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Major: Natural Sciences

Lessons of Embryology

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Contents

Figures list

Tables list

Introduction

I am honored to present this polycopy: Lessons in Embryology, which is the study of the development of embryos from the fertilization of the egg cell by sperm to the formation of a complete organism. These lessons are aimed at first-year students of middle and secondary school teacher in the Higher Normal School of Technological Education of Skikda. According to the approved program, I have divided the content into 12 main chapters. The first three chapters cover male and female reproductive functions and their neurohormonal regulation. Chapters four through eight study the stages of fetal development from fertilization to the fourth week, focusing on the most important stages and changes that occur during this period.

Chapters nine and ten are dedicated to the final development of both appendages and Three Embryonic Germ Layers. Chapter eleven discusses the features of the fetus during the first and last months of uterine life, in addition to childbirth. The final chapter addresses the most important anomalies in fetal development. These lessons are reinforced with schematic drawings and real images to facilitate understanding and simplify the concepts.

Sex cells are formed: sperm at the level of the male reproductive system (in large numbers and continuously) and eggs at the level of the female reproductive system (one periodically). After fertilization, when the sperm enters the reproductive tract and reaches the fallopian tube, fertilization occurs, which is the fusion of the nuclei of the sperm and egg, resulting in a fertilized egg, or zygote. The zygote undergoes successive divisions known as cleavage to form a group of cells that differentiate into three germ layers: ectoderm, mesoderm, and endoderm, From these germ layers, all tissues and organs of the body develop (organogenesis).

The study of fetal development is divided into three stages: the pre-embryonic stage, fertilization, and embryonic development.

1. Pre-embryonic stage: This includes the study of reproductive organs and the formation of sex cells (gametogenesis).

2. Fertilization: It is the union of the male gamete or sperm with the female gamete or egg to form a fertilized egg.

3. Embryonic development: Embryonic development is divided into two stages: the stage of embryonic formation (embryogenesis) and the stage of organ formation (organogenesis).

3.1. Embryogenesis phase: This stage of embryonic formation involves the initial formation of organ primordia and is further divided into three phases:

3.1.1. Pre-morphogenetic phase: This phase involves segmentation and the sequence of events during the first week of embryonic development. The fertilized egg undergoes a series of cleavages to produce cells called blastomeres, which organize into a compact mass called a morula. After the appearance of a cavity (blastocoele) inside it, the morula transforms into a blastocyst.

3.1.2. Primary morphogenetic phase: This phase corresponds to implantation and the temporary formation of the two germ layers (pre-gastrulation) and then the three definitive germ layers (gastrulation). Beginning in the second week of pregnancy, the blastocyst implants into the uterine lining, and the embryo becomes bilaminar (with an inner and outer layer) from day seven until day 16 of pregnancy, known as the pre-gastrulation. The period of gastrulation involves the establishment of the third germ layer, the mesoderm, in the third week of pregnancy. This is quickly followed by neurulation or the formation of the central nervous system.

3.1.3. Secondary morphogenetic phase: This phase corresponds to the establishment of the basic organ primordia and closure of the embryonic ventral region. It is also considered a transitional stage between embryonic formation (Embryogenesis) and organ formation (Organogenesis). This phase mainly involves:

- Individualization of the fetus, taking on its final shape.
- Development of the nervous system, which begins during the third week and ends around day 29.
- Appearance of metameric segments (somites) at the level of the trunk.
- Formation of the organ primordia during the individualization of the fetus.
- All of these stages occur during the first month (four weeks) of embryonic development, followed by the organogenesis stage.

3.2. Organogenesis stage: This stage begins from the end of the fourth week until the end of the second month of embryonic development, followed by the fetal period or the tissue formation stage (Histogenesis). During organogenesis, the structural development of various organs becomes apparent.

As pregnancy approaches its end, several processes occur, leading to childbirth and the expulsion of the placenta. The fetus moves towards the cervix, and with the assistance of abdominal muscles, it is delivered from the uterus. Shortly after delivery, the placenta is expelled

Before starting the 12 chapters, it's important to present some important and necessary definitions for the science of embryology in general:

- The embryo at various stages of development is referred to using three terms:

- **Germ:** Corresponds to the initial stages of development while the external form is more or less spherical.
- **Embryo:** Corresponds to the stage from which a recognizable overall form appears. This term is used during the first 8 weeks of development.

- **Fetus:** Corresponds to the stage from which the embryo begins to resemble a living being (from the 60th day onwards). This term is used after the 8th week until the end of gestation.

- Development: is the gradual modification of anatomical structures of embryo during the period from conception to maturity.

- The sections used in the study of embryonic development are primarily longitudinal sections and transverse sections (Figure 1):

- **Longitudinal sections include:**
- ✓ **Median sagittal sections:** These sections pass through the axis of symmetry in the embryo, providing two equal sections.
- ✓ **Para-sagittal sections:** These sections are parallel to the median sagittal section.
- **Transverse sections:** These sections can pass through any level in the embryo, remaining perpendicular to the longitudinal sections.

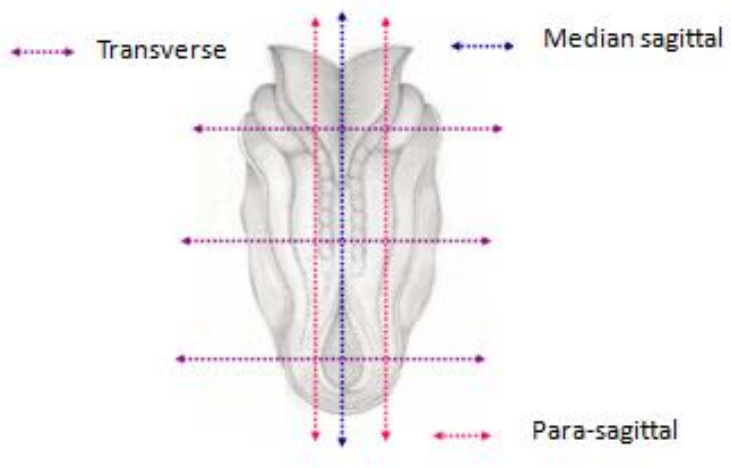

Figure 1: Different types of sections.

Chapter One: Male Sexual Function

1. Male genitalia: The group of organs and pathways responsible for the function of reproduction, which ensures the production, transport, nourishment, and storage of male germ cells or sperm, as well as their delivery into the female reproductive tract during mating. The male reproductive system can be divided according to the pathway of sperm into: the testes, the spermatic ducts, the accessory glands, and the penis (Figure 2).

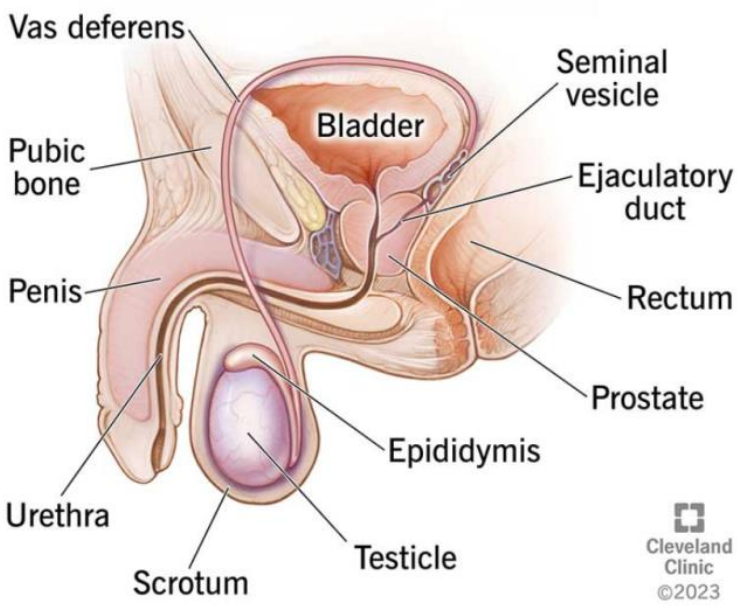

Figure 2: Male genitalia.

1.1. Testes: A dual organ, housed within a skin pouch called the scrotum. Which is a flexible and contractile sac that contains sebaceous and sweat glands, as well as a layer of fibrous and elastic tissue. This layer divides the scrotum into two compartments, each containing one testis. The primary function of this sac is to carry the testes outside the body because sperm production requires a lower temperature than that of the body, typically 2 to 3 degrees Celsius lower. The muscular fibrous layer assists in either bringing

the testes closer to or moving them away from the body through contraction and relaxation, responding to external temperature conditions. Each testis is approximately 3-5 cm in length, 2-3 cm in height, 2.5 cm in width, and weighs between 15-25 grams. The surface of the testis is covered by dense fibrous tissue called the Tunica albuginea, which forms intermediate extensions (Septa) dividing the testis into 200 to 300 testicular lobules. The Tunica albuginea extends into the testis to create the mediastinum testis (Highmore). Each lobule contains 2 to 4 seminiferous tubules, which are responsible for sperm production (Figure 3). The testis is considered a mixed gland. The inner part of secretion involves Leydig cells, which are situated in masses within the spaces between the seminiferous tubules and secrete the testosterone. The outer part of secretion involves the production and release of sperm into the lumen of the seminiferous tubules.

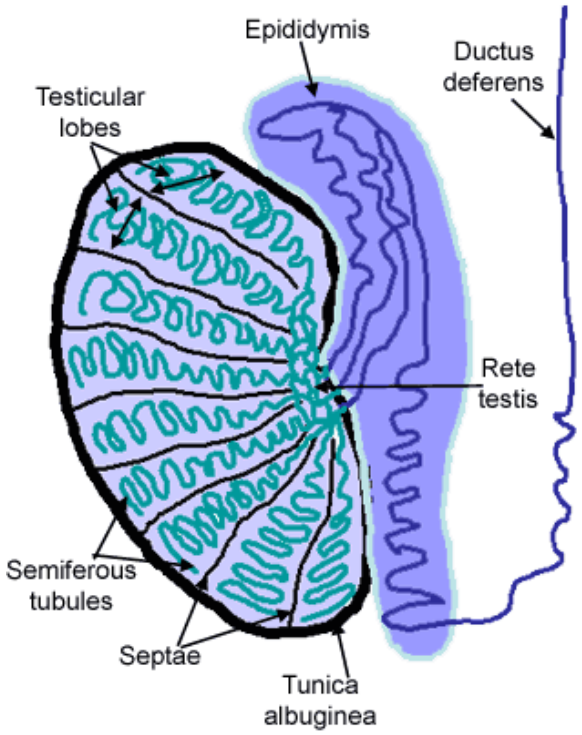

Figure 3: Structure of testis.

The two testes in a male fetus initially develop inside the abdomen. They then descend under the influence of the male sex hormone (testosterone) through the

inguinal canal. As the fetus grows, they continue to descend until they fully emerge into the scrotum during the eighth month of embryonic life (Figure 4).

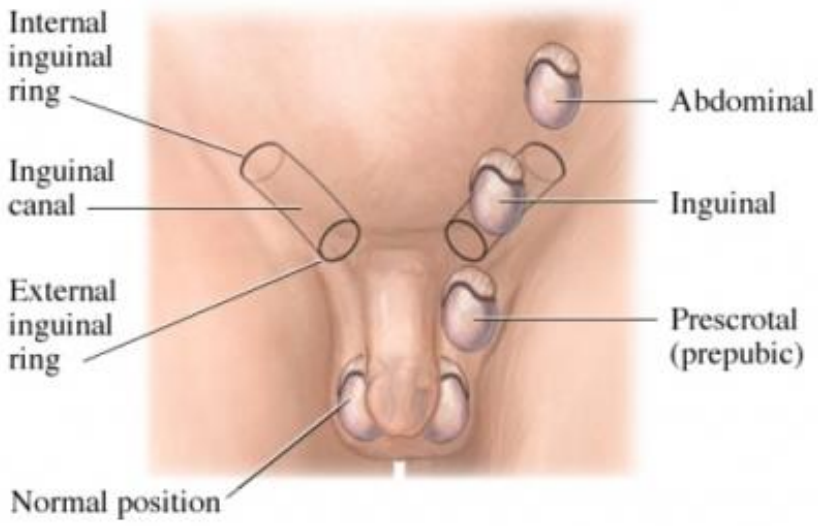

Figure 4: Descendance of testes.

After the descent of the testes, the inguinal canal narrows, allowing only the passage of structures like the vas deferens, which joins with arteries, veins, and nerves to form the spermatic cord (Figure 5).

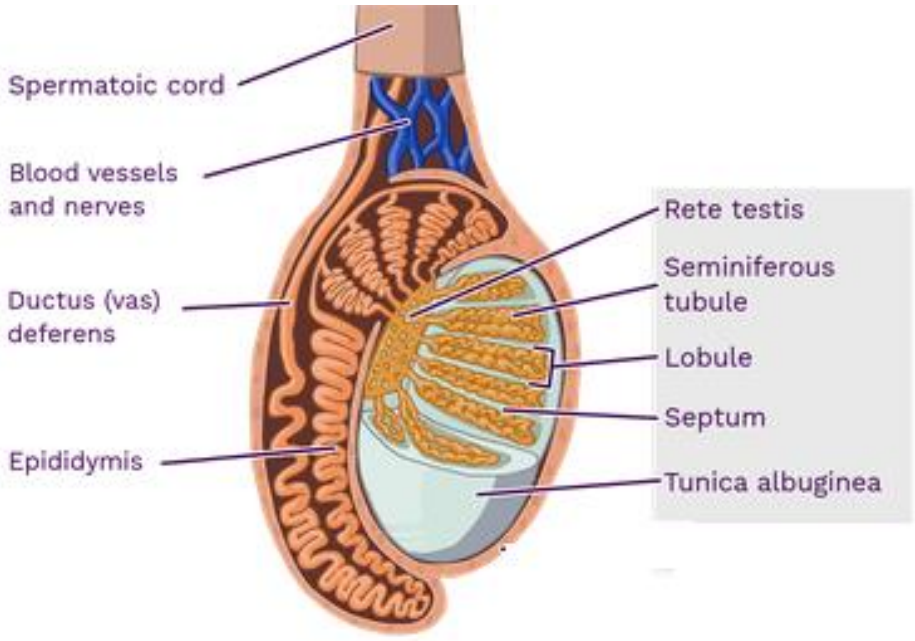

Figure 5: Spermatic cord.

1.2. Spermatic pathways: The area where sperm production and secretion take place is called the male reproductive tract. This system begins with the seminiferous tubules in the testes, where sperm production occurs, and it ends at the opening of the penis.

a. Internal spermatic pathways: The internal spermatic pathways consist of the seminiferous tubules, the rete testis, and the ductus epididymis. The seminiferous tubules are responsible for sperm production and lead directly into the straight tubules, which in turn terminate in the rete testis (Figure 6).

- Seminiferous tubules: These are blind tubes, blocked at one end and open at the other end, connecting to the straight tubules at the level of the mediastinum testis. Each one of these tubules, has a length ranging from 30 to 70 cm and a diameter of 150 to 250 microns. It is lined with a basement membrane made of connective tissue that contains smooth muscle cells, aiding in the movement of sperm. The lining of these tubules is the seminal epithelium, where spermatogenesis takes place. The seminal epithelium consists of two types of cells: germ cells in various stages that eventually develop into sperm, and larger pyramidal-shaped support cells called Sertoli cells. They provide protection, support, and nourishment to the germ cells. These tubules are distributed in several lobules, and each tubule terminates in a straight portion.

- Straight tubules: These are the fine tubes found in the lobules of the testes, with a length of 1-2 mm and lined with cuboidal epithelial tissue. They originate from the seminiferous tubules and terminate in the rete testis. Each straight tubule receives 5-6 seminiferous tubules.

- Rete testis: They form a tangled group of tubules, originating from the union of the straight tubules at the mediastinum testis, and are lined with cuboidal epithelial tissue.

b. External spermatic pathways: These pathways ensure the transport of sperm and consist of the efferent ductules, the epididymal duct, the ductus deferens (Figure 6), and the ejaculatory duct.

- Efferent ductules: These are convoluted ducts, numbering approximately 12-15 canals that exit from the center of the testis and ascend to converge into a single canal known as the rete testis.

- Epididymal duct: It is a single, coiled tube that wraps around the upper and side surfaces of the testis. When stretched out, its length can reach up to 6 meters, with a diameter of 4 mm. This tube is divided into three parts: the head, which is located at the front of the testis, the body, which is situated on the upper edge of the testis, and the tail, from which the ductus deferens emerges. The lumen of the epididymal duct narrows in the head region and widens as you move towards the tail, aligning with the tail's primary function, which is the storage of sperm. The epididymis serves several functions, including:

- ✓ Secretion of specific substances in the head of the epididymis from the lining epithelial cells to nourish and activate sperm (such as glycogen).
- ✓ Sperm storage site (in the tail of the epididymis).
- ✓ During the storage period, sperm complete their final maturation stages by shedding their cytoplasmic droplet. They also lose their ability to fertilize an egg by acquiring a protein coat, where a glycoprotein substance deposits on the head of the sperm to protect the acrosome until they are released into the female reproductive tract (during ejaculation).
- ✓ The epididymis acts as a graveyard for sperm that were not ejaculated or did not exit with urine.

- Vas deferens: The ductus deferens, also known as the vas deferens, continues upward in parallel to the longitudinal axis of each testis. It increases in size and wall thickness, becoming rich in smooth involuntary muscle, forming what is called the vas deferens, known for its firmness. A single ductus deferens exits from each testis, ascending to the abdomen, where it expands to join the seminal vesicle. The length of this duct measures 35-45 cm, and it has a diameter of 2 mm.

- Ejaculatory duct: It connects to the prostatic urethra and opens into the urinary tract, with a length of 2 cm. The ejaculatory duct is responsible for the release of the sperm-laden seminal fluid into the prostatic urethra.

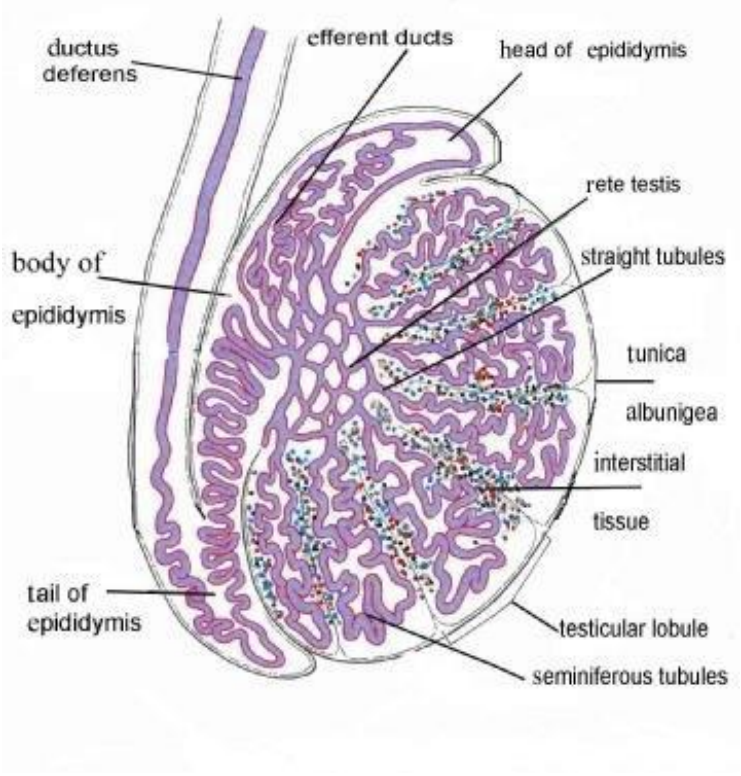

Figure 6: Internal and external spermatic pathways.

1.3. Accessory glands: These are external accessory glands that secrete the seminal fluid, which serves as a carrier and nourishment for sperm and, in addition to the epididymal secretions and sperm, forms the semen. This fluid is

discharged into the described pathways above. The wall of these glands consists of involuntary smooth muscles. These glands typically include:

- Seminal vesicles: These are a pair of glands located behind the bladder. Each vesicle is lobulated and opens into the terminal part of the ejaculatory duct. Their function is to secrete a portion of the seminal fluid responsible for nourishing sperm, which is particularly rich in fructose, prostaglandins, and peptide hormones. This fluid makes up more than 50% of the volume of ejaculated semen (Figure 7).

- Prostate gland: This is a single, cluster-like gland located at the base of the bladder, with a weight of 20-25 grams. It is crossed by the ejaculatory ducts, where they meet and converge into the prostatic urethra, which is the common canal for both urine and semen. The prostate gland has both secretory and mechanical functions. It manufactures a portion of seminal fluid and contains muscular structures that allow the passage of both urine during urination and sperm during ejaculation. The fluid secreted by the prostate gland contains very high concentrations of minerals, particularly zinc, which plays a crucial role in protecting sperm plasma against bacteria. It also contains calcium, magnesium, potassium, and spermine, which imparts the distinctive odor to semen (Figure 7).

- Bulbourethral or Cowper's glands: These are small in size, composed of a pair of glands located on each side of the prostatic urethra. Their primary function is to secrete viscous substances that are directly deposited into the urethra. These secretions serve to wash the male reproductive and urinary tract of any residual urine remnants, which may have harmful effects on sperm during ejaculation (Figure 7).

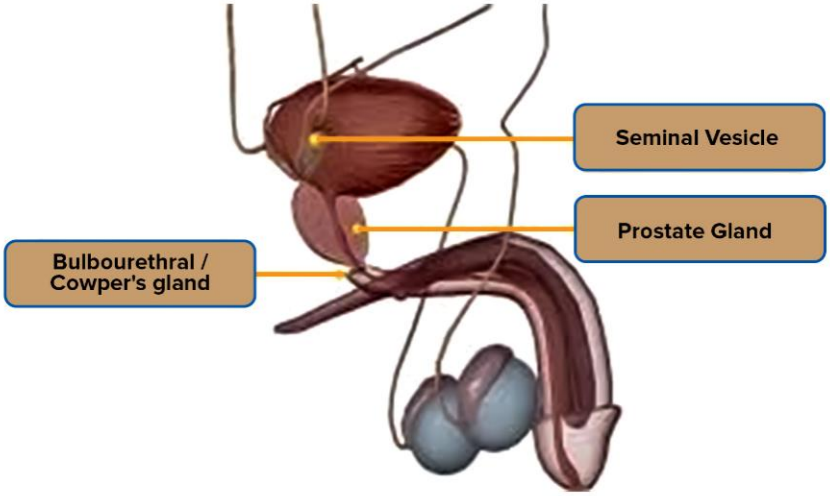

Figure 7: Accessory glands.

1.4. Somatic cells:

- Sertoli cells: They extend from the base of the seminiferous tubule to its lumen, anchoring to the basal membrane. Their apices face the lumen of the seminiferous tubule (Figure 8). These cells fill the spaces between the germ cells, and their cytoplasm is rich in glycogen, proteins, and lipids. They contain large and pale nuclei near the basal membrane. Sertoli cells have several important functions, including nourishing sperm, engulfing excess cytoplasmic bodies in sperm, releasing proteins into circulation related to hormone transport, such as Androgen Binding Protein (ABP) responsible for testosterone transport, releasing Inhibin that plays a regulatory role of FSH, and also secreting a hormone that inhibits the Muller canal (Anti Mullerien Hormon or AMH) during fetal life.

- Leydig cells: These are spindle-shaped or spherically shaped cells with round, prominent, and clear nuclei. They have a single, large, and distinct nucleus. These cells occupy the spaces between the seminiferous tubules alongside connective tissue where blood vessels run (Figure 8). They release testosterone, a hormone produced from cholesterol.

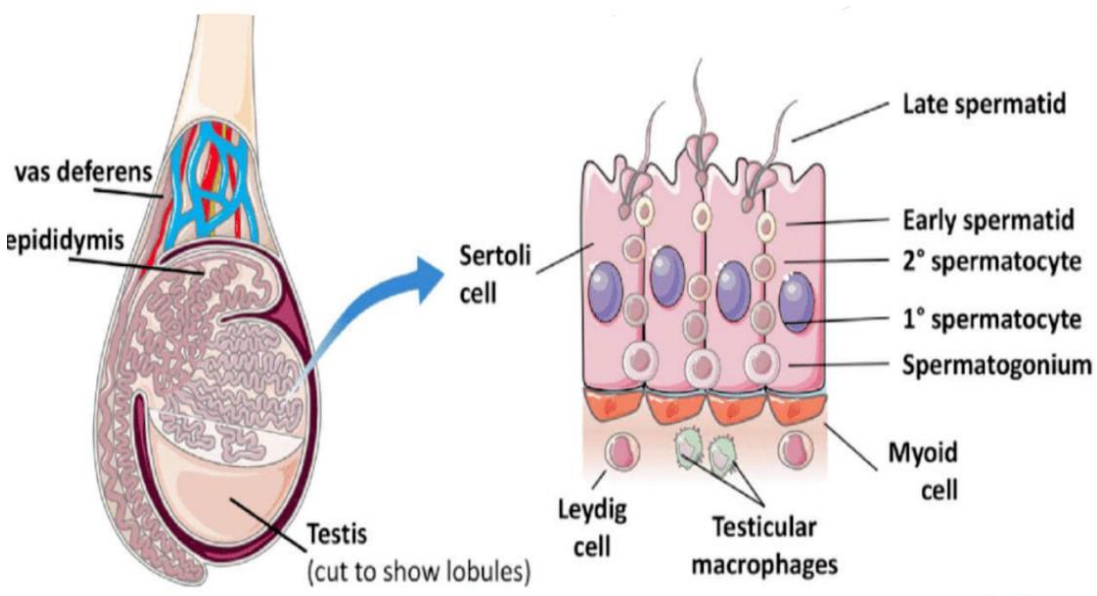

Figure 8: Somatic cells.

1.5. Penis: This is the common canal through which both urine and semen exit the body during ejaculation. It is also the male reproductive organ responsible for sexual intercourse. The male genitalia comprises erectile tissues that enable erection, and there are two types of these tissues (Figure 9):

- **Corpus Spongiosum**: This tissue surrounds the urethra and plays a role in maintaining its patency during erection. It also helps propel semen during ejaculation.

- **Corpus Cavernosa:** These are two cylinders extending from the branches of the pubic bone, and they fill with blood during arousal to create an erection. The expansion of the corpus cavernosa causes the penis to become erect. Together, these erectile tissues enable sexual function and are crucial for both urination and ejaculation.

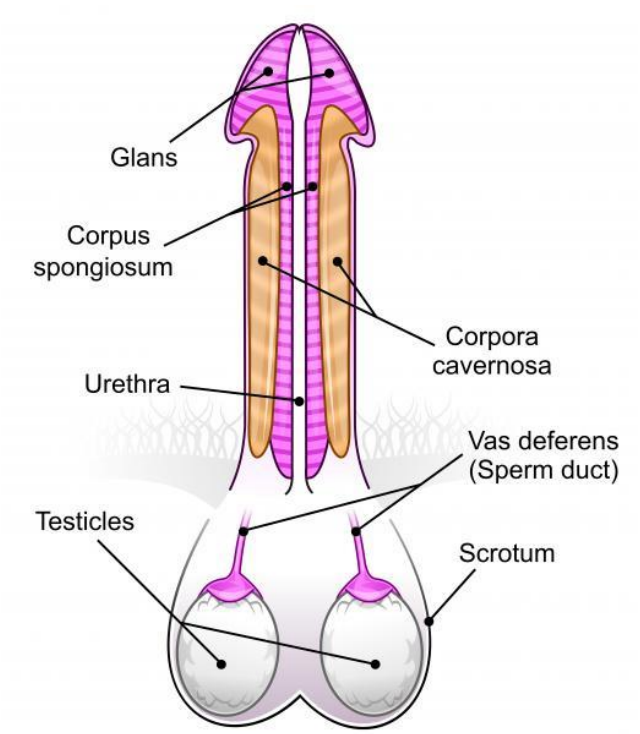

Figure 9: Structure of Penis.

2. Sperm cell or spermatozoa: is a motile cell with a length of approximately 60 µm. Its lifespan typically ranges from 48 to 72 hours. It consists of three main parts (Figure 10):

- Head: It is oval and flattened, containing a condensed nucleus that primarily contains DNA and associated proteins. At the top of the head is the acrosome, which is responsible for assisting in the fusion of the sperm with the egg during fertilization. The acrosome contains enzymes that help dissolve the egg's membranes.

- Midpiece: It is the region between the head and the tail. It contains the mitochondria, which are essential for providing energy for the sperm's movement and the initiation of events that lead to egg division following fertilization.

- Tail: It is the longest part of the sperm and is responsible for its movement, facilitating fertilization. It contains proteinaceous fibers that are contractile

and composed of actin and myosin. These fibers are responsible for the whip-like motion that propels the sperm forward.

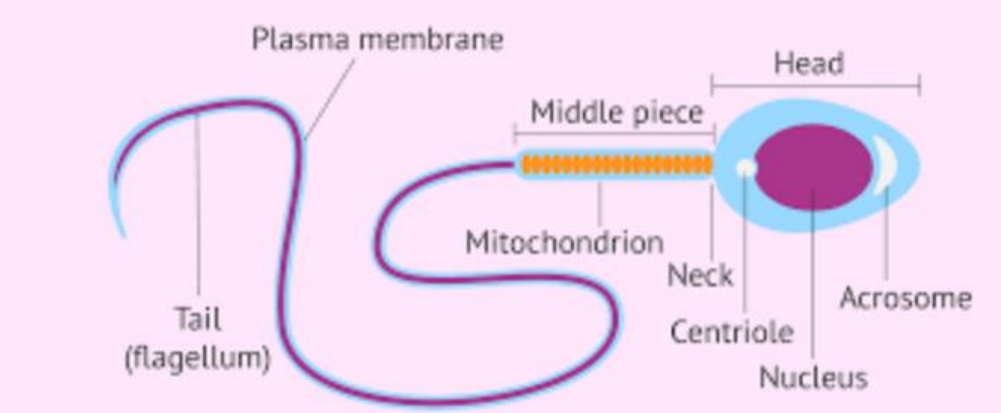

Figure 10: Sperm cell or spermatozoa parts.

3. Semen: This is the result of ejaculation and contains both sperm and seminal fluid, which includes secretions from the accessory glands such as the seminal vesicles, prostate gland, and Cowper's glands (Figure 11). Semen is a viscous, dense, slightly yellowish fluid with a distinctive odor. It has a slightly alkaline pH of around 7.2-7.8. The total volume of ejaculate typically ranges from 2 to 6 milliliters, with about 10% being sperm and the remaining 90% consisting of seminal fluid. The seminal fluid produced by the accessory glands plays a crucial role in nourishing and transporting sperm, as well as facilitating their movement. In a single milliliter of semen in humans, you can find approximately 20-250 million sperm, of which at least 80% should exhibit normal size and appearance under normal conditions.

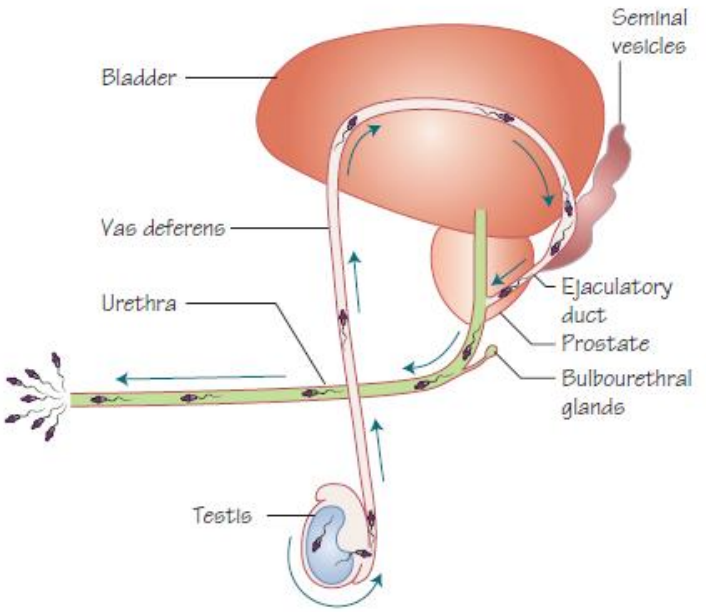

Figure 11: Semen pathway.

4. Spermatogenesis: The formation of sperm occurs through a series of stages in which the original sperm cells, known as spermatogonia, undergo a process. These spermatogonia are diploid cells, meaning they have a double set of chromosomes, and eventually transform into mature sex cells or spermatozoa, which are haploid cells with a single set of chromosomes capable of fertilization. Sperm formation takes place continuously and permanently within the seminiferous tubules in the testes, with a duration of approximately 74 days in humans. It is devided to 4 phases (Figure 12):

4.1. Multiplication Phase: Duration: 27 days; Spermatogonia undergo mitotic divisions. Dark chromatin (Ad) spermatogonia divide, giving rise to two daughter cells: Ad cell, identical to the mother cell for the renewal of original sperm cells, and another cell (Ap) with pale chromatin, somewhat different from the mother cell. The Ap cell further divides to produce B spermatogonia. Division of spermatogonia B occurs through regular mitotic divisions, resulting in two primary spermatocytes with a diameter of about 25 microns.

4.2. Growth Phase: The size of first-order spermatocytes increases, with an increase in cytoplasmic volume in preparation for entering the equatorial division phase.The diameter becomes approximately 25 µm with a duration of 23 days.

4.3. Maturation Phase: First-order spermatocytes (Spermatocytes I) enter the first stage of equatorial division (Meiosis), a reductional division. Each first-order spermatocyte (Spermatocyte I) produces two second-order spermatocytes (Spermatocytes II) with 1N chromosome and double DNA content. One of these contains a sex chromosome X, and the other a sex chromosome Y.

Second-order spermatocytes (Spermatocytes II) are rarely found in anatomical sections due to their short lifespan (24 hours).They quickly mature, undergo equational division in the second meiotic phase, resulting in spermatids. The brief duration of this phase is attributed to the non-duplication of DNA during the second prophase. Each second-order spermatocyte produces two spermatids, each with 1N chromosome and the same DNA content.

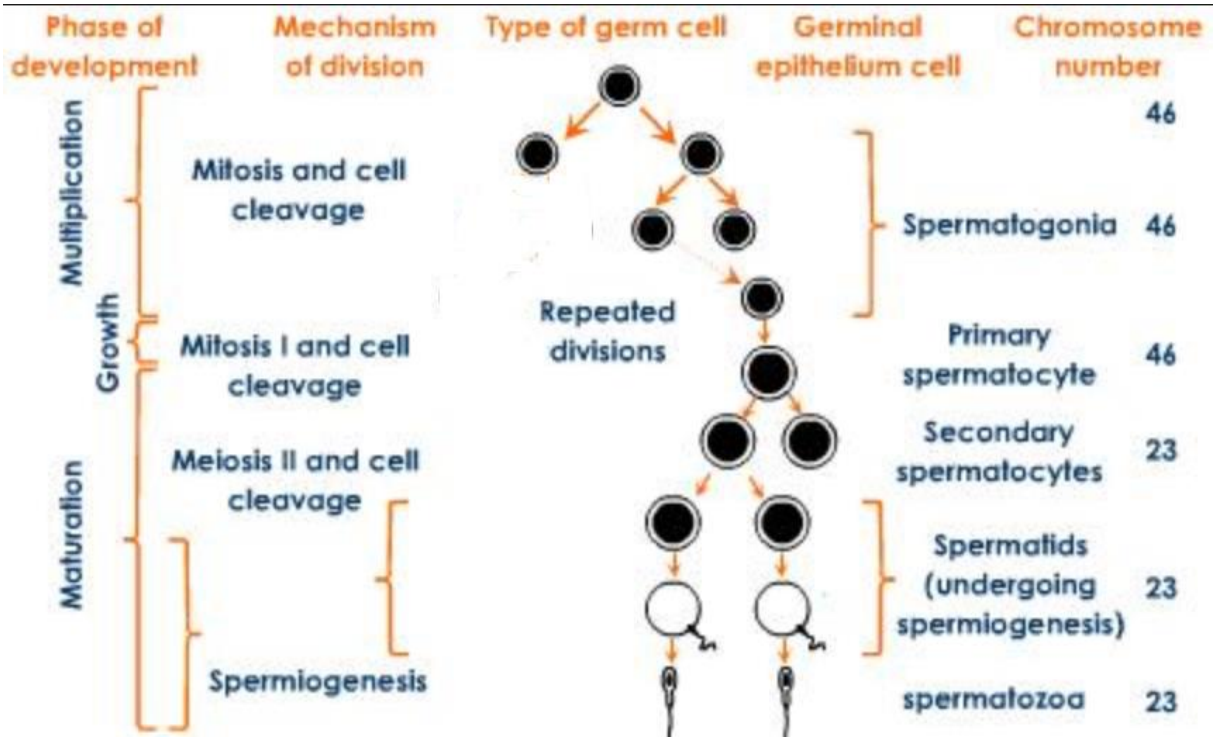

Figure 12: Phases of Spermatogenesis.

4.4. Differentiation Phase or spermiogenesis: No division occurs in this phase. Spermatids undergo differentiation, transforming into sperm capable of fertilization over a period of 23 days, undergoing changes in both the nucleus and cytoplasm (Figure 13).

Key Components of Spermatids:

- **Nucleus:** Undergoes elongation, transitioning from a circular shape. Chromatin undergoes changes to protect against physical and chemical stresses, condensing by replacing histones with protamines. This renders it insensitive to the ADNase enzyme found in the male reproductive tract, which degrades foreign DNA. Microtubule systems appear in the cytoplasm, aiding the nucleus in changing its shape.

- **Acrosome:** Golgi apparatus becomes very active, secreting small vesicles that coalesce to form the acrosomal vesicle which moves towards the anterior pole of the nucleus, attaching to the nuclear membrane. Its contents homogenize, forming the acrosome, rich in enzymes such as hyaluronidase, acrosin, and C.P.E (Corona Penetrating Enzyme).

- **Tail (Flagellum):** The proximal centriole near the nucleus is inactive, while the distal centriole produces microtubules that form the flagellar axis (central pair and 9 peripheral pairs). The cytoplasm flows around the tail, carrying organelles.

- **Midpiece:** Characterized by a helical arrangement of mitochondria. The remaining mass of cytoplasm contains ribosomes, lipid droplets, degenerated mitochondria, and remnants of Golgi apparatus called residual bodies. These remain in the seminiferous tubule cavity until phagocytosed by Sertoli cells. A tiny part of the cytoplasm known as the cytoplasmic droplet remains attached to the sperm near the front of the midpiece. This droplet disappears during the sperm maturation process at the level of the epididymis.

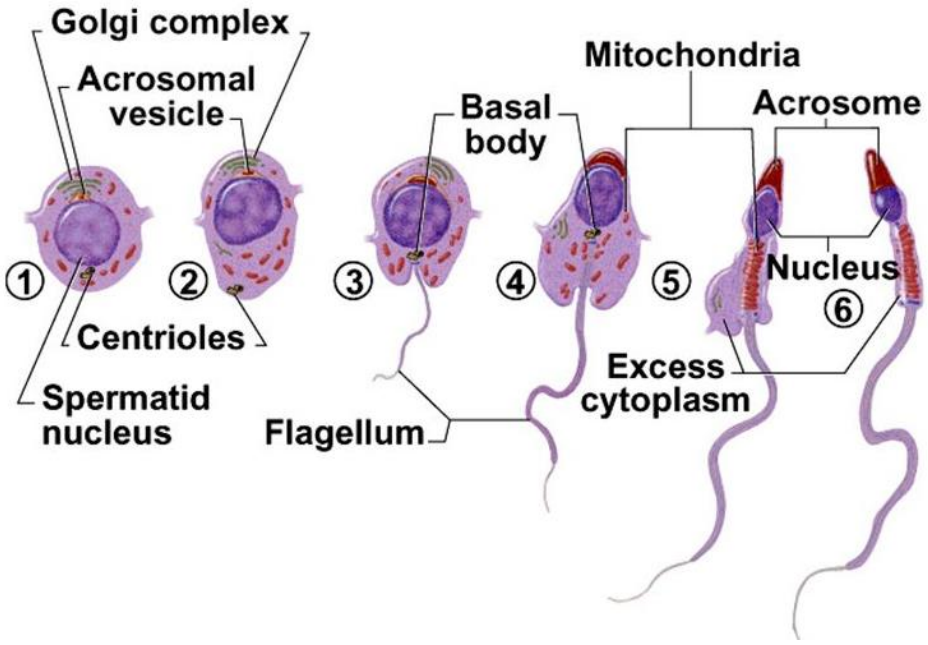

Figure 13: Changes of sperm cell in differentiation Phase or spermiogenesis.

Note: Theoretically, each Ap spermatogonium produces two B spermatogonia, four primary spermatocytes, eight secondary spermatocytes, and sixteen spermatids, which then transform into sixteen spermatozoa. However, microscopic observations in testicular biopsies indicate that 25% of sperm cells degenerate between the primary spermatocyte stage and spermatids.

5. Factors affecting the formation and abnormalities of sperm:

- Heat.
- Hormonal imbalance.
- Localized blood deficiency (ischemia) for an hour is sufficient to eliminate original sperm cells.
- Radiations (x, y).
- Certain types of bacterial infections.
- Consumption of certain medications for treating specific types of cancer.
- Exposure to certain chemicals (tobacco, drugs, alcohol) .

Because of these factors, sperm may take several abnormal shapes, manifested as morphological deformities:

- Sperm with small or large heads.
- Sperm with two heads or tails.
- Sperm without tails.

Chapter Two: Female Reproductive Function

1. Female Genitalia: A set of organs responsible for producing female sex cells or eggs, receiving and transporting sperm, fertilization, the migration and implantation of the fertilized egg, fetal development during pregnancy, and ultimately childbirth (Figure 14).

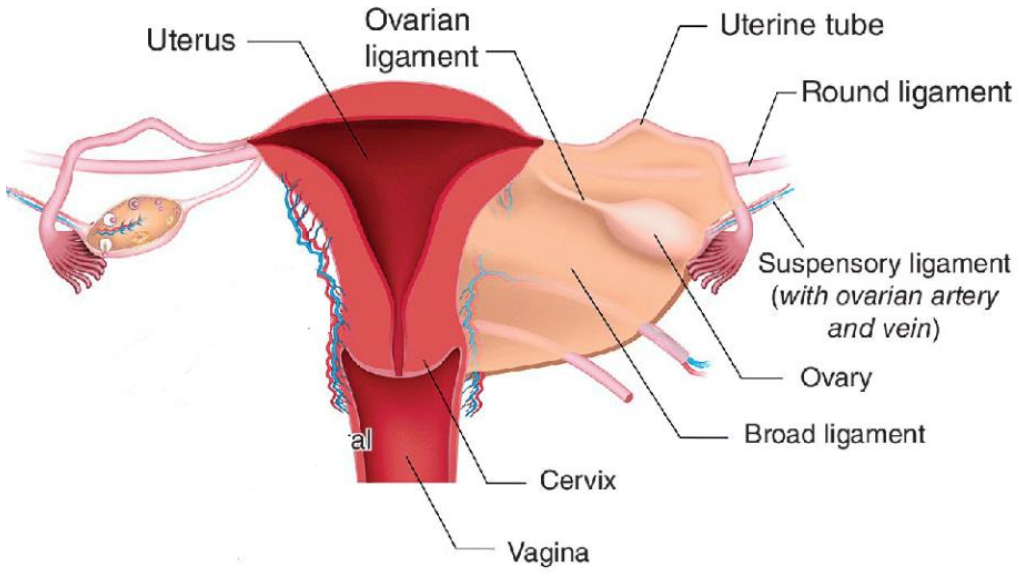

Figure 14: Female genitalia.

1.1. Internal Organs:

a. Ovaries: Two female sexual glands oval in shape, each measuring 4 cm in length, 1 cm in width, and weighing 8-10 grams, lined with cuboidal epithelium called germinal epithelium . They are located in the pelvis, in the middle of the abdominal cavity next to the kidneys, secured by short ligaments called the ovarian ligaments (Mesovarium). Each ovary consists of the cortical region containing eggs, follicles, corpus luteum, and the medullary region containing blood vessels and nerves (Figure 15). The ovary functions as a dual-secretion gland, producing estrogens and progesterone internally. Externally, it produces and releases eggs during ovulation.

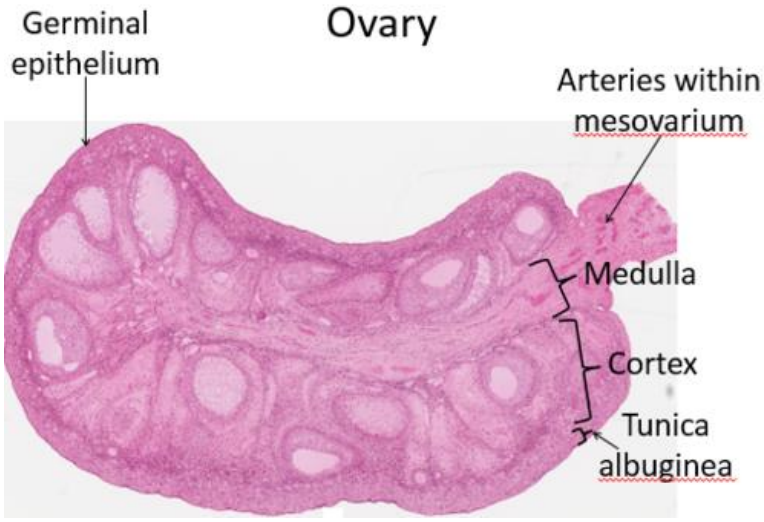

Figure 15: Structure of ovary.

b. Fallopian Tubes: Each extends from the uterus to the ovary, approximately 11 cm in length. Each tube represents the conduit between the uterus and the ovary, lined with ciliated cells that aid in pushing the egg as it exits the ovary towards the inner uterine cavity. The cells also nourish the embryo in its early days with secretions rich in necessary ions, proteins, and acids like pyruvate, lactate, Na, P, Mg, Ca. They are divided into three parts (Figure 16):

- ✓ The infundibulum, the most mobile part, about 2-3 cm in length, closely associated with the adjacent ovary, branching and resembling a funnel shape (Fimbriae) to capture the egg during ovulation;
- ✓ The ampulla, the middle part of the tube, serving as the ideal site for sperm-egg fusion (length 7-8 cm);
- ✓ the isthmus, the short section adjacent to the uterus (length 3-4 cm).

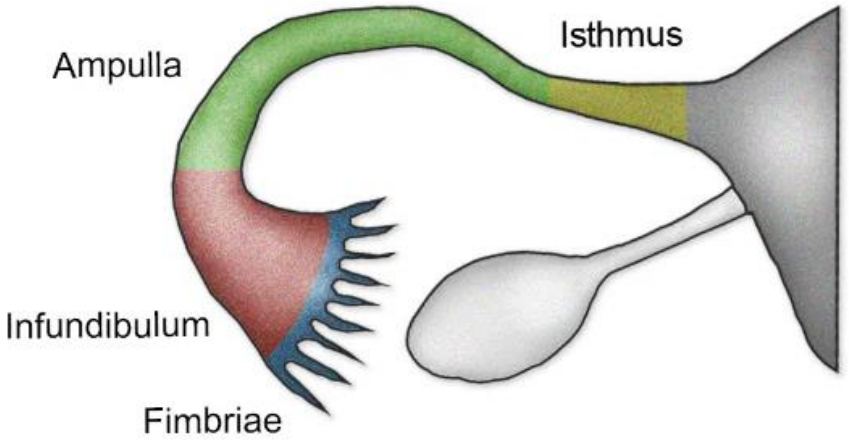

Figure 16: Fallopian Tube parts.

c. Uterus: A single muscular organ resembling an inverted pear, measuring 7.5 cm in length and 5 cm in width. The uterus consists of three layers: the serous layer (perimetrium), an extension of the broad ligament that connects the reproductive system to the abdominal cavity; the thick uterine wall layer, containing smooth muscles called the myometrium, pivotal during childbirth, interspersed with numerous blood vessels and sympathetic nerves, with a thickness of 5 cm. The inner lining of the uterus (Endometrium) consists of epithelial tissues, connective tissues (basal layer, spongy layer, and compact layer), and numerous uterine glands that thicken before menstruation, shedding during the menstrual bleeding to regenerate a new layer (Figure 17). The uterus serves as the site for embryo implantation, development, and birth.

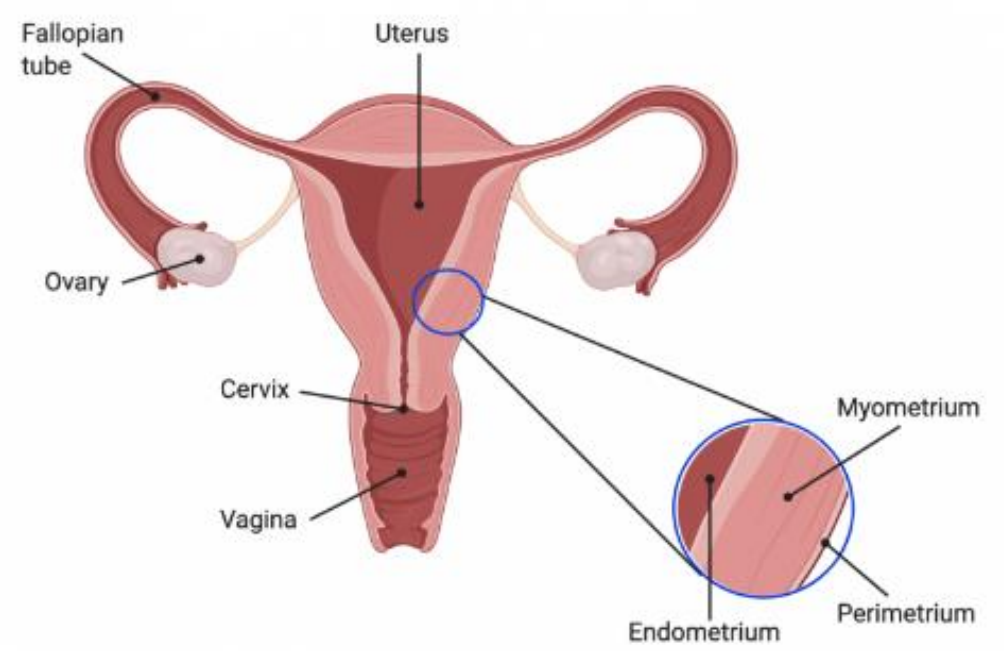

Figure 17: Uterus layers.

d. Cervix: The uterus ends with a narrow muscular part called the cervix. It's a cylindrical organ measuring 7-10 cm in length and 3-4 cm in diameter, protruding into the vaginal cavity (Figure 18). It has two openings: the internal opening into the uterus and the external opening into the vagina. The cervix is composed of sturdy, contractile muscles capable of closing the passage and expanding to accommodate the fetus during childbirth. Its lining consists of columnar epithelial cells interspersed with goblet cells that secrete cervical mucus, composed of a fluid part containing water, mineral salts, organic compounds, and proteins, along with a solid part, a network of interlinked fibers that can change during the menstrual cycle. This cervical mucus acts as a gatekeeper, allowing only healthy sperm into the uterine cavity while preventing foreign bodies and sperm proteins. Additionally, it actively combats microbes and serves as a reservoir for sperm, providing the necessary energy for their activation.

e. Vagina: Is the copulatory organ, extends from the cervix to the external genitalia (approximately 8 cm in length). The superficial cells lining the vaginal cavity continuously shed and, together with mucus from cervical glands, form vaginal secretions (Figure 18). The vagina harbors microscopic organisms called lactobacilli or Döderlein's flora, which convert glycogen within vaginal cells into lactic acid, rendering the vagina acidic. The hymen, found in the anterior part of the vagina, consists of a horizontal fold that tears during the first sexual intercourse. Its wall is composed of mucosal and muscular layers.

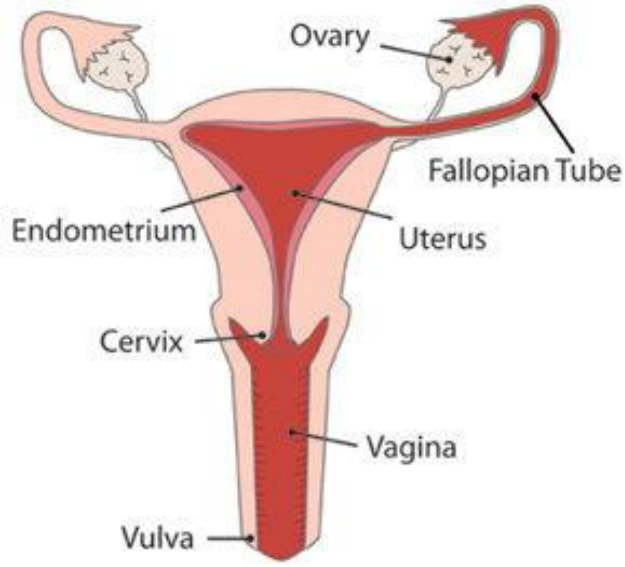

Figure 18: The location of cervix and vagina.

1.2. External organs or vulva: Contain 4 parts (Figure 19) as follows

a. Labia majora (outer lips): Bilateral prominent folds of skin that meet at their loose edges, concealing the other visible external reproductive organs.

b. Labia minora (inner lips): Thin, elongated folds of smooth, delicate skin situated behind the larger labia and surrounding the vaginal opening, providing complete coverage. Their role is protective.

c. Clitoris: Equivalent to the penis in males, terminating in the urethral opening.

d. Bartholin's glands: Located on either side of the vagina, these glands secrete mucous substances that facilitate penis entry.

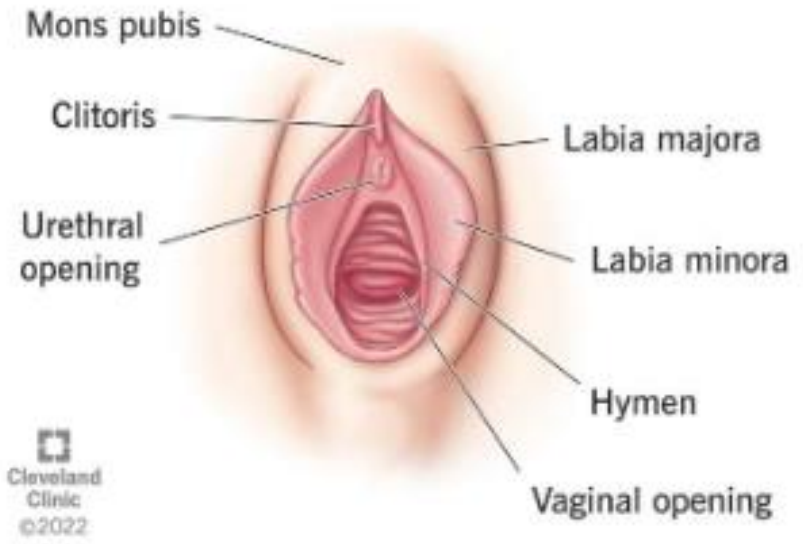

Figure 19: External female sexual organs.

2. Oogenesis: The formation of eggs involves a series of stages through which the primary egg cells (oogonia) with a chromosome configuration of 2n undergo development in the ovarian cortex, which includes the outer layer and surrounds the medulla, culminating in the production of a single egg cell with 1n chromosomes capable of fertilization. Egg cells are periodically produced and released through the process of ovulation, which typically occurs in the middle of the menstrual cycle, approximately every 28 days from puberty until menopause (Figure 20).

1.1. Multiplication Phase: Egg cell formation begins in the fourth month of fetal life with regular cell division (mitosis) of the primary egg cells or oogonia found in the ovarian cortical region. Between the seventh and eighth months of fetal life, these cells are surrounded by some follicular cells, becoming

primordial follicles, marking the end of the multiplication phase. These cells then undergo the initial phase of division, becoming first-grade egg cells (Oocyte I) with 2n chromosomes. However, they soon halt in the final stage of the preparatory phase I (prophase I) and remain in this state for several years (until puberty). At the end of this stage, a million primordial egg cells are formed.

1.2. Growth Phase: A few months before puberty and under the influence of sex hormones, a group of privileged primordial follicles enters an active phase. Within each primary follicle, the size of the Oocyte I increases from 40 to 60 microns, surrounded by a proteinaceous sugar coat called the zona pellucida. During this phase, a large number of primordial follicles and their enclosed egg cells disappear, leaving approximately 400,000 at the time of puberty.

1.3. Maturation Phase: The maturation of the first-grade egg cells occurs concurrently with the maturation of the follicles. This maturation involves only a few follicles: 300 to 400. Each month from puberty to menopause, within a maturing follicle, the primary egg cell completes its reduction division and transforms into a second-grade egg cell (oocyte II) + a polar body, each having a 1n chromosome configuration. Then, the oocyte II directly enters the second phase of meiotic division (equational division of meiosis), halting again at metaphase II during ovulation. The entire meiotic division concludes only upon fertilization, which happens when the sperm enters the egg cell. The oocyte II completes the second and final separation phase, yielding the ovum on one side and the second polar body on the other. In the absence of fertilization, the oocyte II quickly disintegrates, halted in the metaphase stage of the second division.

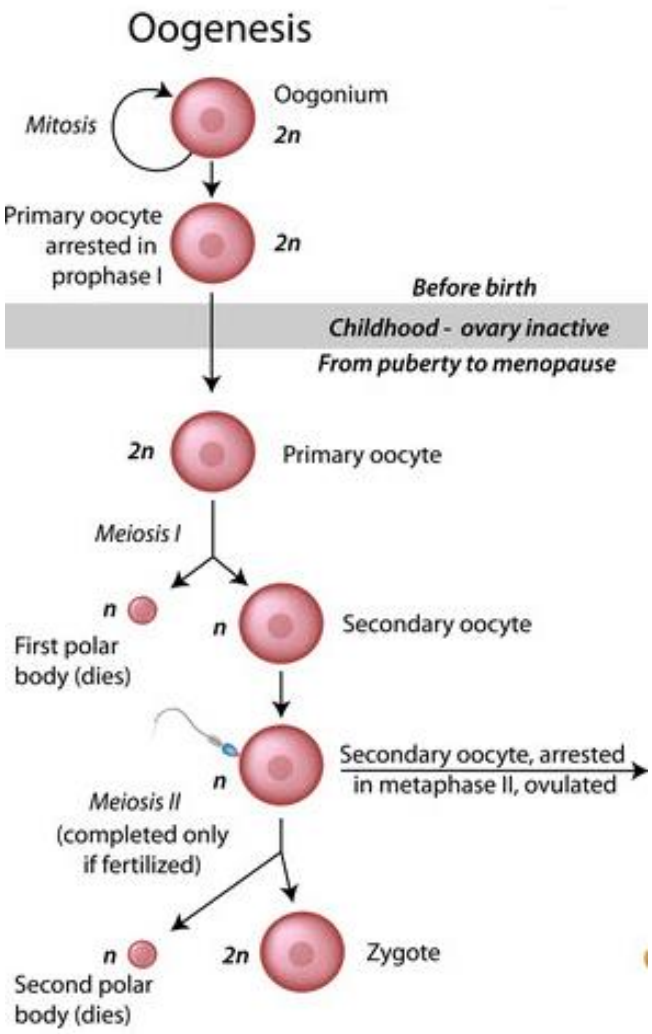

Figure 20: Oogenesis phases.

Note: Each matured egg produces one ovum and three polar bodies, which subsequently disintegrate.

3. The ovum: It is along with its follicular cells, is a large and stationary cell (lacking motility) compared to the sperm, measuring 120 micrometers in diameter. It emerges from the follicle as a secondary oocyte (meaning half the chromosomes or 32). The nucleus stops at the second meiotic division, and this division is only completed if fertilization occurs. The cytoplasm is gel-like, rich in mitochondria and RNA, ready for various protein-building processes, along with other specific metabolic elements during early development. The ovum is

poor in Alécithe (nutritional content) and feeds on the surrounding corona radiata cells. They are separated by a transparent zone, serving as a site for exchanges between them. The connections between the corona radiata cells loosen post-ovulation, interlinked by hyaluronic acid bridges. The ovum is surrounded by scattered cumulus oophorus cells. A secondary oocyte can survive within the female reproductive tract for approximately 24 to 48 hours. The ovum contains two poles: an animal pole housing the nucleus and polar bodies that disappear later, and a vegetal pole concentrated with yolk granules.

4. Folliculogenesis: Follicles are structures composed of female germ cells surrounded by granulosa cells, establishing a close relationship between the follicle and the ovum since the egg cell is an essential component of the follicle, making it the suitable place for ovum formation. The follicles are always situated in the outer layer of the ovary or the cortex and go through several developmental stages before becoming mature follicles carrying the egg cells. These mature follicles release the egg cells outside the ovary in a process known as ovulation. During each cycle, numerous follicles enlarge, but typically, only one gradually matures while the others regress, transforming into atretic follicles. Consequently, only one egg cell matures under normal circumstances in each ovarian cycle. Folliculogenesis includes several stages (Figure 25):

4.1. Primordial follicle: A small follicle measuring 40-50 micrometers, consisting of a single layer of flattened epithelial cells called follicle cells surrounding the primary oocyte, which is in the primordial stage of the first meiotic division (Figure 21).

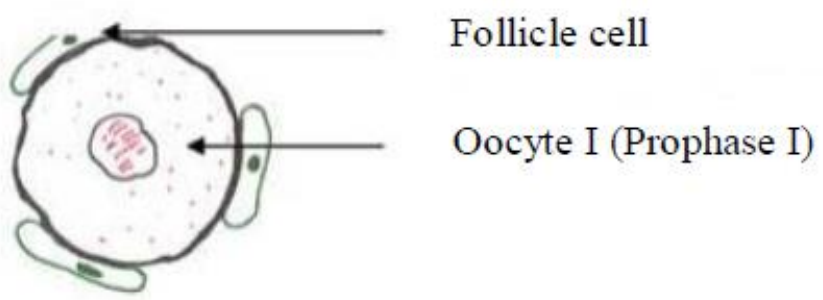

Figure 21: Primordial follicle.

4.2. Primary follicle: Differs from the primordial follicle due to the follicle cells becoming cuboidal. Its size reaches 40-50 micrometers, and it is surrounded by a fibrous membrane known as Slavjanski's membrane, separating it from the ovarian cortex. A glycoprotein membrane, the pellucid or zona pellucida, forms around the ovum (Figure 22).

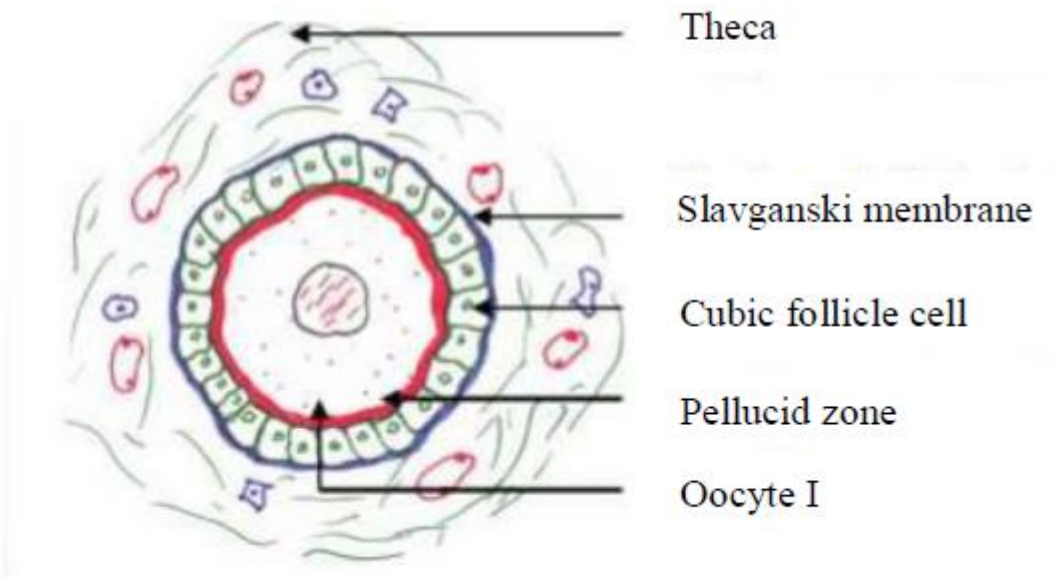

Figure 22: Primary follicle.

4.3. Secondary follicle: Its diameter increases from 50 to180 micrometers, characterized by the formation of a second layer of granulosa cells. The thecal layer differentiates into an outer fibrous thecal area and an inner thecal area traversed by blood vessels (Figure 23).

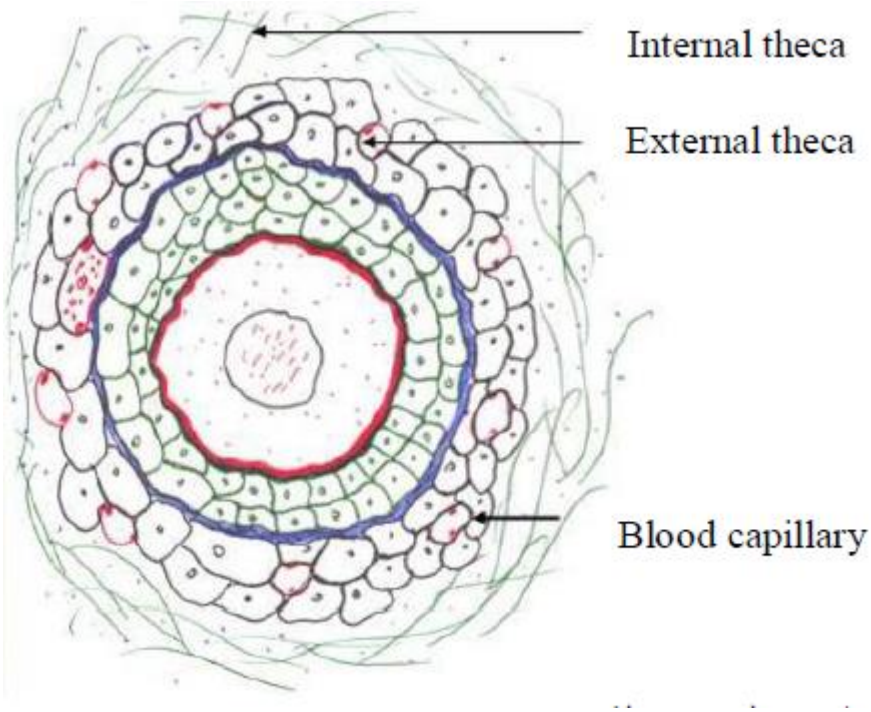

Figure 23: Secondary follicle.

4.4. Tertiary follicle: Its diameter reaches around 5 mm, distinguished by the formation of a third layer or more of granulosa cells called the granulosa layer. Irregular spaces filled with a fluid called follicular fluid appear within this layer (Figure 24).

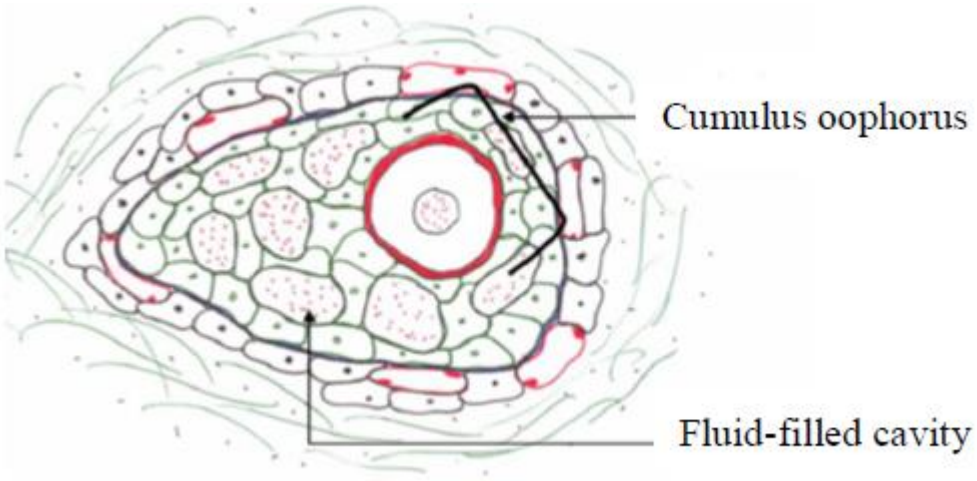

Figure 24: Tertiary follicle.

4.5. Mature follicle or Graafian follicle: At this stage, the cavities in the granulosa layer merge, forming a single cavity called an antrum. The egg cell, still surrounded by granulosa cells known as the corona radiata at this stage, protrudes into the cavity from one side and is connected to the rest of the follicle on the other side through the cumulus oophorus. The mature follicle's diameter reaches about 20 mm, and inside it, there's the egg cell I, measuring 120-140 microns, with a bulge visible on the surface of the ovary (Figure 25).

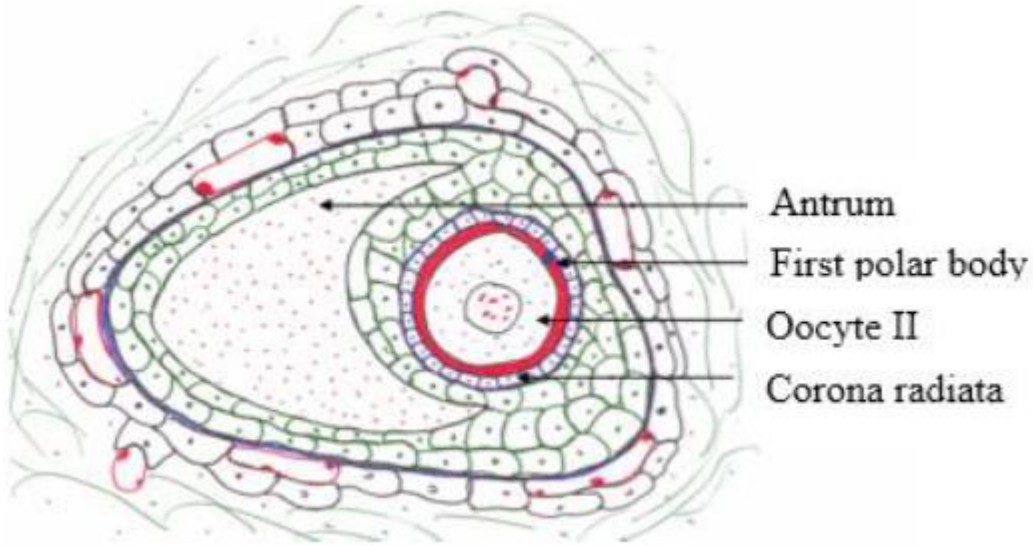

Figure 25: Mature or Graafian follicle.

After ovulation, the remnants of this follicle transform into a structure called the Corpus Luteum, where the granulosa cells enlarge and fill with fatty material containing a yellowish pigment. There are two types (Figure 26):

- ✓ **Cyclic Corpus Luteum:** This structure diminishes in the absence of fertilization and transforms into a white body known as the Corpus Albicans. It appears as a scar on the surface of the ovary, which can be counted to estimate the approximate age of the female.

- ✓ **Gestational Corpus Luteum:** In the case of fertilization, this corpus luteum remains during the first trimester of pregnancy due to the hormone hCG, ensuring a high production of progesterone to maintain the pregnancy. It's later replaced by the placenta.

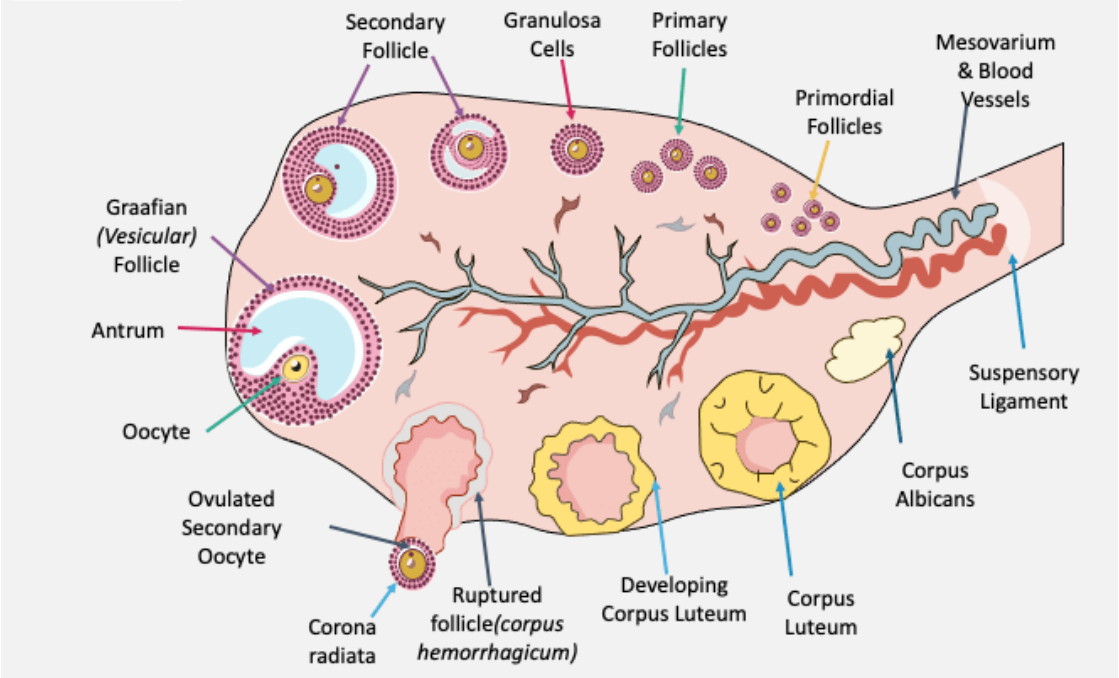

Figure 26: Different steps of folliculogenesis and types of corpus luteum.

5. Women's sexual cycle: lasts around 28 days (± 2) from puberty to menopause and is distinguished by two main phases:

5.1. Ovarian Cycle: This cycle is subdivided into (Figure 27):

a. Follicular Phase (Pre-Ovulation): Characterized by follicular growth where typically one follicle, termed the Graafian follicle, matures. This phase lasts approximately 13 days.

b. Ovulation: Occurring around the midpoint of the cycle (day 14), marked by the thinning of the mature follicle walls due to specific enzymes. As a result of ovarian contractions, the secondary oocyte in the metaphase is released and drawn into the Fallopian tube by the fimbriae.

c. Luteal Phase (Post-Ovulation): The remaining follicle transforms into a yellowish body called the corpus luteum, where granulosa cells proliferate and it fills with a yellow substance.

5.2. Uterine cycle: This cycle can be divided into (Figure 27):

a. Menstruation: This phase prepares the uterine lining for potential embryo implantation, reaching its peak around day 21, potentially the time for implantation. If fertilization doesn't occur, the uterine lining sheds due to blood vessel contractions and bursts, resulting in the shedding of the lining along with non-clotting blood due to an anti-clotting factor released by the uterus, leading to menstrual bleeding.

b. Proliferative Phase: Following menstruation, the uterine lining thickens due to the proliferation of mucosal cells and blood vessels, under the influence of estrogens.

c. Secretory Phase: Influenced by estrogens, the uterine lining further thickens, and the glands secrete mucus-rich secretions, particularly rich in glycogen.

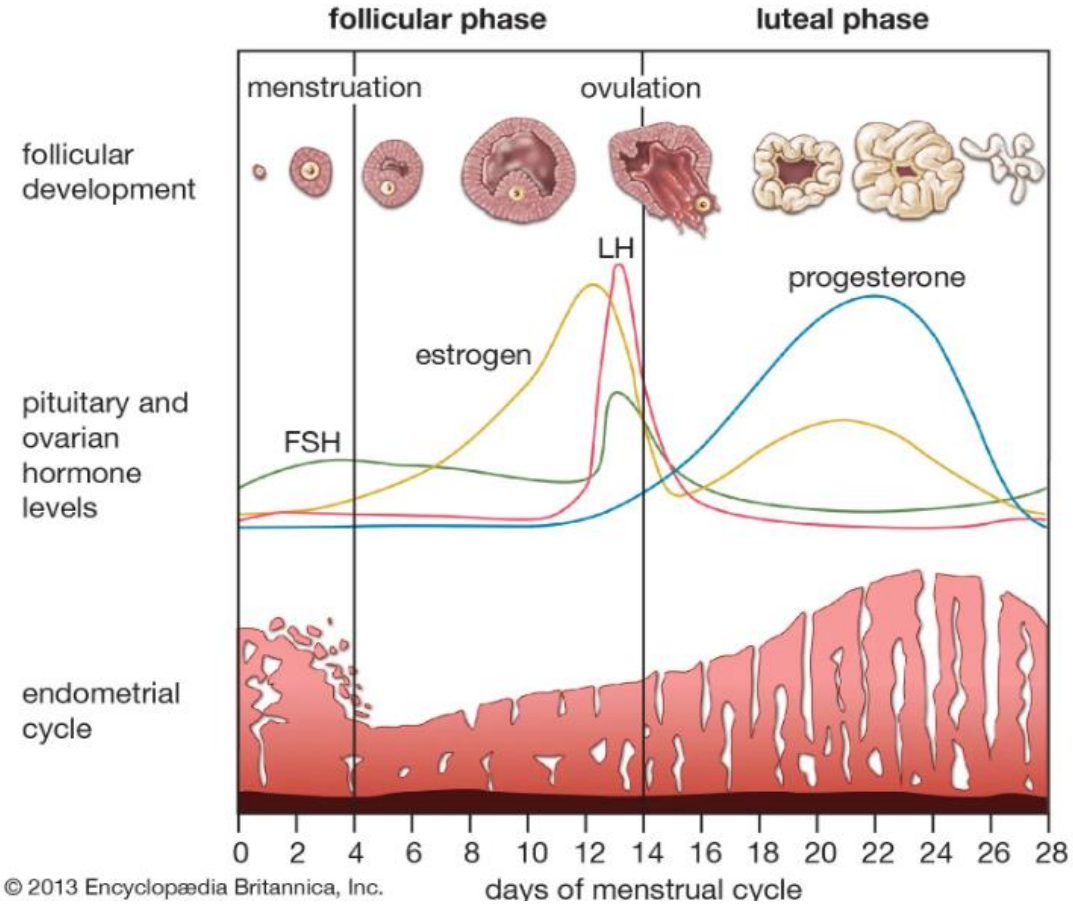

Figure 27: Ovarian and uterine cycles phases.

6. Menopause: The cessation of ovarian cycles leads to the onset of menopause, attributed to the depletion of follicle reserves in the ovaries. Consequently, the secretion of ovarian hormones ceases, ultimately leading to the cessation of menstruation.

Chapter Three: Regulation of Sexual Function

Male and female sexual functions are subject to dual regulation: neural and glandular. The hypothalamus and pituitary gland serve as pivotal regulators for both functions. The hypothalamo-hypophyseal complex is an anatomical unit comprised of the hypothalamus and the pituitary gland, two endocrine structures located at the base of the brain. This complex plays a fundamental role in hormonal regulation and is involved in numerous physiological processes.

1. Hypothalamus: It lies the interface between the autonomic nervous system and the endocrine system through the pituitary gland. The hypothalamus, occupies the largest part of the interbrain, situated below the thalamus and above the brain stem. It exists in the brains of all mammals, including humans. At puberty and under external stimuli, specific neurons in this area secrete Gonadotropin Releasing Hormone (GnRH), an amino acid-based hormone that stimulates the release of sex hormones from the anterior pituitary gland cells.

2. Anterior Pituitary Gland: The pituitary gland is a pea-sized gland located at the base of the brain, it consists of two distinct parts: the anterior lobe, which constitutes 80% of the pituitary gland's weight and the posterior lobe. These lobes are connected to the hypothalamic region through a stalk containing blood vessels and nerve projections (nerve fibers or axons).

GnRH stimulates the anterior pituitary gland cells to release gonadotropic hormones, such as Follicle-stimulating hormone (FSH) and Luteinizing hormone (LH) (Figure 28).

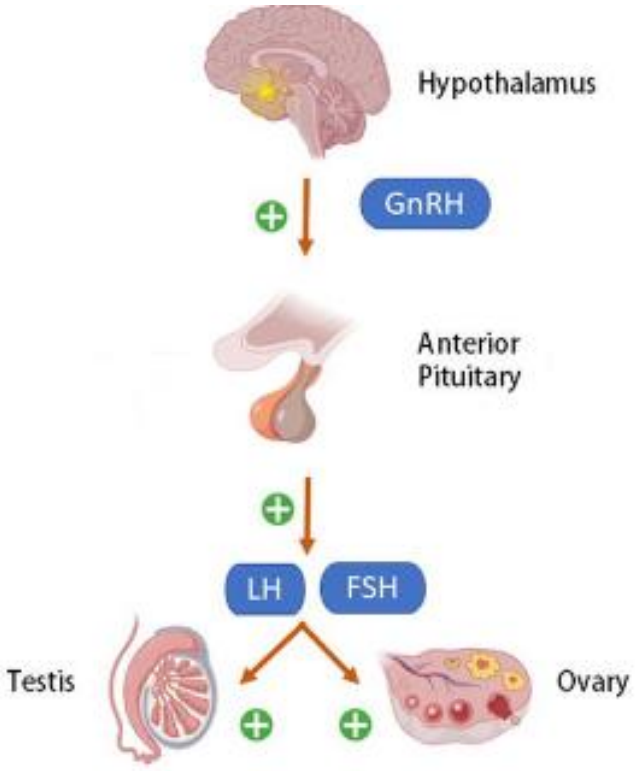

Figure 28: Hypothalamic-anterior pituitary axis.

3. Regulation of male sexual function: Described in Figure 29.

3.1. FSH: It binds to membrane receptors on Sertoli cells, which play a triple role:

- ✓ Stimulating the formation of male germ cells (spermatozoa) through the support of Sertoli cells.
- ✓ Inducing the secretion of the inhibin hormone. The latter affects FSH secretion through negative feedback control. It either indirectly affects the hypothalamic neurons by decreasing GnRH secretion or directly impacts the anterior pituitary gland cells.
- ✓ Stimulating the production of the Androgen Binding Protein (ABp).

3.2. LH: is primarily responsible for stimulating Leydig cells in the testes to produce testosterone. Testosterone, in turn, has several functions:

- ✓ It positively affects the reproductive tracts and accessory glands.
- ✓ It negatively impacts LH secretion, either indirectly by affecting hypothalamic neurons and reducing GnRH secretion or directly affecting the anterior pituitary gland cells.
- ✓ Additionally, it's responsible for the development of secondary sexual characteristics in males.
- ✓ Responsible for the descent of the testes into the scrotum during fetal development.

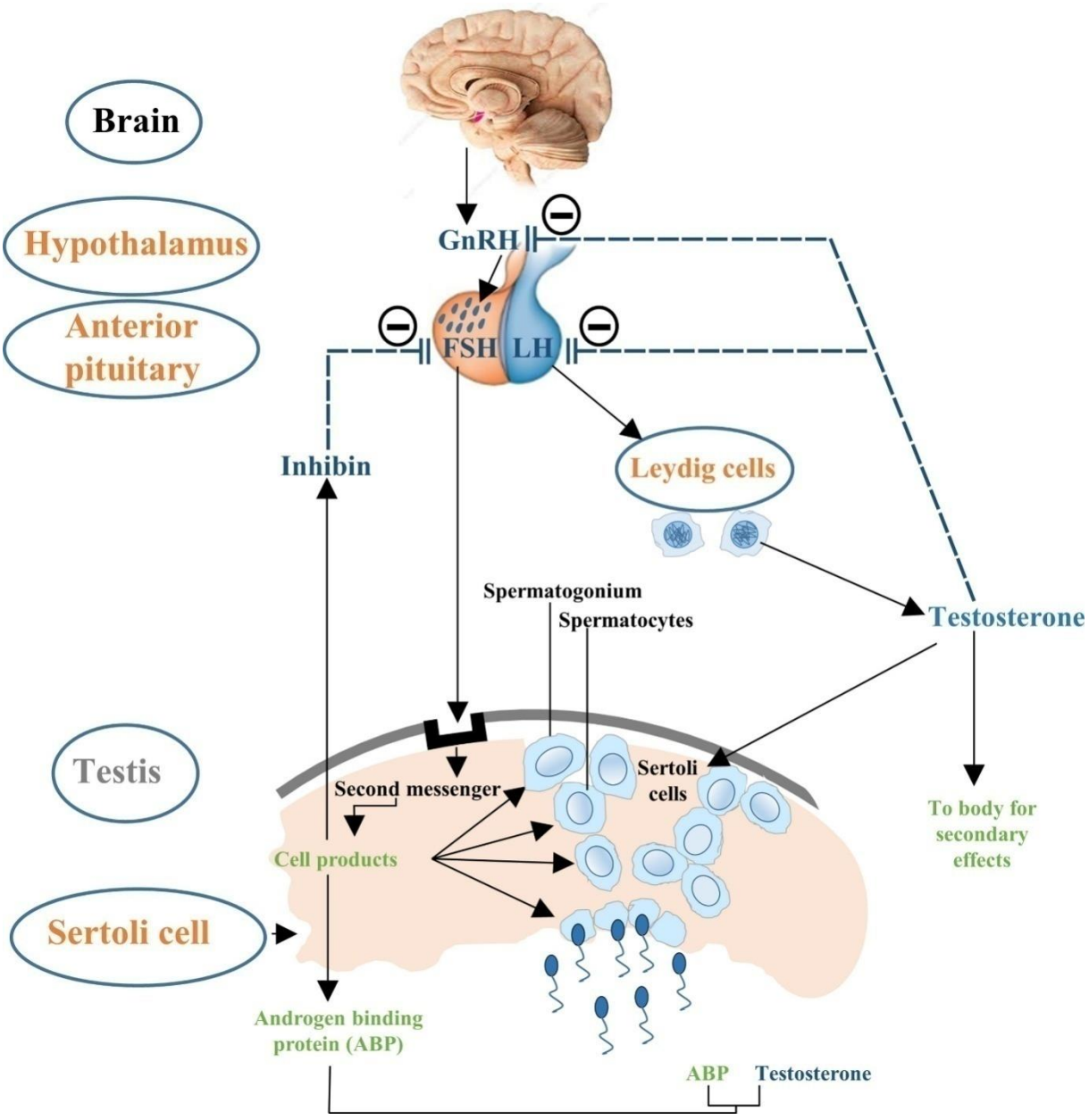

Figure 29: Regulation of male sexual function.

4. Regulation of female sexual function: Described in Figure 30.

4.1. Ovarian cycle:

a. Follicular Phase: FSH prompts the growth of several follicles, leading to the development of a dominant follicle that matures into a Graafian follicle. These follicles secrete estrogens, which further stimulates LH, causing ovulation.

b. Ovulation Phase: Peak LH levels around day 14 of the cycle trigger the rupture of the mature Graafian follicle and the release of the ovum.

c. Luteal Phase: Remaining follicle components transform into the corpus luteum, which secretes progesterone and some estrogens, preparing the uterus for pregnancy. If fertilization occurs, the corpus luteum sustains pregnancy during the first trimester; otherwise, it regresses, leading to reduced hormone levels, menstruation, and the end of the cycle.

4.2. Ovarian cycle hormones:

a. Estrogens: Secreted by the inner layer of the ovarian follicles, estrogens induces uterine contractions, affects uterine mucosa, and is responsible for female secondary sexual characteristics.

b. Progesterone: Produced by the corpus luteum, progesterone thickens the uterine wall in the secretory phase, inhibits FSH secretion, and maintains pregnancy by facilitating embryo attachment.

4.3. Uterine cycle:

a. Menstrual Phase: Lasting 3-5 days, characterized by shedding of the endometrial lining due to decreased levels of progesterone and estrogens.

b. Proliferative Phase: Lasting approximately 10 days post-menstruation, involving the thickening of the uterine lining due to estrogens effects.

c. Secretory Phase: Lasting from ovulation for around 12-14 days, driven by progesterone, which prepares the endometrium for potential embryo implantation by increasing its thickness and glycogen-rich secretions.

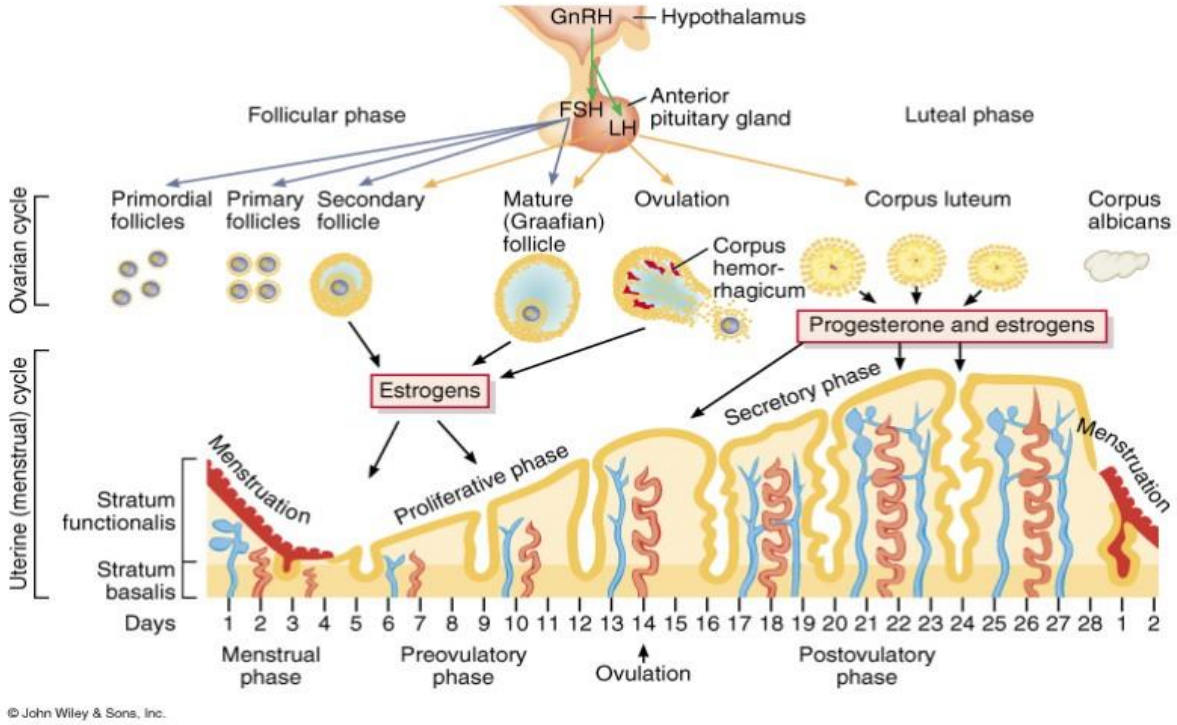

Figure 30: Regulation of male sexual function.

Chapter Four: The First Week of Fetal Development: Fertilization - Segmentation.

During the first week of fetal development, fertilization occurs followed by the process of Segmentation.

1. Fertilization:

1.1. Definition: It's the union of the nucleus of the male gamete (sperm) and the nucleus of the female gamete (egg) to form the fertilized egg (zygote), representing the initial stages of fetal development. Its significance lies in:

- ✓ Formation of the fertilized egg and return to the 2n chromosome number.
- ✓ Contribution of both the father and mother to half of the genetic material (diversity).
- ✓ Determination of the fetus's gender.
- ✓ Activation of the egg cell and initiation of the division process (cleavage).

1.2. Timeframe and Location: Fertilization can occur during the lifespan of gametes. The lifespan of an egg within the female reproductive tract is estimated to be about 48 hours, while sperm can survive for up to 72 hours. Hence, for fertilization to happen, intercourse should occur within 48 hours before and after ovulation.

Fertilization occurs in the fallopian tube: the ampulla (Figure 31).

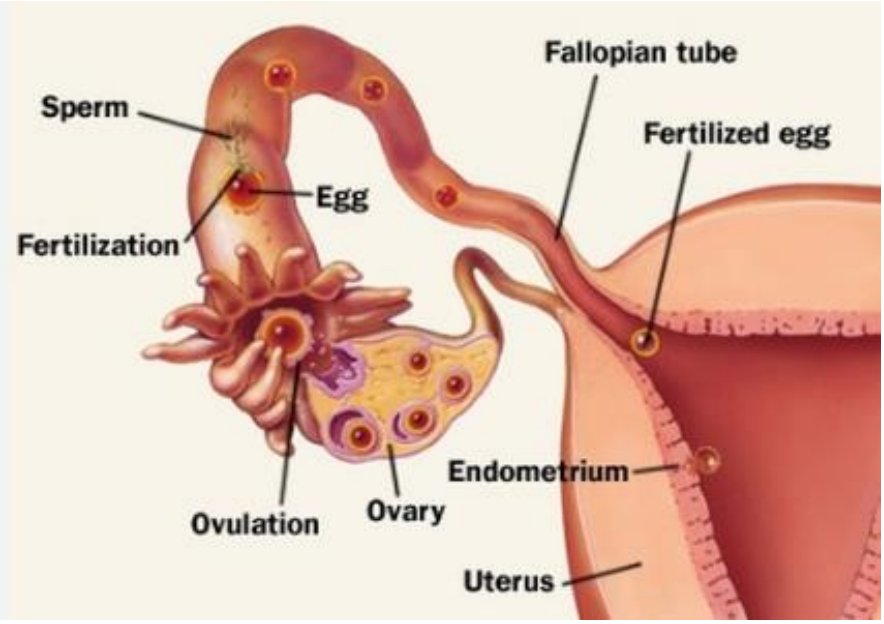

Figure 31: Location of fertilization in fallopian tube (Ampulla).

1.3. Conditions:

For females, these conditions can be summarized as follows:

- ✓ Adequate cervical mucus viscosity.
- ✓ Occurrence of actual ovulation.
- ✓ Integrity of the female reproductive tract from any infections, with a necessity for sperm to be present in the female reproductive tract within 48 hours prior to ovulation.

In males, it revolves around the quality of semen (semen analysis) as mentioned in table 1.

Table 1: Biological Characteristics of Human Semen and its Abnormalities:

Characteristics	**Normalities**	**Abnormalities**
Volume	2- 6 ml	Less than 2 ml
Ph	7.2- 7.8	More or less
Viscosity	Liquefaction within one hour after ejaculation	-liquefaction
Number of spermatozoa	20- 250 million /ml	Less than 20m/ml = Oligospermia
Mobility of spermatozoa	50- 70% mobile spermatozoa	Less than 50% = Asthénospermia
Vitality of spermatozoa	Less than 30% of dead spermatozoa	More than 30% = Necrozoospermia
Malformation of spermatozoa	Less than 40% of malformed spermatozoa	More than 40% = Tératospermia

Note: The complete absence of spermatozoa is termed azoospermia.

1.4. Stages: Preceding the fertilization process, the release of the egg carrying a haploid chromosome through ovulation occurs. The egg is captured by the fimbriae and remains arrested in the metaphase of the second (equational) division, which it completes in the event of fertilization. It is enveloped from the inside out by (Figure 33):

- ✓ **The plasma membrane:** the outer layer of the egg, which contains fine villi directed toward the granulosa cells, indicating the vital exchanges

between these cells and the egg cell. The plasma membrane also contains specific membrane receptors that play a role in fertilization.

- ✓ **The zona pellucida region:** which protects the egg and is composed of numerous glycoproteins known as ZP1, ZP2, and ZP3 glycoproteins. ZP1 forms a three-dimensional network by linking the chains of ZP2 and ZP3 through disulfide bonds (Figure 32).

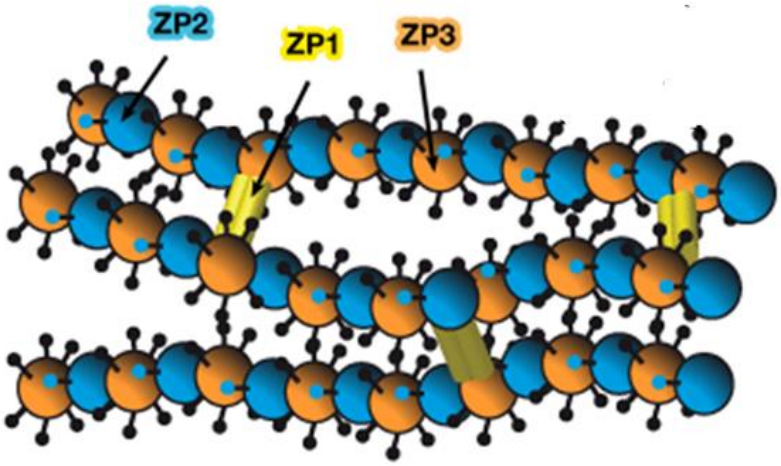

Figure 32: Composition of Zona Pellucida.

- ✓ **The corona radiata:** is the layer closest to the zona pellucida and is closely associated with the egg cell. It also possesses microvilli on its membrane.
- ✓ **Cumulus oophorus:** a group of loosely connected granulosa cells unlike the corona radiata, which is more cohesive.

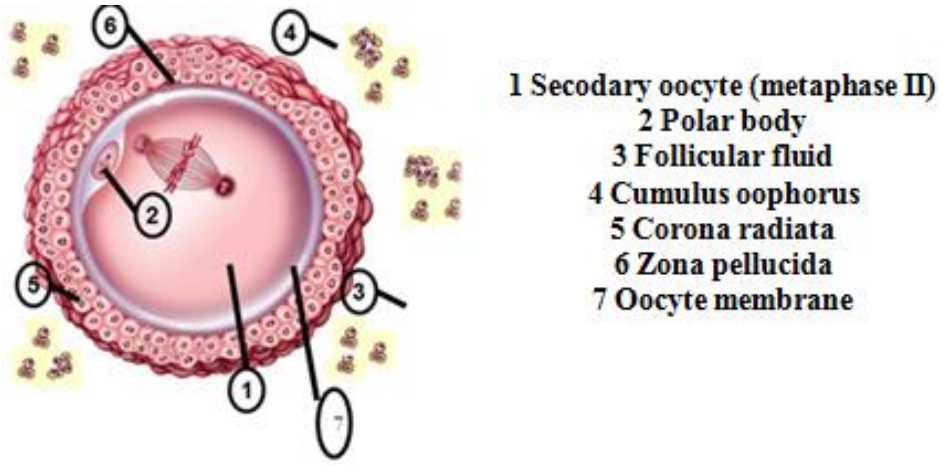

Figure 33: Ovulated egg composition.

As for the sperm, also haploid, it is released through ejaculation into the female reproductive tract and is part of the seminal fluid (composed of secretions from the seminal vesicles, prostate, and Cowper's glands), collectively forming semen. Spermatozoa have a distinct structure (head, midpiece, and tail), and they are enveloped from the inside out by (Figure 34):

- ✓ **The inner acrosome membrane:** containing specialized membrane receptors for ZP2 at the level of the zona pellucida.
- ✓ **The outer acrosome membrane:** which fuses with the plasma membrane of the sperm during the acrosome reaction.
- ✓ **The sperm plasma membrane:** which has specific membrane receptors for ZP3 at the level of the zona pellucida and also specific membrane receptors for the egg cell.

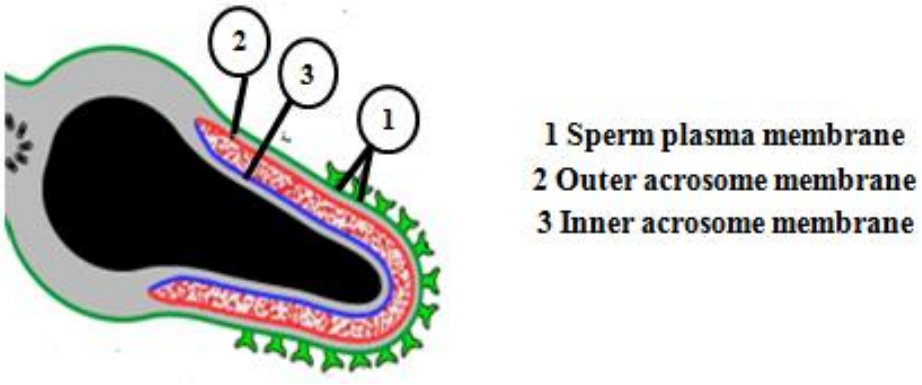

Figure 34: Sperm head membranes.

The stages of fertilization are as follows:

a. Passage of the sperm through the female reproductive tract from the vagina to the fallopian tube:

- The seminal fluid is ejaculated into the upper part of the vagina near the cervix. Although the vagina is acidic (pH = 3-4) due to the presence of Lactobacillum bacteria that convert glycogen into lactic acid, the seminal fluid is alkaline (protective for sperm). However, many sperm die at this stage despite the protective fluid. The cervix is alkaline (suitable for sperm), the cervical mucus undergoes changes during ovulation (Figure 35). Several phenomena occur at this level, including the liquefaction of seminal fluid and the preparation of the sperm.

- This cervical mucus ensures the selection of healthy and well-moving sperm, not allowing passage of dead, immotile, immature sperm, or bacteria still adhering to it . Hence, a large number of sperm die at this stage (approximately 2 million reach the uterus).

- The semen is dense (coagulated) due to proteins from prostatic fluid (fibrinogen), it gets liquefied by enzymes (fibrinolysin), becoming unmixable with mucus (viscous), and is ejaculated into the vagina and then outside the body, leaving only sperm behind.

- At this level, sperm capacitation occurs, enhancing motility and functional maturity by removing the sperm plasma: decreasing molecular weight and removing the tough protein coat surrounding the sperm head (exposing receptors to penetrate the egg wall) via enzymes secreted by the cervical glands (proteolytic enzymes).

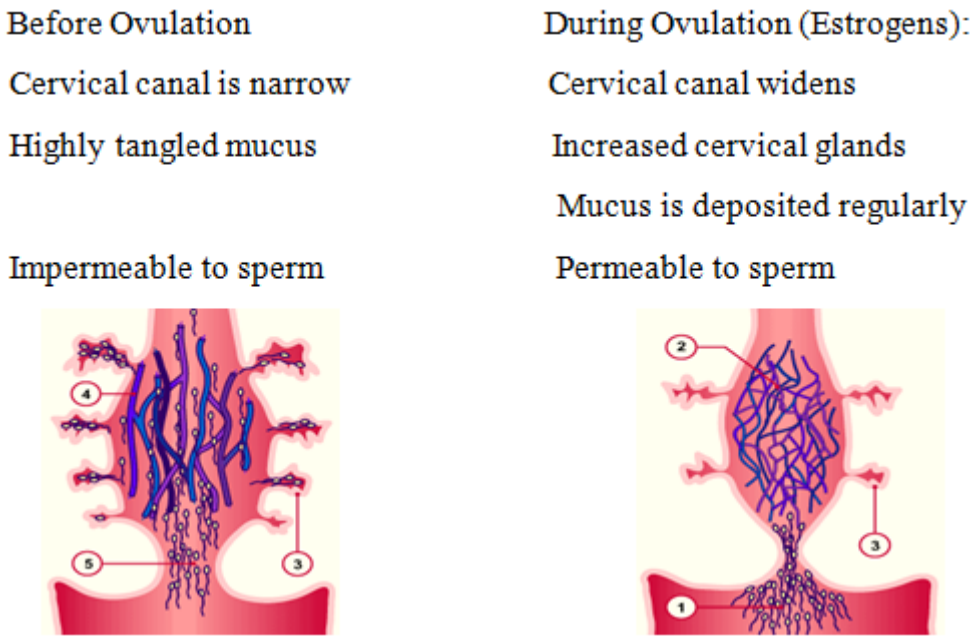

Figure 35: Cervical mucus changes before and during ovulation.

- During female sexual arousal (intercourse): The pituitary hormone oxytocin is released, causing the contraction of vaginal, cervical, and uterine muscles and fallopian tubes, aiding sperm movement up the female reproductive tract in addition to their own motility.

b. Sperm Arrival at the Fallopian Tube (Ampulla): About an hour later (with the best and fastest sperm actually reaching it within 30 minutes), around 200 sperm reach this level: the ampulla (alkaline-rich with potassium, glycogen, and bicarbonates). Here, fertilization occurs in the true sense across three stages: penetration of the corona radiata and zona pellucida, penetration of the zona pellucida, and finally, the fusion of sperm and egg membranes.

b.1. Penetration of the cumulus oophorus and corona radiata: Enzymes secreted by the acrosome (Hyaluronidases) work to separate the cells of the cumulus oophorus and corona radiata by breaking down the substance binding them: hyaluronic acid and CPE (Corona Penetrating Enzyme), which disrupts the corona radiata cells, allowing sperm (with a healthy acrosome) to progress toward the zona pellucida (Figure 36).

b.2. Penetration of the zona pellucida: ZP3 (the zona pellucida) serves as a receptor for sperm. After the acrosome binds to this protein, it releases its enzymes (Acrosin), which break down the sugar proteins of the zona pellucida, creating a narrow passage for the sperm head to penetrate into the egg's cytoplasm. This is known as the acrosomal reaction, allowing the fusion of the membranes (sperm and egg) (Figure 36).

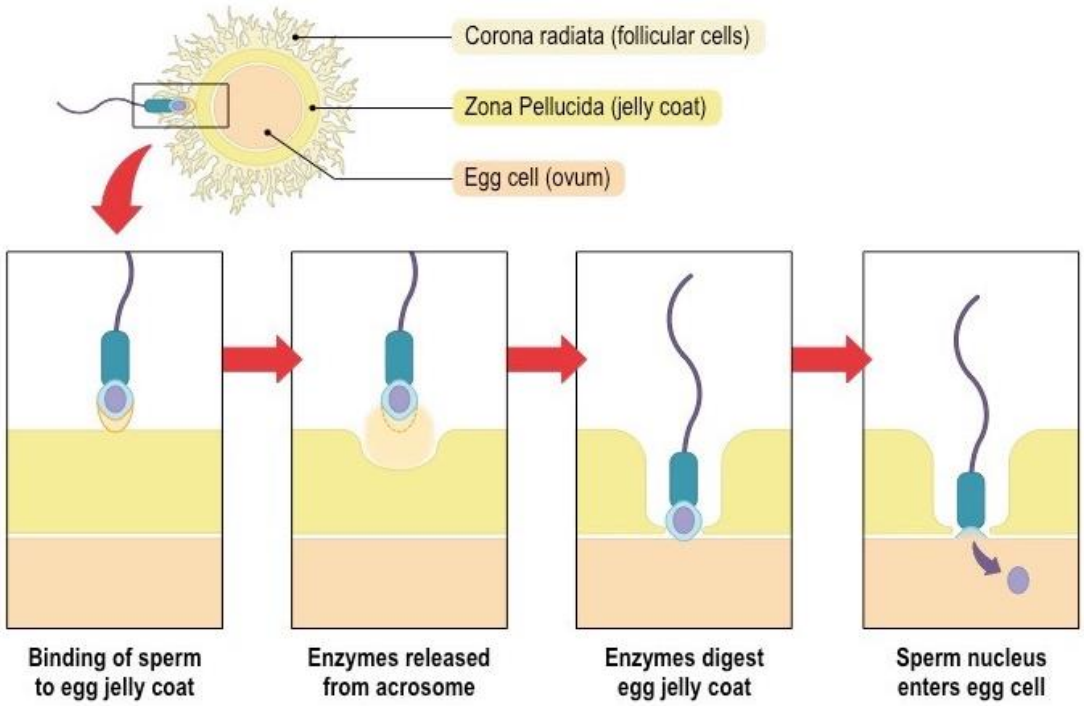

Figure 36: Penetration of the cumulus oophorus, corona radiata and zona pellucida.

b.3. Outcomes of sperm entry into the egg's cytoplasm: Upon contact with the egg's membrane, the two cytoplasmic membranes merge, allowing the sperm's head and tail to enter the egg's cytoplasm, leaving the membrane outside, followed by:

✓ **The cortical reaction (blockage of polyspermy):** cortical granules (formed during egg maturation as a result of Golgi vesicles) are expelled outside the cytoplasmic membrane through exocytosis, releasing their enzymatic content (along with enzymes, proteins, molecular residues, and metabolic products from within the egg). These substances break down sperm receptors and alter the structure of the zona pellucida, making it thicker and tougher, thereby preventing the entry of other sperm and forming what's known as the fertilization membrane (Figure 37).

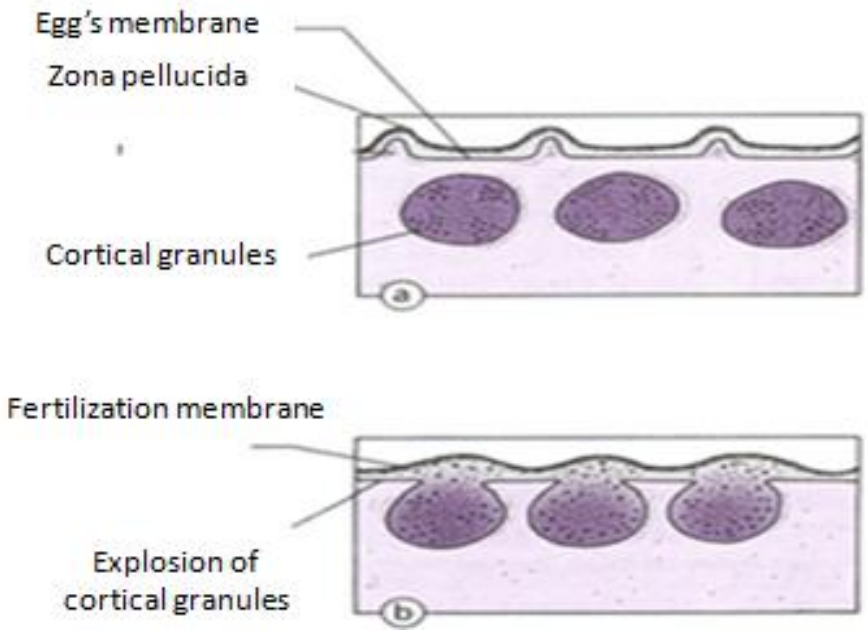

Figure 37: Cortical reaction.

✓ **The completion of the egg's second division:** Due to the disappearance of plasma membrane polarization and the release of calcium in the internal

environment, a mature egg forms with dense cytoplasm and a polar body containing little cytoplasm, each containing the same amount of DNA.

✓ **Formation of the fertilized egg:** After completing its second division, the precursor of the female nucleus forms. Similarly, the sperm loses its tail, and the precursor of the male nucleus forms. Then, the centrosome doubles to form the spindle, and the DNA in each nucleus duplicates. The nuclear membranes fade away as the chromosomes condense and mix to form a single nucleus with 2n chromosomes. The chromosomes align along the equatorial plane to initiate the first division of cell division (cleavage) (Figure 38).

Ultimately, the zygote, with 2n chromosomes, is formed, determining the gender of the embryo (whether the sperm carries an X or Y chromosome), and cleavage begins.

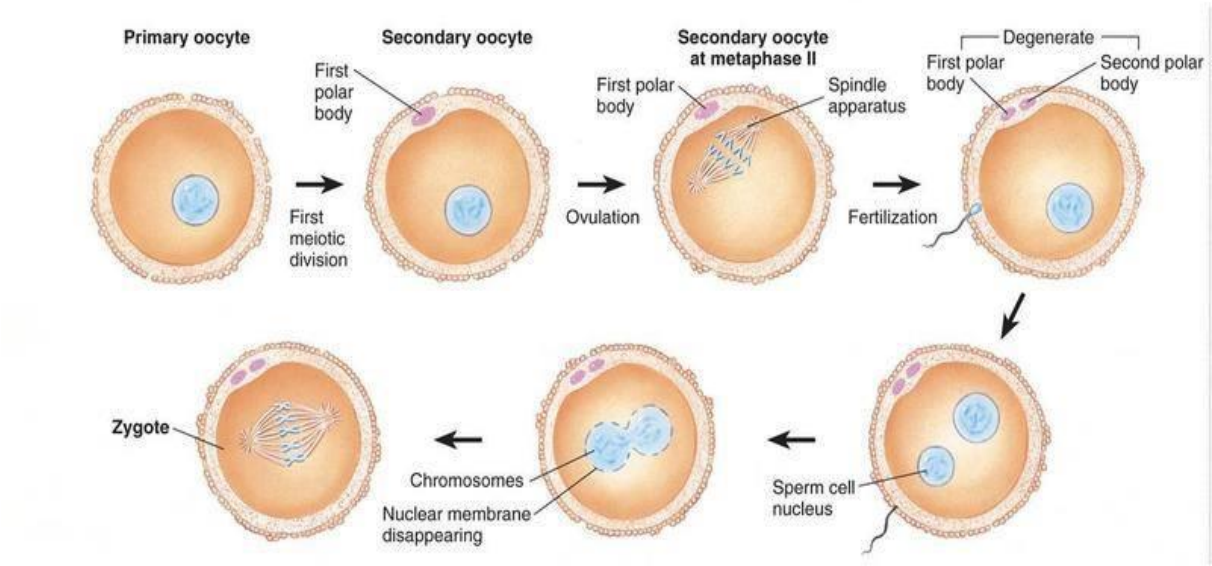

Figure 38: Zygote formation.

2. Sgmentation: The process of "Segmentation" or "Cleavage" refers to the series of mitotic cell divisions undergone by the zygote, leading to the formation of a multicellular structure known as the blastula or morula. This process involves several stages.

2.1. Definition: Segmentation involves the division of the fertilized egg (zygote) through mitosis, resulting in blastomeres (cells). Initially, these blastomeres are larger, but they become progressively smaller as cleavage progresses. The process culminates with the formation of the blastula, which marks the end of the segmentation phase. Before starting segmentation, the zygote undergoes internal preparation by duplicating its genetic material (DNA). In humans, the egg is holoblastic and undergoes complete, equal divisions (Figure 39).

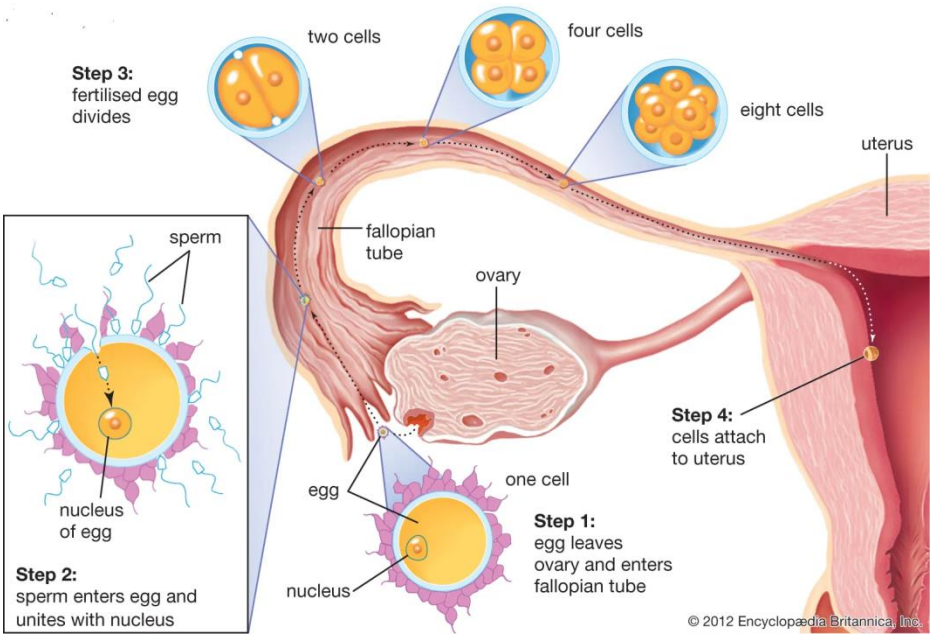

Figure 39: Segmentation.

2.2. Characteristics:

- ✓ Initially regular, segmentation becomes random and successive, making it challenging to track each division.

- ✓ The single-cell zygote transitions into a multicellular structure without growth; cells become smaller with each division.
- ✓ The overall shape remains the same, except for the appearance of a cavity in the blastula known as the blastocoel.

2.3. Stages: Described in (Figure 40)

- ✓ **Migration through the Fallopian tube:** As cleavage progresses, the egg migrates through the Fallopian tube (oviduct). The number of divisions varies, with two cells at 25-30 hours post-fertilization, four cells at 36-40 hours, and eight cells at 40-50 hours. These blastomeres are oval-shaped and separate from each other.
- ✓ **Formation of the morula:** After 50-80 hours (around day 3 or 4) post-fertilization, a cellular mass of 16-64 cells forms, resembling a mulberry (morula in Latin). Its size remains around 150 microns, constantly surrounded by the zona pellucida. The outer cells become smaller than the inner cells, and intercellular connections allow metabolic exchanges, ensuring cohesion and monitoring of exchanges between the morula and the external environment.

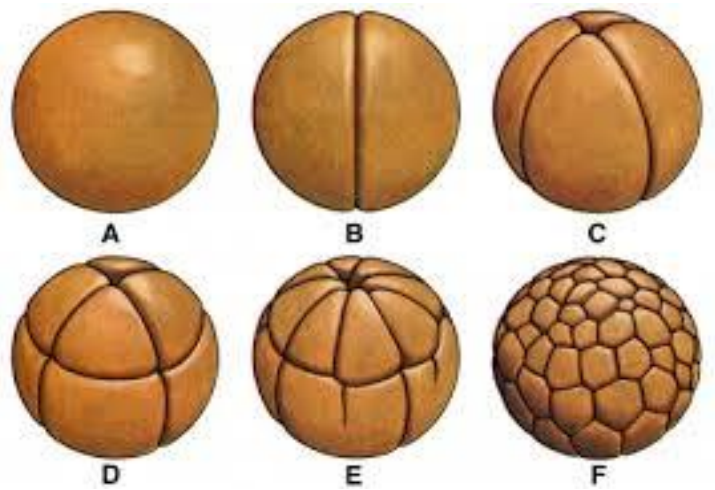

Figure 40: Segmentation stages.

- ✓ **Formation of the blastula or blastocyst:** With around 60 cells, some cavities appear within the inner cells, coalescing into a single cavity known as the blastocyst cavity. This cavity contains fluid from uterine secretions. The trophoblast, a layer of small peripheral cells, forms the nutritive layer, while the larger inner layer or embryoblast gives rise to the embryo and most associated structures (such as the amnion and chorion) (Figure 41).
- ✓ This phase concludes with the blastocyst becoming free to move within the uterus but still influenced by the mother's secretions. Around days 6-7 post-fertilization (day 21 of the menstrual cycle), the subsequent stage begins: implantation, where the blastocyst attaches to the uterine lining, directing the embryoblast toward the endometrium after hatching from zona pellucida.

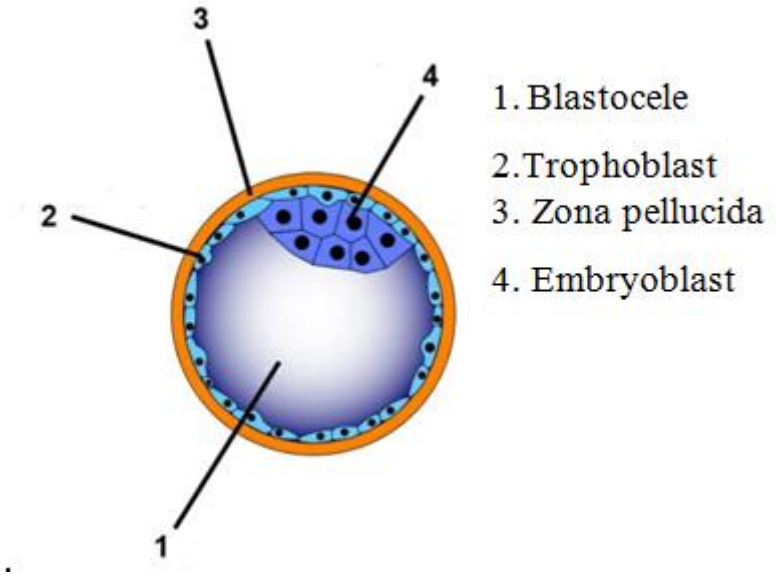

Figure 41: The blastocyst.

Chapter five: The second week of embryonic development

It is characterized by implantation, which marks the beginning of pregnancy.

Implantation (Nidation):

1. Definition: Implantation (Figure 42) is the process by which the embryo attaches itself within the prepared lining of the uterus, facilitated by progesterone and estrogens secreted by the corpus luteum. The duration of implantation occurs during the second week of embryonic development (around days 6-14). It starts with zona pellucida hatching and liberating the blastocyst.

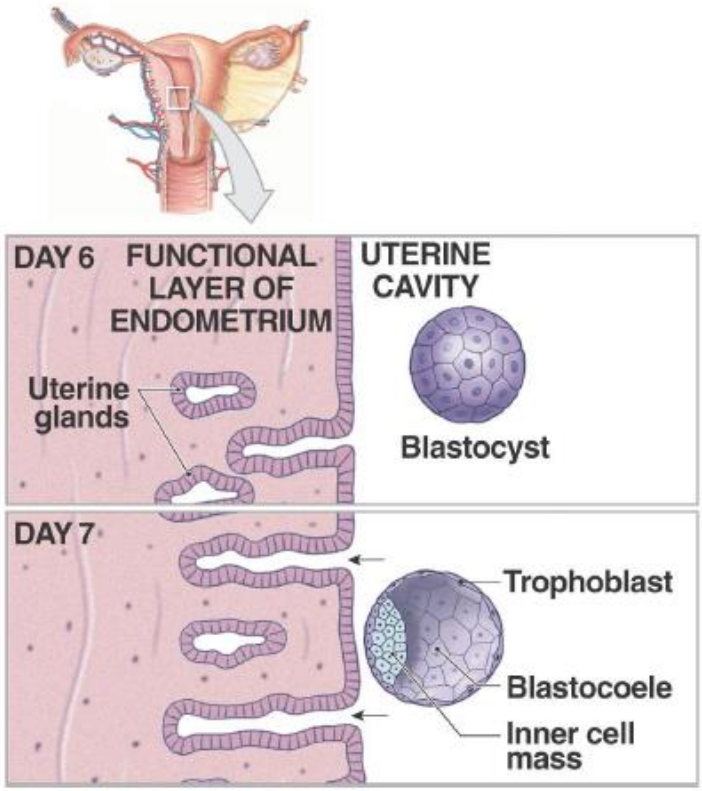

Figure 42: Implantation.

2. Site of implantation: Implantation usually occurs in the upper lateral part of the uterus (the 2 sides) and rarely in the anterior part (Figure 43).

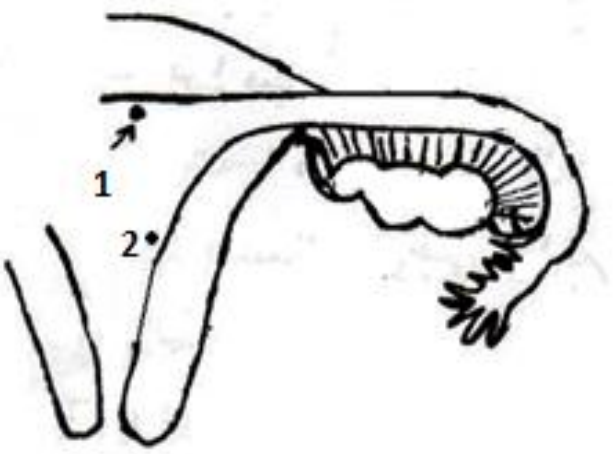

Figure 43: Normal sites of implantation (1: Anterior part, 2: upper lateral part).

3. Stages: Embryonic Development during Implantation:

During implantation, the nourishing cell layer secretes a hormone that helps maintain the corpus luteum (up to the first trimester of pregnancy) and alters the uterine immune reaction towards the embryo, making it appear non-foreign (detectable in a woman's urine around day 6-9 post-conception in a pregnancy test). This hormone, structurally similar to LH, is called HCG (Human Chorionic Gonadotropin).

3.1. Day 6 to 8: After hatching from zona pellucida (Figure 44), the nourishing cell layer divides rapidly and penetrates into the uterus with the help of enzymes it secretes, differentiating into two layers (Figure 44):

- **Cytotrophoblast:** Larger, with membranes and large nuclei.
- **Syncytiotrophoblast:** Envelopes the previous layer, membrane-less (dissolves), forming a multi-nucleated cell mass.

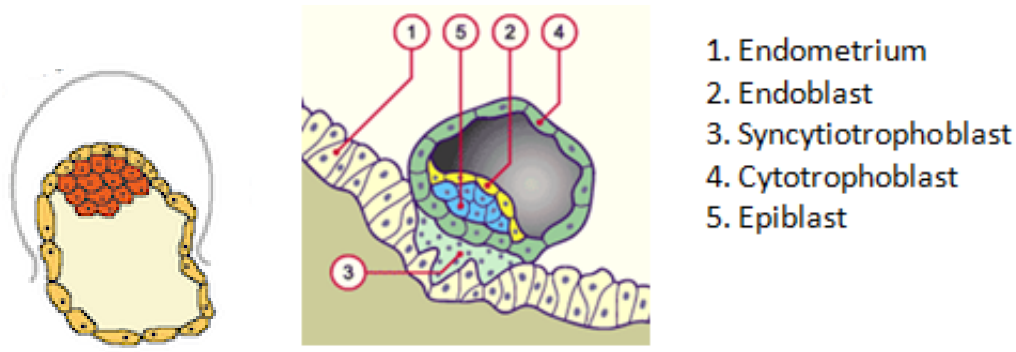

Figure 44: Hatched blastocyst and start of implantation.

The inner cell mass differentiates into (Figure 45):

- **Endoblast:** A layer of small cuboidal cells.
- **Epiblast:** A layer of tall columnar cells that will give rise to the outer and middle layers.

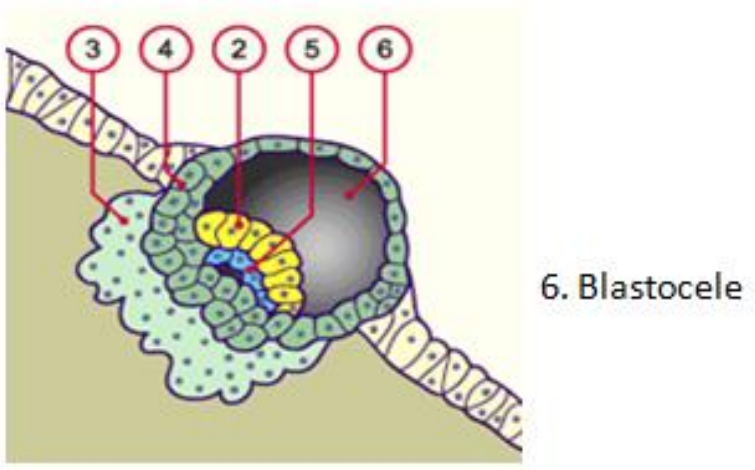

Figure 45: Implantation day 8.

- At this stage, the embryonic disc becomes bilaminar or two-layered.

- The outer layer cells attach to the nourishing layer, then detach, forming the amniotic cavity and surrounding cells are called amniotic cells.

3.2. Day 9 to 12:

- The embryo embeds deeper into the uterine lining, and its entry point is sealed by a fibrous clot.

- Small gaps appear in the nourishing layer, joining to form wider lacunae, known as the lacunar stage (Figure 46).

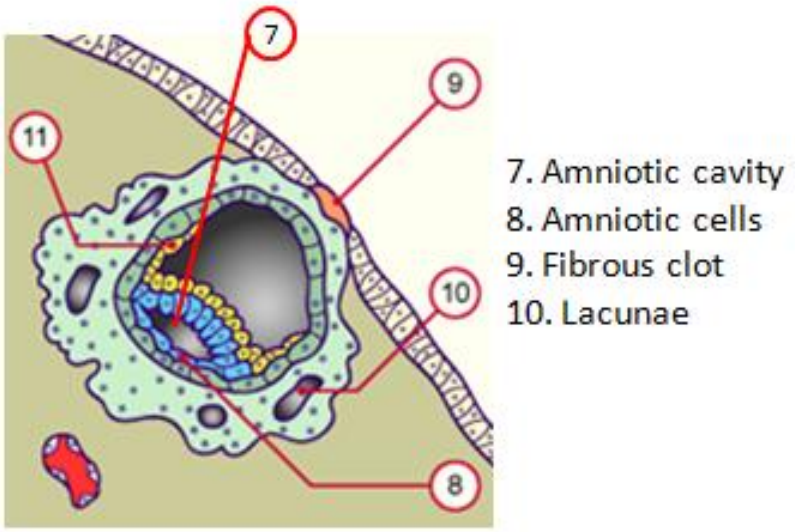

Figure 46: Implantation day 9.

- The uterine lining secretes glycogen.

- Endoblast cells muktiplicates forming a thin membrane around them known as Heuser's membrane.

- The cavity boundaries outside the general cavity form the primary yolk sac, then other layers separate and form the extra-embryonic mesoderm, which surrounds the amniotic and yolk sac.

- Complete embedding of the embryo, and the entry point disappears.

- The lacunae in the nourishing layer expand, breaking the uterine capillaries, establishing direct connections between maternal blood and the space (Figure 47).

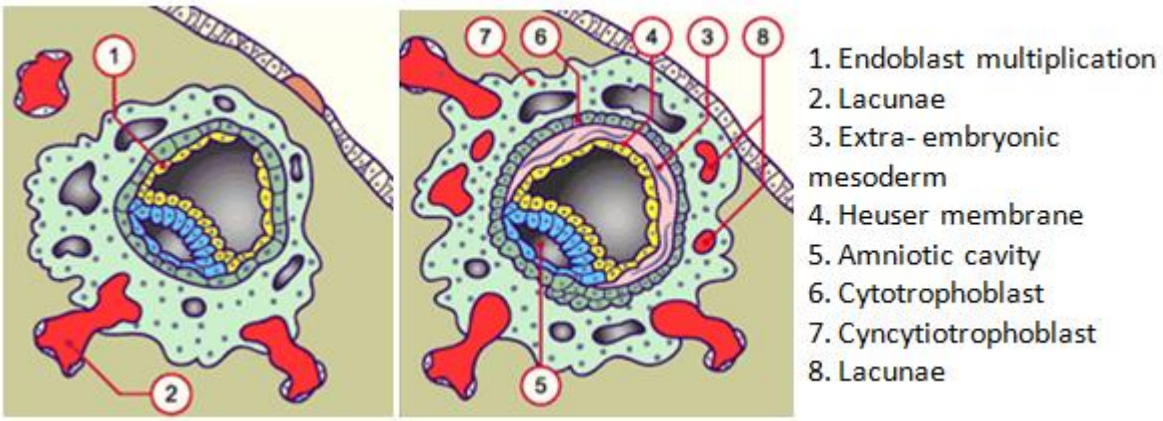

Figure 47: Implantation day 12.

3.3. Day 13 to 14:

- The mesoderm proliferates, forming cavities that come together, creating the chorionic cavity (Figure 48).

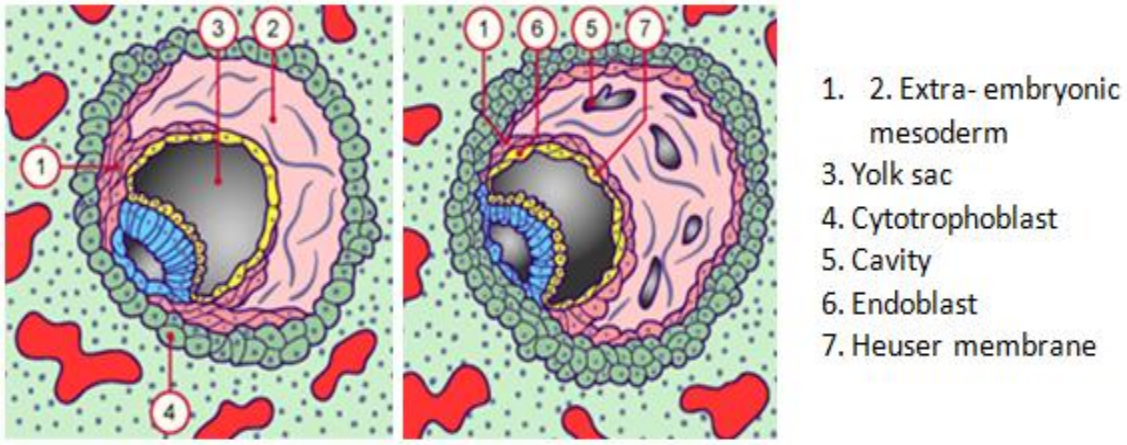

Figure 48: Implantation day 13.

- The connecting region between the embryo and the nourishing layer, the embryonic stalk (Embryonic pedicle), forms; later, it develops into the umbilical cord.

- The entry point disappears completely, replaced by a renewed uterine lining.

- Occasionally, bleeding might occur due to increased maternal blood flow, around day 28 of the cycle, causing confusion with normal menstruation and misjudging the gestation period.

- The inner layer cells continue to multiply, forming flat cells lining Heuser's membrane, defining a smaller new cavity called the secondary yolk sac, pulling remnants of Heuser's membrane with it (Figure 49).

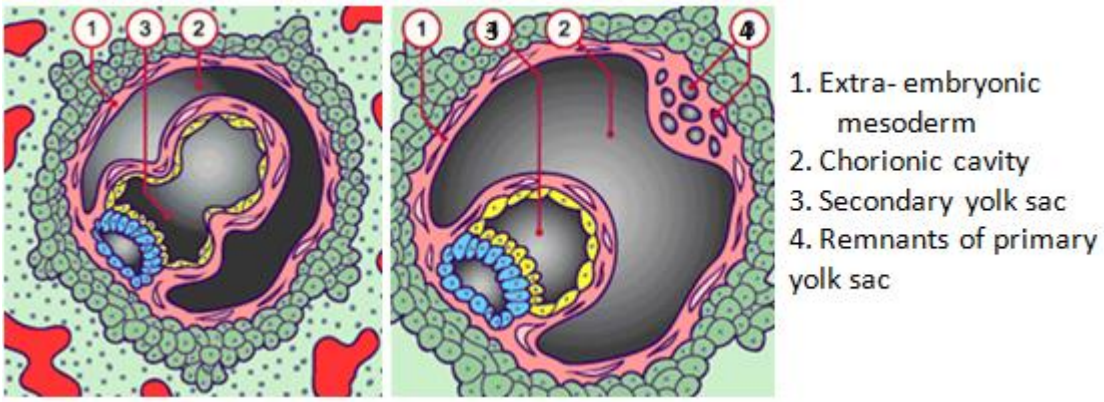

Figure 49: Implantation day 14.

At the end of this stage:

- ✓ The embryo firmly embeds within the uterine lining during the second week (around day 6-15) and receives nourishment from the mother's blood through the uterine blood vessels (lacunar spaces of the syncytiotrophoblast).
- ✓ The embryo consists of two embryonic layers or leaflets, and by the end
- ✓ of the second week, the first signs of the primitive streak appear, the first step towards gastrulation.
- ✓ Formation of the first embryonic attachments (amnion, chorion, and the secondary yolk sac).

Chapter six: the third week of embryonic development.

The third week of embryonic development is characterized by several phenomena, including the development of some embryonic structures (the amnion, blood islands, and chorionic villi), gastrulation (formation of the intermediate germ layer), and the establishment of the notochord, which initiates the nervous system (formation of the neural tube).

1. Embryonic Annexes:

1.1. Allantois: On day 16, the secondary yolk sac extends toward the attachment stalk, forming the allantois. By day 20, spherical cells known as the primordial germ cells appear within the mesenchymal core surrounding the allantois (Figure 50).

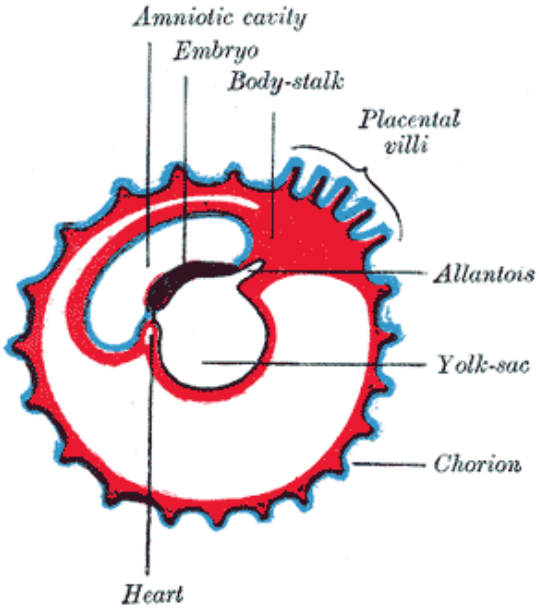

Figure 50: Allantois.

1.2. Blood Islands (Wolff and Pander Islets): On day 17, cellular masses representing blood islands appear within the mesenchyme.

✓ Around the attachment stalk (Embryonic pedicle), near the allantois: They contribute to the venous circulation of umbilical corde.

✓ Within the extraembryonic mesenchyme: They give rise to the first blood cells.

✓ Within the chorionic plate: They form the vascular network of the chorionic villi (Figure 51).

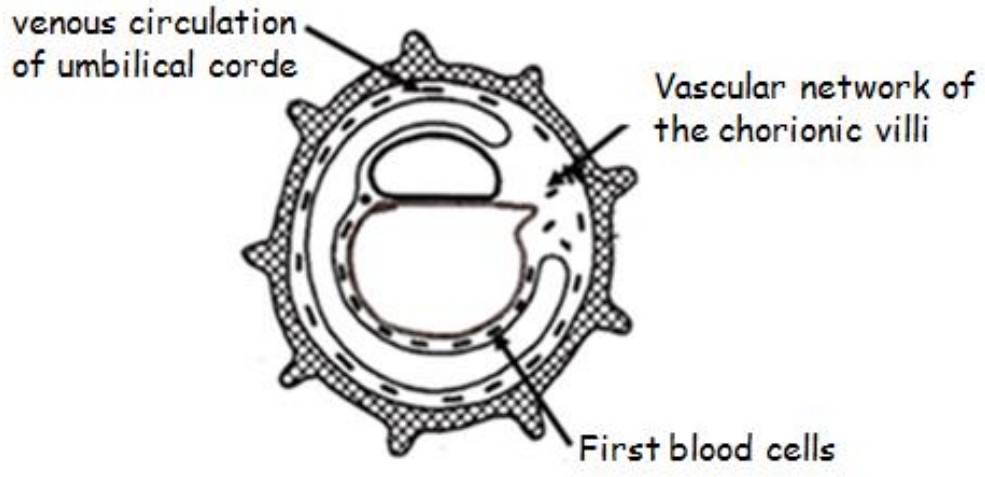

Figure 51: Blood Islands (Wolff and Pander Islets).

1.3. Development of the Placenta: On day 13, within the syncytiotrophoblast layer and the chorionic plate, cellular masses called primary villi appear. By day 15, the mesenchyme of the chorionic plate enters the axis of these villi, making them secondary villi. Between days 18 and 21, primary blood islands differentiate within the mesenchyme axis inside the secondary villi, transforming them into tertiary villi (Figure 52).

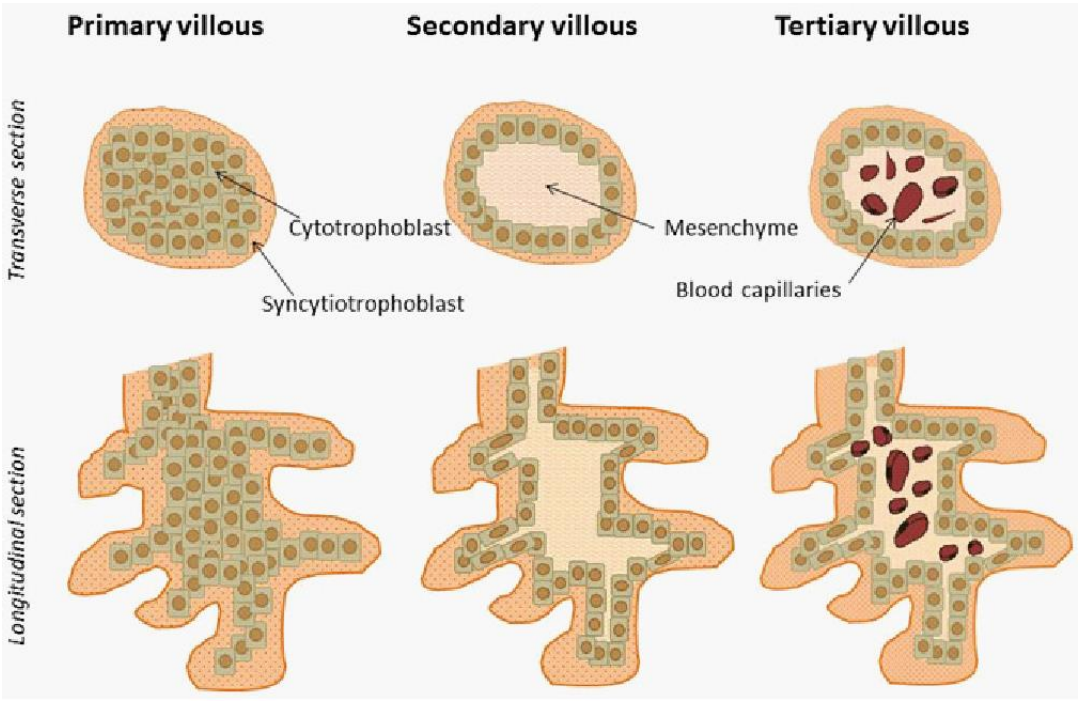

Figure 52: Development of the placental villi.

At the level of the chorionic plate: Vascular lacunae filled with maternal blood coalesce, forming inter-villous spaces between the villi.

2. Gastrulation: It's a series of cellular movements aimed at forming the third germ layer (mesoderm).

2.1. Formation of the Primitive Streak: On day 16, cell clusters appear on the surface of the outer layer (they condense). Then, a line forms within those clusters: the primitive streak, with its endpoint known as the Hensen's node. Through the Hensen's node, the distinction between the head (cranial) and tail (caudal) ends can be recognized (before it: caudal end, after it: cranial end) (Figure 53).

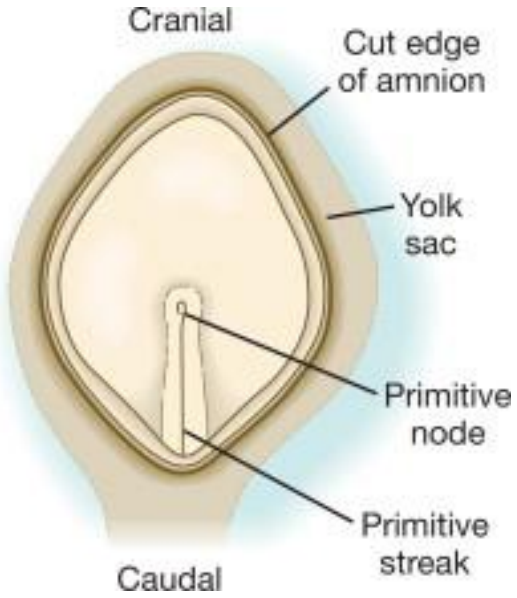

Figure 53: The primitive Streak.

2.2. Formation of the Middle or Mesodermal Germ Layer (Mésoblaste ou Mésoderme): On day 17, cells from the thickening outer layer separate and spread towards both right and left sides, sandwiched between the outer and inner layers, forming the mesodermal or middle germ layer. This differentiation defines the outer layer.

In two specific regions, the outer and inner layers remain connected: the oral and anal plates (Figure 54).

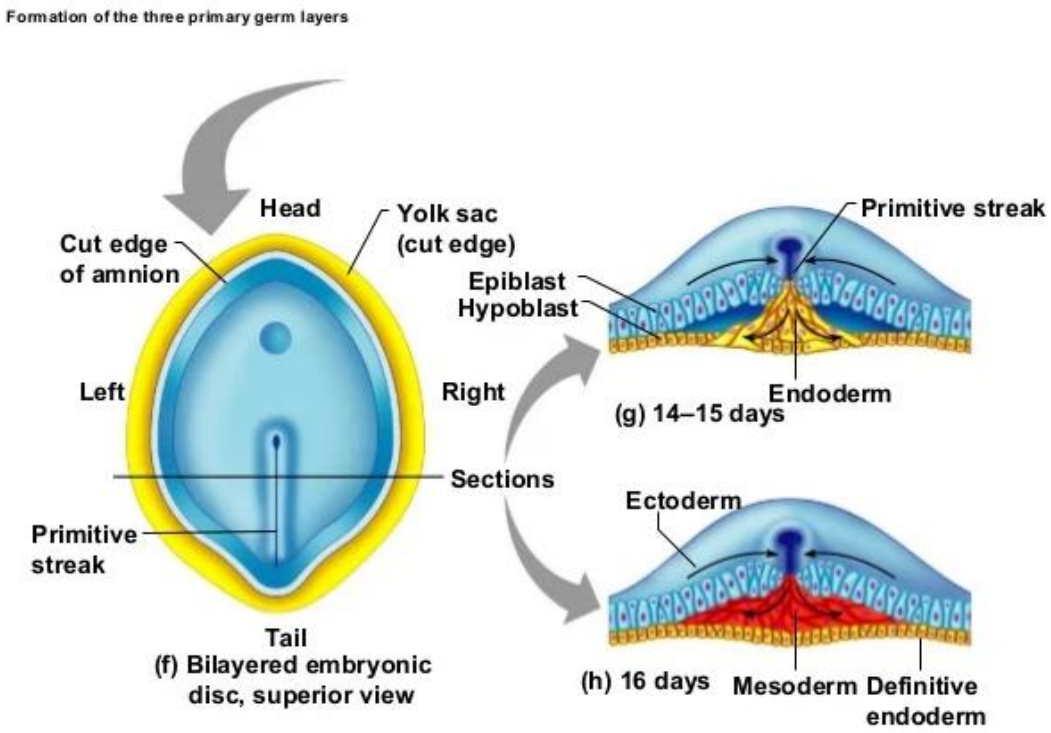

Figure 54: Formation of mesoderm.

3. Formation of the Notochord: After day 17, some cells originating from the outer layer move inwards towards the middle layer through the Hensen's node, extending axially forward between the inner and outer layers, forming the vertical extension primarily made of materials composing the cord (Figure 55). During days 18 and 19, the embryonic disc grows wider in the front and longer in the back. Simultaneously, the vertical extension grows, forming a canal known as the notochordal canal, its base adhering to the roof of the secondary yolk sac. At this stage, there are disruptions in several points concerning the base of the notochordal canal and the roof of the secondary yolk sac, allowing the latter to connect with the amniotic cavity.

By day 19, the bend in the outer layer concludes, and the primitive streak regresses. Consequently, only outer tissue cells remain on the surface as all other cells have differentiated during their penetration between the layers to form the intermediate tissue. Additionally, disruptions extend along the base of the

notochordal canal and the roof of the secondary yolk sac, creating an inverted trough shape. This structure then expands into a plate, known as the notochordal plate, occupying the middle region of the roof of the yolk sac and remaining connected to the inner tissue.

By the end of day 19, at the Hensen's node location, a gap called the Lieberkühn canal persists, allowing direct communication between the amniotic cavity and the secondary yolk sac. The fetus begins to bend, making its dorsal region convex, while the oral and anal plates take on a diagonal shape concerning the fetus's longitudinal axis. The notochordal plate assumes a trough shape, and the inner tissue closes, forming the spinal cord, which later develops into the spinal column and the tail base of the skull.

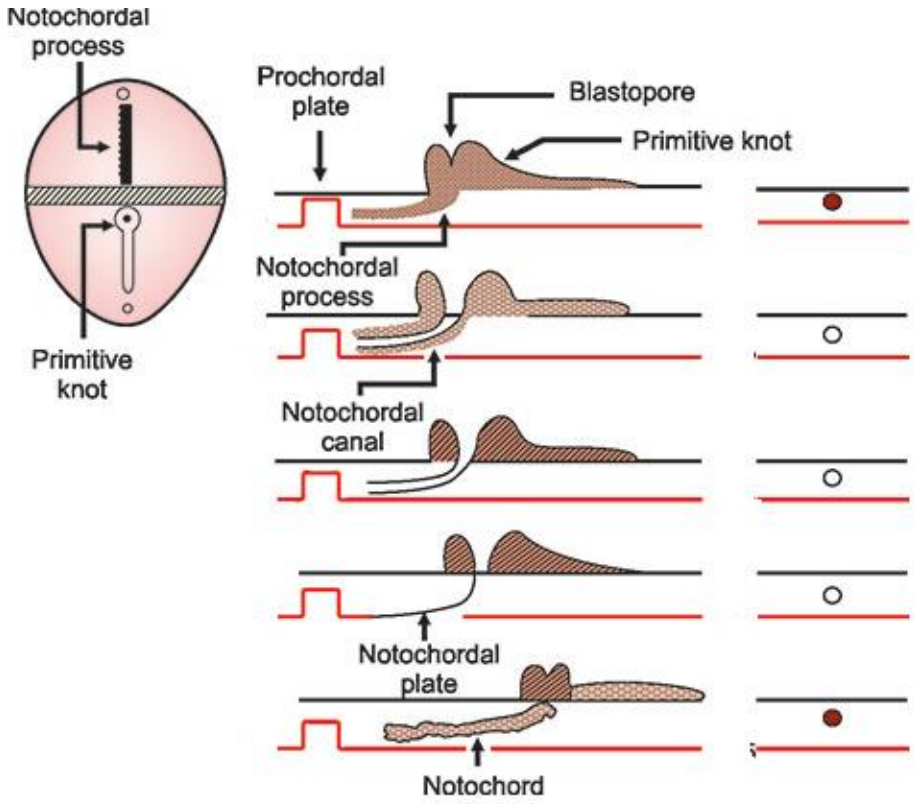

Figure 55: Formation of notochord.

4. Neurulation: It progresses through three stages (Figure 56):

4.1. Neural Plate: On day 18, the thickness of the outer embryonic tissue (beside the Hensen's node) increases and extends to become shaped like a paddle: the neural plate. Neural tissue forms at the level of the outer layer along with the remaining tissue.

4.2. Neural Groove: On day 19, the edges of the plate rise to form the neural groove. The remaining tissue still attached to the edges of the groove is known as neural crests.

4.3. Neural Tube: The edges of the neural groove gradually start to close, forming the neural tube. As the edges of the groove unite, the neural crests become isolated. Neural tube closure concludes in week 4 with the closing of the posterior and anterior neural openings (on days 26 and 28).

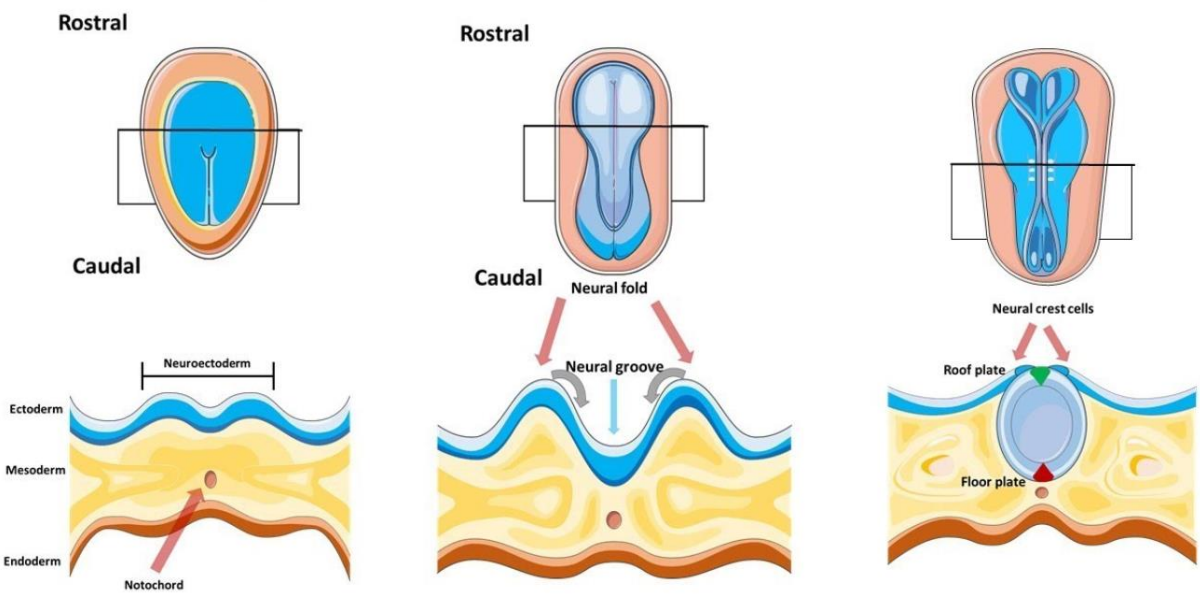

Figure 56: Neurulation stages.

5. The differentiation of the mesoderm: At the end of neurulation, the intermediate mesoderm (Figure 57) differentiates into para-axial tissue, intermediate tissue, and lateral tissue: splanchnic and somatic.

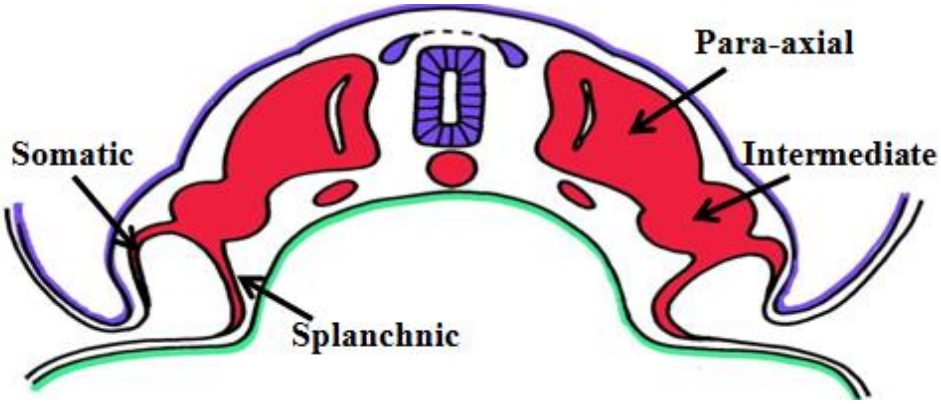

Figure 57: Differentiation of the mesoderm.

The para-axial one begins to divide to form the dorsal pieces or somites (3 pairs by day 21) (Figure 58).

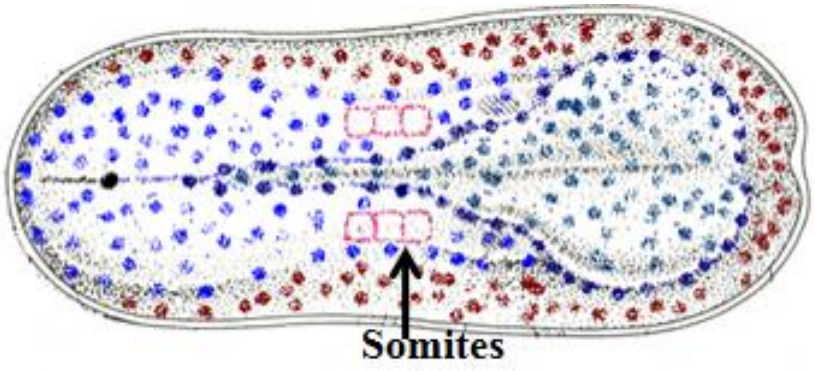

Figure 58: Somites (3 pairs by day 21).

In this third week, several embryonic structures begin to form, making the embryo three-layered. The neural axis starts to take shape, and some dorsal segments begin their development. These stages mark the beginning of a new phase: Organogenesis.

Chapter Seven: The Fourth Week of Fetal Development:

The fourth week of fetal development is characterized by several phenomena, including: the isolation of the fetus, completion of neural formation, development of the mesodermal tissue, and differentiation of the outer tissue

1. Embryonic Isolation (embryo delimitation): This involves the wrapping of the embryo's edges around the abdominal region, which later becomes the genital region. Its outcome: the embryo becomes isolated from its attachments, connected only by the umbilical cord, a process also known as the rotation of the fetus (Figure 59).

- ✓ The rapid growth of neural tissue leads to the rotation of the cephalic end towards the abdominal region.
- ✓ Growth of the amniotic cavity from the tail end.
- ✓ Their growth (neural tissue and amniotic cavity) contributes to the convergence of the cephalic and caudal regions, thereby exerting pressure on the secondary yolk sac.
- ✓ The roof of the secondary yolk sac forms a longitudinal tube: the primitive gut.
- ✓ What remains of the secondary yolk sac forms the umbilical or vitelline vesicle.
- ✓ Ultimately, the amniotic cavity occupies the entire general cavity: the embryonic or chorionic cavity.
- ✓ The attachment site becomes located in the abdominal region opposite the secondary yolk sac, and at this level, the primary umbilical cord forms from two attachments: the allantois and the umbilical vesicle, covered by the amnion wall.

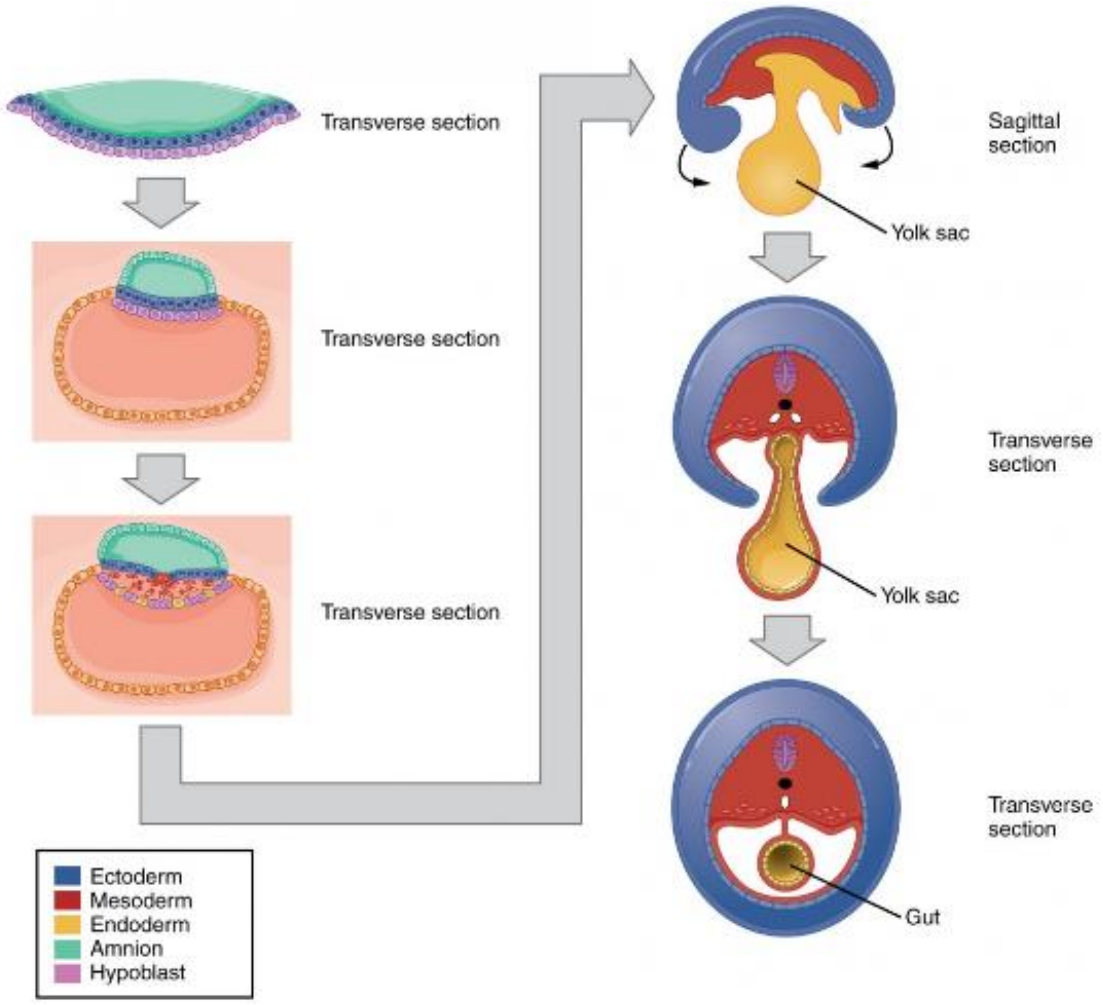

Figure 59: Embryo delimitation.

2. Completion of Neural Formation: Closure of the neural tube and the anterior and posterior openings (on days 26 and 28 respectively).

- ✓ The Neural Tube: Later gives rise to the central nervous system, where the cranial region of the tube eventually widens to form the brain, while the remainder forms the spinal cord.
- ✓ At the end of the fourth week: Appearance of three regions in the brain: the anterior, middle, and posterior brain (Figure 60).
- ✓ Neural Crests: Later give rise to the peripheral nervous system (spinal ganglia and nerves).

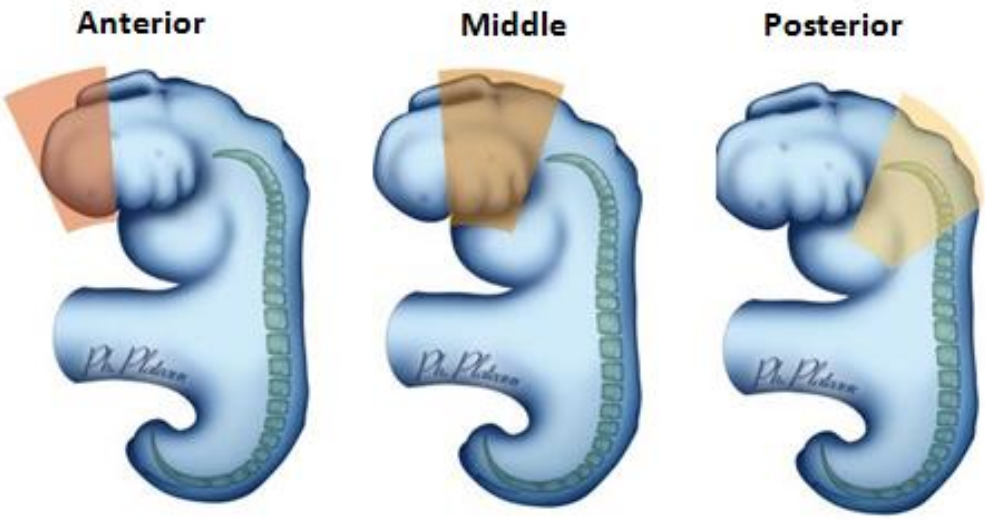

Figure 60: The three regions of the brain.

3. Development of the Intermediate Tissue:

3.1. Para-axial: The medial intermediate tissue undergoes segmentation, forming somites or dorsal segments: 7 pairs on day 22, 10 pairs on day 23, 14 pairs on day 25, and 25 pairs on day 28 (Figure 61). These segments subsequently divide into two parts: muscular, giving rise to muscles, and skeletal, forming vertebrae.

Figure 61: Development of para-axial tisue.

3.2. Lateral somatic: The lateral tissue increases, elevating the outer tissue to form the buds. The upper or arm buds emerge on day 27, and the lower limb or leg buds appear on day 28 (Figure 62).

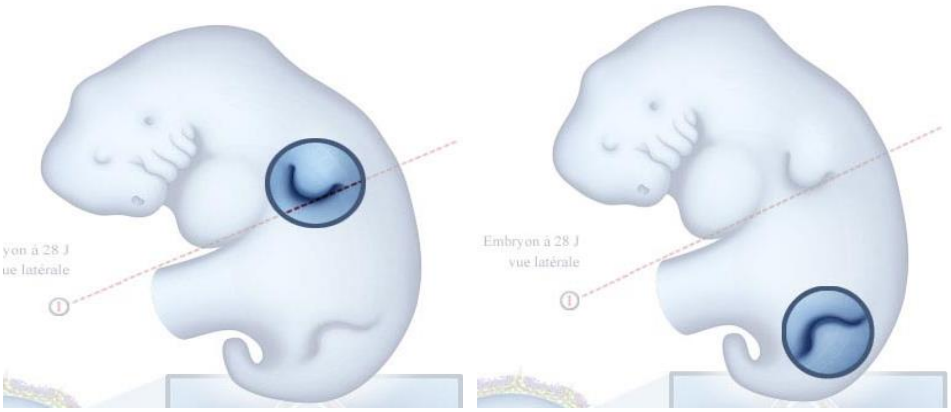

Figure 62: Development of lateral somatic tisue.

4. Formation of pharyngeal arches: Appearance of three pharyngeal arches iat the last of this week (Figure 63).

5. Differentiation of Outer Tissue or ectoderm: To form sensory vesicles (auditory, olfactory, and optic) (Figure 63).

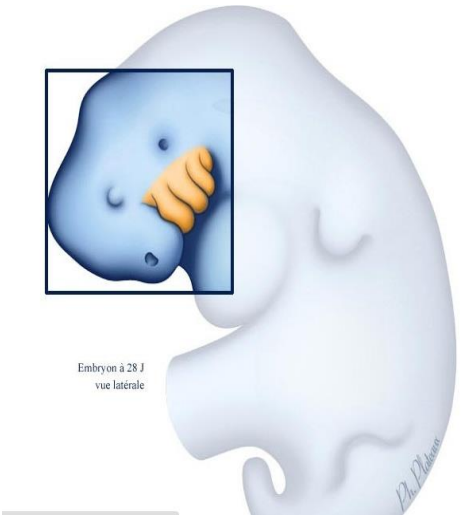

Figure 63: Formation of pharyngeal arches and differentiation of ectoderm.

Chapter Eight: Study of the external appearance and cross-sections of a fetus aged of 28 days:

1. External Appearance:

- The fetus measures 4.25 millimeters with distinct boundaries: connected to appendages through the umbilical cord and covered by the amnion.
- Closure of both the anterior and posterior neuropores (on days 25 and 28, respectively).
- Notable: optic and auditory vesicles, pharyngeal arches or pouches, and 25 pairs of somites.
- Emergence of the hand plate or limb bud (Figure 64).

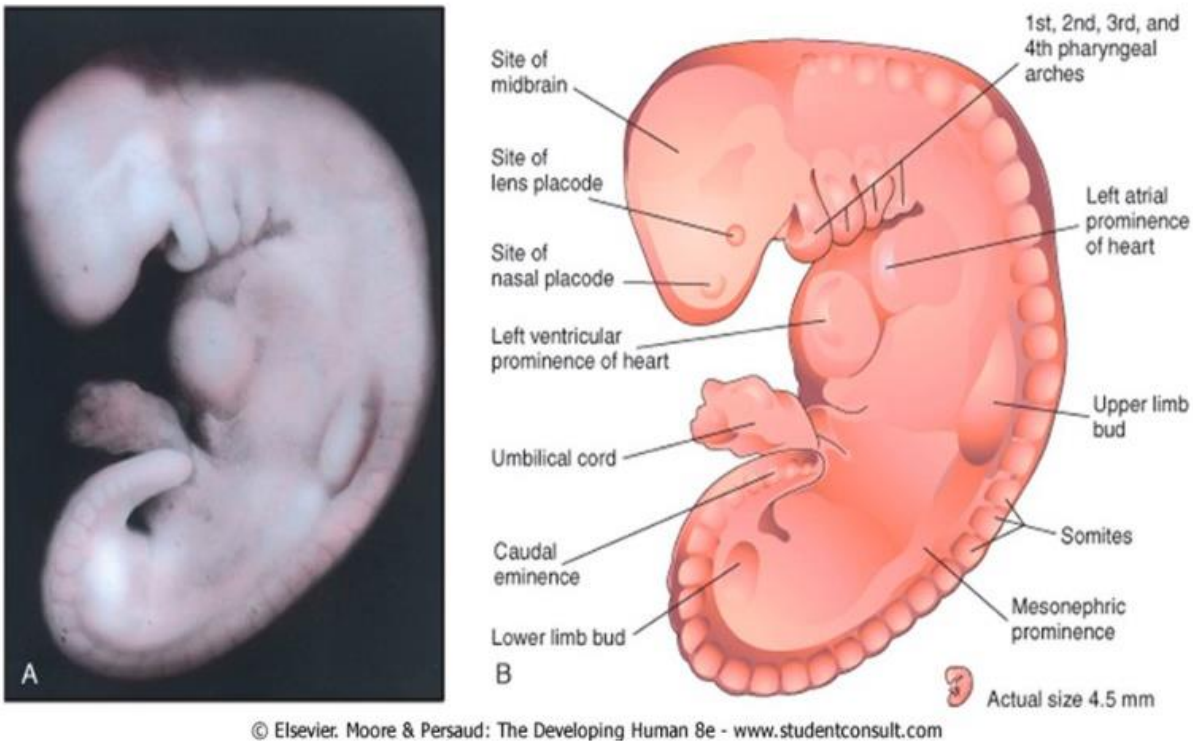

Figure 64: External appearance and cross-sections of a fetus aged of 28 days.

2. Full Sagittal Section:

- Formation of the neural tube and differentiation of 3 brain vesicles: anteriorbrain, middle and posterior brain.
- Emergence of the pituitary gland primordium.
- Continuity between the digestive tube and the umbilical cord.
- This digestive tube contains: a pancreatic and liver bud.
- The heart is positioned ventrally.
- As a result of fetal development: convergence of the umbilical cord and the allantois (Figure 65).

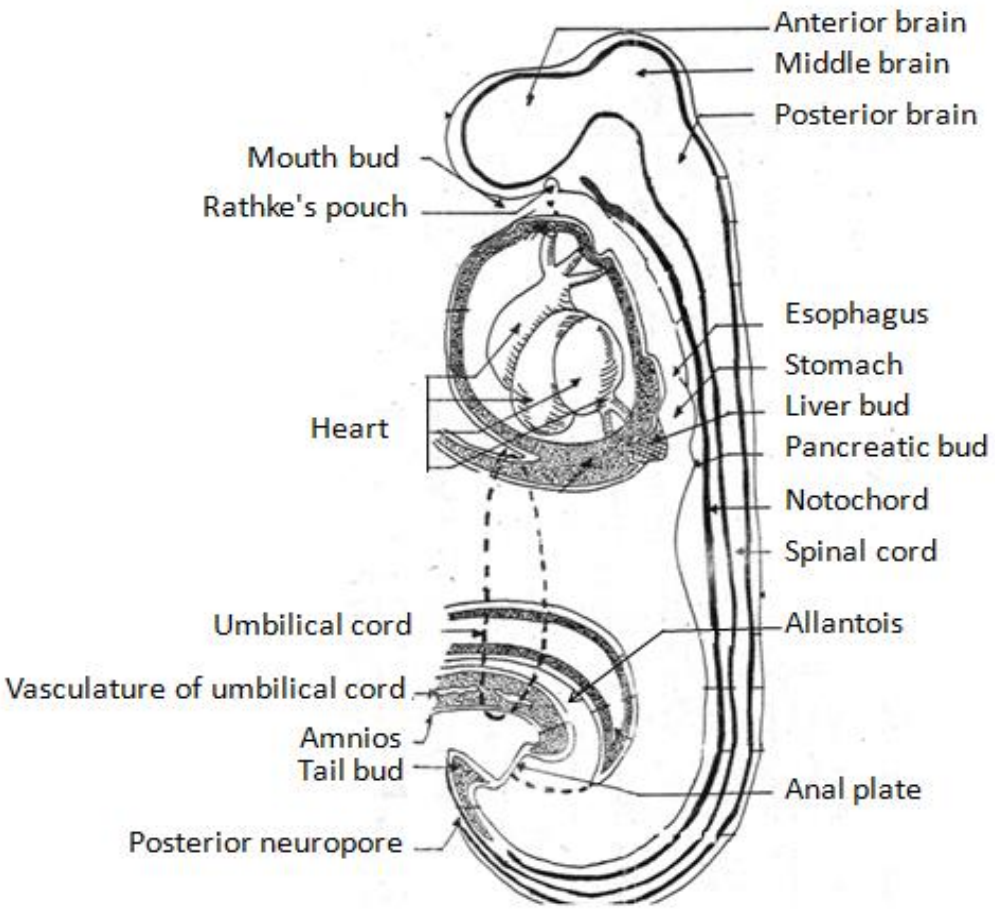

Figure 65: Median sagittal section of a fetus aged of 28 days.

Chapter Nine: Final Development of Fetal Appendages

This chapter details the final development of fetal appendages, including: the umbilical corde,

1. Umbilical corde:

1.1. Primitive umbilical corde: It forms from two parts:

- **Allantois:** The allantois develops inside the umbilical cord and elongates slightly. It eventually merges with the yolk sac to form the primitive umbilical cord.

- Yolk Sac: The yolk sac doesn't contain nutritional reserves in humans and is relatively small. It closes during the fourth week of development, forming the **primary gut** for the embryo. The remaining part becomes the **vitelline or umbilical vesicle**.

- **The vitelline vesicle** joins with the **allantois** to form the **primitive umbilical cord** (Figure 66).

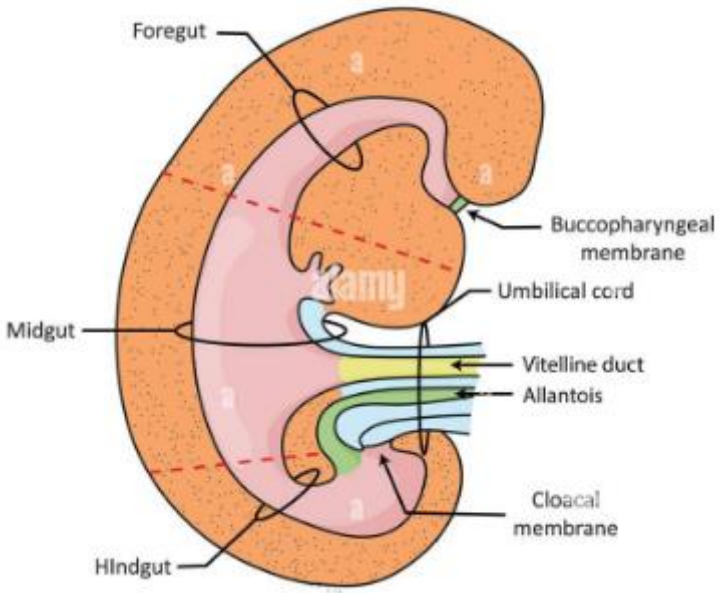

Figure 66: Primitive umbilical cord.

1.2. Umbilical corde: It forms by the merging of the allantois, the vitelline vesicle, blood vessels from the chorion, within the connecting stalk (embryonic pedicle). It connects the fetus to the placenta and can reach about 50 cm in length and 1.5 cm in thickness, containing two umbilical arteries (carrying blood from the fetus to the placenta) and one umbilical vein (carrying blood from the placenta to the fetus) (Figure 67).

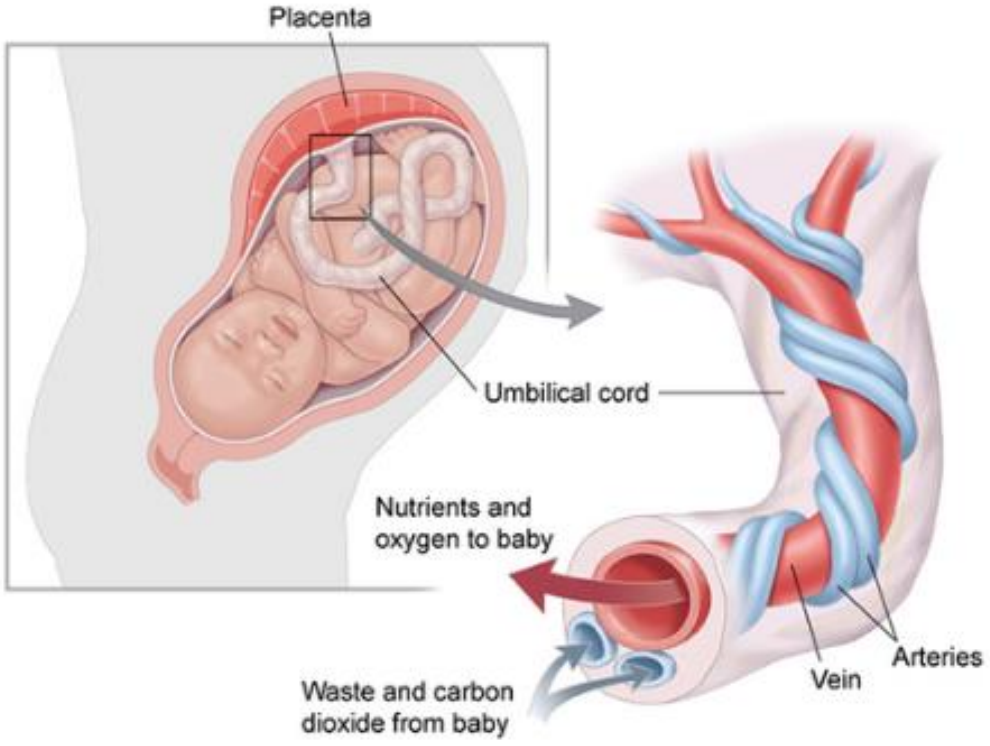

Figure 67: Umbilical cord.

2. Amniotic membrane and Amniotic fluid:

2.1. Amniotic membrane: It's a thin, sealed membrane surrounding the fetus, forming a sac filled with amniotic fluid. Initially formed by amniotic cells, most of the fluid comes from the mother, with contributions from the fetus through urine and sweat. Its volume increases as the fetus grows, reaching its peak in the seventh month (1.5 liters), gradually decreasing to around 1 liter before birth (Figure 68).

2.2. Characteristics of Amniotic fluid: Transparent in early pregnancy, turning slightly yellowish-white towards the end. It has a salty taste, a scent resembling semen, and is composed of 98-99% water, with minerals, proteins, mucus, grape sugar, and some white blood cells. The fetus starts swallowing amniotic fluid in the fifth month, absorbing it into its bloodstream, passing it back into the amniotic sac through the placenta. Towards the end of pregnancy, the fetus can swallow around 400 ml daily. Insufficient amniotic fluid or excessive accumulation (polyhydramnios) can indicate abnormalities.

2.3. Functions of Amniotic Fluid:

✓ During Pregnancy:

- Provides nourishment to the fetus, aiding its growth.

- Protects the fetus from sudden shocks and allows movement, aiding muscular development.

- Maintains fetal temperature.

- Prevents adhesion of the fetus to the amniotic membrane, allowing for proportional growth.

✓ During Birth:

- Distributes pressure during uterine contractions.

- Helps in cervical dilation.

- Contains substances that stimulate uterine contractions during delivery.

✓ Additionally, studying amniotic fluid can help determine the fetus's gender, identify sexual anomalies, diagnose gender-related diseases, and determine the fetus's blood group.

3. Chorion: It's the outer membrane in fetal membranes, originating from the nutritive layer of the trophoblast and adjacent to the extraembryonic mesoderm. It initially has primary villi, which later change to secondary and tertiary villi, contributing to placental formation (Figure 68).

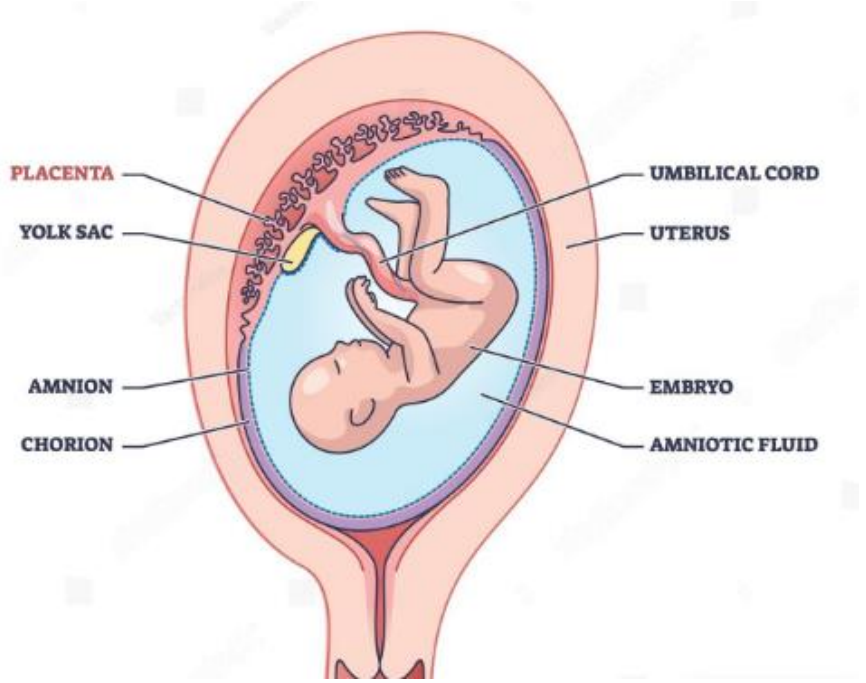

Figure 68: Amnion and chorion.

4. Placenta: It's a highly vascular disc-shaped or oval organ responsible for vital functions between the mother and fetus. Formation begins in the third week of intrauterine life and is expelled from the uterus after birth. It has maternal and fetal sides, with the fetal side covered by the amniotic membrane. It facilitates nutrient and waste exchange between maternal and fetal tissues.

From the end of the third week until the end of pregnancy, nutrients, oxygen, and metabolic waste are transferred through the placenta. The placenta is connected to the fetus via the umbilical cord (Figure 69).

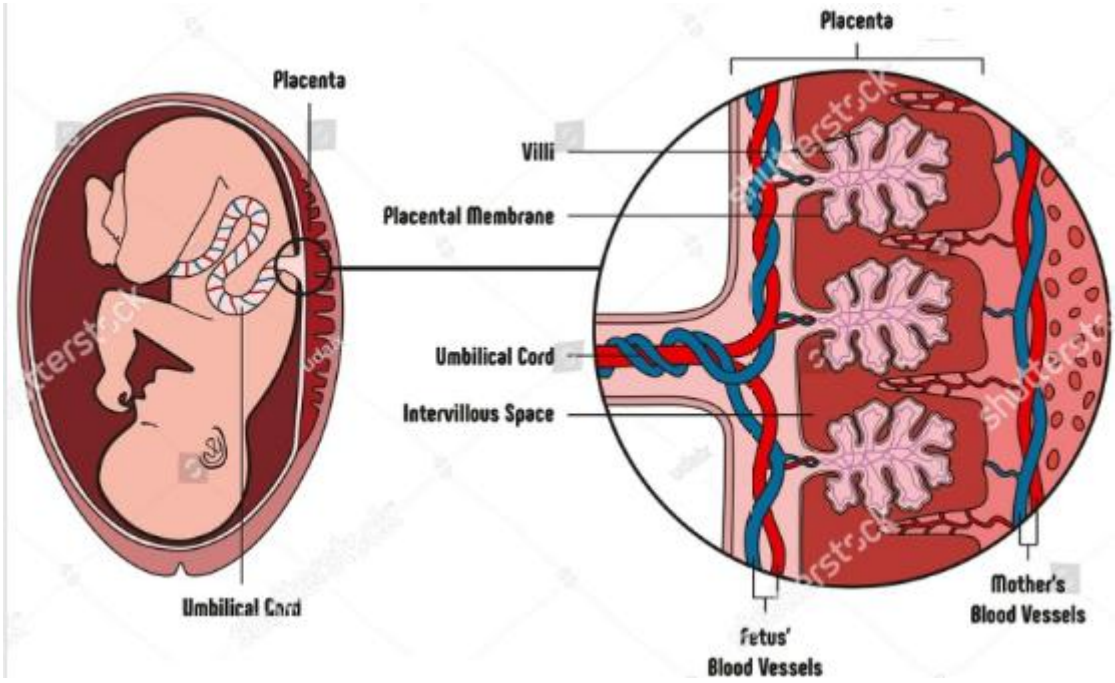

Figure 69: Placenta structure.

Functions of the placenta include:

- ✓ Nutrition: The absence of yolk sac in the human egg causes the complete dependence of embryonic development on various nutrients provided by the uterine environment. These nutrients are carried through a continuous blood flow that reaches the fetus via the placenta. Notably, there's no mixing of the maternal tissue structure with the fetal tissue structure because each has its separate and distinct circulatory system. There is no mixing of the mother's blood with the fetal blood or vice versa; the two circulations remain entirely separate, each with its own barrier - the placental barrier.
- ✓ Transporting oxygen from the mother's body to the fetus.
- ✓ Removing waste products (such as carbon dioxide and urine) from the fetus to the mother's blood.
- ✓ Producing essential hormones for maintaining pregnancy and facilitating fetal development (like progesterone).

- ✓ Acting as a barrier against germs and bacteria, protecting the fetus from their passage.

Chapter Ten: Final Development of the Three Embryonic Germ Layers:

Ectoderm (outer), Mesoderm (middle), and Endoderm (inner)

Ectoderm, mesoderm, and endoderm, which are the three primary germ layers originate during embryonic development, form all tissues and organs in the body (Table 2).

Table 2: Final Development of the Three Embryonic Germ Layers.

1. Ectoderm	Nervous tissue	Neural tube	Central nervous system
		Neural crests	Peripheral nervous system + Melanocytes
	Other tissue	Skin + Sensory organs	
2. Mesoderm	Para-axial	Bones + Skeletal uscles	
	Intermediate	Urinary and Reproductive system	
	Lateral	Somatic	Upper and lower limbs
		Splanchnic	Heart + Smooth muscles
3. Extra-embryonic mesoderm	Blood cells		
4. Endoderm	Respiratory and Digestive system		

Chapter Eleven: Fetal Development During Early and Late Months + Birth.

1. Fetal Development During Early and Late Months:

1.1. First Month:

- ✓ Head development in the fetus.
- ✓ Formation of sensory buds, heart, liver, and digestive system.
- ✓ Length: 0.5 cm (Figure 70).

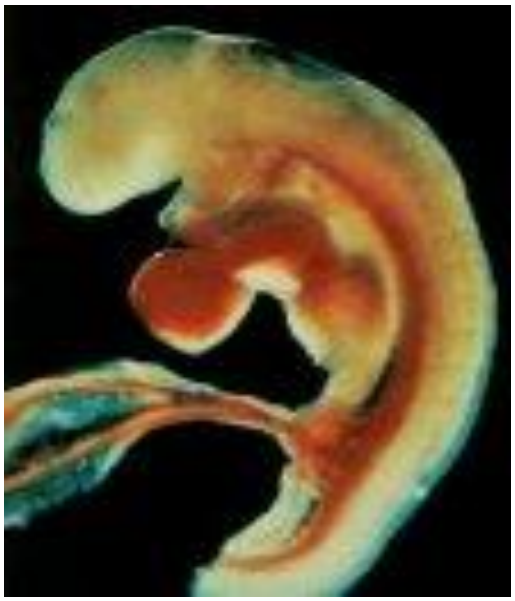

Figure 70: Fetal Development: First month.

1.2. Second Month:

- ✓ Development of arms and legs starts.
- ✓ Heart forms with four chambers and begins pumping blood.
- ✓ Brain development begins, facial features and various body organs start to form (eyes, ears, digestive system, kidneys).
- ✓ Length of the fetus: 5 cm (Figure 71).

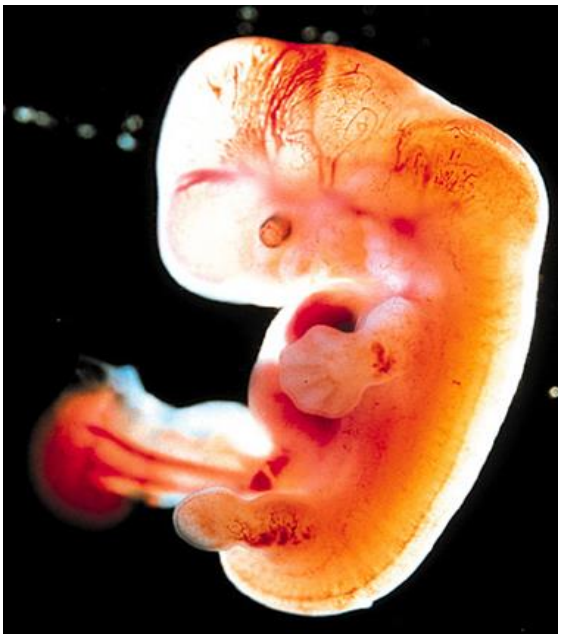

Figure 71: Fetal Development: Second month.

1.3. Third Month:

- ✓ Fetal movement begins.
- ✓ Rapid fetal growth.
- ✓ Weight: 26g, length: 8 cm.
- ✓ Gender can be distinguished by the end of the month (Figure 72).

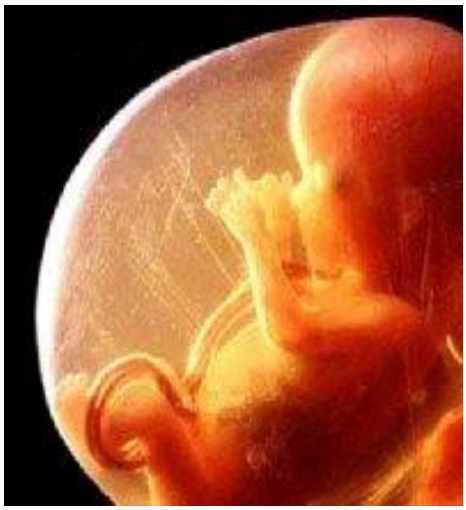

Figure 72: Fetal Development: Third month.

1.4. Fourth Month:

- ✓ All fetal organs complete their formation, resembling a small baby.
- ✓ Increased fetal activity and movement.
- ✓ Weight: 114g, length: 15 cm.
- ✓ By the end of the month, kidneys start producing urine, and the liver secretes bile (Figure 73).

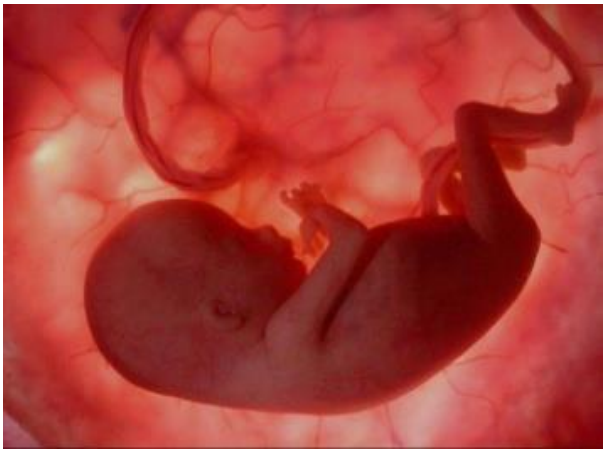

Figure 73: Fetal Development: Fourth month.

1.5. Fifth Month:

- ✓ Fetal heartbeats can be heard using a stethoscope.
- ✓ Stronger fetal movements.
- ✓ Weight: 228g, length: 25 cm.
- ✓ Appearance of hair and fingernails.
- ✓ Development of milk teeth in the jaw (Figure 74).

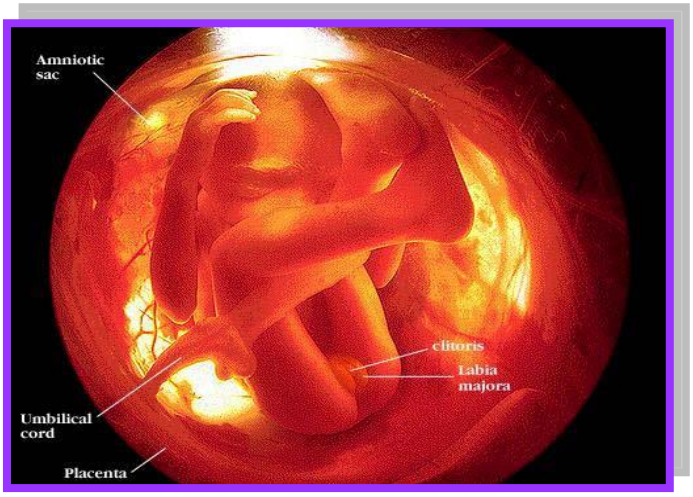

Figure 74: Fetal Development: Fifth month.

1.6. Sixth Month:

- ✓ More vigorous fetal movements.
- ✓ Fetal facial skin appears red and wrinkled.
- ✓ Fetal survival unlikely if born in the fifth or sixth month due to incomplete brain and respiratory system development.
- ✓ Weight: 680g, length: 30 cm (Figure 75).

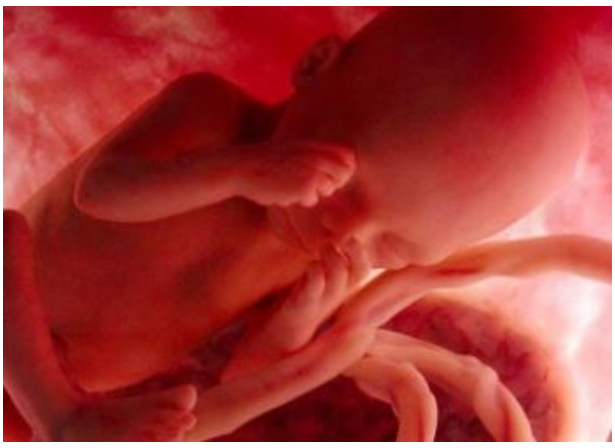

Figure 75: Fetal Development: Sixth month.

1.7. Seventh Month:

- ✓ Fetus may occasionally open its eyes.
- ✓ Ability to hear sounds.

- ✓ Formation of fingernails.
- ✓ Fetus starts to position its head downward.
- ✓ Nervous and respiratory systems mature.
- ✓ Weight: 1.13kg, length: 38 cm (Figure 76).

Figure 76: Fetal Development: Seventh month.

1.8. Eighth Month:

- ✓ Increased fetal movements.
- ✓ Skin wrinkles start to disappear.
- ✓ Fetus assumes the birthing position.
- ✓ Weight: 1.80kg, length: 42 cm.
- ✓ In males, testicles completely descend (Figure 77).

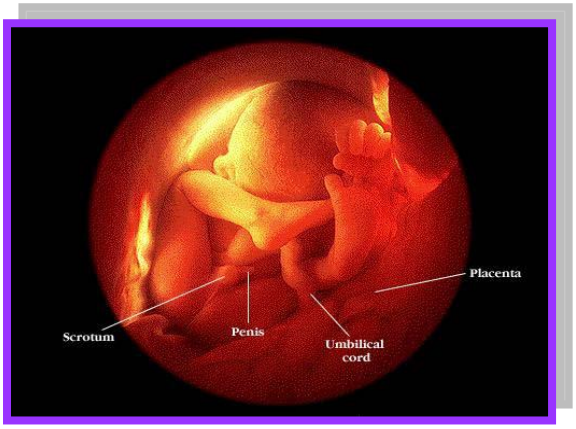

Figure 77: Fetal Development: Eighth month.

1.9. Ninth Month:

- ✓ Slower growth during this month.
- ✓ Fetus fully formed, covered in hair on the head.
- ✓ Weight: 3.25kg, length: 50 cm or more (Figure 78).

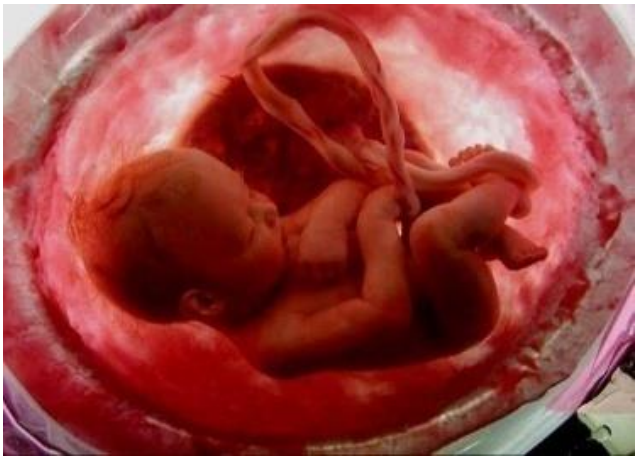

Figure 78: Fetal Development: Ninth month.

2. Birth:

The fetus becomes ready for birth after the completion of organ formation, typically after nine months.

A few weeks before birth, the fetus changes position, with its head pointing towards the mother's pelvis to prepare for delivery.

Hormonal activities regulating childbirth involve the secretion of estrogen by the placenta, stimulating oxytocin release, which triggers uterine contractions. The placenta also secretes relaxin and prostaglandins.

2.1. Birth stages: Childbirth can be divided into three stages (Figure 79):

a. Cervical Dilation: (2 - 12 hours)

Uterine contractions widen the cervix, allowing the fetus to exit.

Contractions initially occur every 20 minutes, gradually increasing to one minute.

The mother feels labor pains in the lower back area, extending to the front abdomen.

Rupture of the amniotic sac occurs, releasing amniotic fluid for the fetus to exit.

The fetus is pushed out due to uterine and abdominal muscle contractions.

b. Delivery of the Baby: (0.5 - 2 hours)

The baby's head emerges from the birth canal.

The frequency of contractions increases.

The baby is born connected to the umbilical cord, which is cut and tied by the doctor, leaving a part known as the umbilicus or belly button.

The newborn begins breathing on its own.

c. Delivery of the Placenta: (15 - 30 minutes)

After birth, the placenta separates from the uterus and is expelled from the mother due to uterine contractions and voluntary contractions of the abdominal muscles.

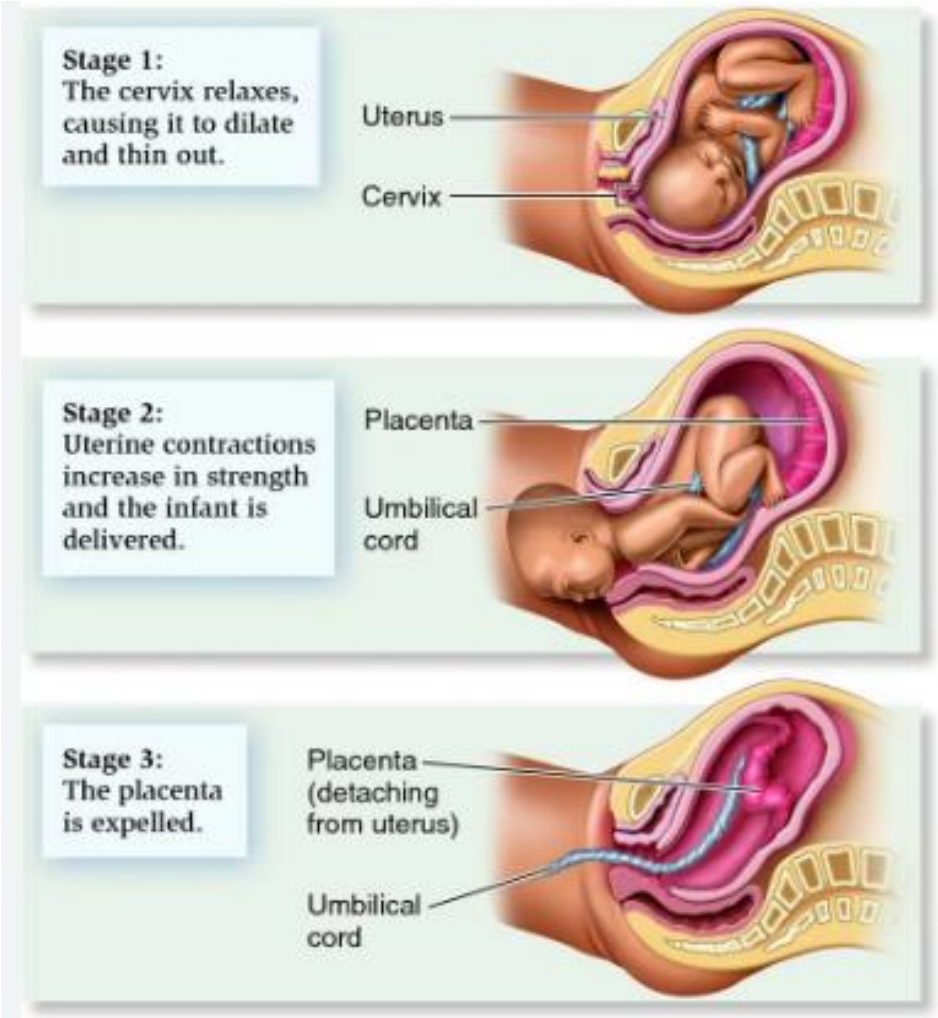

Figure 79: Childbirth stages.

2.2. Control of Birth:

Pregnancy requires achieving a complex hormonal balance resulting from ovarian, placental, and pituitary secretions. At the end of pregnancy, there is an imbalance in placental hormonal secretions under the influence of cortisol secreted by the adrenal gland of the fetus, resulting in a decrease in progesterone secretion, leading to the relaxation of the uterine muscle contractions. Under the influence of uterine nerve signals and placental estradiol, the posterior pituitary gland stimulates an increasing secretion of oxytocin, where both oxytocin and prostaglandin enlarge uterine contractions. The secretion of relaxin from the ovary, which softens the connective tissues in

the pelvic region and softens the bones in that area, decreases progesterone secretion, making the uterine wall membranes sensitive to oxytocin (Figure 80). The amount of blood reaching the fetus from the placenta decreases, leading to an increase in carbon dioxide levels and causing increased fetal movement and consequently increased muscular contractions of the uterine wall. The fetus moves towards the cervix, and the amnion facilitates the passage, with the help of abdominal muscles, the fetus is expelled from the uterus, and the natural position of the fetus during birth is the head coming out first.

The fetus becomes ready for birth after the completion of its organ formation, i.e., after 9 months. Several weeks before delivery, its position changes, and its head turns towards the cervix to prepare for delivery.

Regarding hormonal activities in regulating the birthing process:

- ✓ The placenta secretes estrogen.
- ✓ The pituitary gland stimulates the mother and the fetus to release oxytocin (which acts on uterine muscle contraction) and in turn stimulates the placenta to secrete relaxin and prostaglandins.
- ✓ The concentration of progesterone hormone in the blood decreases, stimulating the muscles of the uterine wall to contract in successive waves.

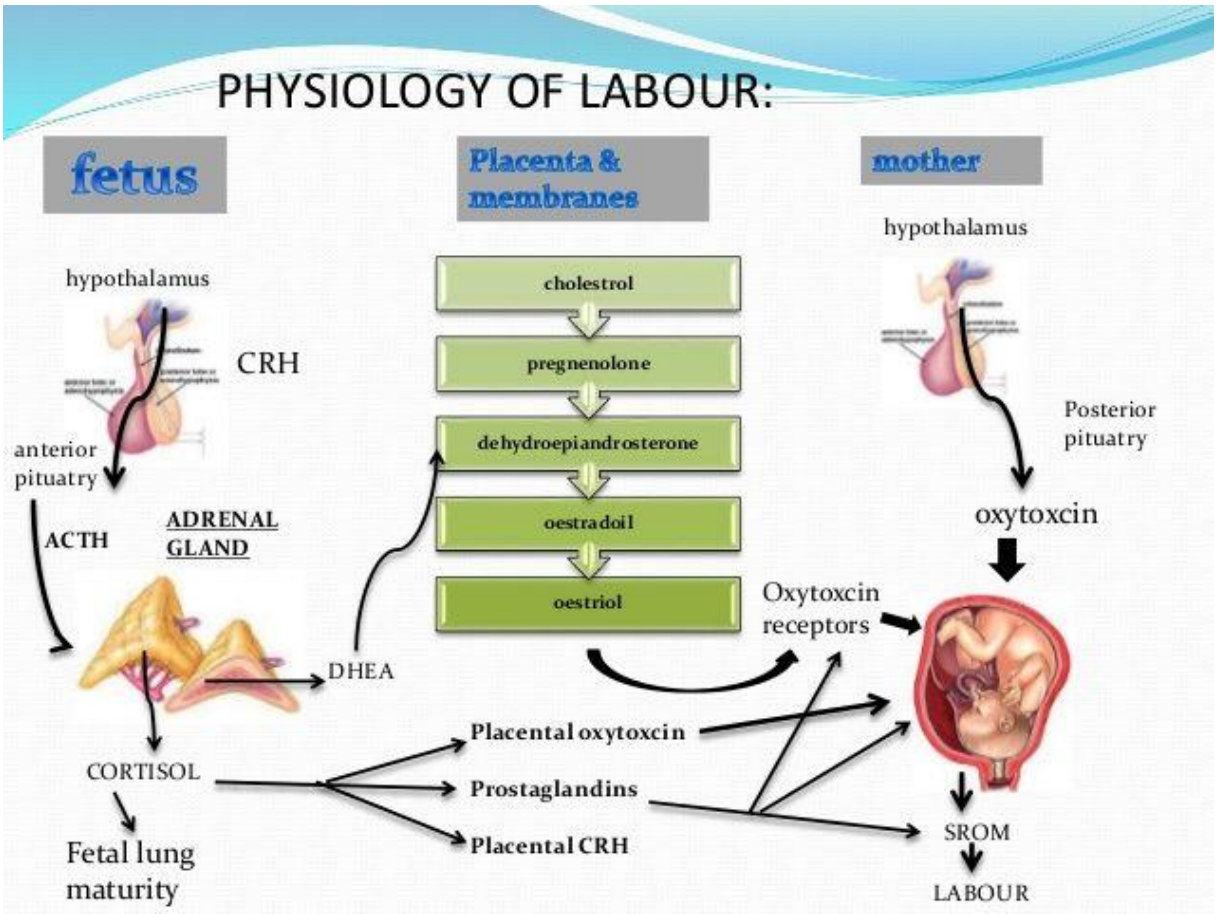

Figure 80: Control of birth.

Chapter Twelve: Abnormalities of Fetal Development

Fetal abnormalities refer to unusual or unexpected conditions in a baby's development during pregnancy. Fetal abnormalities may also be known as congenital anomalies or birth defects. They have many causus like:

1. Chromosomal disorders:

A chromosomal disorder occurs when there is a change in the number or structure of the chromosomes. This change in the amount or arrangement of, the genetic information in the cells may result in problems in growth, development and/or functioning of the body systems. The most often reason is mistake which occurs during the cell division. It is connected with wrong development of the sperm or ovum, age of parents and Influence of the environment. There are two types:

1.1. Abnormalities in chromosomal structure:

- **Translocation:** A part of one chromosome is transferred to another chromosome.
- **Deletion :** it is characterized by the loss of a part of chromosome.
- **Isochromosomes :** they are created by the incorrect division of centromere. Normally centromere divides vertically. In this case it divides horizontally.
- **Inversion :** are typical two breakages in the different part of the chromosome. The newly created segments then replace each other.

1.2. Abnormalities in chromosomal number:

Aneuploidy in human sex chromosomes

- **X_ female (Turner Syndrome):** Short stature; sterile (immature sex organs); often reduced mental abilities. About 1 in 2500 human female births
- **XXY male (Klinefelter syndrome):** Often not detected until puberty, when female body characteristics develop. Sterile; sometimes reduced mental abilities; testosterone shots can be used as a partial treatment; About 1 in 500 human male births.
- **XYY male (XYY syndrome):** Usually tall, with heavy acne; some correlation with mild mental retardation and with aggressiveness; usually still fertile. About 1 in 1000 human male births
- **XXX female (triple X syndrome):** Usually just like XX females, except for having 2 Barr bodies in somatic cells. HOWEVER, more likely to be sterile, and if fertile, more likely to have XXY and XXX children. About 1 in 1000 human female births. Aneuploidy in human autosomes
- **Autosomic monosomy:** Appears to be invariably fatal, usually very early in pregnancy. Most autosomic trisomy is fatal, but sometimes individuals trisomic for autosomes 13, 15, 18, 21, or 22 survive to birth and even beyond. Chromosome number reflects size; bigger number = smaller size, and usually fewer genes. Extra 13, 15, or 18 lead to multiple defects and usually death well before 1 year of age. Extra 22 is much like extra 21 (Down syndrome, covered below), but usually more severe, with shorter life expectancy.
- **Trisomy 21 (Down syndrome):** The only autosomal trisomy condition in humans that allows an appreciable number of individuals to survive to adulthood Found in about 1 in 750 live births. A phenotypic ally identical condition occurs that is not due to a true trisomy (it involves a chromosomal translocation, covered later) Traits

include abnormal facial appearance, high likelihood of mental retardation (degree varies considerably), and increased likelihood of developing leukemia and Alzheimer's disease Likelihood of a child being born with Down syndrome increases with the age of the mother rate is as high as 1 in 16 live births for mothers age 45 and over at conception. Not completely clear why the odds go up so dramatically, likely a combination of factors. It is clear that Nondisjunction is more common in eggs than sperm.Appears that spontaneous rejection of aneuploids pregnancies is more common in younger women (Figure 81).

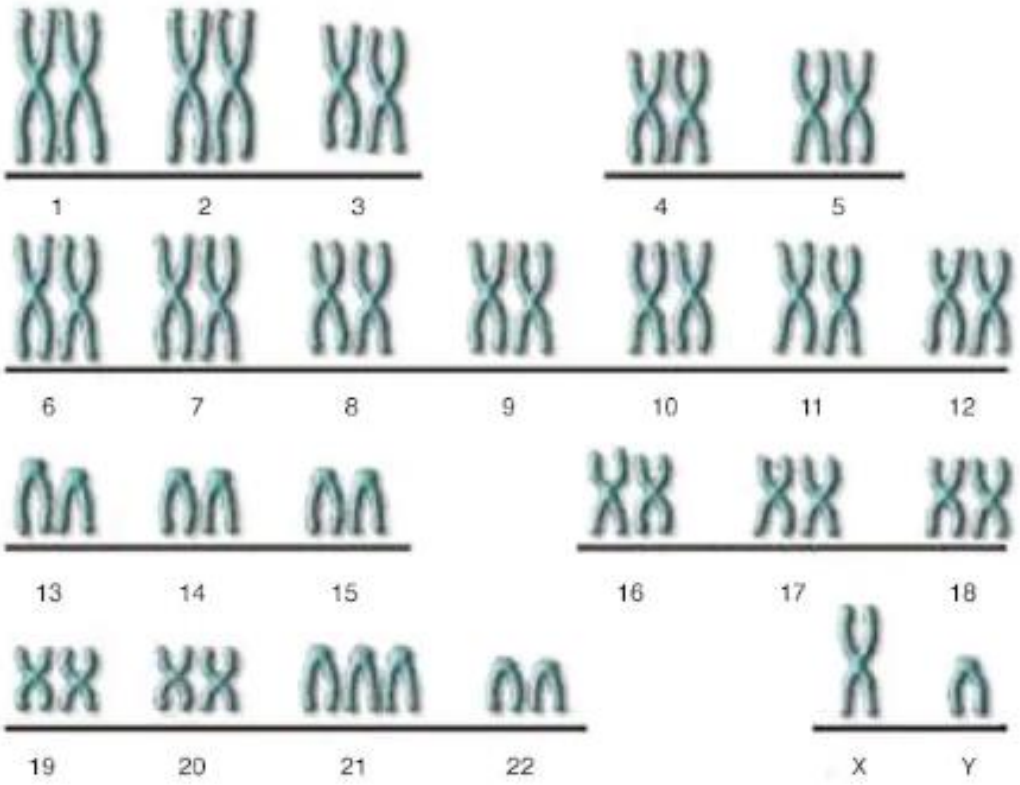

Figure 81: The genetic basis of Down syndrome.

2. Conjoined twins:

They represent one of the rarest forms of congenital anomalies. The incidence of conjoined twinning is estimated to be 1 in 50,000 to 1 in 1,00,000 deliveries.

The most well known conjoined twins were Chang and Eng Bunker who were born in Siam in 1811. The acceptable theory explaining their etiology is that the embryonic tissue divides incompletely, remaining fused at some point or points.

The anatmomic sites shared by conjoined twins can be complex, the current nomenclature being derived from the most prominent site of conjunction which can be (Figure 82):

- **Thoracopagus (Thoracic cage)**
- **Omphalopagus or Xiphopagus (**usually joined anteriorly from the xiphoid to the umbilicus)
- **Pygopagus (**joined at the glueteal region with fusion of the sacrum).
- **Ischiopagus (joined** at the pelvic level with sharing of genitourinary structures, rectum and liver).
- **Craniopagus (**at the skull involving the brow, vertex or parietal bone).
- Craniothoracopagus, a rare variety with a singlci fused head and two faces looking in opposite direction is referred to as **Janiceps** twins
- **Heteropagus (**asymmetric forms. There may be parasitic attachment in non-duplicated fashion to any portion of the body or even within the body as a fetus in fetus. Sometimes one may be less complete and depend on the other).

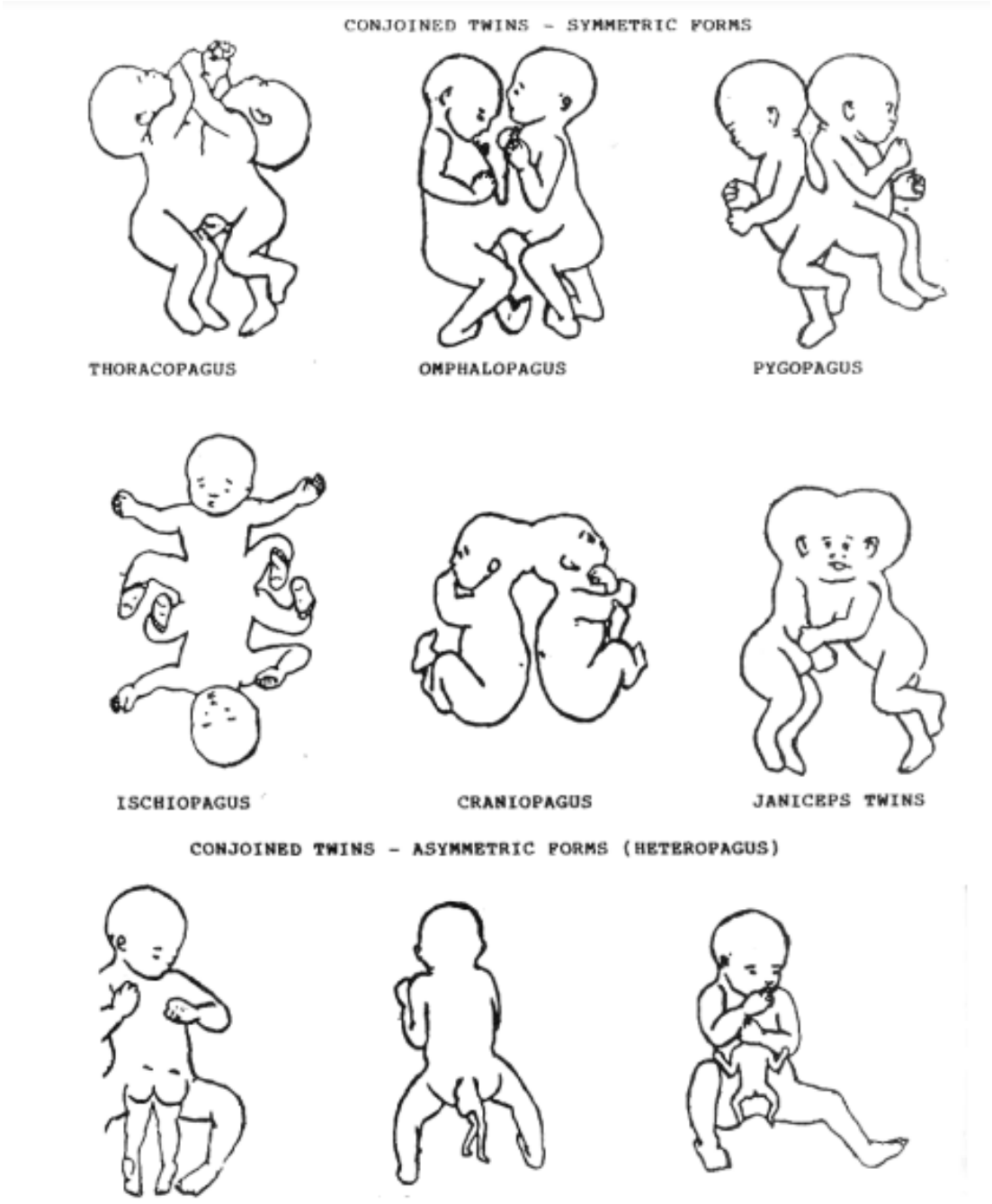

Figure 82: Types of conjoined twins.

Majority of conjoined twins are dead born or die soon after birth. Attempt at surgery is done in only a few cases and probably a large number of unsuccessful operations are not reported in the literature. The results of surgery depend on the type of conjoined twin, the degree and type of organs shabby the twin,

associated malformations general condition of the twins and finally on the medical and surgical treatment available.

3. Implantation:

Usually, implantation occurs in the upper lateral part of the uterus and rarely in the anterior part. However, in abnormal cases (Figure 83):

- ✓ **Tubal implantation:** It occurs in one of the sections of the fallopian tube: the ampulla, the isthmus, or the narrow part (between the tube and the uterus). In this case, the fetus grows until the space is insufficient for its further development (maximum duration being two months), leading to internal bleeding that requires emergency surgery and consequently fetal death.
- ✓ **Lower implantation** (lower part of the uterine cavity): It leads to cervical dilation and fetal death before the due date.
- ✓ **Intracavitary implantation:** In the broad ligament of the ovary or in the intestinal mucosa, requiring emergency surgery at the beginning of pregnancy to remove the fetus.
- ✓ **Ovarian implantation:** Inside the ovary.

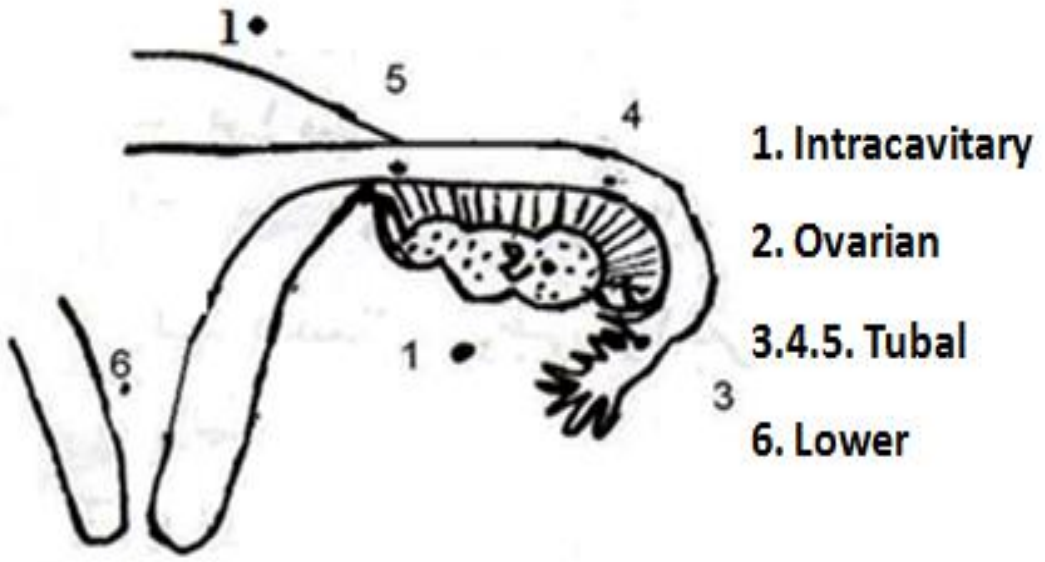

Figure 83: Implantation abnormal locations.

Implantation may not occur in cases of low levels of human chorionic gonadotropin hormone (hCG).

4. Neurulation: In humans, the neural tube closes during the period between 21 and 28 days of embryonic development; anomalies affecting this closure are characterized by inadequate fusion of the neural tube in the developing embryo. The prevalence of neural tube defects (NTDs) ranges from 1 pregnancy in 300 to 1 pregnancy in 1,000 and is affected by ethnic, genetic, and dietary factors (the highest rates of NTDs are observed in the United Kingdom and the United States, while the lowest rates are observed in Japan). Some chronic maternal medical conditions increase the risk of NTDs, including poorly controlled maternal insulin-dependent diabetes (OR, 11.5), conditions requiring the use of antiepileptic drugs (valproic acid, carbamazepine), conditions requiring treatment with folate antagonists, and maternal obesity (OR, 3.5). NTDs are described based on their anatomical location and the type of neural content, as follows (Figure 84):

✓ **Spina bifida** (failure of closure of the rostral folds of the neural tube) 50%: 93% of Meningomyelocele (neural placode at the base of the NTD) and 7% of Myeloschisis (Meningocele: a quarter dural sac only; Meningomyelocele: neural elements attached to the dural sac).

✓ **Anencephaly** (failure of closure of the caudal folds of the neural tube causing failure of brain development) 40%.

✓ **Encephalocele** (herniation of the brain through a skull bone anomaly; occipital encephalocele is the most common [anterior and lateral locations]) 8.5%.

✓ **Inencephaly / Craniorachischisis** (abnormal development of the skull and upper part of the spine) 1.5%.

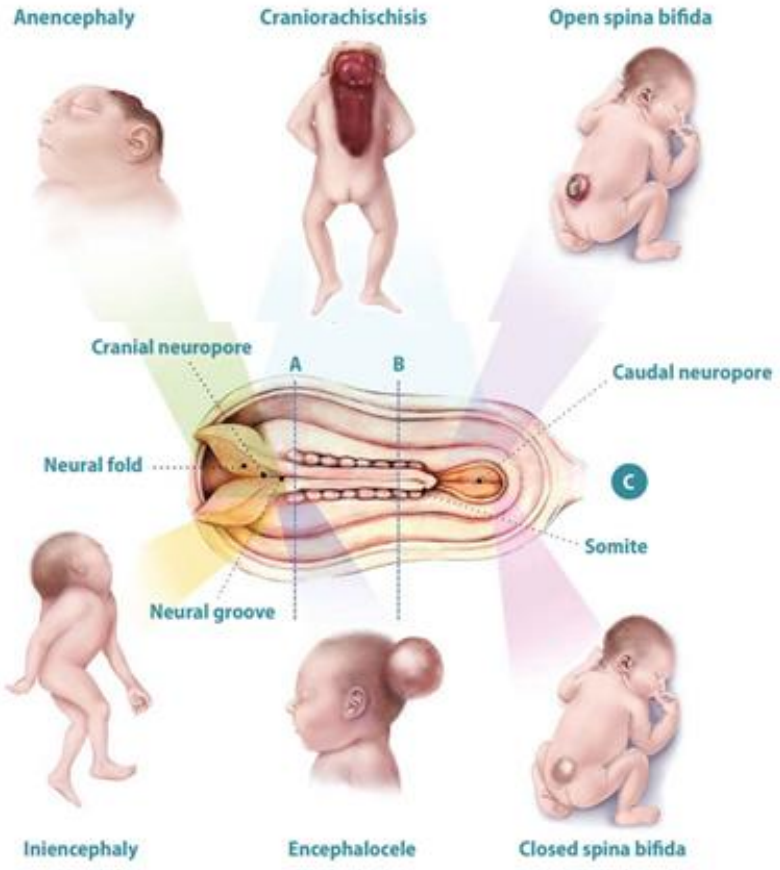

Figure 84: Neural tube defects.

Remarque: Fetal development can halt at any later stage due to several reasons, including inadequate nutrition, hormonal imbalance, or due to any incident the pregnant woman may encounter.

Conclusion

In conclusion, this polycopy provided a comprehensive exploration of the exciting field of embryology, from the earliest stages of fertilization to birth, encompassing the various complexities of embryonic formation.

Throughout its chapters, we have gained a deeper appreciation for the marvels of embryological development and the underlying cellular and physiological mechanisms involved. We have learned about the crucial role of signaling pathways, neurohormonal regulation in orchestrating the formation of tissues, organs, and ultimately, entire organisms, with some abnormalities.

Moreover, it has underscored the significance of embryology in various scientific disciplines, including developmental biology. By understanding the principles of embryological development, we are better equipped to address challenges in areas such abnormalities, infertility and regenerative medicine.

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