:- Variation in Chromosome Structure and Number :- (Unit-II)

* Genetic variation refers to differences between members of the same species or those of different sp.

* Chromosomes of each sp has a characteristic morphology (structure) and number

* Sometimes due to certain accidents or irregularities at the time of cell division, crossing over or fertilization some alterations in the morphology & number of chromosome take place.

* Chromosomal aberration causes structural abnormalities in chromosome structure. They alter the sequence or the kind of genes present in chromosome.

Chromosomal aberration are substantial changes in chromosom structure.

These typically affect more than one gene, also called Chromosomal mutation.

Teacher's Signature : .....

* Chromosome mutation are inherited once they occur and are of following type :-

OR

* There are two primary ways in which the structure of chromosomes can be altered.

STRUCTURAL CHANGES

1.) The total amount of genetic information in the chromosome can change OR Change in number of genes

a) Loss/decrease :- Deletion
b) Addition/Increase :- Duplication

2. The genetic material may remain same, but is rearranged OR Changes in gene arrangement

a) Rotation of a group of genes 180°C within one chromosome: Inversion

b) Exchange of parts between chromosomes of different pair :- Translocation

NUMERICAL CHANGES

a) Loss or gain of a part of chromosome set Aneuploidy
b) Loss or gain of whole chromosome set Euploidy
=> 1) Loss of an entire set of chromosomes Haploidy
=> 2) Addition of one or more set of chromosomes Polyploidy

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To understand the abnormalities of chromosome structure, we have to consider two important feature of chromosome behaviour

1) During prophase-I of meiosis, homologous regions of chromosome show a great affinity for pairing and they often go through considerable contortions in order to pair. This results in many curious structures observed in cells containing one normal chromosome set plus an aberrant set.

2. Structural changes usually involve chromosome breakage

Types of Structural Changes in Chromosome

* Structural abnormalities can occur in both homologous chromosome of a pair or in only one of them

* When both homologous chromosomes are involved, they are called Structural homozygotes eg:- deletion & duplication homozygotes

* When only one homologous chromosome is involved, it is called Structural heterozygotes eg:- Translocation heterozygote
Translocation homozygote

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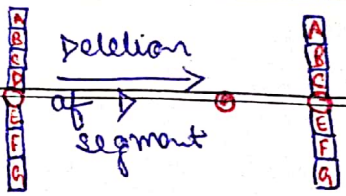


1. Deletion

* It means breakage in the chromosome followed by loss of the chromosomal segments.

* These deleted fragment is acentric, lag in anaphase movement and are lost from recoginizing nuceli OR lost from multiple rounds of cell division. Such loss of a portion of a chromosome is called deletion

*

* The chromosome with deletions can never revert to a normal conditions, because the DNA is gone degraded.

* If gametes arise from the cells, having deleted chromosome, this deletion is transmitted to the next generation

* Deletions start with chromosome breaks induced by.
  - ⇒ Heat or Radiation (Ionizing)
  - ⇒ Chemicals
  - ⇒ Viruses
  - ⇒ Errors in recombination

*

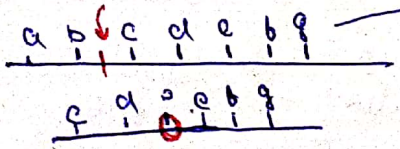
Deletion

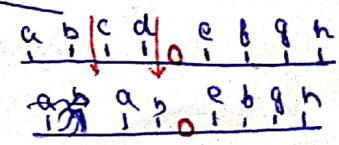
Terminal

* A terminal section of a chromosome is absent, it is resulted by only one breakage

Intercalary

* An intermediate portion of a chromosome is lost & it is usually by two breakage





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* A diploid cell has a homologous of the chromosome which has lost a segment. The corresponding segment of the intact homologue will have alleles of the genes that the cell has lost. Such a cell is said to be heterozygous for a deficiency.

* A very small deficiency in the heterozygous state is viable, but if homozygous it is lethal

* The occurence of a deficiency can sometimes be inferred from the results of a genetic cross when a rare recessive phenotype unexpectedly appears in the progeny.

$D D \times d d$

D control dominant expression trait

d is a recessive allele.

$\downarrow$

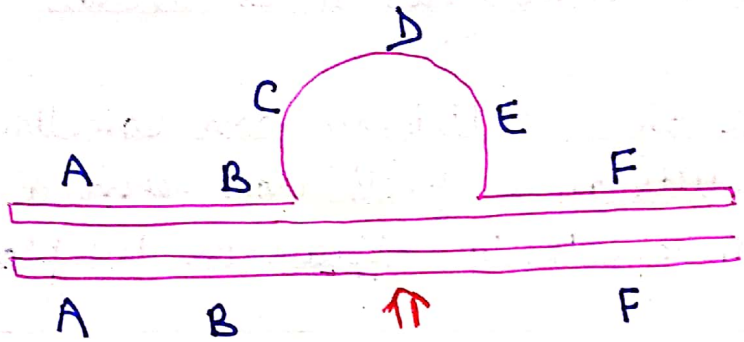
Dd.

In this cross dominant trait F_1 shows the dominant trait & have genotype Dd.

* If on the contrary, some F_1 individuals show the recessive phenotype, one explation could be sought in a deletion of the chromosomal segment bearing gene D. It is best to confirm the occcurence of deficiency from a cytological study of the chromosome.

Teacher's Signature : .....

* If one of the homologues is deficient over a small lenght, the corresponding portion of the second homologue has nothing to pair with. It therefore, forms a loop, which is clearly visible in cytological studies.
* Deletion loop are also detected in polytene chromosome of Drosophila,



Deletion involving C, D & E.

Genetical Effect of Deletion

* Deletion of some chromosome regions produce their own unique phenotype.
* A good example of this is a dominant notch-wing mutation in Drosophila. This is a small deletion and acts as a recessive lethal.

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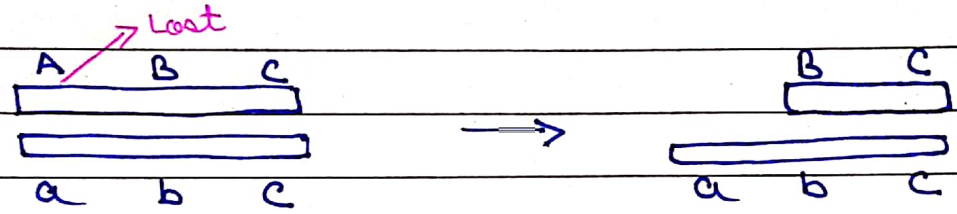
* So, In the presence of a deletion, a recessive allele of the normal homologous chromosome will behave like a dominant allele, i.e. it will be phenotypically expressed. this phenomenon is called pseudodominance



ABC Normal heterozygotes

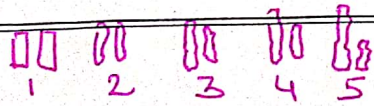
a-BC exhibits pseudodominance.
a is dominant which is phenotypically expressed.

Examples of pseudodominance.

1) Cri du chat (cry of the cat) syndrome

* This disease is resulting from the deletion of the part of the short arm of chromosome 5. ~~Hence~~ This syndrome was first described by Lejeune et al., 1963.

* Sufferers are also mentally retarded (IQ below 20), have malformation in larynx, saddle nose, small head & malformed low set ears.



– short chromosome arm

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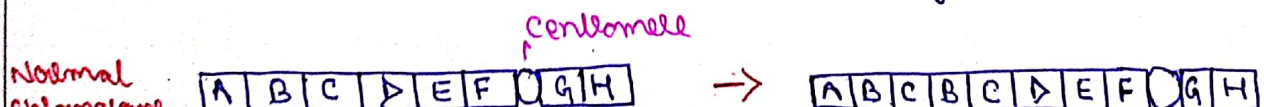
2. duplication

* duplication result from doubling of chromosomal segments, and occur in a range of size & location.
* Due to duplication some genes are present in a cell in more than two doses.
* If duplication is present only one of two homologous chromosome bearing the duplicated segment form a loop to maximize the juxtaposition (during pairing) of homologous region.
* Extra segment in a chromosome may arise in a variety of ways such as follows

1) Tandem Duplication

* This duplications are adjacent to each other in same order.
* It can occur due to unequal crossing over where homologous chromosomes pair inaccurately during meiosis-I



For eg:- ABCDEF.GH gene sequence in a chromosome & if the chromosomal segment containing the genes BC is duplicated the sequence of gene in tandem duplication will be ABCBCDEF.GH

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2. a) Reverse tandem duplication

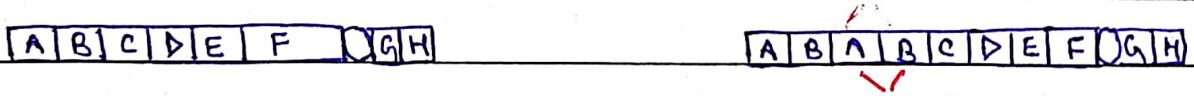
* It results in genes arranged in the opposite order/reverse of a normal sequence.

Eg:- The sequence of genes will be ABCCBDEF·GH

Reverse gene sequence

b) Terminal tandem duplication

When tandem duplication occur at the end of chromosome is called terminal tandem duplication.



Terminal duplication

4 Non tandem duplication.

* It may result from crossing over during meiosis within segments of the chromosome that contain inversions or translocations

5) Displaced Duplication

* In this duplicated region is not situated adjacent to the normal section.

* depending on whether the duplicated portion is one the same side of the centromere as the original section or on the other side, the displaced duplication can be termed either homobranchial or heterobranchial.

Homobranchial — ABC.▷EFG ▷EFH
Heterobranchial — A▷EFB.C.▷EFGH.

6) Transposed duplication

* The duplicated portion of chromosome becomes attached to a non-homologous chromosome.

ABC.▷EFGH
LMNOPQ.RST

↓

ABC.GH and LMN▷EFOPQ.RST

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Extra-chromosomal duplication

In the presence of centromere the duplicated part of a chromosome act as independent chromosome.

Genetic effects of duplication

1) Bar eye in duplication

- It is characterized by narrower, oblong, bar-shaped eye with few facts.
- It is determined by a X-linked recessive allele B.
- The classical studies of Bridge (1936) showed that the bar trait of Drosophila is associated with the duplication of a segment of the X chromosome called section 16A, observed in salivary gland chromosome
- Each added section 16A intensifies the bar phenotype (i.e duplication behave genetically as a dominant factor). However, the narrowing effect is greater if the duplicated segments are on the same chromosome called Positive effect.

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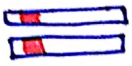
Comparison of genotype and phenotype for bar eye in Drosophila female showing positive effect of 16A segment

	X Chromosome		Phenotype	Mean No of Facets
1.	16A/16A		Normal	779
2.	16A, 16A/16A		Heterozygous Bar eye	358
3.	16A, 16A/16A, 16A		Homozygous Bar eye	68
4.	16A, 16A, 16A/16A		Heterozygous · Ultrabar (= double bar)	45
5.	16A, 16A, 16A/16A, 16A, 16A		Homozygous · ultra bar	25

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3. Inversion

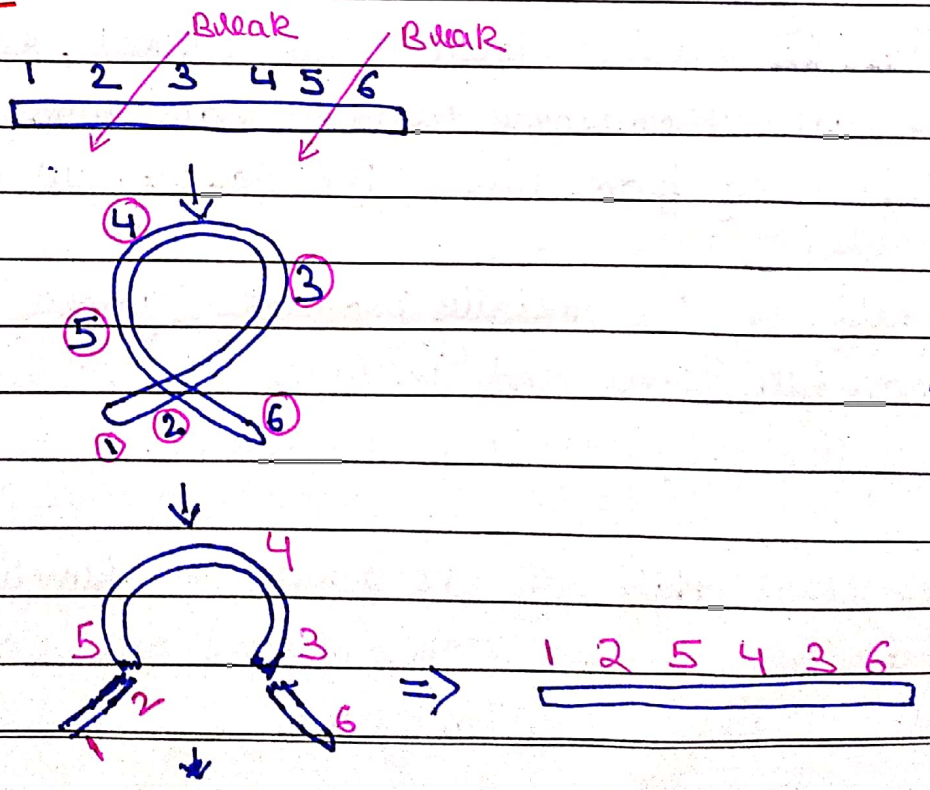
Inversion was first detected by Strutevant & Plunkett in 1926.

+ Inversion involves a rotation of a part of chromosome or a set of genes by 180° on its own axis. It essentially involves occurence of breakage and reunion.

+ The net result of inversion is neither a gain nor a loss in genetic material, but simply rearrangment of the gene sequence.

Eg: Normal order of segments within a chromosome is 1-2-3-4-5-6; break occurs in region 2-3 and 5-6 and broken piece is reinserted in reverse order.

1-2-5-4-3-6



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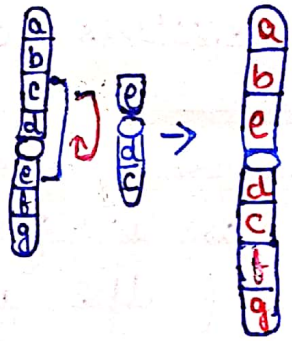
* An inversion heterozygotes has one chromosome in the inverted order and its homologue in the normal order

* Inversion may be classified into 2 types

1) Pericentric inversion

when inversion includes the centromere.



Crossing over in pericentric inversion

- Crossing over in a heterozygous pericentric ~~is~~ result in deletions and duplications and also produce rod shaped (acrocentric) chromosome.

- The 1st meiotic figure appear normal, but the two chromatids of each chromosome usually have arms of unequal lenght depending from where the crossing over occured.

- Half of the meiotic products (gamets/Pollen grains) are non functional and inviable due to the presence of duplication & deletion in them.

- The other half of the gametes are functional; one-quarter have the normal chromosome order, one-quarter have the inverted arrangment.

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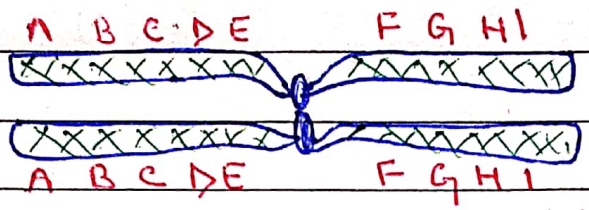
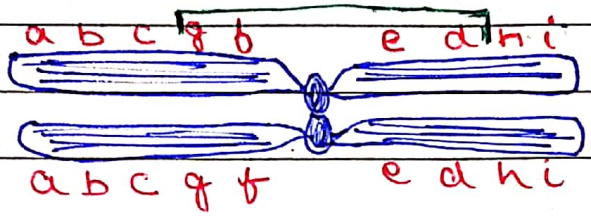
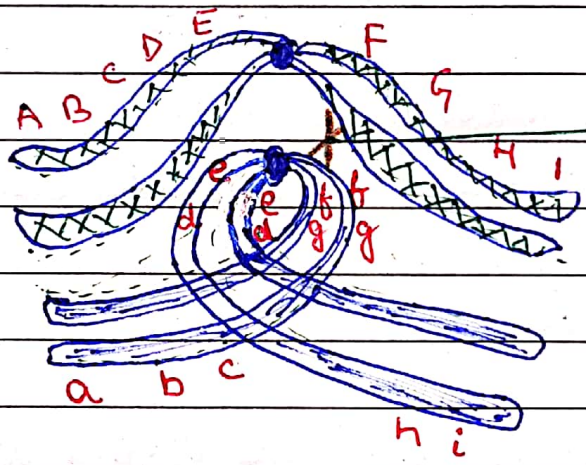


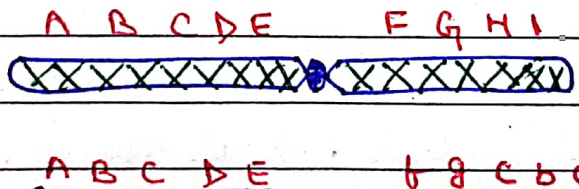
NORMAL



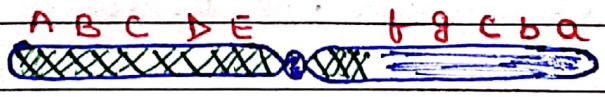
WITH INVERSION



Crossover site

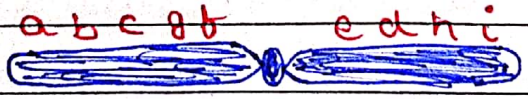


NORMAL PRODUCT



— Duplication/Deletion

— Duplication/Deletion



INVERSION PRODUCT

Pericentric Inversion

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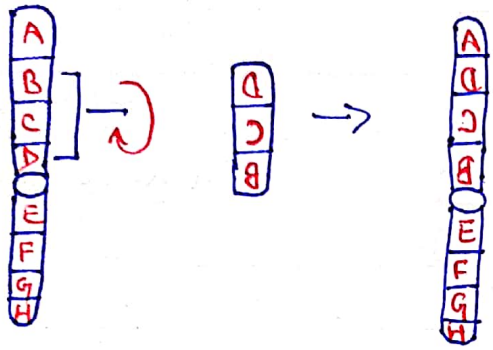
2. Paracentric Inversion

* If the centromere is not included in the inversion.



Crossing over in paracentric inversion

- Crossing over in the inverted region of a heterozygote paracentric inversion produces a dicentric chromosome (2 centromere) which form a from one pole to other during first anaphase
- The bridge will rupture along its lenght and resulting fragments will contain duplication or deletion.
- Here, an acentric fragment is also formed & it usually fails to move either pole, it is not included in any meiotic product
- Half of the meiotic products are non-functional, one-quarter are functional with normal chromosome and one-quarter are functional with an inverted chromosome.
- Heterozygotes for paracentric inversions are highly sterile & Produce only parent like progeny.

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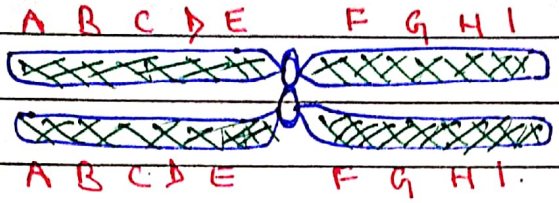
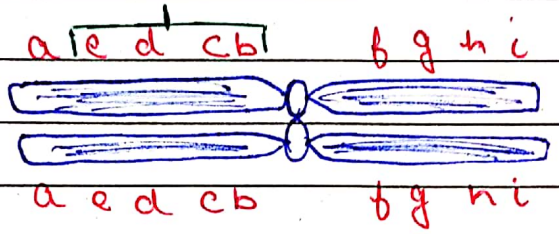
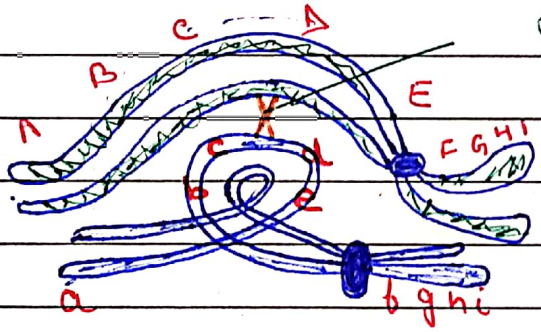


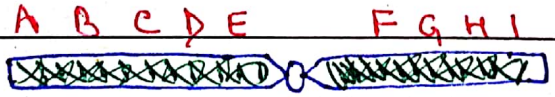
NORMAL



WITH INVERSION

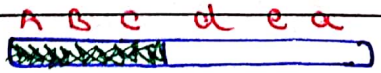


Crossover sites

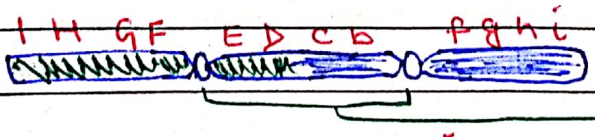


Normal Product

Deletion Product

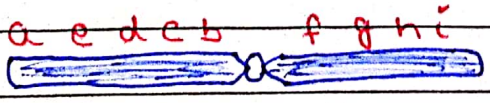


Acentric fragment



Dicentric chromosome

Dicentric bridge



Inversion Product

Pracentric Inversion

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4. Translocation

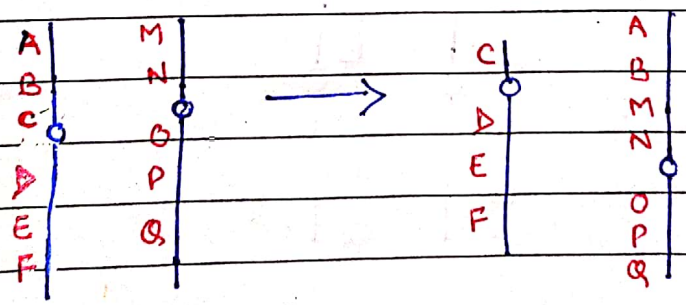
* The shifting or transfer of a part of a chromosome or a set of genes to a non-homologous one is called Translocation.

* There is no addition or loss of genes during translocation only a rearrangement (i.e change in the sequence & position of a gene).

* Translocation may be following 3 types

1) Simple translocation

They involve a single break in a chromosome. The broken piece gets attached to one end of a nonhomologous chromosome.



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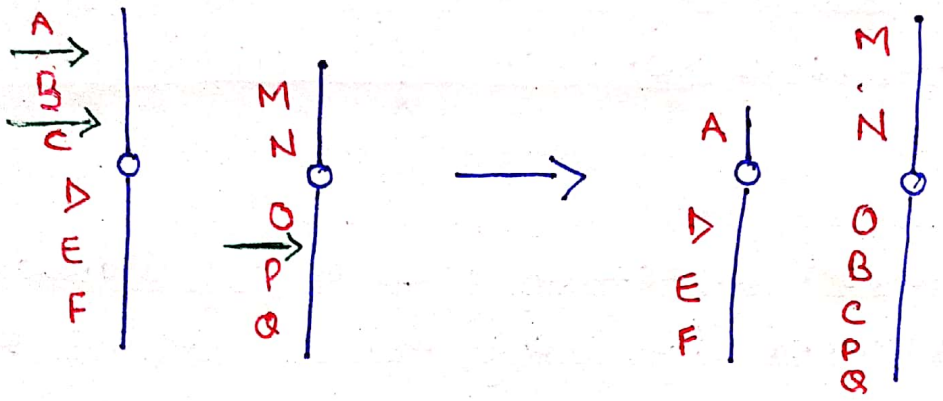
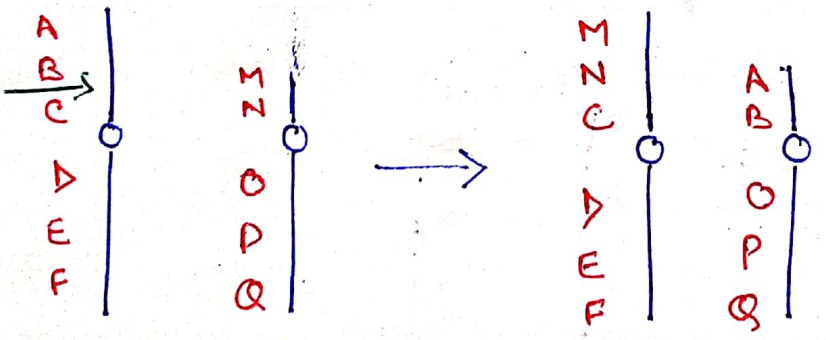
2. Shift translocation

* In this type, the broken segment of one chromosome get inserted interstitially in a nonhomologous chromosome



3. Reciprocal translocation

In this case, a segment from one chromosome is exchanged with a segment from another nonhomologous one, so that in reality two translocation chromosomes are simultaneously achieved



→ Indicate the point of breaks.

Cytology of Translocation Heterozygotes

In reciprocal translocation two non-homologous chromosomes exchange genetic material. Usually generate so-called balanced translocation

It is usually without phenotypic consequences. It can result in positive effect.

Balanced Lethal and Gametic Completes.

* Individuals carrying balanced translocations have a great risk of producing gametes with unbalanced combinations of chromosomes.
* This depends on the segregation pattern during meiosis-I.
* During meiosis-I, homologous chromosomes synapse with each other
* For the translocation or translocated chromosome to synapse properly, a translocation cross must form.

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Meiotic segregation can occur in one of three ways.

1. Alternate Segregation

- Chromosomes on opposite sides of the translocation cross segregate into same cell
- It Leads to balanced gametes
- Both contain a complete set of genes & thus viable.

2. Adjacent-1-Segregation

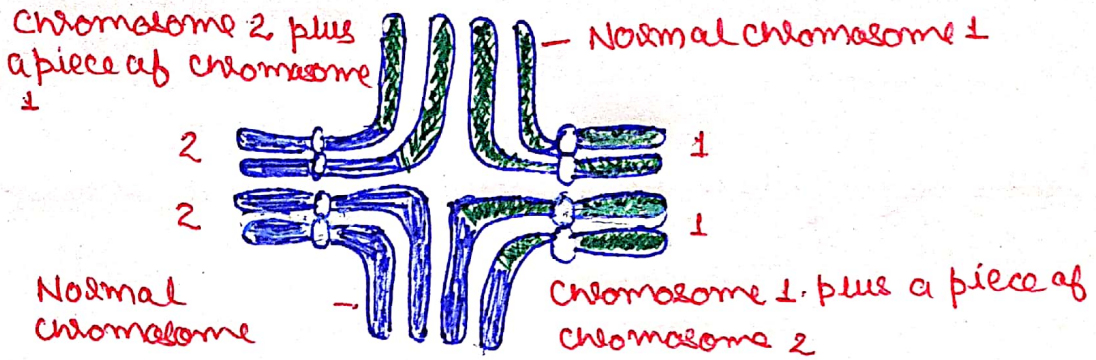
- Adjacent non-homologous chromosomes segregates into the same cell
- Leads to unbalanced gametes
- Both have duplications & deletions are thus inviable

3. Adjacent-2-Segregation

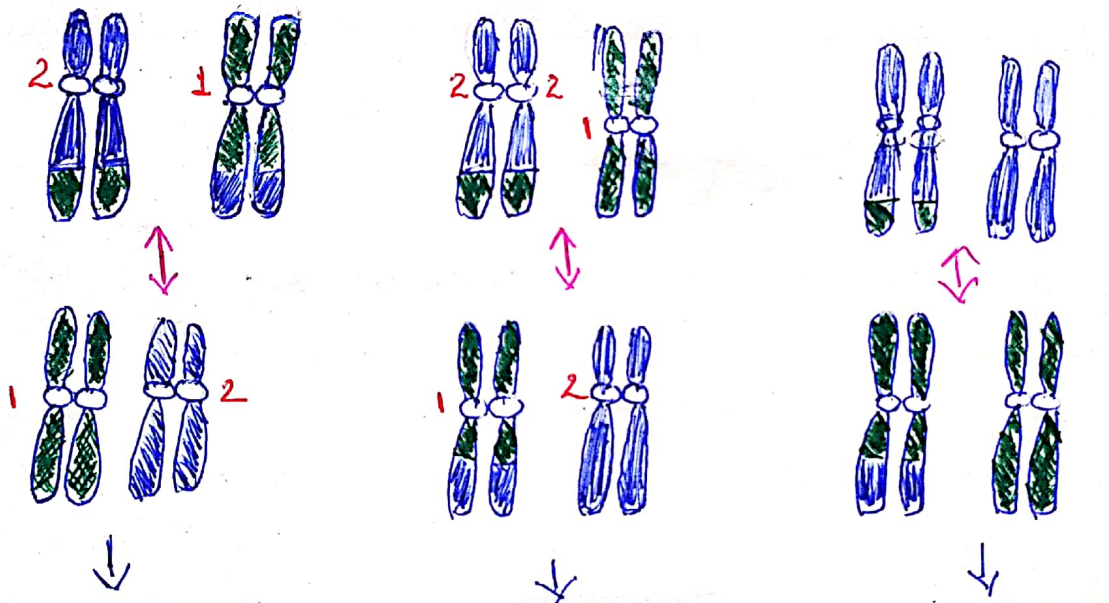
- Adjacent homologous chromosomes segregate into the same cell.
- Leads to unbalanced gametes
- Both have duplications and deletion & thus inviable

Teacher's Signature : .....

Translocation cross



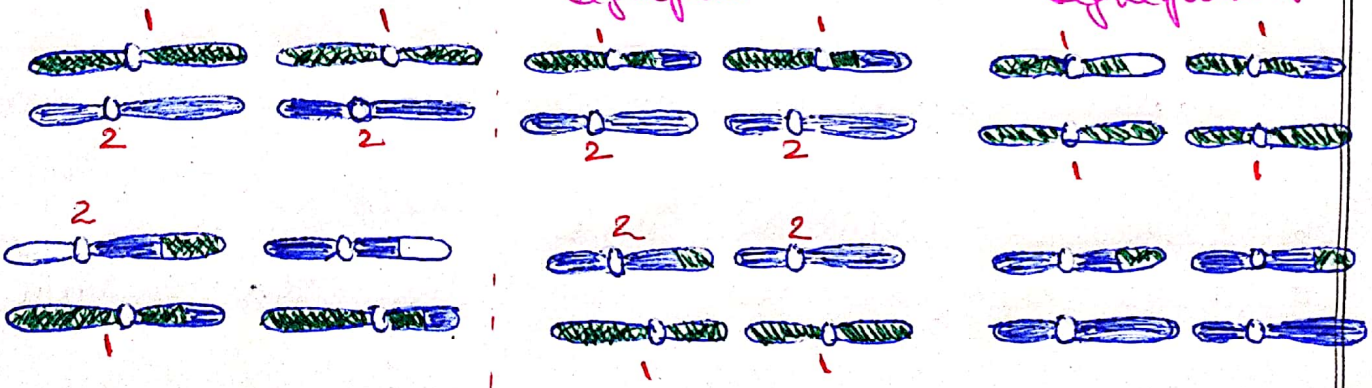
Possible segregation during anaphase I



a) Alternate segregation

b) Adjacent-1 segregation

c) Adjacent-2 segregation



Two normal cells + 2 cells with balanced translocation

All 4 cells unbalanced

All 4 cells unbalanced

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