## CHROMOSOMAL ABERRATIONS

Aberration alters the chromosome structure but do not involve a change in chromosome number. The mechanics signify chiefly a rearrangement through loss, gain or reallocation of chromosomal segments. The chromosome set of a species remains relatively stable over long periods of time. However, within populations there can be found abnormalities involving the structure or number of chromosomes. Their consequences are usually deleterious, giving rise to individuals who are unhealthy or sterile, though in rare cases alterations provide new adaptive opportunities that allow evolutionary change to occur. In fact, the discovery of visible chromosomal differences between species has given rise to the belief that radical restructuring of chromosome architecture has been an important force in evolution.
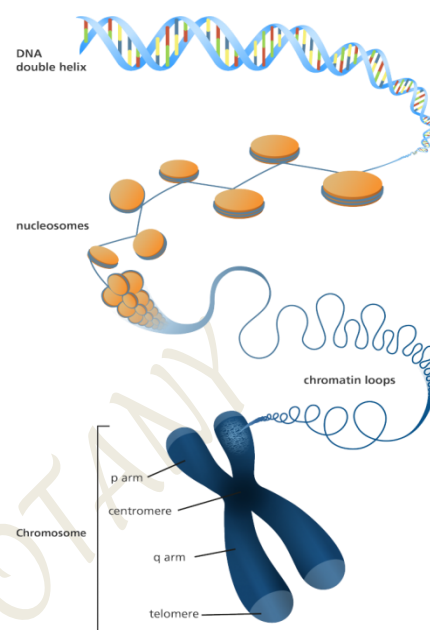
Changes in chromosome structure

Two important principles dictate the properties of a large proportion of structural chromosomal changes. **The first principle** is that any deviation from the normal ratio of genetic material in the genome results in genetic imbalance and abnormal function. In the normal nuclei of both diploid and haploid cells, the ratio of the individual chromosomes to one another is 1:1. Any deviation from this ratio by addition or subtraction of either whole chromosomes or parts of chromosomes results in genomic imbalance. **The second principle** is that homologous chromosomes go to great lengths to pair at meiosis. The tightly paired homologous regions are joined by a ladder like longitudinal structure called the synaptonemal complex. Homologous regions seem to be able to find each other and form a synaptonemal complex whether or not they are part of normal chromosomes. Therefore, when structural changes occur, not only are the resulting pairing formations
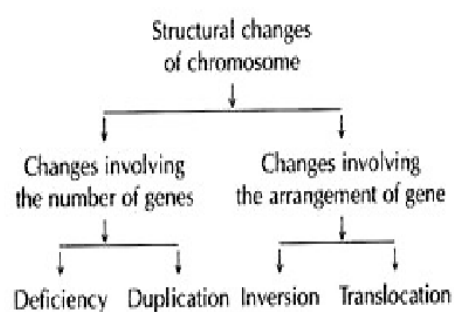
highly characteristic of that type of structural change but they also dictate the packaging of normal and abnormal chromosomes into the gametes and subsequently into the progeny.

(i) Deficiency (parts of chromosome lost or deleted),

(ii) Duplication (parts of chromosome added or duplicated),

(iii) Inversion (sections of chromosome detached and reunited in reverse order), and

(iv) Translocation (parts of chromosome detached and joined to non-homologous chromosome).

Deficiency of Chromosomal Aberration:

Deficiency or deletion represents a loss in chromosomal material and was the first chromosomal aberration indicated by genetic evidence. This evidence, presented by Bridges in 1971 in Drosophila melanogaster, showed a deletion of the X-chromosome that included the Bar locus.

Deficiency or deletions are of two types:

(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.

Origin:

Origin of intercalary deficiency is represented in Fig. Terminal deficiency might seem less complicated and more likely to occur than those involving two breaks.
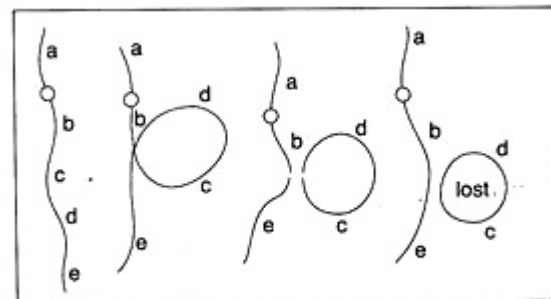

The origin of a deletion

Meiosis:

Heterozygous deficiencies during meiosis form a loop in a bivalent and it can be observed in the pachytene stage.

Effect of Chromosomal Aberration:

Deficiencies have an effect on inheritance also. In presence of a deficiency, a recessive allele will behave like a dominant allele and this phenomenon is called pseudo dominance. This principle of pseudo dominance exhibited by deficiency heterozygotes has been utilized for location of genes on specific chromosomes in Drosophila.
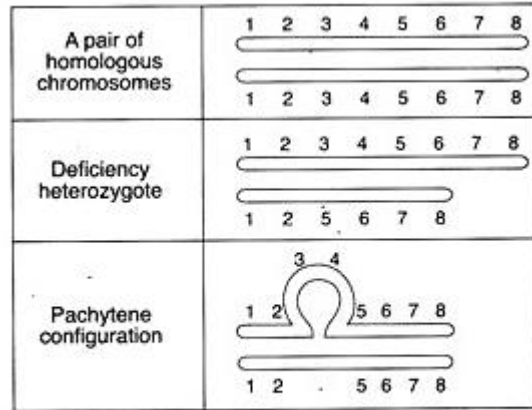
Chromosome pairing in a deficiency hetero-zygote

Thus chromosome deficiencies have greatly facilitated the checking of linkage maps.

A somatic cell that has lost a small chromosome segment may live and produce other cells heterozygous like itself, each with deleted section of a chromosome. Phenotypic effects sometimes indicate which cells or portions of the body have descended from the originally deficient cell.

If the deficient cell is a gamete that is subsequently fertilized by a gamete carrying a non-deficient homologue, all cells of the resulting organism will carry the deficiency in the heterozygous condition.

Recessive genes on the non-deficient chromosome in the region of deficiency may express themselves. Heterozygous deficiencies thus usually decrease the general viability.

Duplication of Chromosomal Aberration:

Duplication represents additions of chromosome parts. A chromosome segment is present in more than two copies.

Origin of Duplication of Chromosomal Aberration:

Duplication originates out of unequal crossing over.
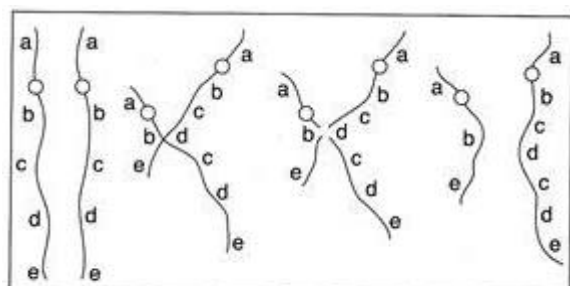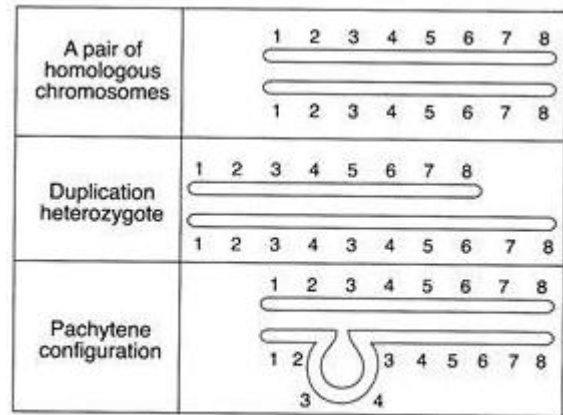
The origin of a duplication

Meiosis:

If duplication is present only on one of the two homologous chromosomes, at meiosis (i.e., pachytene) a characteristic loop is obtained.

Effect of Duplication of Chromosomal Aberration:

The duplication was-critically examined in the B (bar) locus of the X-chromosome of Drosophila. Barred eye is a character where eyes are narrower as compared to normal eye shape. This phenotypic character is due to duplication for a part of a chromosome. The Bar character is due to duplication in region 16A of X-chromosome.

A pair of homologous chromosomes	1 2 3 4 5 6 7 8 1 2 3 4 5 6 7 8
Duplication heterozygote	1 2 3 4 5 6 7 8 1 2 3 4 3 4 5 6 7 8
Pachytene configuration	1 2 3 4 5 6 7 8 1 2 3 4 5 6 7 8 3 4

Chromosome pairing in a duplication heterozygote

Barred eye individuals (16A 16A) give rise to ultrabar (16A 16A 16A) and normal wild type (16A) due to unequal crossing over. Barred eyes have different phenotypes in homozygous bar and heterozygous ultrabar individuals although in each case, number of 16A segments remains the same. This was called **position effect**.
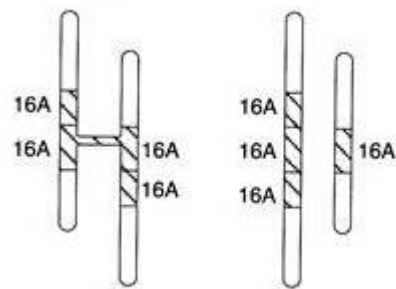
An ultrabar condition resulting from 'Bar' due to unequal crossing over

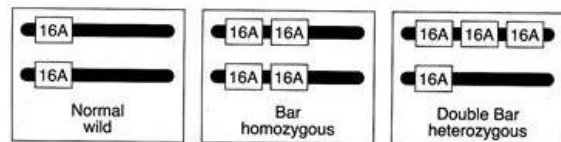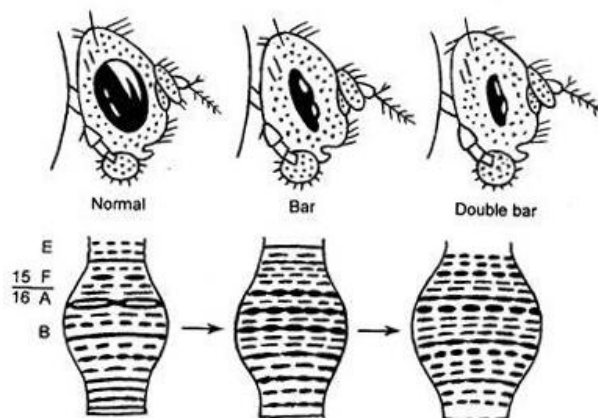| Normal wild	Bar homozygous	Double Bar heterozygous

Diagram showing position effect

A normal eye, bar eye and a double bar eye with corresponding chromosome segments (salivary gland chromosomes) showing duplications

Types of Duplication of Chromosomal Aberration:

Duplications are of different types on the basis of position of duplicated segment:

(i) Tandem duplication – adjacent region;

(ii) Displaced homo-brachial duplication – at a displaced position of the same arm;

(iii) Displaced heterobrachial duplication – on the different arm of the same chromosome;

(iv) Transposed duplication – on a different chromosome;

(v) Reverse tandem duplication – duplicated segment found as a reverse repeat at adjacent region.

(i) 1 2 3 2 3 4 5 6
Tandem duplication

(ii) 1 2 3 4 2 3 5 6
Displaced homobrachial duplication

(iii) 1 2 3 4 5 3 4 6
Displaced heterobrachial duplication

(iv) 1 2 3 4 5 6   7 8 3 4 9 10 11 12
Transposed duplication

(v) 1 2 3 3 2 4 5 6
Reverse tandem duplication
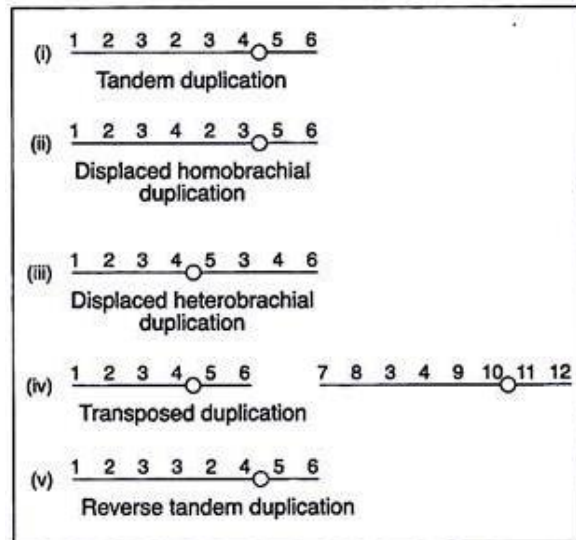
Different kinds of duplications

Inversion of Chromosomal Aberration:

Inversion represents reverse gene order in the chromosome.

Origin:

Inversions originate when parts of chromosome become detached, turn through 180°, and are reinserted in such a way that the genes are in reversed order. Some inversions presumably result from entanglements of the threads during the meiotic prophase and from the chromosome breaks that occur at that time.

For example, a certain segment may be broken in two places, and the two breaks may be in close proximity because of a chance loop in the chromosome.
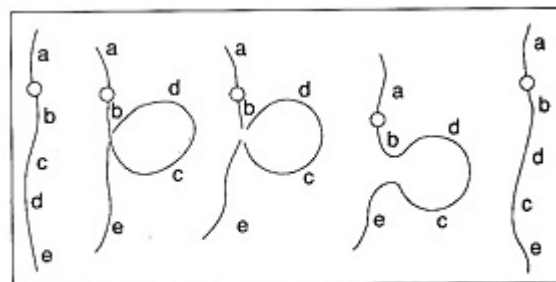
The origin of an inversion

When they rejoin, the wrong ends may become connected. The part on one side of the loop connects with a broken end different from the one with which it was originally connected. This leaves the other two broken ends to become attached. The part within the loop thus becomes turned around and inverted.

Meiosis:

Inversions may survive the meiotic process and segregate into viable gametes. Chromosome pairing is essential in the production of fertile gametes. The mechanism by which homologous chromosomes heterozygous for inversions accomplish such pairing in the meiotic sequence is depicted in Figs. The products of crossing over and subsequent stages of meiosis are different for the two types of inversions.

Types of Inversions:

Inversions can be of two types:

(i) Paracentric inversion and

(ii) Pericentric inversion

Paracentric inversions are those inversions where inverted segments do not include centromeres. On the other hand, in a pericentric inversion, inverted segment includes centromere.
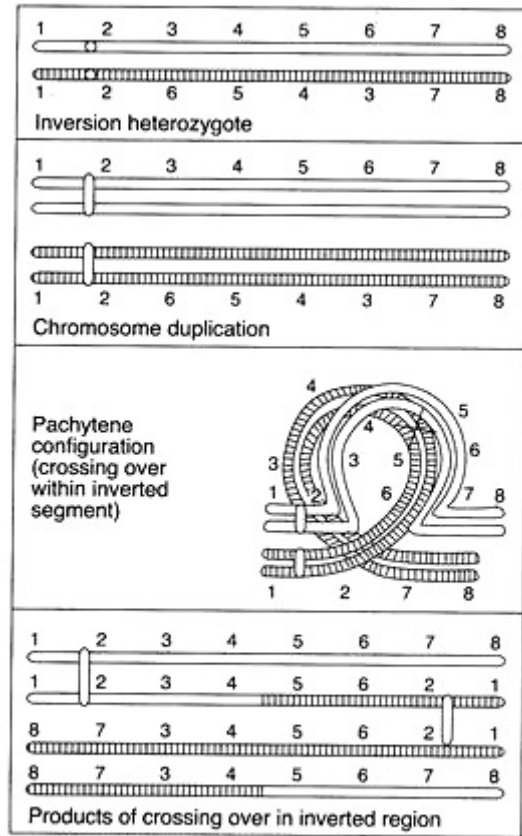

Chromosome pairing and products of crossing over in a paracentric inversion heterozygote (after P. K. Gupta)

Paracentric Inversion:

In paracentric inversion, a single crossover or an odd number of crossovers in inverted region results in the formation of a dicentric chromosome (having two centromeres) and an acentric .chromosome (with no centromere). Of the remaining two chromatids, one remains normal and the other carries the inversion.
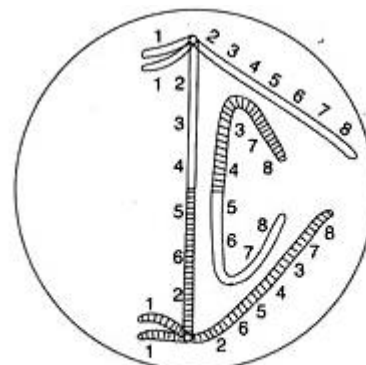
The dicentric chromatid and the acentric chromatid are observed at anaphase I in the form of a bridge and a fragment. Crossing over within and outside inversion lead to various kinds of deficiencies and duplications.

Pericentric Inversion:

In pericentric inversion, the pachytene configuration observed is similar to that of paracentric inversion. But the products of crossing over and configurations at subsequent stages of meiosis differ. Two of the four chromatids will


Dicentric bridge and an acentric fragment at anaphase I

have deficiencies and duplications. No dicentric bridge or acentric fragments are formed.

As the two chromatids resulting from crossing over have deficiencies and duplications, the gametes having these chromosomes do not function and lead to considerable gametic or zygotic lethality. The plants show pollen sterility. The only crossovers which can be recovered are double crossovers, and the observed frequency of recombination between any two genes is considerably reduced.

Thus inversions are called crossover suppressors. This property of inversion has been utilized in the production of CIB stock, used by Muller for detection of sex linked lethal mutations. Three different kinds of non-crossover progenies (1 : 2 : 1) are obtained by selfing of an inversion heterozygote.
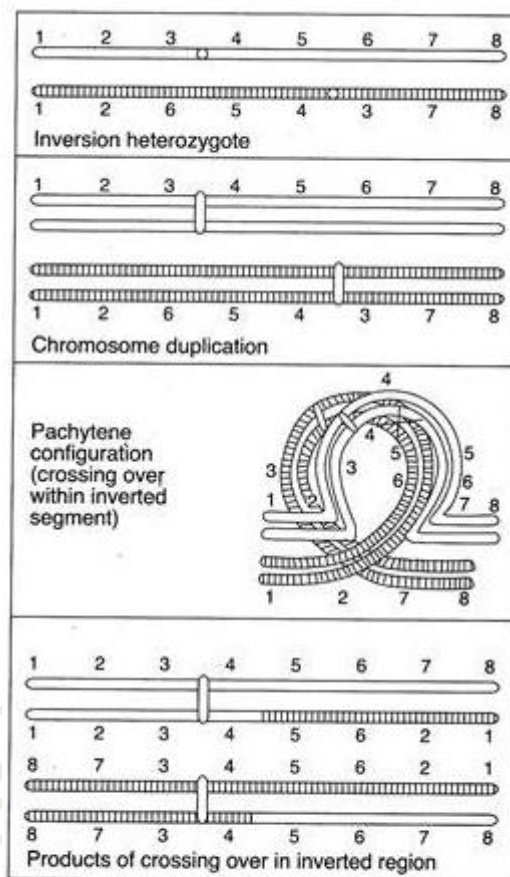
Chromosome pairing and products of crossing over in a pericentric inversion heterozygote (after P. K. Gupta)

Translocation of Chromosomal Aberration:

Sometimes a part of a chromosome becomes detached and joins to a part of a non-homologous chromosome, thus producing translocation. Translocations have been described in a number of plants and are important factors in the evolution of certain plant groups such as Datura and Oenothera.

The origin of a translocation

Types of Translocation:

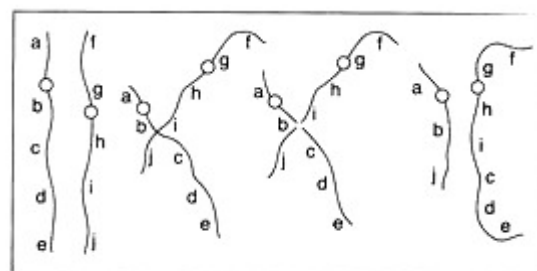Three types of translocations are observed:

(i) Simple translocation:

The broken part gets attached to one end of non-homo¬logous chromosome.

(ii) Shift translocation:

Broken part gets inserted interstitially in a non-homologous chromosome.

(iii) Reciprocal translocation:

When parts of chromosomes belonging to members of two different pairs become exchanged.

Meiosis:

If a translocation is present in one of the two sets of chromosomes, that will be a translocation heterozygote. In such a plant, normal pairing into bivalents will not be possible among chromosomes involved in translocation.

Due to pairing between homologous segments of chromosomes, a cross shaped (+) figure involving four chromosomes (quadrivalent) will be observed at pachytene. This ring of four chromosomes at metaphase I can have one of the following three orientations:
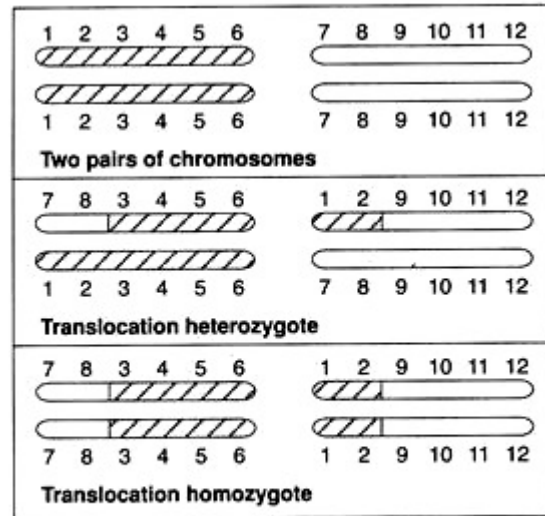
Chromosome constitution of a structural heterozygote and a homozygote

Alternate:

In this orientation, alternate chro¬mosomes will be oriented towards the same pole.

This is possible by attaining an "eight" (8) like configuration.

Adjacent I:

In this orientation, adjacent chrotromeres will orient towards opposite poles. A mosomes having non-homologous centromeres ring of four chromosomes will be observed.

Adjacent II:

In this orientation, adjacent chromosomes having homologous centromeres will orient towards the same pole. A ring of four chromosomes is obtained.
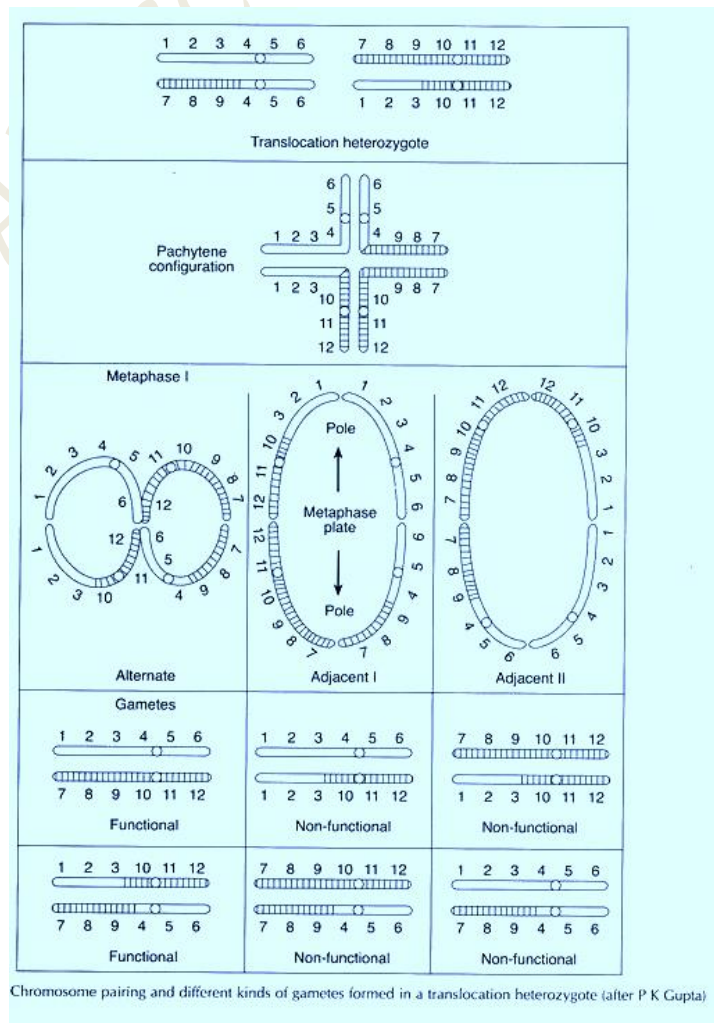
Chromosome pairing and different kinds of gametes formed in a translocation heterozygote (after P K Gupta)

Alternate disjunction gives functional gametes. Adjacent I and Adjacent II will form gametes, which would carry duplications or deficiencies and as a result would be nonfunctional or sterile. Therefore, in a plant having a translocation in heterozygous condition, there will be considerable pollen sterility.

The different kinds of progenies in the ratio 1:2:1 are obtained due to self-fertilization in a translocation heterozygote through alternate disjunction. The first

A ring of 6 pairs of chromosomes (12) in Rhoeo with heterozygote translocations (Courtesy: Prof. Sumitra Sen)

case of translocation was found in Oenothera. Tradescantia and Rhoeo also have translocations in heterozygous conditions.

Balanced Lethals and Balanced Heterozygosity:

When translocation involves more than two non-homologous pairs of chromosomes, meiotic rings containing six, eight or more chromosomes can be obtained. These events are not rare and are extensively seen in Oenothera.

Oenothera has the following characteristics:

(i) Some of its races produce new hereditary types at a frequency that is much higher than that commonly expected for mutation.

(ii) Many Oenothera races, such as O. lamarckiana, produce seeds that are about 50 percent lethal when ordinarily self- pollinated but fully viable when outbred to other races.

iii) All Oenothera races have seven pairs of chromosomes. The first meiotic meta- phase configuration ranges from seven individual bivalents through various combination of rings and bivalents to a single ring of 14 chromosomes.

In O. lamarckiana a ring of 12 chromo¬somes instead of a ring of 14 chromosomes is observed. Since alternate segregation is almost exclusively observed for these rings, duplications and deficiencies are generally absent and entire translocation complexes segregate as a unit in each gamete.

Each is also bearing the 1.2 chromosome of the segregating bivalent. Any other type of segregation in the heterozygote would produce unbalanced gametes. Thus each complex of six chromosomes is considered as a linkage group. These two were named as gaudens and velans by Renner.

O. lamarckiana does not produce either velans / velans or gaudens / gaudens, although both homozygotes are chromosomally balan-ced. Apparently, recessive lethals are main¬tained in

both the velans and gaudens com¬plexes, so that homozygous combinations are lethal. This lethality affects the zygotes, so that half the seeds do not germinate. The gametic or zygotic lethality leads to survival of only heterozygotes.

In gametic lethality, only one of the two types of gametes function on the male side, the other type being functional on the female side, thus giving rise to only one type of progeny, which is heterozygous. In zygotic lethality on the other hand, both types of gametes will function on male as well as on female side, but the homozygote progeny due to recessive lethal genes does not survive.

Similar to Oenothera, Rhoeo discolor is a structural heterozygote where there is a ring of 12 chromosomes in meiosis.

Other Forms of Chromosomal Aberrations:

Centric Fusion and Fission:

Centric fusion is a process that leads to a decrease in chromosome number. Two acrocentric chromosomes join together to produce a metacentric chromosome. This phenomenon is also called **Robertsonian translocation**.

Dissociation or fission is process that leads to an increase in chromosome number. In dissociation, a metacentric (commonly large) and a small supernumerary metacentric fragment become trans-located, so that two acrocentric or sub-metacentric chromosomes are produced.

Direct fission of centromere of metacentric chromosome leads to two telocentric chromosomes (misdivision). Fusion and fission are the main mechanisms by which the chromosome number can be decreased and increased during evolution of the majority of animals and in some groups of plants.

Iso-chromosomes:

A new type of chromosome may arise from a break (i.e., a misdivision) at the centromere. As shown in Fig, the two resultant telocentric chromosomes may open up to produce chromosomes with two identical arms (i.e., iso-chromosomes). This type of chromosome is produced in irradiated material. At meiosis they may pair with themselves or with a normal homologue.

Sister Chromatid Exchange:

A sister chromatid exchange is an interchange of DNA between sister chromatids in a chromosome, presumably involving DNA breakage followed by fusion. Sister chromatid exchanges are difficult to find using common cytological methods because the chromatids are morphologically identical.

Such chromatid exchanges were first described in studies in which 3H-thymidine was added during a replicating cycle which was followed by another cycle in a non-radioactive medium. Analysis of this phenomenon has been greatly facilitated by the use of bromodeoxyuridine (BrdU), a thymidine analogue that can be incorporated into the DNA of replicating cells instead of the original base.

If BrdU is followed by a fluorescent dye (Hoechst 33528), the fluorescence of the segments that contain BrdU is greatly diminished in comparison with those of the original base. Furthermore, there is also a similarly decreased staining with the Giemsa stain.

The use of this technique, however, has been unable to discover whether the chromatid exchange could occur spontaneously or whether it is induced by the BrdU.

It has, though, been of great help in differentiating the various inherited diseases characterized by chromosome fragility, which has an increased frequency of sister chromotid exchanges and a tendency to have associated neoplasia. Some of the diseases (e.g. Bloom's syndrome, Fanconi's anemia, and ataxia- telangiectasia) are presumably related to defects in DNA repair.

Sister chromatid exchange has also been important in studying the effect of mutagens on the chromosomes. Various mutagenic drugs that are alkylating agents, such as mitomycin C and nitrogen mustard, produce a great number of breaks and chromatid exchanges. The intimate association of sister chromatid exchange with mutagenesis and carcinogenesis may have important medical implications.

Effects of Chromosomal Aberration:

- In most cases, homozygosity for deficiencies or deletions has a deleterious effect and leads to death. Duplications may have more desirable effects than the loss of chromosome substances. Even in this category, there is a disturbance of chromosome balance and in instances of large duplications, a reduction in fertility as well as in vigour may occur.

- Translocation in Oenothera lamarckiana produces 50% non-viable seeds. The viable

seeds are all translocation heterozygotes (balanced lethal system). In Rhoeo discolor, the only translocation heterozygotes are survivors. In Clarkia, Paeonia, translocation and normal homozygotes are also common.

- Sometimes in Oenothera, Rhoeo, chromosomes disjoin in an irregular manner, new translocations are produced and crossing over between different complexes may take place. All these changes produce recognisable phenotypic effects.

- The occurrence of inversions is less recorded than translocations. In flowering plants with vegetative reproduction, for instance, in Tulipa, heterozygosity for inversions has, however, turned out to be frequent and in Paris quadrifolia, every plant seems to be heterozygous for one or several inversions (Muntzing).

- That, inversions are common in plants with vegetative reproduction is due to the fact that structural alterations arise and accumulate in them without particular disadvantages. Reproduction is not affected on account of structural aberrations. Since these plants in question reproduce exclusively or pre-dominantly in vegetative way, the aberrations affecting sexuality and seed setting are of no prime importance.

Detection of Chromosomal Aberrations:

- ❖ The alterations of chromosome structure can however be detected through comparative analysis of karyotypes. The gross chromosomal changes and their location can conveniently be studied through clarification of chromosomal details and their comparison with unaltered genotypes.

- ❖ The study of meiosis too provides with a powerful method of detection, provided the changes are adequate to bring out the detectable changes in meiotic behaviour.

- ❖ The study of detection includes formation of loops for the deficiency, inversion bridges for inverted segments as well as ring formation for structural heterozygotes. The formation of multivalent also clearly indicates the duplication of chromosomes. As such, meiotic analysis can provide clear indication of the changes the chromosomes have undergone affecting their structure.

- ❖ However, gradually a number of modified methods have come up through which finer segments of chromosome can be microscopically differentiated. These methods permit identification of minute chromosome segments which otherwise become difficult to resolve through karyotype or pachytene analysis or study of meiotic details.

❖ The two methods which are now widely applied for detection of chromosomal and genomic alterations are (1) chromosome banding and (2) In situ hybridization (ISH).

Type	Change in Chromosome Structure
Deficiency	Loss of a segment of chromosome.
1. Terminal deletion	Lost segment includes telomere.
2. Interstitial deletion	A segment between telomere and centromere is lost.
Duplication	A chromosome segment present in more than two copies in the same nucleus.
1. Tandem duplication	The additional chromosome segment located just after the normal segment, gene sequence being the same.
2. Reverse tandem duplication	Same as above but the gene sequence of the additional segment is inverted.
3. Displaced duplication	The additional segment located in the same chromosome but away from the normal segment.
4. Transposed duplication	The additional segment located in a nonhomologous chromosome.
Inversion	A chromosome segment contains genes in a sequence which is reverse of the normal.
1. Paracentric inversion	The inverted segment does not contain centromere.
2. Pericentric inversion	The inverted segment contains centromere.
Translocation	Chromosome segment integrated into nonhomologous chromosomes.
1. Simple translocation	A segment of a chromosome integrated into a nonhomologus chromosome.
2. Reciprocal translocation	A segment of chromosome integrated into a nonhomologous chromosome from which a segment is integrated into the first one.