Lecture 30
Chromosomal theory of inheritance

Learning objectives

- **Number of chromosomes in somatic cells and gametes.**
- **Mitosis (Definition – stages)**
- **Meiosis (Definition – stages)**
- **Abnormal number of chromosomes and birth defects results from that abnormalities.**
- **Introduction:**

Humans have approximately 35,000 genes on 46 chromosomes. In somatic cells, chromosomes appear as 23 homologous pairs to form the diploid number of 46 (2n). There are 22 pairs of matching chromosomes, the autosomes, and one pair of sex chromosomes.

If the sex pair is XX, the individual is genetically female; if the pair is XY, the individual is genetically male. One chromosome of each pair is derived from the maternal gamete, the oocyte, and one from the paternal gamete, the sperm.

Thus each gamete (sex cell) contains a haploid number (23) of chromosomes (n), and the union of the gametes at fertilization restores the diploid number of 46.

✓ A single chromosome consists of two characteristic regions called arms (p arm = short arm; q arm = long arm), which are separated by a centromere (Fig.1).

✓ During cell division, single chromosomes undergo DNA replication, which essentially duplicates the arms. This forms duplicated chromosomes, which consist of two sister chromatids attached at the centromere (Fig. 1).

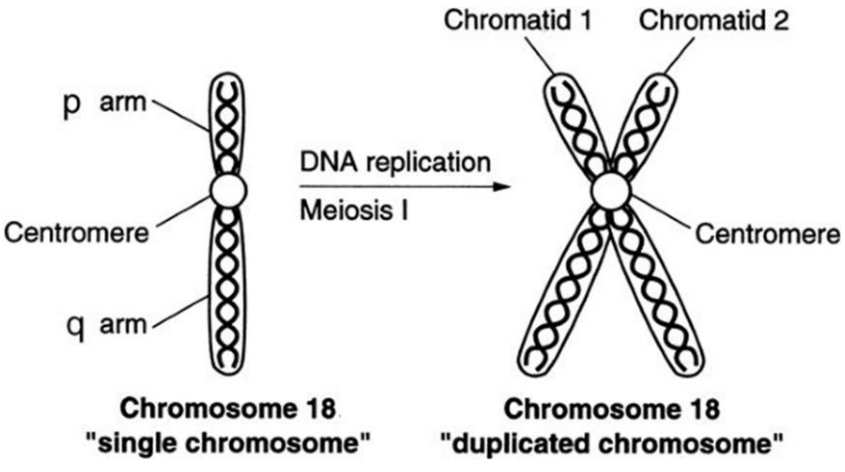

Fig. 1: Structure of chromosome

MITOSIS

●**Definition of Mitosis:** is the cell division that takes place in somatic cells giving rise to two daughter cells that are genetically identical to the parent cell. Each daughter cell receives the complete complement of 46 chromosomes

√ Before a cell enters mitosis, it enters in interphase where each chromosome replicates its DNA. During this replication phase, chromosomes are extremely long, they are spread diffusely through the nucleus, and they cannot be recognized with the light microscope (Fig. 2).

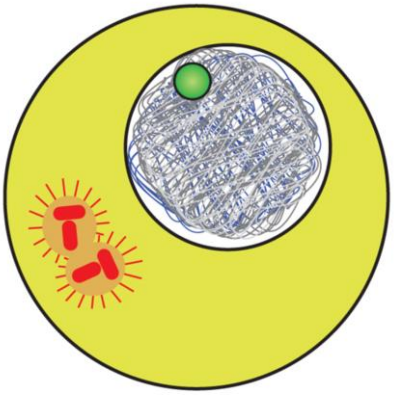

Fig. 2: Interphase stage

√ During mitosis, the centromeres divide, the sister chromatids separate, and one of each kind of chromosome goes into each daughter cell. Therefore, each daughter cell gets a complete set of chromosomes and is 2n. Since each daughter cell receives the same number and kinds of chromosomes as the parental cell, each is genetically identical to the other and to the parental cell (Fig. 3).

❖ **Stages of Mitosis:**

1-Prophase (Fig:4):

- The chromosomes begin to coil, contract, and condense; these events mark the beginning of prophase. Each chromosome now consists of two parallel subunits, chromatids, that are joined at a narrow region common to both called the centromere. Throughout prophase, the chromosomes continue to condense, shorten, and thicken.
- The two pairs of centrioles outside the nucleus begin moving away from each other toward opposite ends of the nucleus .

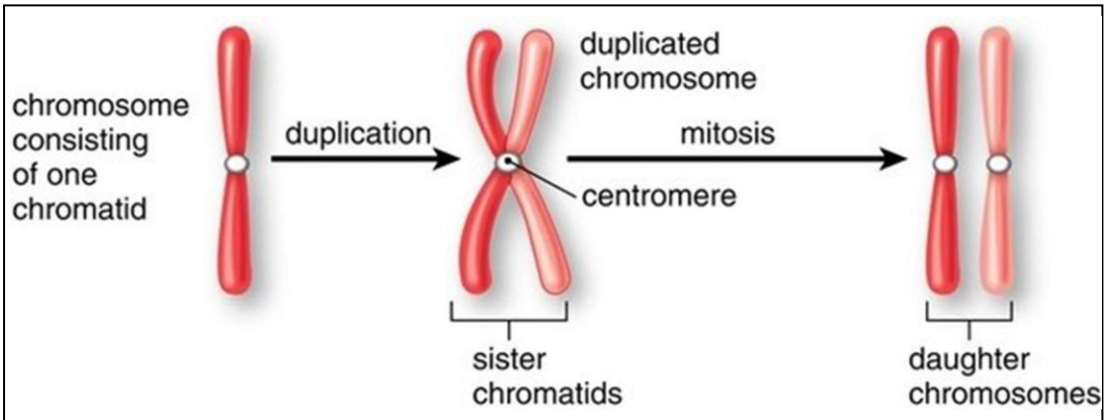

Fig.3:Duplication and division of chromosomes

- Spindle fibers appear between the separating centriole pairs .
- The nuclear envelope begins to fragment.
- The nucleolus begins to disappear.
- During mitosis, the centromeres divide, the sister chromatids separate, and one of each kind of chromosome goes into each daughter cell. Therefore, each daughter cell gets a complete set of chromosomes and is 2n.
- Since each daughter cell receives the same number and kinds of chromosomes as the parental cell, each is genetically identical to the other and to the parental cell.

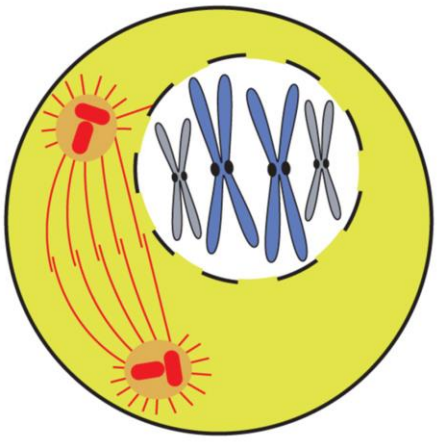

Fig.4: Prophase stage

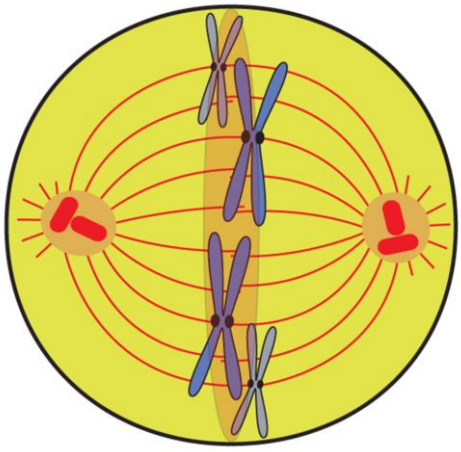

Fig.5: Metaphase stage

2- Metaphase (Fig.5):

- During metaphase, the nuclear envelope is fragmented completely, and the spindle occupies the region previously occupied by the nucleus.

- The chromosomes line up in the equatorial plane, and their doubled structure is clearly visible. Each is attached by microtubules extending from the centromere to the centriole, forming the mitotic spindle.

3-Anaphase (Fig. 6):

- The centromere of each chromosome divides, marking the beginning of anaphase, followed by separation of the sister chromatids and migration of chromatids to opposite poles of the spindle.
- Separation of the sister chromatids ensures that each cell receives a copy of each type of chromosome and thereby has a full complement of genes .

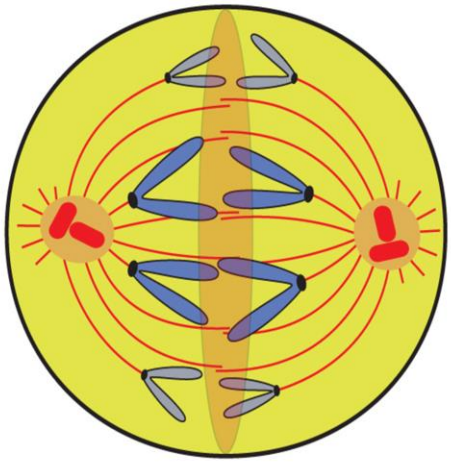

Fig.6: Anaphase stage

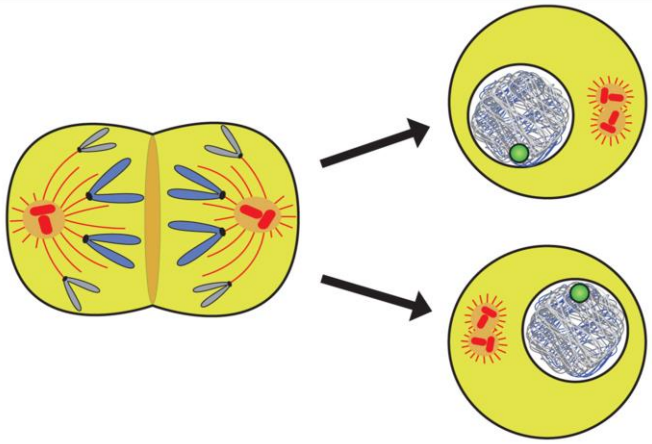

Fig. 7: Telophase and Cytokinesis

4-Telophase (Fig. 7):

- Telophase begins when the chromosomes arrive at the poles .
- The spindle disappears as nucleoli appear, and nuclear envelope reforms. The cytoplasm divides.
- Telophase is characterized by the presence of two daughter nuclei.

✓ **Cytokinesis (Fig.7):**

Cytokinesis is division of the cytoplasm and organelles. A slight indentation called a cleavage furrow passes around the circumference of the cell. Actin filaments form a contractile ring, and as the ring gets smaller and smaller, the cleavage furrow pinches the cell in half.

As a result, each cell becomes enclosed by its own plasma membrane. Each daughter cell receives half of all doubled chromosome material and thus maintains the same number of chromosomes as the mother cell.

MEIOSIS

● **Definition of Meiosis:** is the cell division that takes place in the germ cells to generate male and female gametes, sperm and egg cells, respectively each one contains the half number of chromosomes (haploid number).

.Meiosis requires two cell divisions, meiosis I and meiosis II, to reduce the number of chromosomes to the haploid number of 23 (half the number of chromosomes as the parental cell)

- The parental cell has the 2n number of chromosomes, while the daughter cells have the n number of chromosomes. Therefore, meiosis is often called reduction division.
- At the beginning of meiosis I, male and female germ cells (primary spermatocytes and primary oocytes) replicate their DNA so that each of the 46 chromosomes is duplicated into sister chromatids.
- During meiosis I, the homologous chromosomes of each pair come together and line up side-by-side due to a means of attraction still unknown.
- This so-called synapsis results in a tetrad, an association of four chromatids that stay in close proximity until they separate.
- During synapsis, nonsister chromatids may exchange genetic material

❖ **Synapsis**: is pairing of homologus chromosome.

Or Each chromosome (2 sister chromatids) pairs up with homologus chromosome and binds to form tetrade (4 chromatids) (Fig. 8).

❖ **Crossovers (Fig. 9)**: are the interchange of chromatid segments between paired homologous chromosomes.

- Segments of chromatids break and are exchanged as homologous chromosomes separate. As separation occurs, points of interchange are temporarily united and form an X-like structure, a **chiasma.**
- Crossing-over is significant because it increases the genetic variability of the gametes and therefore the offspring.

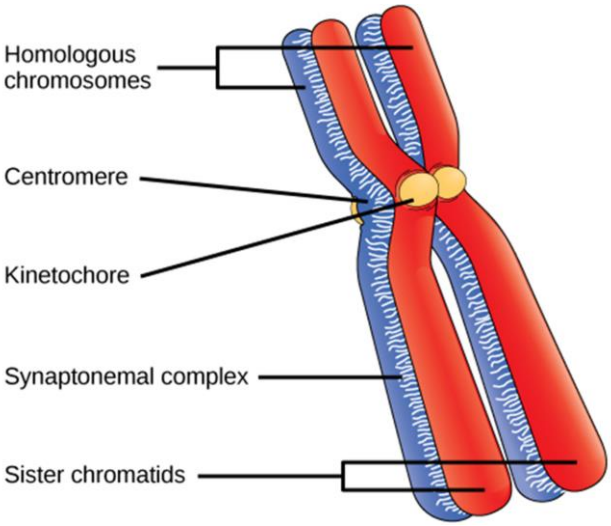

Fig. 8: Synapsis

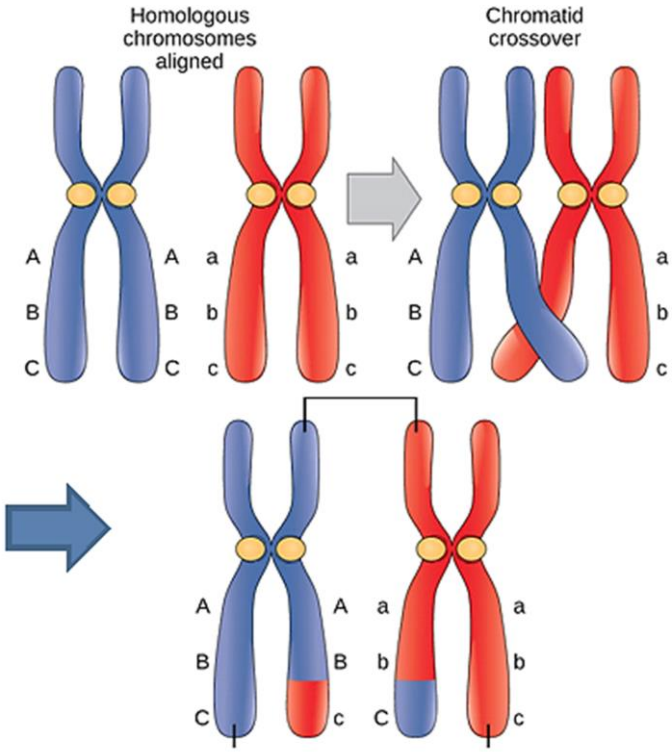

Fig. 9: Cross overs and synapsis

Stages of Meiosis

- **The First Division (meiosis I)(Fig. 10):**

During prophase I, the chromosomes begin to coil, contract, and condense, spindle appears while the nuclear envelope fragments and the nucleolus disappears. The homologous chromosomes, each having two sister chromatids, undergo synapsis, forming tetrads. Crossing-over occurs now .

In metaphase I, tetrads line up at the equator of the spindle.

During anaphase I, homologous chromosomes of each pair separate and move to opposite poles of the spindle.

During telophase I, nucleoli appear, and nuclear envelopes form as the spindle disappears. **During cytokinesis I**, the plasma membrane furrows to give two cells. Each daughter cell contains only one chromosome from each homologous pair. The chromosomes has two sister chromatids.

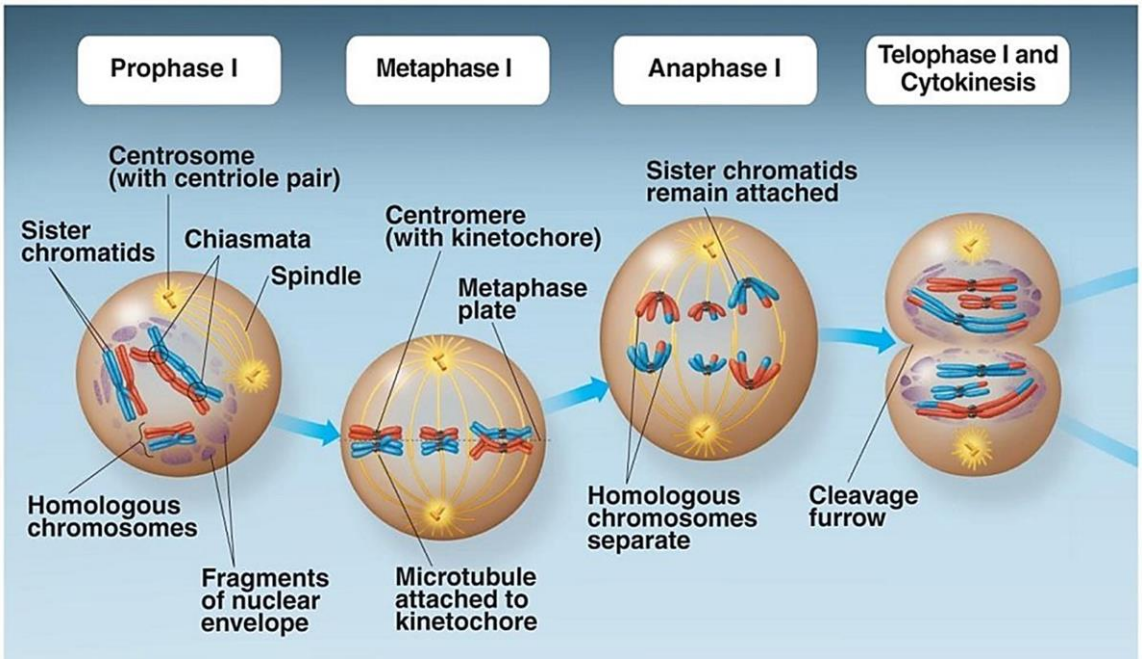

Fig.10: The First Division (meiosis I)

- **The Second Division (meiosis II): (Fig. 11)**
- It resembles the mitotic division.No duplication of DNA at start of meiosis II .

At the beginning of prophase II, the chromosomes continue to condense, shorten, and thicken.

Spindle fibers start to appear between the separating centriole pairs, the nuclear envelope begins to fragment. The nucleolus begins to disappear.

In metaphase II, the chromosomes line up in the equatorial plane, and their doubled structure is clearly visible.

At the start of anaphase II, the centromeres split. The sister chromatids move toward the poles. Each pole receives the same number of chromosomes.

In telophase II, the spindle disappears as nuclear envelopes form. During cytokinesis II, the plasma membrane furrows to give two complete cells, each of which has the haploid, or n, number of chromosomes. Since each cell from **meiosis I** undergoes meiosis II, there are four daughter cells altogether.

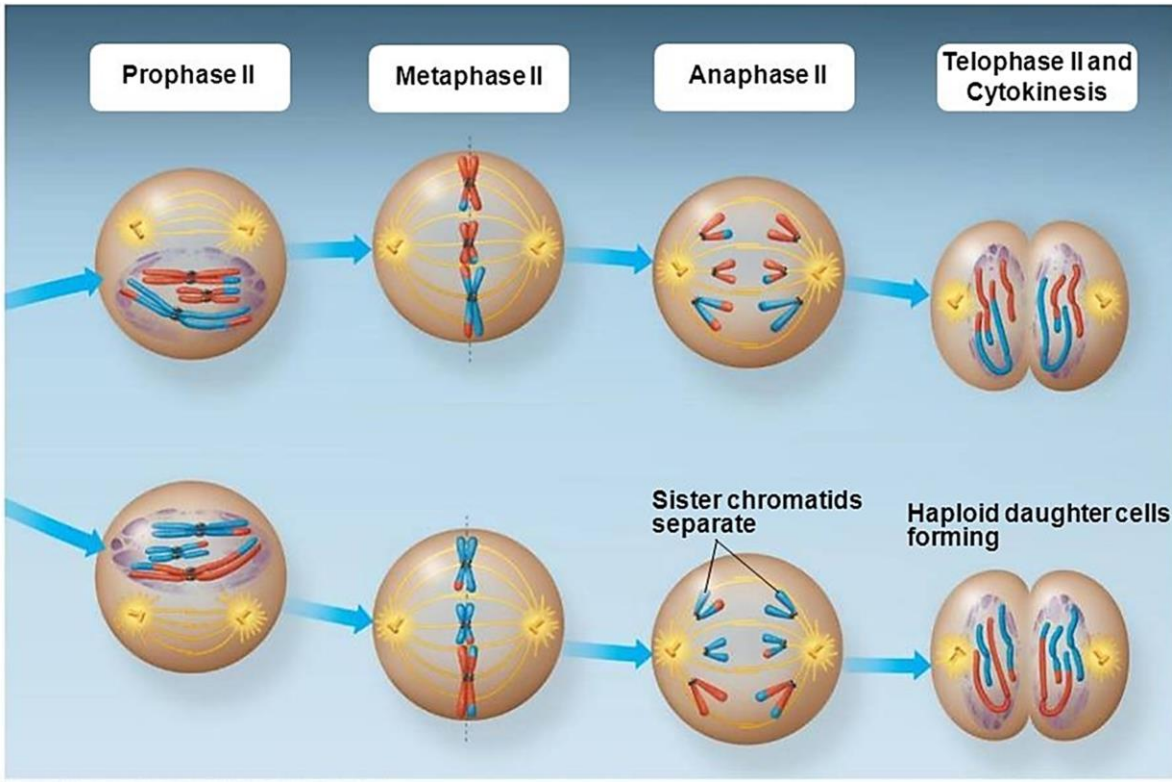

Fig. 11: The Second Division (meiosis II)

Karyotyping

A karyotype test is a type of genetic testing. It looks at the size, shape, and number of chromosomes in a sample of cells from your body (Fig. 12).

❖ **A karyotype test checks the chromosomes in your cells to**:

1-See whether you have a full set of 46 chromosomes (check for the number of chromosomes). Having too many or too few chromosomes can cause serious problems with health, growth, and normal development, such as Down syndrome (extra chromosome 21) and Turner syndrome (missing X chromosome).

2- Look for changes in the structure of chromosomes, such as broken, missing, or extra parts. These changes may cause a wide variety of problems depending on which chromosome is affected.

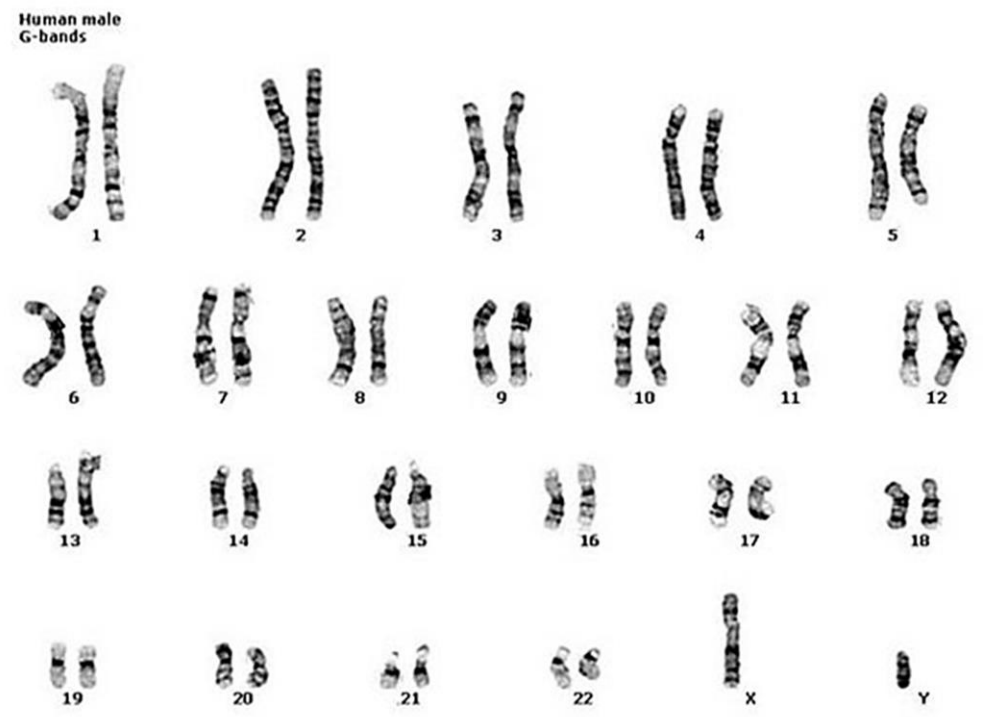

Fig. 11: Normal human karyotype

CHROMOSOMAL ABNORMALITIES (Numerical and Structural abnormalities):

❖ **Numerical Abnormalities**

The normal human somatic cell contains 46 chromosomes; the normal gamete contains 23. Normal somatic cells are diploid, or 2n; normal gametes are haploid, or n .

Trisomy: it is usually applied when an extra chromosome is present or when one is missing **(monosomy)**

Abnormalities in chromosome number may originate during meiotic or mitotic divisions Figs. 12, 13, 14). In meiosis, two members of a pair of homologous chromosomes normally separate during the first meiotic division so that each daughter cell receives one member of each pair**.**

Sometimes, however, separation does not occur (nondisjunction), and both members of a pair move into one cell. As a result of nondisjunction of the chromosomes, one cell receives 24 chromosomes, and the other receives 22 instead of the normal 23. (Fig. 12) When, at fertilization, a gamete having 23 chromosomes fuses with a gamete having 24 or22 chromosomes, the result is an individual with either 47 chromosomes (trisomy) or 45 chromosomes (monosomy).

❖ **Structural abnormalities:**

Sometimes chromosomes break, and pieces of one chromosome attach to another. Such **translocations** resulted in birth defects.

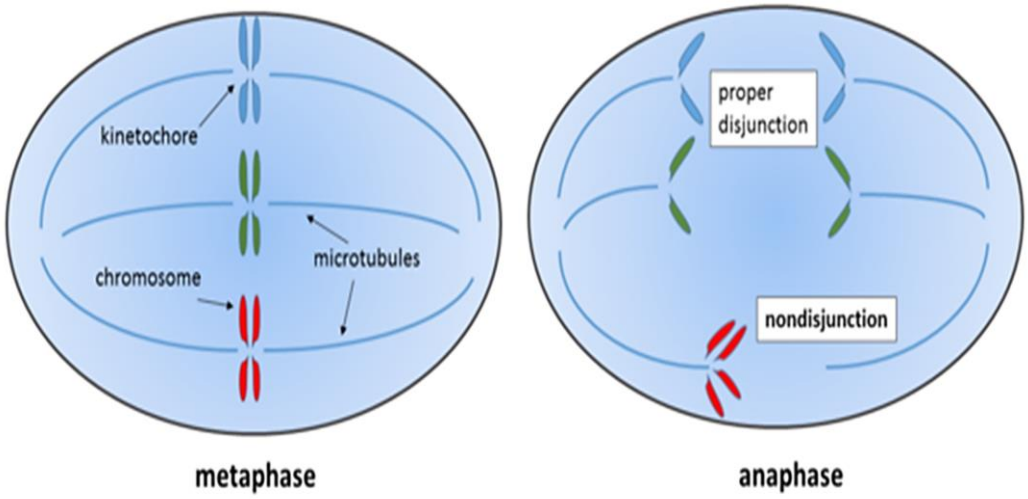

Fig. 12: Normal Versus Nondisjunction

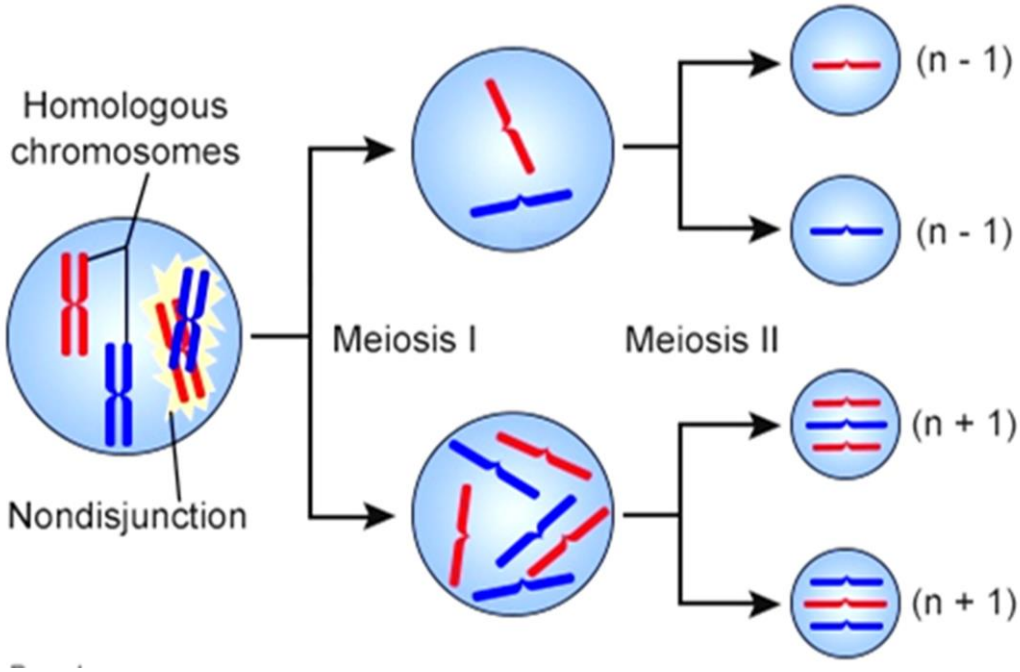

Fig. 13: Nondisjunction in meiosis I

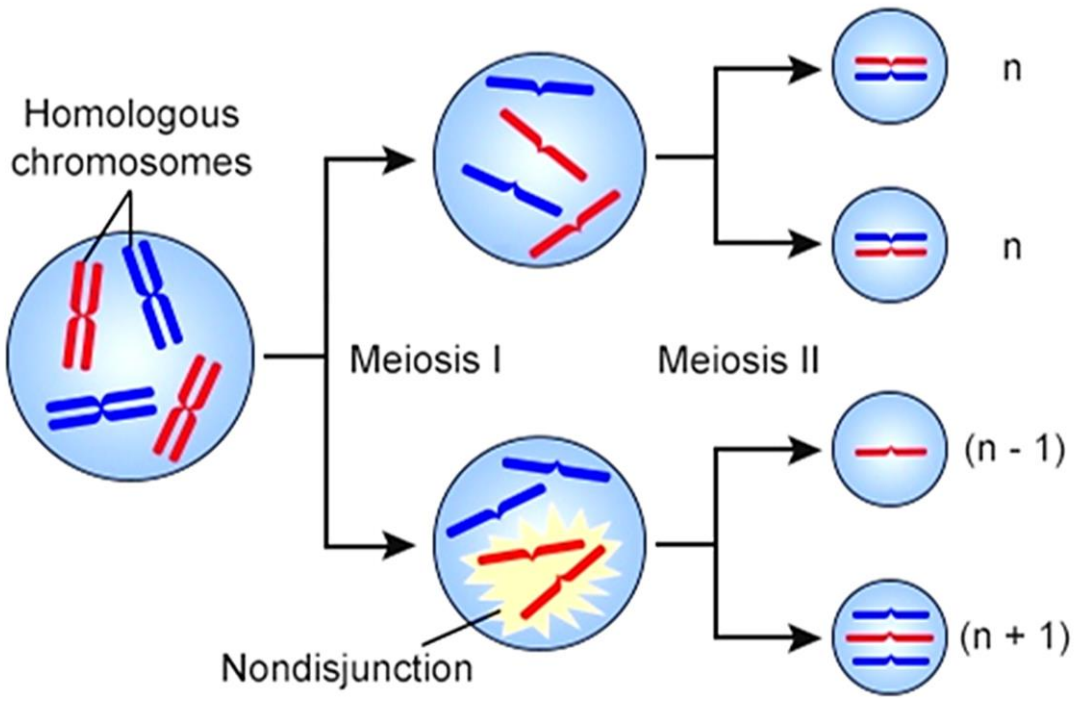

Fig. 14: Nondisjunction in meiosis II

DOWN SYNDROME

Down syndrome (Fig. 15) is called trisomy 21 because the individual usually has three copies of chromosome 21 .In most instances, the egg had two copies instead of this chromosome.

❖ Causes of Down Syndrome:

Abnormal karyotype – approximately 95% of cases result from chromosomal non-disjunction of chromosome 21 (47,XX,+21 or 47,XY,+21) at conception.

❖ Down syndrome is easily recognized by these characteristics (Fig. 16) :

- Growth retardation (short stature)
- Mental retardatio ‹
- Craniofacial abnormalities, including upward slanting eyes, epicanthal folds [extra skin folds at the medial corners of the eyes], flat facies, and small ears.
- a wide gap between the first and second toes, a large, fissured tongue, a palm crease (the so-called simian line),
- Cardiac defects.
- Hypotonia

- The chance of a woman having a Down syndrome child increases rapidly with age, starting at about age 40.

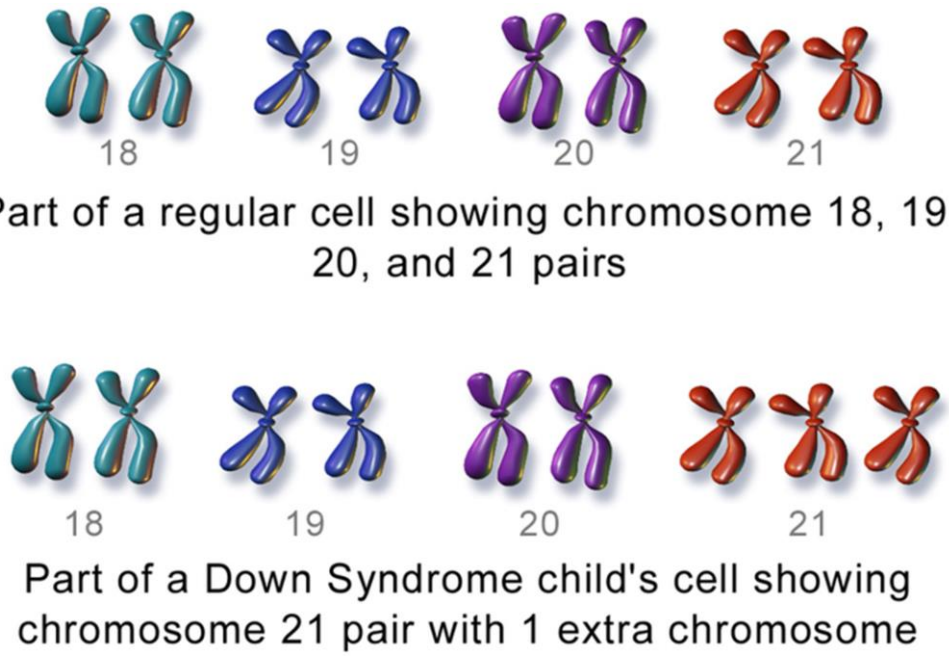

Fig. 15: Down syndrome – chromosomal pattern

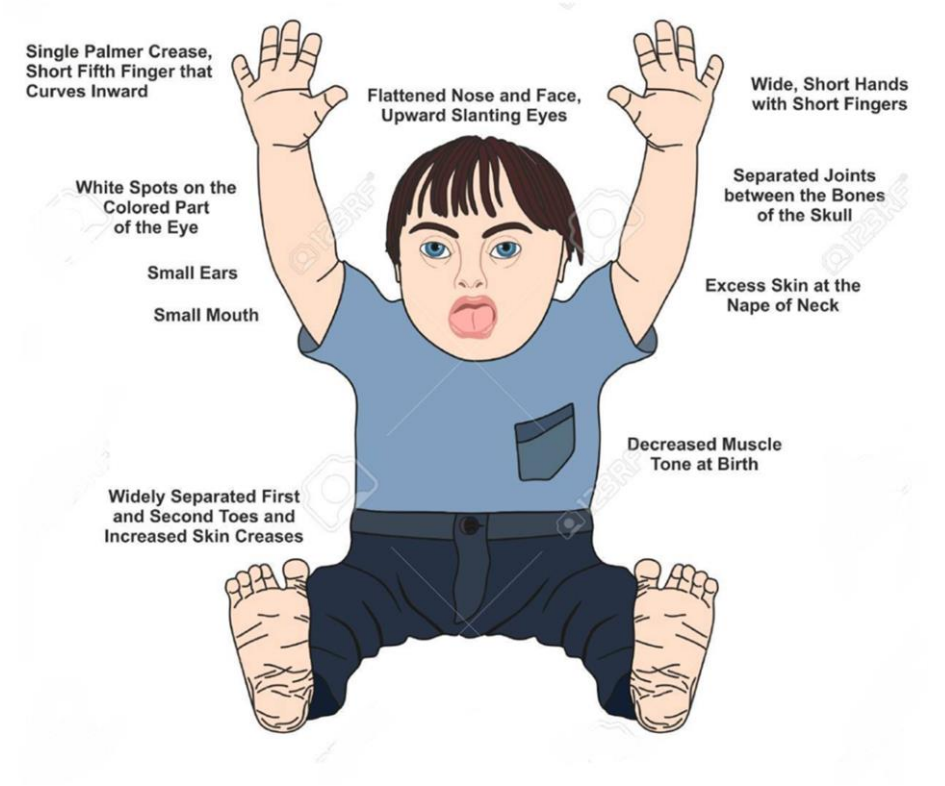

Fig. 16: Down syndrome –

TURNER SYNDROME (FIG. 17)

It is a chromosomal disorder characterized by a structurally normal X chromosome and the partial or complete absence of a second sex chromosome. Monosomy (45,X) is the classical karyotype in TS.

- These females are short, with a broad chest with widely spaced nipples and a webbed neck, absence of ovaries (gonadal dysgenesis).
- Turner females do not undergo puberty or menstruate, and there is a lack of breast development. They are usually of normal intelligence and can lead fairly normal lives, but they are infertile even if they receive hormonal supplements.

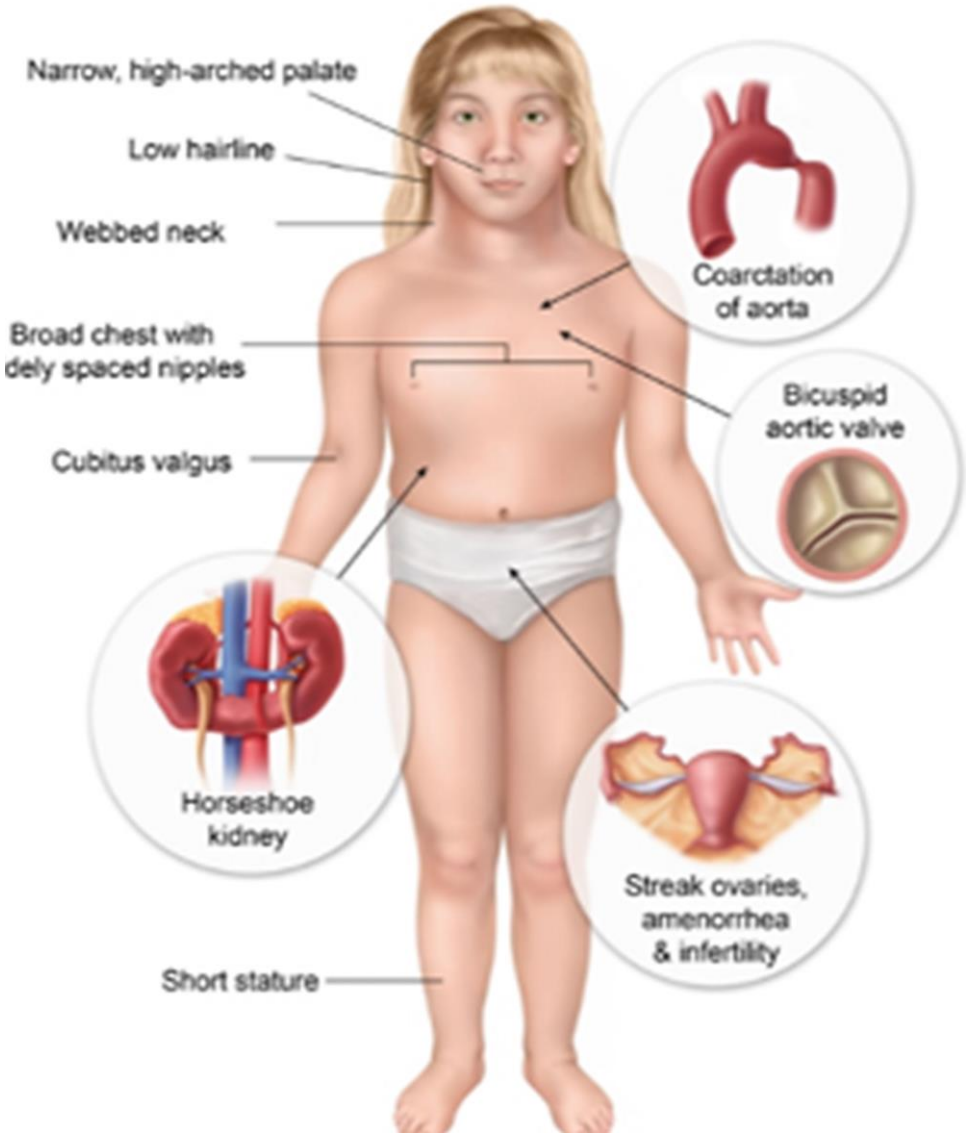

Fig. 17: Turner Syndrome

KLINEFELTER SYNDROME (Fig. 18)

The clinical features of Klinefelter syndrome, found only in males and usually detected at puberty, are sterility, testicular atrophy, hyalinization of the seminiferous tubules, and usually gynecomastia .

The cells have 47 chromosomes with a sex chromosomal complement of the XXY type, males. Although mental retardation is not generally part of the syndrome.

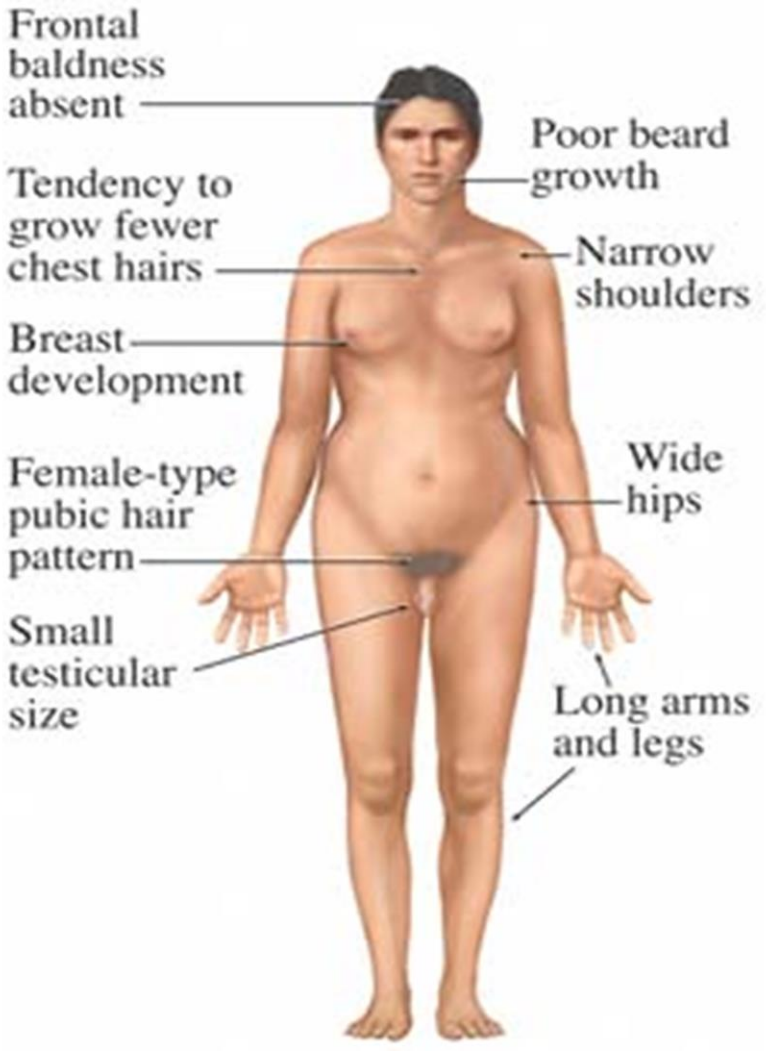

Fig. 18: KLINEFELTER SYNDROME