Course Name- Human Cytogenetics

Paper code: (MZO-508)

Unit 3: Chromosomal Abnormalities

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Chromosomal Abnormalities

- The most common type of chromosomal abnormality is knows as anupioid , an abnormal chromosome number due to an extra or missing chromosome. Most people with aneuploidy have trisomy (three copies of a chromosome) instead of monosomy (single copy of a chromosome).
- Chromosome anomalies usually occur when there is error in cell division – meiosis or mitosis.
- There are many types of chromosome abnormalities. They can be organized into two basic groups, numerical and structural abnormities.

Abnormal Human karyotypes

- The normal chromosome number or man is 46, but various types of chromosomal abnormalities either in their number or morphology have been observed.
- These chromosomal abnormalities are expressed in defective phenotype, i.e., various defects occur in the morphology and physiology of organism all of which cause different symptoms of a particular disease and called a syndrome.
- The chromosomal abnormalities following heading:

A. Autosomal abnormalities:

a) Numerical autosomal aberrations: The man following kinds of autosomal numerical variations have been observed:

1. **Polyploidy in man:** In man some type of polyploidy are commonly encountered. A severely defective male child was found to be a triploid with total of 69 chromosome(66 autosomes+ two X-chromosomes+ one Y chromosome). Further, an extensive survey of human cytogenetics have revealed the fact that most human individuals are mosaics, have both diploid and triploid cells in skin and tetraploid cells in liver
2. **Aneuploidy in man:** In man several kinds of autosomal aneuploidies have been reported. Certain commonly known trisomic and monosomic aneuploidies of man are following:

(i) Down's syndrome (21-Trisomy):

- One of the most familiar human aneuploidy is trisomy 21.

- Removes the nuances of associating mental retardation with any particular group of people.
- Originally studied by Langdon Down in 1866, it has been termed monogoloid idiocy or mongolism because of certain facial characteristics that suggested resemblance to oriental features. The condition is now referred to as Down's syndrome which diplomatically removes the nuances of associating mental retardation with any particular group of people.
- Down's syndrome is a congenital syndrome, usually recognizable at birth by an experienced physician, and one that is associated with multiple malformations (characteristic facial features, palmprint abnormalities, etc.; severe mental retardation and markedly defective development of the central nervous system.

- The face of such a patient has a special moon-like aspect, with oblique palpebral fissures increased, separation between the eyes and a skin fold at inner part of the eyes.
- The nose is flattened, the ear are malformed, the mouth is constantly open and the tongue protrudes.
- The heart, hands and feet too remain defective in a mongoloid.

ii) Trisomy-18:

- The patient child in which trisomy occurs in chromosome 18 remains small and weak.
- The head of such a patient is laterally flattened and the helix of the ear scarcely developed.
- The hands are short and show little development of the second phalanx; the digital imprints are rather simple. These children are very retarded mentally and usually die before one year of age.

iii) Trisomy-13:

- The patients having a trisomy of the 13- characterized by multiple and severe body malformations as well as profound mental deficiency.
- The head is small and the eyes are often small, or absent. Harelip, cleft palate and malformations of the brain are frequent.
- The internal organs are severely malformed, and in most cases death occurs soon after birth.
- Meiotic non-disjunction is thought to be the cause of this chromosomal aberration.

(iv) Monosomy-21 :

- When one chromosome of the pair of chromosome 21 become completely deleted monosomy-21 occurs and it remains lethal to the patient. But when large part of one 21 chromosome is lacking, children exhibit morphological characteristics, just opposite to mongolism or Down's syndrome.
- In 21- monosomics the nose remains prominent, the distance between eyes is shorter then normal, the ears are large and the muscles are contracted.

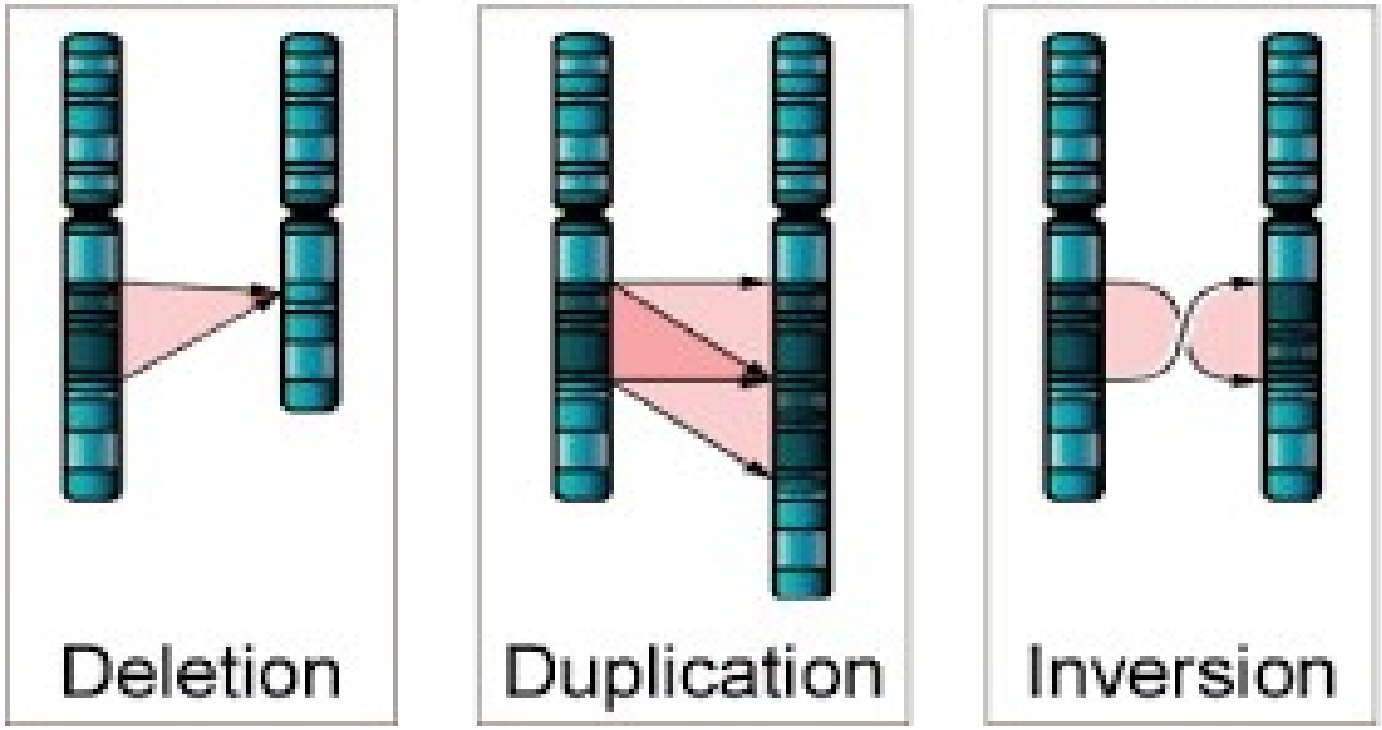
(v) Monosomy-18:

- This is the opposite syndrome in which a partial deletion of one chromosome of the pair occurs.(Grouchy et al.,1966).
- The ears are voluminous, the fingers long and the digital imprints are complex and convoluted.

b) Structural autosomal aberrations: Cases carrying all kinds of structural aberrations have been reported in man. Translocations of several types, deletion, duplications, ring chromosomes, inversions and isochromosomes have frequently been associated with congenital diseases. These chromosomal abnormalities appear sporadically in the general population, and they usually lead to characteristic phenotypic change.

- **Deletions:** A portion of the chromosome is missing or deleted
- **Duplications:** A portion of the chromosome is duplicated, resulting in extra genetic material.
- **Translocations:** A portion of one chromosome is transferred to another chromosome.

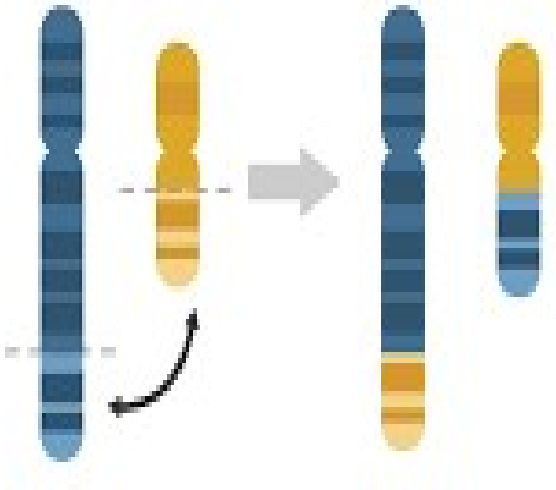
Large Chromosomal Changes



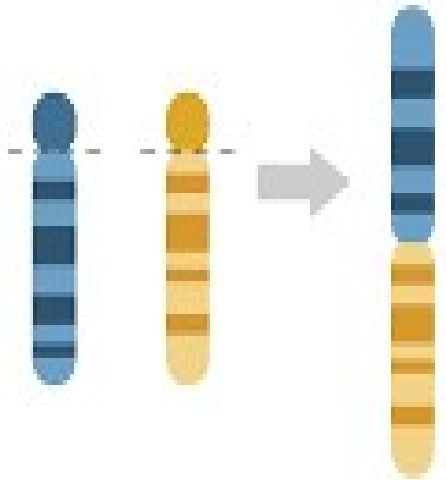
There are two main types of translocations.

- **Reciprocal translocation:** segments from different chromosomes have been exchanged.
- **Rebertsonian translocation:** An entire chromosome has attached to another at the centromere-In human these only occur with chromosomes 13,14,15,21 and 22.
- **Inversion:** A portion of the chromosome has broken off, turned upside down, and reattached, therefore the genetic material is inverted.
- **Insertions:** A portion of a one chromosome has been deleted from its normal place and inserted into another chromosome.
- **Rings:** A portion of a chromosome has broken off and formed a circle or ring. This can happen with or without loss of genetic material.

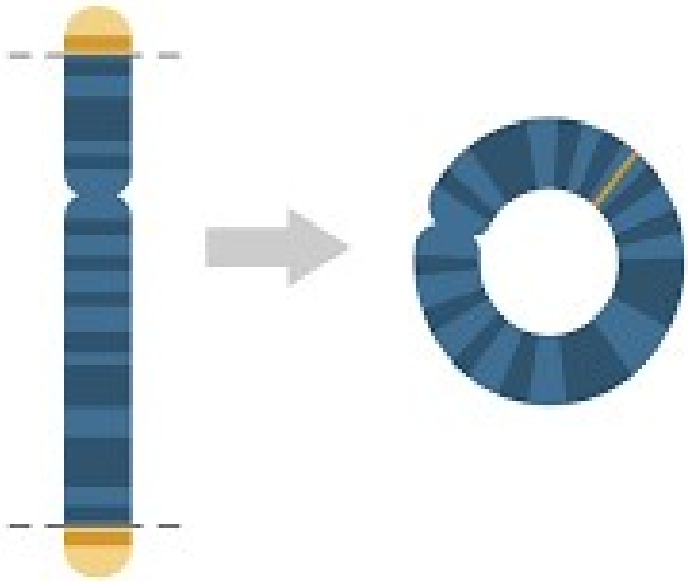
Reciprocal translocation



Robertsonian translocation



Ring chromosome



- Isochromosome: Formed by the mirror image copy of a chromosome segment including the centromere.

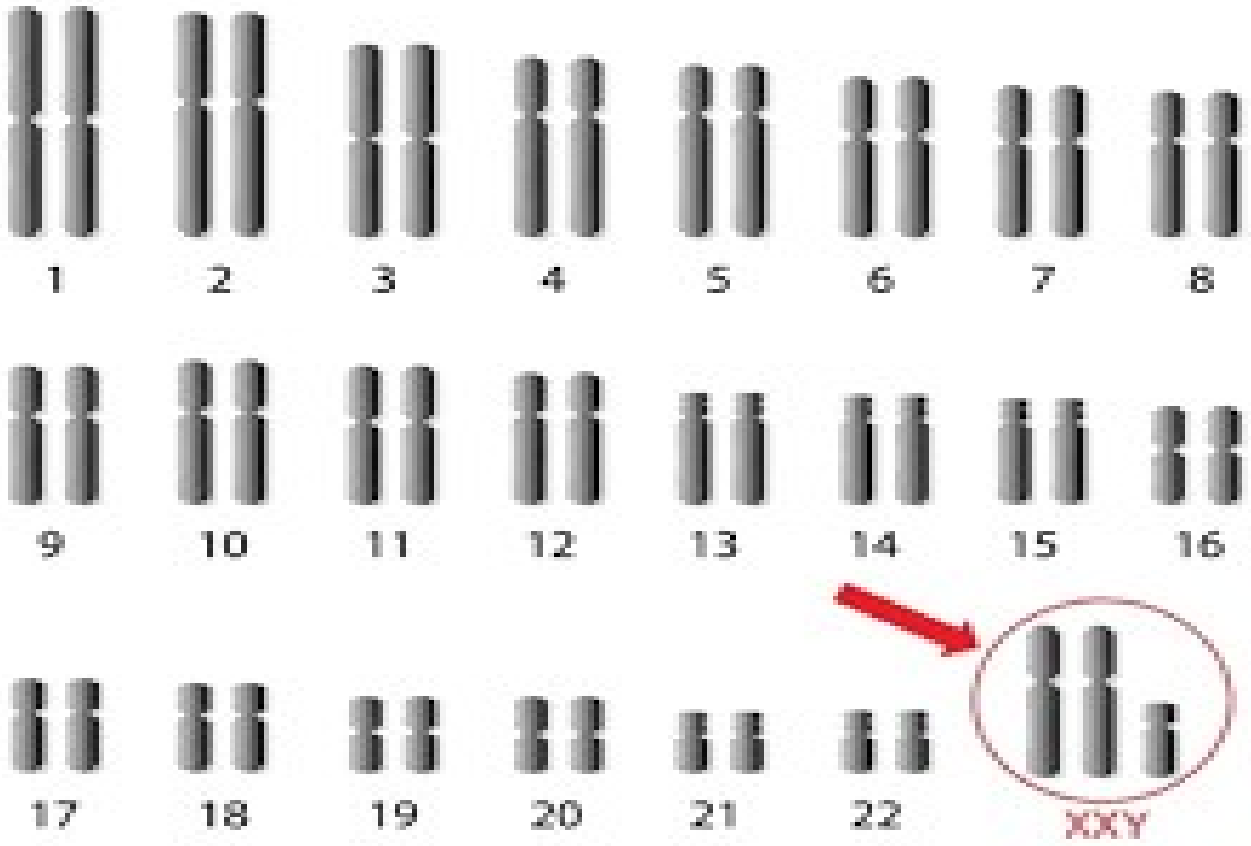
B. Sex- chromosomal Abnormalities :

In man different kinds of sex chromosomal numerical aberrations have been detected. Most of them are caused either by mitotic non-disjunctions or meiotic non-disjunctions .

They are expressed phenotypically in the following different kinds of syndromes.

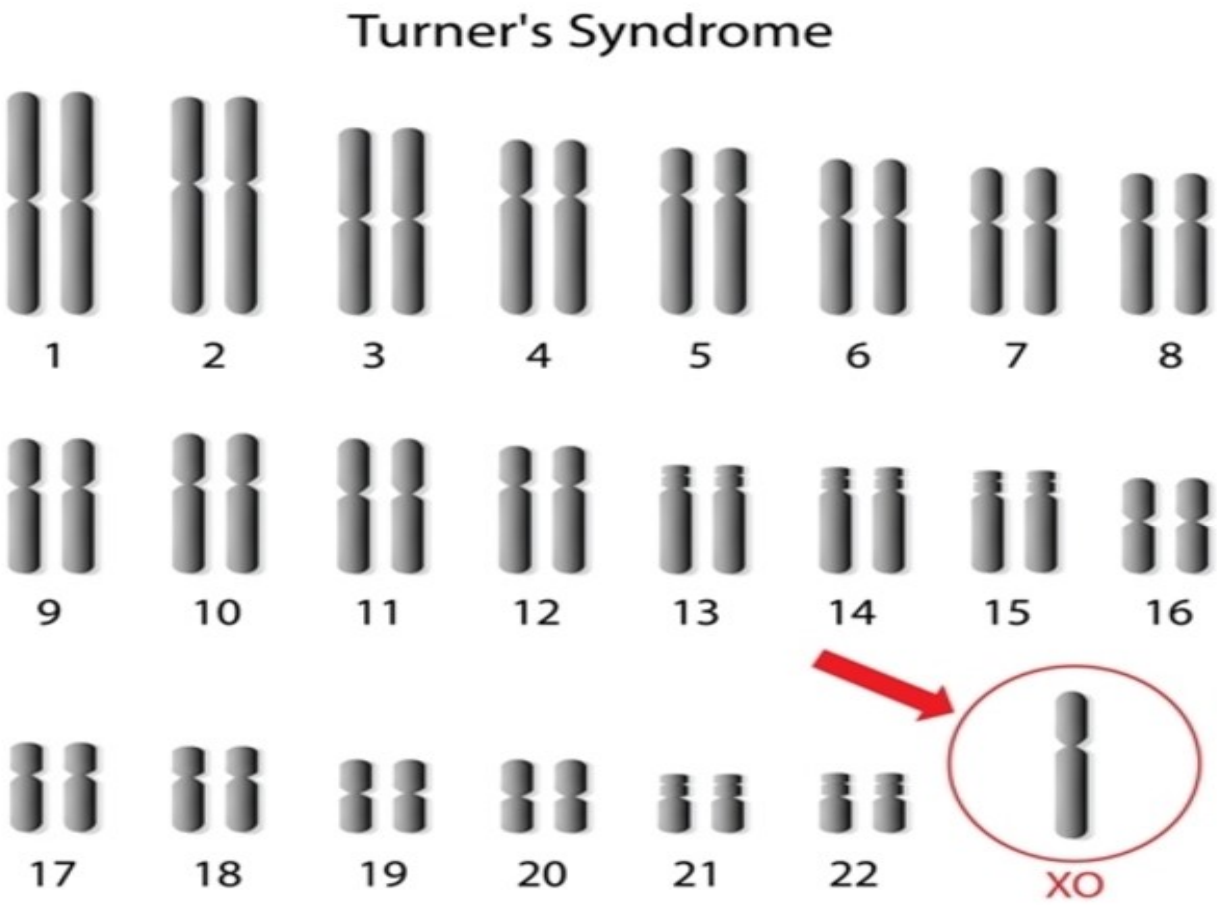
- **(i) Klinefelter syndrome:** Persons with klinefelter syndromes or somniferous tubule dysgenesis have been found to contain a positive sex chromatin and 47 chromosome: 44 autosomes, two X-chromosomes and Y-chromosome (44autosomea+XXY). The patients with klinefelter syndrome.

Klinefelter Syndrome



(ii) Turner's syndrome:

- The persons with the karyotype of 45 chromosomes (44 autosomes and one X-chromosomes) have the symptom of disease called female gonadal dysgenesis Turner's syndrome. Such persons have female phenotype, but with rudimentary gonads and without menstruation cycle during puberty.
- Further, a patient of Turner's syndrome is characterized by short stature, congenital malformation, shield chest, pronounced webbing of the neck, short fourth metacarpel, hypoblastic nails (nails are small, narrow and deep set in nail pit or square with increased lateral curvature), recessive X-linked condition s such as colour blindness and diabetes and usually impaired intelligence.


Turner's Syndrome
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