crossing over
  - Occurs during prophase I of meiosis at the bivalent stage
  - Non-sister chromatids of homologous chromosomes exchange DNA segments

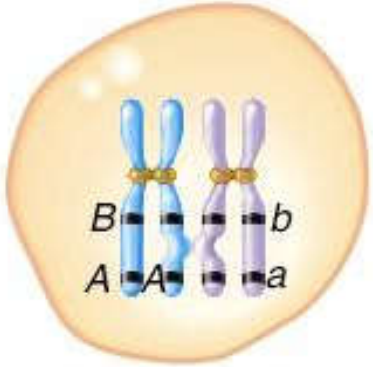
- Figure 5.1 illustrates the consequences of crossing over during meiosis



The haploid cells contain the same combination of alleles as the original chromosomes

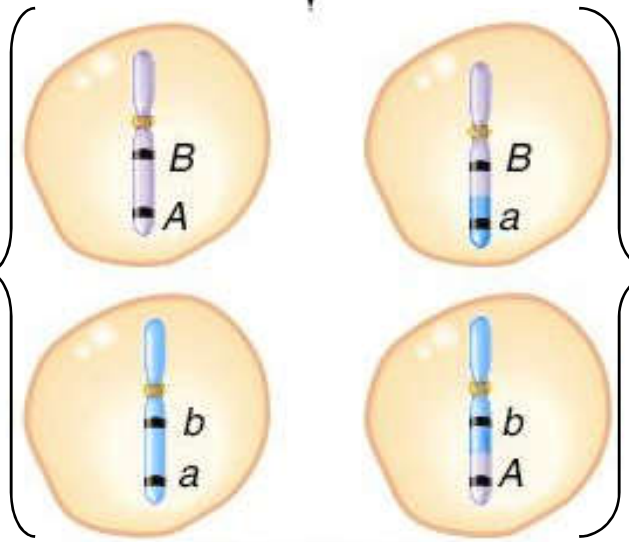
The arrangement of linked alleles has not been altered

Figure 5.1 **(a)** Without crossing over, linked alleles segregate together.



Diploid cell after chromosome replication

Meiosis



Possible haploid cells

These are termed parental or non-recombinant cells

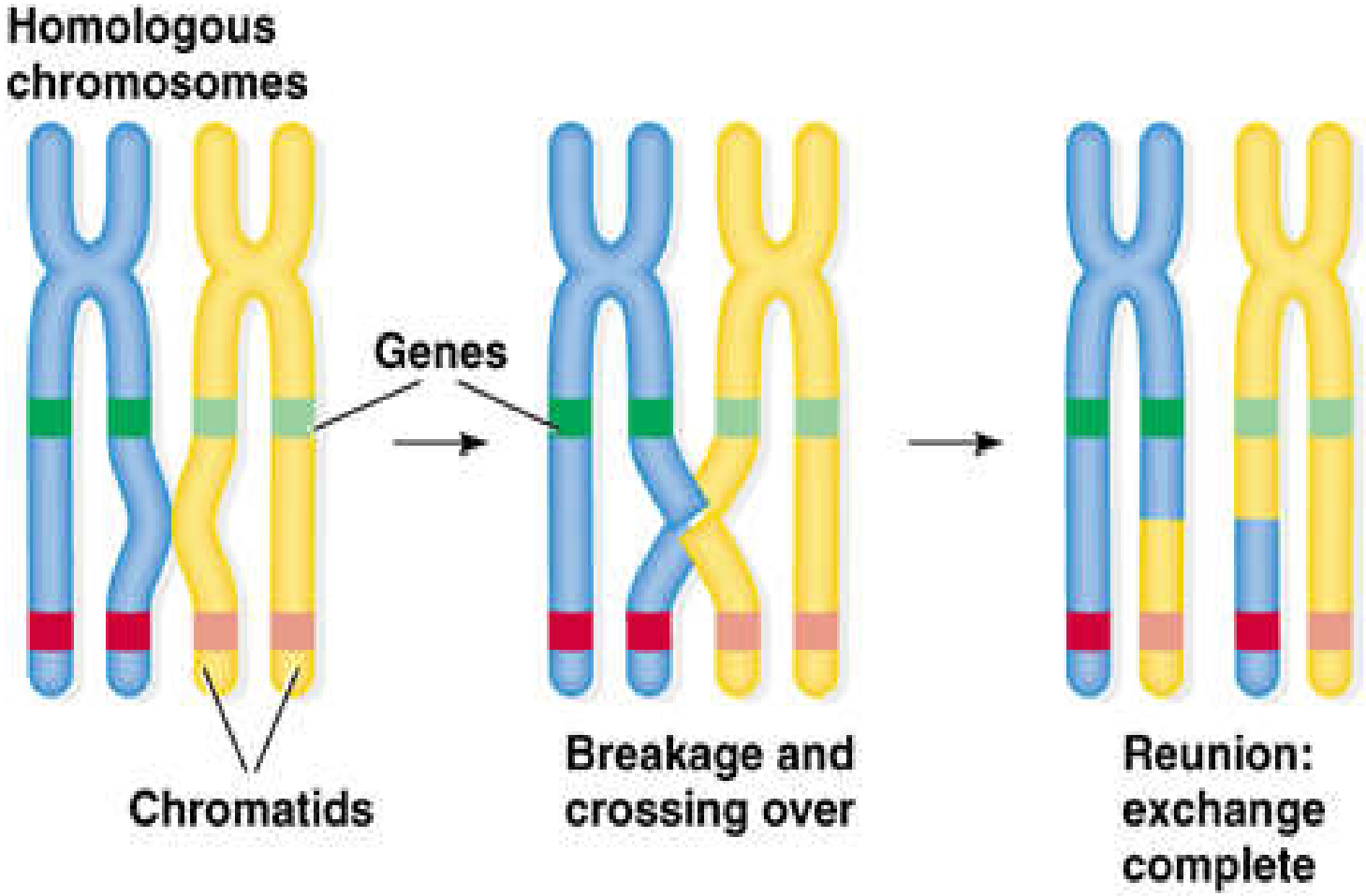
These haploid cells contain a combination of alleles NOT found in the original chromosomes

This new combination of alleles is a result of genetic recombination

These are termed nonparental or recombinant cells

Figure 5.1 **(b)** Crossing over can reassort linked alleles.

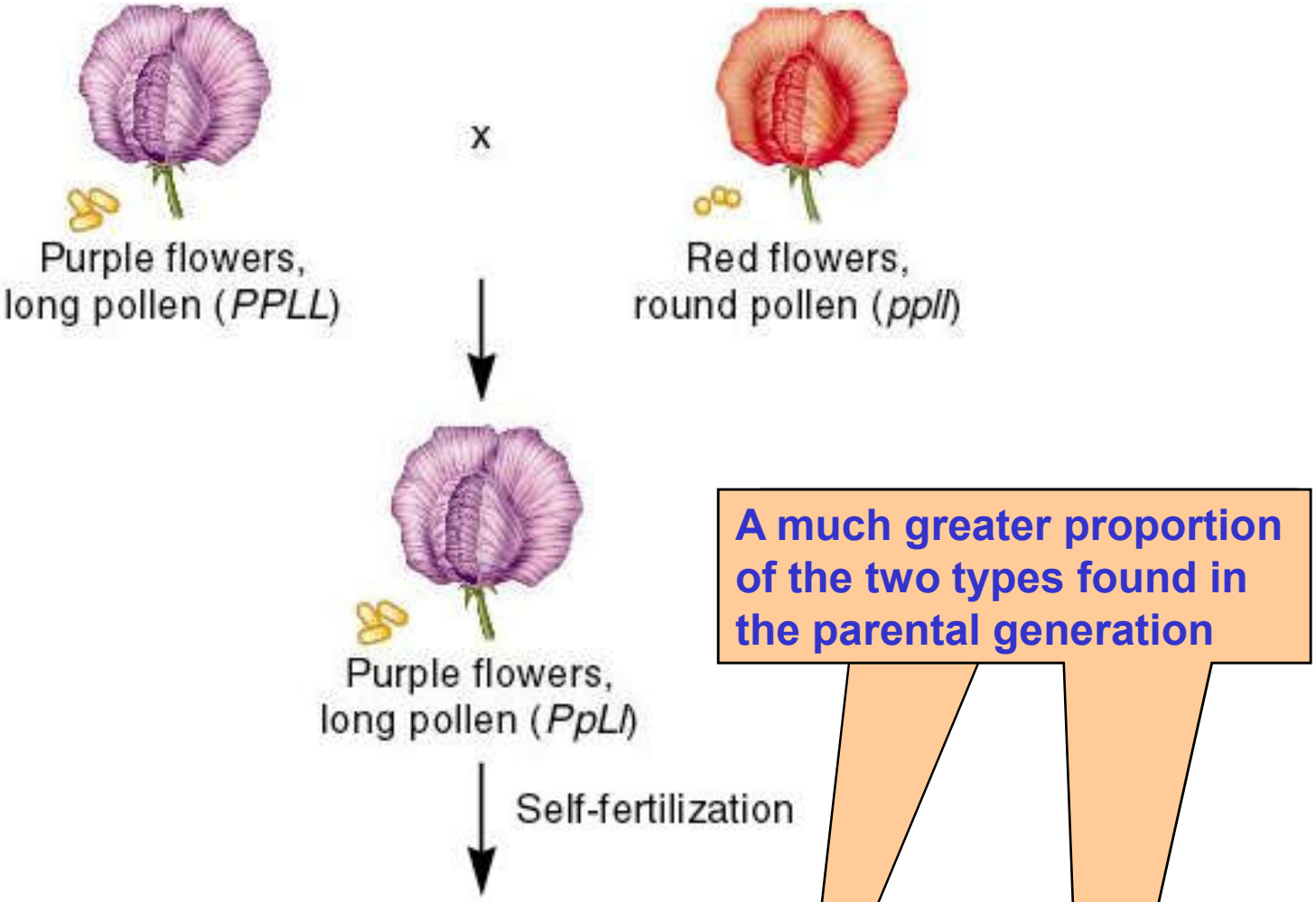
Fig. 13.2 Mechanism of crossing-over



Bateson and Punnett Discovered Two Traits That Did Not Assort Independently

- In 1905, William Bateson and Reginald Punnett conducted a cross in sweet pea involving two different traits
  - Flower color and pollen shape
- This is a dihybrid cross that is expected to yield a 9:3:3:1 phenotypic ratio in the F_2 generation
  - However, Bateson and Punnett obtained surprising results
- Refer to Figure 5.2

Figure 5.2



A much greater proportion of the two types found in the parental generation

F_2 offspring	Observed number	Rat	Expected number	Ratio
Purple flowers, long pollen	296	15.6	240	9
Purple flowers, round pollen	19	1.0	80	3
Red flowers, long pollen	27	1.4	80	3
Red flowers, round pollen	85	4.5	27	1

Bateson and Punnett Discovered Two Traits That Did Not Assort Independently

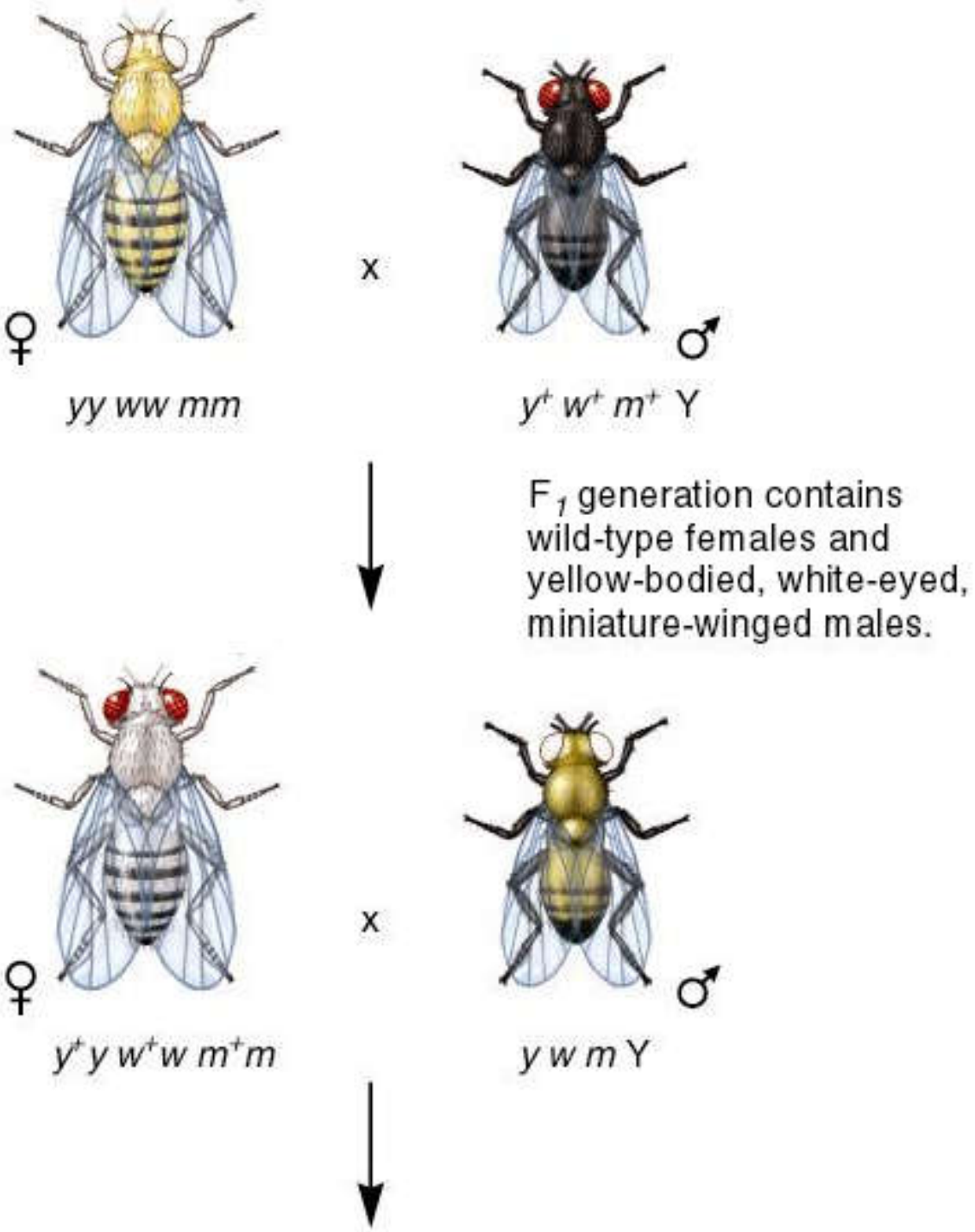
- They suggested that the transmission of the two traits from the parents was somehow coupled
  - The two traits are not easily assorted in an independent manner

- However, they did not realize that the coupling is due to the linkage of the two genes on the same chromosome

Morgan Provided Evidence for the Linkage of Several X-linked Genes

- The first direct evidence of linkage came from studies of Thomas Hunt Morgan
- Morgan investigated several traits that followed an X-linked pattern of inheritance
- Figure 5.3 illustrates an experiment involving three traits
  - Body color
  - Eye color
  - Wing length

Figure 5.3


♀
x
♂
yy ww mm
y+ w+ m+ Y
F1 generation contains wild-type females and yellow-bodied, white-eyed, miniature-winged males.
F1 generation
♀
x
♂
y+y w+w m+m
y w m Y

F_2 generation	Females	Males	Total
Gray body, red eyes, normal wings	439	319	758
Gray body, red eyes, miniature wings	208	193	401
Gray body, white eyes, normal wings	1	0	1
Gray body, white eyes, miniature wings	5	11	16
Yellow body, red eyes, normal wings	7	5	12
Yellow body, red eyes, miniature wings	0	0	0
Yellow body, white eyes, normal wings	178	139	317
Yellow body, white eyes, miniature wings	365	335	700

P Males

P Females

- Morgan observed a much higher proportion of the combinations of traits found in the parental generation
- Morgan's explanation:
  - All three genes are located on the X chromosome
  - Therefore, they tend to be transmitted together as a unit

Morgan Provided Evidence for the Linkage of Several X-linked Genes

- However, Morgan still had to interpret two key observations
  - 1. Why did the F_2 generation have a significant number of nonparental combinations?
  - 2. Why was there a quantitative difference between the various nonparental combinations?

- Let's reorganize Morgan's data by considering the pairs of genes separately

Gray body, red eyes	1,159
Yellow body, white eyes	1,017
Gray body, white eyes	17
Yellow body, red eyes	12
Total	2,205

But this nonparental combination was rare

Red eyes, normal wings	770
White eyes, miniature wings	716
Red eyes, miniature wings	401
White eyes, normal wings	318
Total	2,205

It was fairly common to get this nonparental combination

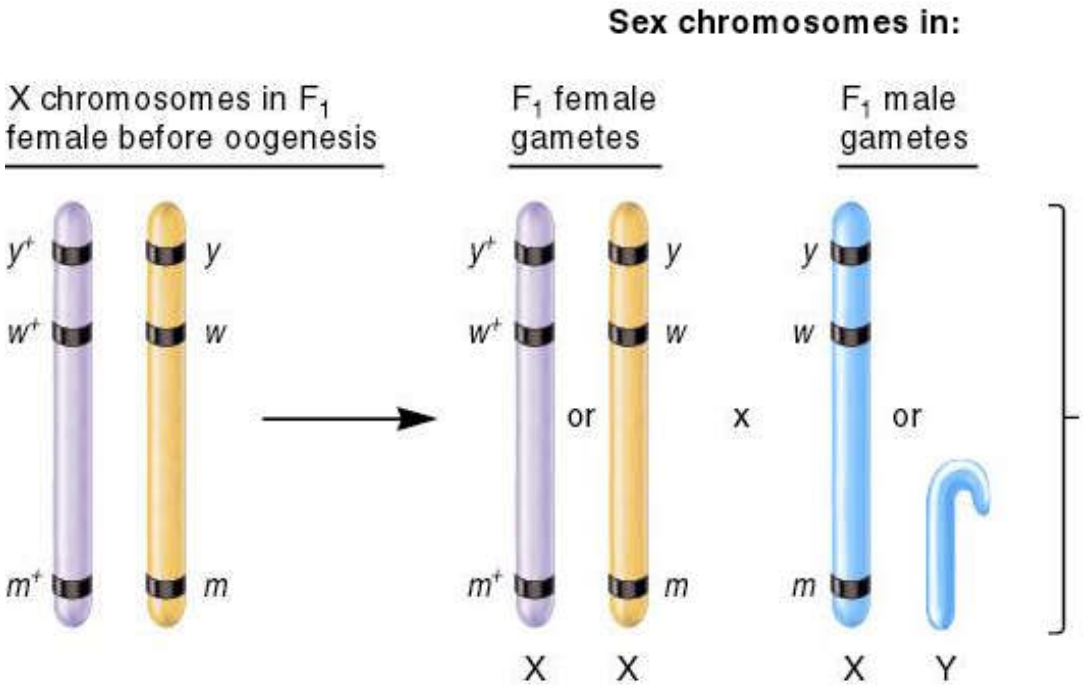
- To explain these data, Morgan considered the previous studies of the cytologist F.A Janssens

- Janssens had observed chiasmata microscopically
  - And proposed that crossing over involves a physical exchange between homologous chromosomes

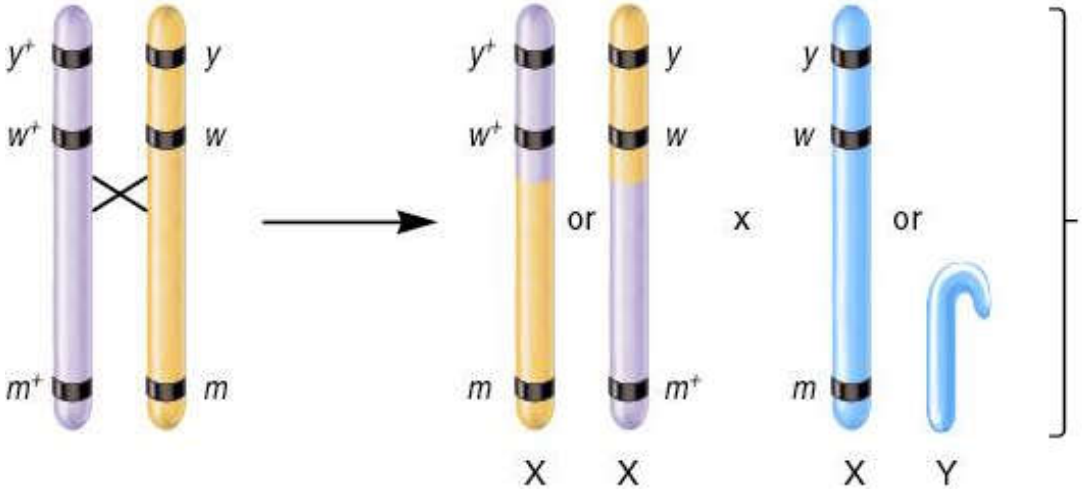
- Morgan shrewdly realized that crossing over between homologous X chromosomes was consistent with his data

- Crossing over did not occur between the X and Y chromosome
  - The three genes were not found on the Y chromosome

- Morgan made three important hypotheses to explain his results
  - 1. The genes for body color, eye color and wing length are all located on the X-chromosome
    - They tend to be inherited together
  - 2. Due to crossing over, the homologous X chromosomes (in the female) can exchange pieces of chromosomes
    - This created new combination of alleles
  - 3. The likelihood of crossing over depends on the distance between the two genes
    - Crossing over is more likely to occur between two genes that are far apart from each other
- Figure 5.4 illustrates how crossing over provides an explanation for Morgan's trihybrid cross



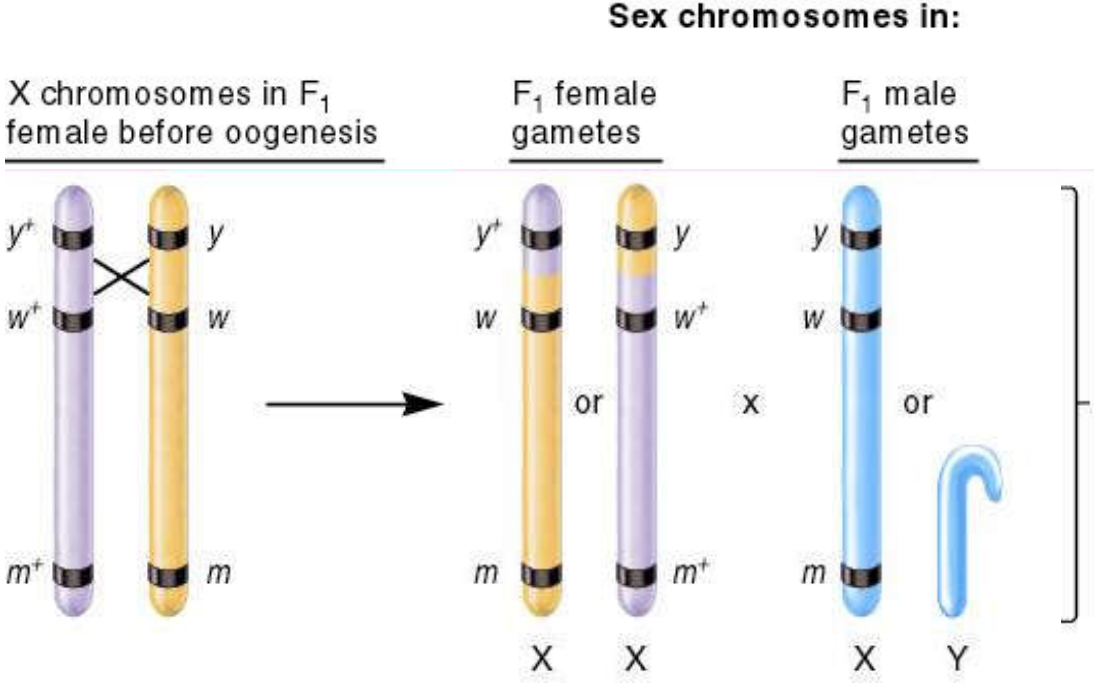
(a) No crossing over between y^+ and m^+ (most likely)



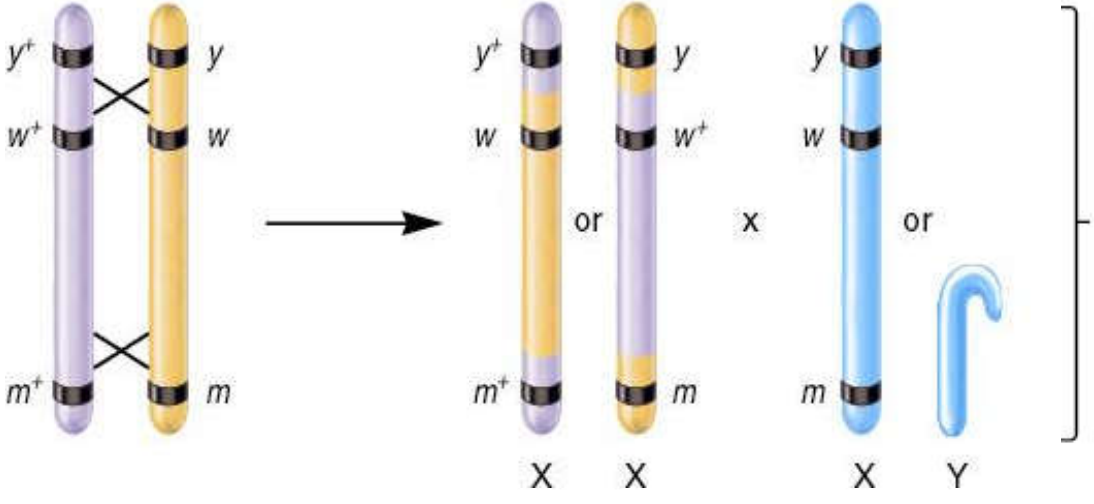
(b) Crossing over between w^+ and m^+ (fairly likely) because the genes are far apart

Figure 5.4

Figure 5.4



(c) Crossing over between y^+ and w^+ (unlikely) **because the genes are very close together**



These recombinant offspring are very unlikely
1 out of 2,205

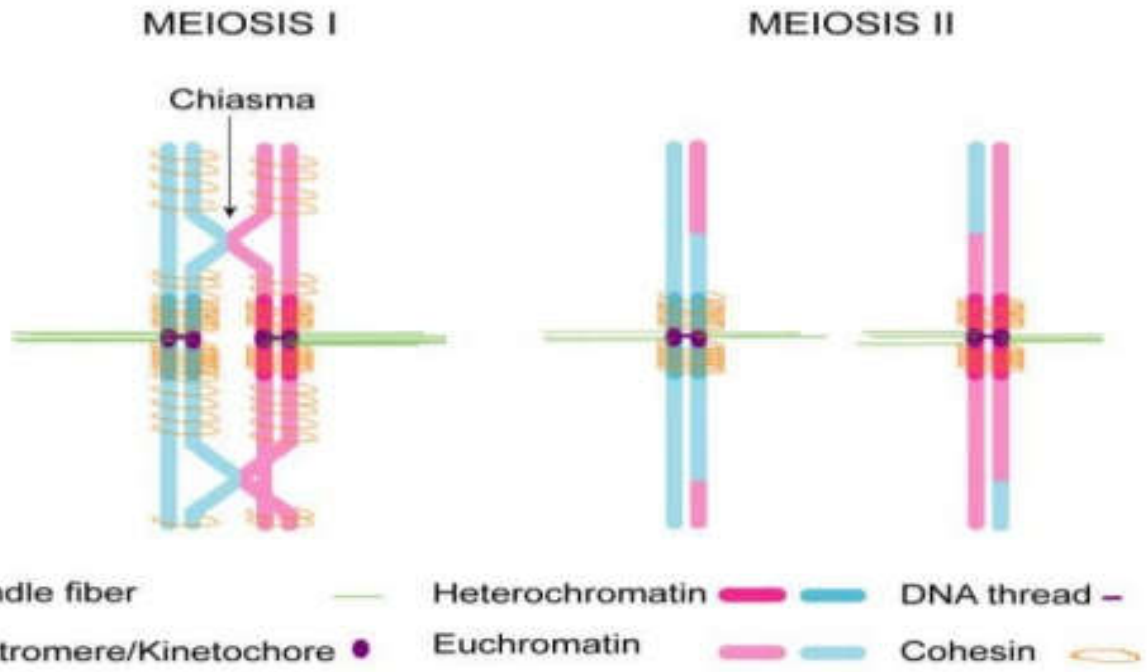
(d) Double crossing over (very unlikely)

Types of Crossing over

- **Single crossing over**:

Chromosomal crossover (or **crossing over**) is the exchange of genetic material between homologous chromosomes that results in recombinant chromosomes. It is one of the final phases of genetic recombination, which occurs during prophase I of meiosis (pachytene) during a process called synapsis.

single crossing over



Double crossing over

Two simultaneous reciprocal breakage and reunion events between the same two chromatids.

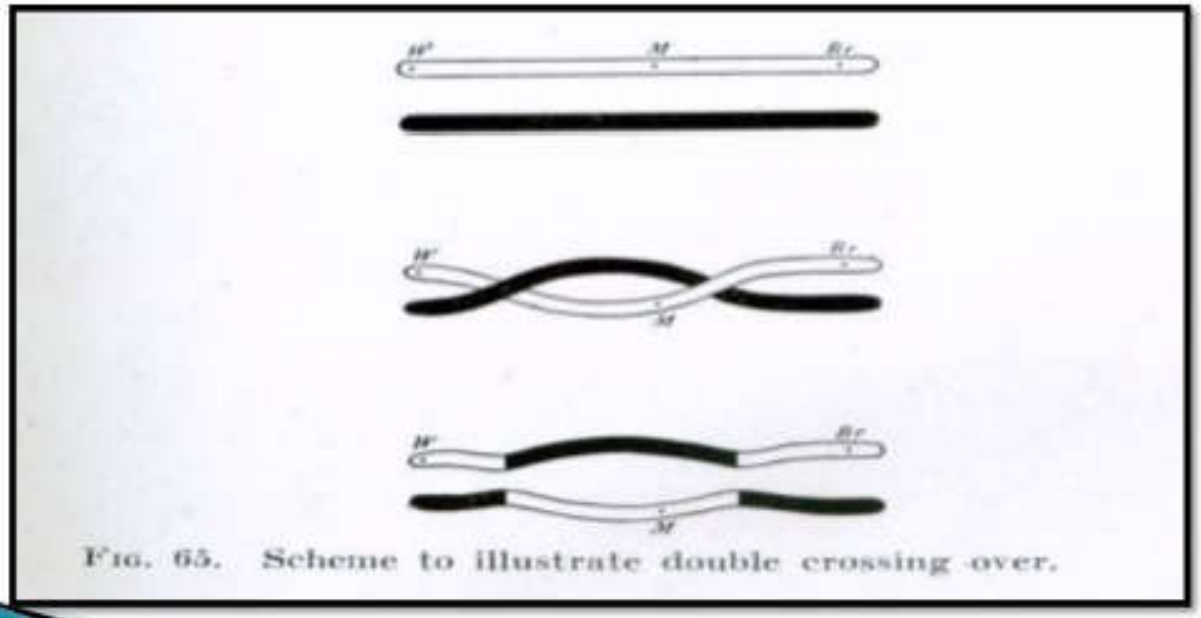


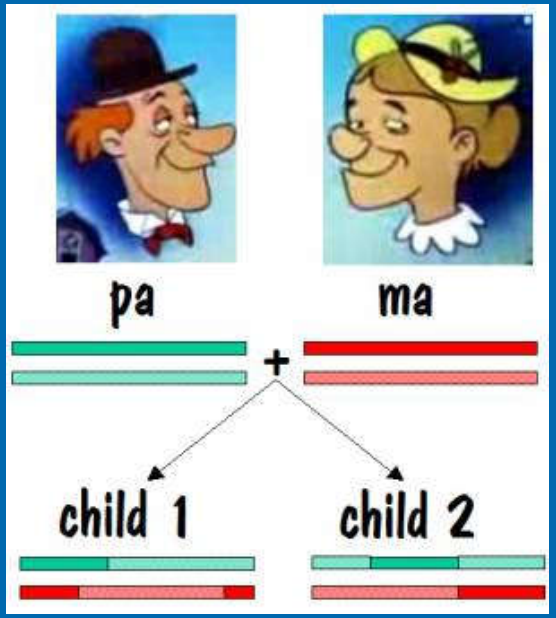
FIG. 65. Scheme to illustrate double crossing over.

Factors affecting crossing over

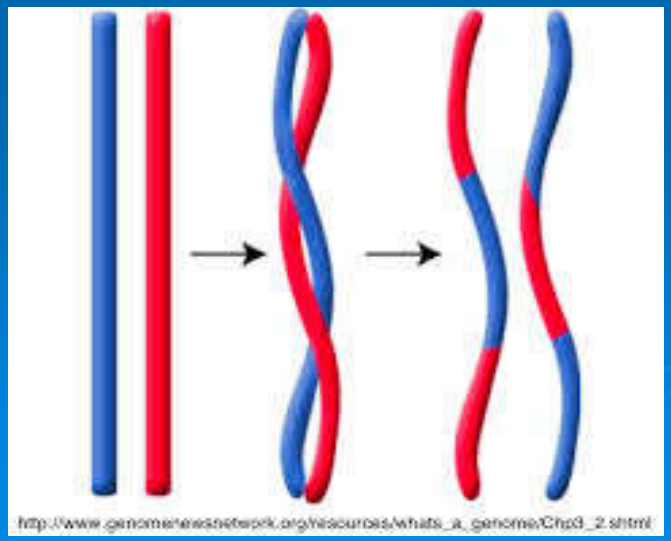
- Age
- Sex
- Temperature
- Radiation
- Chemicals
- Physical distance between genes

Significance of crossing over

- Crossing over is universal in occurrence, occurs in plants, animals, bacteria, virusesand moulds.
- Meiotic crossing over allows a more independent selection between the two alleles that occupy the positions of single genes, as recombination shuffles the allele content between sister chromatids
- Helps in proving linear arrangement of genes. Recombination does not have any influence on the statistical probability that another offspring will have the same combination. This theory of "independent assortment" of alleles is fundamental to genetic inheritance.



Chromosome Mapping



Chromosome mapping is a technique used in autosomal DNA testing which allows the testee to determine which segments of DNA came from which ancestor. In order to **map** DNA segments on specific **chromosomes** it is necessary to test a number of close family relatives

Recombination : in meiosis , recombination generates haploid genotypes differing from the haploid parental genotypes . The recombinants can be most easily **visualized by test crosses**.

Gene Linkage All the genes that are located on the same chromosome and that control the dissemination of one or two trait of certain

Linkage : is a method that allows us to determine regions of chromosomes that are likely to contain a risk gene , and rule out areas where there is a low chance of finding a risk gene , number of linkage as number of chromosome in organism ex: 23 pairs of chromosome in human= 23 linkage .

Kinds of Linkage :

1- Complate linkage : The genes closely located in the chromosome show complete linkage as they have no chance of separating by crossing over and are always transmitted together to the same gamete and the same offspring . Thus , the parental combination of traits is inherited as such by the young one .

2- In complete Linkage : The gene distantly located in the chromosome show incomplete linkage because they have a chance of separation by crossing over and of going into different gametes and offspring .

chromosome Theory of Linkage :

1- Genes are found arranged in a linear manner in the chromosomes

2- Genes which exhibit linkage are located on the same chromosomes

3- Genes generally tend to stay in parental combination , except in cases of crossing over

4- The distance between linkage genes in a chromosome determines the strength of linkage

Recombination by crossing over :

1- Recombinant frequency significantly less than 50% shows that the genes are linkaged .

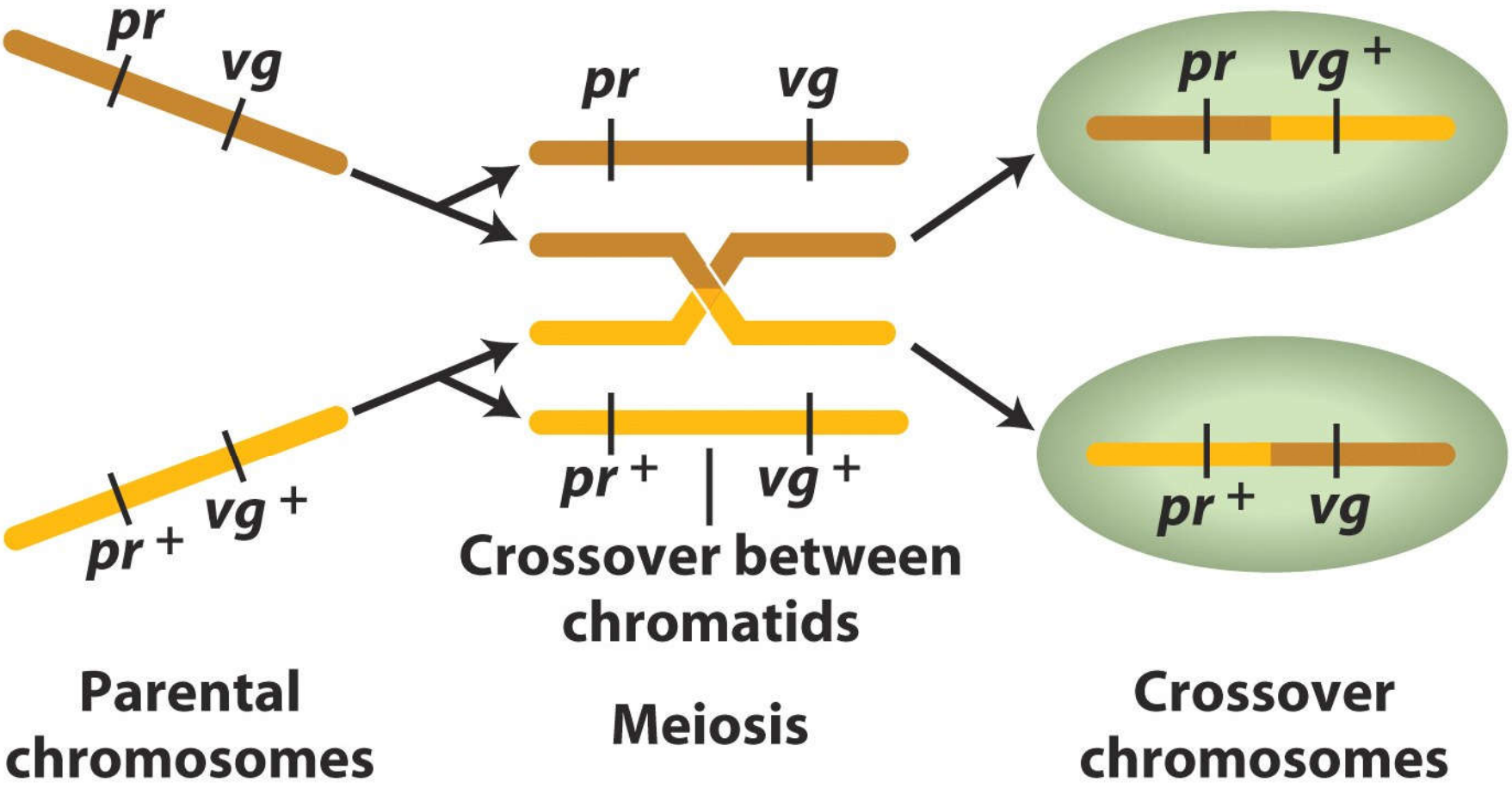
2-Recombinant frequency significantly 50% generally means that the genes are un-linkaged on separate chromosomes .

Note :

1- 0 % Less than 50% is considered a full link

2- Less than 50% is considered a link but not fully

3- more than 50% is considered a unlink


pr
vg
pr +
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Crossover between chromatids
pr
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vg
Parental chromosomes
Meiosis
Crossover chromosomes

Creating a genetic map : which shows the order of and relative distance between genes on chromosome , can be made by noting the frequency of crossing over between genes on sister chromatids . The unit of distance in a genetic map is called a map unit : one map unit is equal to one percent recombination .

Gene mapping has important applications :

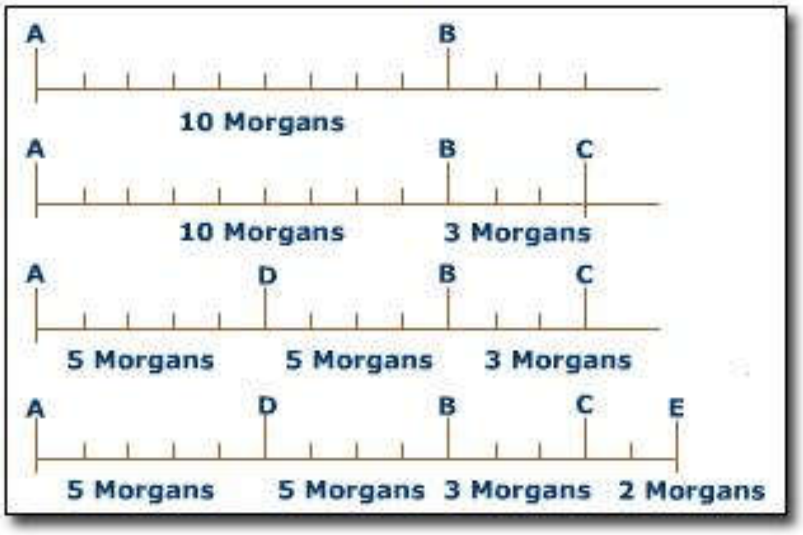
1- locating the position of genes on chromosomes

2-Estimation genetic risk

3-Human genome project is the mapping of all human genes

Chromosome map unit :

Unit of map distance between genes , and is termed as centi-morgan (cM) by Morgan geneticist .



The three-point test cross:

Example :

In Drosophila , on X chromosome the genes have recessive mutations , and are linked in these chromosome : The mutations (vermillion eyes (V) , cross-veinless wings (cv) , and cut wings(ct)) . Female **homozygous** has vermillion eye was mated with male **homozygous** has cross veinless and cut wing edge , if you have the following F2 generation ,

1- calculate the recombination and draw the map distance between these genes :

2-Consider the following data for the percents of crossing over between the genes

3- **What is the order of the three genes?**

F2 progeny:

PHENOTYPE	GAMETES	# PROGENY
vermillion eyes, normal wing vein, normal wing edges	*v* *cv*+ *ct*+	580
normal eyes, no cross vein, cut wing edges	+ *cv* *ct*	592
vermillion eyes, no cross vein, normal wing edges	*v* *cv* *ct*+	45
normal eyes, normal wing vein, cut wing edges	*v*+ *cv*+ *ct*	40
vermillion eyes, no cross vein, cut wing edges	*v* *cv* *ct*	89
normal eyes, normal cross vein, normal wing edges	*v*+ *cv*+ *ct*+	94
vermillion eyes, normal cross vein, cut wing edges	*v* *cv*+ *ct*	3
normal eyes, no cross vein, normal wing edges	*v*+ *cv* *ct*+	5
		1448

Step 1: identify non-crossover classes: (parental types as the most frequent pair of products)

Step 2: identify double crossover classes (as least frequent pair of products)

Step3: identify Single cross over classes. Usually these can be divided into groups of two with roughly equal numbers in each of the two classes in a group.

Step 4: calculate recombinant frequencies

Map Distance :

Crossing 1 + Crossing 3 / total X 100 = % m.u.

Crossing 2 + Crossing 3 / total X 100 = % m.u.

Step 5: Compare the parental and double crossover products to determine the order of the three gene loci

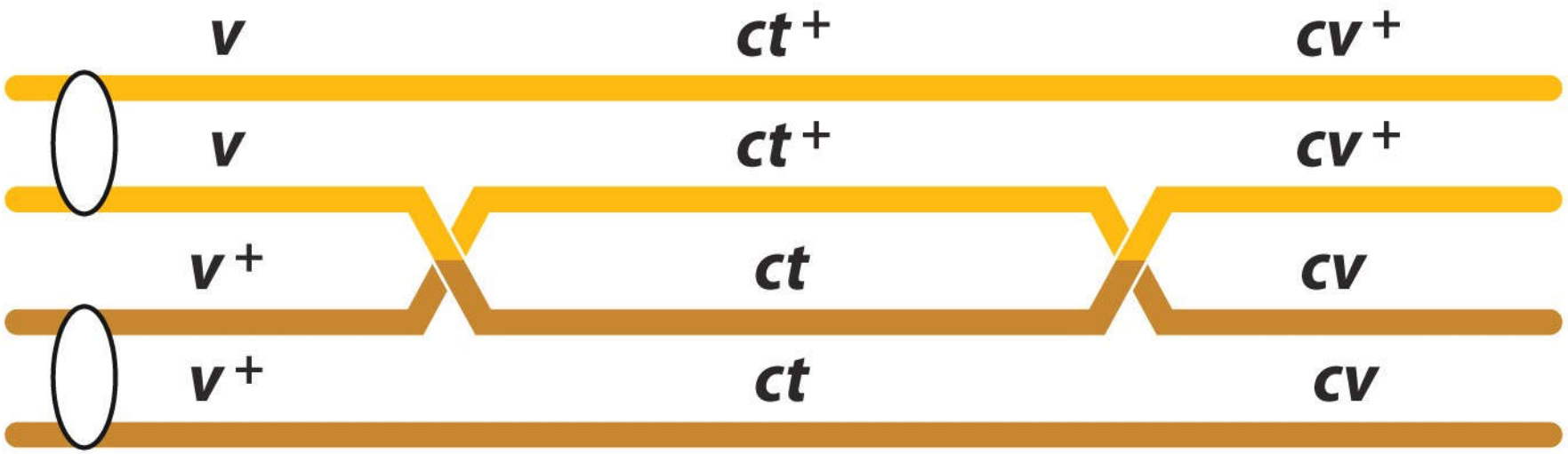
using double recombinants to deduce gene order

Double recombinants have the middle gene"flipped" relative to parental arrangement:

parental:	**v**	**cv$^+$**	**ct$^+$**
	v$^+$	**cv**	**ct**
Double :	**v**	**cv$^+$**	**ct**
(DCO)	**v$^+$**	**cv**	**ct$^+$**

This is flipped must be in the middle

So, the right order of the genes is: **v** **ct** **cv**



In dco products, the central marker is displaced relative to the parental types

Recombination frequency *v* and *ct*= $\frac{89+94+3+5}{1448}$X100= 13.2%

Recombination frequency *cv* and *ct*=$\frac{40+45+3+5}{1448}$ X 100= 6.4%

Question ;

On chromosome 3 in drosophila , there are the following mutations :

Lyra (LY) , bright red eyes (br) and between of them there is a stubble mutation (Sb) .

A Female homozygous for the 3 mutations was mated to a wild type male . If you have the following F2 generation ,

1- calculate thyhe recombination and draw the map distant between these genes :

2-Consider the following data for the percents of crossing over between the genes

Phenotype	**Genotype**	**F2 generation**
Lyra, stubble, bright red	LY Sb br	404
Wild type	+ + +	422
Lyra	LY + +	18
Stubble , bright red	+ Sb br	16
Lyra ,bright red	LY + br	75
stubble	+ Sb +	59
Lyra,stubble	Ly Sb +	4
bright red	+ + br	2
Total		1000

Sex Linked Inheritance

Sex Influence Inheritance

Sex Limited CHaracters

- There are two types of chromosomes, Autosomes and Sex chromosomes
- *Autosomes* are those chromosomes that are not involved in sex determination.
- Sex chromosomes are those chromosomes that determine the sex of an organism.
- A human somatic cell has two sex chromosomes: XY in male (hetero-gametic) and XX in female (homo-gametic).
- In birds the female (ZW) is hetero-gametic and male (ZZ) is homo-gametic.
- Ordinarily, F_1 and F_2 generations from reciprocal crosses yield identical results and it does not matter if the female or male parent had the recessive character. Further male and females in the progeny show identical ratios.

- This ratio change in reciprocal cross due to phenomenon of sex linkage.
- Sex linkage is an association of a character with sex of the progeny during inheritance.
- Sex linkage refers to the association of a hereditary trait with sex chromosomes.
- Most genes for sex link traits are present only on the X-chromosome. The Y-chromosome is smaller (Very few genes are located on Y chromosome).
- Because of their location in the sex chromosomes, they are said to be *"sex linked traits"*.

- Certain sex linked genes are located only on X chromosomes (in XY system) or on the Z chromosome (ZW system) and their alleles are absent from Y chromosome.
- Characters for which genes are located on sex on X chromosomes are known as sex linked traits.
- Genes controlling these traits are called sex linked genes.
- Linkage of such genes is referred to as sex linkage.
- Inheritance of such genes or characters is known as sex linked inheritance.
- X-linked inherited diseases occur more frequently in males because they only have one X chromosome.

- X linked inheritance may be X - linked dominant, X-linked recessive or X - linked co dominant.

- Sex linked genes show the dominance recessive relationship only in homogametic sex (e.g. female in humans) because it can carry two alleles at the sex linked locus. So, female can be homozygous or heterozygous.

- In the heterogametic sex (males in humans and females in birds) do not show dominance recessive relationship because the existence of only a single X or Z chromosome.
- The term ***hemizygous*** is used for X linked gene in males as they carry only one allele with regard to sex linked trait (In birds the female is hemizygous).

- ***Pseudo-dominance*** is phenomenon in which a single copy of recessive allele is phenotypically expressed because a second copy of the gene is absent. This pseudo dominance found in male in humans and in female in birds because they are hemizygous.

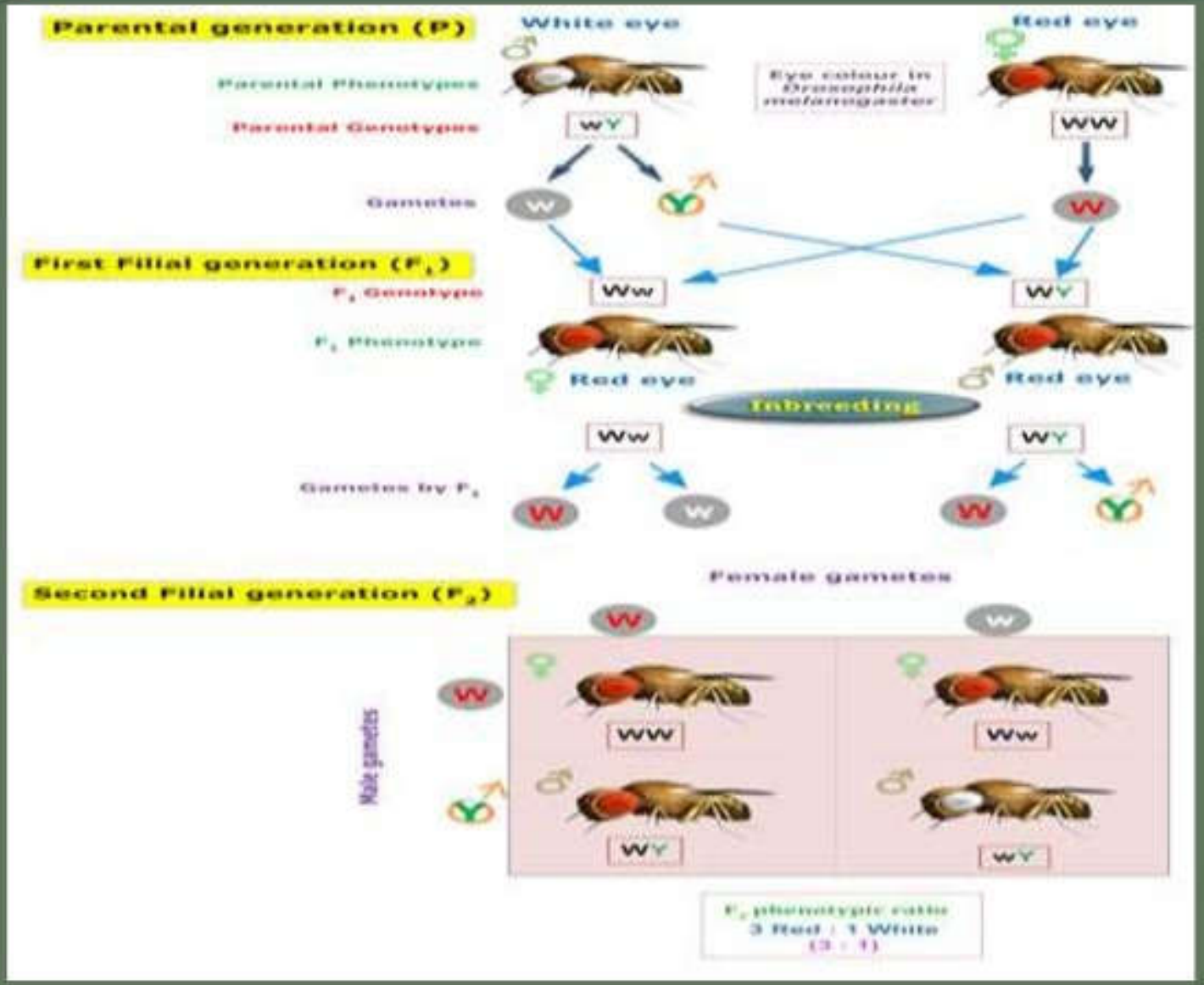
CHARACTERISTICS OF SEX LINKED INHERITANCE

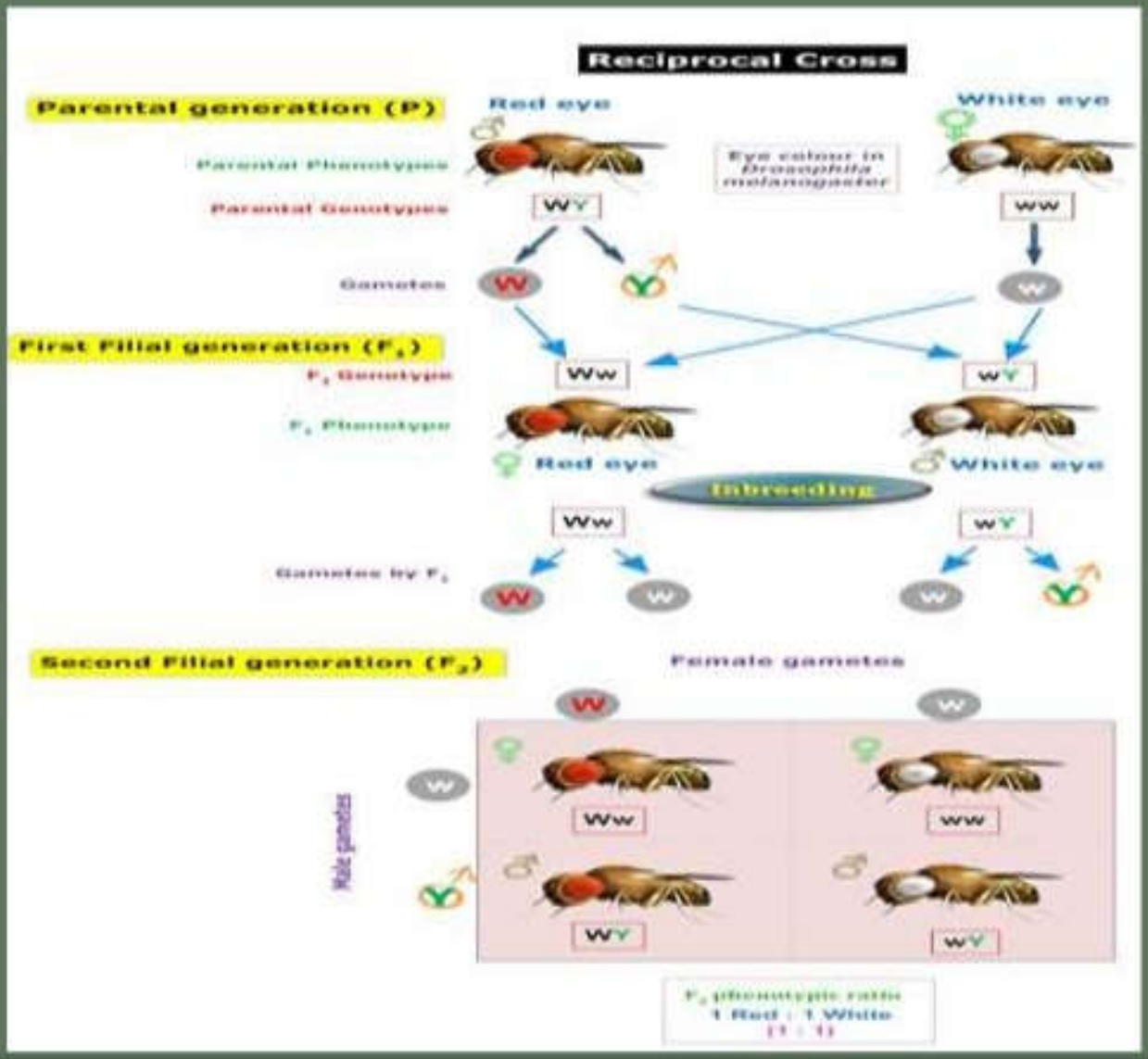
- The frequency of individuals showing a recessive sex linked trait is markedly higher in heterogametic sex than that in the homogametic sex.
- The gene governing the sex linked traits are not transmitted from male parent to directly their male progeny. e.g. white eye gene is not transmitted from male to male in drosophila fly.
- The sex linked gene are located on X chromosomes only but not present on Y chromosome

- Inheritance of sex linked characters does not follow normal segregation pattern.
- In human and drosophila fly, male transmits its sex linked genes to all its daughters.
- These daughters transmit this gene to half of their male progeny.
- As a result, a sex linked recessive gene is transmitted from male to its female progeny and then to half of male progeny of such females.
- Thus the ***sex linked genes pass from male female and then back to male***, this type inheritance pattern is called as ***criss-cross inheritance pattern***.

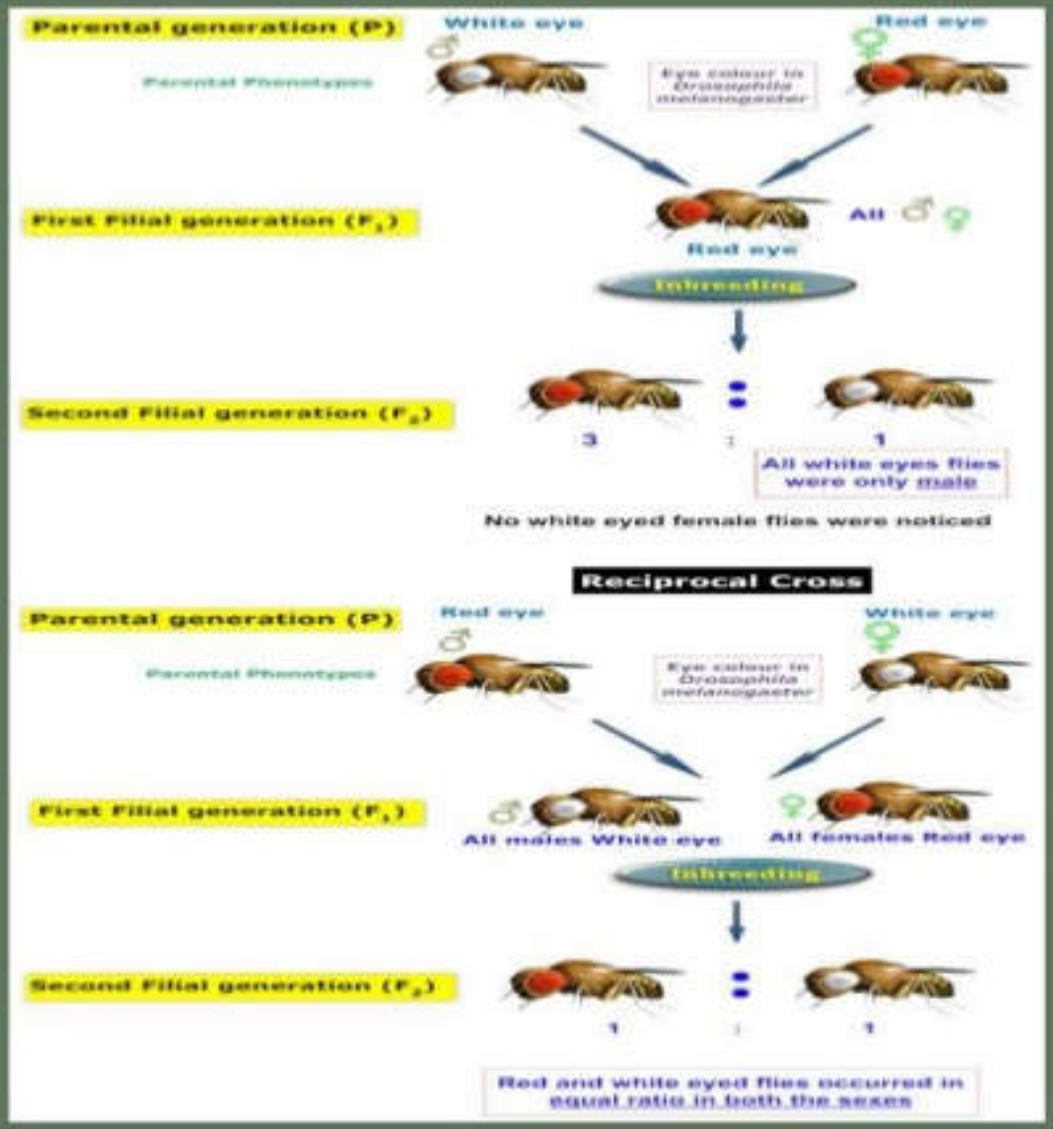
X-LINKED RECESSIVE

- In X-linked dominance, both males and females can display the trait or disorder by having only one copy of the allele. E.g. barred pattern in poultry.
- In X-linked recessive, male can display the trait by having only one copy allele but in female it display when both recessive alleles are present Examples are:
- Eye color in drosophila
- Colour blindness in Human
- Haemophilia in Human
- Feather pattern in poultry
- Rate of feathering in poultry
- Down colour pattern in poultry
- Thomas Hunt Morgan (1910) observed a male *Drosophila melanogaster* with white eyed (mutant) mated fly with a red eyed (Normal) female and got the following result. (As per mention in figures)


Parental generation (P)
White eye
Red eye
Parental Phenotypes
Parental Genotypes
Eye colour in Drosophila melanogaster
wY
WW
Gametes
w
Y
W
First Filial generation (F1)
F1 Genotype
F1 Phenotype
Ww
WY
Red eye
Red eye
Inbreeding
Ww
WY
Gametes by F1
w
w
W
Y
Second Filial generation (F2)
Female gametes
Male gametes
W
w
WW
Ww
WY
WY
F2 phenotypic ratio
3 Red : 1 White
(3 : 1)


Reciprocal Cross
Parental generation (P)
Red eye
White eye
Parental Phenotypes
Eye colour in Drosophila melanogaster
Parental Genotypes
XᵂXᵂ
XʷY
Gametes
Xᵂ
Y
Xʷ
First Filial generation (F1)
F1 Genotype
XᵂXʷ
XᵂY
F1 Phenotype
Red eye
White eye
Inbreeding
Gametes by F1
Xᵂ
Xʷ
Second Filial generation (F2)
Female gametes
Male gametes
XᵂXʷ
XʷXʷ
XᵂY
XʷY
F2 phenotypic ratio
1 Red : 1 White
(1 : 1)

- In F_2 generation, equal number of red and white eyed individuals with normal sex ratio appeared. (That finding different from normal autosomal gene inheritance in which there is no difference in reciprocal crosses). The white-eye colour gene is located on the X-chromosome.


Parental generation (P)
White eye
Red eye
Parental Phenotypes
Eye colour in Drosophila melanogaster
First Filial generation (F_1)
All ♂ ♀
Red eye
Inbreeding
Second Filial generation (F_2)
3 : 1
All white eyes flies were only male
No white eyed female flies were noticed
Reciprocal Cross
Parental generation (P)
Red eye
White eye
Parental Phenotypes
Eye colour in Drosophila melanogaster
First Filial generation (F_1)
All males White eye
All females Red eye
Inbreeding
Second Filial generation (F_2)
1 : 1
Red and white eyed flies occurred in equal ratio in both the sexes

- Males have only one X chromosome, a single recessive allele on that X chromosome will act as pseudo dominance and cause the disease.
- Females have two X chromosome, so two copies of the recessive allele are required for the disease to express in females.
- Males never pass the disease to their sons because there is no male-to-male transmission of the X chromosome.
- Males pass the defective X chromosome to all of their daughters, who are described as obligate carriers.

- Transmission of the sex linked disease from affected males to male grand children through carrier daughters is described as a *"Nasse's Law".*
- Female carriers pass the defective X chromosome to half their sons.

Haemophilia

It is a hereditary defect which is governed by recessive gene and is inherited through females.

In case of a marriage between hemophilic woman and normal man, the disease will be transmitted to 50% of the sons even if the gene is in heterozygous condition in the carrier.

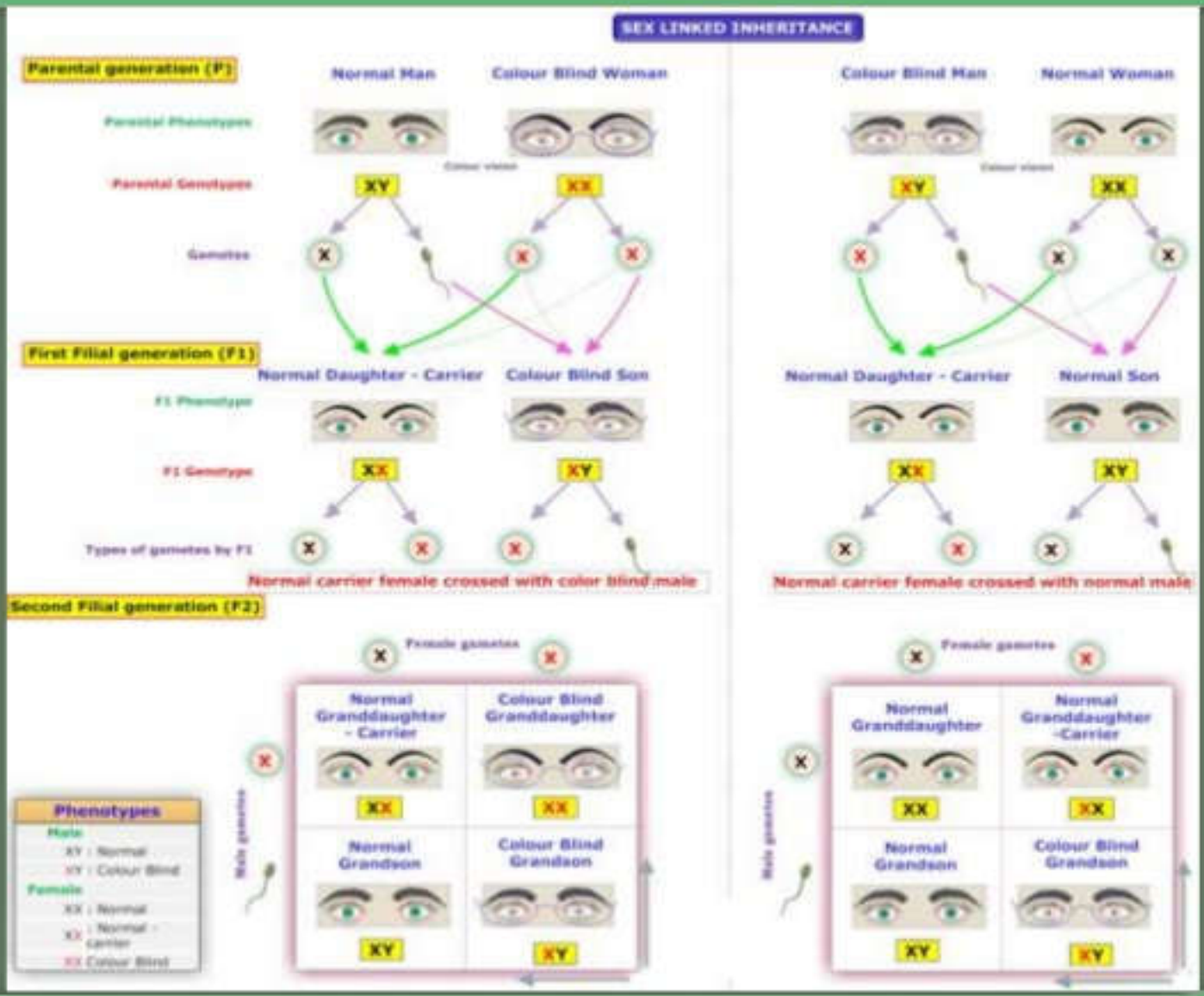
Parents	Haemophilic woman	Normal man
Genotypes	X^hX^h	X^HY
	Sperms	
	X^H	Y
Ovum	X^h	X^HX^h (Normal) / X^hY (haemophilic)

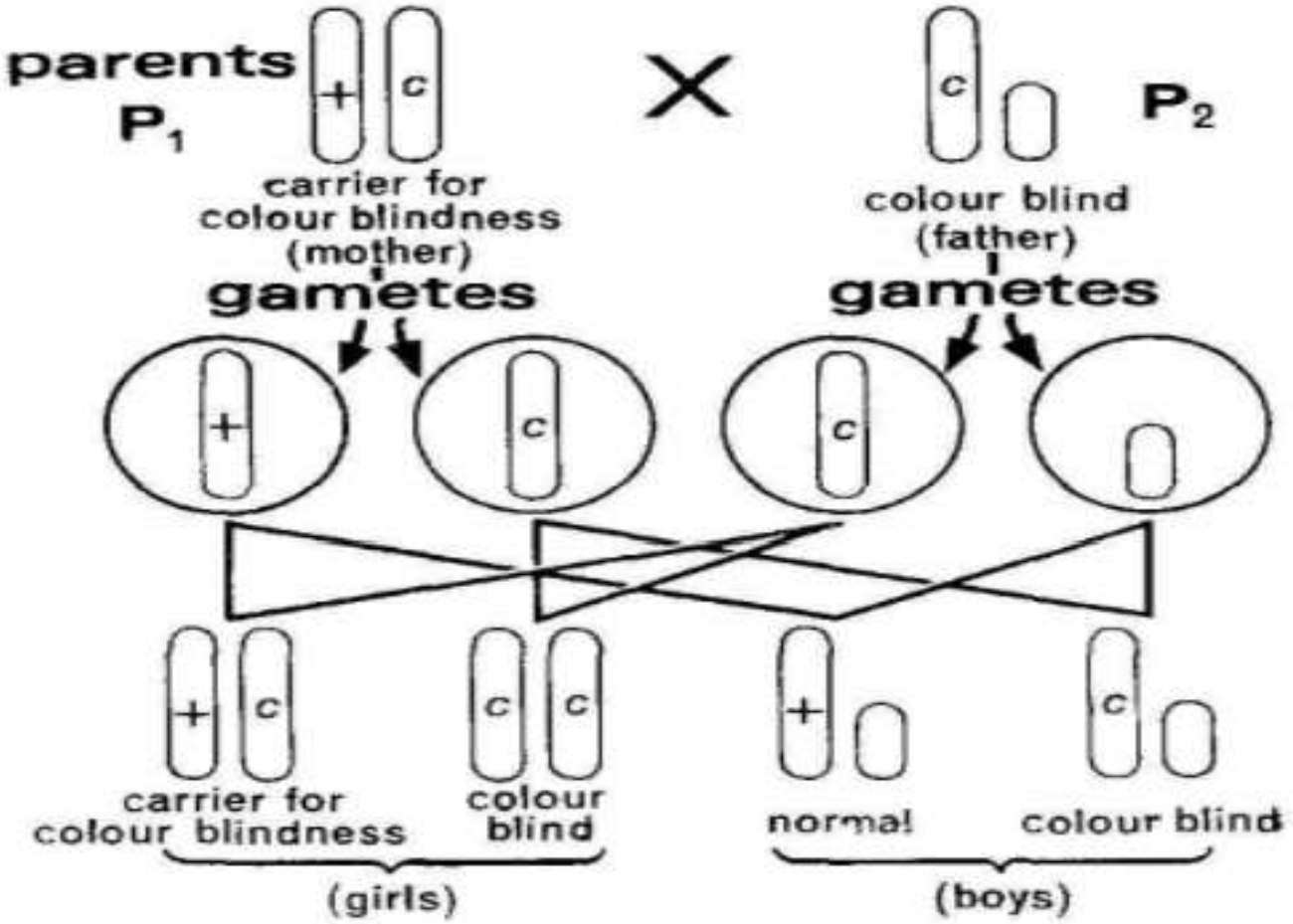
Parents	Normal woman	Haemophilic man
Genotypes	X^HX^H	X^hY
	Sperms	
	X^h	Y
Ovum	X^H	X^HX^h (Normal) / X^HY (Normal)
	X^H	X^HX^h (Normal) / X^HY (Normal)

Normal but Carrier for haemophilia

Colour blindness

- This trait is governed by a recessive gene located on X chromosome.
- A person having such defect cannot differentiate between red and green colour.
- Sons from the marriage between colour blind man and normal woman will be normal, but daughters will carry such genes in heterozygous condition.
- Marriage of such carrier girl with colour blind boy will produce children in which both male and female children will be colour blind each in 50% cases.


SEX LINKED INHERITANCE
Parental generation (P)
Normal Man
Colour Blind Woman
Colour Blind Man
Normal Woman
Parental Phenotypes
Parental Genotypes
XY
XX
Gametes
First Filial generation (F1)
Normal Daughter - Carrier
Colour Blind Son
Normal Daughter - Carrier
Normal Son
F1 Phenotype
F1 Genotype
XX
XY
Types of gametes by F1
Normal carrier female crossed with color blind male
Normal carrier female crossed with normal male
Second Filial generation (F2)
Female gametes
Male gametes
Normal Granddaughter - Carrier
Colour Blind Granddaughter
Normal Grandson
Colour Blind Grandson
Normal Granddaughter
Normal Granddaughter -Carrier
Phenotypes
Male
XY : Normal
YY : Colour Blind
Female
XX : Normal
XX : Normal - carrier
XX Colour Blind



Inheritance of sex linked colour blindness in human

Sex linked dominance

Sex linkage in poultry

In poultry, female individual is heterogametic having only one X-chromosome (XO condition) and male is homogametic having two X-chromosomes (XX). Therefore, inheritance pattern in relation to sex will be reversed in this case.

Barred plumage is a popular example of sex linked character in poultry. In an individual, which has barred plumage, feathers are banded with bars of black on a white background.

Barred ♀ x Non barred ♂

- If barred (BW) female individual is crossed with non barred male (bb) individual, (barred is normal and dominant over non barred), only barred males and non barred females are obtained in F_1 generation.
- In F_2 generation, barred and non barred individuals appear in 1 : 1 ratio, among male as well as female populations.

Non barred ♀ x barred ♂

- When non barred female individual (bW) is crossed with barred male (BB), all progeny (male as well as female) would be barred in F_1 generation.
- In F_2 generation 50 % females will be barred and rest 50 % non barred while all males would be barred.

Barred (♀) (BW) x Non barred (♂) (bb)

Male Gametes		Female Gametes	
		B	W
b	Bb Barred Male	bW Non barred Female	

1:1 = Barred: Non barred

F_2 Generation

Female Gametes		Male Gametes	
		B	b
b	Bb Barred Male	bb Non Barred Male	
W	BW Barred Female	bW Non Barred Female	

1:1 = Barred: Non barred
50 % barred : 50% non barred
50% male barred & 50% male non barred
50% female barred & 50% female non barred

Non Barred (♀) x Barred (♂)
(bW) (BB)

Male Gametes		Female Gametes	
		b	W
B	Bb Barred Male	BW Barred Female	

100% barred

F_2 Generation

Female Gametes		Male Gametes	
		B	b
B	BB Barred Male	Bb Barred Male	
W	BW Barred Female	bW Non Barred Female	

3:1 = Barred: Non barred
100% male barred
50% female barred & 50% female non barred

Genes Linked with Y Chromosome

- Non-homologous portion of Y chromosome contains few genes.
- Two genes appear to be located in this region in Drosophila for male fertility.
- Seventeen genes are present in the non-homologous portion of human Y chromosome.
- Genes which are present in Y chromosome are known as holandric genes.
- The best example of holandric condition is presence of excessive hair on ears in man, the condition is known as hypertrichasis, which is a Y linked character.
- Y-linked genes would be transmitted directly from father to son and never appears in female. Examples are :

- Histocompatability gene (H-Y) present on the short arm of human Y - chromosome.
- SRY (Sex-determining Region Y) genes.
- The hair on pinna of the ear in man has been interpreted as due to holandric gene.

Features of sex-linked recessive diseases

- The frequency is higher in heterogametic than homogametic sex.
- It is transmitted from affected man through normal daughter to half of the grandsons.
- Does not occur in a woman unless her father has it.
- All the sons of the woman having this trait are affected.

Features of sex-linked dominant diseases

- More common in females.
- All female offspring of affected male will be affected
- If mother is normal sons will not be affected with the diseases.

APPLICATION OF SEX LINKAGE

Sexing of day old chicks

- **Auto-sexing** is method of sexing in day old chicks by their different appearances when they have hatched.
- The chicks are sexed at hatching as poultry farmers/breeders are interested to keep only the female chicks for egg production in future.
- In traditional method of sexing is vent method (Japanese method).
  Time consuming, Laborious, Expensive and require experience
- While the sexing by sex linkage is less expensive, more accurate more convenient.

- In birds (butterflies, silkworm, moths, fishes) males are homogametic (ZZ) and females are heterogametic (ZW).
- The 'barring' pattern is sex-linked. That is the males have two chromosomes for barring and the females only one chromosome resulting in to, a day old chicks have a light coloured patch on the top of the head.
- When these light coloured patches are combined with brown colour, there is a very clearly defined stripe the body.

- The male chicks on the other-hand have a light patch covering most of the head and there is only a very blurred resulting in to unclear body stripe.
- The first auto-sexing breed was developed and described by Punnett and Pease (1930).
- Some autosexing traits in poultry:
  - Barred (B) and non-barred (b) plumage pattern in Plymouth Rock
  - Silver plumage (S) in Sussex x Golden plumage (s) in Rhode Island Red and New Hampshire
  - Slow feathering (K) x Fast feathering (k)

Reducing cost of broiler chick production:

- Sex linked dwarfing gene (dw) offers potential value by reducing cost of commercial broiler chick production.
- The normal size of hen who used for production of broiler chicks are heavy and required much feed, space, excess fat deposition and produce abnormal eggs. The adult dwarf mother (dw W) weigh 30 % less than the normal sized hen (Dw W).
- When this dwarf (dw W) mother mated with normal sized male (Dw Dw). The commercial chicks resulting from this mating have normal size (Dw dw ♂ and Dw W♀).

Sex Influenced Traits

- The traits which are controlled by genes present on autosomes but whose expression is influenced by the sex of individual are called sex influence traits.
- A trait which is influenced by the sex of the individual is called sex-influenced trait.
- Sex-influenced traits are those that are dominant in one sex but recessive in the other. This is due to the different cellular environments in males and females provided by sex hormones.
- Different hormonal environments affect expression of heterozygote of a trait but homozygotes are unaffected and express the trait unrelated of the hormones produced.

These genes have three main features:

1. Located in the autosomes.
2. Express more frequently in one sex than other.
3. Expression of such characters appears to be governed by sex hormones
4. No difference between reciprocal crosses in F_1 and F_2.
5. Dominance in the heterozygous condition depends on the sex of the individual

Coat Colour in Ayershire cattle			Sex influence characters	Pattern of baldness in humans		
Genotype	Phenotype			Genotype	Phenotype	
	Bull	Cow			Man	Woman
MM	Mahogany	Mahogany		BB	Bald	Bald
Mm	Red	Red		Bb	Bald	Non bald
mm	Red	Red		bb	Non bald	Non bald

Example: Horned condition in sheep

Dorset horn – both males and females horned

Suffolk – both males and females hornless (polled)

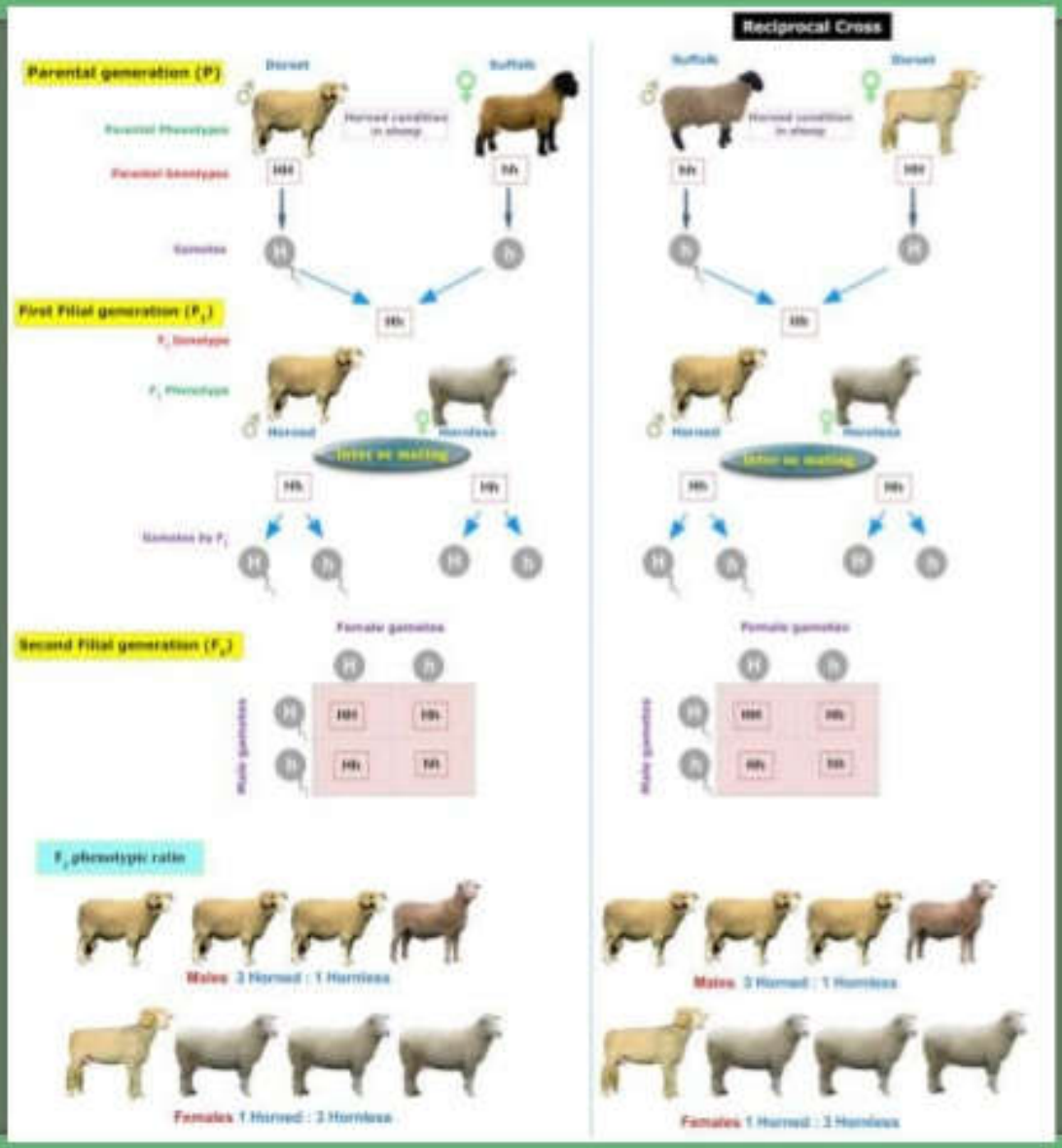
Dorset (HH) x Suffolk (hh)

Hh Horned if male progeny

Hornless (polled) if female progeny

In F_2 Generation

Horned condition in sheep		
Genotype	Phenotype	
	Male	Females
HH	horned	horned
Hh	horned	hornless
hh	hornless	hornless


Reciprocal Cross
Parental generation (P)
Dorset
Suffolk
Parental Phenotypes
Horned condition in sheep
Parental Genotypes
HH
hh
Gametes
H
h
First Filial generation (F_1)
F_1 Genotype
Hh
F_1 Phenotype
Horned
Hornless
Inter se mating
Gametes by F_1
Second Filial generation (F_2)
Female gametes
Male gametes
F_2 phenotypic ratio
Males 3 Horned : 1 Hornless
Females 1 Horned : 3 Hornless

Sex Limited Traits

- Some autosomal genes express characters in only one sex (either male or female).
- These are autosomal genes but can be expressed only in particular sex. As their expression is limit to only one sex, they are called sex-limited traits. **Or**
- Those traits whose development is limited to only one sex are known as sex limited traits.

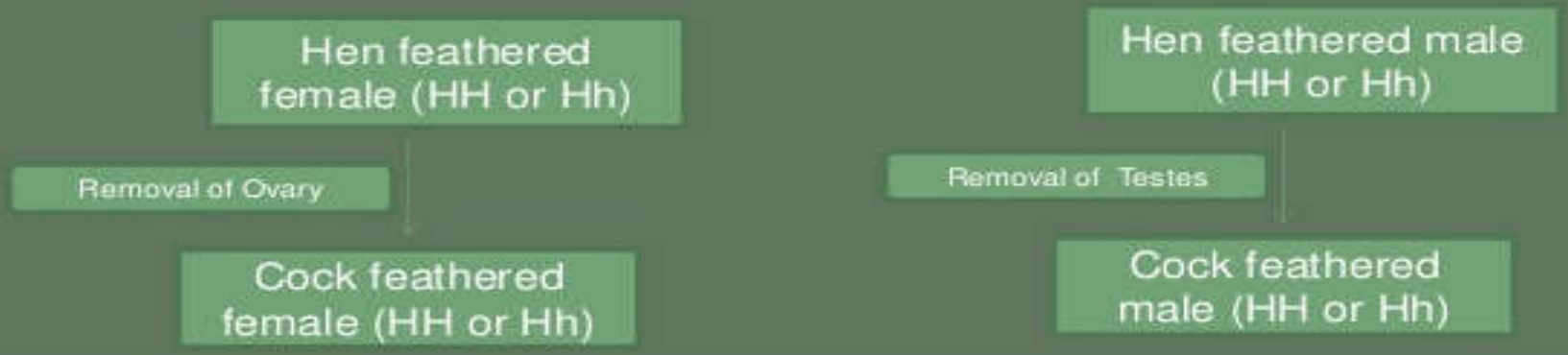
Main characteristics:

1. They express in one sex only and not in the other sex.
2. Sex limited genes may be located either in sex chromosome or autosomes.
3. Sex limited genes control the expression of primary and secondary sex characters

Examples are:

- Milk production in mammals
- Egg production in chicken
- Genes responsible for secondary sexual characteristics as well as primary sexual characters like… Development of Hair, mammary gland etc
- Cock-feathering trait in bird

- Hen- feathering result from a single gene "H" and cock-feathering result from its allele, "h".
- The expression of gene “H” and “h” depends upon the sex hormones.
- The “h” gene produces hen feathering if female hormone is present, cock-feathering if female hormone is absent.
- This was proved by removing the ovaries in female or testes in male birds, which possesses hen feathered, results in production of cock feathering eventhough “H” allele present.



SEX LIMITED INHERITANCE

Plumage pattern in Poultry

Genotype	Phenotype	
	Cock	Hen
HH	 Hen feathered	 Hen feathered
Hh	 Hen feathered	 Hen feathered
hh	 Cock feathered	 Hen feathered

	Sex Linked Characters	Sex Limited Characters
1	Genes are located on sex or X chromosomes.	Genes ate located on sex chromosomes or autosomes.
2	Can express in both the sexes.	Express in one sex only.
3	Include characters not related to sex.	Include primary and secondary sex characters.
4	Examples- White eye in Drosophila, Hemophilia and Colour blindness in man	Examples – Milk production, Egg Production

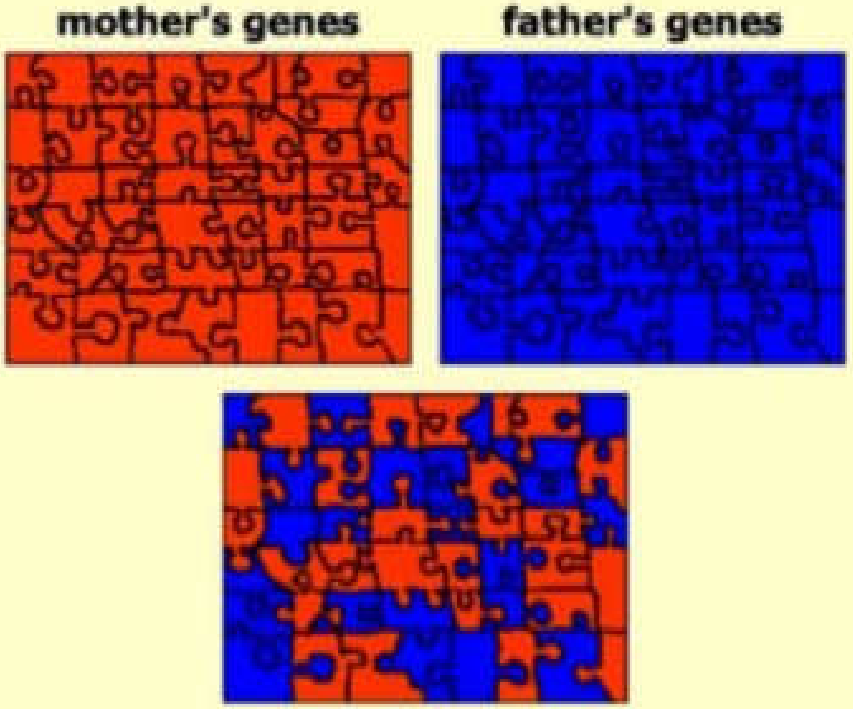
SEX-LINKED INHERITANCE

BY: MRS. PRECILLA C. STEPHEN

DEFINITION

- It is the inheritance of a trait(phenotype) that is determined by a gene located on one of the sex chromosome.

INHERITANCE OF TRAITS

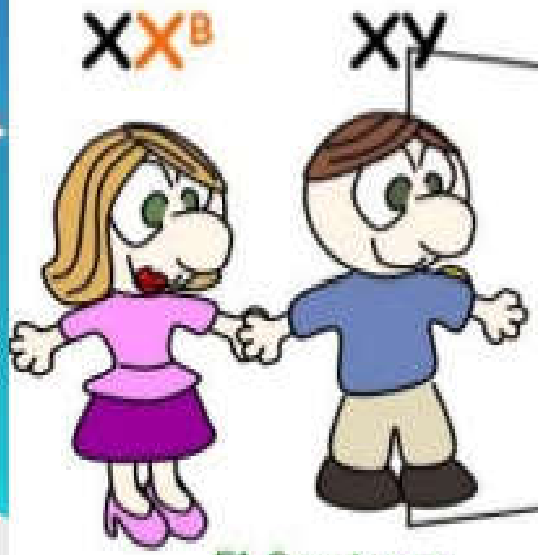


X-LINKED DOMINANT INHERITANCE

- Dominant gene is carried on the X-gene
- Male – get their X-chromosome from their mother
- Females – get their X-chromosome from both of their parents
- If the mother is a carrier of the mutated gene
- 50% of the son or/and daughter will be affected
- 50% of the son or/and daughter will be normal

SEX-LINKED TRAITS

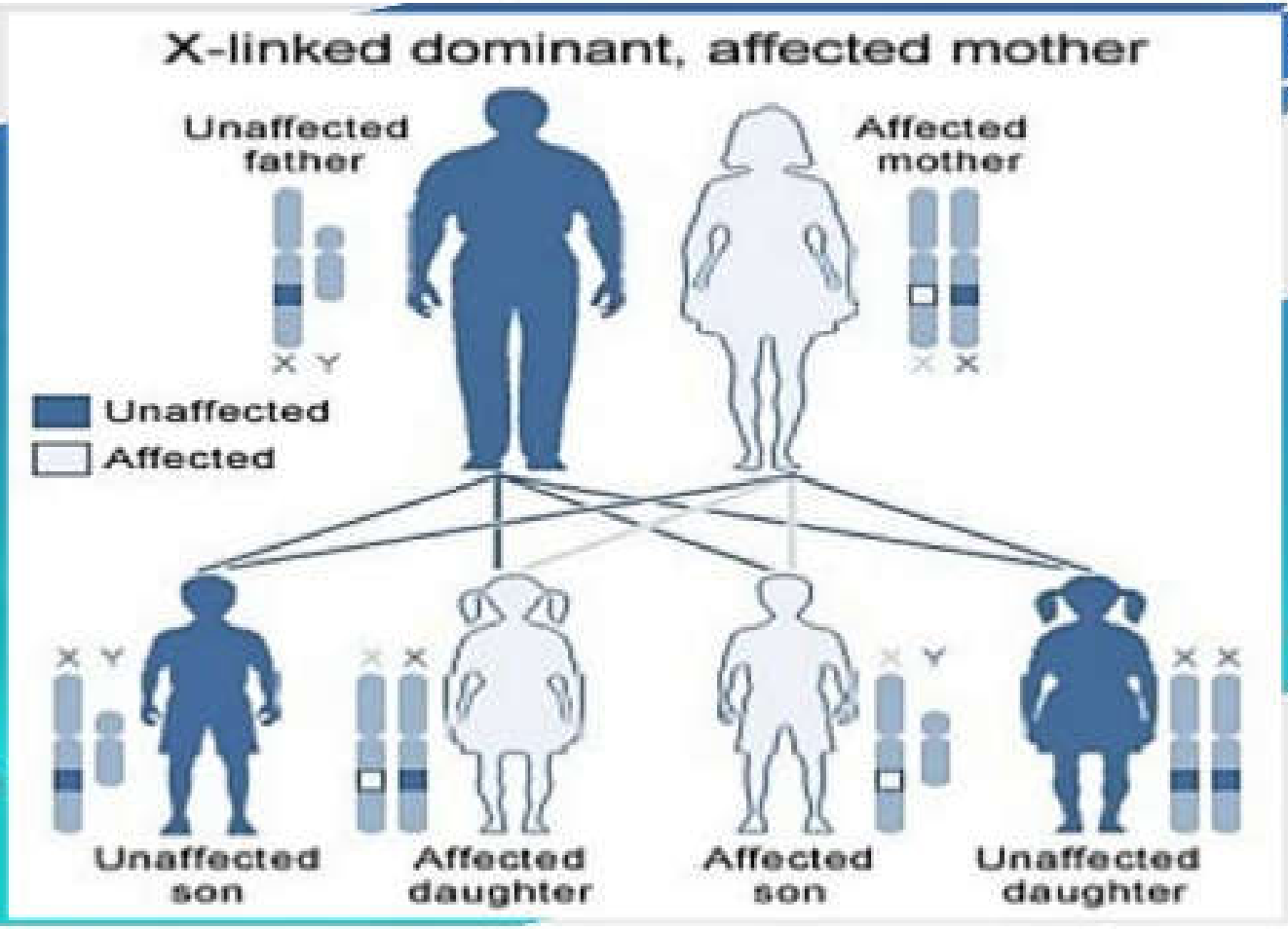
So how is baldness inherited?



	X	Y
X	XX	XY
X^B	XX^B	X^BY

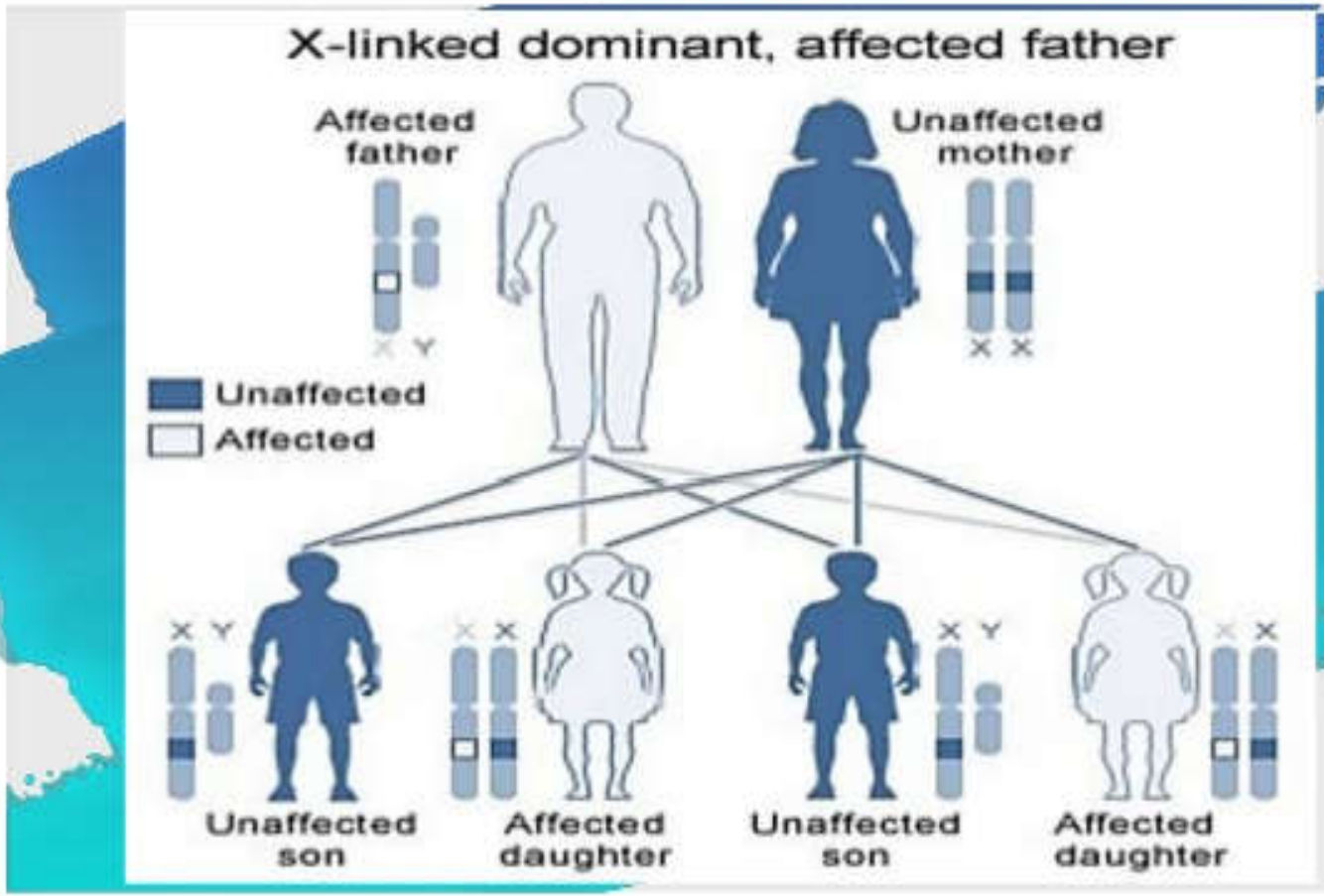
F1 Genotypes:
25% XX, 25% XX^B, 25% XY, 25% X^BY

F1 Phenotypes:
50% of males are bald. Females are "normal" (wild type)


X-linked dominant, affected mother
Unaffected father
Affected mother
X Y
X X
Unaffected
Affected
X Y
X X
X Y
X X
Unaffected son
Affected daughter
Affected son
Unaffected daughter

X-LINKED DOMINANT INHERITANCE

- If the father is a carrier of the mutated gene
- 100% of his daughter will have the disorder
- 0% of his son will have the disorder


X-linked dominant, affected father
Affected father
Unaffected mother
Unaffected
Affected
Unaffected son
Affected daughter
Unaffected son
Affected daughter

X-LINKED DOMINANT INHERITANCE

- If both parents are a carrier of the mutated gene
- 100% of his daughter will have the disorder
- 50% of his son will have the disorder
- 50% of his son will be unaffected or normal

X-LINKED RECESSIVE INHERITANCE

A mode of inheritance on the X-Chromosome that causes the phenotype to be expressed

Female carriers have only copy of the gene and usually don't express the phenotype.

Ex: Color blindness, haemophilia

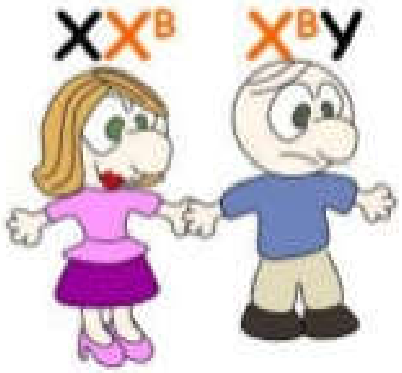
Y- LINKED INHERITANCE

- Holandric Inheritance
- Y-chromosome is small and doesn't contain numerous genes
- Y-linked diseases or disorder are very rare
- It occurs between fathers and his sons.

SEX-LINKED TRAITS

How is this possible?!

If the father is bald, and the mother is a carrier, then half of her children will become bald



	X^B	Y
X	X^BX 	XY 
X^B	X^BX^B 	X^BY 

SEX-LINKED TRAITS

So how is hemophilia inherited?

In the same way as baldness, hemophilia is inherited usually because the mother is a carrier. Once again, usually male children are affected

XX^H XY

	X	Y
X	XX	XY
X^H	XX^H	X^HY

10. Sex Determination in Animals

The development of a zygote into male or female is called ***sex determination.***

Sex is a character. It has two alternatives, namely ***maleness*** and ***femaleness.*** The male produces the sperm and the female produces the egg.

Sex is determined by the following factors:

1. *Chromosomes*
2. *Environment*
3. *Hormone*
4. *Metabolism*
5. *Parasites.*

Sex Determination in Man

The development of an organism into male or female is called ***sex determination.***

Sex is a character. It has two alternatives, namely ***maleness*** and ***femaleness.*** The male produces the sperm and the female produces the egg.

In man, sex is determined by three factors, namely-

1. *Chromosomes*
2. *Barr body*
3. *Hormones*

1. Sex Determination by Chromosomes

The determination of sex by chromosomes is called ***chromosomal theory*** of sex determination. It was proposed by *Mc Clung*

The female has two X chromosomes and the male has one X chromosome and one Y chromosome.

The female is ***homogametic*** and it produces only one type of eggs all carrying one X chromosome.

The male is ***heterogametic*** and it produces two types of gametes; one type of sperm carries one X chromosome and the other

In human beings, the sex is determined by the sperms. When a sperm carrying X chromosome fuses with the egg, the resulting baby is female. When a sperm carrying Y chromosome fuses with the egg, the resulting baby is male. Thus, ***father*** determines the sex of a baby.

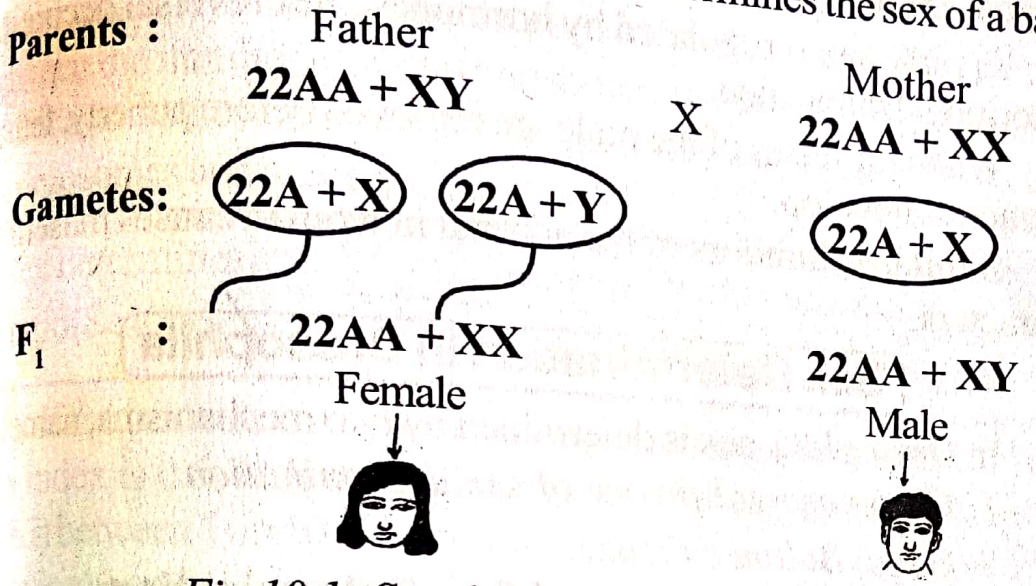


Fig.10.1: Sex determination in Man.

2. Sex Determination by Barr body

The darkly stained inactivated X chromosome attached to the inner surface of nuclear membrane is called ***Barr body.*** It was discovered by ***Barr.*** It is also called ***sex-chromatin.***

The Barr body is the ***inactivated X chromosome.***

The sex is identified by the presence or absence of Barr body.

The male has no Barr body in the nucleus.

The female has one Barr body.

The triploid female has two Barr bodies.

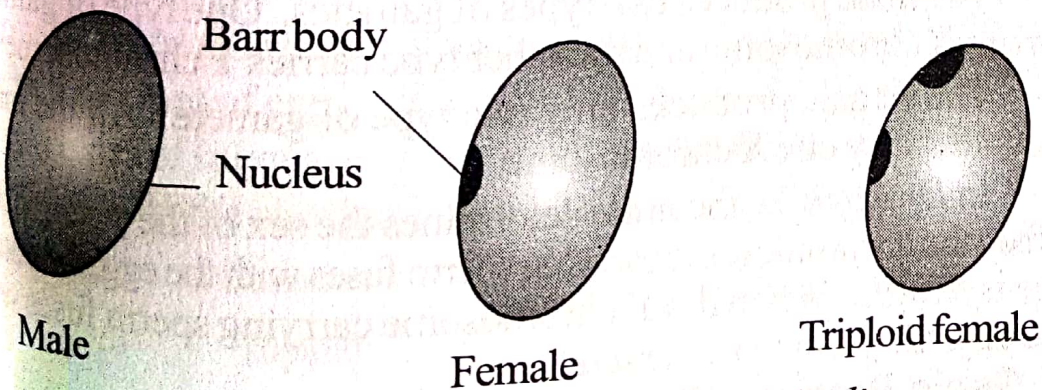


Fig.10.2 : Sex determination by Barr bodies.

The number of Barr bodies is always one less than the expected number of X chromosomes. The normal females have 2X chromosomes. So the number of Barr body is 2-1 = 1.

The normal males have one X chromosome. So there is no Barr body (1-1 = 0). The triploid female has 3X chromosomes. So it has 2 Barr bodies (3-1).

3. Sex Determination by Hormones

In man, sex is regulated by hormones. Sex reversal occurs due to hormonal unbalance.

When the testes of the male are removed before puberty, female characters develop.

Similarly, tumours of the adrenal in woman causes masculine characters.

Sex Determination in Drosophila

In *Drosophila,* sex is determined by two mechanisms, namely

1. *Chromosomal theory of sex determination*
2. *Genic Balance theory*

1. Chromosomal Theory of Sex Determination

According to chromosomal theory, sex chromosomes determine the sex of *Drosophila.* The female has XX chromosomes and it is ***homogametic.*** The male has XY chromosomes and it is ***heterogametic.***

Drosophila has 4 pairs of chromosomes. Of these 3 pairs are ***autosomes*** and one pair is ***allosomes*** (sex chromosomes).

The male has 3 pairs of autosomes and one pair of sex chromosomes. The sex chromosomes are ***XY.***

The female has 3 pairs of autosomes and one pair of sex chromosomes. The sex chromosomes are ***XX.***

The male produces two types of gametes. One type of gamete carries ***X*** chromosome and the other type carries ***Y*** chromosomes.

The female produces only one type of gamete. All the male gametes carry one ***X*** chromosome.

In *Drosophila,* the ***male*** determines the sex of the young ones. When the ***X***-chromosome carrying sperm fuses with the egg, the young one is ***female.*** When the ***Y***-chromosome carrying sperm fuses with the egg, the young one is ***male.***

2. Genic Balance Theory

This theory was formulated by ***Bridges.*** According to this theory, sex is determined by the relative number of X chromosomes and autosomes. It is actually the ratio between the X chromosomes and autosomes determi...

The X chromosomes carry female stimulating genes and the autosomes (A) seem to carry the male stimulating genes. There is no sex influencing genes in Y chromosomes. Haploid sets of autosomes are represented as n (A) and diploid sets of autosomes are represented as 2n(A). The sex of an animal is determined by the ratio between the number of X chromosomes and the number of haploid sets of autosomes. The ratio is the quantitative balance between X chromosomes and autosomes.

$$\text{Sex determining ratio (Sex index)} = \frac{\textit{Number of X chromosomes}}{\textit{Number of haploid sets of autosomes}}$$

If the sex index is 1, the individual develops into female. If the sex index is 0.5, it develops into male. If the ratio is intermediate (0.67) between 1 and 0.5 the resulting individual is an ***intersex***. If the ratio is above 1 (1.5), the sex is super female and if the ratio is below 0.5 (0.3), the sex is supermale.

In male *Drosophila,* there are 2 sets of autosomes 2n(A) and one X chromosome. Hence the ratio is X/2n(A)+1/2=0.5. In female, there are two sets of autosomes 2n(A) and two X chromosomes. Hence the ratio is 2/2 = 1.

Bridges also explained the formation of supersexes and intersexes in *Drosophila.* He found some *Drosophila* females with triploid sets of chromosomes 3n(A) XXX. These triploid females are much like the normal diploid ones in appearance and are fertile. Bridges crossed this triploid female with normal diploid male. The diploid normal male produces two types of sperms. The triploid female produces four types of eggs. When the four types of eggs are fertilized by two types of sperms, eight sexually distinct kinds of offspring are produced as in the checker board.

Parents: Female Triploid **3n(A)+XXX** X Male Diploid **2n(A)+XY**

Gametes: 2n (A)+X; n (A)+XX; 2n (A)+XX; n (A)+X; n A+X; n A+Y

1.	Superfemale	3X	2n(A)
2.	Triploid female	3X	3n(A)
3.	Diploid female	2X	2n(A)
4.	Intersex	2X	3n(A)
5.	Intersex	2XY	3n(A)
6.	Normal male	X	2n(A)
7.	Super male	X	3n(A)
8.	Exceptional female	2XY	2n(A)

mating within a race normal flies appear and intersexes do not appear because of balance between factors of maleness and femaleness. But when mating occurs between different races intersexes appear along with normal flies.

Any zygote with a weak cytoplasmic factor and a strong male X chromosome factor will be female intersex. Any zygote with a strong female factor and a weak male determining factor will be a male intersex. If an European female (weak) is crossed with a japanese male (strong), the males, are normal. But the females become intersex because the female determining factors are inherited from weak female. In the same way, if a European male (weak) is crossed with a Japanese female (strong), the female offspring are normal while a male develops into intersex.

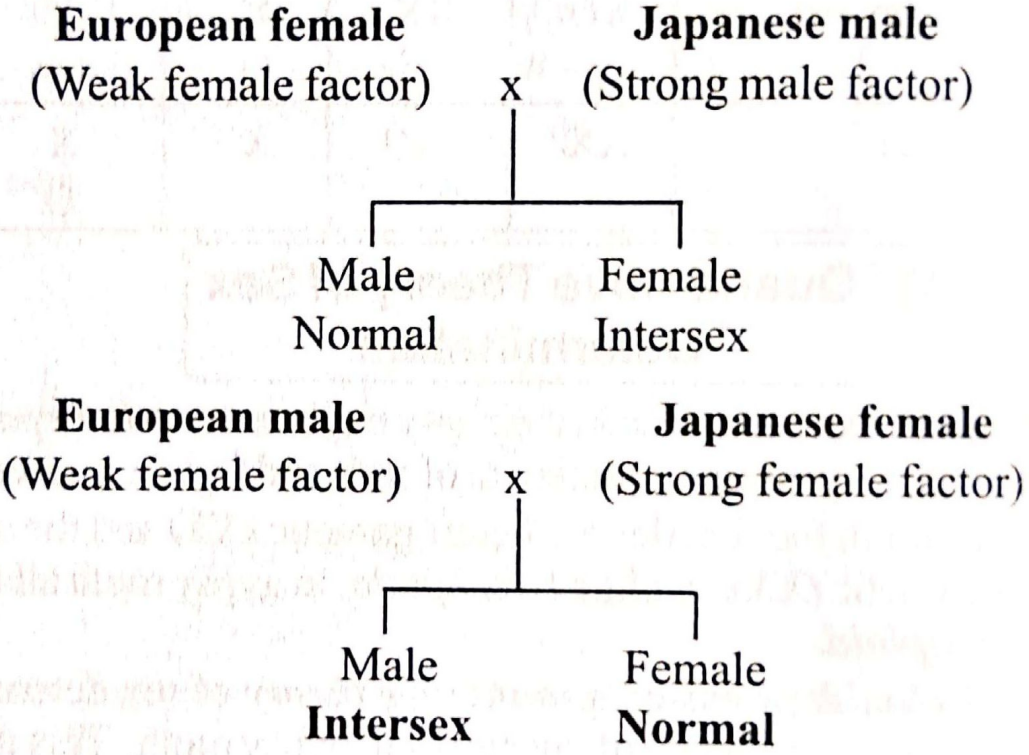


Fig.10.9: Crosses between different races of gypsy moths.

Gynandromorphs

Gynandromorphs are *individuals which show male characters on some parts of the body and female characters on other parts of the body.* They are also called ***gynanders.*** The gynandromorphs are ***sterile.***

Gynanders are rare. They occur in *Drosophila,* butter flies, beetles, wasps, bees, silk worms, etc.

There are three types of gynanders. They are the following:

1. Bilateral Gynanders: These have male traits on one lateral side of the body and female traits on the other lateral side. Eg. *Drosophila.*

2. Anteroposterior-gynanders: They have features of one sex on the anterior half of the body and those of the other sex on the posterior half of the body. Eg. *Beetles.*

3. Sex pie balds: These are gynanders having a mixture of male and female tissues in the body.

Gynandromorphism is produced in two ways.

One type is produced by the loss of one X chromosome in a blastomere. Another type is produced by a binucleate egg.

1. Loss of X Chromosomes

A gynander begins its development with 2n(A) +XX chromosomes. But in the course of cell division, and X gets lost from one of the products of cell division. So one daughter cell possess 2n(A) +XX chromosome and other 2n(A) + X. In case, this should happen during first zygotic division two blastomeres with unequal number of X chromosomes are formed. The blastomere with 2n(A) + XX chromosomes develops into female half, while the second blastomere with 2n(A) + X chromosomes produces male half.

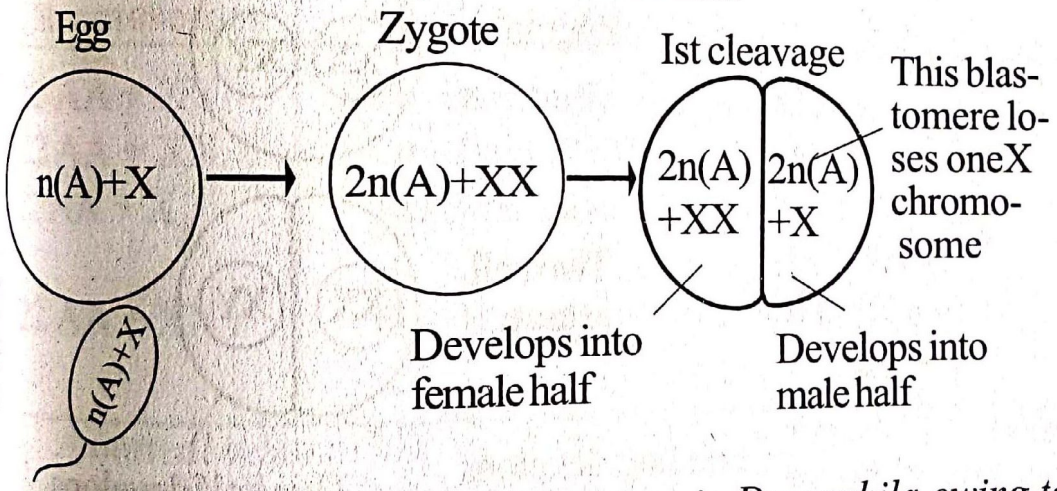


Fig.10.10: Development of gynanders in Drosophila owing to the loss of one X chromosome.

2. Binucleated Eggs

This mechanism was explained by ***Goldschmidt*** in silkworm moths. In silk worm, females are ***XY*** and males are ***XX.*** During oogenesis, ***X*** and ***Y*** chromosomes normally separate, one passing into egg and the other into the polar body.

Sometimes, both the nuclei are present in the egg and a binucleate egg (***XX*** and ***XY***) is produced. The binucleate egg may be fertilized by two sperms, each fertilizing one egg nucleus. After fertilization and cleavage, one blastomere (***XX***) develops into male parts and the other blastomere (***XY***) develops into female parts.

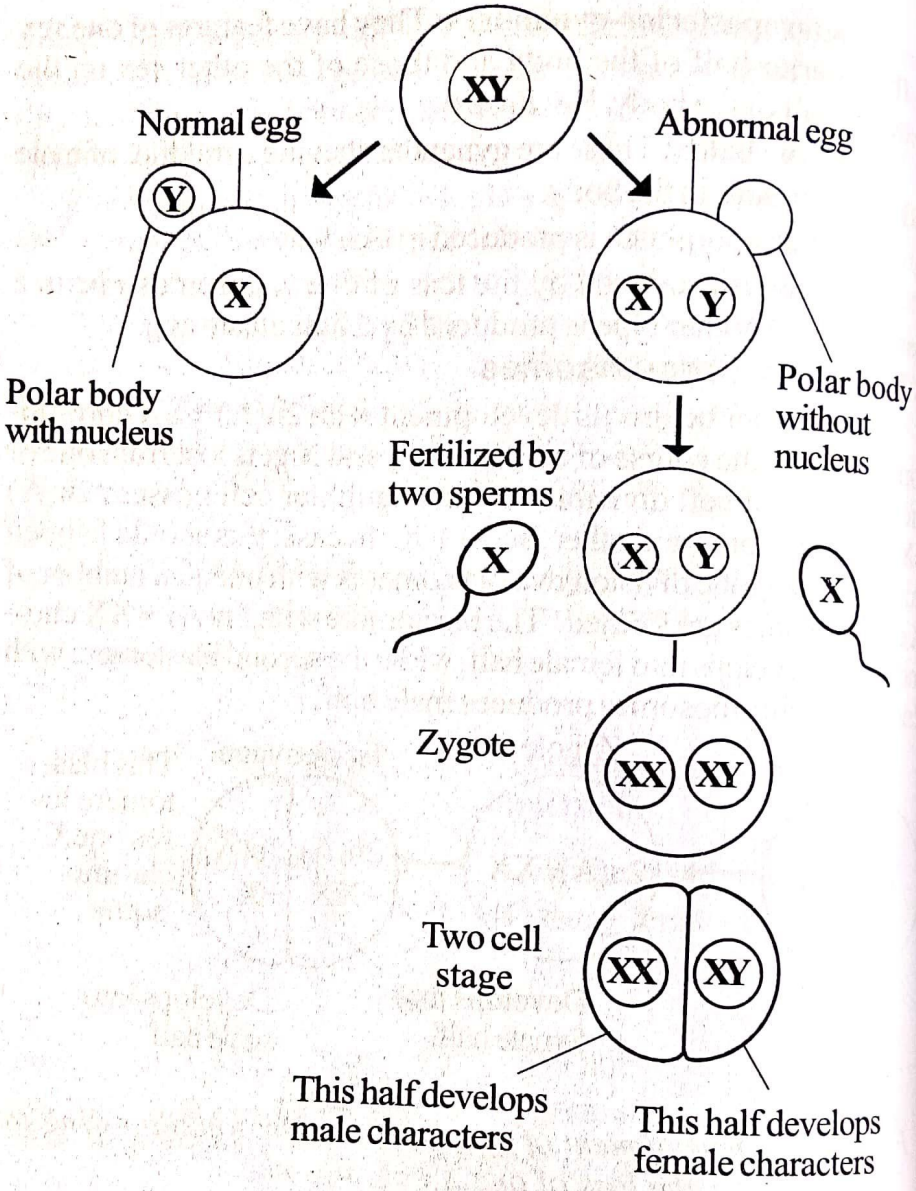


Fig.10.11: Formation of gynanders in silkworm.

Barr Body or Sex Chromatin

A darkly staining chromatin body present in the nucleus is called ***Barr body.*** It is also called ***sex chromatin.***

It was discovered by ***Barr*** 1949. The Barr body is attached to the inner surface of the nuclear membrane. It contains a large amount of ***heterochromatin*** and lesser amount of ***euchromatin***. Hence it contains large amount of RNA and lesser amount of DNA.

It is nothing but the ***inactivated X chromosome.***

22. Mutation

Mutation is a *sudden change of a gene or chromosome fro one form to another.* It produces an alteration in the character und its control. ***Dobzhansky*** stated that mutation is a ***mistake*** or ***mispri*** in cell division. The term ***mutation*** was introduced by ***De Vries.***

Genes are exceedingly stable units. They are reproduced an copied exactly during meiosis or gamete formation. Neverthele mistakes occasionally occur during the copying or replication of gene during meiosis. These mistakes represent mutation. Once a mutatio occurs, it is then reproduced and copied exactly during meiosis. ***Mu tations*** are *the basis of discontinuous variation in populatio* Mutations may occur at ***chromosomal level*** or ***gene level.***

I. Genome Mutations (Chromosomal Mutations)

The changes in the structure and number of chromosome (genome) are called ***genome mutations.*** Since these mutations oc cur at the chromosomal level, they are also called ***chromosomal ab errations.***

The ***genome*** is defined as the total genetic material containe within the chromosomes of an organism. Humans have 46 chromo somes. Our 46 chromosomes represent our genome. Genome muta tions occur at a frequency of 1/10000 to 1/1000000.

Genomic mutations take place due to abnormalities in cell div sions, especially during gametogenetic meiosis. They may occur du to change in structure of chromosomes or due to change in the chro mosome number. Any change in individual genes has not been consi ered in genome mutations. Genomic mutations are analyzed with cy tological investigations of cells.

Genome mutation is of two types, namely

1. Changes in the structure of chromosomes.
2. Changes in the number of chromosomes

1. Change in the Structure of Chromosome

The chromosome contains genes. The change in the structure of chromosome bring about changes in the number and arrangement of genes. These are of 4 types, namely

1. *Deletion*
2. *Duplication*
3. *Inversion*
4. *Translocation*

1. Deletion

Deletion is *a chromosomal aberration where a segment of the chromosome is lost.* Here some genes are lost.

Deletion is of two types, namely ***terminal deletion*** and ***intercalary deletion.*** In terminal deletion, a terminal segment is lost. In intercalary deletion, an intermediate segment of the chromosome is lost.

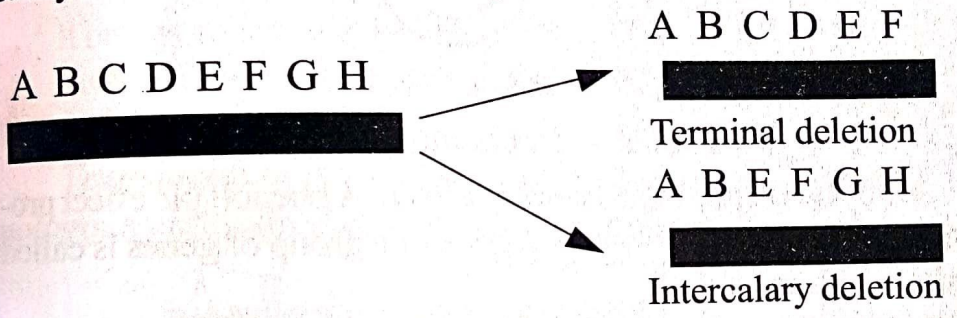


Fig.22.1: Deletion.

When deletion occurs in one member of a homologous chromosome, a ***deletion loop*** is produced in the normal homologous chromosome. The deletion loop is formed by the segment opposite to the deleted segment. It occurs during pairing in meiosis.

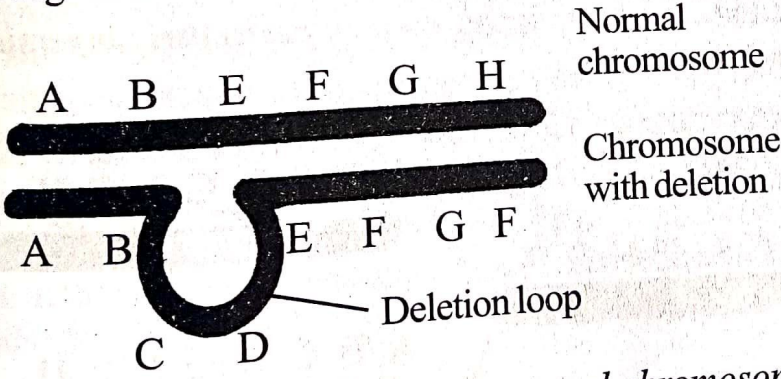


Fig.22.2: Deletion loop in a normal chromosome.

In human babies, deletion of a segment of chromosome number 5 causes a disease called ***cridu chat syndrome.*** The baby cries like a cat; it is mentally retarded with small head.

2. Duplication

Duplication is a chromosomal aberration where a segment is repeated. Hence a set of genes is present in double doses.

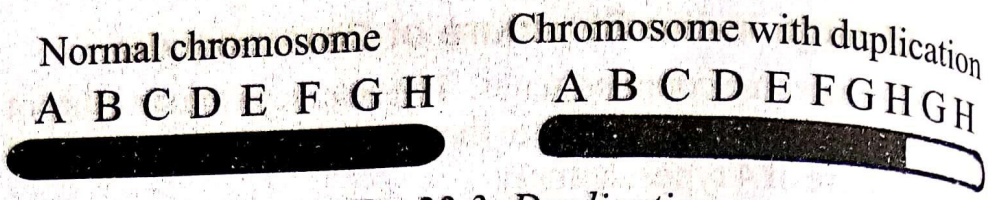


Fig.22.3: Duplication.

During meiosis, the duplicated segment forms a ***loop.***
In *Drosophila,* ***bar eye*** is due to duplication.

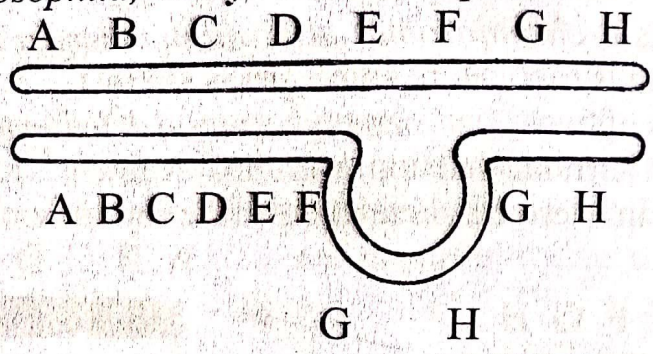


Fig.22.4: Duplication loop.

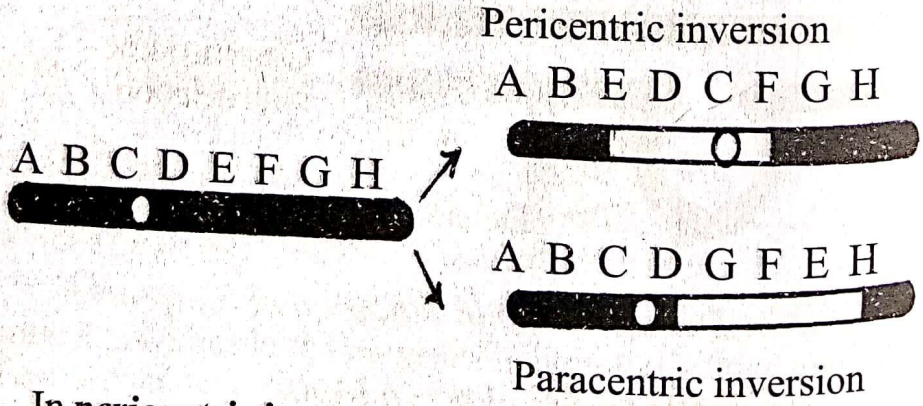
Duplication produces ***position effect***. A phenotypic effect produced by change in position of a gene or a group of genes is called ***position effect.***

3. Inversion

Inversion is *a chromosomal aberration where a segment of chromosome breaks and reunites in the reverse order.*

In inversion, there is no loss or gain of genes. But the genes are rearranged in reverse order.

Inversion is of two types, namely ***pericentric inversion*** and ***paracentric inversion.***



In ***pericentric inversion,*** the centromere is included in the inverted segment.

In ***paracentric inversion,*** the centromere is not included in the inverted segment.

1. Monosomy
2. Nullisomy
3. Trisomy

1. Monosomy

Monosomy is *a chromosomal aberration where one chromosome is lost from a pair.* It is represented by 2n-1. The monosomic individual has one chromosome less from the normal number of chromosomes.

A monosomic *Drosophila* has 8 –1=7 chromosomes. A monosomic man has 46-1=45 chromosomes.

It is an ***aneuploidy.***

It is produced in woman when an egg without an X chromosome fuses with a sperm containing, an X chromosome. It causes a syndrome called ***Turner's syndrome.***

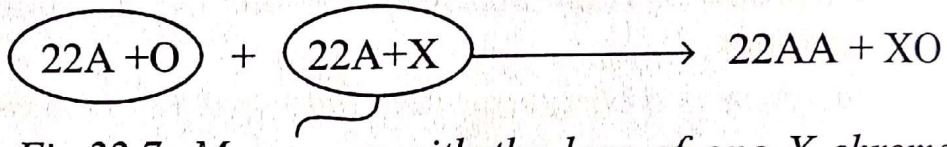


Fig.22.7: Monosomy with the loss of one X chromosome. Turner's syndrome.

2. Nullisomy

Nullisomy is *a chromosomal aberration where both chromosomes of a pair are lost.* It is represented by 2n-2.

It is an ***aneuploidy.***

A nullisomy is produced by the fusion of gametes having one chromosome less.

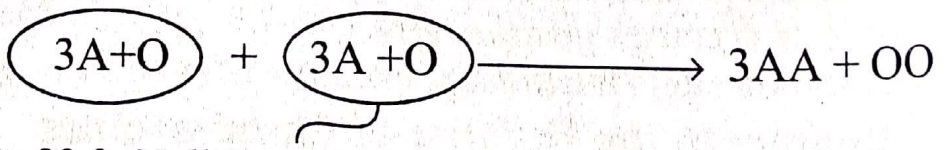


Fig.22.8: Nullisomy with the loss of a pair of chromosomes.

Nullisomic individuals cannot survive.

3. Trisomy

Trisomy is *a chromosomal aberration where one chromosome is added to a pair.* It is represented by 2n+1. A trisomic individual has an additional chromosome from the normal number.

Thus a trisomic *Drosophila* has 8+1=9 chromosomes. A trisomic man has 46+1=47 chromosomes.

It is an ***aneuploidy.***

Trisomy is caused by ***non-disjunction.***

There are two types of trisomy, namely ***trisomy of autosomes*** and ***trisomy of sex chromosomes.***

Trisomy of autosome is due to the addition of one chromosome to any one homologous pair of autosome. When a chromosome is added to 21st pair of autosome, it is called ***trisomy-21.***

Trisomy-21 in man causes a syndrome called ***Down's syndrome*** (Mongolism). A trisomic man has 47 chromosomes instead of 46. They are mentally retarded. They have broad face and flat stubby nose.

Trisomy of sex chromosome is due to the addition of one sex chromosome. When an X chromosome is added to a man, he has 47 chromosomes, 22AA+XXY. It causes a syndrome called ***Klinefelter's syndrome.***

2. Euploidy

Euploidy is *a chromosomal aberration involving change in the number of chromosome sets.* It is of two types, namely

1. Haploidy
2. Polyploidy

1. Haploidy or Monoploidy

The basic set of chromosome in any species is haploid; each chromosome is represented singly; that is (N) number.

The gametes carry haploid number of chromosomes. During fertilization the parental chromosomes unite together by the fusion of gametes forming diploid number (2N) of chromosomes.

Sometimes in the life of an animal a set of chromosomes will be lost and this leads to haploidy. So some characters which are present in any parent, will be lost from the resulting individual.

2. Polyploidy

Polyploidy is the condition in which an organism contains more than the usual two sets of chromosomes. Such animals are said to be ***polyploid.***

Polyploid organisms may have three, four or more sets of chromosomes and they are called ***triploids*** (3N); ***tetraploids*** (4N); ***pentaploids*** (5N); ***hexaploids*** (6N) ***hectaploids*** (7N); ***octoploids*** (8N); ***nanaploids*** (9N); ***decaploids*** (10N) and so on.

Polyploidy may be ***autopolyploidy*** or ***allopolyploidy.*** In autopolyploidy, the chromosome sets are derived from the same species so no addition of new genes occurs but in allopolyploidy the chromosome sets are derived from distinct species it involves the addition of new genes hence much variations occur in organisms. These variations

21. Inbreeding and Outbreeding

Inbreeding

Mating between closely related individuals is called ***inbreeding.*** ***Self fertilization*** is an ideal inbreeding.

Mendel carried out inbreeding among the F_1 plants in his ***monohybrid*** and ***dihybrid experiments.***

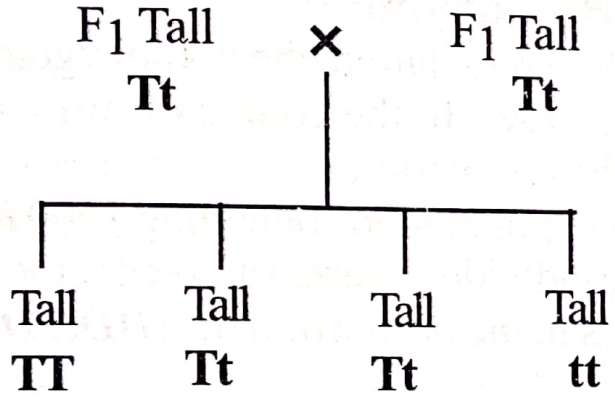


Fig.21.1: Inbreeding in Mendel's experiment.

The marriage between a brother and a sister (not in practice) is an ideal inbreeding.

The Royal family of Egypt including Cleopatra was famous for inbreeding between brothers and sisters.

Cousin marriages are examples of inbreeding.

The mating between a mother cow and an Ox born for the cow is an inbreeding.

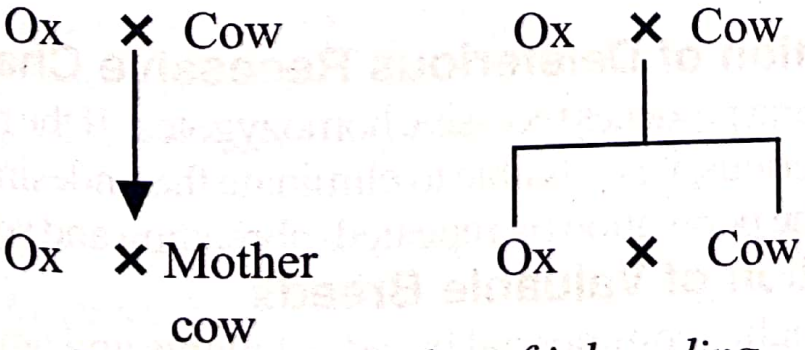


Fig.21.2: Examples of inbreeding.

Significance of Inbreeding

Inbreeding has demerits and merits.

Demerits of Inbreeding

1. Low Yield

Inbreeding results in low yield.

2. Inbreeding Depression

The loss of vigour as a result of inbreeding is called ***inbreeding depression.***

3. Appearance of Deleterious Characters

In human beings, there is a seven-fold increase in phenylketonuric children from cousin marriages than from marriages between unrelated parents.

In corns, inbreeding results in the appearance of deleterious characters such as white seedlings, yellow seedlings and dwarfs.

Merits of Inbreeding

1. Increase of Homozygotes

In an inbreeding population, the homozygotes increase and the heterozygotes decrease. In the course of time, ***heterozygotes*** are ***eliminated*** from the population.

Let us assume a population containing 1600 ***heterozygous*** (Dd) individuals. These individuals mate (inbreed) among themselves and produce offsprings in the proportion of 1***DD:***2***Dd:*** 1***dd*** or 400*DD*: 800***Dd***: 400***dd.***

In the second generation, there will be 600 ***DD***, 400 ***Dd***, 600 ***dd*** and so on.

The heterozygotes will be decreased by half in each generation, with corresponding increase in the frequency of homozygotes.

2. Production of Pure lines

Inbreeding produces ***homozygotes. The homozygotes reproduce only homozygotes by inbreeding***. These homozygotes are ***pure lines*** as they breed pure. Hence inbreeding produces pure lines.

3. Elimination of Deleterious Recessive Characters

Inbreeding produces recessive homozygotes. If the recessive character is deleterious, it is possible to eliminate the undesirable recessive genes from the population by repeated inbreeding and selection.

4. Production of Valuable Breeds

High quality commercial breeds of plants and animals are pro-

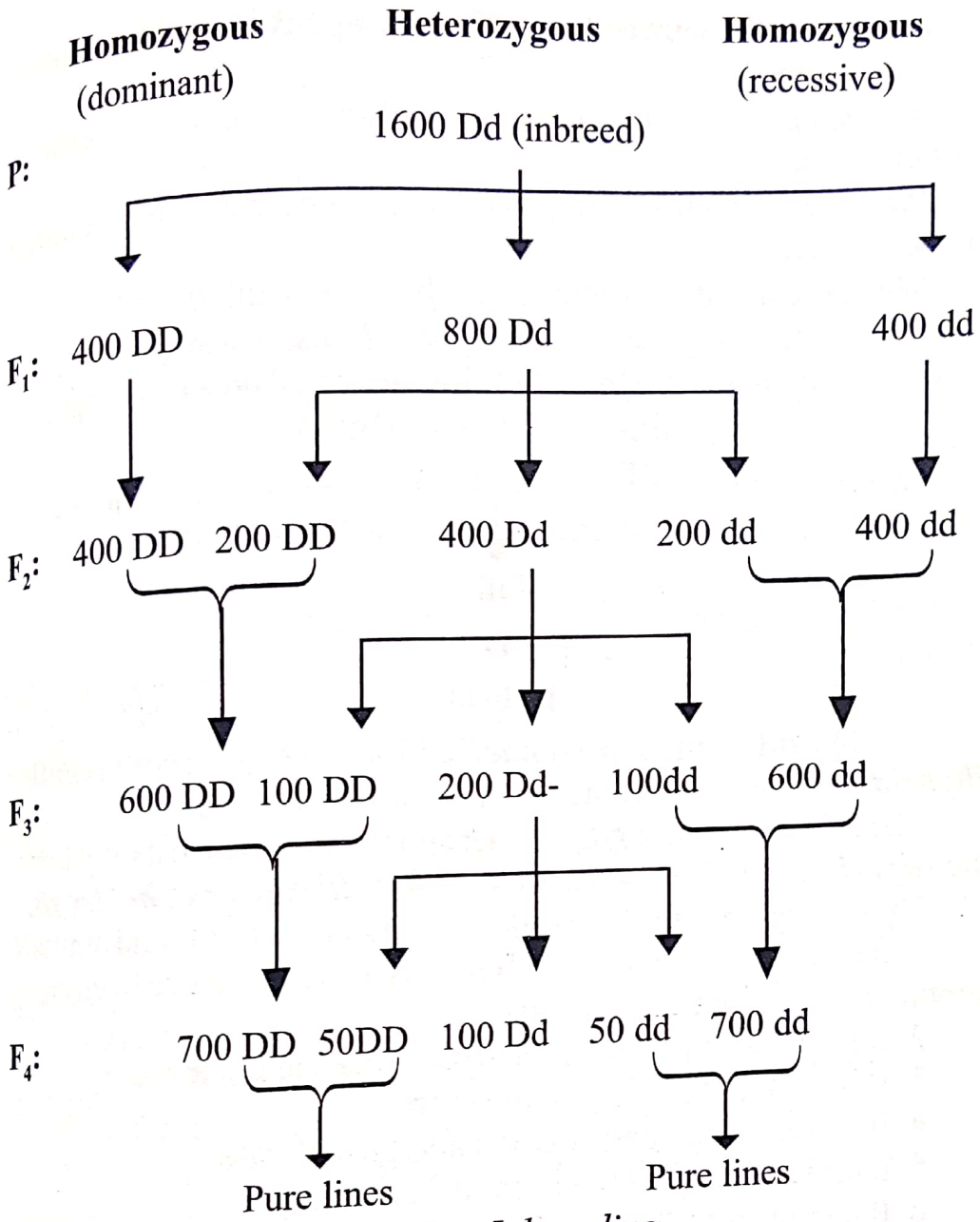


Fig.21.3: Inbreeding.

Outbreeding

The mating of unrelated individuals is called ***outbreeding.*** It is also called ***cross breeding.***

The offspring formed by mating two unrelated parents is called ***hybrids.***

The production of hybrids by mating unrelated parents is called ***hybridization.*** So outbreeding is a hybridization.

Outbreeding is of three types, namely

1. *Intraspecific outbreeding*
2. *Interspecific outbreeding*
3. *Intergeneric outbreeding*

Intraspecific outbreeding is the mating between the members of the same species.

Interspecific outbreeding is the mating between the members of different species.

Intergeneric outbreeding is the mating between the members of different genera.

Mendel carried out outbreeding between a tall pea plant and a dwarf pea plant. The resulting plants are ***hybrids***. These parents differ in only one character. So these hybrids are called ***monohybrids.***

Tall × Dwarf

TT **tt**

↓

Tall

Tt

Hybrid

The hybrid formed in ***Mendel's*** dihybrid experiment is called ***dihybrid*** because the parents differ in two characters.

The hybrids are stronger, heavier and vigourous than their parents. The ***superiority*** of the hybrid is called ***hybrid vigour*** or ***heterosis.***

Hybrid vigour brings the following effects in plants and animals:

1. It increases the height, viability, fertility, resistance to environmental factors, disease and pests.
2. It increases the size of the fruits, seeds and leaves.
3. It increases the yield of the crop.
4. It causes better germination and growth rate.
5. It initiates early flowering and fruit setting.
6. It increases milk production.
7. It increases number of eggs in poultry.
8. It produces better beef and pork.
9. It increases in silk production.

Mule is a hybrid. Mule is born for a ***male donkey*** and a ***female horse.*** Mule is superior to a horse in strength, ability to work and resistance to disease. Mule is more intelligent than their parents. Thus mule exhibits ***hybrid vigour.*** However mule is ***sterile*** and it cannot produce another mule.

Everytime mule is produced a new:

Mule is employed in Indian army in Himalayan mountain.

Zebrankey is a hybrid between Zebra and Donkey.

Hybrid cows born between ***Red Sindhe*** and ***Jershey*** give more milk.

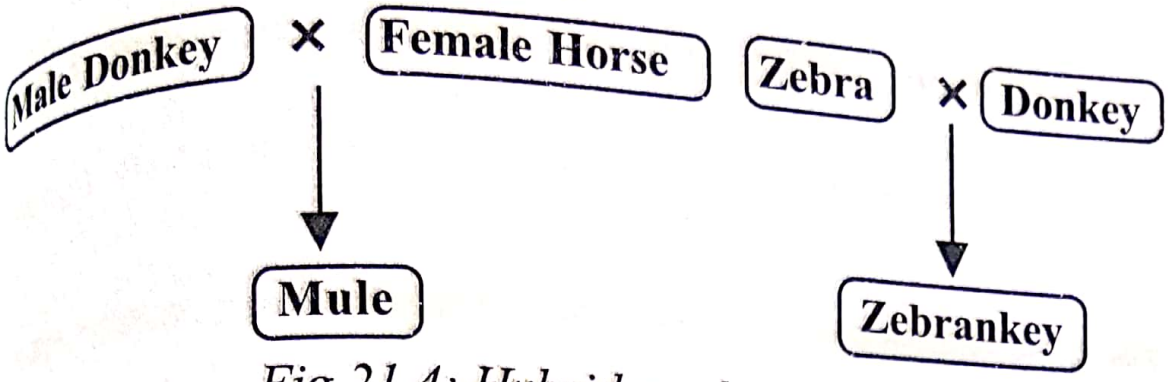


Fig.21.4: Hybrid production.

Among dairy cattle ***Friesian,*** hed ***Dane, Jershey, Sindhi,*** etc. are high yielding hybrid cows produced by outbreeding.

The cattle ***Blue roam*** is a hybrid born for a ***White short horn*** and ***Black Angus cattle.*** This hybrid cattle is known for ***hybrid vigour,*** rapid growth, economical utilization of food and high quality of beef.

Broiler chicks of high class flesh are hybrids and are the products of outbreeding. The hybrid vigour in broiler chicks is in the form of conversion of food into flesh and fast growth.

Hybrid fowl between ***White leghorn*** and ***Plymouth Rock*** gives more yield of eggs.

Hybrid ***silk worm*** produces more silk.

In ***Fisheries,*** hybrid fishes are produced for fast growth. Eg. *Catla.*

Outbreeding produces numerous varieties of better yielding ***crop plants.***

Paddy hybrids produce more grains.

Tall and ***Dwarf*** coconut hybrid yields more number of nuts.

Caddish is a hybrid between cabbage and Radish.

Pomato is a hybrid between Potato and Tomato.

Causes of Heterosis

Heterosis is caused by two main factors, namely

13. Syndromes

Syndromes are caused by non-disjunction. Syndrome is a disease characterized by a group of symptoms.

In man, the following syndromes are produced by non-disjunction:

1. *Klinefelter's syndrome.*
2. *Turner's syndrome.*
3. *Down's syndrome.*

1. Klinefelter's Syndrome (22AA+XXY) = 47

Klinefelter's syndrome is a ***genetical disease*** caused by an additional X chromosome in human ***male.***

It is a sexual abnormality in ***males*** discovered first by ***Harry*** (1942).

It is caused by ***chromosomal aberration.***

It is caused by ***trisomy (aneuploidy)*** where one chromosome is added to a set (2n + 1).

This abnormality is due to the presence of *47* chromosomes instead of 46. The victims possess an additional X chromosome with XY. So the chromosomal make up is ***22AA + XXY.***

It is caused by ***non-disjunction*** of XX chromosomes. When an abnormal egg with XX chromosomes, is fertilized with a sperm with Y chromosome, the resulting baby contains ***XXY.***

They are ***sterile males.***

The testes are small; there is no spermatogenesis.

Male sex glands are poorly developed.

The breasts are enlarged.

They are tall.

Amount of male hormone is low.

Genitalia are poorly developed.

They are ***mentally affected.***

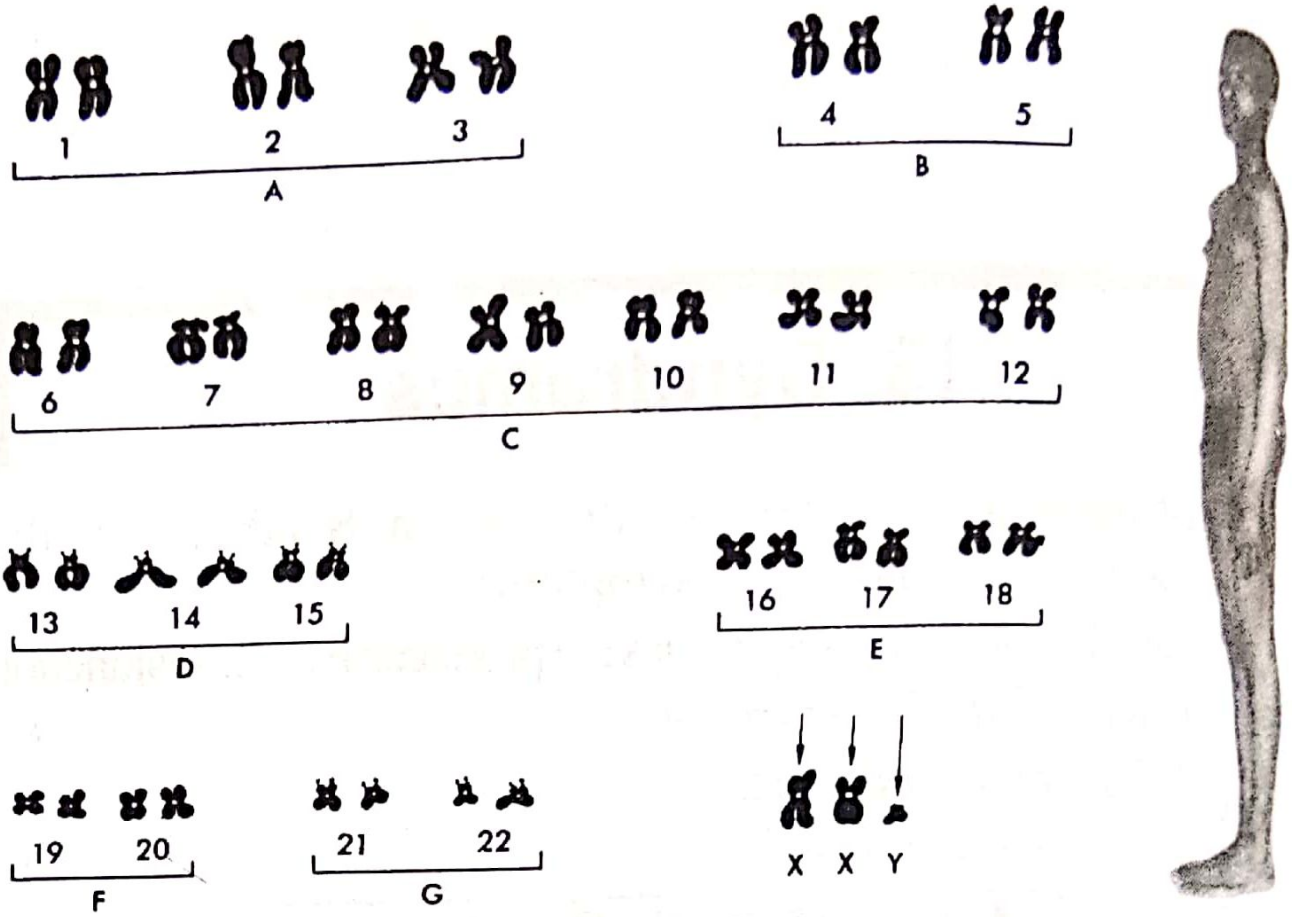


Fig.13.1: The Klinefelter's syndrome in man. Such persons are AAXXY, with 47 chromosomes as shown in the karyotype. External genitalia are male-type, but there is usually some female-like breast development as in this case.

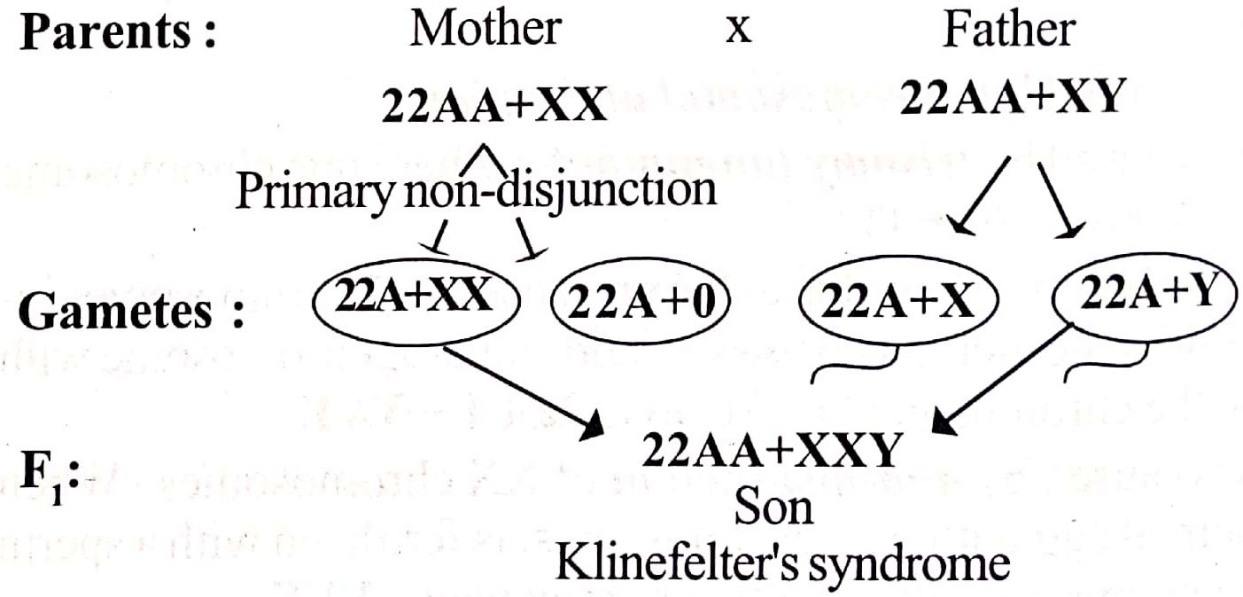


Fig.13.2: Non-disjunction resulting in Klinefelter's syndrome.

This abnormality is due to *45* chromosomes instead of 46. The missing chromosome is one X chromosome. Hence the chromosomal make up is ***22AA + X = 45.***

It is caused by ***non-disjunction*** of XX chromosomes. When an abnormal egg without any X chromosome is fertilized by a sperm with X chromosome, the resulting baby contains ***XO*** chromosomes.

The baby develops into a ***sterile female***. She has female phenotypes. But there is ***no menstruation.***

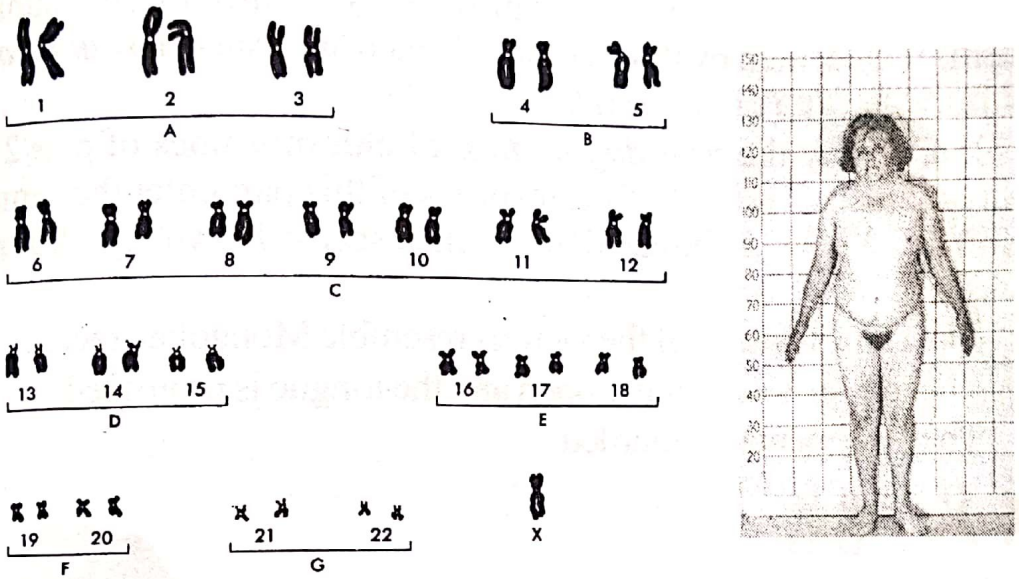


Fig.13.3: The turner's syndrome in woman. Such persons are AAXO, with only 45 chromosomes as shown in the karyotype. Note, external female genitalia, webbed neck, broad chest, underdeveloped breasts and short stature. Turner individuals have a small uterus and vestigial ovaries.

Parents : Mother **22AA+XX** x Father **22AA+XY**

Non-disjunction

Gametes : (**22A+XX**) (**22A+O**) (**22A+X**) (**22A+Y**)

$\mathbf{F_1}$: **22AA+XO**

Daughter

Turner's syndrome

Fig.13.4: Non-disjunction resulting in Turner's syndrome.

Ovaries are represented by ridge of whitish tissue called ***streak gonad.***

Female hormones are low. The chest is broad. Breasts are poorly developed. They are dwarf. Mentally retarded.

3. Down's Syndrome (Mongolism or Mongoloid idiocy)- 21AA+ A+XX

This abnormality was described by ***Down*** in 1866.

It is caused by ***chromosomal aberration.*** It is due to ***trisomy*** in 21st pair of ***autosome.***

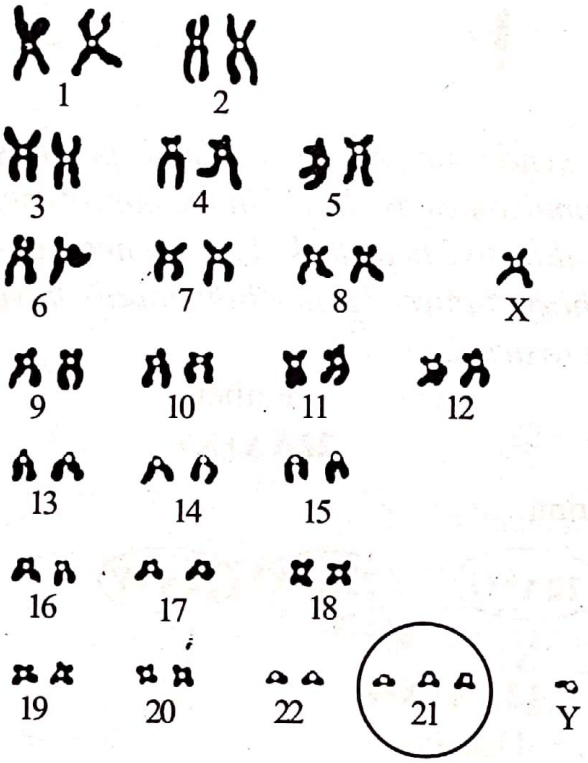
It is due to 47 chromosomes instead of 46; chromosome number 21 is represented by three copies. Hence, it is caused by ***autosomal aneuploidy (21-trisomy).***

It arises by the ***non-disjunction*** of chromosomes of pair 21 during meiosis. Hence both autosomes of this pair enter the same egg. When this egg is fertilized by a normal sperm, Down's syndrome results.

The facial features of the victims resemble Mongolian race.

The mouth is constantly open and the tongue is protruded.

They are mentally retarded.



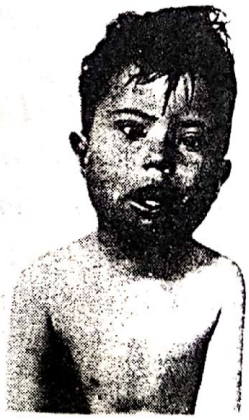


Fig.13.6: Down's syndrome (Mongoloid idiocy) in a child.

Fig.13.5: Karyotype of trisomic mongoloid idiot having 47 chromosomes (triplo-21).

The neck is short and broad. She is dwarf.

The nose is oblique.

The ears are malformed.

This syndrome appears much more frequently in children born to women in the later part of the reproductive life.

Parents : Mother **22AA+XX** Non-disjunction x Father **22AA+XY**

Gametes : **22A+A+X** **21A+X** **22A+X** **22A+Y**

F_1 : **22AA+A+XX**

Daughter

Down's syndrome

Fig.13.7: Non-disjunction resulting in Down's syndrome.

15.Twins

The two babies born at a time for a mother are called *twins.* Twins are due to ***multiple pregnancy.*** There are three types of twins. They are the following:

1. *Identical twins*
2. *Fraternal twins* and
3. *Siamese twins*

1. Identical Twins

Identical twins are *extremely similar in their characters.* They are ***developed from a single zygote.*** So they are also called ***monozygotic twins.***

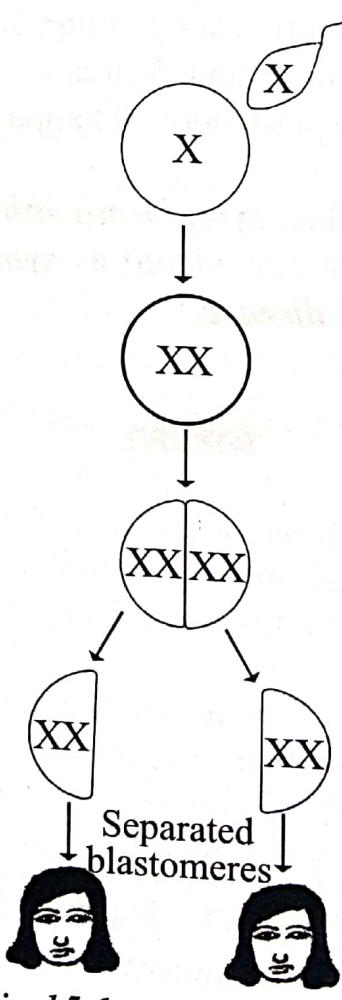


Fig.15.1: Identical twins.

The identical twins develop from a single zygote. During cleavage, the zygote divides into two ***blastomeres.*** These blastomeres separate and each blastomere develops into a baby. Hence the two babies are similar in all respects.

Sometimes, the identical twins are joined together producing ***siamese twins.***

They are of the ***same sex.***

They have the ***same type of genes.***

They have the same type of ***blood group.***

They have very similar temperaments, disposition and mental capacities.

They are generally opposite handed. One of the twin is right handed and the other is left handed.

They show similar whorls of hair on the head but in a reverse order like mirror image.

2. Fraternal Twins

Fraternal twins are like ordinary brothers and sisters born in one birth. They develop from ***two independent zygotes.*** So they are also called ***dizygotic twins.***

They are formed by the fertilization of two eggs by two sperms.

They may be of the same sex or opposite sexes.

They have different genotypes. So they have dissimilar characters. So they are called ***non-identical twins.***

Generally a lady produces only one egg at a time. But some times two eggs are produced simultaneously. The two eggs are fertilized by two sperms producing fraternal twins. If both the eggs are fertilized by sperms containing X chromosomes, female babies are produced. If both the eggs are fertilized by sperms containing Y chromosomes, male babies are produced. If one egg is fertilized by X carrying sperm and another by Y carrying sperm, both male and female babies are produced. (Fig.15.2).

3. Siamese Twins

These twins were born for the first time in ***Siam;*** hence they are called ***siamese twin. Siamese*** twins are similar to ***identical twins.*** They develop from a single egg. So they are ***monozygotic twins.*** They are ***joined together physically.***

The zygote divides into two blastomeres. The blastomeres are partially separated. These blastomeres develop into two babies. They

They may have a double head and a single trunk. Sometimes they are double in the trunk region and single in the head region. On certain occasions, they are double in the head and leg regions and united only in a small area at the hips. They are also called ***double monsters*** or ***abnormal twins.*** They survive very rarely.

The siamese twins are of the same sex. They have the same type of genes.

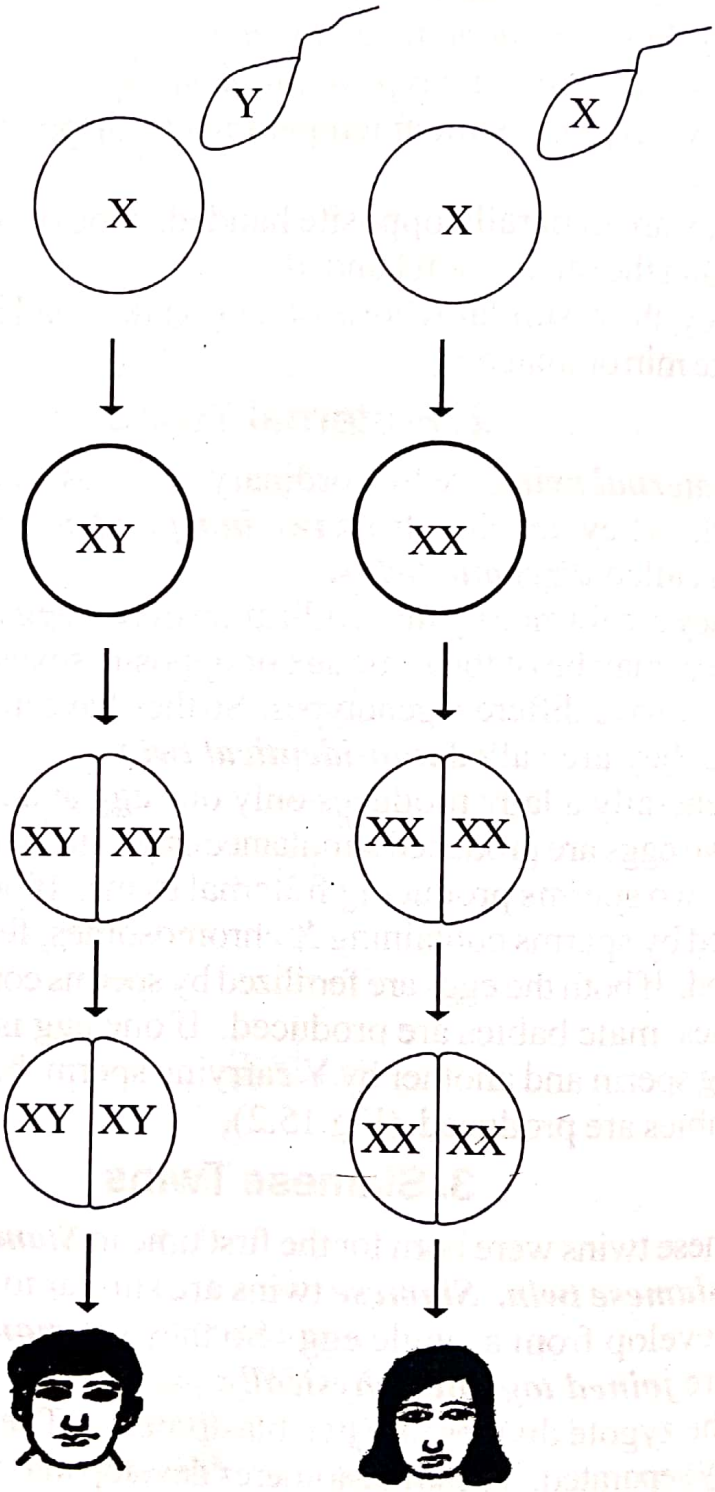


Fig.15.2: Fraternal twins.

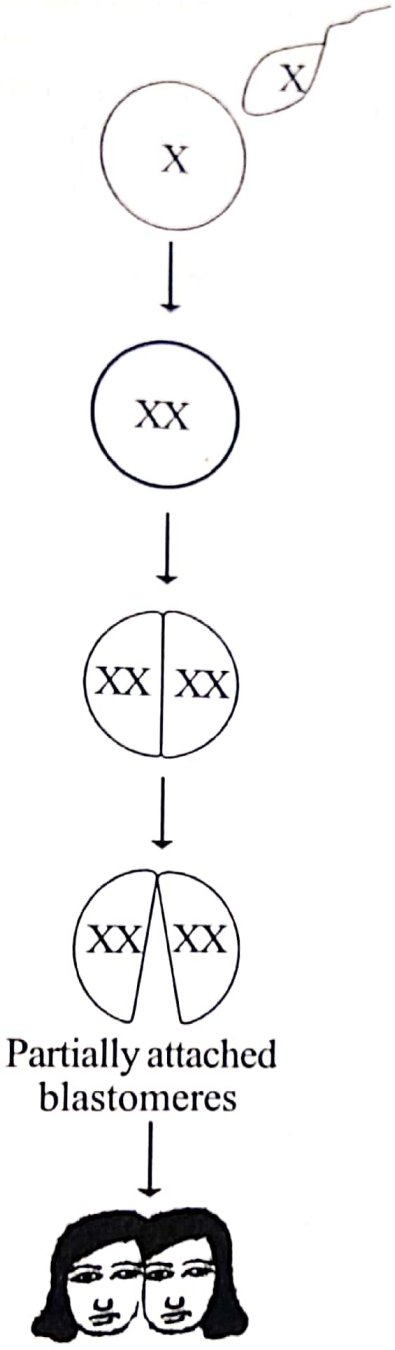


Fig.15.3: Siamese twins.

Importance of Twin Study

1. The study of the heredity of twins helps to understand the hereditary and environmental characters. The identical twins contain the same type of genes because they develop from one egg. So all the characters which are similar are hereditary characters. The character which is present in one of the twin and absent from the other is produced by the environment. Observation of this shows that intelligence, diabetes, feeble mindedness, etc. are hereditary characters.

2. The study of twins also helps to understand the influence of environment on twins. If the environment is similar, twins show practically no difference. If the twins are reared apart, there is definitely difference in the hereditary characters. These differences are caused by the environment.

The ***human genome project*** is a *multinational research project to determine the genomic structure of man (Homo sapiens.)* It is aiming at sequencing all DNAs of man and at determining the location of various genes in the DNAs. Many Government and Private sectors took part in the project.

The genome project was initiated in 1988 and completed in 2003. It was under the International Administration of the ***'Human Genome Organization'*** (HUGO). It was funded by the ***Department of Energy*** (DOE) and ***National Institutes of Health*** (NIH) in the USA, the ***European Commission*** (EC) and Britain's ***Welcome Trust.***

The research works in the project was conducted in research laboratories in six nations. The most important among them were the ***National Human Genome Research Institute*** (USA) and ***Sanger Centre*** (England).

Methodology

A somatic cell of human being contains 23 pairs of chromosomes. Each chromosome is composed of a long double-stranded DNA and histone protein. It is estimated that there are 3.2 million basepairs in the DNA of all these chromosomes. Among them, 2 million basepairs are already sequenced. The general methodology of the genome project is outlined below:

Obtaining DNA

A cell culture containing a human cell line is homogenized in ***sucrose*** solution using a pestle.

The homogenate so obtained is subjected to ***differential centrifugation*** to get a chromosomal fraction.

This fraction is added with a ***lysis buffer*** and again ***centrifuged*** using an ultracentrifuge to separate different chromosomes according to their sizes. Thus human chro... numbered ...

In the chromosomes, DNA is wrapped around ball-like histone proteins. These DNA wrapped units are called ***nucleosomes***.

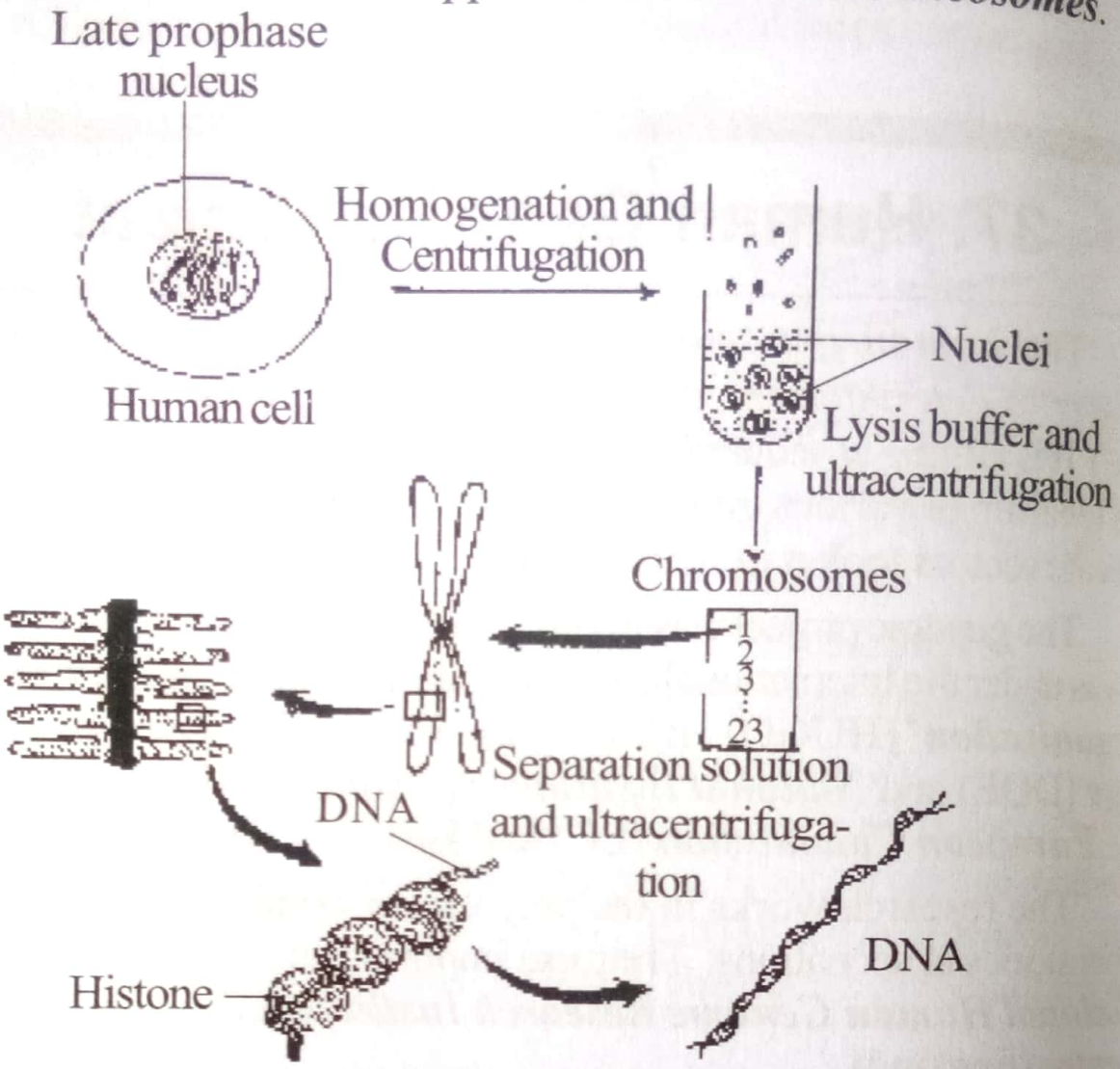


Fig.37.1. Obtaining DNA for genome study.

Each chromosome, is suspended in a solution containing Tris-HCl, EDTA and NaCl and is stored at-20°C. This treatment releases histones from the nucleosomes, releasing the DNA free.

The DNA is isolated from it by ***Cesium chloride density gradient centrifugation***. Each DNA is about 5 feet long.

Preparation of DNA for Study

The long DNA of a chromosome is cut into small pieces of 5000 -10,000 nucleotides using a ***restriction enzyme*** that cuts the DNA at long distances.

The individual pieces of DNA are separated by agarose gel ***electrophoresis*** on the basis of restriction fragment length polymorphism (RFLP). Each and every DNA fragment so obtained, is placed in a vial and stored at 20°C for future use.

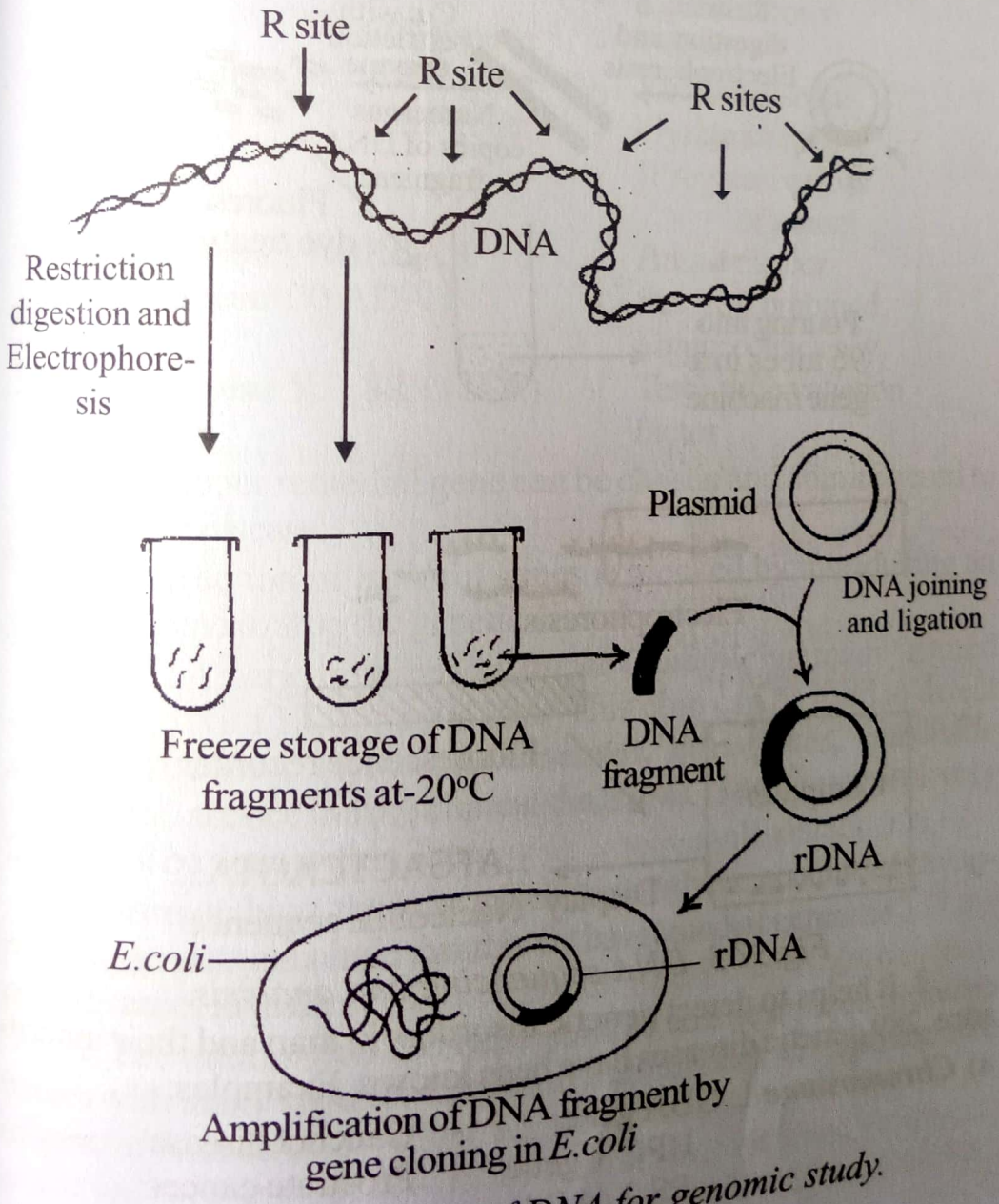
One DNA fragment is inserted into a plasmid DNA to construct a ***rDNA***. The rDNA is introduced into *E.coli* for *invivo* ***amplification*** of that DNA fragment. Consequently billions of copies of that

DNA fragments are made. In this way each and every DNA fragment is amplified.

Sequencing and Analysis

The amplified rDNA is isolated from the bacterial cells and the ***target DNA*** is separated. It is cut with a restriction enzyme to generate ***small DNA fragment.***

Fluorescent dye visible under laser light is added to the terminal nucleotide of each DNA fragment. The resulting DNA solution is poured into 96 tubes inside the ***DNA sequencing machine***. In the tubes, the DNA fragments are electrophoresed very fast and this can be observed by a ***fluorescence recorder*** in the gene machine.



Amplification of DNA fragment by gene cloning in *E.coli*

Fig.37.2. Preparation of DNA for genomic study.

The bases in the overlapping segments are identified and assembled in a linear order by using computer database. In this way, all DNA fragments of a chromosome are sequenced to recreate its original nucleotide sequence.

Such a study is conducted on all 23 chromosomes of human genome to understand the exact genome structure of man.

Applications of Genome Project

1. Genome project provides database information of DNA sequences of man. Biotechnology based companies may use the information to manufacture human proteins which are of much use in the human disease treatments.

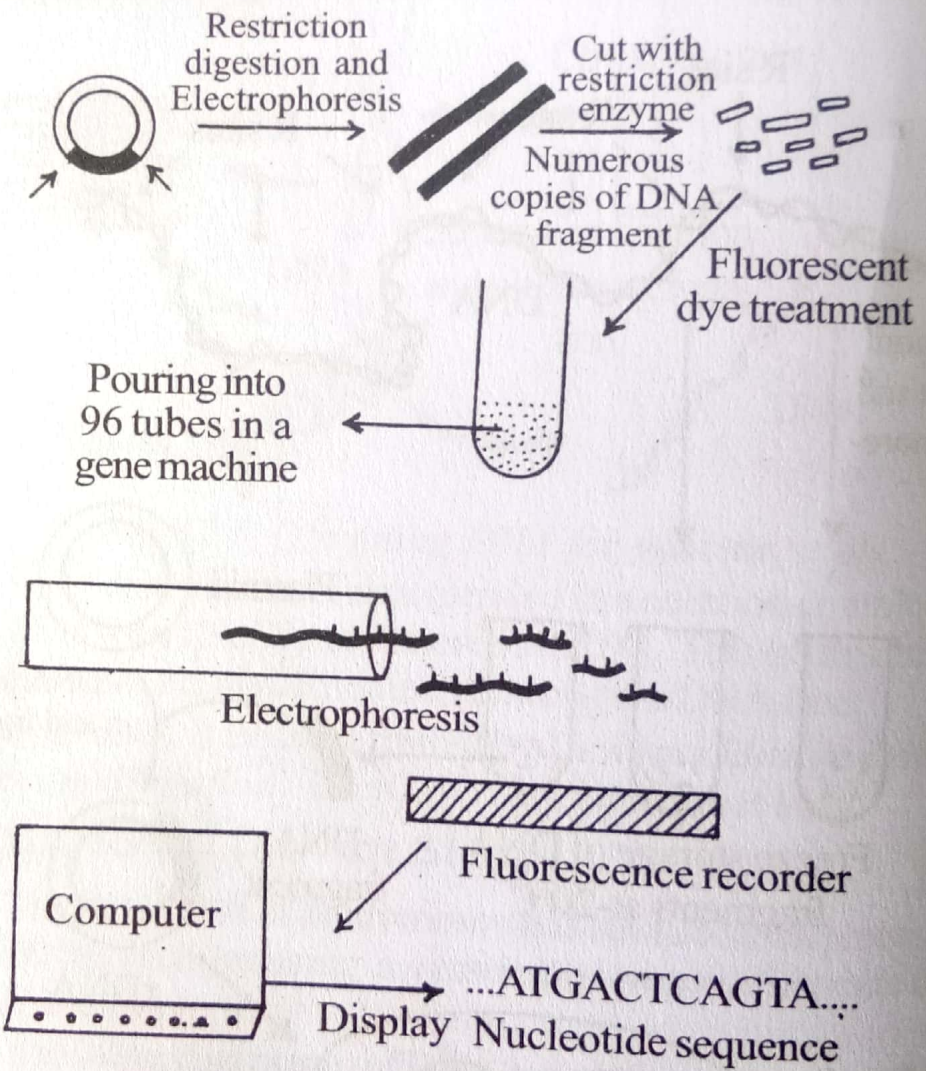


Fig.37.3. DNA sequencing and analysis.

2. It helps to detect genetic disorders in man and their inheritance. 289 genetic diseases have been known. Examples:

a) ***Chromosome*** 1: GBA gene - Gaucher disease
HPC 1 gene - Prostrate cancer
PS 2 (AD4) - Alzheimer's disease

b) *Chromosome* 2:	CREB	-	Loss of memory
	PAx3	-	Waardenberg syndrome (Mismatching in colours)
c) *Chromosome* 6:	SCA 1 gene	-	Spinocerebellar atrophy (Loss of contraction)
	IDDM 1 gene	-	Diabetes associated with kidney failure
	EPM 2 A	-	Epilepsy
d) *Chromosome* 7:	GCK gene	-	Diabetes
	CFTR	-	Cystic fibrosis
	OB gene	-	Obesity
e) *Chromosome* 10:	PAHX gene	-	Refsum disease
	OAT gene	-	Gyrate atrophy (Progressive loss of vision)
f) *Chromosome* 17:	BRCA 1	-	Breast cancer
g) *Chromosome* 20:	ADA 1	-	Severe Combined immunodeficiency
h) *Chromosome* Y:	SRY (TDF)	-	Testis differentiation factor

3. A proper remedial gene can be chosen and administered to treat genetic disease.

4. The action of harmful genes is blocked by introducing an antisense gene to stop the genetic disease.

5. The American company, ***Incyte Genomic*** has manufactured a gene chip with 10,000 gene kits. This chip can be used to detect ***genetic diseases, infectious diseases, oncogenes, parasitic worms,*** etc. at once during clinical diagnosis. The diagnosis is very fast; it will be done within 3hrs.

6. By matching, the human genome with the genome of *Drosophila*. Scientists conclude that this fly has remedial genes for 177 genetic diseases in man.

7. The information about the genome will be utilized to design babies with many superior characters such as skill, strength and free of genetic disorders.

17. Pedigree Analysis

A pedigree is a systematic listing of the parents and grand parents of a given individual. It is the family tree for ***a large number of individuals.***

A pedigree chart contains different types of symbols to indicate different types of individuals and they are as follows:

1. Normal male members of a family are shown by ***squares*** and normal females by ***circles.***

2. Mating is presented by a square and a circle connected by a ***horizontal line***.

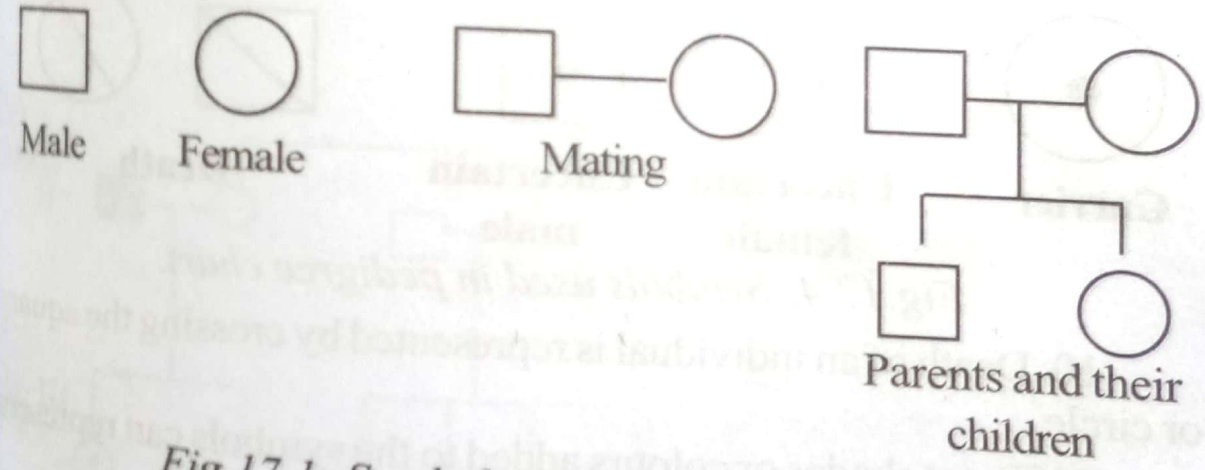


Fig.17.1: Symbols used in pedigree chart.

3. Parents and their children are presented by connecting the children with the mating line of parents.

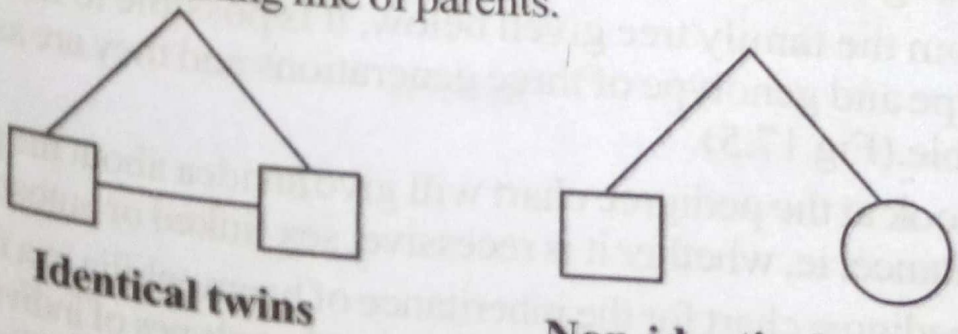


Fig.17.2: Symbols used in pedigree chart.

4. Identical twins are indicated by the children ... inverted 'V' line ...

Non-identical twins are indicated by children connected by an inverted 'V' line.

6. Affected males are presented by closed squares and females by closed circles.

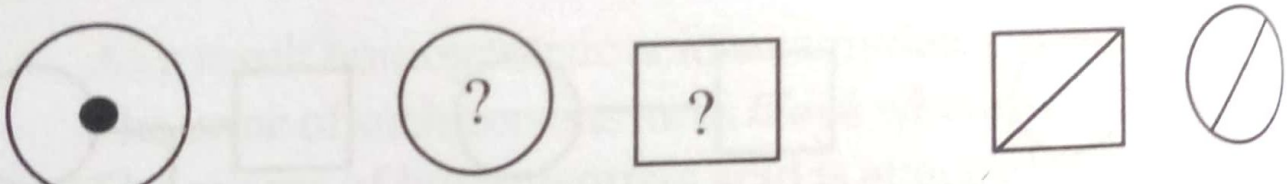
Affected male **Affected female** **Heterozygous male** **Heterozygous female**

Fig.17.3: Symbols used in pedigree chart.

7. Heterozygous males are represented by half - closed squares and females by half - closed circles.

8. Carrier of sex linked recessive is represented by a circle with dot inside.

9. For uncertain phenotype of the individual, a question mark is placed in the symbol.



Carrier **Uncertain female** **Uncertain male** **Death**

Fig.17.4: Symbols used in pedigree chart.

10. Death of an individual is represented by crossing the square or circle.

Different shades or colours added to the symbols can represent various phenotypes.

Each generation is listed on a separate row.

From the family tree given below, it is possible to find out the phenotype and genotype of three generations and they are as shown in the table.(Fig.17.5).

A look at the pedigree chart will give an idea about the pattern of inheritance, ie, whether it is recessive, sex linked or autosomal. The trait in a family

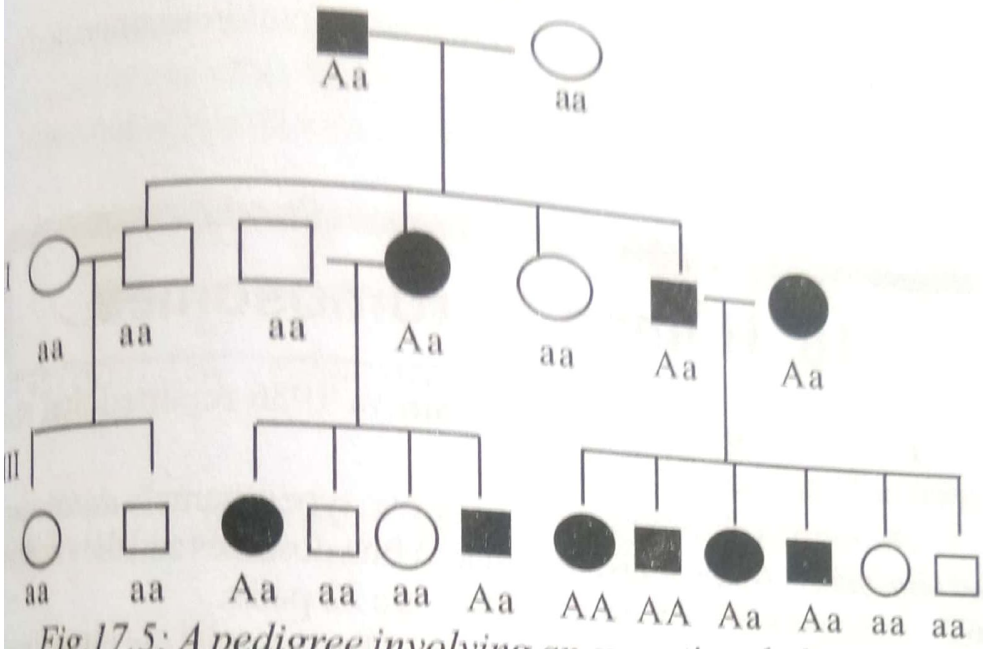
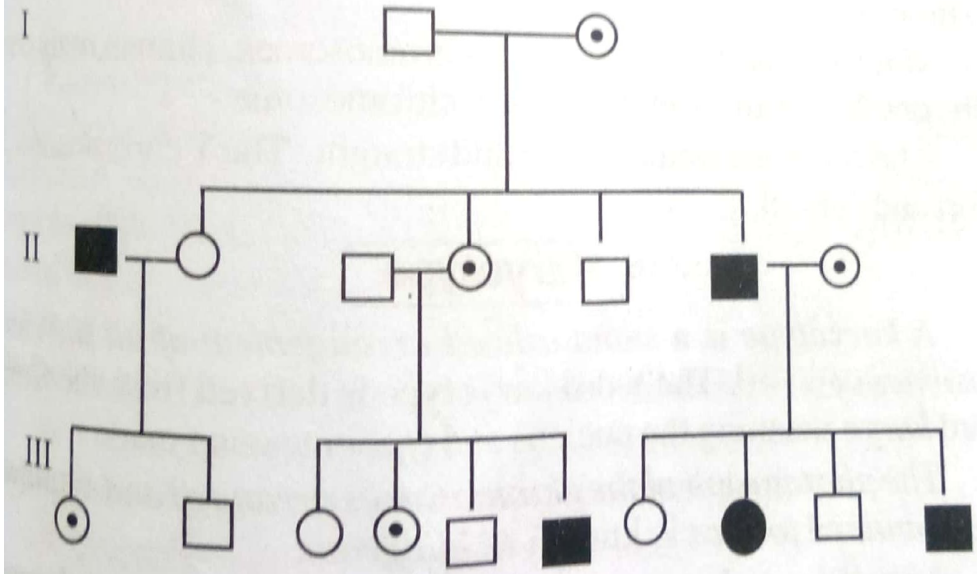


Fig.17.5: A pedigree involving an exceptional phenotype con olled by recessive allele "a". (Normally gene sym bols are not iven in pedigrees).



g.17.6: The Pedigree chart for the sex linked disease-Haemophilia.

Genetic engineering deals with the manipulation of genes. It refers to the artificial synthesis, modification, removal, addition and repair of the genetic material (DNA) to get a desired and useful phenotype. In this technique the DNA or genes of different origins are joined to produce a hybrid DNA called ***recombinant DNA.*** The science of genetic engineering is in its infancy.

Tools Used in Genetic Engineering

The following tools are used in genetic engineering:

1. Host
2. Vector
3. Desired DNA and
4. Enzyme

1. Host

Host is a cell where the recombinant DNA is allowed to multiply to produce thousands of copies. Bacteria, yeasts, etc. are used as hosts. Among bacteria *Escherichia coli* is used extensively as the host.

2. Vector

Vectors are the vehicles which are used to transfer the foreign DNA from one cell to another. The commonly used vector is the ***plasmid.*** It is an extrachromosomal, circular, double stranded DNA present in bacterial cells.

3. Desired DNA

It is the DNA to be cloned and transferred. It can either be synthesized artificially or be obtained from other cells. Eg. *Nitrogen fixing gene (NiF genes), insulin genes,* etc.

4. Enzymes

Enzymes are used in genetic engineering as ***chemical knives*** and ***sutures.*** They are used to cut and link DNA molecules. There are two types of

1. Restriction endonucleases: These enzymes are used as ***chemical knives.*** They cut DNA strands. These enzymes produce staggered cuts and the resulting fragments terminate in short single strandard projections called ***sticky ends.*** The important endonucleases are as follows: ***Eco R1, Hind III, Bam I, hae III,*** etc.

2. Ligase: These are used as ***chemical sutures.*** They link the cut ends of ***DNA*** strands. The fragments which have annealed together have ***nicks*** which can be covalently ***sealed*** by this enzyme.

Mechanism of Genetic Engineering

The mechanism of genetic engineering can be studied by transferring a ***Nif gene*** (nitrogen fixing gene) from a bacterium to a dicotyledonous plant. The Nif genes help the bacteria to convert free N_2 into nitrates. But dicotyledonous plants do not contain Nif genes; so they cannot use free N_2. When Nif genes are transferred from bacteria to plants, the plants get the ability to use free N_2. So the plant need not be given artificial fertilizers. This saves money labour and increases the yield.

The following steps are involved in genetic engineering:

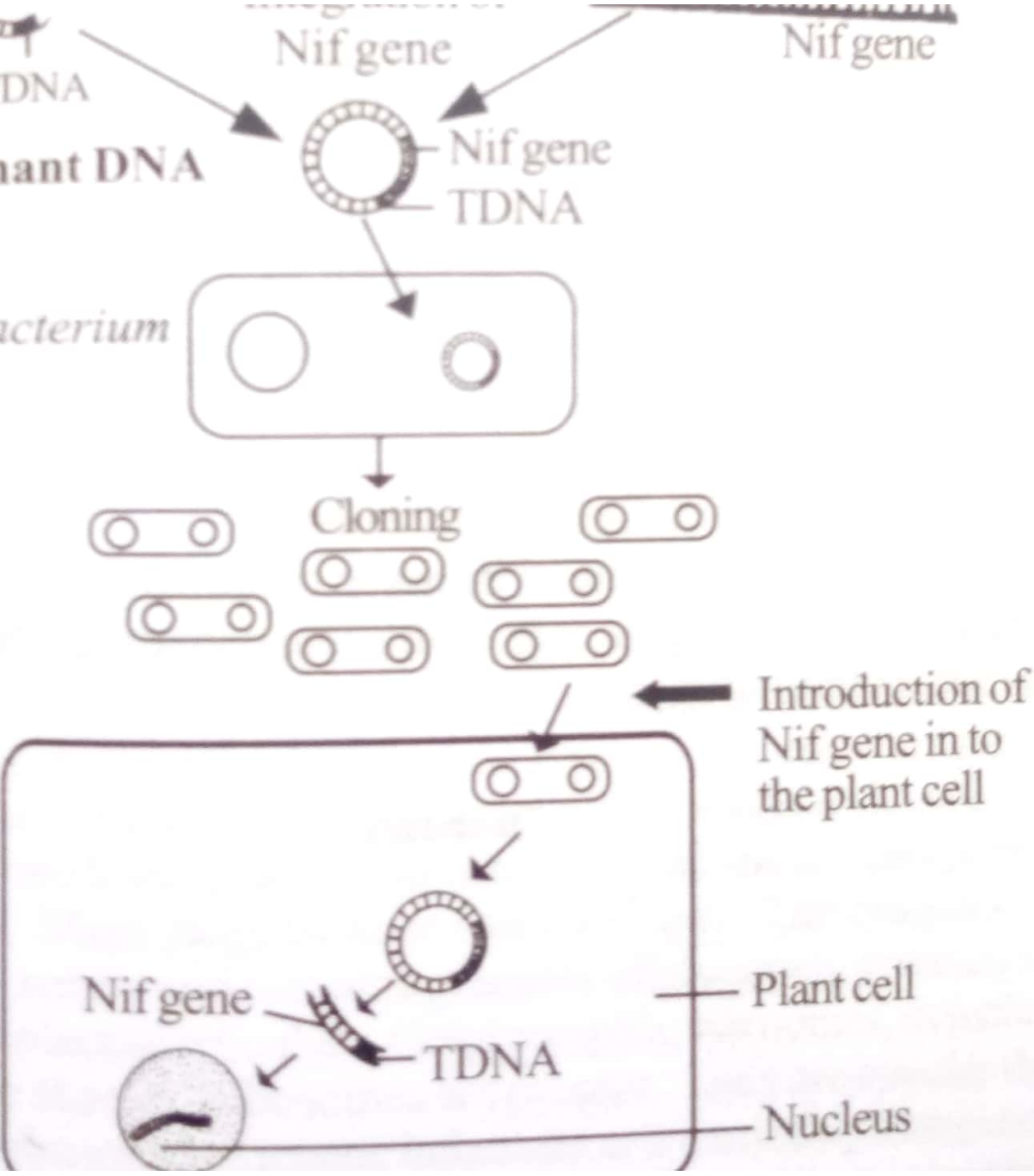
1. Isolation of Nif gene.
2. Integration of Nif gene.
3. Cloning the Nif gene.
4. Introduction into the plant genome.
5. Culture of plant cells into trees.

1. Isolation of Nif gene

Nif genes are present in the nitrogen fixing bacteria *Rhizobium.* The bacterial cell is opened by the enzyme ***lysozyme.*** The DNA is treated with a specific ***restriction endonuclease.*** It produces DNA fragments with ***sticky ends.*** These fragments carry Nif genes.

2. Integration of Nif gene in the vector

Vector is the vehicle which transfers the Nif gene to the plant genome. For transferring Nif genes, the commonly used vector is the ***Ti plasmid*** present in the soil bacterium *Agrobacterium tumefaciens.*



genes are also replicated. Thus thousands of copies of Nif genes are produced.

4. Introduction into the Plant Genome

Now the bacterium containing the recombinant plasmid is introduced into the plant cell. In the cell, the T-DNA containing the Nif

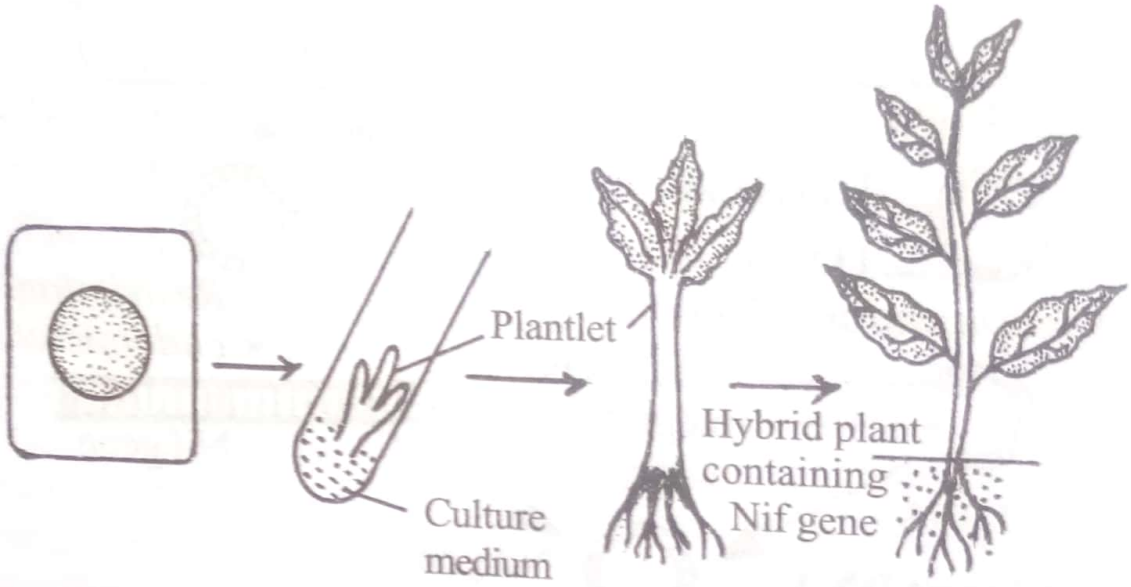


Fig.41.2: Culture of plant cell containing Nif gene

gene of the plasmid

Nucleic acid *is a macromolecule with acid property and it was isolated from the nucleus of cells and hence it is named as* ***nucleic acid.*** It is made up of ***C, H, O, N*** and ***P.***

The nucleic acid was first isolated in 1868 by ***Miescher*** from the nuclei of pus cells on hospital bandages. He called it ***nuclein***. ***Altmann*** (1889) gave the name nucleic acid.

Nucleic acids are found in all organisms such as ***plants, animals, bacteria*** and ***viruses.*** They are found in the nucleus as well as in the cytoplasm.

Nucleic acid molecule is a long chain polymer. It is composed of monomeric units, called ***nucleotides***. Each nucleotide consists of a ***nucleoside*** and a ***phosphate group***. Each nucleoside consists of a ***pentose sugar*** and a ***nitrogenous base***. The sugar is ***ribose*** in the case of RNA and ***deoxyribose*** in the case of DNA.

The nitrogenous bases are of two types, namely ***purines*** and ***pyrimidines***. There are two main purine bases, ***adenine*** and ***guanine***. Similarly there are three main pyrimidine bases. They are ***cytosine, thymine*** and ***uracil***. DNA contains all these bases except ***uracil***. RNA contains all these base except ***thymine***.

Nucleosides

A base combined with a sugar molecule is called a ***nucleoside***. In DNA, four different nucleosides are present. They are ***adenosine, guanosine, cytidine*** and ***thymidine***. In RNA, deoxyribose sugar is replaced by ribose and the base thymine is replaced by Uracil.

Nucleotides

A nucleotide is derived from a nucleoside by the addition of a molecule of phosphoric acid. The DNA contains four different types of nucleotides. They are adenylic acid, guanylic acid, cytidylic acid

and thymidylic acid. The RNA contains uridylic acid instead of thymidylic acid.

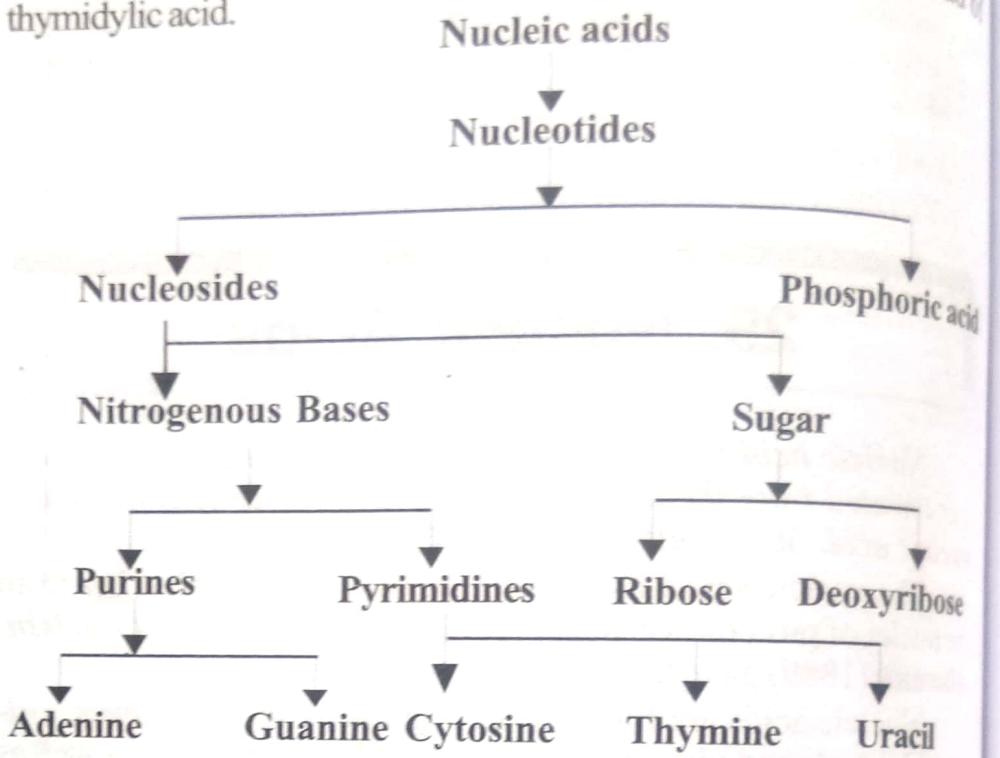


Fig.29.1: Components of Nucleic Acids.

Polynucleotide: A number of nucleotide units link with one another to form a ***polynucleotide chain*** or ***nucleic acid.***

Nucleic acids are broadly classified into two types based on the type of sugar present in them. They are

1. Deoxyribonucleic acid (DNA)
2. Ribonucleic acid (RNA)

The ribonucleic acid is further divided into three types, namely

1. messenger RNA (mRNA)
2. transfer RNA (tRNA)
3. ribosomal RNA (rRNA)

Deoxyribonucleic Acid (DNA)

Deoxyribonucleic acid (DNA) is the molecule of heredity. It functions as the ***genes***.

DNA is present in all cells except plant virus. In eukaryotic cells, DNA is present in the chromosomes of nucleus. In addition, the mitochondria and plastids also contain DNA.

In ***eukaryotic nucleus,*** the DNA is in the form of a ***double helix***. In bacteria, mitochondria and plastids the DNA molecules are ***circular***. In viruses and bacteriophages, they are ***coiled***.

The number of DNA molecules in eukaryotic cells corresponds to the number of chromosomes per cell.

DNA is made up of three chemical components, namely *1. Sugar 2. **Phosphoric acid*** and *3. **Nitrogenous bases.***

1. Sugar

The sugar present in the DNA is called ***deoxyribose***. It is a pentose sugar which contains five carbon atoms ($C_5H_{10}O_4$). It contains one O atom less than the ribose sugar. The second carbon of deoxyribose bonds with ***two hydrogen*** atoms; but in ribose sugar, the second carbon atom bonds with one hydrogen atom and one hydroxyl group (OH).

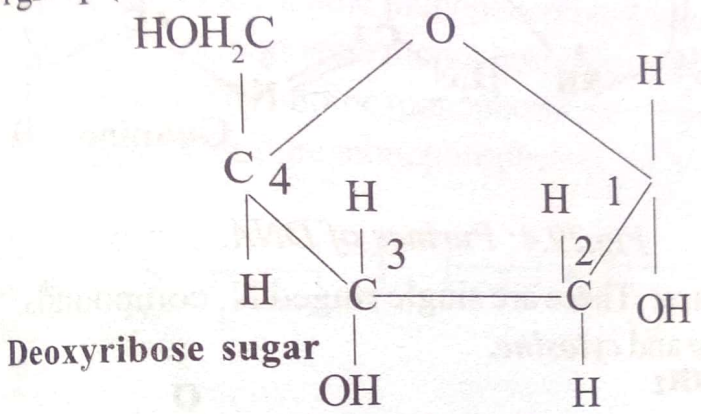


Fig.29.2: Deoxyribose-ring structure.

2. Phosphoric Acid (H_3PO_4)

Phosphoric acid links consecutive nucleotides by joining their pentose sugars with a ***phosphate diester*** bond. This bond links carbon 5′ in one nucleoside with carbon 3′ in the next nucleoside.

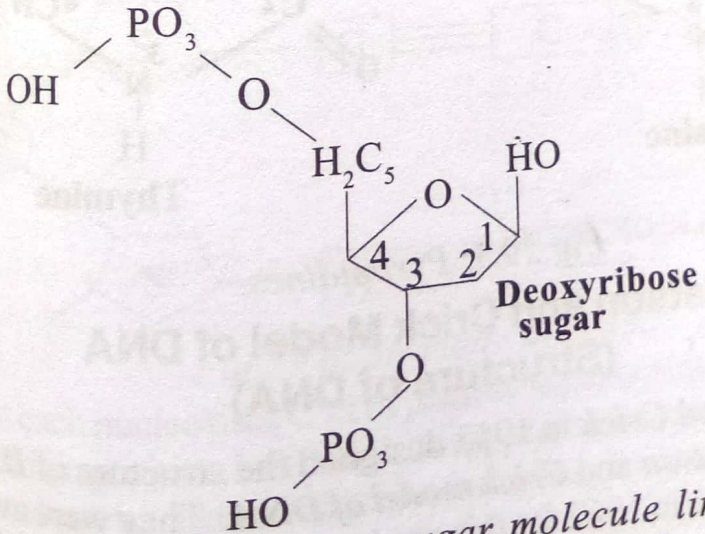


Fig.29.3: Deoxyribose sugar molecule linked with one phosphate group at 5th position and another phosphate group at 3rd position.

3. Nitrogenous Bases

These are N_2 containing organic compounds. They are of two types, namely ***purines*** and ***pyrimidines***.

Purines: Purines are two-ringed N_2 compounds. They include ***adenine*** and ***guanine***.

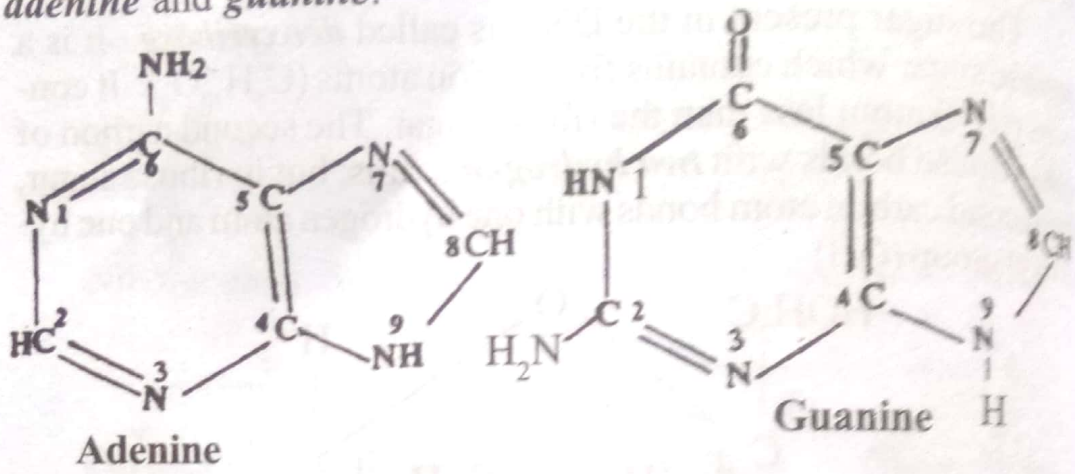


Fig.29.4: Purines of DNA.

Pyrimidines: These are single ringed N_2 compounds. They include ***thymine*** and ***cytosine.***

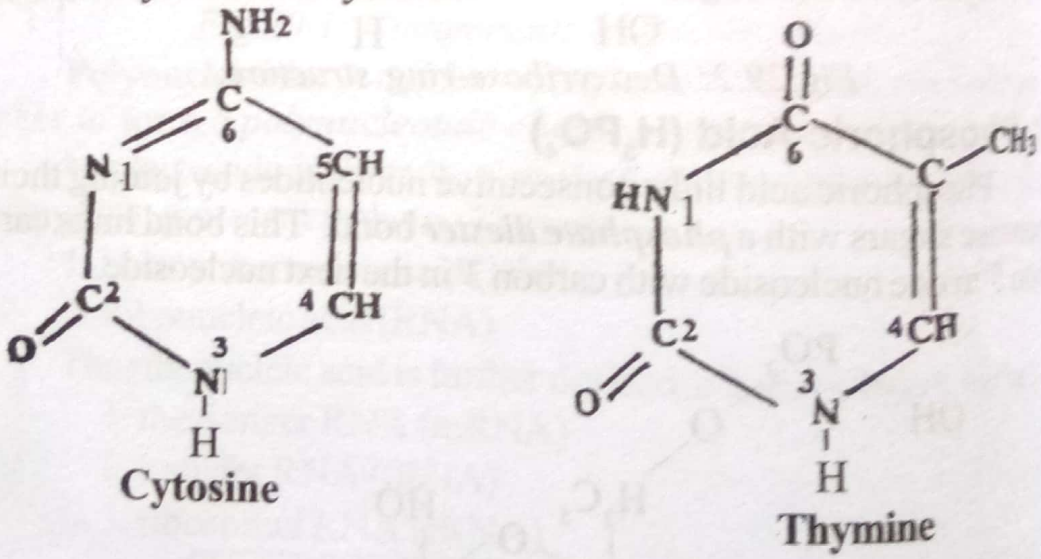


Fig.29.5: Pyrimidines.

Watson and Crick Model of DNA (Structure of DNA)

Watson and ***Crick*** in 1953 designed the structure of ***DNA***. It is called the ***Watson*** and ***Crick model of DNA***. They were awarded with Nobel Prize in 1962 for this work.

According to ***Watson*** and ***Crick,*** DNA is in the form of a ***double helix.***

DNA is a ***nucleic acid.*** It is a ***macromolecule***. It is made up of two ***chains***. Each chain is a ***polynucleotide chain***. Each polynucleotide is made up of many small units called ***nucleotides***. Each nucleotide is made up of three chemical components, namely a ***phosphoric acid***, a ***deoxyribose sugar*** and a ***nitrogen base***.

The nitrogen bases are ***adenine, guanine, thymine*** and ***cytosine***.

The nucleotides of DNA are named according to the type of nitrogen bases present. As there are four types of nitrogen bases, DNA contains four types of nucleotides, namely

1. AMP - Adenosine monophosphate (Adenylic acid)
2. GMP - Guanosine monophosphate (Guanylic acid)
3. TMP - Thymidine monophosphate (Thymidylic acid)
4. CMP - Cytidine monophosphate (Cytidylic acid)

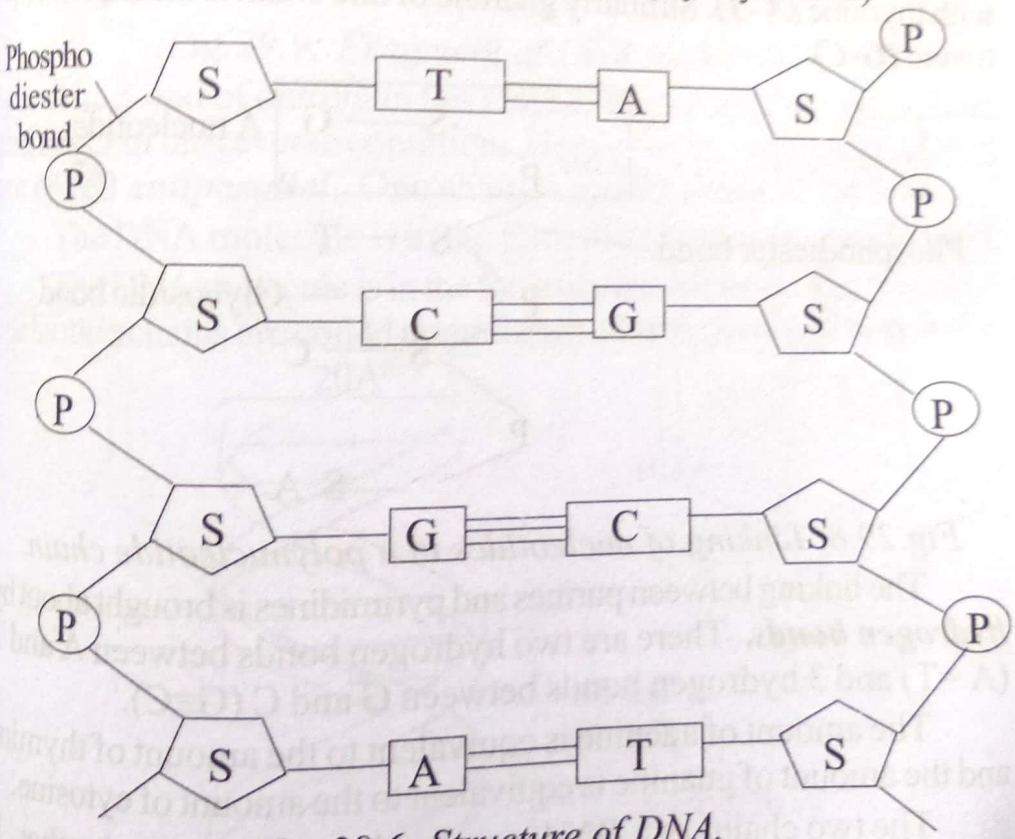


Fig.29.6: Structure of DNA.

In each nucleoside, C - I of pentose sugar is attached with nitrogen atom (in position 1 of purine or in position 9 of pyrimidine) of the nitrogen base by a glycosidic bond. A phosphoric acid molecule is linked with the sugar of nucleoside to form a nucleotide.

Many nucleotides are linked together to form a ***polynucleotide chain.*** Two nucleotides are joined by a ***phosphodiester bond.*** It is

ponent of another nucleotide.

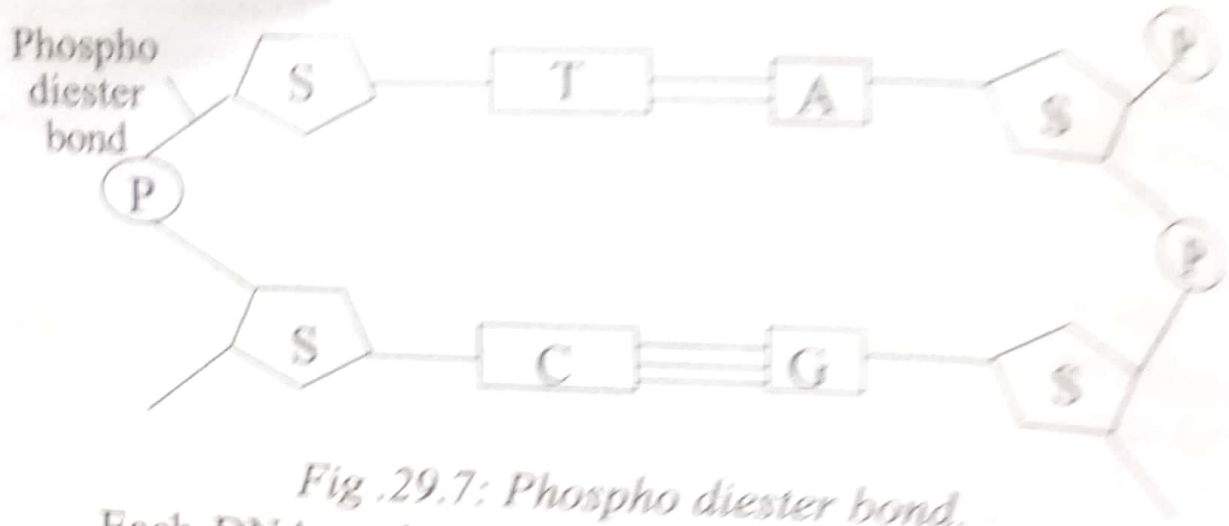


Fig .29.7: Phospho diester bond.

Each DNA molecule has two polynucleotide chains. The nucleotides of adjacent chains are linked. Adenine is always linked with thymine ***(A -T)***. Similarly guanine of one chain is linked with cytosine ***(G-C)***.

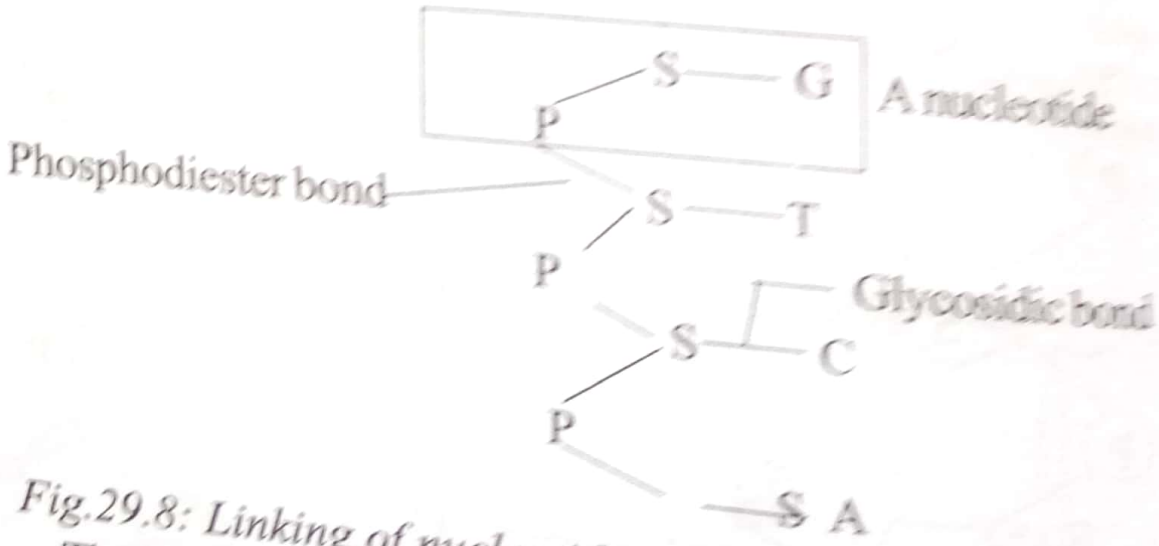


Fig.29.8: Linking of nucleotides in a polynucleotide chain.

The linking between purines and pyrimidines is brought about by ***hydrogen bonds.*** There are two hydrogen bonds between A and T (A =T) and 3 hydrogen bonds between G and C (G≡C).

The amount of adenine is equivalent to the amount of thymine and the amount of guanine is equivalent to the amount of cytosine.

The two chains of a ***DNA*** are ***complementary*** to each other. If the sequence of base in ***one chain*** is ***A, G, A, T, G, C,*** then the sequence of base in the ***second chain*** is ***T, C, T, A, C, G.***

At one end of the polynucleotide chain, the 3 rd carbon of the sugar is free and it is not linked to any nucleotide. This end is called ***3 prime (3′) end.*** At the other end, the 5 th carbon of the sugar is free and this end is called ***5 prime (5′) end.***

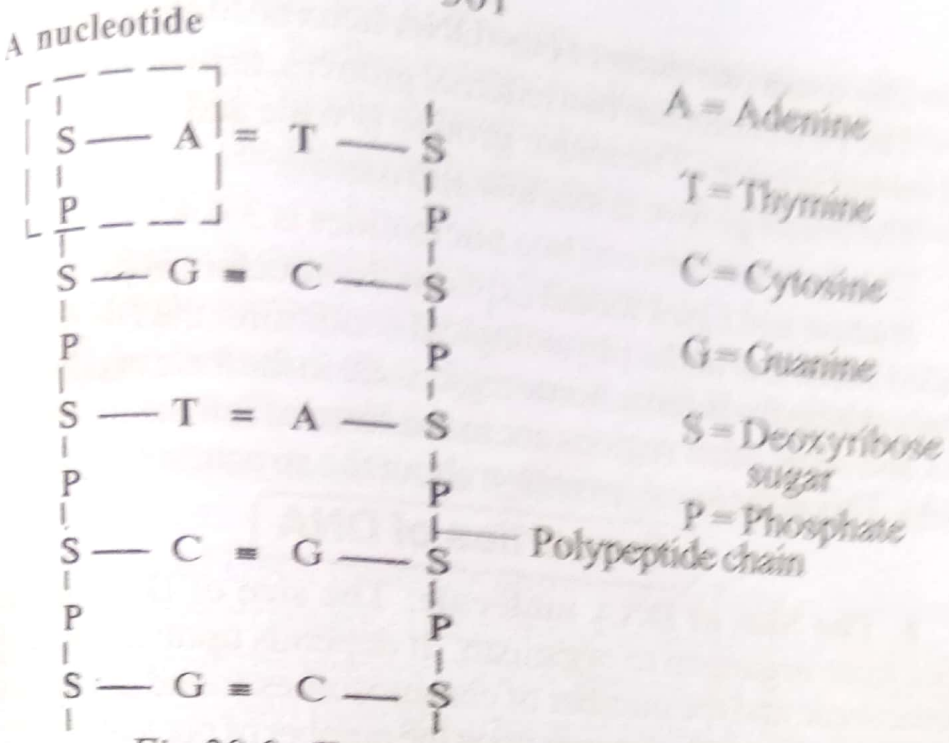


Fig.29.9: Fragment of DNA molecules.

The 3′ end of one chain lies close to the 5′ end of the other chain and never in the reverse condition. Hence the two strands of a DNA are called ***antiparallel***. One chain is ***upside down*** to the other.

The DNA molecule is in the form of a spiral stair case (ladder).

The DNA molecule is in the form of a double helix. The two polynucleotide chains are coiled around each other to form a ***double helix.***

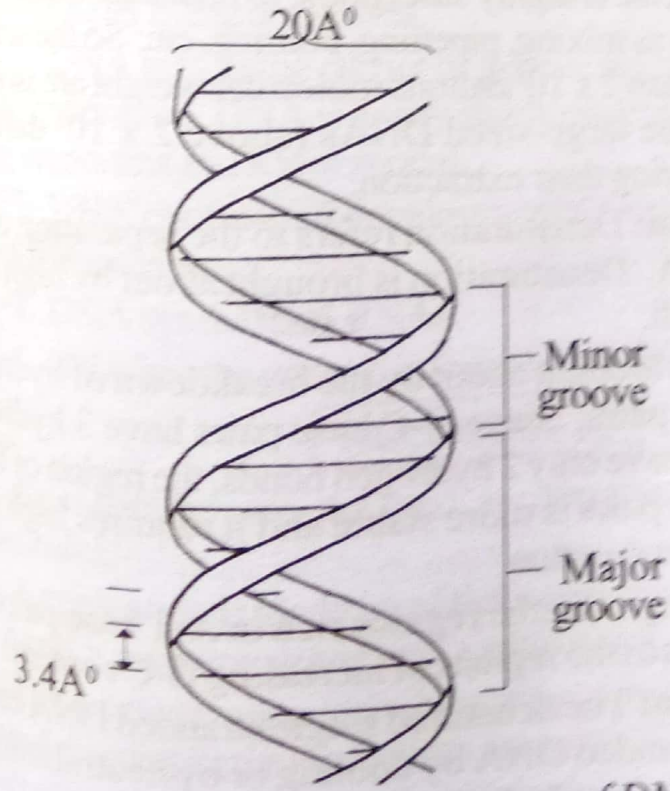


Fig.29.10: Structure of DNA.

The width (diameter) of the DNA helix is 20A°.

The DNA helix has two external grooves, namely ***major groove*** and ***minor groove.*** The major groove is wide and deep.

The minor groove is shallow and narrow.

The distance between two nucleotides is 3.4 A°.

Watson and ***Crick*** model explains the structure of β-DNA (right handed helix. But under physiological conditions, the DNA does not always exist in the β-form. Some regions are in the form of right handed helix and some other regions are in the form of left handed helix (A-DNA). This is the latest invention about the structure of DNA.

Properties of DNA

1. The Size of DNA molecule: The size of DNA molecule varies from organism to organism. It depends upon the size of the chromosome and the number of chromosomes found in each living cell. The size basically depends upon the number of nucleotides present in each DNA molecule. The size of DNA molecule ranges from 0.7 mm to 40, 000 mm (4 cms).

2. Fragility of DNA molecule: The DNA molecule is highly fragile. The fragility of DNA molecule is determined by its length. Larger molecules break easily. But smaller molecules are not susceptible to breakage.

The DNA molecule is highly susceptible to breakage during handling operations, such as mixing, pipetting, pouring, etc. So the smaller molecules with less than 2×10^8 daltons molecular weight are isolated without damage. The large-sized DNAs (above 2×10^8 daltons) undergo breakage during their extraction.

3. Denaturation: Denaturation refers to the separation of the two strands of a DNA. Denaturation is brought about by high temperature, acid or alkali.

Denaturation is brought about by the breakdown of hydrogen bonds between base pairs. Since G-C base pairs have 3 hydrogen bonds and A-T pairs have only 2 hydrogen bonds, the region of DNA containing G-C base pairs is more stable and it requires high temperature or pH for denaturation.

Denaturation begins in the regions rich in A-T base pairs and progressively extends to the regions of increasing G-C content.

5. Effect of pH on DNA: The DNA is stable around the neutral pH in the solution. Further increase in pH (alkali treatment) causes strand separation and finally denaturation occurs above pH 11.3.

6. Stability: The DNA is a highly stable molecule. The stability is due to two forces:

a. Hydrogen bonding between the bases.

b. Hydrophobic interactions between bases.

7. Hyperchromic Effect: DNA molecule absorbs light energy. This is a property of individual bases.

The intact DNA absorbs less light energy as its bases are packed into a double helix.

A denatured DNA molecule absorbs more light as its bases in single strands are exposed. The increase in the absorption of light occurs eventhough the amount of DNA remains the same. This phenomenon of increased light absorption is called ***hyperchromic effect.***

A single stranded DNA does not show the hyperchromic effect. This phenomenon of hyperchromic effect can be used to distinguish single or double stranded DNAs in the sample.

Functions of DNA

DNA plays an important role in all biosynthetic and hereditary functions of all living organisms.

1. DNA acts as the carrier of genetic information from generation to generation. DNA is a very stable macromolecule in almost all living organisms and it is immortal.

The nitrogen base may be a ***purine*** or ***pyrimidine***. The purines are two types, namely ***adenine*** and ***guanine***. The pyrimidines are of three types, namely ***thymine***, ***cytosine*** and ***uracil***.

The nucleotides are named according to the purines and pyrimidines. They are the following:

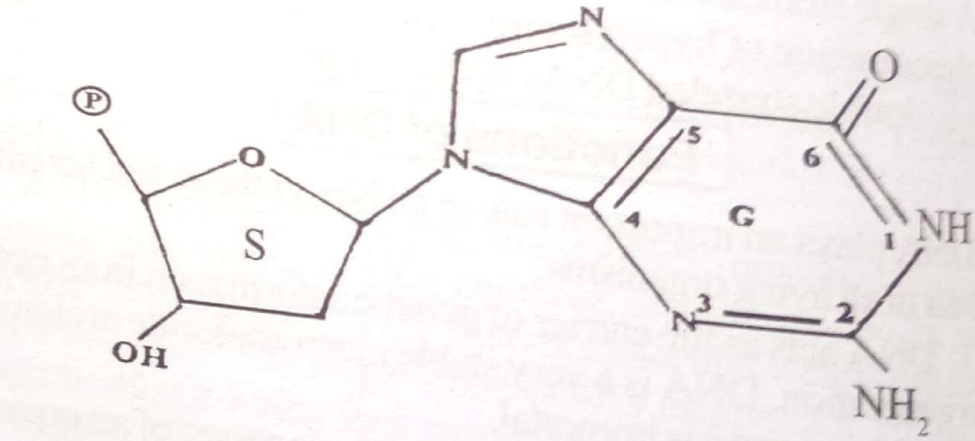
1. Adenylic acid or Adenosine monophosphate (AMP)
2. Guanylic acid or Guanosine monophosphate (GMP)
3. Thymidylic acid or Thymidine monophosphate (TMP)
4. Cytidylic acid or Cytosine monophosphate (CMP)
5. Uridylic acid or Uridine monophosphate (UMP)

These five nucleotides form the basic units of nucleic acids, DNA and RNA.

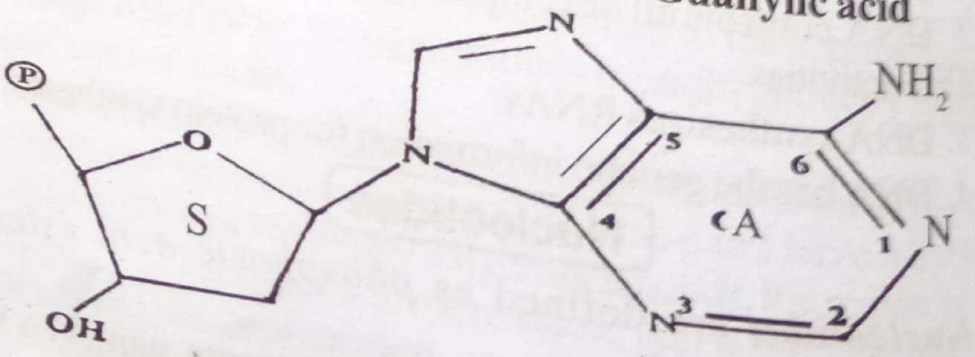
In addition, many nucleotides occur freely in the tissues. They are the following:

ADP - Adenosine diphosphate

ATP - Adenosine triphosphate, etc.



Guanylic acid



Adenylic acid

Fig.29.11: Nucleotides of DNA.

A typical nucleotide is composed of three chemical components, namely a nitrogen base, a pentose sugar and a phosphoric acid. The base and phosphoric acid are attached to th

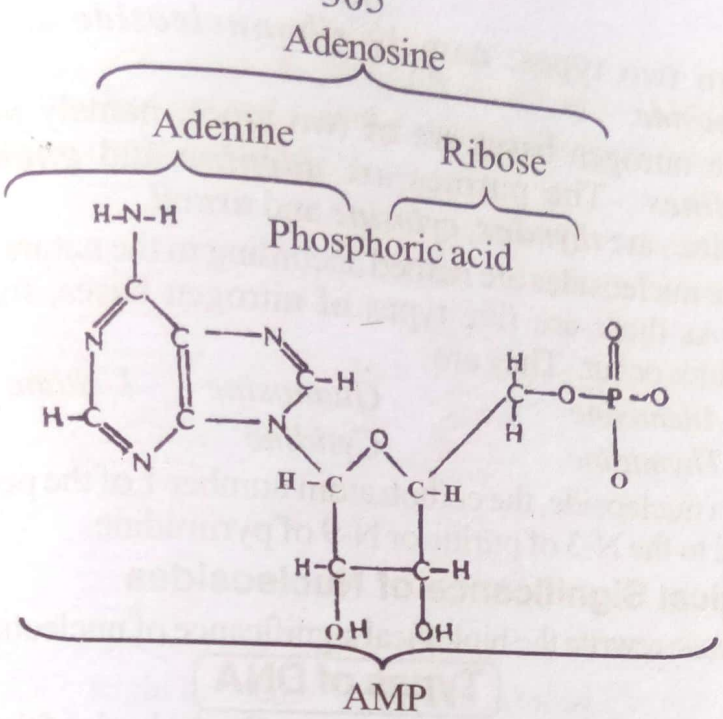


Fig.29.12: Structure of AMP.

On hydrolysis, the nucleotide splits into ***phosphoric acid*** and a ***nucleoside***. The nucleoside is made up of a base and a pentose sugar.

Biological Significance of Nucleotides

1. Components of Nucleic acid: Nucleotides form the main component of nucleic acids.

2. Genetic material: Deoxyribonucleotides of DNA function as the genetic material. They transmit hereditary characters from parents to offspring.

3. Source of High energy: Nucleotides functions as the source of high energy. Eg. *ATP, UTP, CTP*, etc.

4. Oxidative phosphorylation: ATP is involved in oxidative phosphorylation.

5. Coenzymes: Certain nucleotides function as coenzymes. Eg. *UDPG, CoA, FMN, FAD,* etc.

6. Vitamins: Certain nucleotides function as vitamin- B. Eg. *FMN, FAD, NAD*, etc.

Nucleosides

Compounds that contain nitrogen bases linked to pentose sugars are called ***nucleosides.***

The pentose sugars are of two types, namely ***ribose*** sugar and ***deoxyribose*** sugar. Accordingly, the nucleosides are broadly classi-

fied into two types, namely ***ribonucleoside*** and ***deoxyribonucleoside***.

The nitrogen bases are of two types, namely ***purines*** and ***pyrimidines***. The purines are ***adenine*** and ***guanine***. The pyrimidines are ***thymine***, ***cytosine*** and ***uracil***.

The nucleosides are named according to the nature of nitrogen bases. As there are five types of nitrogen bases, five types of nucleosides occur. They are

Adenosine	*Guanosine*	*Uridine*
Thymidine	*Cytidine*	

In a nucleoside, the carbon atom number 1 of the pentose sugar is linked to the N-3 of purine or N-9 of pyrimidine.

Biological Significance of Nucleosides

Please rewrite the biological significance of nucleotides.

Types of DNA

DNA is classified in various ways. On the basis of the number of strands, DNA is classified into two types, namely ***double stranded DNA*** and ***single stranded DNA.***

On the basis of number of nucleotide residues, DNA is classified into 4 types. They are : 1. ***A-DNA*** 2. ***B-DNA*** 3. ***Z-DNA*** 4.***RL helix Model.***

On the basis of the shape, DNA is classified into three types, namely a. ***Circular DNA,*** b. ***Relaxed DNA*** c. ***Supercoiled DNA.***

On the basis of the nature of nucleotide sequence in duplex DNA, they are of two types. 1. ***Palindromic DNA*** 2. ***Repetitive DNA*** or ***Satellite DNA.***

1. Double Stranded DNA

Double stranded DNA is otherwise known as ***double helical DNA.*** In most of the organisms, except a few viruses, the DNA has a double stranded structure.

2. Single Stranded DNA

DNA of some viruses such as φ x 174 infecting *E. coli* is single-stranded.

3. A-DNA

It is a double helical DNA having 11 residues per turn. It is a ***right handed helix***. It is formed by the dehydration of B-DNA. Double stranded RNA also exists in A-form. It has 11 basepairs per turn.

The sugar phosphate backbone is regular.

The repeating units are ***mononucleotides.***

4. B-DNA

This is the ***Watson*** and ***Crick*** double helix having 10 residues per turn. It is a ***right handed*** DNA.

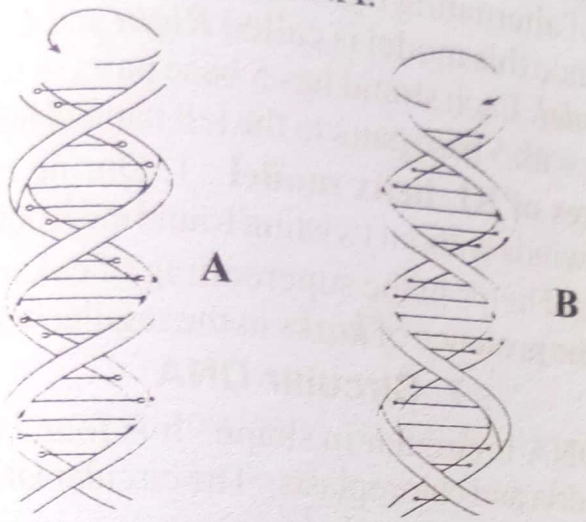


Fig.29.13:A.B DNA; B.Z DNA.

5. Z-DNA

It is a left handed double helix having 12 base pairs per turn. The sugar phosphate backbone is ***Zig-Zag*** in orientation (Fig.29.13B).

The ZDNA has some alternating repeated units of dinucleotides throughout the DNA.

The ZDNA model was proposed by ***Rich***. It plays a role in genetic ***recombination.***

Table 29.1: Difference between Z-DNA and B-DNA.

S.No.	Z-DNA	B-DNA
1	Left handed.	Right handed.
2	Phosphate backbone is **Zigzag**.	phosphate backbone is ***regular***.
3	Its repeating units are dinucleotide.	Its repeating units are mononucleotides.
4	It has 12bp for every twist of 360°.	It has 10bp.
5	One complete helix is 45A°.	One complete helix is 34A°.
6	The angle twist of one helix is 60°.	Angle twist of one helix is 36°.
7	Diameter is 18A°.	Diameter is 20A°.

6. RL helix model of DNA

According to ***Rodley*** *et.al* and ***Sasi Sekharan,*** the DNA duplex is formed of alternating right and left handed helices arranged side by side. Hence this model is called ***Right*** and ***Left helix model*** or ***R-L helix model***. Each strand has 5 base pairs in the right handed helix alternating with 5 base pairs in the left handed helix.

Advantages of RL helix model : 1. During replication, the DNA duplex unwinds without twisting round each other.

2.This model helps in the supercoiling of eukaryotic chromosomes without the presence of ***kinks*** in the regular helix.

7. Circular DNA

Circular DNA is circular in shape. It is found in bacteria, viruses, mitochondria and chloroplasts. The circular DNA may be ***single stranded*** or ***double stranded.***

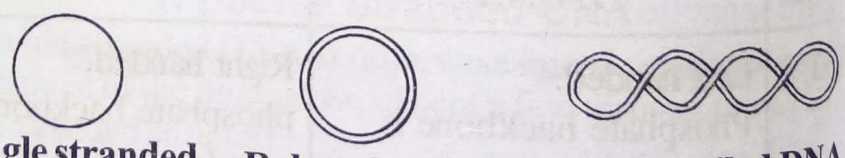
Single strand circular DNA is made up of a single strand. It is found in some viruses like φ x 174. Double strand circular DNA is found in bacteria, most of the viruses, mitochondria, chloroplasts, etc.

8. Relaxed DNA

Circular DNA without any helical coiling is called ***relaxed DNA.***

9. Supercoiled DNA

In supercoiled DNA, the axis of the double helix itself it twisted to form a super helix. It can produce negative supercoiling and positive supercoiling. The degree of coiling is controlled by ***topoisomerases*** and ***gyrases***.



Single stranded DNA **Relaxed double stranded DNA** **Super coiled DNA**

Fig.29.14: Shapes of DNA.

10. Palindromic DNA

Palindrome is a *word or sentence that reads the same both forwards and backwards.* ***Palindromic DNA*** is *a DNA containing palindromic sequences of nucleotides.* In ***palindromic sequence,*** *the sequence of nucleotides goes in one direction in one strand and in another direction in the second strand. It is an inverted sequence.*

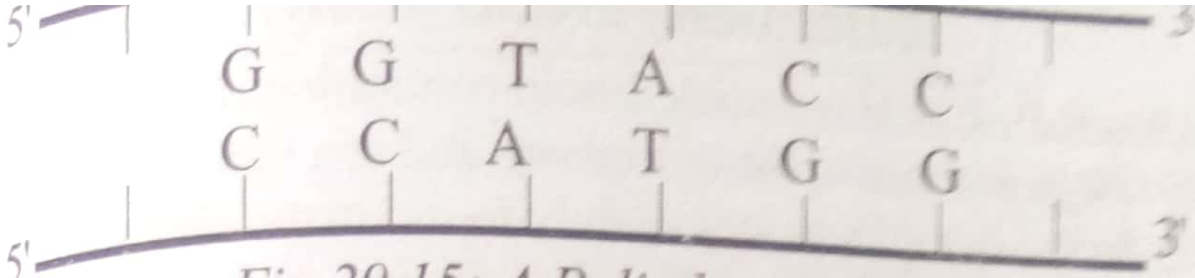


Fig.29.15: A Palindromic DNA.

The term ***palindromic DNA*** was first used by ***Wilson*** and ***Thomas*** in 1974.

Palindromic sequences are found in the DNA of both prokaryotes and eukaryotes. The palindromic sequences may have a length of 3 to 10 nucleotides or hundreds or thousands of nucleotides. Comparatively, the palindromic sequences of eukaryotes are longer than that of prokaryotes.

The palindromic sequences of DNA strands transcribe the same RNA. Endonuclease recognises the specific palindromic sequence in DNA and produces a staggered cut which results in ***sticky ends.***

11. Repetitive DNA or Satellite DNA

When very short sequences of base pairs are repeated many times in DNA, the DNA is called ***repetitive DNA*** or ***satellite DNA.*** In repetitive DNA, some genes are repeated in tandem several hundred or thousand times.

All eukaryotes, except yeast, contain repetitive ***DNA. Repetitive DNA*** is absent ***from prokaryotes.***

In *Xenopus laevis,* the genes for 18S rRNA and 28S rRNA are repeated about 450 times. The repeated genes are tandemly arranged and are separated by ***spacer regions.***