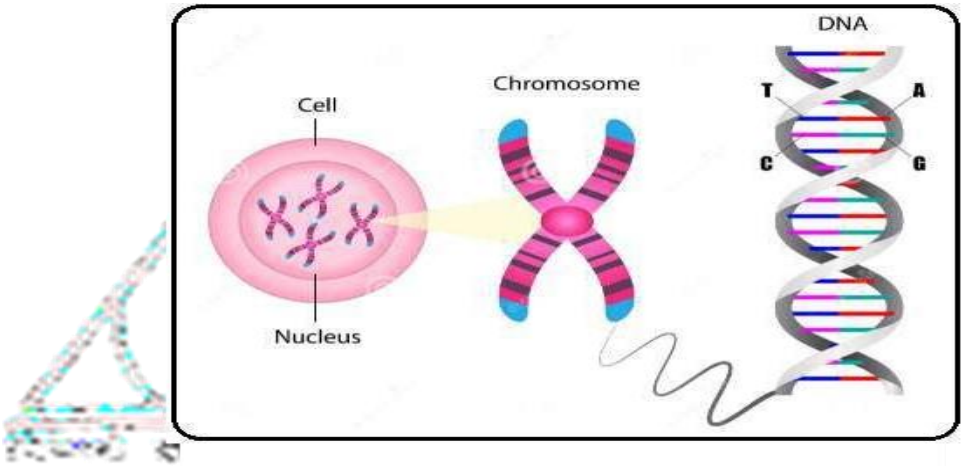
Chromosomal Aberrations (Structural changes of Chromosomes)

CC13
UNIT-3

DR. ARINDAM MANDAL
Assistant Professor
Bejoy Narayan Mahavidyalaya
Itachuna, Hooghly
West Bengal

Chromosomes

- **Chromosomes are thread-like structures located inside the nucleus of animal and plant cells.**
- **Each chromosome is made of protein and a single molecule of deoxyribonucleic acid (DNA). Thus, chromosomes are actually a nucleoprotein complex.**
- **They carry the genetic information form generation to generation.**
- **The DNA molecule contain genes, which are the basic physical and functional unit of heredity**

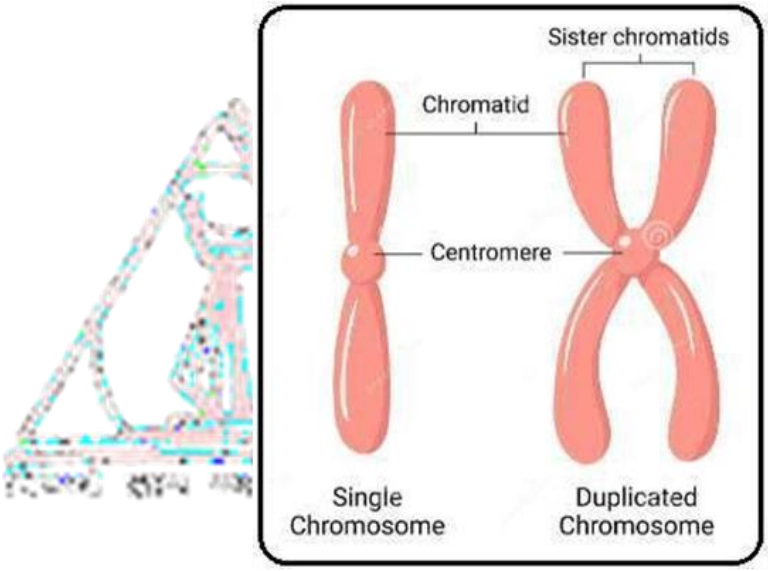


Chromosomes

During cell division, the chromosomes can be seen to consist of 2 parallel strands, which is known as chromatids. Two strands are called as sister chromatids.

Two sister chromatids are held together at one point that is known as centromere. Chromosomes are found in pairs in diploid organisms, termed as homologous chromosomes.

Centromere contains a complex structure of proteins to which microtubules attach during cell division, which is called as kinetochore.

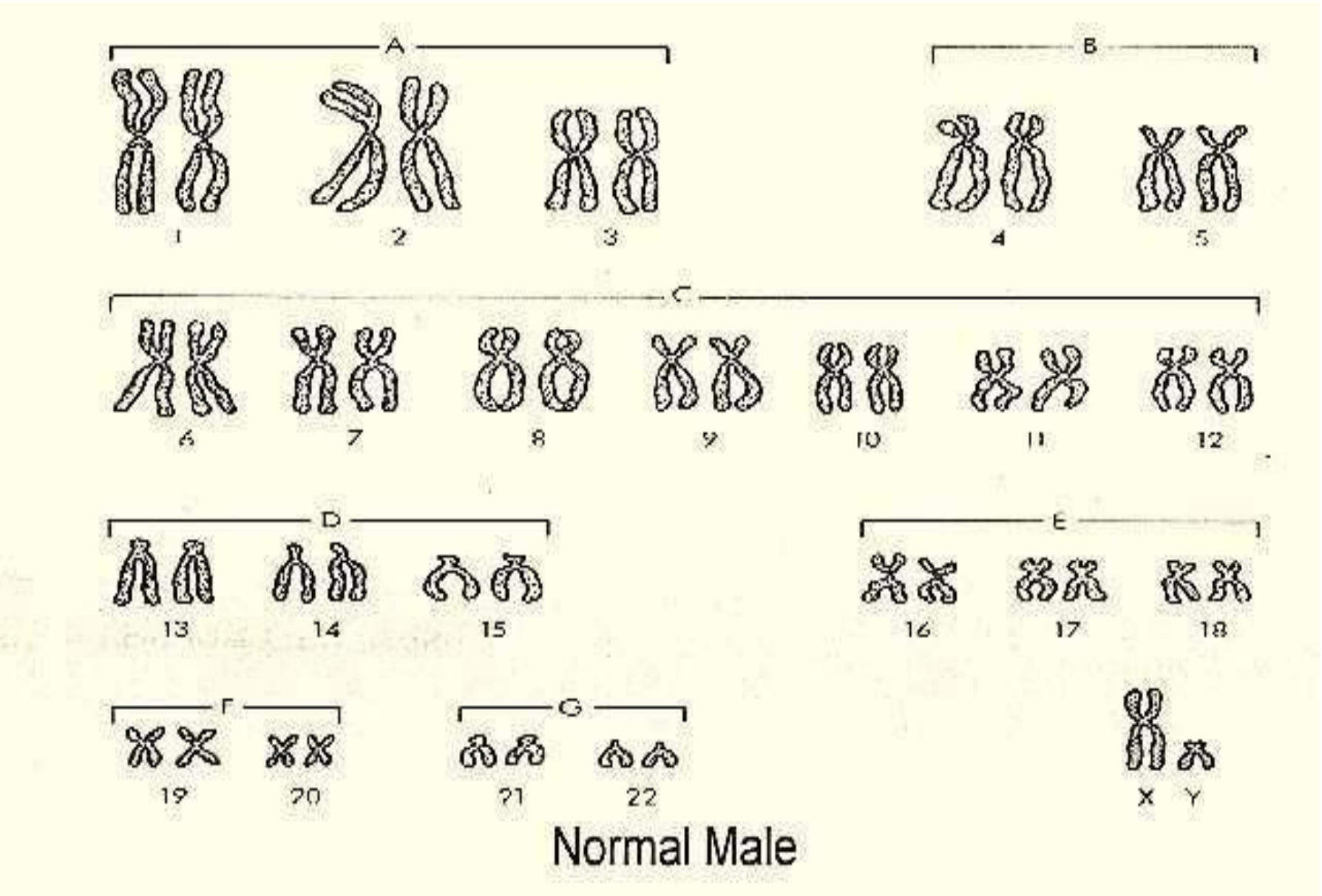


Karyotype

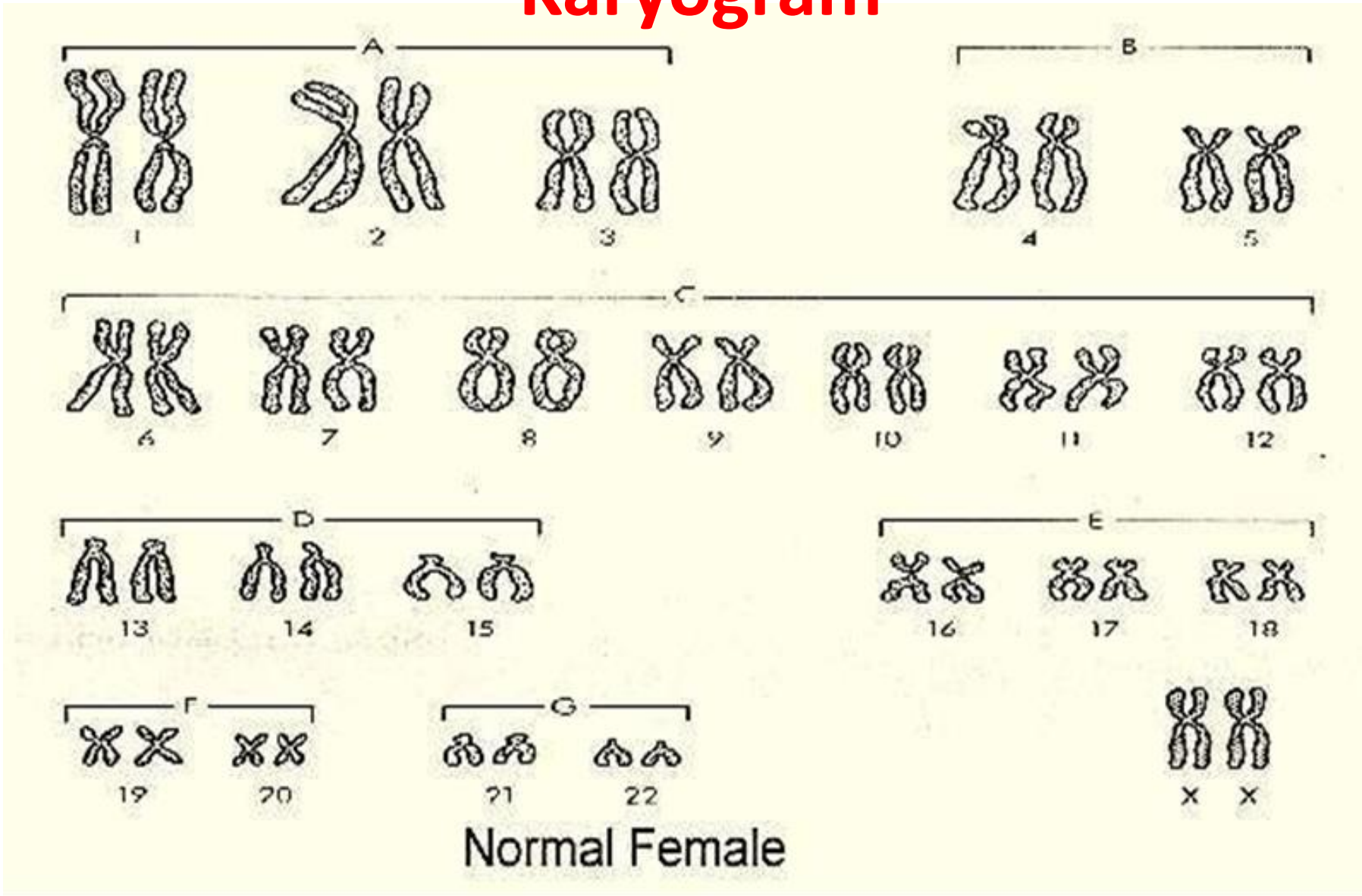
- It is the set of chromosomes of an individual.
- It is the systematized arrangement of the chromosomes of a single cell.
- In the human cell, there are 46 chromosomes or 23 pairs (diploid number); of these 23 pairs, 22 are similar in both sexes and are called the autosomes. The remaining pair is called sex chromosomes : XX in the female cells and XY in the male cells.

Karyogram: A display of the chromosomes of a cell, sorted into pairs.

Karyogram


A
B
C
D
E
F
G
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y
Normal Male

Karyogram


A
B
C
D
E
F
G
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X X
Normal Female

Karyotype

- **Asymmetric karyotype is defined as the huge difference between the largest and smallest chromosome as well as less number of metacentric chromosomes in a chromosome complement.**
- **Similarly, symmetric karyotype is defined as the small difference between the largest and smallest chromosome as well as more number of metacentric chromosomes in a chromosome complement.**

Chromosomal aberration

Two types:

1. Structural chromosomal aberration: Structural chromosome abnormalities occur when part of a chromosome is missing, a part of a chromosome is extra, or a part has switched places with another part leading to too much or too little genetic material. It may be of following types

Deletion

Duplication

Inversion

Translocation

Chromosomal aberration

2. Numerical chromosomal aberration: Numerical chromosomal abnormalities occur when there is a different number of chromosomes in the cells of the body from what is usually found. So, instead of normal number of chromosome, there may be extra or less number of chromosomes.

Polyploidy

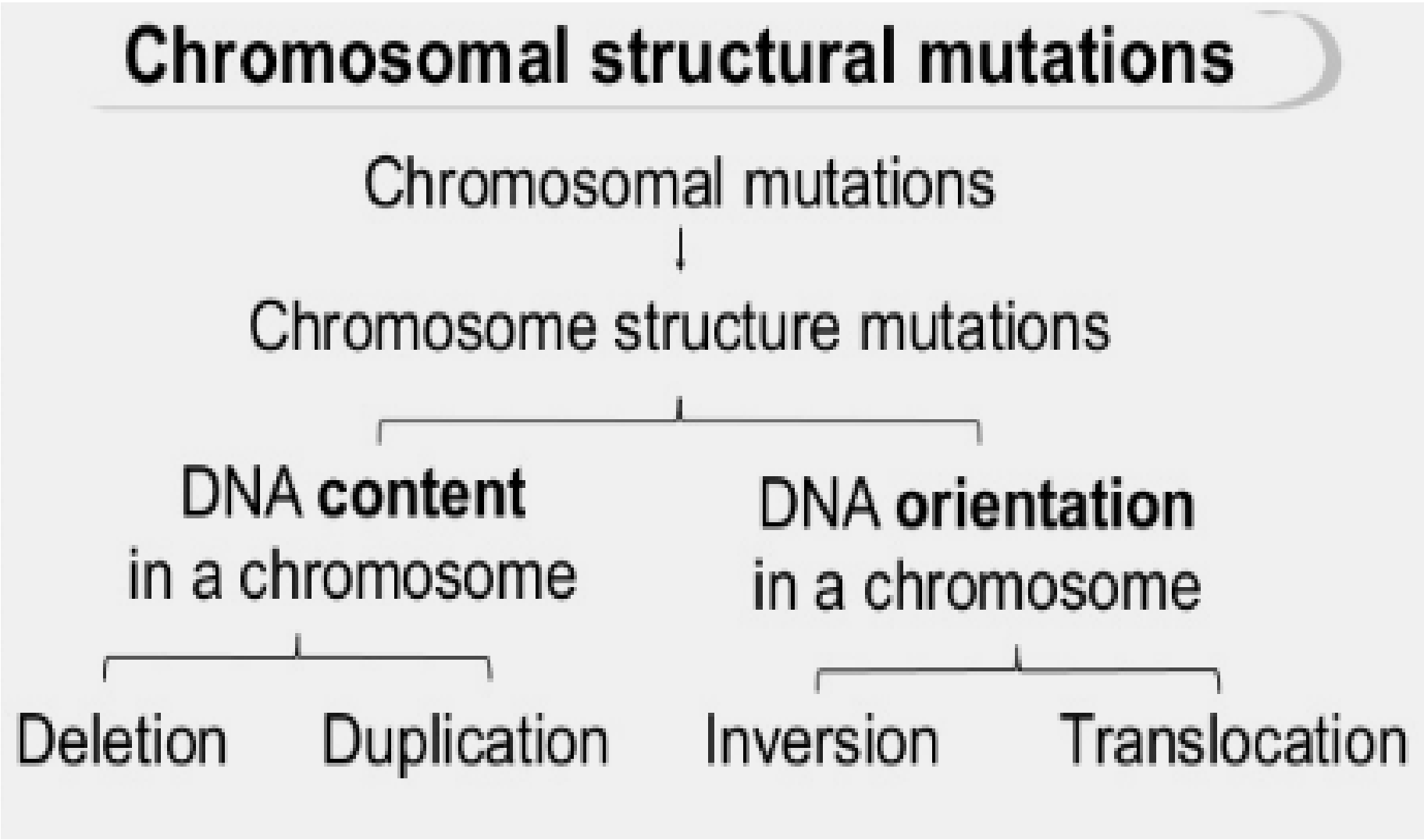
Aneuploidy

Introduction

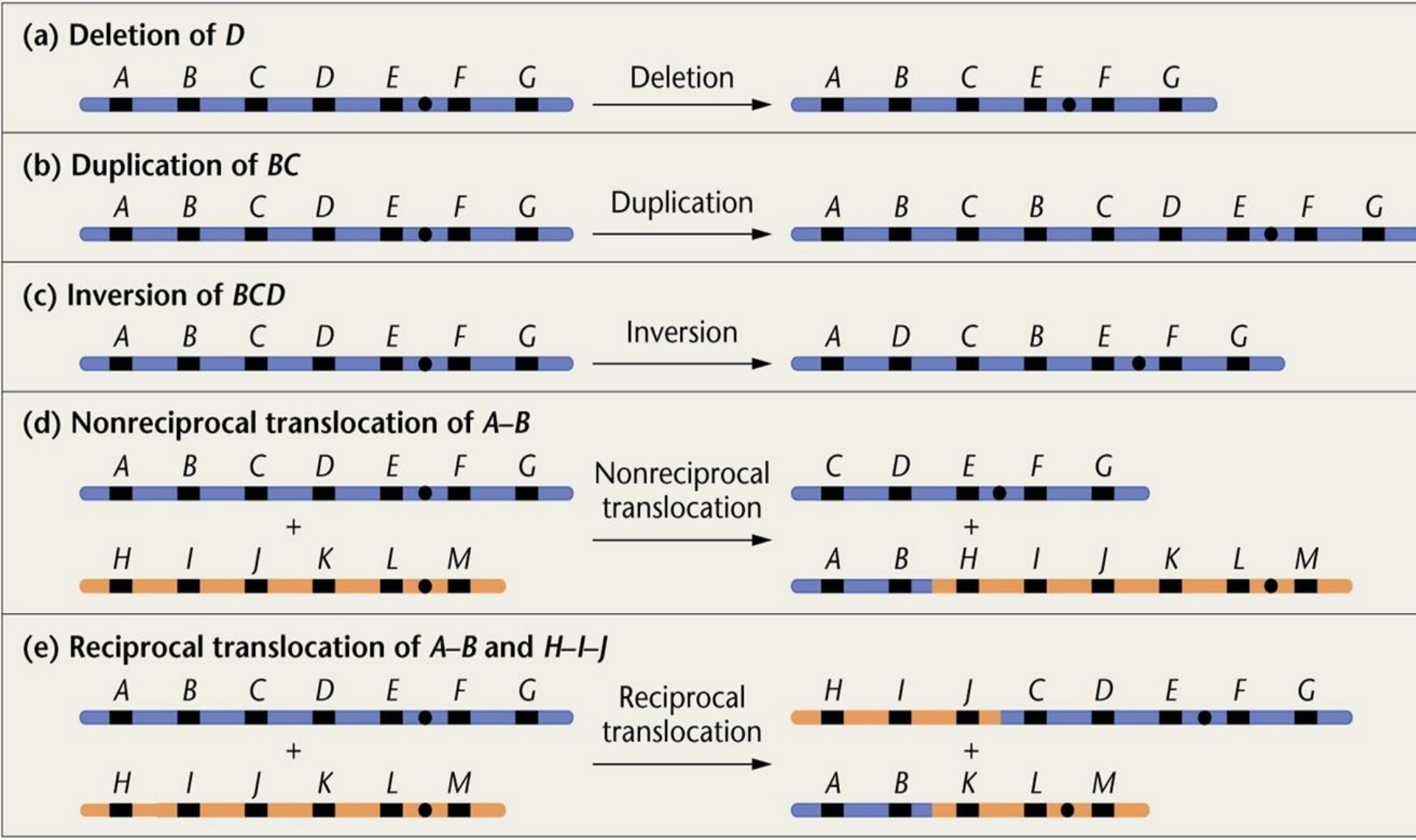
Also called chromosome rearrangements

- **Deletion**: loss of segment
- **Duplication**: gain of segment
- **Inversion**: reversal of region
- **Translocation**: movement of segment to another chromosome

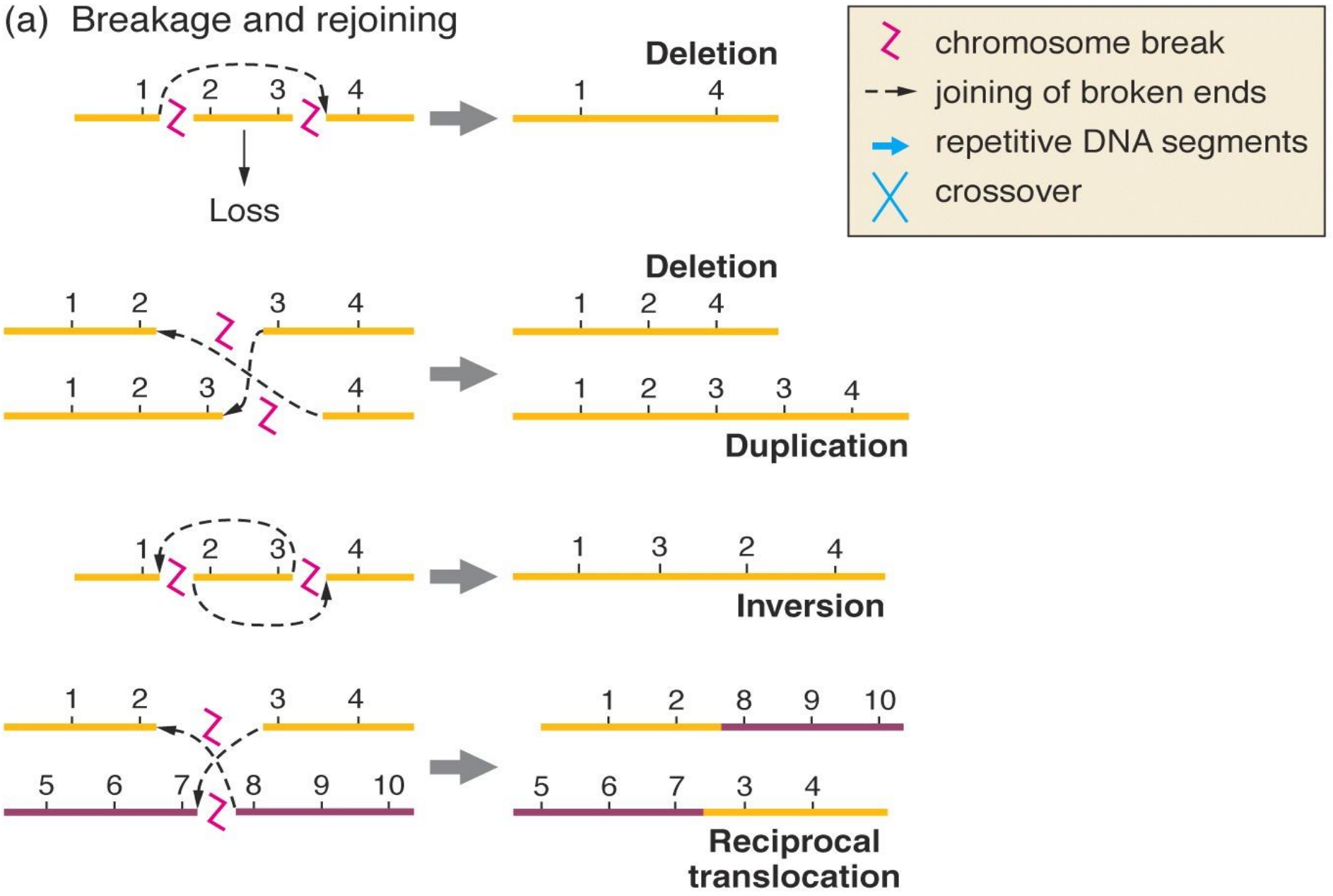
Chromosomal structural mutations



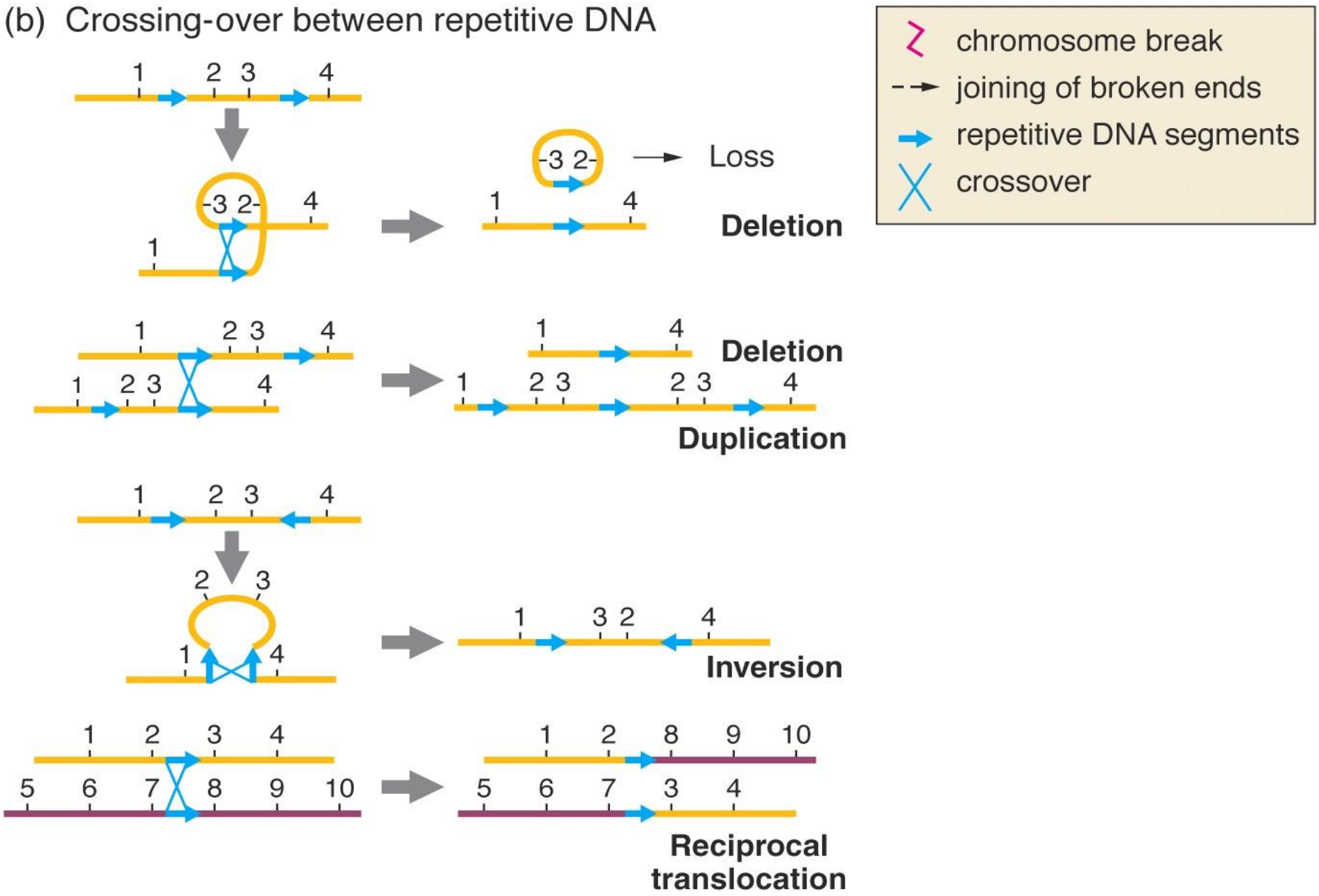
Types Of Aberrations



Origin


(a) Breakage and rejoining
Deletion
1 2 3 4
Loss
1 4
chromosome break
joining of broken ends
repetitive DNA segments
crossover
Deletion
1 2 3 4
1 2 3 4
1 2 4
1 2 3 3 4
Duplication
1 2 3 4
1 3 2 4
Inversion
1 2 3 4
5 6 7 8 9 10
1 2 8 9 10
5 6 7 3 4
Reciprocal translocation

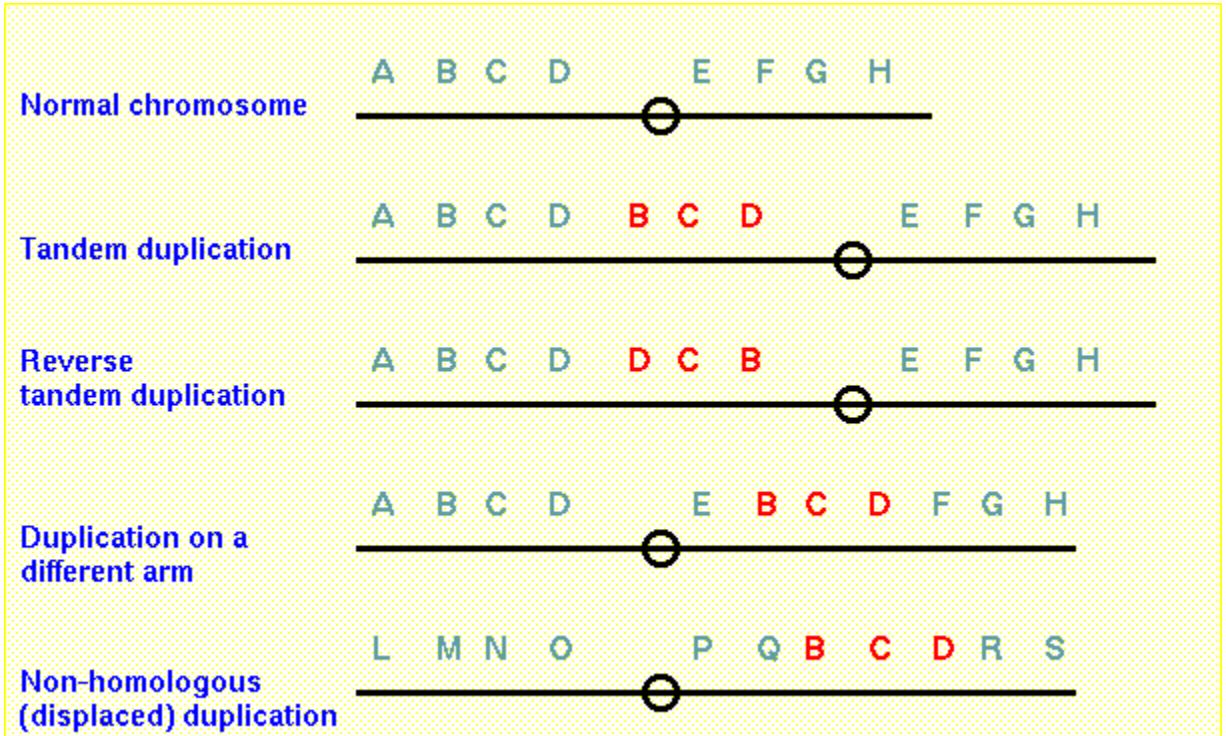
Origin


(b) Crossing-over between repetitive DNA
chromosome break
joining of broken ends
repetitive DNA segments
crossover
Loss
Deletion
Deletion
Duplication
Inversion
Reciprocal translocation

Duplication types

(i) Direct tandem duplication in which the duplicated gene sequence lies just next to normal corresponding section.

(ii) Reverse tandem duplication in which the duplicated section with reverse gene sequence lies adjacent to normal sequence.

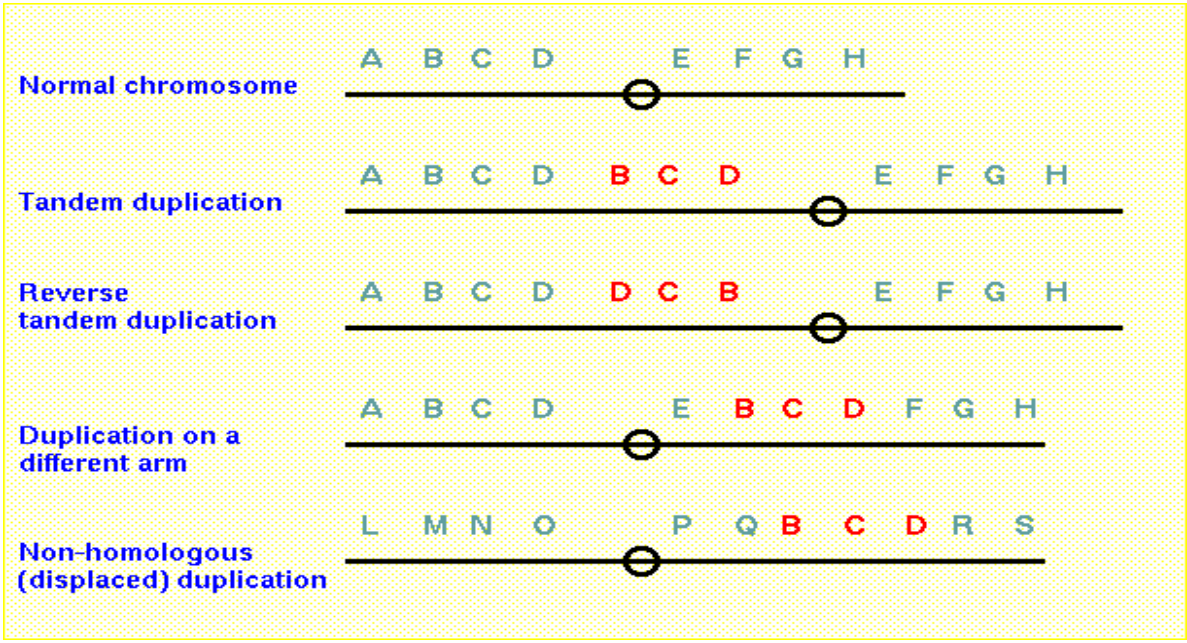


Duplication types

(iii) Displaced direct duplication in which the duplicated section is not adjacent or contiguous with the normal section (i.e., separated by other segment).

(iv) Displaced Reverse duplication in which the duplicated section with reverse gene sequence is separated from normal segment by other segment

(v) Transposed duplication in which the duplicated gene sequence is attached to another position owing to inter-chromosomal duplication.



Duplication

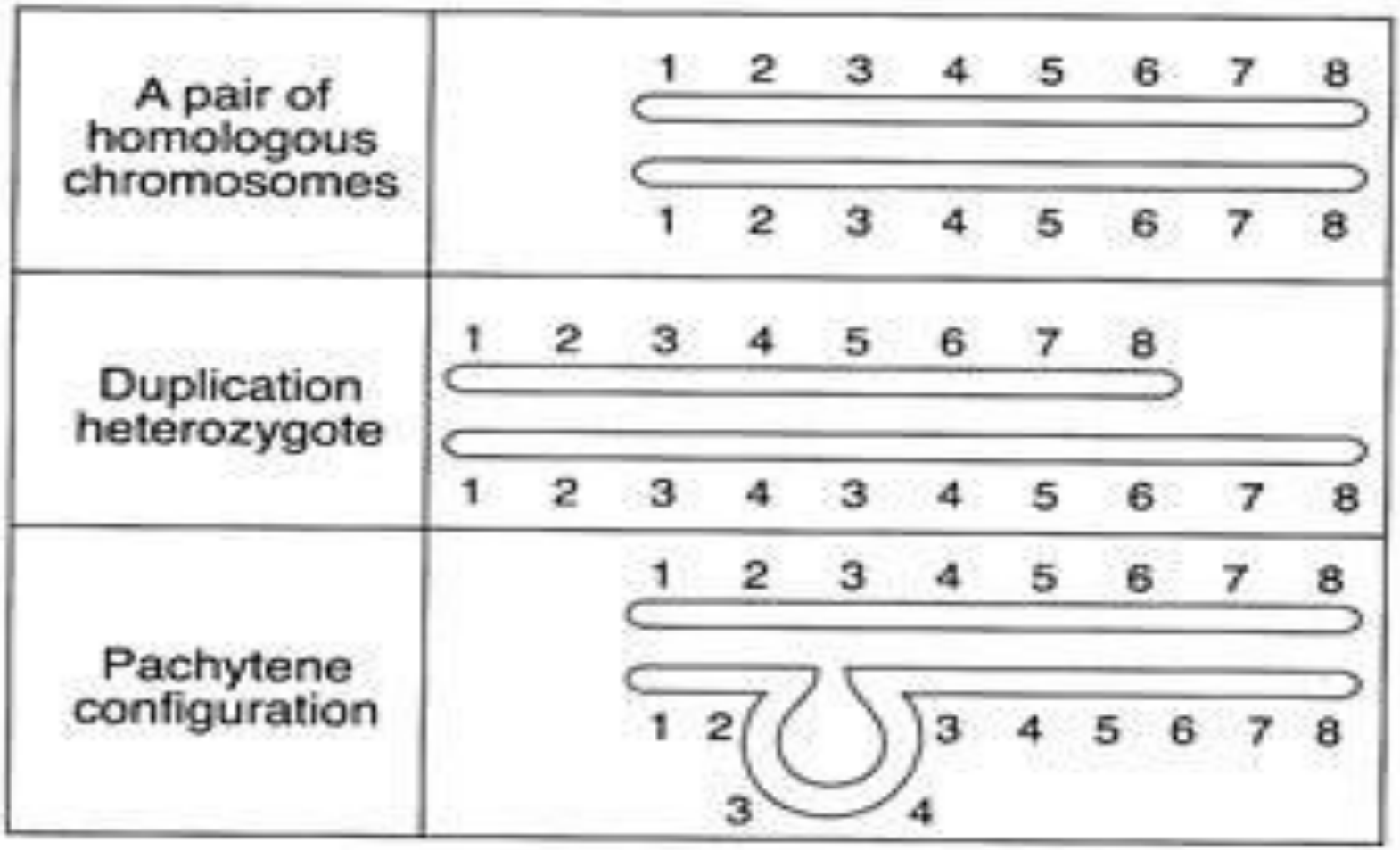
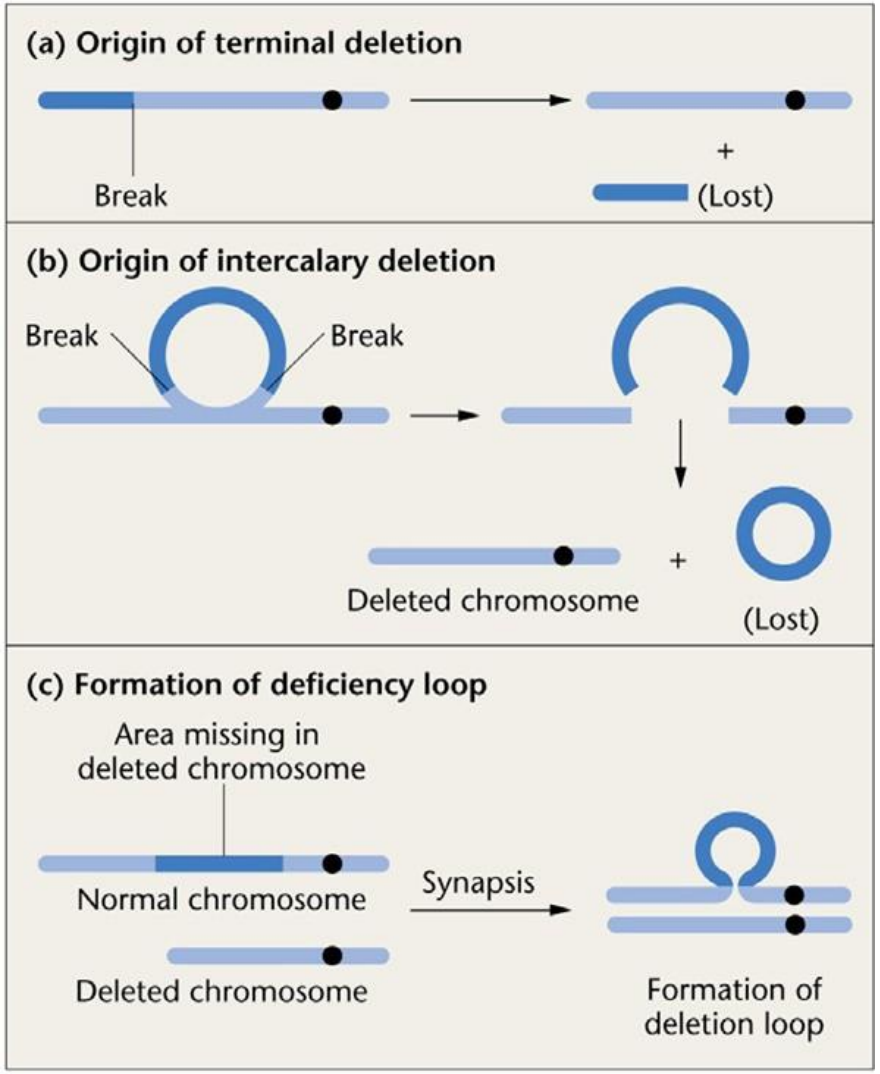


Fig. 12.7: Chromosome pairing in a duplication heterozygote

Deletion

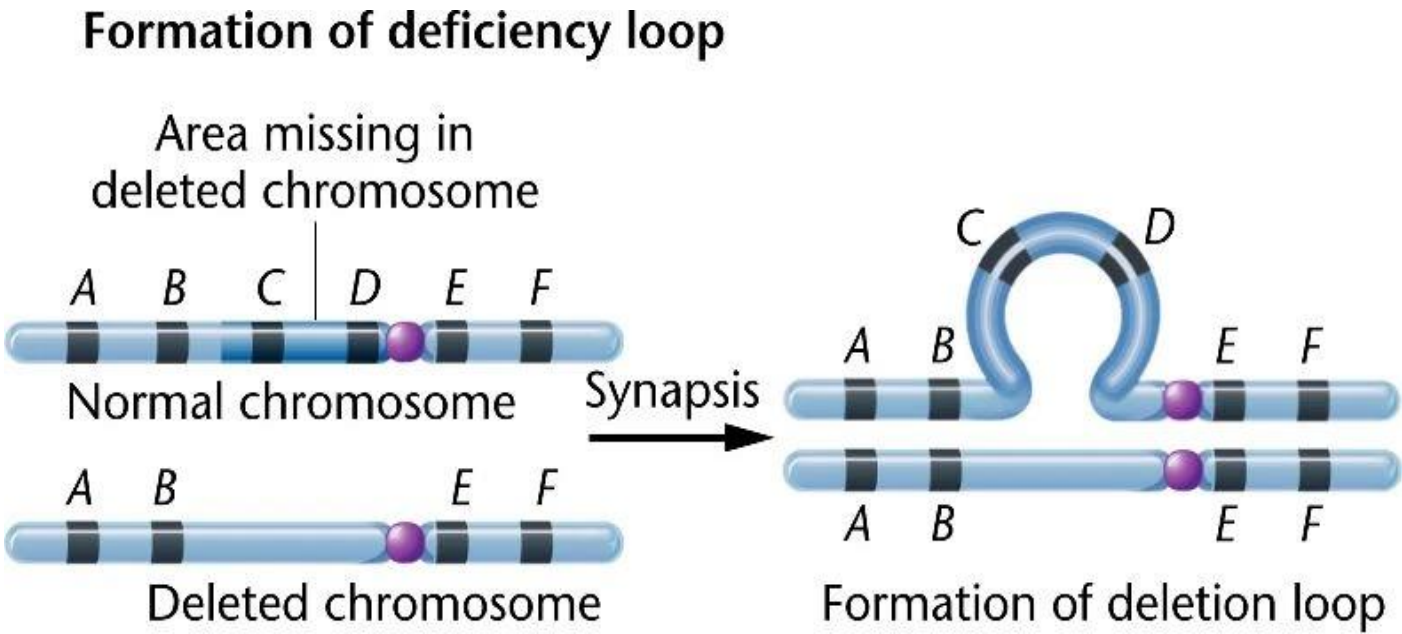
(i) Terminal deletion: A single break near the end of a chromosome would be expected to result in a terminal deficiency.

(ii) Intercalary deletion: If two breaks occur, a section may be deleted and an intercalary deficiency is created.



Meiotic behavior

- In individuals heterozygous for deletions, the normal chromosome must loop during the pairing of homologs in prophase I of meiosis to allow the homologous regions of the two chromosomes to align and undergo synapsis.
- This looping out generates a structure that looks very much like that seen for individuals heterozygous for duplications.



Effect of deletion

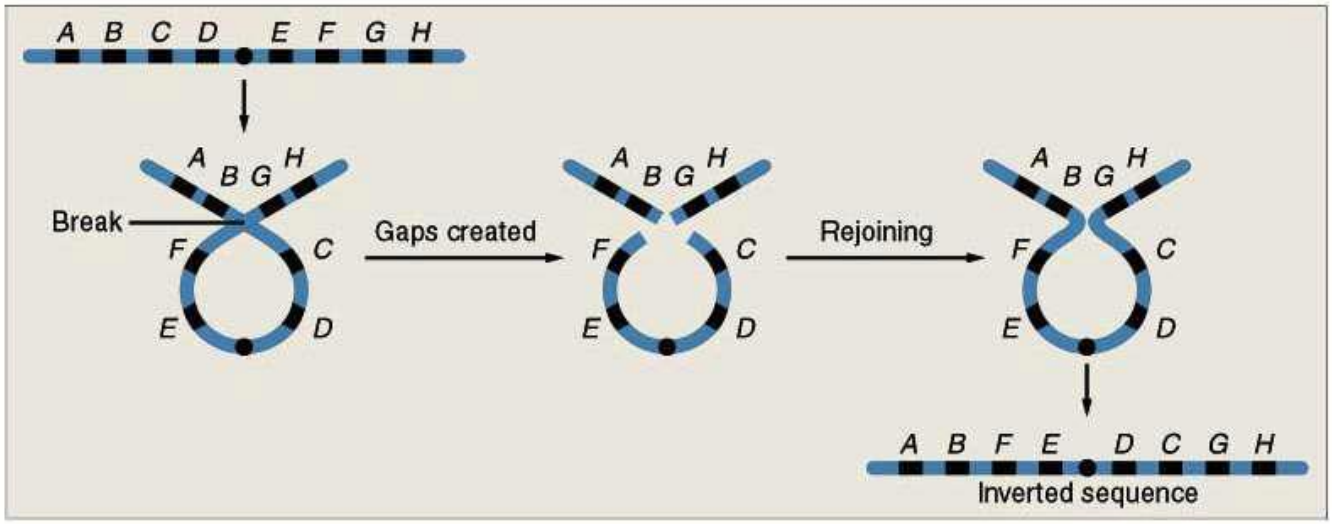
Hemizygous: **Gene is present in a single dose.**

Psuedodominance: **Hemizygous genes are expressed.**

Inversion

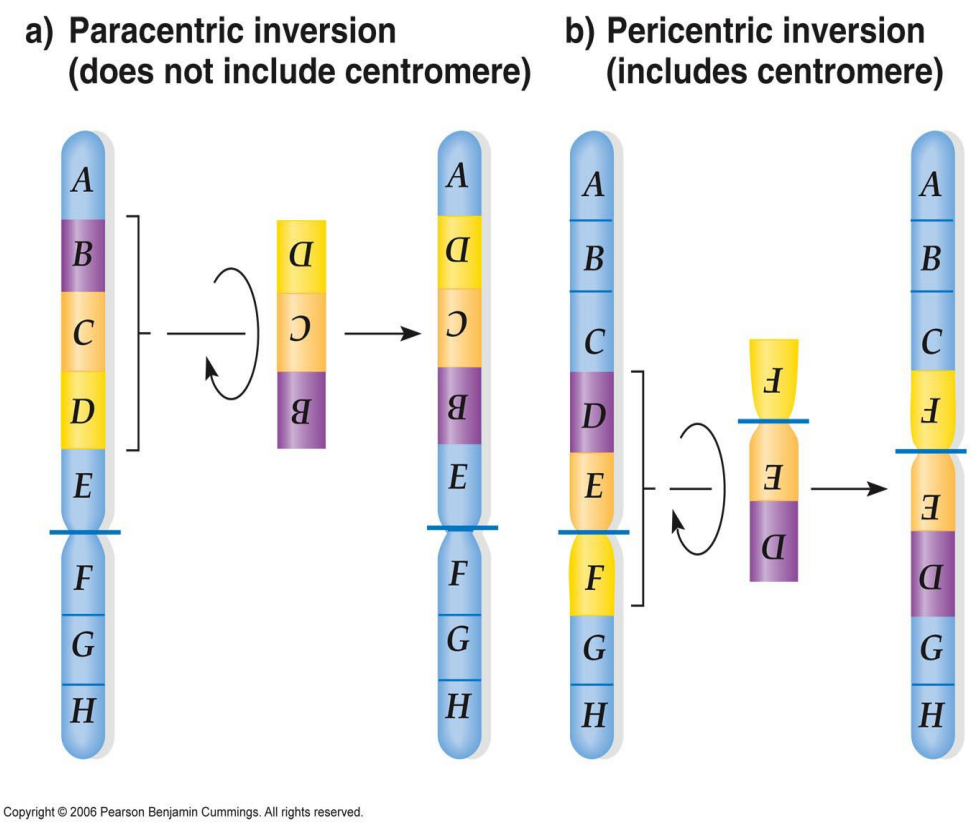
An inversion is a chromosome rearrangement which occurs when a chromosome breaks at two points and the segment bounded by the breakpoints is reinserted in the reversed orientation.

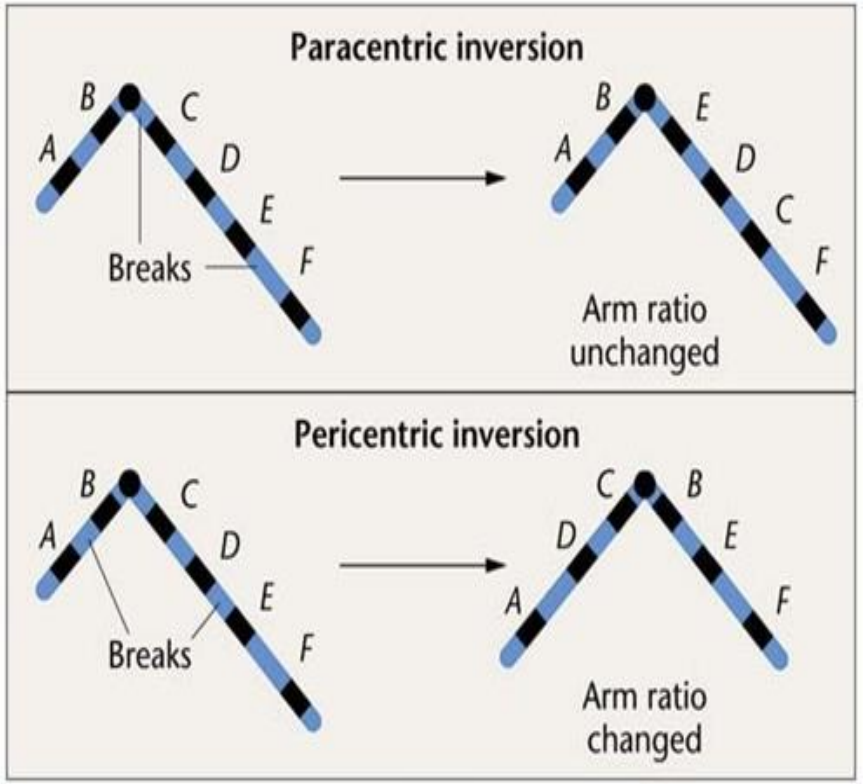
An inversion occurs when a single chromosome undergoes breakage and rearrangement within itself.



Origin of Inversion

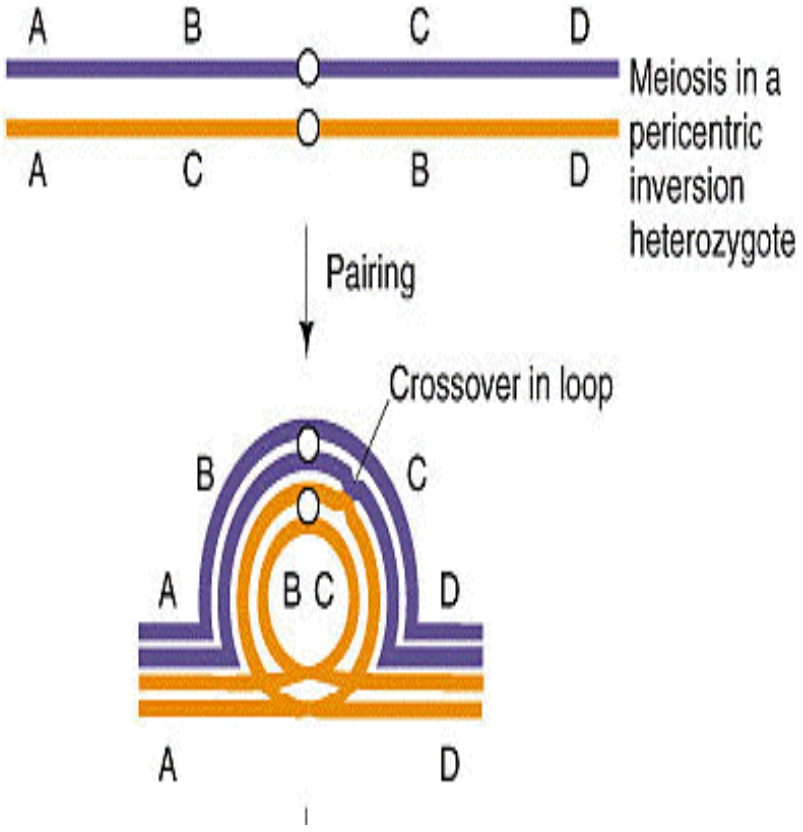
Inversions are of two types- paracentric and pericentric.





Pericentric Inversion

A chromosomal imbalance is produced as a result of a crossover event between a chromatid bearing a pericentric inversion and its noninverted homolog.

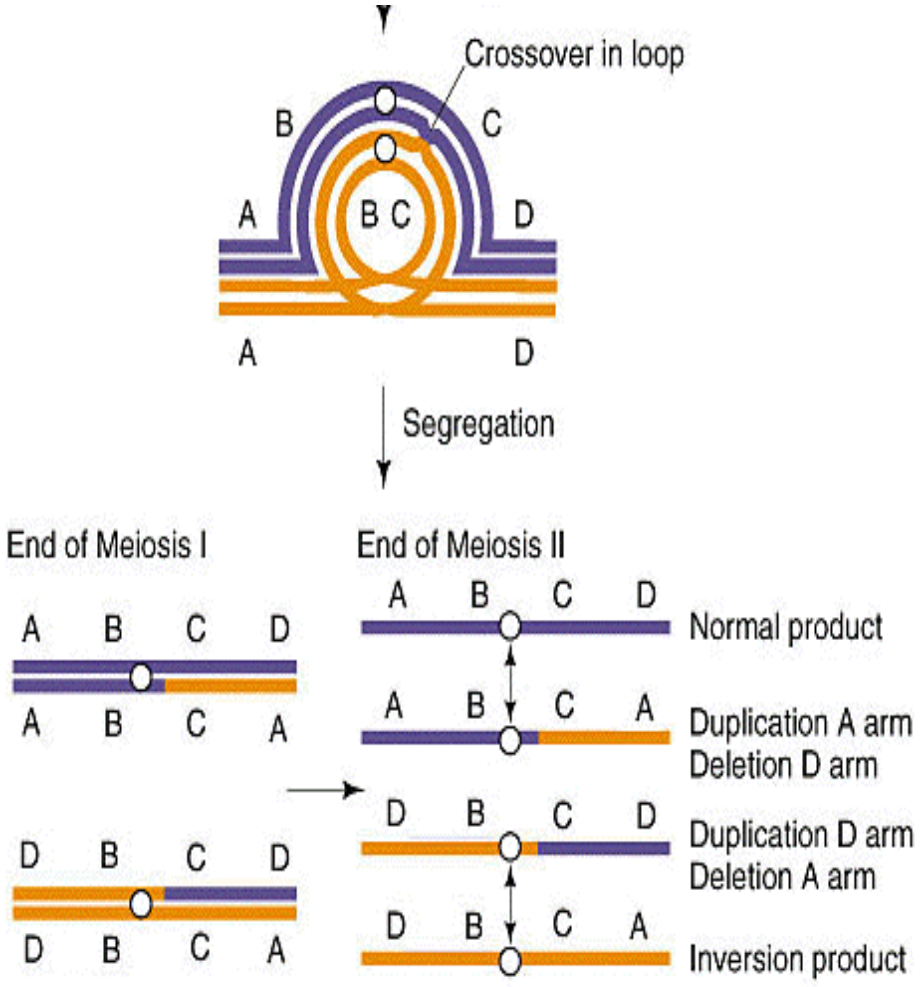


The recombinant chromatids that are directly involved in the exchange have duplications and deletions.

Pericentric Inversion

In plants, gametes receiving such aberrant chromatids fail to develop normally, leading to aborted pollen or ovules. Thus, lethality occurs prior to fertilization, and inviable seeds result.

In animals, the gametes have developed prior to the meiotic error, so fertilization is more likely to occur in spite of the chromosome error. However, the end result is the production of inviable embryos following fertilization.

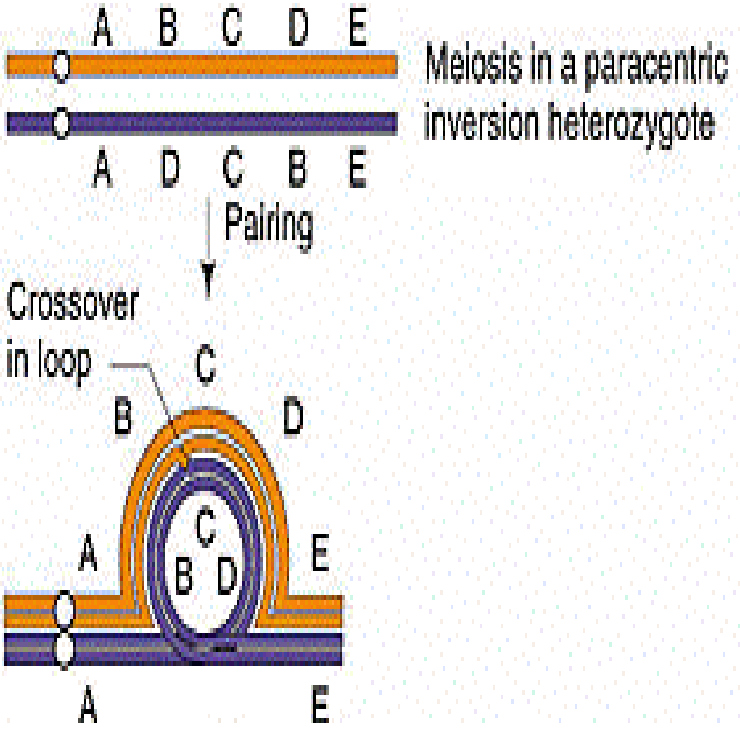


Paracentric Inversion

In prophase I of meiosis, an inversion loop forms, allowing the homologous sequences to pair up.

If a single crossover takes place in the inverted region , an unusual structure results .

The two outer chromatids, which did not participate in crossing over, contain original, non-recombinant gene sequences.

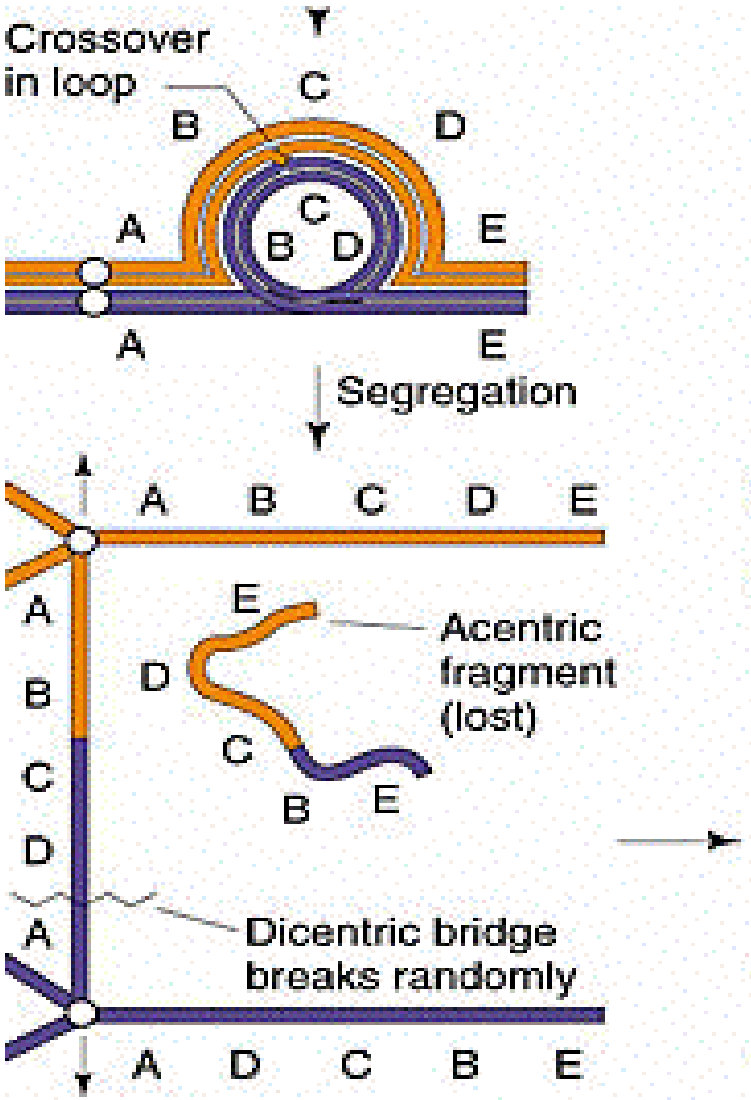


Paracentric Inversion

The two inner chromatids, which did cross over, are highly abnormal: each has two copies of some genes and no copies of others.

One of the four chromatids now has two centromeres and is said to be a dicentric chromatid; the other lacks a centromere and is an acentric chromatid.

In anaphase I of meiosis, the centromeres are pulled toward opposite poles and the two homologous chromosomes separate.

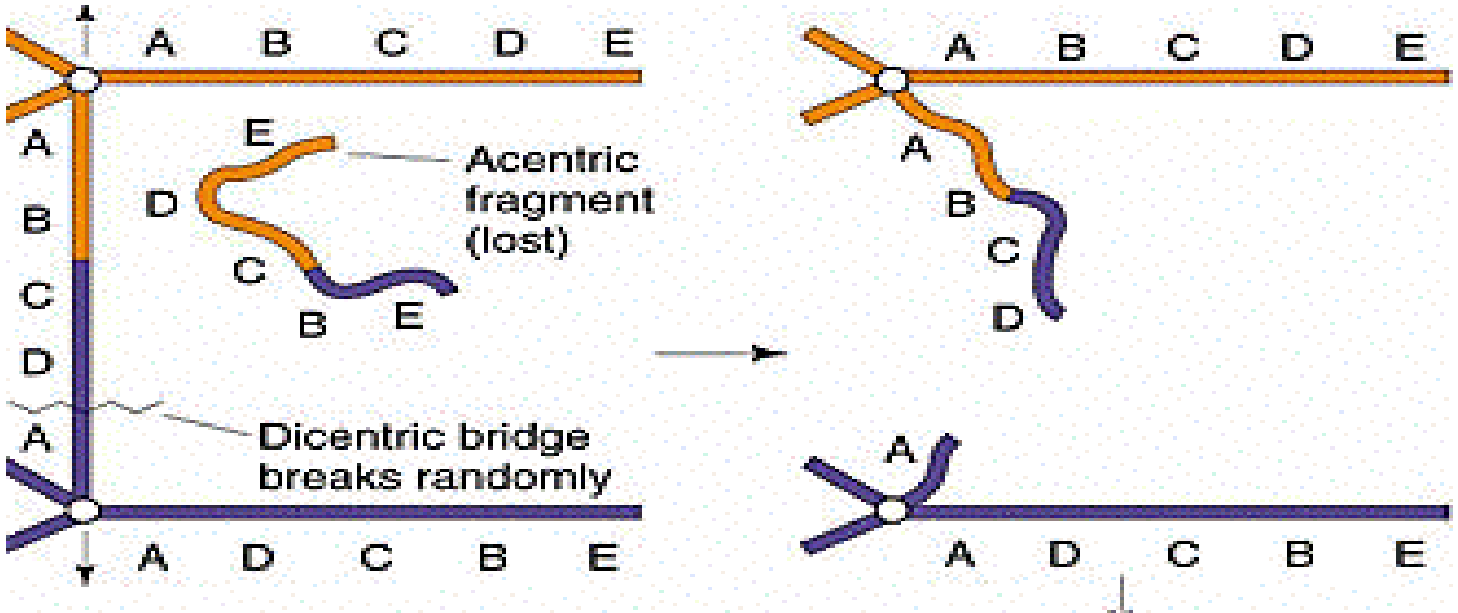


Paracentric Inversion

This action stretches the dicentric chromatid across the center of the nucleus, forming a structure called a dicentric bridge.

Eventually, the dicentric bridge breaks, as the two centromeres are pulled farther apart.

Spindle fibers do not attach to the acentric fragment, and so this fragment does not segregate into a nucleus in meiosis and is usually lost.

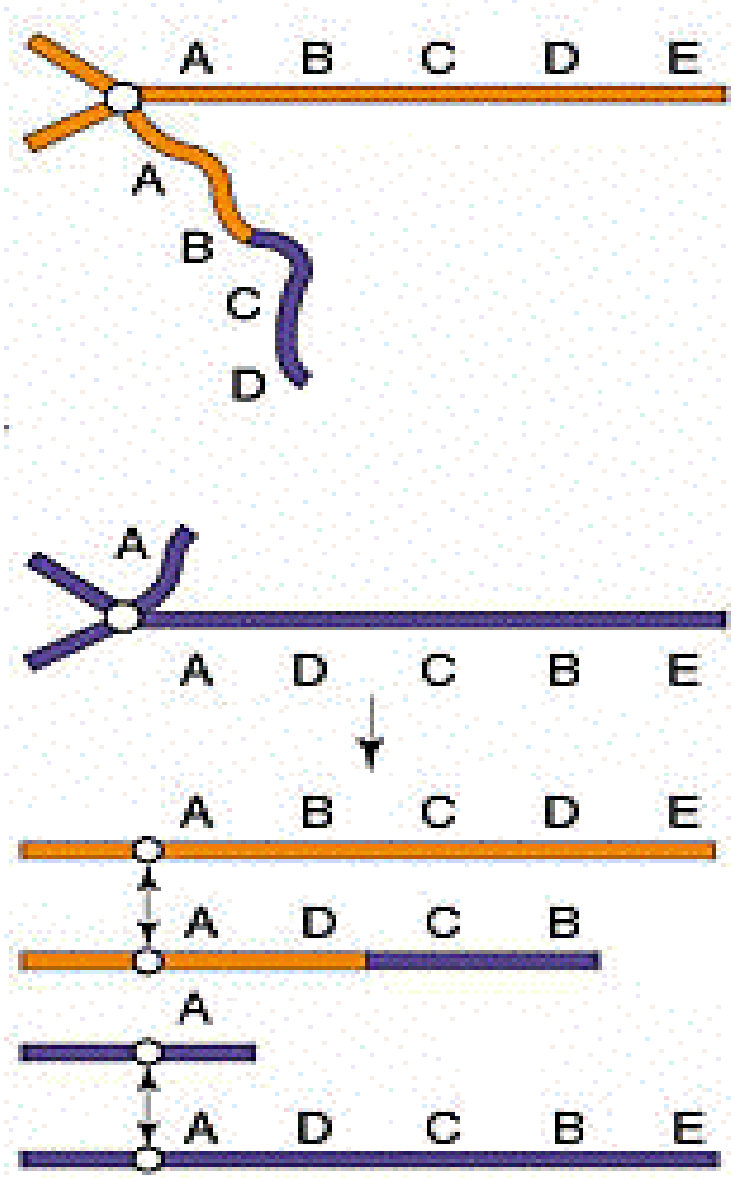


Paracentric Inversion

In the second division of meiosis, the sister chromatids separate and four gametes are produced.

Two of the gametes contain the original, non-recombinant chromosomes . The other two gametes contain recombinant chromosomes that are missing some genes; these gametes will not produce viable offspring.

Thus, no recombinant progeny result when crossing over takes place within a paracentric inversion.



Translocation

Translocations (movement of a chromosomal segment from one location to another)

Types

1. Nonreciprocal (1 segment moves to a new location without an exchange)

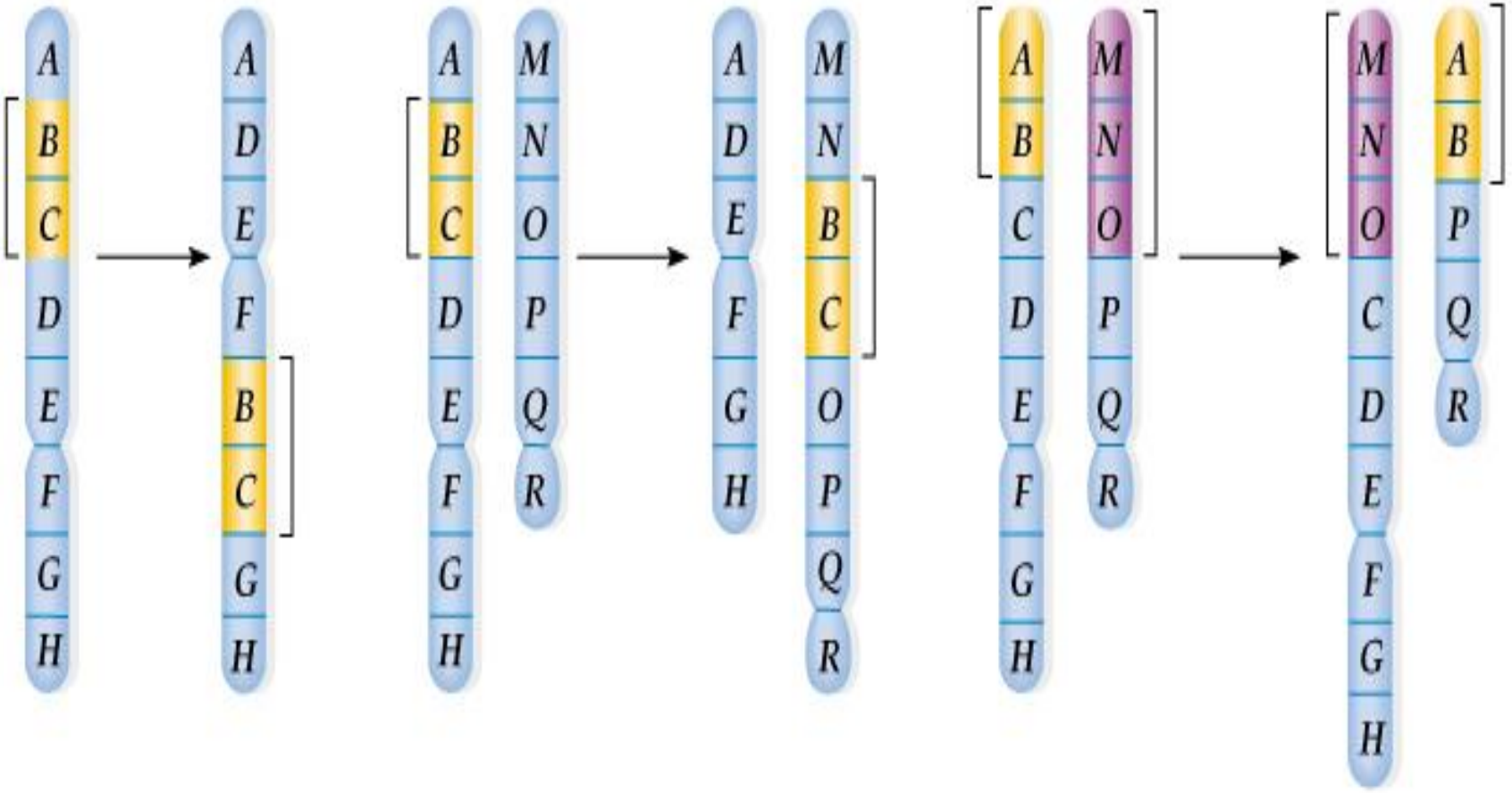
2. Reciprocal (exchange of segments)

Reciprocal translocations require two breaks in two different chromosomes followed by rejoining of the ends.

a) Nonreciprocal intrachromosomal translocation

b) Nonreciprocal interchromosomal translocation

c) Reciprocal interchromosomal translocation



Origin of translocations

1. **Mechanical shear: Breaks occur frequently due to mechanical shear because of chromosome entanglement at interphase or prophase. The broken chromosome segments then reunite with non-homologous chromosome to produce translocations.**
2. **Formation of interlocked bivalents: Interlocking during prophase of meiosis when a non-homologous chromosome passes through a loop of two homologous chromosomes that are in the process of pairing. The interlocked bivalents subsequently separate at anaphase-I, but during this process breakage and reunion takes place.**

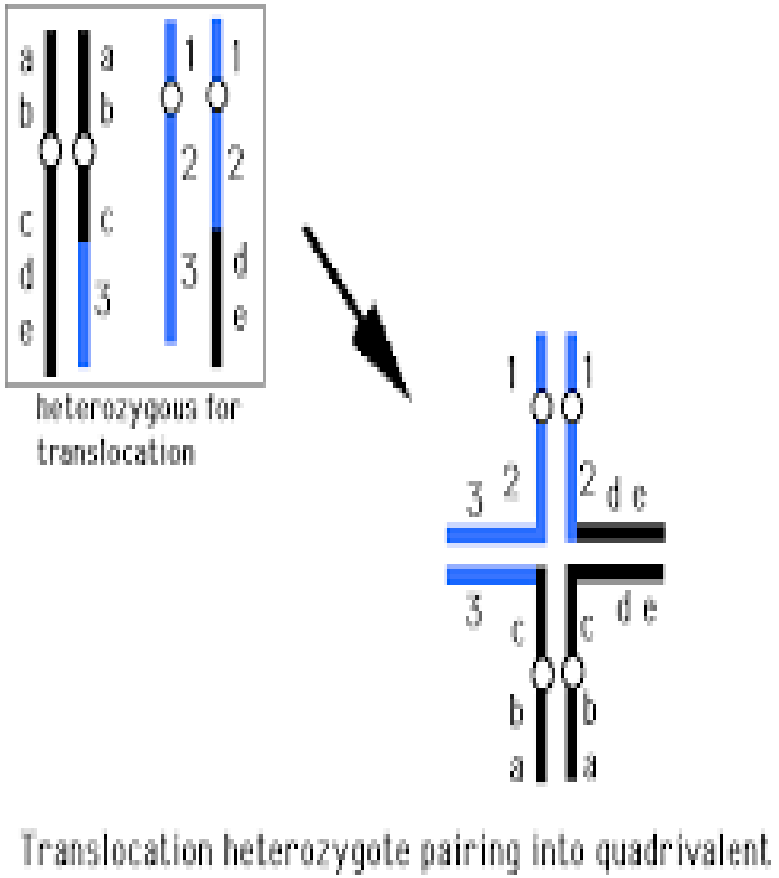
Origin of translocations

3. Physical and chemical agents: Physical mutagens (like X-rays) and various chemical agents induce breaks in the chromosomes. If, two or more breaks occur simultaneously in the non-homologous chromosomes, may result in translocations. Most of the naturally occurring translocations are due to these mutagenic agents because the organisms are continuously exposed to these agents, in the environment.

4). Crossing over in homologous regions: Some times, some duplicated segments are found between non-homologous chromosomes. These duplicated segments are homologous to each other and crossing over between these segments may lead to translocations

Cytology of Translocated Heterozygotes

In meiosis I cells heterozygous for the Translocation, cross conformation forms to get proper alignment of the homologous chromosomes.

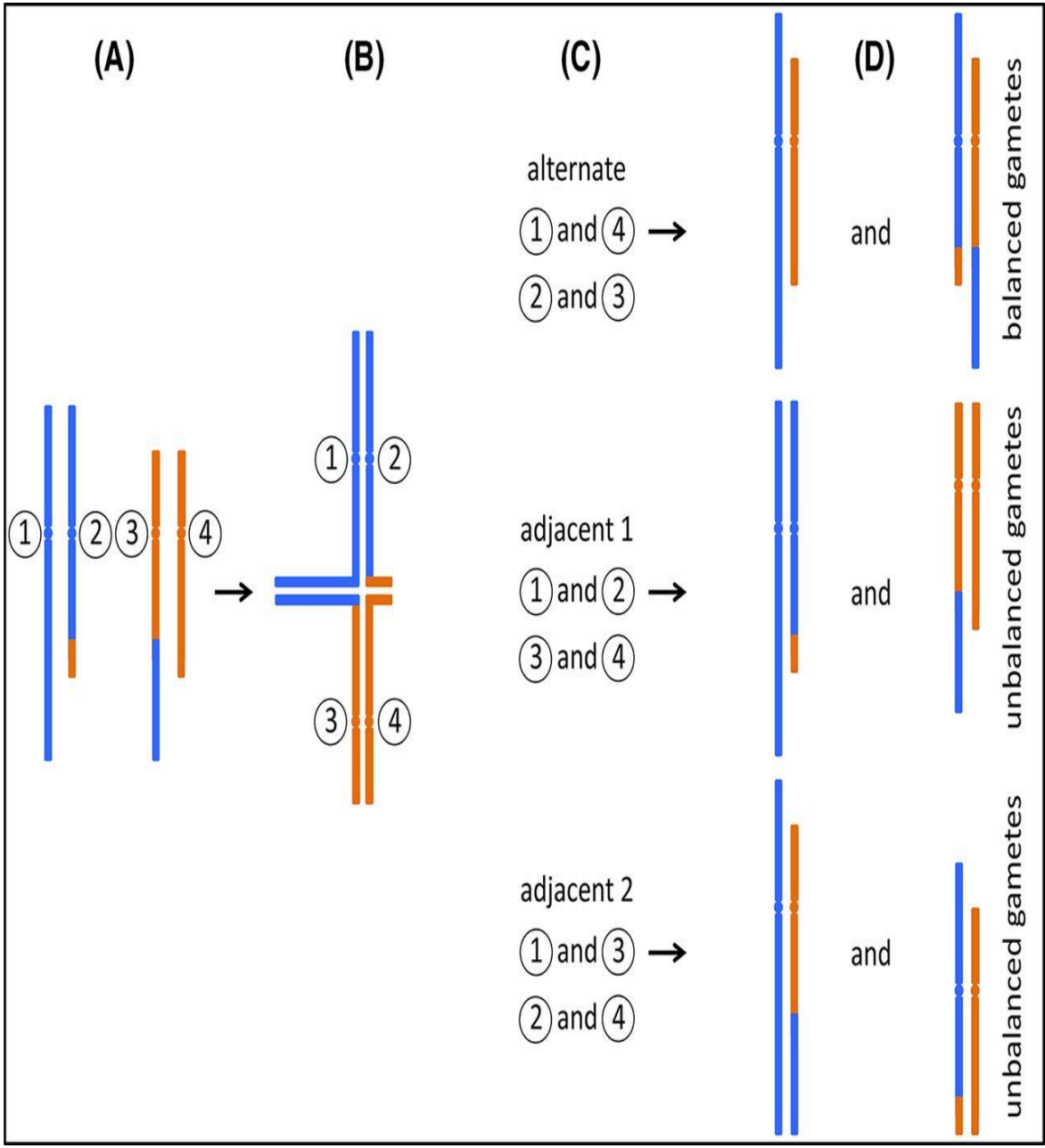


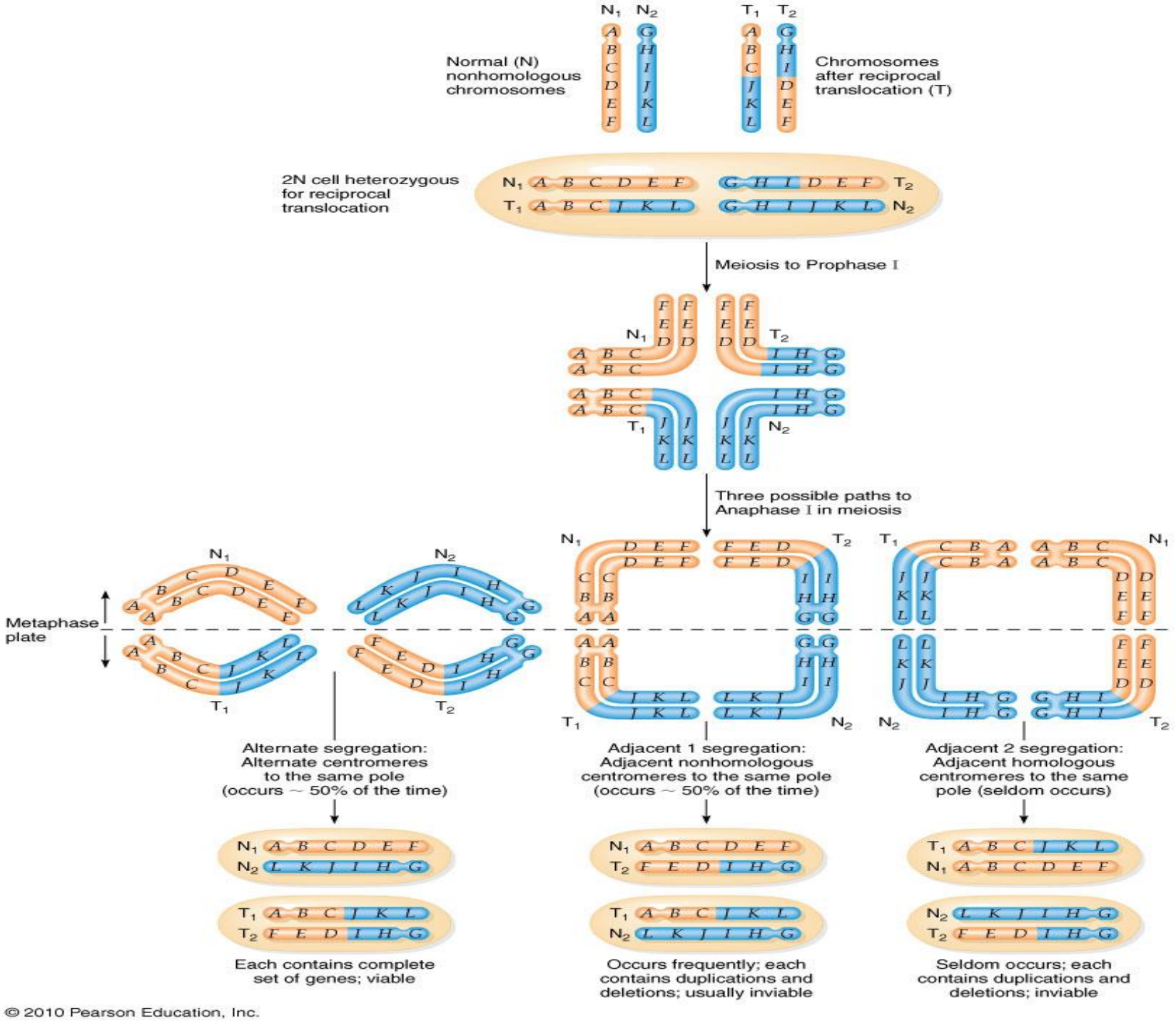
Translocation heterozygote pairing into quadrivalent

1.Alternate: In this case, alternate chromosomes will be oriented towards the same pole, or the adjacent chromosomes will orient towards opposite poles.

2.Adjacent-I: In this type of orientation adjacent chromosomes having non-homologous centromeres are oriented towards the same pole.

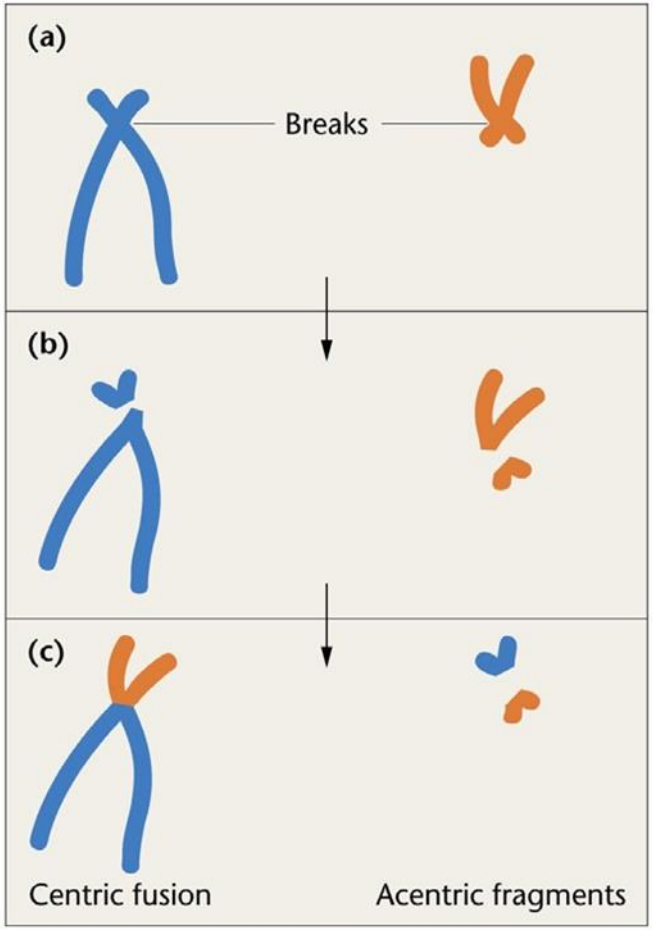
3.Adjacent-II: In this type of orientation, adjacent chromosomes with homologous centromeres will move towards the same pole at anaphase.





Robertsonian translocations

- The fusion of two acrocentric chromosomes with the subsequent loss of the two short arms is termed Robertsonian translocation or centric fusion.
- Although this translocation causes loss of the short arms, it is maintained as a balanced translocation. This is explained by the fact that the genes on the short arms are most rRNA genes that are present in many copies on other chromosomes; thus deletion of these copies doesn't have much phenotypic manifestation.
- One of the commonly seen such translocation is between chromosome 14 and 21.



Effect of translocations

1. **Semisterility:** due to adjacent segregation in meiosis
2. **Position effects:** altered expression of a gene when it is moved to a new location

Detection

1. Genetic

a) Semisterility

b) Apparent linkage of genes on separate chromosomes

c) Position effects

2. Cytological

a) Can change the location of the centromere

b) Change in the size of the chromosome

c) Cross formation in meiosis I