Medical Embryology

1st lecture
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Introduction

- **Embryology**: It's the science that deals with the origin and development of the individual organism.
- **Development**: is a gradual bringing to completion, both in structure and in function.
- Development in mammals can be divided into two periods: **Prenatal** (before birth) and **Postnatal** (after birth).
- For a long time, attention was focused on the events taking place before birth, later it was realized that important changes (other than growth) continue to occur even to the adult state, like developments of brain, teeth and male and female gonads.

So the boarder concept of embryology:

It's all the developmental events resulting from sexual reproduction till completion of development, which include infancy, childhood and adolescence.

- Throughout these periods a gradual remodeling of body shape and completion of some organs happened.

Gametogenesis:

- Normal somatic cells are **diploid** or 2n.
- Normal gametes are **haploid**, or n.
- Occurs in the ***gonads*** (sex organs)
- Two types of gametogenesis:

Spermatogenesis—production of sperm cells
Oogenesis—production of egg cells (***ova***)

- In males, spermatogenesis occurs within the testes
- In females, oogenesis occurs within the ovaries
- Spermatogenesis of 1 parent cell results in the production of ***4 sperm cells***
- Oogenesis of 1 parent cell results in the production of ***1 ovum and 3 "polar bodies"***.

Development begins with fertilization, the process by which the male gamete, the **sperm, and the** female gamete, the **oocyte, unite to give rise to a zygote.** Gametes are derived from **primordial germ cells** that are formed in the epiblast during the second week of development that move to the wall of the yolk sac.

During the fourth week these cells begin to migrate from the yolk sac toward the developing gonads, where they arrive by the end of the fifth week. Mitotic divisions increase their number during their migration and also when they arrive in the gonad.

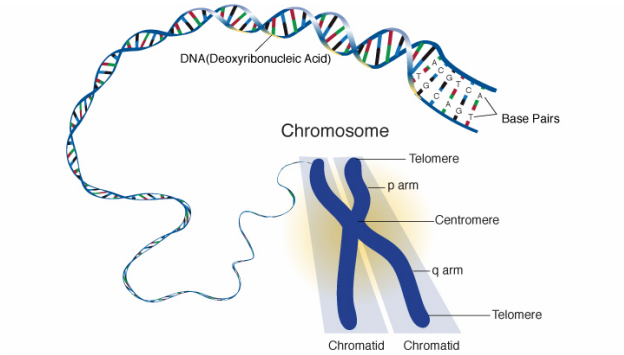
In preparation for fertilization, germ cells undergo **gametogenesis,** which includes meiosis, to halve the number of chromosomes and **cytodifferentiation to complete their maturation.**

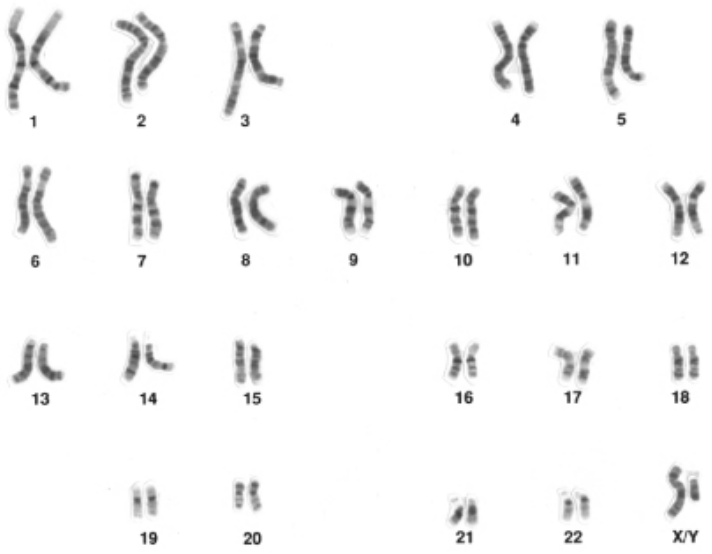
☒ **The Chromosome:**

Humans have approximately 35,000 genes on 46 chromosomes. Each chromosome now consists of two parallel subunits, **chromatids, that are joined at a** narrow region common to both called the **centromere. (**Only at prometaphase do the chromatids become distinguishable).

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 contains a haploid number of 23 chromosomes, and** the union of the gametes at **fertilization restores the diploid number of 46.**



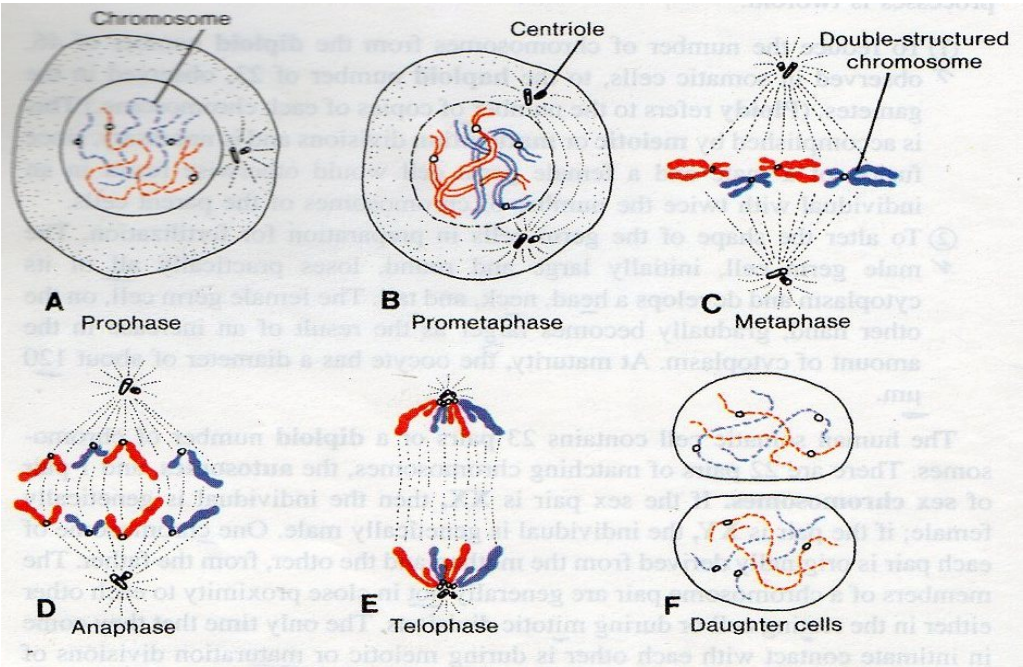


HUMAN MALE KARYOTYPING

Mitosis:

Is the process whereby one cell divides, giving rise to two daughter cells that are genetically identical to the parent cell. With the onset of mitosis:

1. Before a cell enters mitosis, each chromosome replicates its DNA.
2. The chromosomes begin to coil, contract, and condense; these events mark the beginning of prophase.
3. During metaphase the chromosomes line up in the equatorial plane, and their doubled structure is clearly visible.
4. The chromosomes attached by microtubules extending from the centromere to the centriole, forming the mitotic spindle.
5. Then the centromere of each chromosome divides, marking the beginning of anaphase followed by migration of chromatids to opposite poles of the spindle.
6. Finally, during telophase, chromosomes uncoil and lengthen, the nuclear envelope reforms, and the cytoplasm divides. Each daughter cell receives half of all doubled chromosome material and thus maintains the same number of chromosomes as the mother cell.



Meiosis:

Meiosis is the cell division that takes place in the germ cells to generate male and female gametes. Meiosis requires two cell divisions, with one-time DNA replication**,** to halve the number of chromosomes to the haploid number of 23.

The process starts:

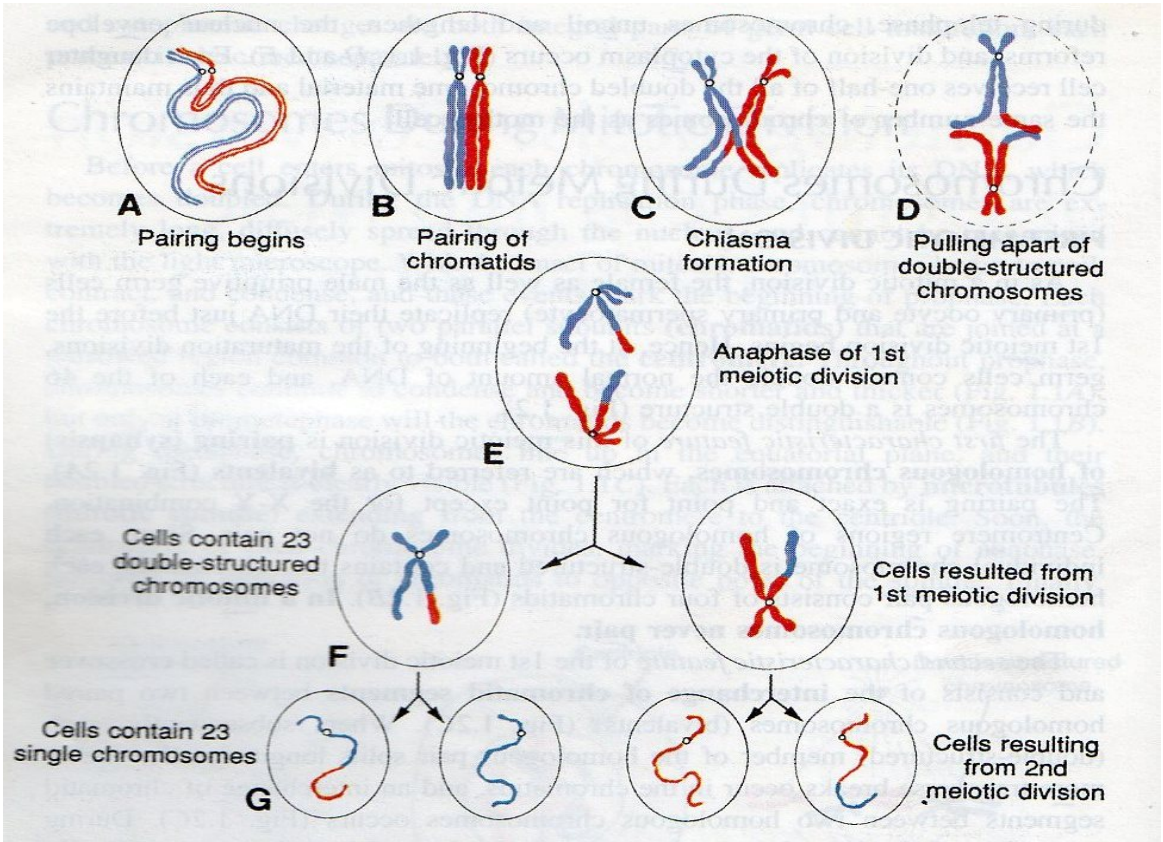
1. As in mitosis, male and female germ cells (**spermatocytes and primary oocytes) at the beginning of meiosis I replicate** their DNA so that each of the 46 chromosomes is duplicated into sister chromatids.

2. **Homologous chromosomes then align** themselves in **pairs, a process called synapsis (**except for the XY combination)**.**

3. Critical events in meiosis I, are the **interchange of chromatid segments** between paired homologous chromosomes called: crossing over.

4. Crossing over: 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, called a **chiasma.**

5. Homologous pairs then separate into two daughter cells. Shortly thereafter meiosis II separates sister chromatids. Each gamete then contains 23 chromosomes.



- results of meiotic divisions,

(a) Genetic variability is enhanced through crossover, which redistributes genetic material, and through random distribution of homologous chromosomes to the daughter cells; and

(b) Each germ cell contains a haploid number of chromosomes, so that at fertilization the diploid number of 46 is restored.

Chromosomal and Genetic Factors:

Chromosomal abnormalities**,** which may be **numerical** or **structural,** are important causes of birth defects and spontaneous abortions.

1. **Numerical Abnormalities*:***

- **Euploid** refers to any exact multiple of **n**, e.g., diploid or triploid
- **Aneuploid** refers to any chromosome number that is not euploid: when an extra chromosome is present (**trisomy) such as in Down syndrome (trisomy of chromosome 21) or when one chromosome** is missing (**monosomy), such as in Turner syndrome (45 X).**
- Abnormalities in chromosome number may originate during meiotic or mitotic divisions.

❑ Causes of Numerical Abnormalities:

A. **Nondisjunction**:

Incomplete separation of the chromosomes (**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. When, at fertilization, a gamete having 23 chromosomes fuses with a gamete having 24 or 22 chromosomes, the result is an individual with either 47 chromosomes (trisomy) or 45 chromosomes (monosomy). **Nondisjunction, which occurs during either the first or the second meiotic division of the germ cells, may involve the autosomes or sex chromosomes.** In women, the incidence of chromosomal abnormalities, including nondisjunction, increases with age, especially at 35 years and older.

B. **Translocations:** chromosomes break, and pieces of one chromosome attach to another chromosome, **two types of translocation may be present as:**

- **Balanced**: breakage and reunion occur between two chromosomes, but no critical genetic material is lost and individuals are normal
- **Unbalanced:** in which case part of one chromosome is lost and an altered phenotype is produced. For example, unbalanced translocations between the long arms of chromosomes 14 and 21 during meiosis I or II produce gametes with an extra copy of chromosome 21, it's one of the causes of Down syndrome.

TRISOMY 21(Down syndrome)**:** is usually caused by an extra copy of chromosome 21.

- In 95% of cases, the syndrome is caused by trisomy 21 resulting from meiotic nondisjunction.
- In approximately 4% of cases of Down syndrome, there is an unbalanced translocation between chromosome 21 and chromosome 13, 14, or 15.
- The final 1% is caused by mosaicism resulting from mitotic nondisjunction.

Turner syndrome: is the only monosomy compatible with life, with a 45,X karyotype,. 98% of all fetuses with the syndrome are spontaneously aborted. The few that survive are unmistakably female in appearance and are characterized by the absence of ovaries (**gonadal dysgenesis)**

- In 80% of these women, nondisjunction in the male gamete is the cause. In the remainder of women, structural abnormalities of the X chromosome or mitotic nondisjunction resulting in mosaicism are the cause.

2. **Structural Abnormalities*:***

A. **Structural chromosome abnormalities:** which involve one or more chromosomes, usually result from chromosome breakage. Breaks are caused by environmental factors, such as viruses, radiation, and drugs. The result of breakage depends on what happens to the broken pieces. Like:

- **Partial deletion of a chromosome:**
- **Microdeletions:** may result in **microdeletion syndrome or contiguous gene syndrome**

B. ***Gene Mutations:*** **DNA sequence alterations**