# VARIATION IN CHROMOSOME NUMBER

## Objective and Aim

- To observe the nature and consequences of the variation in chromosome numbers in humans and other organisms

- Each species has a characteristic number of chromosomes. Most higher organisms are diploid, with two sets of homologous chromosomes: one set donated by the mother, and the other set by the father.
- Variation in the number of sets of chromosomes (**ploidy**) is commonly encountered in nature.

- It is estimated that one-third of the angiosperms (flowering plants) have more than two sets of chromosomes (**polyploidy**).

- Variation in chromosome number ranges from the addition or loss of one or more chromosomes to the addition or loss of one or more haploid set of chromosomes.

- When an organism gains or loses one or more chromosomes, **but not a complete set**, the condition of **aneuploidy** (uneven) is created.
- **Euploidy** (even) is a condition where one or more complete haploid sets of chromosomes are found or lost.

# Euploidy

- **Monoploid**:- Have only one set of chromosomes (n) and is characteristically found in the nuclei of some lower organisms such as fungi.
- Monoploids in higher organisms are usually smaller and less vigorous (viable) than the normal diploids. Few monoploid animals survive. Monoploid plants are known but are usually sterile.

- **Triploid**:- Three sets of chromosomes (3n) can originate by the union of a monoploid gamete (n) with a diploid gamete (2n).
- The extra set of chromosomes of a triploid is distributed in various combinations to the germ cells.
- This will result in genetically unbalanced gametes.
- Triploids are sterile, therefore not commonly found in natural populations.

- **Tetraploids**:- Four sets of chromosomes (4n) can arise in body cells by the somatic doubling of the chromosome number.
- Doubling is accomplished either spontaneously or it can be induced in high frequency by exposure to chemicals such as colchicines.
- They are also produced by the union of unreduced diploid (2n) gametes.

## Extra Reading

- Read and make notes on the following:
  (i) autotetraploid
  (ii) allotetraploid
  (iii) polyploid

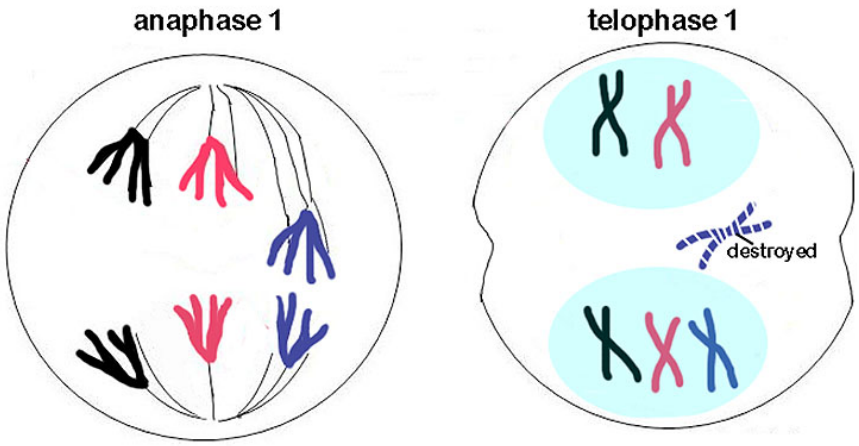
# Aneuploidy

- Variations in chromosome number may occur which do not involve whole sets of chromosomes, but only parts of a set.
- The term aneuploidy is given to variations of this nature.
- The suffix *"-somic"* is part of their nomenclature. It refers to a particular organism and its chromosome number.

- The most common examples of aneuploidy, where an organism has a chromosome number other than an exact multiple of the haploid set, are cases in which only part of a set, is either added to or lost from a normal diploid set.
- Aneuploidy can arise when there is primary or secondary nondisjunction.

- In man, aneuploidy will arise from failure of paired chromosomes or sister chromatids to disjoin at anaphase.
- It can also arise due to delayed movement of a chromosome at anaphase so that it is trapped or captured in one cell instead of the other. This is called **anaphase lag.**

## Anaphase lag

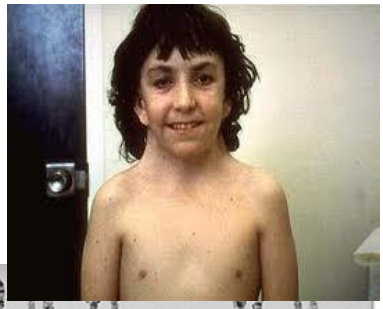


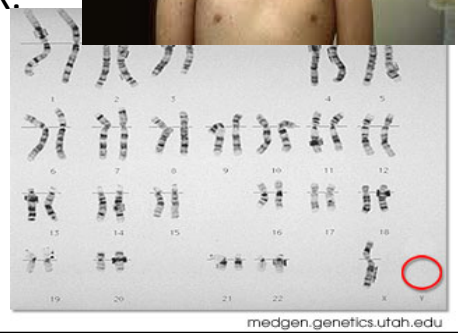
# Monosomy

- Monosomics: Diploid organisms which are missing one chromosome of a single pair are monosomics.
- Their genomic formula is 2n – 1.
- The single chromosome without a pairing partner may go to either pole during meiosis, but more frequently will lag at anaphase and will fail to be included in either nucleus.

# Monosomy

- Turner Syndrome (45 X).
- A female has only one X chromosome instead XX.





## Monosomy

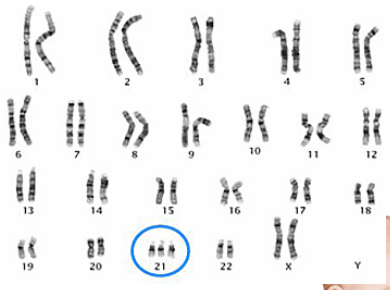
- Monosomics can form two kinds of gametes, i.e. (n) and (n – 1).
- In animals, loss of one whole chromosome often results in genetic imbalance which is manifested by high mortality or reduced fertility.

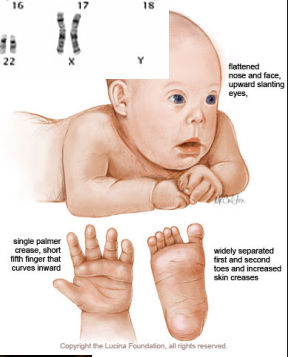
## Trisomy

- **Trisomic**:- Diploids which have one extra chromosome are trisomics.
- They are represented by chromosomal formula 2n + 1
- They can thus form gametes of (n + 1) and (n)

# Trisomy 21

- Also called Down syndrome or "mongolism"
- Easily recognized phenotype
  - Short stature
  - Eyelid fold
  - Flat face
  - Stubby fingers etc.
- Genes responsible for characteristics of syndrome located on bottom third of chromosome 21





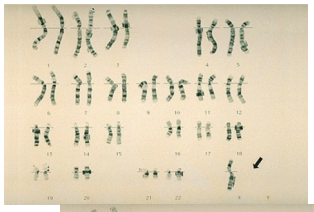

# Nullisomy

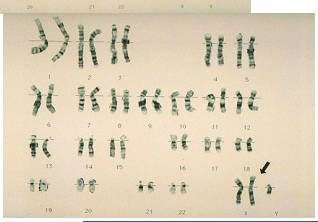
- **Nullisomic**:- An organism which has lost a chromosome pair is a nullisomic.
- The result is usually lethal to diploids.
- It has a formula: 2n – 2
- Some polyploids, however, can lose two homologues of a set and still survive.

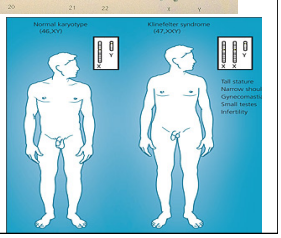
- Example: several nullisomics of hexaploid wheat (6n – 2) exhibit reduced vigour and fertility but can survive to maturity because of genetic redundancy in polyploids.

## Changes in Sex Chromosome Number

- Turner Syndrome (XO)
- Klinefelter Syndrome (XXY)
- Poly-X Females (XXX)
- Jacobs Syndrome (XYY)







## VIABILITY IN HUMAN ANEUPLOID CONDITIONS

- The reduced viability of individuals with recognized monosomic and trisomic conditions leads us to believe that many other aneuploid conditions may arise but, the affected fetuses do not survive to term.

- The above observation has been confirmed by karyotypic analysis of spontaneous aborted fetuses.
- About 65% of spontaneous abortuses demonstrating chromosomal abnormalities are aneuploids.

- The highest incidence of aneuploid condition among abortuses is the 45X, which produces an infant with Turner Syndrome if the fetus survives to term.

## CHROMOSOMAL ABERRATIONS (MUTATION)

- Different cells of the same organism and different individuals of the same species have as a rule, the same number of chromosomes.
  - Except that, gametic cells have only half as many chromosomes as somatic cells.
- Homologous chromosomes are also uniform in the number and order of genes they carry.

- The chromosomes of an organism may evolve by changes not only in their **number and size, but also in their organization:**
  - i.e. segments or parts may change their location within a chromosome or move from one chromosome to another.

- These changes, in terms of number, size, and organization of chromosomes are known as chromosomal ***aberrations, mutations***, or ***abnormalities***.

# CLASSIFICATION OF CHROMOSOMAL CHANGES

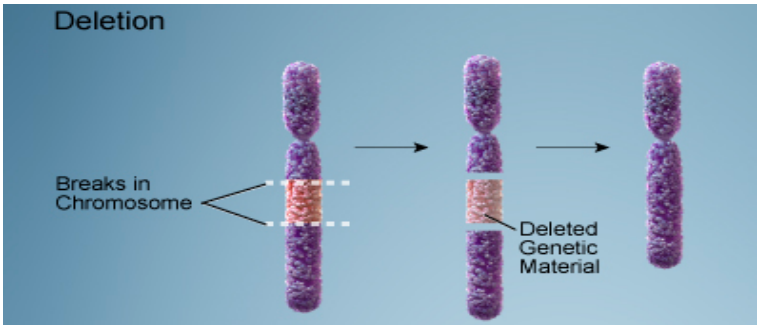
- Chromosomal aberrations can be subdivided as follows:
  - **Changes in the structure of chromosomes (Structural aberration).**
  - **Changes in number of chromosomes (Numerical aberration).**

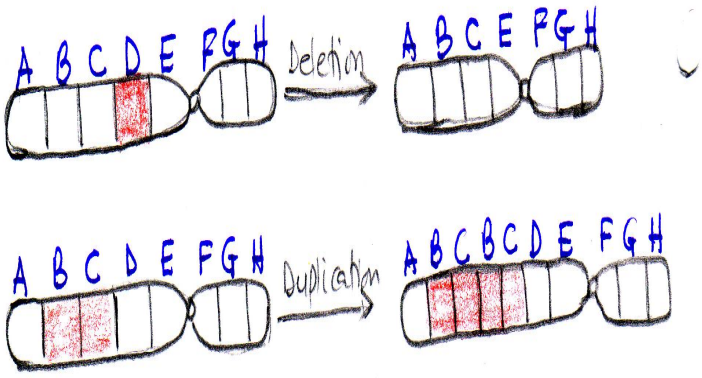
# Structural aberrations

- Changes in the **number of genes** in chromosomes (deletion and duplications).
- Changes in the **location of genes** on the chromosomes (inversions and translocation).

# Deletions or Deficiency:

- It is the loss of a chromosomal segment.
- They are usually lethal in homozygous conditions.
- However, very small deletions that are not lethal in the homozygous condition have been detected in corn, *Drosophila* and other organisms.

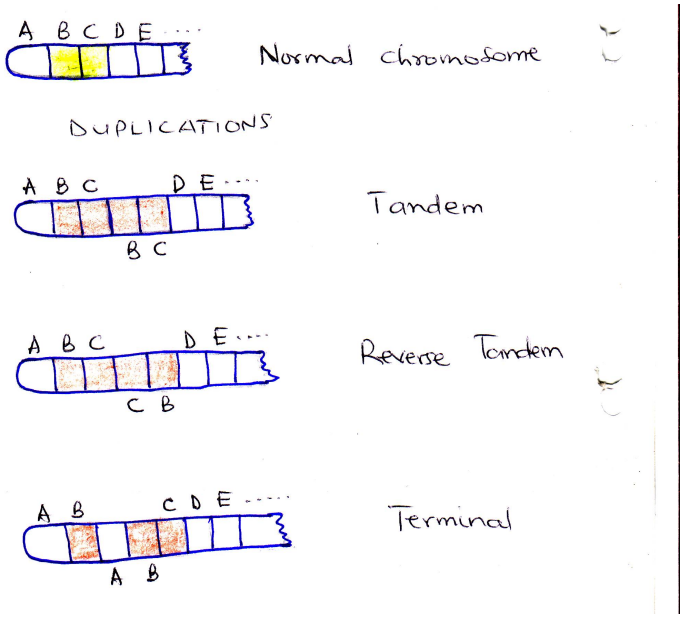


- In humans, the *cri-du-cat* (cry of the cat) syndrome is associated with the heterozygous deficiency in the short arm of chromosome 5.
- The syndrome is characterized by severe growth abnormalities, and mental retardation.
- Death usually occurs in infancy or early childhood.

## Duplication or Repeat:

- The presence of a chromosome segment more than once in the same chromosome or in a nonhomologous chromosome is known as a duplication or a repeat.
- Duplicated segments often occur in tandem, i.e. adjacent to each other.




- A *reverse tandem* duplication occurs when the order of genes in the duplicated segment is opposite.
- When the duplicated segment is at the end of the chromosome, the duplication is called *terminal*.

- Duplications are sometimes detected because individuals that are expected to be homozygous for a recessive allele fail to manifest the recessive phenotype, owing to the presence of a dominant allele in the duplicated segment.

- Many duplications and deletions arise from chromosome breakage through mechanisms such as;

  (i) radiation

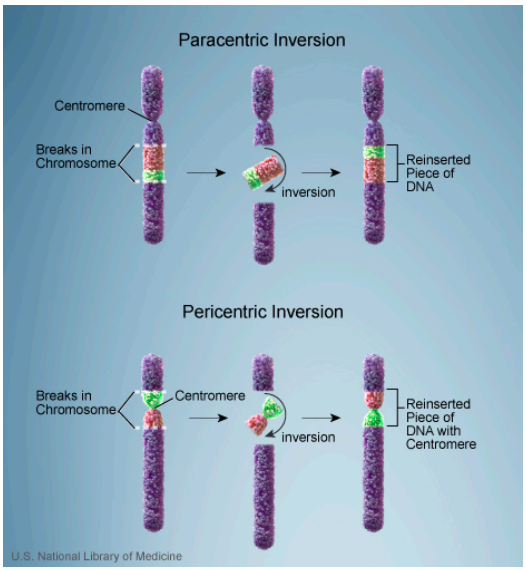
  (ii) chemicals and

  (iii) viruses

  They may also arise by unequal crossing over.

# Inversions

- They are 180$^{o}$ reversals of chromosomal segments.
- They do not change either the number of chromosomes or the number of genes in the chromosomes.



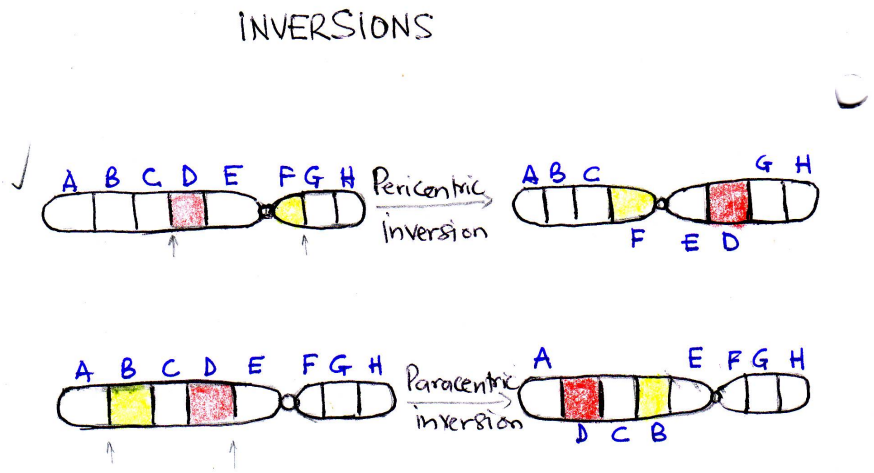

- Example: if the gene sequence of a chromosome is represented as

  **ABCDEFGH**,

  inversion of the segment **BCD** will result in a chromosome with the sequence

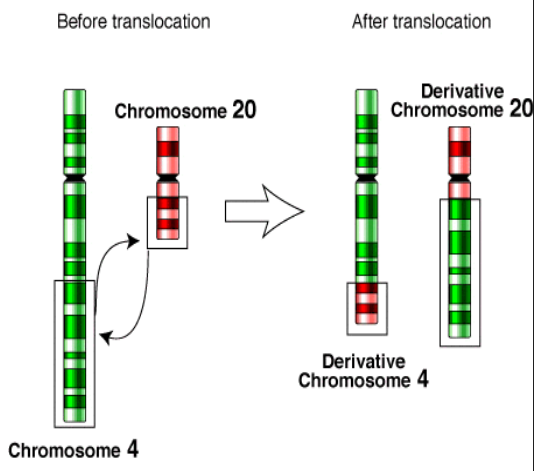
  **ADCBEFGH**

- ***Pericentric*** inversions include the centromere in the inverted segment whereas ***Paracentric*** inversions do not.



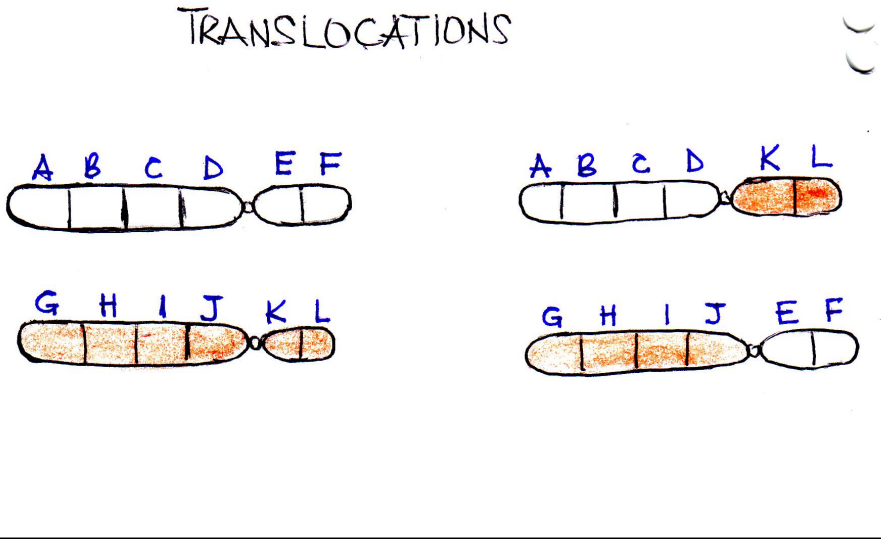
# Translocations:

- Reciprocal translocations involve the interchange of block of genes between two nonhomologous chromosomes.
- Assuming the gene sequences in two non-homologous chromosomes are represented as




**ABCDEF** and **GHIJKL,**

the sequences **ABCDKL** and **GHIJEF** will represent the translocated chromosome.




- In the above example, the **KL** genes are now linked to **ABCD** after the translocation, and no longer linked to **GHIJ**.

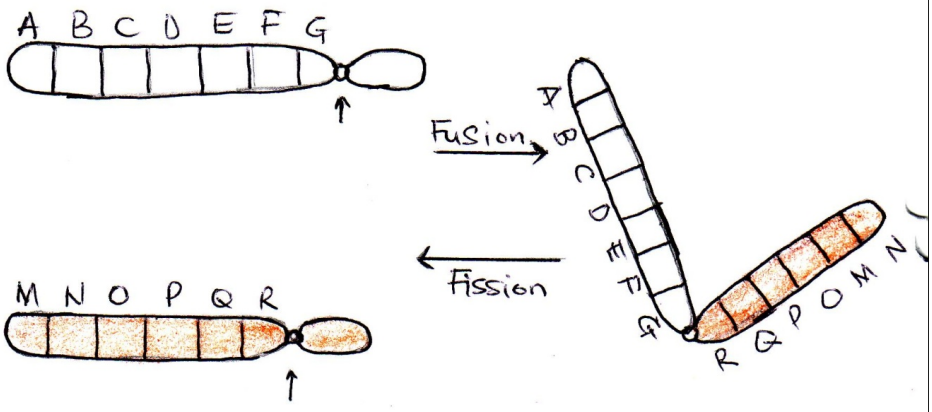
## Numerical aberration

- Chromosomes occasionally undergo spontaneous rupture, or can be induced to rupture in high frequency by ionizing radiation.
- The broken ends of such chromosomes may rejoin into nonhomologous combinations.

## Centric Fusions and Fissions

- Are sometimes called Robertsonian changes.
- ***Centric fusions*** result when two non-homologous chromosomes join at the centromere to become one single metacentric chromosome.
- ***Centric fissions*** or ***dissociations*** are the reciprocal of fusions.
- One metacentric chromosome splits into two telocentric chromosomes.

# Centric Fusions and Fissions




# Human Chromosomal Abnormalities

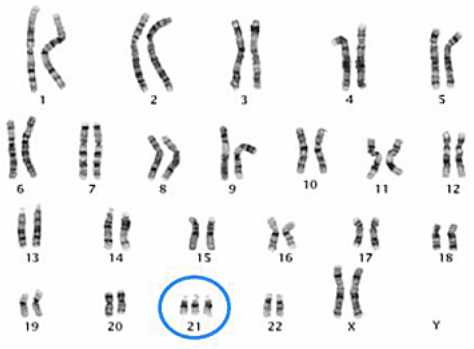
**Down syndrome (47, +21)**

- Most cases of the syndrome are due to the presence of 47 chromosomes, with chromosome 21 being represented three times rather than twice as a result of non-disjunction at the first meiotic division.

- It is the best known and most common chromosome-related disease syndrome.

# Down Syndrome

- It is also known as **trisomy 21 or "*mongolism*"**.
- The overall incidence is 1 in 700 live births among Europeans.




- The incidence of the syndrome increases with the mother's age.
- It must be noted that, most, and perhaps all cases of trisomy in humans can be explained by nondisjunction at meiosis.

## Clinical Features:

- Patients are short in stature, and had an epicanthal fold (mongolism).
- Have wide nostrils, large tongues with distinctive furrowing, and stubby hands.
- They are characterized as low in mentality, but they can be trained in routine mechanical skills.

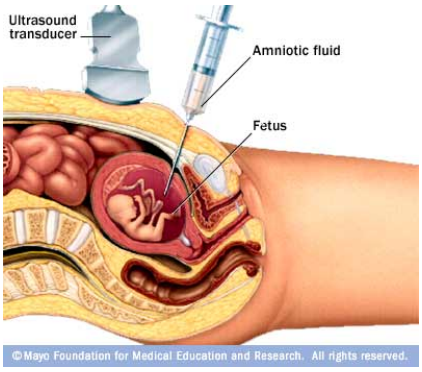
- They usually have IQ less than 50.
- In rare cases, Klinefelter syndrome co-exist.
- Affected persons rarely reproduce.
- The males are infertile.

## ***Amniocentesis for detecting Aneuploidy***:

- A fetus may be checked in early changes of development by karyotyping the cultured cells obtained by a process called ***amniocentesis.***

## Process of amniocentesis:

- A sample of fluid is drawn with a needle from the amniotic sac.
- After culturing the fetal cells for about three weeks, chromosomes in dividing cells can be stained and observed.
- If three number 21 chromosomes are present, then, Down syndrome is confirmed.



# Patau Syndrome (47, +13)

- It arises as a result of parental nondisjunction at the first and second meiotic division.
- It occurs in about 1 in 20,000 newborns.
- The syndrome is rare in children and non-existent in adults.
- The symptoms are very severe and results in early death.

- 50% of affected individuals will die within a month and only 10% will survive the first year.
- It is also called trisomy 13 and is due to trisomy for chromosome 13.

## Clinical Features

- Symptoms include small brain, apparent mental deficiency, deafness, cleft lip, polydactyly, heart defects, and numerous other internal and external abnormalities.

## Edward syndrome (47, +18)

- Like Patau syndrome, Edward syndrome is due to autosomal aneuploidy.
- It is due to trisomy for chromosome 18.
- The incidence of the syndrome is 1 in about 10,000.
- Most infants with this syndrome die at an early stage.

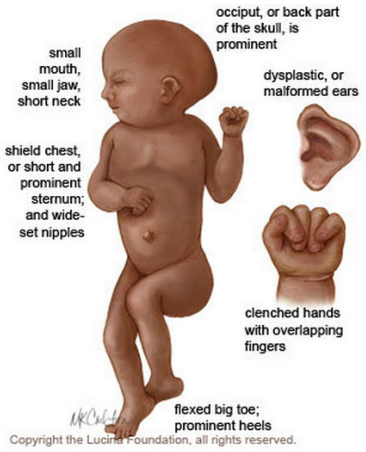
- Most affected individuals are females, with 80 to 90 % mortality by two years of age.
- However, a few affected individuals have been reported to be alive in their teens.
- 95% of all Edward cases are aborted spontaneously.

- It arises as a result of parental nondisjunction at the first and second meiotic division.

# Diagnostic Features

Affected individuals have:

- Low birth rate.
- Mental deficiency.
- Malformed ears, receding mandible, small mouth and nose.
- They also show profound developmental delay.




# Aneuploidy for human sex chromosomes

- Like nondisjunction of autosomes, nondisjunction of sex chromosomes also occurs during meiosis.
- This is however, less deleterious than aneuploidy for autosomes.
- A variety of conditions with abnormal complements of sex chromosomes have been identified in humans.

- Three comparatively common conditions are **XO** females, **XXY** males, and **XYY** males.

## Turner syndrome (45,X)

- It is due to the presence of one X and no Y chromosome. (XO females)
- It is the only known viable type of monosomy known in humans
- Occurrence is about 1 in 10,000 live female births.

- XO females can result from nondisjunction in male or female parents.
- An X-carrying sperm can fertilize an ovum with no X **or** an ovum with an X can be fertilized by a sperm lacking a sex chromosome.
- In 75% of all cases, the maternal X chromosome is present.
- More than 90% abort spontaneously.

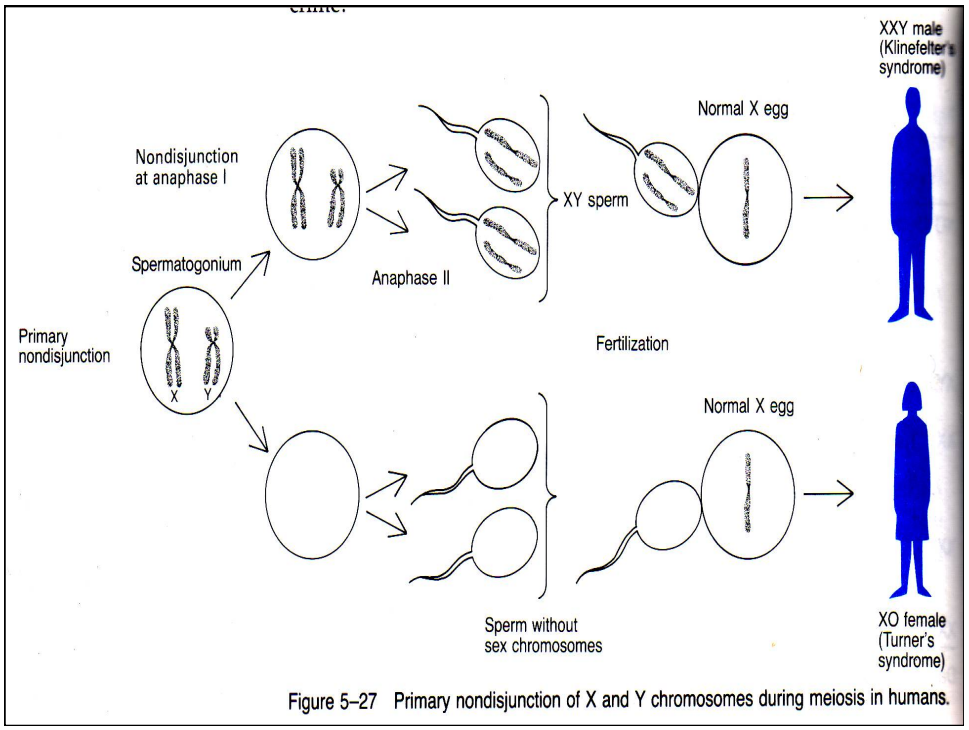



Figure 5–27 Primary nondisjunction of X and Y chromosomes during meiosis in humans.

## Clinical Features:

- Affected females have normal life expectancy, and on the average, reduced intelligence.
- They are sterile, having no or only rudimentary ovaries.
- There is limited development of the secondary sexual characteristics.

- They are somewhat shorter than average.
- Have a webbed or broad neck.
- Have a shield-like or broad chest.

## Klinefelter Syndrome (47,XXY)

- It is due to the presence of two X chromosomes and a single Y chromosome in addition to 44 autosomes (XXY males).
- Other karyotypes like XXXY, XXXXY etc. are also associated with the syndrome.
- Affected individuals are born at a frequency of 0.13%.

- XXY males can result from the nondisjunction in the male or female parent.
- Nondisjunction during the first meiotic division produces sperm containing an X and a Y chromosome.
- If an XY-carrying sperm fertilizes a normal X-carrying ovum, an XXY zygote will result.

- Nondisjunction can also occur in the female to produce an XX-carrying ovum. If that ovum is fertilized by a normal Y-carrying sperm, an XXY zygote will result.

## Clinical Features:

- Individuals with the syndrome have genitalia and internal ducts that are male, but they are sterile.
- Have normal life expectancy, and on the average, reduced intelligence.
- Although masculine development occurs, feminine sexual development is not entirely suppressed (enlarged breast).
- About 25% of XXY males are mildly mentally retarded.

# XYY males

- It can be produced by the nondisjunction of the Y chromatids during the second meiotic division.
- Males with an XYY constitution are born at a frequency of about 0.15%.
- Clinically, XYY males are taller than average, they become sexually mature at an early age, and are completely fertile.

- There is a controversy about behavioral abnormalities among XYY males.
- There has been a suggestion that XYY males are predisposed towards violent crimes.

# Review Questions

Q.1: In addition to XO and XXY karyotypes, XXXX chromosome complements are present at a very low frequency in humans. Diagram possible ways that an XXXX zygote could be produced.

Q.2: Discuss the genetic effects of the equational division with and without prior crossing-over between homologous chromosomes.