Unit: 7 Genetics and Evolution

Chapter: 5 Principles of Inheritance and Variation

Module: 9 Chromosomal Disorders in Human

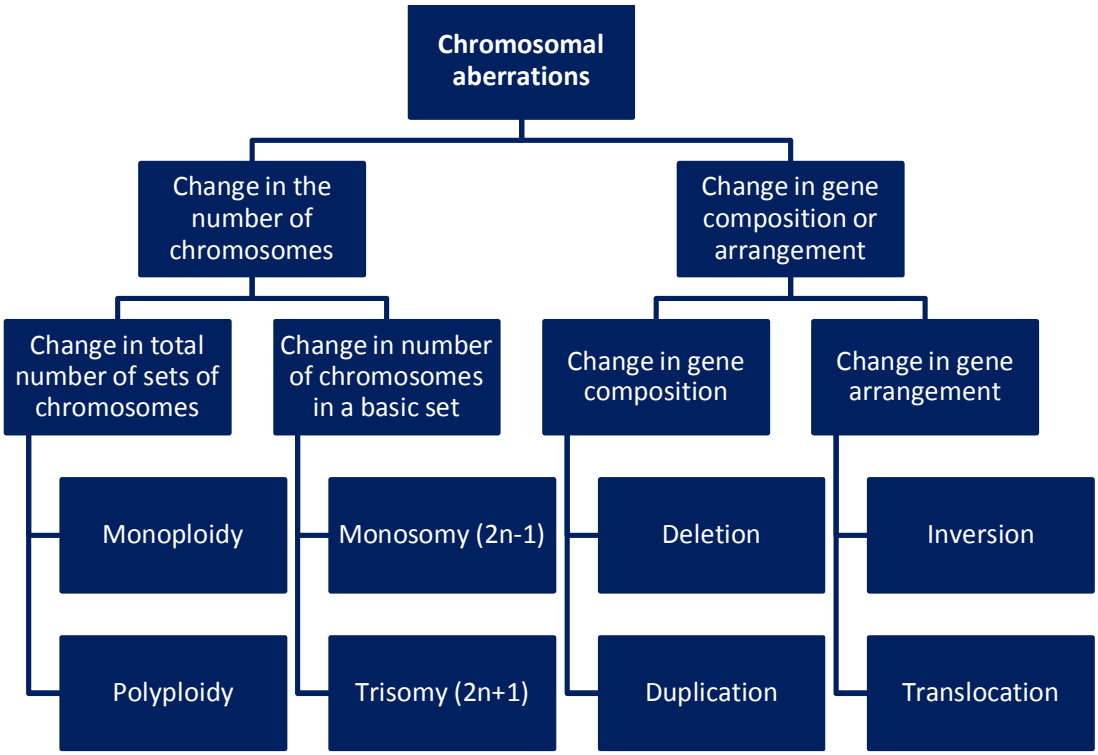
Objectives: This module aim to give an idea about various human genetic disorders arise due change in the chromosome number

Learning points: After going through this module the learner will understand:

- Different types of chromosomal aberrations
- Types of aneuploidy in human
- Down syndrome
- Klinefelter syndrome
- Turner syndrome

Introduction:

Chromosomal aberrations: Diploid organisms normally contain two haploid sets of chromosomes. Sometime they deviate from this. Change in the total number of chromosomes, the deletion or duplication of genes or rearrangements of the genes either within or among chromosomes are the variation from the normal pattern seen in the organisms.



Change in the number of chromosome

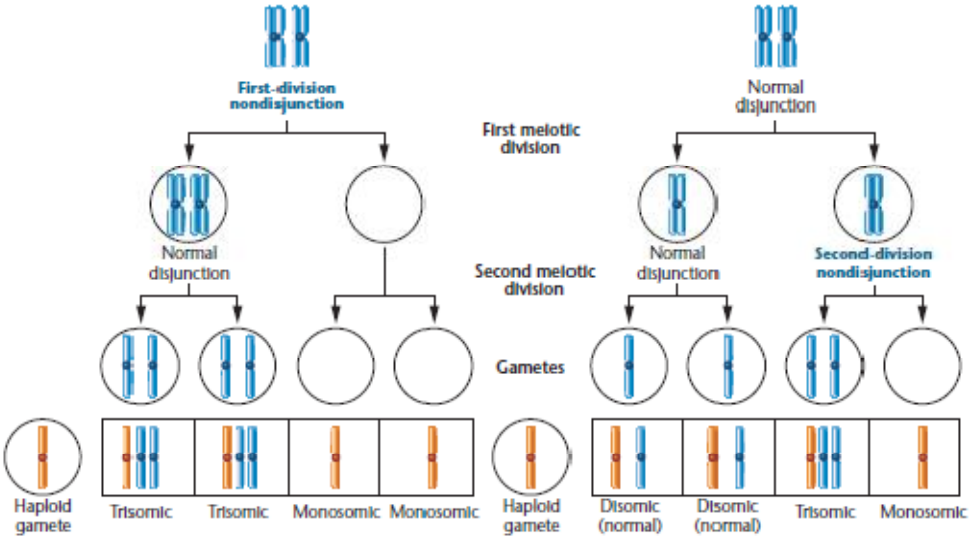
Euploidy: Change in the number of basic sets of chromosomes.

- **Monoploidy**: Presence of only one set of chromosomes.
- **Polyploidy**: Presence of more than two sets of chromosomes.

Aneuploidy: Change in the number of chromosome in one set.

- **Trisomy**: Addition of extra chromosome in a set (2n+1).
- **Monosomy**: Deletion of a chromosome in a set (2n-1).

Nondisjunction: Failure of separation of paired homologs chromosome during anaphase I, or sister chromatids during anaphase II. This process disrupts the normal distribution of chromosomes into gametes and leads to formation of gametes with the n+1 and n-1 chromosome composition.



To be redrawn

Change in composition and arrangement of genes in chromosome.

Deficiency or Deletion: Loss of single genes or a segment of chromosome from the genome.

Addition or Duplication: Presence of single gene or a segment of chromosome more than once in the genome.

Inversion: A segment of a chromosome is turned around 180 degrees within a chromosome. Inversion does not involve loss or gain of genetic information but rearranges the gene sequence in a chromosome.

Translocation: Translocation involves the exchange of segments between two nonhomologous chromosomes. As a result there is movement of a chromosomal segment to a new location in the genome.

Human aneuploidy

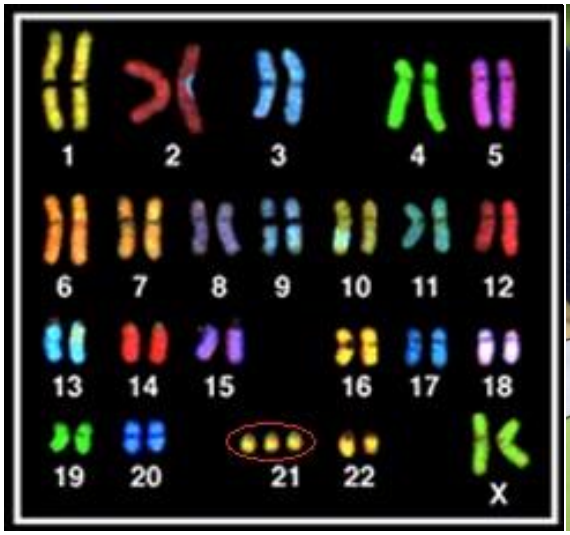
In normal human being 23 pairs of chromosomes are present. The chromosomes differ in their size, shape and staining properties. The chromosomes are arranged based on their size and shape. This is called karyotype. The normal human karyotype contains 22 pair of autosomes and one pair of sex chromosome. The sex chromosome of female and male are XX and XY respectively. The genetic disorder due to aneuploidy can be detected by karyotype analysis.

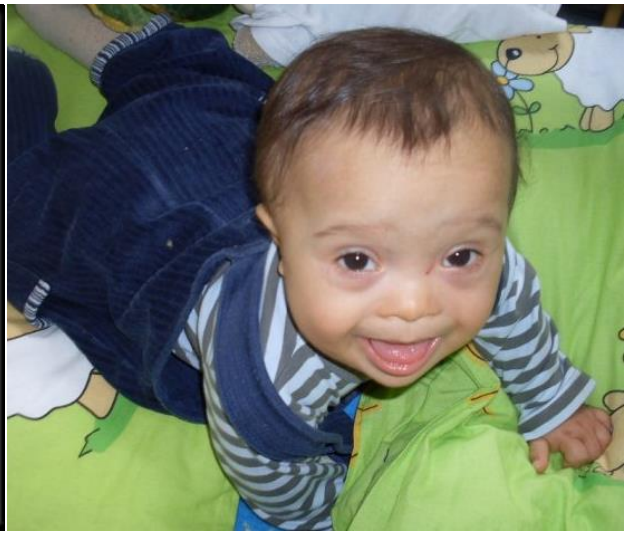
- **Autosomal aneuploidy**
  - Down Syndrome (47, 21+); Trisomy of 21 chromosome
  - Edwards Syndrome (47, 18+); Trisomy of 18 chromosome
  - Patau Syndrome (47, 13+); Trisomy of 13 chromosome

- **Sex chromosomal aneuploidy**
  - Klinefelter syndrome (47, XXY); Trisomy of X chromosome in human male
  - Turner syndrome (45, XO); Monosomy of X chromosome in human female
  - Super male (47, XYY); Trisomy of Y chromosome in human male

Down syndrome (47, 21+)

Down syndrome was first described by Langdon Down (1866).
Trisomy of 21 chromosome (presence of an additional copy of chromosome number 21).
The most common autosomal aneuploidy in humans.
Most children with Down syndrome are born to normal parents.
The incidence of Down's syndrome increases among children born to older mothers.



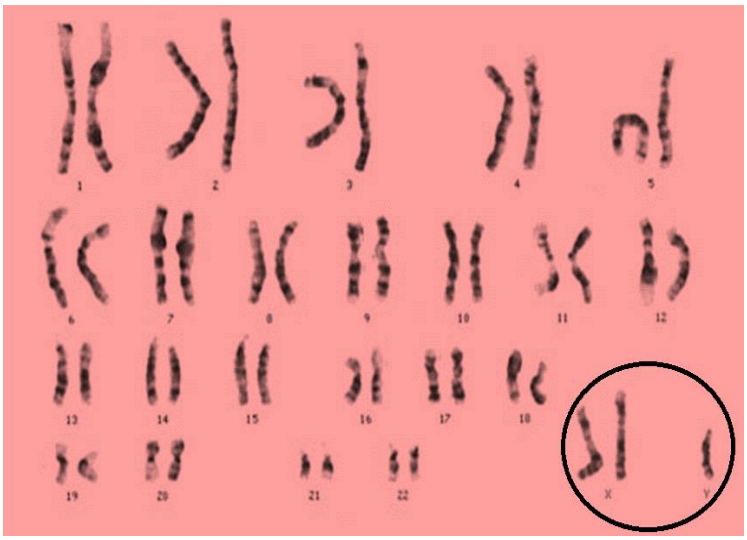


Features of Down syndrome

- Short statured
- Flat face
- Small round head
- Prominent epicanthic fold in each eye
- Protruding, furrowed tongue (This causes the mouth to remain partially open)
- Broad palm; presence of characteristic palm crease and fingerprint pattern
- Retarded physical, psychomotor and mental development

Klinefelter syndrome (47, XXY)

Trisomy of X chromosome (Presence of additional X chromosomes in human males)
Most often they have an XXY complement in addition to 44 autosomes
The karyotypes 48, XXXY; 48, XXYY; 49, XXXXY and 49, XXXYY are phenotypically similar to 47, XXY.
Klinefelter syndromes are males, characterized by presence of Barr body

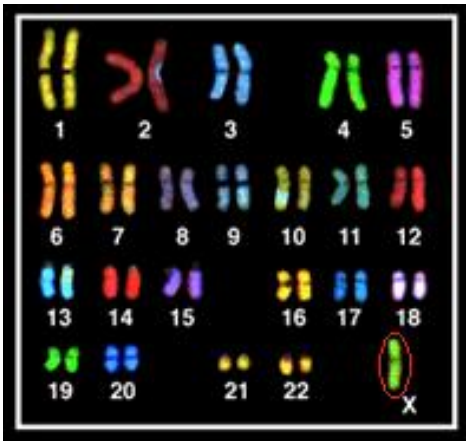


Features of Klinefelter syndrome

- Individuals with Klinefelter syndrome are generally tall and have long arms and legs and large hands and feet.
- They usually have male genitalia and internal ducts, but their testes are rudimentary and fail to produce sperm; sterile.
- Shows feminine sexual development such as slight enlargement of the breasts (gynecomastia).
- Intelligence is often below the normal range.

Turner syndrome (45, XO)

Monosomy of X chromosome (Absence of one X chromosome in human females) They are females, characterized by absence of Barr body.



Features of Turner syndrome

- Lack of secondary sexual characters
- Affected individual has female external genitalia and internal ducts, but the ovaries are rudimentary; sterile.
- Short stature
- Cognitive impairment,
- Skin folds on the back of the neck
- Underdeveloped breasts.

Check yourself

1. Which of the following group of chromosomal disorders in human represents trisomy of chromosome
    a) Turner syndrome, Down syndrome, Edward syndrome
    b) Down syndrome, Super male, Klinefelter syndrome
    c) Turner syndrome, Down syndrome, Edward syndrome
    d) Cri du chat syndrome, Down syndrome, Patau syndrome
2. Monosomy of sex chromosome is seen in
    a) Klinefelter syndrome
    b) Down syndrome
    c) Turner syndrome
    d) Super female
3. Which of the following represents female phenotype and characterized by absence of Barr body
    a) Super female
    b) Turner syndrome
    c) Klinefelter syndrome
    d) Down syndrome
4. Which of the following pair is correctly matched?
    a) Down syndrome - (47, +21)
    b) Klinefelter syndrome – (47, +18)
    c) Turner syndrome – (47, XXY)
    d) Edward syndrome – (45, X0)
5. Which of the following statement about Down syndrome is **incorrect**?
    a) They are always male
    b) They may be born to normal parents
    c) There are increase chances of Down syndrome in the children born to old age mothers
    d) They can be diagnosed by karyotype analysis
6. Simian crease, epicanthal folds and protruding furrowed tounge are the features of

a) Autosomal monosomy
b) Sex chromosome monosomy
c) Klinefelter syndrome
d) Down syndrome

7. Assertion (A): Their karyotype of Klinefelterôs syndrome is 47, XXY
   Reasoning (R): Sex of Klinefelterôs syndrome is females because of presence of two óXô chromosomes.
   a) Both (A) and (R) is correct and (R) is correct explanation of (A)
   b) Both (A) and (R) is correct but (R) is not correct explanation of (A)
   c) (A)is correct but (R) is wrong
   d) (R) is correct but (A) is wrong

Q No.	1	2	3	4	5	6	7
Ans	a	c	d	b	a	d	c