

3. Inversions: Inversions would involve two breaks followed by reunion of interstitial segment in a reverse order i. e., the segment rotates by 180° . Gene sequence in an inverted segment is exactly the opposite of that in its normal homologous pair.

(Let us imagine that a chromosome 1-2-3-4-5-6-7-8 gives rise to another chromosome having the order 1-2-6-5-4-3-7-8. the segment 3-4-5-6 has rotated here at 180° giving an inverted order of genes 6-5-4-3). Even though gene order is changed in an inversion, many inversions do not cause abnormal phenotypes.

Inversions can be of two types depending upon whether centromere is involved or not in inversions.

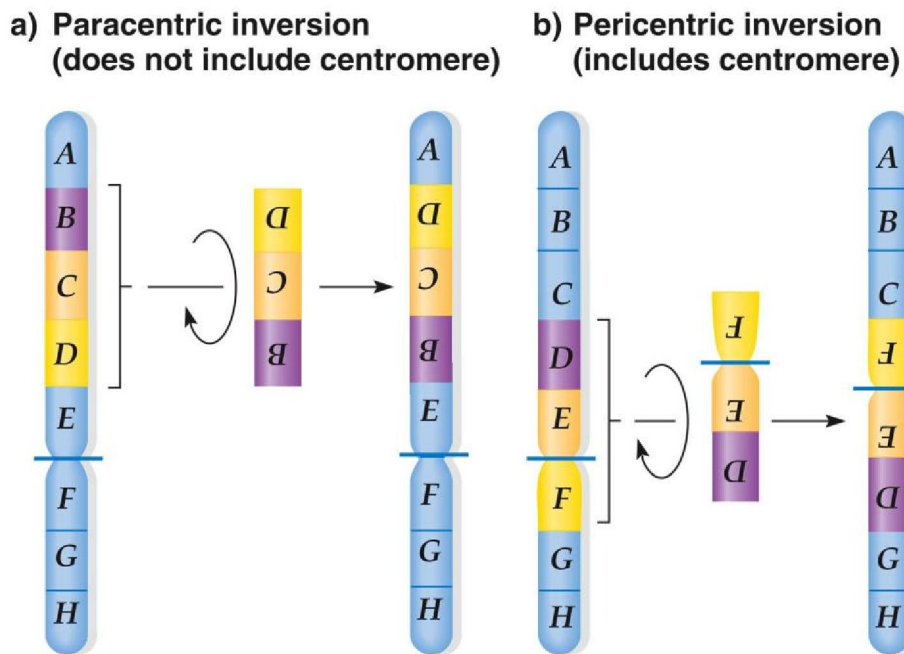
(a) Paracentric inversions and (b) Pericentric inversions.

3. Differentiate between paracentric inversion and pericentric inversion

Paracentric inversion	Pericentric inversion
1. Inverted segment do not include centromere and hence involves only one arm of the chromosome	1. Inverted segment include centromere. Since centromere is involved, both arms of the chromosome are involved in this type of inversion (pericentric means surrounding the centromere).
2. Crossing over within the inversion loop results in the formation of a dicentric bridge (chromatids having two centromeres) and acentric fragment at anaphase-1	No dicentric bridge (chromatids having two centromeres) and acentric fragment are formed at anaphase-1
3. The crossover products (meiotic products or gametes) are non viable due to chromosomal deletions	The crossover products (meiotic products or gametes) are non viable due to chromosomal deletions and duplications
4. Paracentric inversions do not alter the arm ratio and karyotype of chromosomes are not changed	Pericentric inversions alter the arm ratio of chromosomes and hence karyotype is changed.

Why paracentric inversions are called crossover suppressors?

The products of single crossing over will not function and the only crossover products recovered will be double cross overs, the observed frequency of recombination between any two genes of interest will be considerably reduced. Due to this reason, inversions (especially paracentric inversions) are often called crossover suppressors. This reduction in crossing over is not the actual reduction in cytological crossing over, but is the result of lack of recovery of the products of single cross overs (that is gametes of single cross overs are non-viable). This property of inversion has been utilized in the production of CIB stock used by Muller for the detection of sex-linked lethal mutations in *Drosophila melanogaster*.

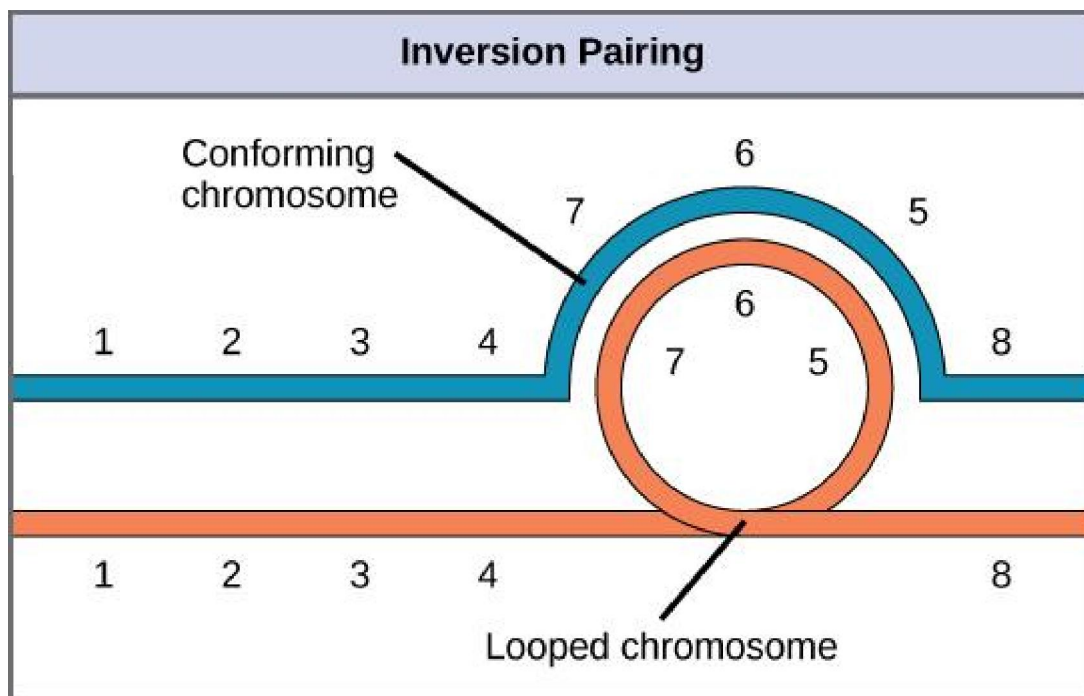


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Origin and production of inversions: Inversions can originate spontaneously and can also be produced artificially. Due to their spontaneous origin, inversions are found abundantly in wild populations of certain organisms such as salivary glands of *Drosophila*. There is some evidence that inversions are produced naturally through the activity of transposable elements (unusual DNA sequences capable of moving from one chromosomal position to the other). During their movement, these elements break a chromosome into pieces. The broken pieces then reattach in an aberrant way, producing an inversion. Chromosome breakage can also occur by mechanical shear or as a result of chromosome entanglement at interphase or during replication. Inversions can also be induced artificially using X-rays or gamma rays or chemical mutagens. These

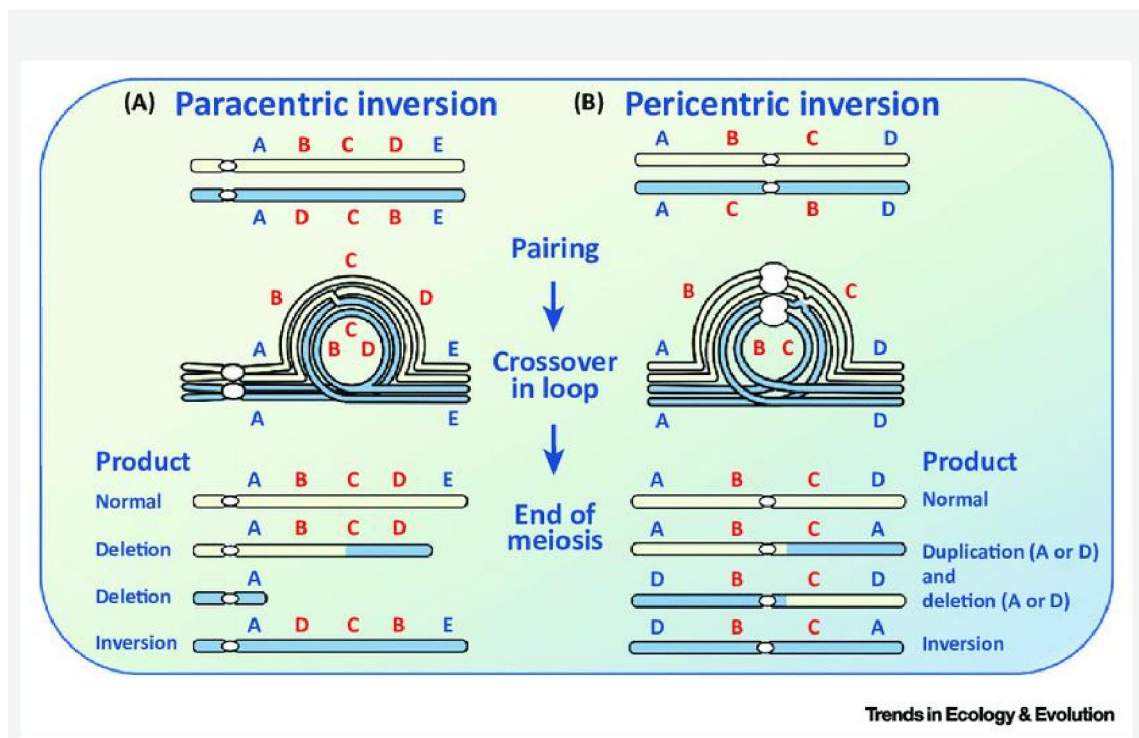
mutagens have the ability to induce breaks in the chromosome. The broken segments sometimes turn around or rotate at 180° and then reattach resulting into an inversion.

Meiotic pairing in inversion heterozygote: during pairing of homologous chromosomes in an inversion heterozygote, the inverted segment must pair with its counterpart with the help of a loop formation at pachytene stage of meiotic prophase. Sometimes the characteristic inversion loop may be absent due to lack of synapsis in the inverted region or due to non-homologous association in the inverted region leading to formation of rod bivalent (McClintock).



Cytological crossing over and its consequences in inversion Heterozygote: Paracentric Inversion: Crossing-over within the inversion loop of a paracentric inversion produces a **dicentric bridge** (the two centromeres remain linked by the bridge) and **acentric fragment**—a fragment without a centromere. As the chromosomes separate in anaphase I, tension eventually breaks the bridge, forming two chromosomes with terminal deletions. The acentric fragment cannot align itself or move and is, consequently, lost (Figure below). The gametes containing such deleted chromosomes are inviable and the zygotes that they eventually form are inviable. Hence, a crossover event, which normally generates the recombinant class of meiotic products, instead produces inviable gametes.

Paricentric Inversion: In a paricentric inversion, because the centromeres are contained within the inverted region, the chromosomes do not form dicentric bridge and acentric fragment. However, the crossover produces chromatids that contain a duplication and a deficiency for different parts of the chromosome (Figure below). Since gametes (cross-over products) having such chromosomes are inviable and the zygote dies. Therefore in higher plants both pollen and ovule abortion are expected due to crossing over in the inverted region.



Detection of inversions

1. Genetic analysis and meiotic chromosome cytology are both good ways of detecting inversions. A paracentric inversion in anaphase-I normally produces a dicentric bridge (the two centromeres remain linked by the bridge) and acentric fragment—a fragment without a centromere. If the same chromosomes are always involved in bridge and the fragment and if the acentric fragment size is constant, it is a strong evidence for the presence of paracentric inversion.
2. If the frequencies of chromosomal configurations such as BF (bridge-fragment), BBFF (two bridge-two fragment), LF (loop-fragment), LLFF (two-loop-two fragment) are similar in Anaphase I and Anaphase II, this will be another evidence for the presence of paracentric inversion.

3. Inversions can be detected through mitotic chromosome analysis. A key operational feature is to look for new arm ratios. Due to pericentric inversions, ratio of the long arm to the short arm has been changed from about 4:1 to about 1:1. Paracentric inversions do not alter the arm ratio, but they may be detected microscopically if chromosome banding or other chromosome landmarks are available.

Uses of para and pericentric inversions

- 1) Inversions can be used to study the behavior of chromosomes during meiosis such as chromosome pairing, cytological crossing over, formation of dicentric bridges and acentric fragments as seen in paracentric inversions, deletions and duplications in pericentric inversions etc.,
- 2) A combination of cytological location of inversion breakpoints and genetic linkage can be used for physical location of genes in the chromosome.
- 3) Inversions can be used to study the Position effect: due to inversions euchromatic segment of a chromosome may become located in the vicinity of a heterochromatic region. In such a condition, the euchromatic region may become heterochromatinized. This would cause suppression of gene expression. One of the main effects of inversion is that it changes the position of the gene. Any change in the phenotype due to change in position of the gene is called position effect. Due to position effect, the expression of the gene may be blocked if, e.g. the gene is separated from its regulatory sequences or is placed next to constitutive heterochromatin due to inversion. The normal expression of the gene is also affected due to absence of various kinds of allelic and nonallelic interactions at its new position.
- 4) Inversions act as cross over suppressors: absence of crossing over within the inverted segment maintains that particular gene combinations intact. That is, complete linkage for the concerned genes and such inversions are designated as cross over suppressors. Muller used CIB stock to detect lethal mutations induced by X-rays. In CIB, 'C' represents crossover suppressor gene (inverted chromosome segment).
- 5) Inversions played an important role of in evolution such as formation of different races in drosophila. By studying overlapping inversions, the phylogentic relation of different species can be studied.
- 6) Asymmetrical Inversion breakpoints on the two sides of a centromere in pericentric inversion changes the karyotype of the chromosome. A metacentric chromosome may become a submetacentric or acrocentric depending on the break positions in the two arms. Thus karyotype polymorphism may be generated.
- 7) inversions in combination with other chromosomal changes can be used to control insects Ex: yellow fever mosquito (*Aedes aegypti*).

8) Inversions are used to create duplications in specific chromosome regions for various experimental purposes.

Role of inversions in evolution

1. Spontaneous inversion observed in drosophila. In *Drosophila pseudoobscura*, a species which inhabits western North America, spontaneous inversion led to formation of different races. These Inversion races are restricted to specific localities and were named according to the localities they inhabited, such as Pike's Peak, Estes Park, Cuernavaca etc.
2. By studying overlapping inversions, the phylogentic relation of different species can be studied. Overlapping inversions can be identified by banding patterns and chromosome pairing in F1 hybrids as seen in salivary gland chromosomes.
3. Because of evolutionary benefit, paracentric inversions are more common in drosophila races than pericentric inversions. Paracentric inversions do not show male or female sterility. Sterility is absent in male drosophila as crossing over is absent. Female sterility is absent due to formation of dicentric bridge in meiosis that causes a chromatid tie. In pericentric inversion sterility on female side is observed due to absence of bridge.

Role of inversion in the evolution of Karyotype

1. In paracentric inversion karyotype changes are not observed. In case of pericentric inversions, asymmetrical inversion breakpoints on the two sides of a centromere changes the karyotype of the chromosome. A metacentric chromosome may become a submetacentric or acrocentric depending on the break positions in the two arms. Thus karyotype polymorphism may be generated.
2. Inversions, specifically pericentric inversions can lead to increase or decrease in chromosome number. Tsuchiya in barley observed in the selfed progeny of a trisomic type for chromosome 6, a 16-chromosome type was obtained which had a pair of new metacentric chromosome 6 in excess. The new metacentric chromosome 6 was shorter than any of the 14 chromosomes of normal barley complement and showed a heteropycnotic nature at late prophase in somatic mitosis. The 16-chromosome plants were observed to exhibit 8_{II} or $7_{II}+2_{I}$ at meiosis.

Breeding behaviour of translocation heterozygotes:

The presence of translocation heterozygosity can be detected by the presence of semisterility and low seed set. This can in turn be confirmed by cytological analysis, where a characteristic translocation ring is observed at diakinesis or metaphase stages of meiosis. We have already seen that only alternate disjunction results in the formation of functional gametes. During selfing of a translocation heterozygote, two types of gametes are formed on male and female side, one carrying normal chromosomes, and the other type carrying translocated chromosomes. Random fertilization between these gametes will produce a progeny of normal, translocation heterozygotes and translocation homozygotes in the ratio of 1:2:1, respectively.

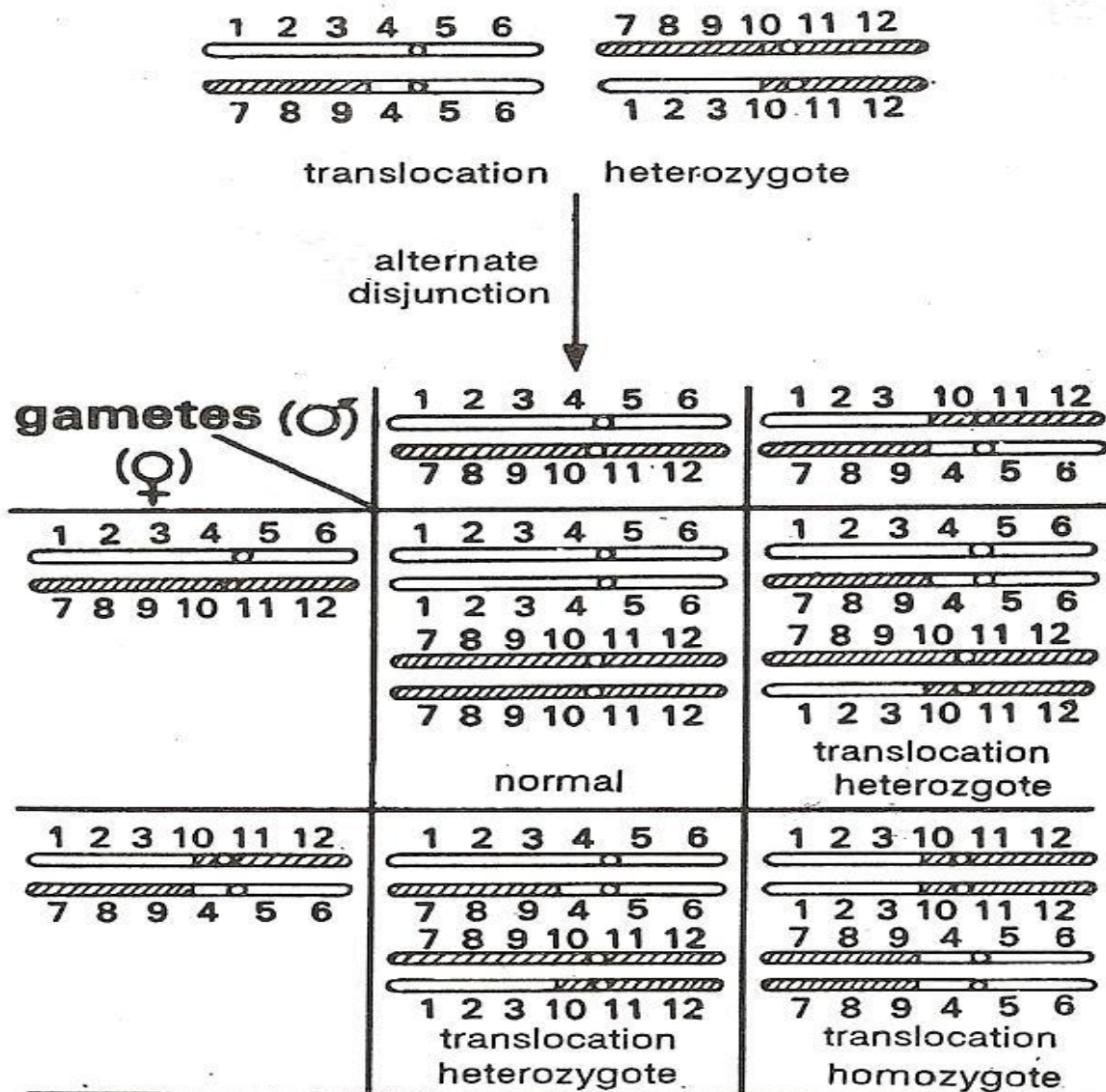


Fig. Breeding behaviour of translocation heterozygote (Drawn from Genetics by PK Gupta)

Rarely, however, an interchange ring may undergo 3:1 disjunction at anaphase, resulting in the formation of $n+1$ and $n-1$ gametes. Although the deficient gamete is non functional, but the gamete with $n+1$ condition on fertilization with normal gamete will lead to the production of variety of trisomics.

Types of translocations

Different types of translocations exist in nature, as given below:

1. Simple translocations

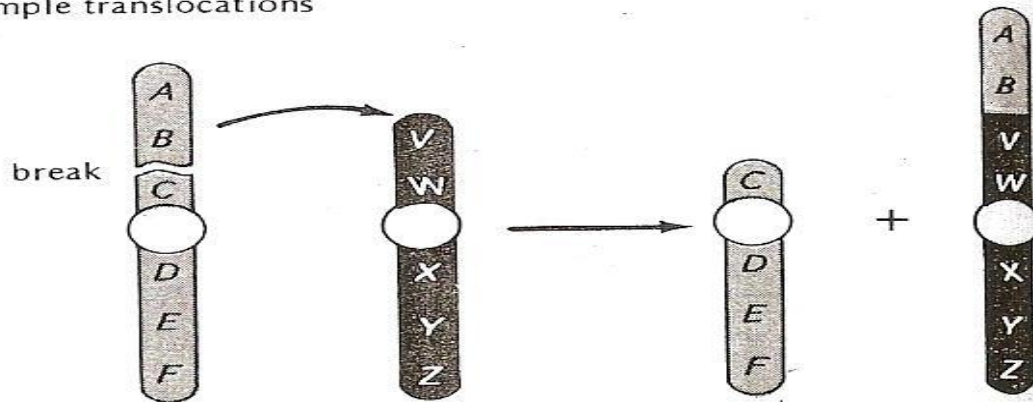
In this case a single break occurs in a chromosome releasing a terminal acentric fragment. This is followed by transfer of this acentric fragment to the end of a non-homologous chromosome. This type of translocation was first reported by **Muller and Painter in 1929**. Simple translocations actually do not exist in nature.

2. Shifts or intercalary translocations: This type of translocation is commonly found in nature and involves atleast three breaks – two breaks in one chromosome releasing an acentric fragment and one break in another non-homologous chromosome. The released acentric fragment is then inserted at the intercalary position near the break produced in the non-homologous chromosome. This type of translocation was first reported by Bridges in 1923. Both simple type and intercalary translocations are also called as non-reciprocal translocations.

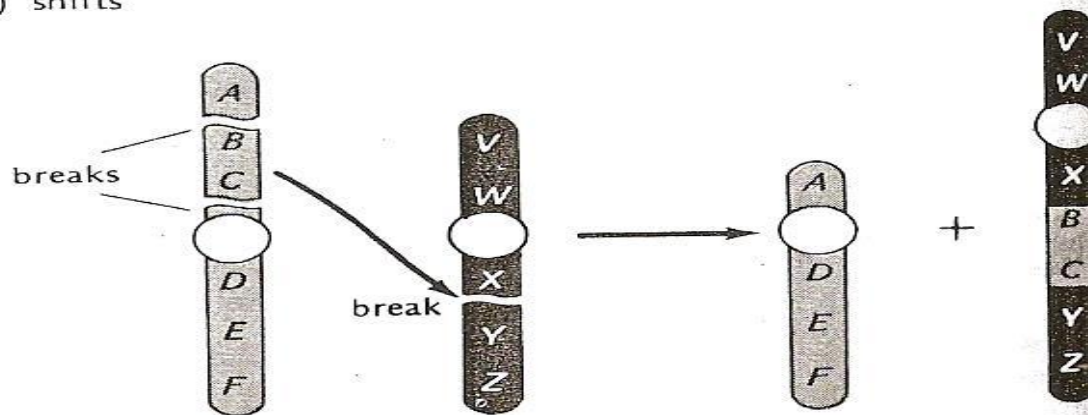
3. Reciprocal translocations: This is the most frequently found and best studied type of translocation. When chromosomal segments are exchanged between two non-homologous chromosomes without any net loss of genetic material, the event is referred to as a reciprocal translocation. In reciprocal translocation, atleast a single break occurs in each non-homologous chromosome, releasing a terminal telomeric fragment. This is followed by mutual exchange of these fragments between the two non-homologous chromosomes, e.g. a part of chromosome-1 is detached and becomes attached to chromosome 2. At the same time, a part of chromosome 2 is detached and becomes attached to chromosome 1. Such translocations are also called interchanges. The net result of this translocation is that genes from one chromosome are transferred to the other, and vice-versa.

Types of translocations (Drawn from Genetics by Strickberger)

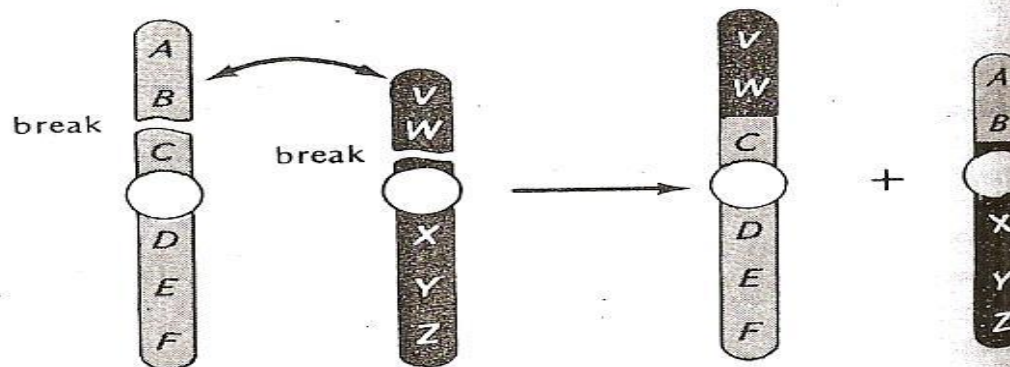
(a) simple translocations



(b) shifts



(c) reciprocal translocations



Permanent translocation hybrids in oenothera: The plant genus *Oenothera* (evening primrose, Onagraceae, $2n = 2x = 14$) due to reciprocal chromosomal translocations, forms extensively multichromosomal rings at meiosis. Meiotic configurations can range from a single ring, where all the 14 chromosomes are involved in catenation, through intermediate forms with rings and bivalents, to solely bivalents. Hence in *Oenothera*, chromosomal end-segments are the only sites throughout the genome where chiasmata are formed. The terminal chiasmata are obligatory for proper and regular meiosis I segregation. However, techniques of classical and molecular genetics show unusually low levels of crossovers, allowing *Oenothera* genomes to be regarded as essentially nonrecombining.

In a *translocation heterozygote* two distinct pairs of homologous chromosomes have reciprocally exchanged nonhomologous segments between one member of each pair. As a result each of the affected chromosome pairs contain both homologous and nonhomologous segments. Put another way, each such pair has one translocated chromosome, and one normal (untranslocated) chromosome. More than two chromosome pairs can be altered in this way so that some or all of the chromosome pairs are composed of a translocated and an untranslocated member. Organisms having all the chromosomes rearranged the form of a ring (sometimes a ring of 12 chromosomes and a bivalent) with genes close to centromere of different chromosomes are linked are said to be *permanent translocation heterozygotes* (permanent hybridity). Due to the way reciprocal translocations are processed during meiosis, all the translocated chromosomes pass to one gamete and all the normal chromosomes pass to the other. As a result, only two types of gametes are produced. One has all the translocated chromosomes and the other has all the normal ones (here "translocated" and "normal" are relative terms since in naturally occurring organisms it is usually unknown which of the two types was original). These two sets of chromosomes ("normal" and "translocated") or linkage groups are known as *Renner complexes*. PTH are always stable because when these complexes meet in the hybrid, they always experience regular meiotic segregation. In well-studied organisms of this type, the various Renner complexes have been assigned formal names.



Oenotheralamarckiana

In one of the best-known permanent translocation heterozygotes, the evening primrose *Oenotheralamarckiana*, the two Renner complexes are called *velans* and *gaudens*. So the karyotype of *O. lamarckiana* is designated as "*velans/gaudens*." Genetic interchange (crossing-over) between Renner complexes is very rare (Renner x Velans).

Aneuploidization is a common stabilization process among permanent translocation heterozygotes because there is an enhanced tendency to produce aneuploid gametes. The result is the production of numerous trisomic forms. But the most common stabilization process seen in organisms of this type occurs when forms with distinct Renner complexes hybridize to produce new forms. For example, hybridization of *O. lamarckiana* with another evening primrose, *O. strigosa*, which has the Renner complexes *deprimens* and *strigens*, yields four different types,

1. *velans/deprimens*,
2. *velans/strigens*,
3. *gaudens/deprimens*,
4. *gaudens/strigens*

Since chromosomes in distinct complexes differ genetically in many respects, some hybrids produced by such recombinations of Renner complexes are reproductively stable and others are not. By this means new stable types can be produced in a single generation. Therefore, a certain level of outbreeding is needed to create new stable [PTH](#) forms. *O. lamarckiana* itself arose by such a process via hybridization between *O. biennis* and *O. hookeri*. This event occurred within the last two or three centuries in Europe where the two parental forms, both native to North America, were introduced. In fact, most of the 18 forms of European *Oenothera* that Renner (1942) treated as species arose in this way.

An explanation for maintenance of permanent hybridity ("*velans/gaudens*") in stable manner in *Oenothera* was given by Muller using Balance Lethal System in *Drososphila*. In Balance Lethals the dominant alleles of two traits, each with a recessive lethal effect, are present in heterozygous repulsion phase. Homozygotes do not survive and permanent hybridity is maintained. There are two balance lethal mechanisms, one involving zygotic lethality and the other involving gametic lethality. There are two gametic complexes in *oenothera*, alpha (α) in functional egg and beta (β) in functional pollen. The full ovule fertility or seed set is due to the fact that only the megaspore

that carries alpha (α) complex. Since alpha (α) complex unite with beta (β) complex in pollen, plants breed true for heterozygous condition.

Robertsonian translocation

A Robertsonian translocation is one that combines the long arms of two acrocentric chromosomes resulting in large metacentric chromosome and a small chromosome, as shown in Figure 17-27. A small chromosome composed of the two short arms also forms; however, this small chromosome may be devoid of genes and may be lost. It is also called centric fusion as the two acrocentric chromosomes fuse at centromere. Such translocations mostly occur in the acrocentric chromosomes such as D group (chromosomes 13,14, and 15) and G group (chromosomes 21 and 22) of human chromosomes. Translocation Down syndrome is caused by a Robertsonian fusion between chromosomes 21 and 14. The translocated chromosome passes down through the generations in unaffected carriers. However, meiotic segregation in the translocation carriers can result in offspring that carry three copies of most of chromosome 21, as shown in Figure 17-27, and these offspring have Down syndrome.

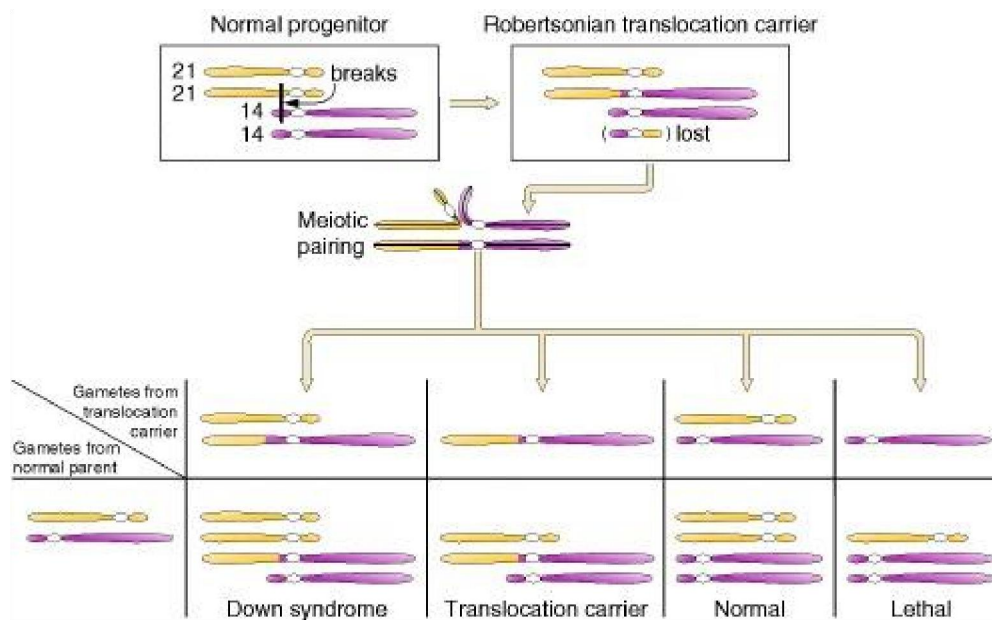


Figure 17-27: How Down syndrome arises in the children of an unaffected carrier of a special type of translocation, called a Robertsonian translocation, in which the long arms of two acrocentric chromosomes have fused. The specific Robertsonian translocation in translocation Down syndrome is between the Down syndrome chromosome 21 and chromosome 14. Translocation Down syndrome accounts for less than 5% of cases.

Effect of Robertsonian translocation:

- 1) Due to loss of small chromosome due to translocation, chromosome number is reduced to 45 in humans. Meiotic cells show association of three chromosomes: i.e., two normal and one large metacentric translocated chromosome.
- 2) The translocated chromosome passes down through the generations in unaffected carriers. However, meiotic [segregation](#) in the translocation carriers can result in offspring that carry three copies of most of chromosome 21, as shown in [Figure 17-27](#), and these offspring have Down syndrome.
- 3) Keith Jones emphasized the role of Robertsonian translocation in the evolution of some members of family Commelinaceae.