

## ~~FERTILIZATION~~

Fertilization is the process of fusion of male and female gametes (pronuclei) to form a zygote. It takes place within 24 hours of ovulation in the most dilated part of the uterine tube – the ampulla. The results of fertilization are (a) determination of genetic sex of embryo, (b) restoration of diploid number of chromosomes, and (c) initiation of cleavage. Fertilization is essential for propagation of species and their evolution.

For a proper understanding, fertilization is described under the following headings: approximation of gametes, fusion of gametes, and results of fertilization.

## Capacitation

The capacitation is the final step of maturation of sperms, which make them competent to fertilize an oocyte. The capacitation occurs after ejaculation of sperms into the female genital tract; it lasts for about 7–10 hours. During capacitation, the glycoprotein coat and seminal plasma proteins covering the plasma membrane of sperm in the acrosomal region are removed by chemicals secreted by uterus. Now sperms' tails start to beat more vigorously. Only capacitated sperm undergoes acrosome reaction and fertilizes the ovum.

## Acrosome Reaction

Acrosome reaction occurs when capacitated sperm comes in contact with the zona pellucida (i.e., acrosome reaction is induced by zona proteins). This reaction leads to release of enzymes, such as **hyaluronidase** and **acrosin**, from acrosomal cap. The antigenic coating of the sperm initiates an immunological reaction between the **oocyte's fertilizin** and the **sperm's antifertilizin**.

## CLINICAL CORRELATION

**Significance of capacitation:** Capacitation of sperms is a prerequisite for fertilization.

It is now confirmed by experiments that the freshly ejaculated sperms are infertile and must be in the female genital tract for at least 7 hours before they can fertilize a secondary oocyte.

During in vitro fertilization, the capacitation of sperms is induced artificially by treating the ejaculate with a solution consisting of gamma-globulin, free serum, follicular fluid, dextran, serum dialysate, and adrenal gland extract.

## Stages of Fertilization (Fig. 5.2)

AN 77.4

To fertilize the ovum (secondary oocyte), the sperm has to break three barriers (may be called **fertilization barriers**) which surround and protect it.

The sequence of events taking place during fertilization is as follows:

1. **Penetration of corona radiata:** About 300–400 capacitated sperms come in contact with corona radiata. They liberate hyaluronidase enzymes, which digest the chemical substance binding the cells of corona radiata. Now the sperm freely penetrates the corona radiata to reach the zone pellucida through the movements of its tail.
2. **Penetration of zona pellucida:** When the head of sperm comes in contact with glycoproteins of zona pellucida, an **acrosome reaction** occurs. The acrosome

releases digestive enzymes (**acrosin and pepsin-like substances**), which cause lysis of the zona pellucida and plasma membrane around the head of the sperm. This allows the sperm to penetrate through the zona pellucida and reach into the perivitelline space. Once the sperm penetrates the zona pellucida, a change in the properties of zona pellucida (**zona reaction**) occurs that makes it impermeable to other sperms to prevent polyspermy.

3. **Penetration of vitelline membrane:** When the plasma membranes of sperm head come in contact with the plasma membrane of oocyte (called vitelline membrane), the latter breaks down at the site of fusion. This allows the head of the sperm to enter into the cytoplasm of the oocyte leaving behind the discarded body and tail of sperm on the oocyte surface. As soon as the head and neck of sperm enters the oocyte, a **calcium wave** appears in the cytoplasm of oocyte that makes oocyte membrane impermeable to other sperms.

N.B. **Polyspermy** is prevented by integrin peptides of vitelline membrane and zona reaction of zona pellucida by not allowing the entry to more than one sperms (vide supra).

4. **Formation of female pronucleus:** The penetration of oocyte by the sperm activates the oocyte to complete its second meiotic division. Thus, two cells are produced: one cell containing all the cytoplasm is called **mature oocyte** and the second cell containing hardly any cytoplasm is called second polar body.

The maternal chromosomes ( $22 + X$ ) of mature oocyte condense and arrange themselves in a vesicular pattern to form the **female pronucleus**.

5. **Formation of male pronucleus:** The sperms move forward to come in close contact with the female pronucleus. Its nucleus becomes swollen and forms the male pronucleus. Morphologically, the male and female pronuclei are indistinguishable. Each chromosome in male and female pronuclei is made of only one chromatid. The pronuclei (both haploid) grow and replicate their DNA, i.e., change from haploid ( $n$ ) to diploid ( $2n$ ). Now each chromosome in male and female pronuclei consists of two chromatids. The oocyte containing two haploid nuclei is called **ootid**.

6. **Formation of zygote:** The male and female pronuclei lose their cell membrane and chromosomes of two nuclei (23 in each) mix together to form diploid (i.e., 46 chromosomes). The ootid becomes a zygote. The chromosomes in zygote become arranged on a cleavage spindle in preparation for cleavage of

## Results of Fertilization

The main results of fertilization are as follows:

1. **Completion of second meiotic division of the female gamete:** As soon as the sperm enters into the secondary oocyte, the latter completes its second meiotic division and extrudes the second polar body into the **perivitelline space**.

- 2. Restoration of diploid number of chromosomes:** The male and female pronuclei (both haploid) fuse with each other to restore normal diploid number of chromosomes.
- 3. Determination of chromosomal sex of the new individual:** The oocytes are only of one type, i.e., they contain only "X" chromosomes, whereas the sperms are of two types: (a) "Y"-bearing sperms (**androsperms**) and (b) "X"-bearing sperms (**gynosperms**). If an oocyte (X) is fertilized by a Y-bearing sperm, the result will be a **male baby**, and if an oocyte is fertilized by an X-bearing sperm, the result will be a **female baby**. *Therefore, it is the father who is responsible for determination of the sex of the baby, and not the mother.*
- 4. Initiation of cleavage:** Fertilization stimulates the zygote to undergo a series of rapid mitotic divisions. This is called **cleavage**.
- 5. Variation of human species:** It occurs due to mingling of maternal and paternal chromosomal complements of two different species. For examples, if the ovum of one species (e.g., tiger) is fertilized by the sperm of other species (e.g., lion), the baby born will be called **liger**. Similarly, if the ovum of a female donkey is fertilized by the sperm of a horse, the baby born will be called **mule**.

**Table 4.1 Distinguishing features between mitosis and meiosis**

Mitosis	Meiosis
Takes place in somatic cells	Takes place in germ cells
Completes in one sequence	Completes in two sequences, i.e., there are two successive divisions, namely, <b>meiosis I</b> <b>and meiosis II</b>
Crossing over of chromatids does not take place	Crossing over of chromatids takes place
Daughter cells have the same number of chromo- somes as parent cells	Daughter cells have half the number of chromosomes as parent cells
Daughter cells are identical to each other and to the parent cell	Daughter cells are not identical to each other and to the parent cell
Equational division	Reductional division

## First Meiotic Division

1. **Prophase:** Prophase of the first meiotic division is very long and complicated. It is therefore subdivided into five stages.

- (a) *Leptotene:* In this stage, the chromosomes, as in mitosis, appear as slender threads. Note: Although each chromosome consists of two chromatids that are joined at centromere, the chromatids are not visible at this stage.
- (b) *Zygotene:* In this stage, the lengthwise pairing of homologous chromosomes begins. One of the two homologous chromosomes is from the father (**paternal chromosome**) and the other is from the mother (**maternal chromosome**). This event is called **synapsis** and each synapsing pair is called **bivalent**.
- (c) *Pachytene:* This stage is very long and may extend even for years. It is characterized by following changes:
  - The chromatids of each chromosome become visible separately. Each bivalent chromosome thus appears to have four chromatids and is called **tetrad**. Each chromatid pair is united

by a **kinetochore**. There are two central chromatids and two peripheral chromatids (one from each chromosome).

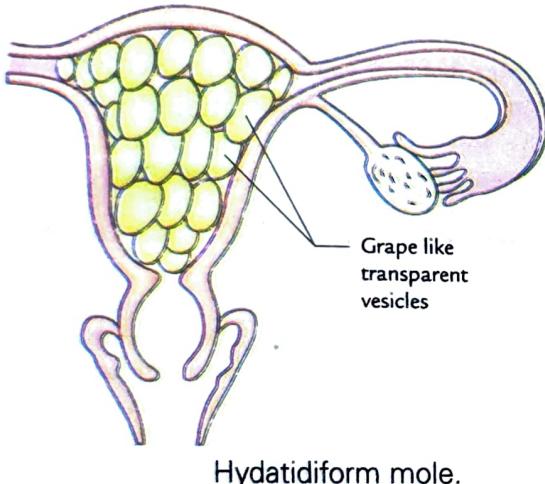
- The two central chromatids (one belonging to each chromosome) of tetrad coil over each other so that they cross at a number of points. This is called **crossing over**. Because of crossing over, the central chromatids present a cross-like configuration called **chiasmata**.

- (d) *Diplotene*: During this process, the paired homologue of tetrad starts separating. The central chromatids break at the point of crossing over and unite to the opposite chromatid. This results in exchange of genetic material between these chromatids.
- (e) *Diakinesis*: The chromosomes become more contracted and migrate toward the nuclear membrane. At the end of prophase, the nuclear membrane disappears.

2. **Metaphase**: The homologous pairs of chromosomes become arranged on the equatorial plane of the spindle.

3. **Anaphase**: In this stage, the homologous chromosomes migrate to the opposite poles of the spindle. Unlike mitosis, the chromosomes move randomly. The shorter chromosomes move earlier than the longer chromosomes.

4. **Telophase**: In this stage, the nuclear membrane is formed around the polarized group of chromosomes. The cell membrane constricts and two daughter cells are formed (**cytokinesis**). Each daughter cell thus formed contains only half the number of chromosomes (**haploid number**) with exchanged genetic material.



Hydatidiform mole.

**N.B.**

- Around 3%–5% of hydatidiform moles undergo malignant change forming **choriocarcinoma**.
- There are two types of hydatidiform moles: (a) complete type in which there is no existence of embryo at all and (b) partial type in which part of the embryo is seen.
- Majority of hydatidiform moles are monospermic, i.e., an empty oocyte having no female pronucleus is fertilized by a single sperm.

## IMPLANTATION

The implantation is a process by which the moving blastocyst is first attached to the epithelial lining of endometrium

and then gets embedded into the uterine endometrium. The embryo remains attached with endometrium till birth.

The implantation occurs in the upper part of the posterior wall of uterine cavity.

The blastocyst surrounded by zona pellucida enters into the uterine cavity on day 5.

The blastocyst enlarges, the zona pellucida disintegrates, and blastocyst is released on day 6, called **hatching of blastocyst**.

Now sticky polar *trophoblast* adheres/binds with the epithelial lining of uterine endometrium, on day 7.

The trophoblast secretes *proteolytic enzymes*, which erodes uterine epithelium to create passage for blastocyst into the uterine endometrium of secretory phase.

**N.B.** Further embedding takes place in 2nd week of development, but brief account is given here for better understanding of students.

The blastocyst burrows deeper and deeper in the endometrium until it completely disappears from the surface.

The polar trophoblast forms finger-like projections called *villi*, which gets intimately associated with maternal tissue (decidua basalis) to form placenta.

The penetration defect in the uterine endometrium is closed by *fibrin plug* made up of blood clot and cellular debris. The implantation is described in detail in Chapter 6.

# EMBRYOLOGICAL TERMS

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Most of the terms used in embryology are of *Latin* (L.) or *Greek* (Gr.) origin. The following text lists only those terms that are commonly used.

1. **Oocyte** (L. *Ovum* = egg): Female germ cells or sex cells produced by ovaries. **Mature oocyte** is called **secondary oocyte**.
2. **Sperm** (Gr. *Sperma* = seed): Male germ cells produced by testes.
3. **Zygote**: Cell formed by union of a sperm and secondary oocyte (ovum). The zygote is the earliest stage of embryo (i.e., the beginning of the new human being).
4. **Conceptus**: Product of conception, i.e., embryo along with its extraembryonic membranes.
5. **Cleavage**: Series of mitotic divisions of the zygote to form early embryonic cells – the *blastomeres*.
6. **Morula** (L. *Morus* = mulberry): Solid ball of 12–32 cells (blastomeres) formed 3–4 days after fertilization, just at the time when embryo enters the uterus.
7. **Blastocyst** (Gr. *Blastos* = bud, *Kystis* = capsule): It forms from late morula stage. It consists of two parts: an outer layer of small, slightly flattened cells called *trophoblasts* and inner cell mass (*embryoblast*) consisting of a group of larger polyhedral cells.  
The cavity of blastocyst (**blastocele**) separates the trophoblast from the inner cell mass except for a small area where they are in contact (embryonic pole). The embryoblast forms embryo, whereas trophoblast forms placenta.
8. **Implantation**: Attachment and subsequent embedding of blastocyst into uterine endometrium, where it develops during gestation.

# CHROMOSOMES

AN 73.1

The chromosomes (Gr. *Chromosome* = a readily staining body) are deeply stained minute rod-like structures in the nucleus of the cell formed by condensation of chromatin during cell division. These contain DNA encoding genetic information inherited from parents. The individual chromosomes are best defined (visible) under microscope only during metaphase stage of cell division.

**Table 29.2** Individual's sex chromosomal constitution and number of Barr bodies per cell

Individual	Sex Chromosomal Constitution	Number of Barr Bodies
Normal male	XY	Nil
Turner syndrome	XO	Nil
Normal female	XX	One
Klinefelter syndrome	XXY	One
Triple X syndrome (superfemale)	XXX	Two

### Classification

The chromosomal abnormalities may be classified in a number of ways.

#### 1. On the basis of type of abnormality:

- (a) **Numerical:** Involving changes in the number of chromosomes, e.g., polyploidy and aneuploidy.
- (b) **Structural:** Involving changes in the structure of chromosomes, e.g., deletion and translocation.

#### 2. On the basis of types of chromosomes involved:

- (a) **Involving autosomes**, e.g., Down syndrome.
- (b) **Involving sex chromosomes**, e.g., Turner syndrome and Klinefelter syndrome.

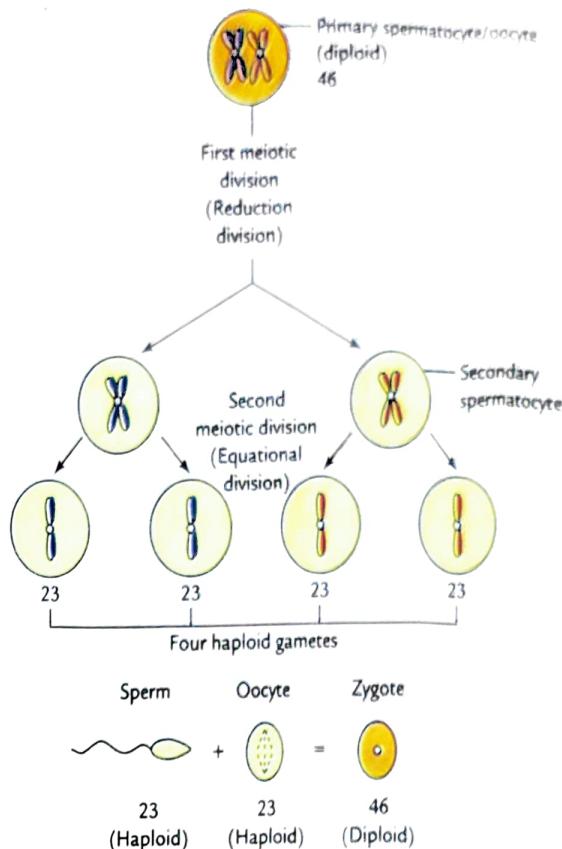
### Numerical Abnormalities

AN 75.1

The numerical abnormalities of chromosomes occur due to failure of meiotic division to occur or due to abnormal meiotic division during the formation of gametes. In normal meiotic division during gametogenesis, both primary spermatocytes and primary oocytes produce four daughter cells, each with 23 chromosomes; and when haploid sperm fertilizes haploid ovum, the diploid zygote (46 chromosomes) is produced (Fig. 29.8).

Sometimes separation of two chromosomes does not occur (**nondisjunction**; Fig. 29.9), either during first meiotic division (Fig. 29.9A) or during second meiotic division (Fig. 29.9B), and then both the members of a pair move into one cell.

As a result of the nondisjunction of the chromosome (Fig. 29.10), one gamete receives 24 chromosomes and the other 22. Consequently, at fertilization, when a gamete (e.g., sperm) having 23 chromosomes fuses with a gamete (e.g., ovum) having 24 or 22 chromosomes, the result will be an individual with either 47 chromosomes (**trisomy**) or 45 chromosomes (**monosomy**), respectively.



**Fig. 29.8** Normal meiotic division producing gametes with 23 chromosomes.

The numerical abnormalities include following conditions:

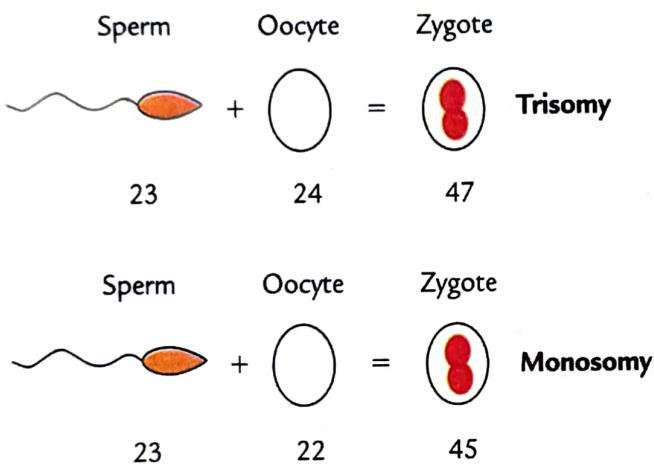
1. **Polyplody:** It is a condition in which chromosome number is increased in a multiple of haploid (23) set of chromosomes, of course, in addition to the diploid number. In other words, polyplody is the condition of extra haploid set/sets of chromosomes (i.e., 23) to normal diploid set of chromosomes (i.e., 46). The examples are given as follows:

(a) **Triploidy:** In this condition, the cells contain 69 chromosomes ( $23 \times 3$ ). It occurs either due to failure of meiosis in germ cell, e.g., fertilization of diploid ovum by a haploid sperm or fertilization of haploid ovum by two haploid sperms (dispermy).

**N.B.** Triploidy results in spontaneous abortion of the conceptus or brief survival of live-born infant after birth.

(b) **Tetraploidy:** In this condition, the cells contain 92 chromosomes ( $23 \times 4$ ). It occurs due to failure of first cleavage division.

**N.B.** Tetraploidy results in spontaneous abortion of the conceptus.



**Fig. 29.10** Nondisjunction during oogenesis. Note that if an abnormal oocyte with 24 chromosomes is fertilized by a normal sperm with 23 chromosomes, a zygote with 47 chromosomes is produced (i.e., trisomy). If an abnormal oocyte with 22 chromosomes is fertilized by a normal sperm with 23 chromosomes, a zygote with 45 chromosomes is produced (i.e., monosomy).

**2. Aneuploidy:** It is a condition in which chromosome number is altered by one, i.e., there is an addition of one chromosome (**trisomy**) or loss of one chromosome (**monosomy**). It occurs due to nondisjunction during meiosis (Figs 29.9 and 29.10).

**N.B.** Trisomy usually results in spontaneous abortion of the conceptus; however, trisomy 13 (Patau syndrome), trisomy 18 (Edward syndrome), trisomy 21 (Down syndrome), and Klinefelter syndrome are found in live-born population.

Monosomy also usually results in spontaneous abortion of the conceptus; however, monosomy of X chromosome (45XO), i.e., Turner syndrome is found in live-born population.

## Structural Abnormalities

These abnormalities involve change in the structure of chromosome. The types of structural abnormalities include **deletions**, **microdeletions**, **translocation**, **fragile sites**, **isochromosomes**, **inversions**, and **breakage**.

The abnormalities in structure cause the following conditions:

**1. Deletions:** It is a condition in which there is a loss of segment of a chromosome, i.e., cri-du-chat syndrome or cat's cry syndrome.

**N.B.** Sometimes, chromosome is deleted at both the ends, and then the two broken ends adhere/unite in the form of ring called **ring chromosome**, commonly seen due to break points of chromosome 14.

**2. Microdeletions:** In this condition, there is a loss of a segment of chromosome, which can be detected only by a high-resolution banding. The clinical conditions caused by microdeletions include *Prader-Willi syndrome*, *Angelman syndrome* or *happy puppet syndrome*, etc.

**3. Translocation:** In this condition, there is breakage and exchange of segments between chromosomes. The examples include the following:

(a) **Robertsonian translocation:** It is a special type of translocation in which breaks occur at the centromeres, e.g., translocation between long

arms of chromosomes 13 and 14 (**most common translocation found in humans**), and chromosomes 21 and 22. The short arms of these chromosomes involved in Robertsonian translocations are generally lost.

- (b) **Reciprocal translocation between chromosome 15 and chromosome 17:** It leads to *acute promyelocytic leukemia*.
  - (c) **Reciprocal translocation between chromosome 9 and chromosome 22 (Philadelphia chromosome):** It leads to *chronic myeloid leukemia*.
4. **Fragile sites:** In this condition, there are gaps or breaks in chromosomes. The clinical examples caused by this condition include **fragile X syndrome** (*Martin–Bell syndrome*).

5. **Isochromosomes:** In this condition, the centromere divides transversely instead of longitudinally. As a result, two arms of a chromosome are separated forming two isochromosomes.

6. **Inversions:** In this condition, a part of chromosome is detached and later unites with the same chromosome in inverted position. As a result, there is a reversal of order of DNA between two breaks in the chromosome. It can be **pericentric** if inversions occur on sides of the centromere, or **paracentric** if inversions occur on the same side of the centromere.

7. **Breakage:** In this condition, there occurs a break in chromosome due to ultraviolet radiation and ionizing radiation.

Here are 5 important differences between DNA and RNA (easy to remember for exams):

Feature	DNA (Deoxyribonucleic Acid)	RNA (Ribonucleic Acid)
Type of sugar	Deoxyribose sugar	Ribose sugar
Nitrogen base	Contains Thymine (T)	Contains Uracil (U) instead of thymine
Strands	Usually double-stranded (double helix)	Usually single-stranded
Location	Mainly in the nucleus (also mitochondria)	In nucleus & cytoplasm (ribosomes)
Function	Stores genetic information	Helps in protein synthesis (mRNA, tRNA, rRNA)

## One-look Summary Table

### Mesoderm Part

Paraxial

### Key Derivatives

Vertebrae, skeletal muscle, dermis

Intermediate

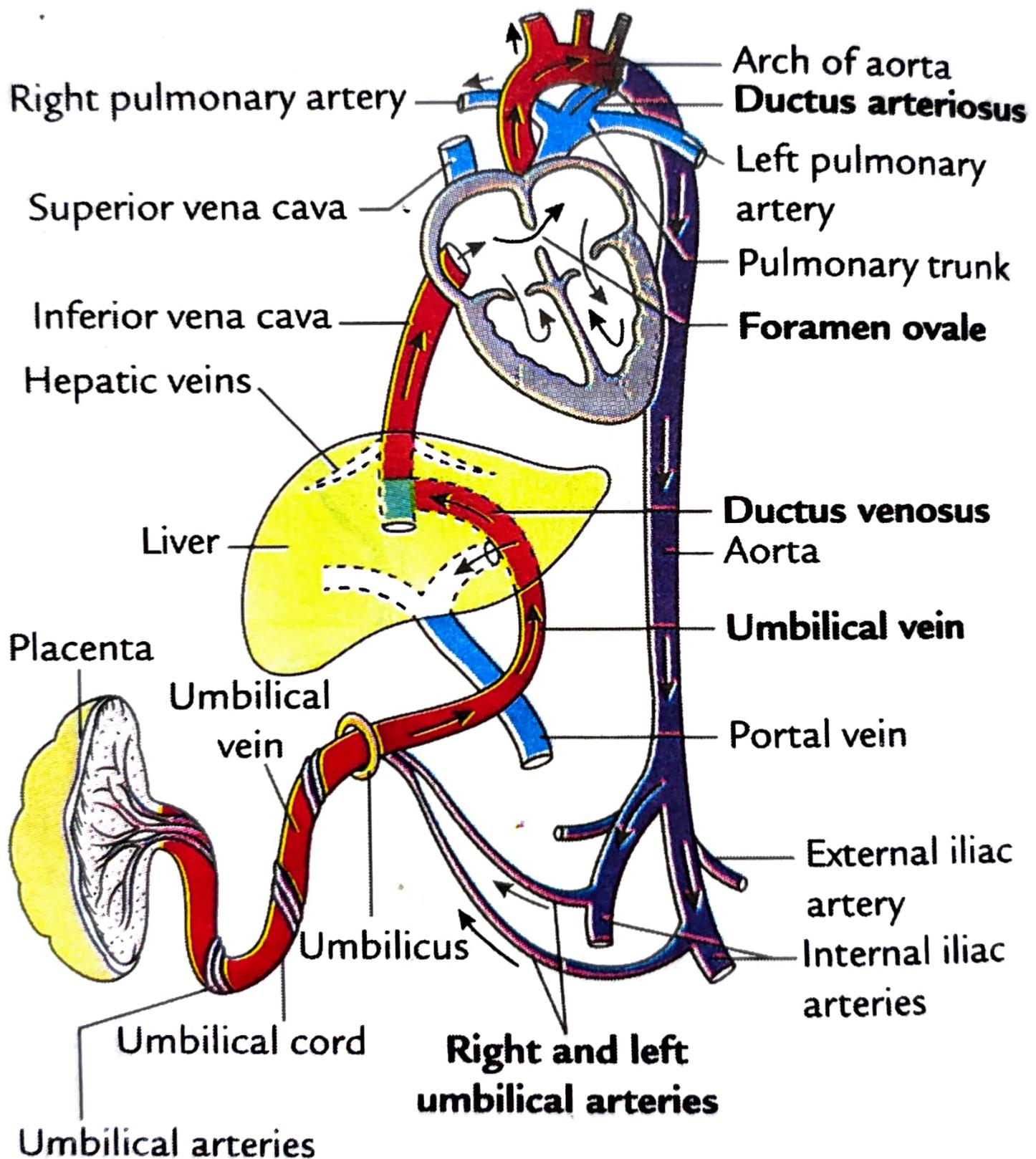
Kidneys, gonads, genital ducts

Lateral plate – Somatic

Body wall, limbs, parietal serosa

Lateral plate – Splanchnic

Heart, vessels, gut smooth muscle



**Fig. 23.25** Fetal circulation.

**Table 10.2 Differences between monozygotic and dizygotic twins**

Monozygotic Twins	Dizygotic Twins
• Form from single zygote	Form from two zygotes
• Incidence is more common	Incidence is less common
• Genetically identical	Genetically not identical
• Twins are of the same sex	Twins are of the same sex or of different sex
• Resemblance is similar	Resemblance is just like any other two siblings
• Mostly have two amniotic sacs, one chorionic sac, with single placenta	Mostly have two amniotic sacs, two chorionic sacs, and two placentas
• Are often called conjoined twins	Not seen as conjoined twins

## Cloaca

The part of hindgut caudal to attachment of allantois is called **cloaca**. It is divided into two parts: ventral and dorsal by a **urorectal septum** (which develops from an angle between the allantois and cloaca).

Ventral part of cloaca is called **primitive urogenital sinus** and dorsal part is called **primitive rectum** (Fig. 24.2).

## Cloaca

- It is a part of primitive hindgut caudal to allantois.
- It is divided into two parts:
  - (a) Primitive urogenital sinus
    - (i) Vesicourethral canal
    - (ii) Definitive urogenital sinus
  - (b) Anorectal canal
- Urinary bladder + primitive urethra (prostatic part above the opening of ejaculatory ducts)
- Remaining urethra except terminal part
- Rectum + upper part of anal canal

In humans, maternal blood is separated from fetal blood by chorionic tissue; hence human placenta is termed hemochorial.

convex areas (lobes) called **cotyledons**. Each cotyledon contains 2–3 anchoring villi. As the pregnancy proceeds, the placenta also enlarges to meet the need of the fetus. At term the placenta covers nearly 30% of the internal surface of the uterus.

## Full-Term Placenta

The fully formed placenta is a disc-shaped compact mass of vascular tissue.

### Features (Fig. 10.11)

- Shape and size: Flat circular disc having a diameter of 15–20 cm, thick in the center (2–5 cm), and thin at periphery.
- Weight: 500–600 g
- Surfaces: Two (maternal and fetal).

**Differences between maternal and fetal surfaces of placenta:** These are given in Box 10.1.

### CLINICAL CORRELATION

After birth, placenta is carefully inspected for missing cotyledons. If the cotyledons remains attached to uterine wall, after birth they may cause severe postpartum bleeding.

## Placental Barrier or Placental Membrane / AN 80.3

The **placental membrane** separates maternal blood from fetal blood within placenta. Thus, there is no mixing of maternal and fetal blood in the placenta.

The intervillous spaces are filled with maternal blood derived from endometrial arteries and drained

by endometrial veins. The chorionic villi contain fetal blood vessels.

The **maternal blood** in the intervillous space is separated from the **fetal blood** within the fetal blood vessels present in the villi by **placental membrane** (also called **placental barrier**) made up of fetal tissue.

It is across this membrane that the exchange of gases, nutrients, and waste products takes place between maternal and fetal blood.

### Constituents of Placental Barrier/Membrane (Fig. 10.12)

#### • In early part of pregnancy

Until about 20 weeks of pregnancy, the placental membrane is thick and made up of five layers. From the maternal side to fetal side, these are:

1. syncytiotrophoblast,
2. cytotrophoblast,
3. basement membrane of cytotrophoblast,
4. mesoderm in the core of villus, and
5. endothelium and basement membrane of fetal capillaries.

#### • In later part of pregnancy

In later part of pregnancy, as the nutritional demands of fetus increases, the placental membrane becomes thin to increase the efficiency of transport of nutrients and gases across it.

Thus, in the early part of pregnancy, i.e., up to 20 weeks, the placental membrane is about 0.025 mm thick, but in the later parts of pregnancy, it remains only 0.002 mm thick.

The placenta is a **fetomaternal organ**. It consists of two components: (a) fetal component and (b) maternal component. The fetal component develops from **chorion frondosum** and the maternal component develops from **decidua basalis**.

## Structural Components of Placenta

The fetal component consists of amnion, extraembryonic mesoderm, chorion, and chorionic villi (made of chorion and *umbilical vessels*), whereas maternal component consists of thin layer of *decidua basalis*, *decidual septae*, *decidual blood vessels* and *blood within placental lacunae*. By the end of 4th month decidua basalis is almost completely replaced by the fetal part of the placenta.

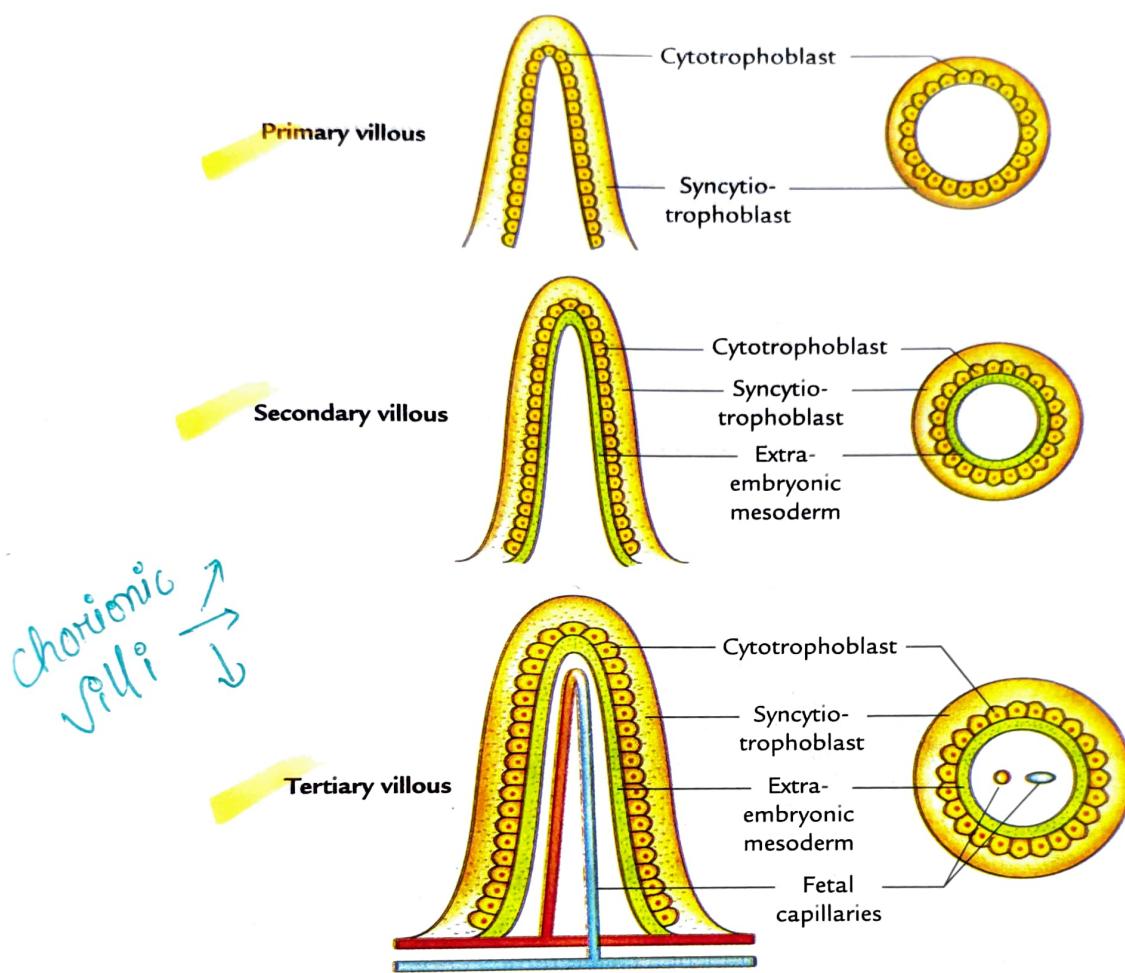
## Functions of Placenta

The placenta subserves the following functions (Fig. 10.14):

1. **Exchange of gases:** This involves supply of O<sub>2</sub> from maternal blood to fetal blood and removal of carbon dioxide (CO<sub>2</sub>) from fetal blood to maternal blood. A full-term fetus takes about 20–30 mL of O<sub>2</sub> per minute from the maternal blood. Therefore, even a short interruption of O<sub>2</sub> supply to the fetus may prove fatal.
2. **Transport of nutrients:** Carbohydrates, fats, proteins, amino acids, vitamins, and electrolytes are transported from maternal blood to fetal blood.
3. **Excretion of waste products** of metabolism like urea, uric acid, etc. into the maternal blood.
4. **Transmission of maternal antibodies:** Maternal antibodies (IgG),  $\alpha$ -globulins, and immunoglobulins can cross the placental barrier and pass from mother to the fetus, and thus provide passive immunity to the fetus against infections/diseases such as diphtheria, measles, and poliomyelitis but not against chicken pox and whooping cough.
5. **Barrier function:** Acts as a barrier to many bacteria and organisms. Some of these or their toxins manage to cross the barrier and may cause fetal defects such

6. Production of hormones and their role in uterine growth and parturition: Placenta also acts as temporary endocrine gland and produces the following hormones:

- Progesterone
- Estrogen
- Human chorionic gonadotropin (HCG)
- Human chorionic somatomammotropin (HCS)
- Human placental lactogen (HPL)
- Relaxin



**Fig. 10.7** Three stages of development of villi. Figures on the right side are the sectional views of three types of villi.

**Table 10.1 Differences in composition of primary, secondary, and tertiary villi**

Types of Villus	Composition
Primary villus	Core of cytотrophoblastic cells covered by a layer of syncytiotrophoblast
Secondary villus	Core of mesoderm covered by a single layer of cytотrophoblast, which in turn is covered by syncytiotrophoblast
Tertiary (definitive) villus	Fetal capillaries appear in the mesodermal core covered by layers of cytотrophoblast and syncytiotrophoblast, respectively

(b) **Zygotene:** In this stage, the lengthwise pairing of homologous chromosomes begins. One of the two homologous chromosomes is from the father (**paternal chromosome**) and the other is from the mother (**maternal chromosome**). This event is called **synapsis** and each synapsing pair is called **bivalent**.

(c) **Pachytene:** This stage is very long and may extend even for years. It is characterized by following changes:

- The chromatids of each chromosome become visible separately. Each bivalent chromosome thus appears to have four chromatids and is called **tetrad**. Each chromatid pair is united

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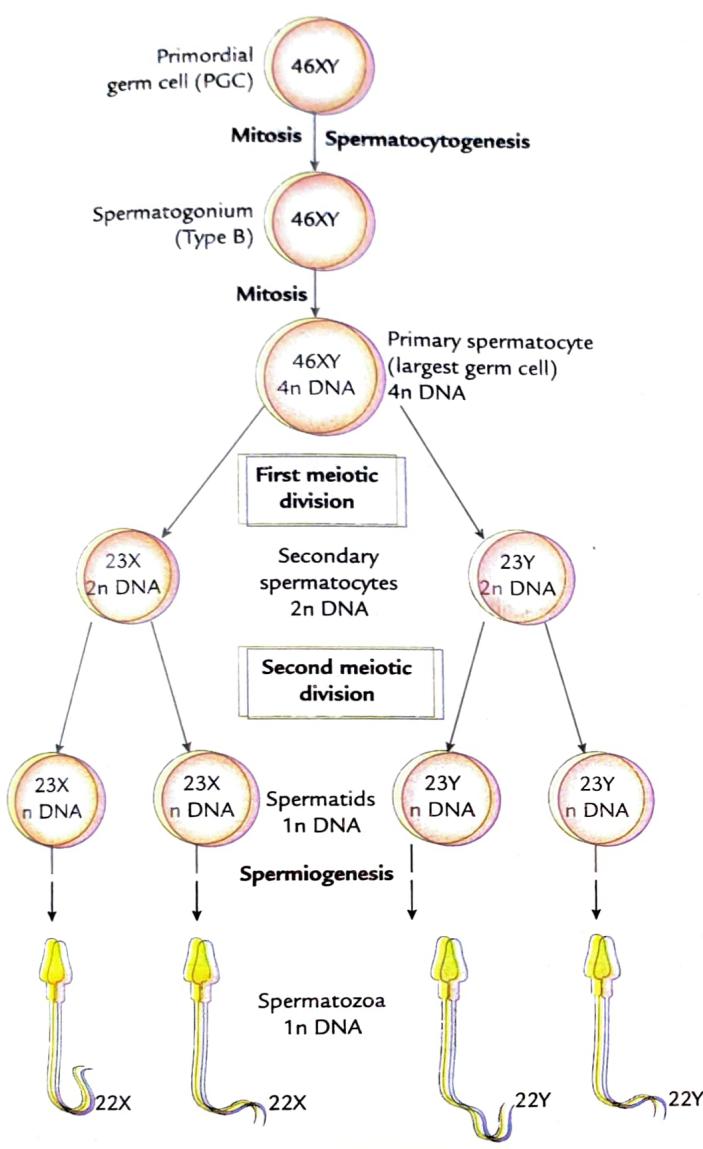


Fig. 4.5 Stages of spermatogenesis.

**N.B.** One primary spermatocyte forms four spermatozoa: two containing X chromosomes and two containing Y chromosomes (Fig. 4.5).

The steps of spermatogenesis are summarized in Flowchart 4.1.

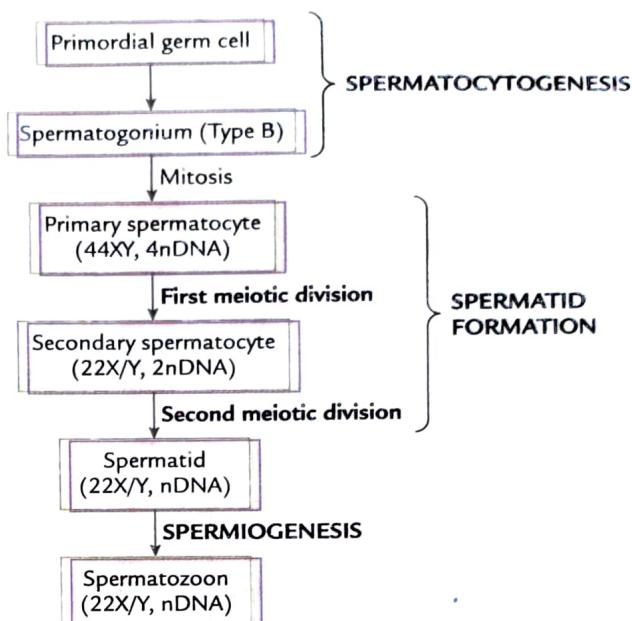
To understand the process of spermiogenesis, the student must first understand the structure of spermatozoon (Fig. 4.6).

### Structure of Spermatozoon (Fig. 4.6)

The spermatozoon (50 microns in length) consists of **head**, **neck**, and **tail**. The tail is further divided into three parts: **middle piece**, **principal piece**, and **end piece**. Tail forms four-fifths of the length.

#### Head

The head of sperm appears somewhat like a spearhead in section. It mainly consists of a **nucleus** that



Flowchart. 4.1 Stages of spermatogenesis.

contains the condensed chromatin material (mostly DNA). Anterior two-thirds of the nucleus is covered by an **acrosomal cap** that contains various enzymes including **hyaluronidase** and **acrosin**.

#### Neck

The neck is narrow. It contains a funnel-shaped **basal plate** and a **centriole**. The centriole gives rise to axial filament that extends throughout the tail.

#### Tail

The tail consists of three parts: middle piece, principal piece, and end piece.

1. **Middle piece:** It contains the axial filament in the center, which is surrounded by spirally arranged mitochondrial sheath. At the distal end of the middle piece there is a ring-like structure through which axial filament passes. It is called *annulus* and is derived from the other centriole.
2. **Principal piece:** It is made of axial filament covered by seven outer dense fibers.
3. **End piece:** It is made of only the axial filament.

#### N.B.

- Structure of the axial filament is very similar to that of the cilium.
- The whole spermatozoon is covered by plasma membrane.

Figure 4.6 shows parts of the mature sperm (on the left) and sections through head, neck, middle piece, principal piece, and end piece along with their composition (on the right).

**N.B.** The axial filament is responsible for the movements of the spermatozoon, while mitochondria supply energy for these movements.

## SPERMIogenesis

The process by which the spermatids are transformed into mature spermatozoa is known as spermiogenesis.

### Process of Spermiogenesis (Fig. 4.7)

The spermatid is more or less a circular cell containing a nucleus, Golgi apparatus, centrosome, and mitochondria. The spermatid is transformed into the spermatozoon as follows:

1. Nuclear material (chromatin) gets condensed and the **nucleus** moves toward one pole of the cell to form the **head of the spermatozoon**.
2. **Golgi apparatus** forms the **acrosomal cap** that covers anterior two-thirds of the nucleus.
3. **Centrosome** divides into **two centrioles**. One centriole becomes spherical and moves toward the posterior end of nucleus to occupy the neck region. It gives rise to the **axial filament**. The other centriole moves away from the first centriole and becomes ring shaped. It forms an **annulus/ring around the distal end of the middle piece** through which axial filament passes.

4. The part of the axial filament between the neck and annulus becomes surrounded by the mitochondria, and together with them forms the middle piece.
5. The remaining part of the axial filament elongates to form the principal and end pieces of tail. Most of the cytoplasm of spermatid is shed off but the cell membrane remains, which covers the entire spermatozoon.
6. Sheding off most of the cytoplasm (residual cytoplasm).

The structural components of the spermatid and the spermatozoon are compared in Table 4.2.

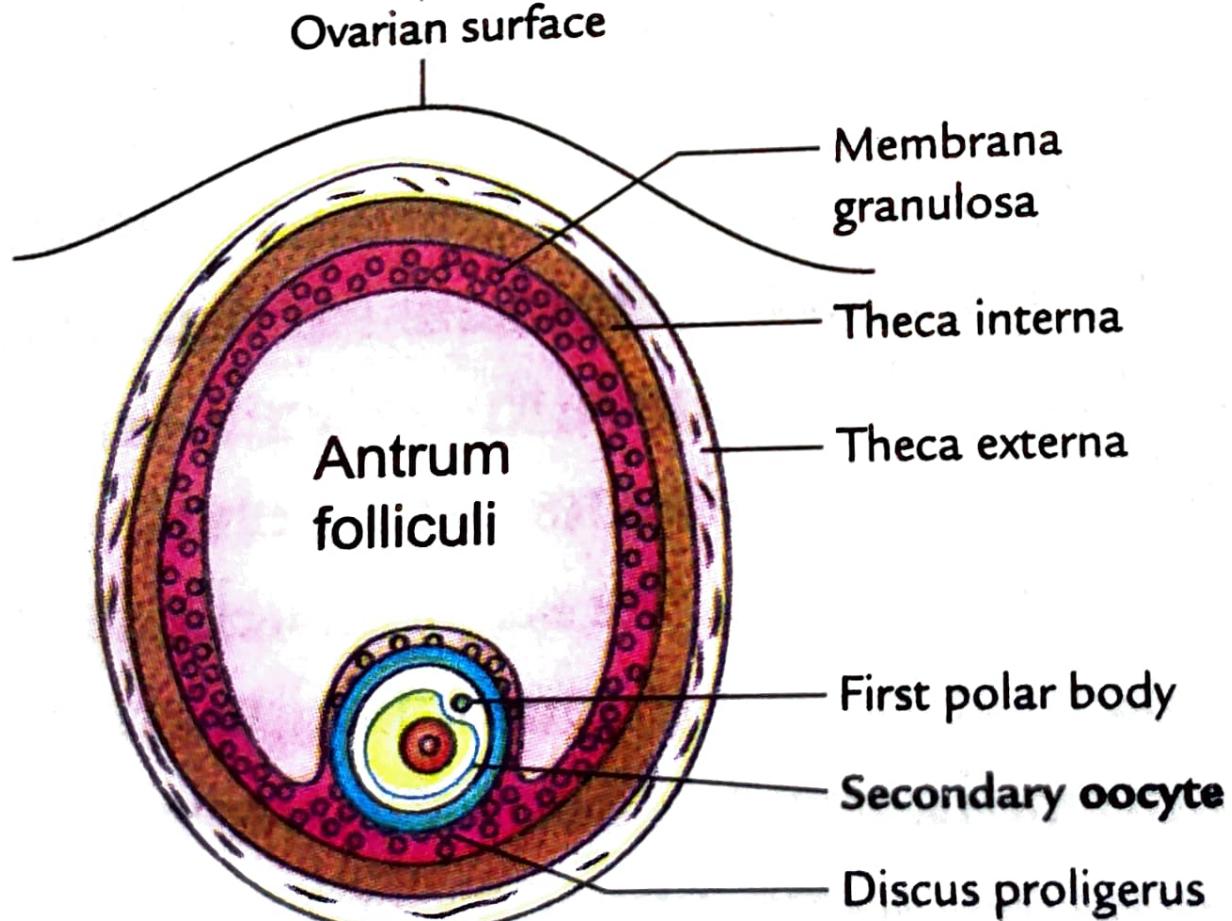
### CLINICAL CORRELATION

#### Abnormal sperms

The abnormality of sperms is common as compared to the oocytes. Morphologically, for clinicians, the sperm consists of two parts of head and tail.

Sperm abnormalities can be categorized as follows:

1. **Morphological abnormalities** (Fig. 4.8):
  - (a) Head and tail of sperms may be abnormal (i.e., two heads, two tails)



**Graafian follicle**

Fig. 4.18 Development of ovarian follicles

## **Meiosis (Fig. 4.3)**

The meiosis is a special type of cell division that takes place only in the germ cells to produce male and female gametes. The meiosis consists of two cell divisions that take place one after the other.

(a) **First meiotic division (meiosis I or reductional division):** In this division, the number of chromosomes of the daughter cells is reduced to half of the mother cell.

(b) **Second meiotic division (meiosis II):** It is the mitotic division similar to the one described above except that there is no duplication of DNA during short interphase.

## GENES

Gene, a *functional unit of DNA*, is the unit of inheritance. The term “**gene**” was coined by Johannsen (1909). *The properties of gene include:*

1. To determine traits, e.g., color of skin, intelligence, and height
2. To undergo replication
3. To undergo mutation

About 50,000–100,000 genes are present in the **human genome**; out of these, about 450 genes are linked to human diseases.

**Table 29.3 Differences between Klinefelter and Turner syndromes**

<b>Klinefelter Syndrome</b>	<b>Turner Syndrome</b>
Trisomic condition found only in males	Monosomic condition found only in females
Chromosomal complement in somatic cells is 47XXY	Chromosomal complement in somatic cells is 45XO
Affected individuals are phenotypically males	Affected individuals are phenotypically females
Long stature	Short stature

## Location of Genes

Each gene occupies a specific **locus** on a chromosome. Both chromosomes of a given pair contain similar genes. The two homologous chromosomes of a pair contain alleles of same genes occupying the same locus. If two allelic genes are identical, the person is **homozygous** for the trait specified by that gene locus. For example, ability to roll one's tongue is coded on a single gene. Since one chromosome of each pair is inherited from father and one from mother, an individual has two genes controlling the ability to roll the tongue. Such paired genes are **alleles**.

## **1. Numerical chromosomal abnormalities affecting autosomes**

(a) **Down syndrome (mongolism) or trisomy 21:** In this disorder, there are three copies of chromosome 21 (trisomy 21), i.e., there is an extra chromosome 21. The karyotype of patient is  $47XY + 21$ .

The trisomy 21 is of two types:

- (i) **Triple-21 (nonfamilial mongolism):** It is common and the affected babies possess 47 chromosomes, including two X chromosomes. It occurs during meiosis due to non-disjunction of 21st pair of chromosomes.
- (ii) **Translocation mongolism (familial mongolism):** In this, an individual possesses 46 chromosomes. In this condition, the extra chromosome becomes attached to one of the other autosomes.

The Down syndrome occurs 1 in every 700 births (1/700).

9. **Gastrulation:** Formation of three germ layers (ectoderm, mesoderm, and endoderm) in the embryo.
10. **Neurulation** (Gr. *Neuron* = nerve): The process by which neural plate forms the neural tube. The embryo at this stage is called *neurula*.

# OVERVIEW

Study of development of the nervous system helps to understand its complex organization and occurrence of various congenital anomalies.

The nervous system develops from ectoderm following induction from notochord.

The specific cell population of early ectoderm, which gives rise to entire nervous system and special sense organs, is termed **neural ectoderm**. The neural ectoderm later differentiates into two structures: neural tube and neural crest cells. The **neural tube** gives rise to the central nervous system (CNS) while **neural crest cells** form nearly entire peripheral nervous system.

## NEURULATION (FORMATION OF NEURAL TUBE) (FIG. 26.1)

AN 64.2

It involves the formation of **neural plate** from ectoderm above notochord and folding of neural plate to form **neural tube**.

In early embryonic disc, at about 16th day of embryonic life, the ectoderm overlying the newly formed notochord thickens in midline forming **neural plate**. Initially the neural plate is flat and slipper shaped with narrow end toward the primitive node. The somatic mesoderm develops on either side of the notochord. The margins of neural plate are elevated as **neural folds**. As a result, center of the plate sinks, creating **neural groove**. The neural folds gradually move together

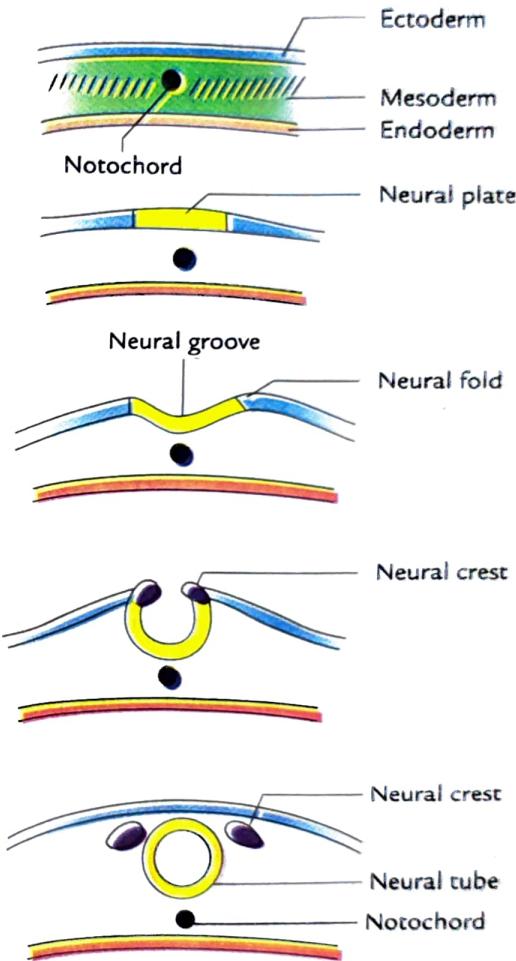


Fig. 26.1 Formation of neural tube and neural crest.

toward the midline and finally fuse to form a cylindrical **neural tube** that loses its connection with the surface ectoderm. The process of neural tube formation is termed **neurulation**.

The fusion of neural folds begins in the middle (region of fourth somite on 20th day of embryonic development) and it simultaneously proceeds in the cephalic and caudal directions. The fusion at the cranial and caudal ends of neural tube is somewhat delayed, forming small openings called **anterior** and **posterior neuropores**. The neural tube and overlying amniotic cavity, therefore, remain temporarily in open communication with each other through these pores. The anterior neuropore closes earlier, in the middle of the 4th week at 18- to 20-somite stage (i.e., on 25th day), and the posterior neuropore closes later at the end of 4th week at about 25-somite stage (i.e., on 27th day). By the time the neural tube is completely closed, it is divided into an enlarged cranial part and an elongated caudal part, which later on give rise to the **brain** and **spinal cord**, respectively.

### **Secondary Neurulation**

The secondary neurulation forms the caudal part of spinal cord distal to S2 spinal segment and the filum terminale.

The **secondary neurulation** begins on day 27, in tissue located within caudal cell mass (representing **Hensen's node**) present caudal to the posterior neuropores at the caudal end of embryo.

First, small tubules form within this tissue (caudal cell mass) which coalesce to form **secondary neural tube**. The secondary neural tube eventually fuse with the neural tube (vide supra).