HATAHET ANATOMY

Introduction to Embryology

Lecture: 23-25

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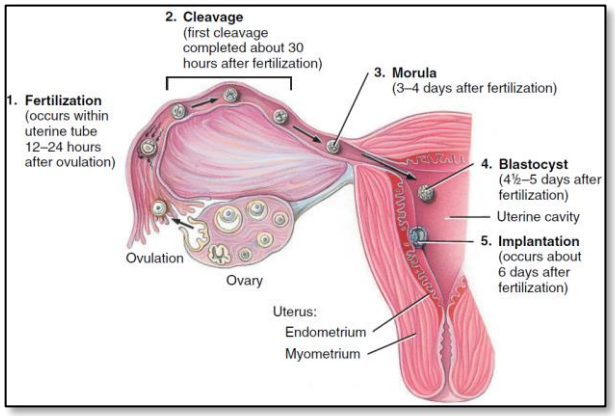
Lecture 23-25: Embryology

▪ **Embryology**: the science concerns in studying the lifetime of an embryo during the **first 8 weeks** of the intrauterine life

First Week

❖ Main event of the First week ❖

❶ **Fertilization & Formation of zygote**
❷ **Cleavage of zygote**
❸ **Morula**
❹ **Blastocyst formation**
❺ **Initiation of implantation of blastocyst**



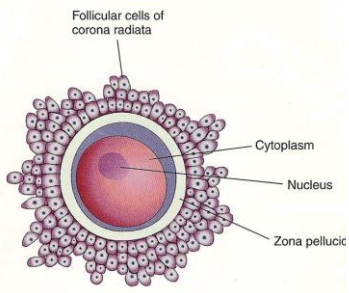
Now, we will discuss the development of zygote By Events:

Fertilization

- Fertilization is the process during which a male gamete (1n) unites with a female gamete (1n) to form the **Zygote** (2n)
- occurs in **Ampulla** of fallopian tube
- fertilization must occur within **24 hours of ovulation**, otherwise it will be transported to the uterus to be degraded
- when ovulation occurs, the ovulated secondary oocyte will have 2 layers surrounding it:

[1] **Zona pellucida**, the thick acellular layer of glycoprotein surrounding the oocyte, appears first at the Early secondary follicle

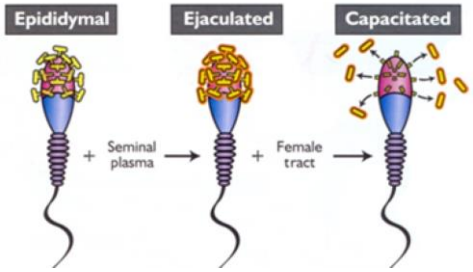
[2] **Corona radiata**, the layer of granulosa that wrap around the secondary oocyte inside Graafian follicle, composed of the remaining follicular cells



- Phases of Fertilization:

➢ Capacitation of sperms

- capacitation is the set of natural physical changes that a spermatozoon undergoes in order to be able to fertilize the ovum
- occurs in vivo following ejaculation when the spermatozoa come into contact with different fluids in the female genital tract



➢ Penetration of Corona radiata

- a proteolytic enzyme called (Hyaluronidase) secreted from acrosome of the sperm that digests corona radiata and allow the sperm to penetrate it

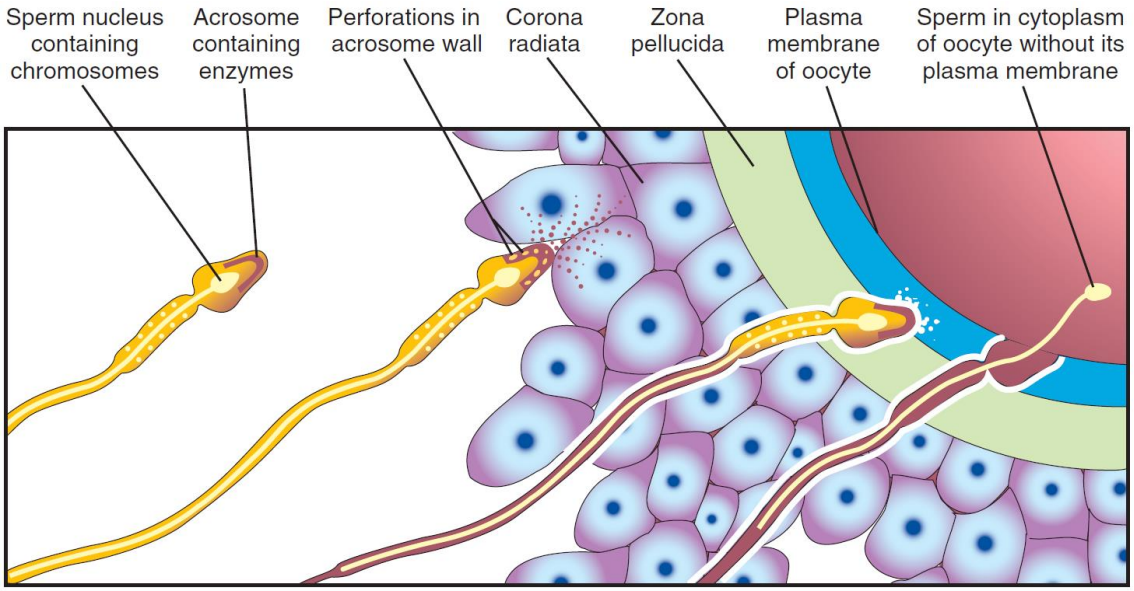
➢ Penetration of zona pellucida

- a proteolytic enzyme called (Acrosin) secreted from acrosome of the sperm that digests zona pellucida to form a path for the sperm to the cell membrane of oocyte

➢ Fusion of plasma membrane of oocyte and sperm

- the inner part of the head & tail enter the cytoplasm of the oocyte

▪ **Zona reaction**: changes in the structural and chemical properties of zona pellucida that makes it impermeable to other sperms; to prevent (**Polyspermy**) abnormal combination of chromosomes (3n, 4n, ...). This is achieved by cortical granules from the oocyte which digest sperm receptors **ZP-2 & ZP-3**



➢ Formation of female pronucleus

- the ovum completes Meiosis II and forms: Mature oocyte & 2nd polar body
- the nucleus of the mature oocyte will become the (**Female pronucleus**)

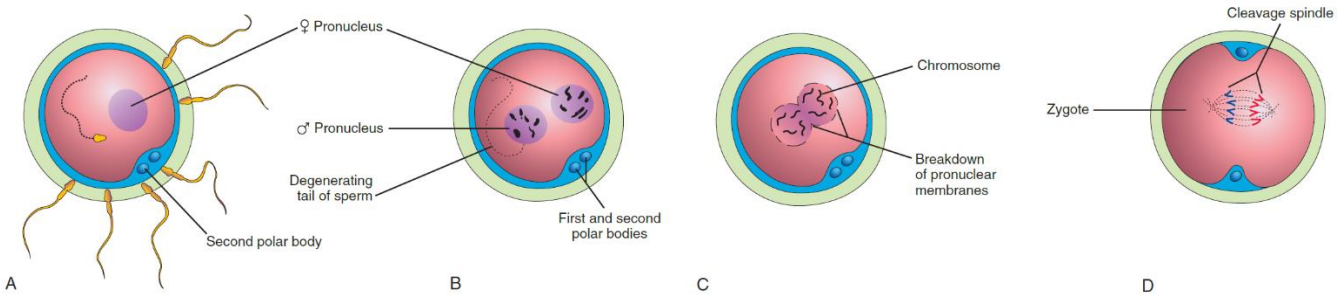
➢ Formation of male pronucleus

- nucleus of the sperm enlarges and becomes rounded, now it is called (**Male pronucleus**)
- tail degenerates

➢ Fusion of both pronuclei and formation of Zygote

➢ Breakdown of pronuclear membrane

- the combination of 23 chromosomes in each pronucleus results in a zygote with 46 chromosomes
- chromosomes are then condensed and arranged for Mitosis, and the first cleavage division of the zygote occurs



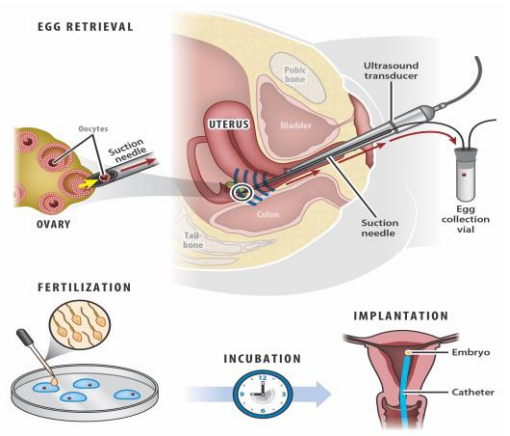
✪ Clinical correlation: In Vitro Fertilization

① collection of several oocytes with **Aspiration & Laparoscopy**

② placement of the oocytes in a special culture medium containing **paternal capacitated sperms**

③ fertilization and cleavage of zygote are monitored

④ transfer of the cleaved cells (4 - 8 cells stage) to the uterus, **how much?** (2 - 3) zygotes are transferred; <u>to ensure that one of these zygotes will survive and form the embryo</u>



Zygote & Morula

- **Cleavage** is the repeated mitotic divisions of the zygote into many cells called (**Blastomeres**), as the following:

  - at 2 - 4 blastomeres stage → 1st and 2nd polar bodies are degraded due to insufficient cytoplasm
  - at 8 - 10 blastomeres stage (**Compaction**) → cells become tightly aligned to form a compact ball
  - at 12 - 32 blastomeres stage (**Morula**) → blastomeres will look like a Mulberry (التوت)

- after 4 days of fertilization, the blastomere's mass will enter the uterus
- note that the zona pellucida is still intact (we are in early day 4 here)

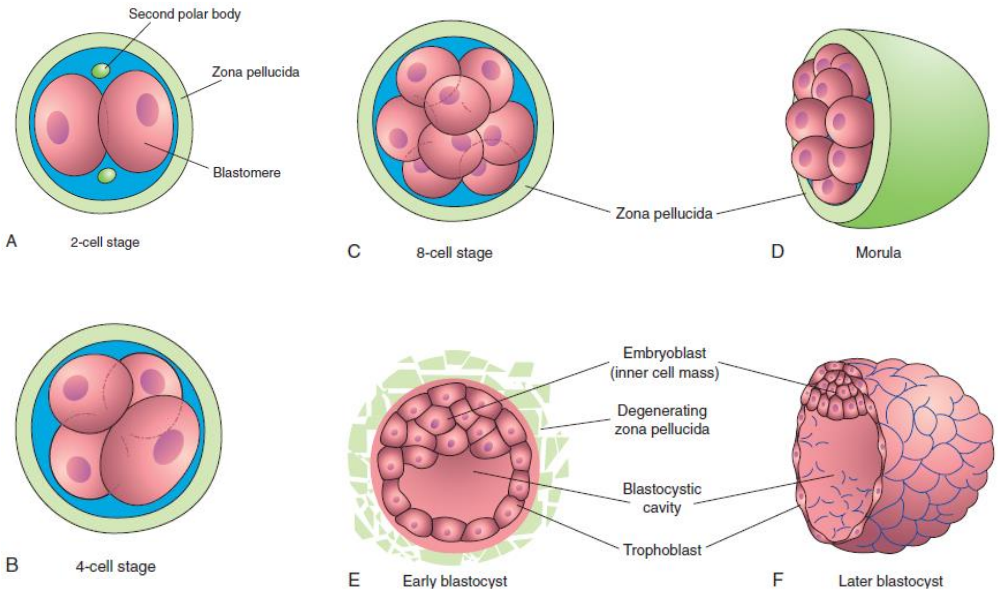
Blastocyst formation

- the formation of blastocyst is accomplished in 2 phases:

  A. **Early blastocyst** (late Day 4) → uterine fluid passes through zona pellucida to form the fluid-filled (**Blastocystic cavity**)
  B. **Late blastocyst** (Day 5) → zona pellucida is shed and disappears completely

- after the formation of blastocyst, blastomeres will have separated into 2 regions:

  A. **Trophoblast** → the outer cell layer, it is the embryonic part of the placenta [Tropho = nourishment]
  B. **Embryoblast** → the inner cell mass of blastomeres gathered at periphery, it gives rise to the embryo



Initiation of Implantation

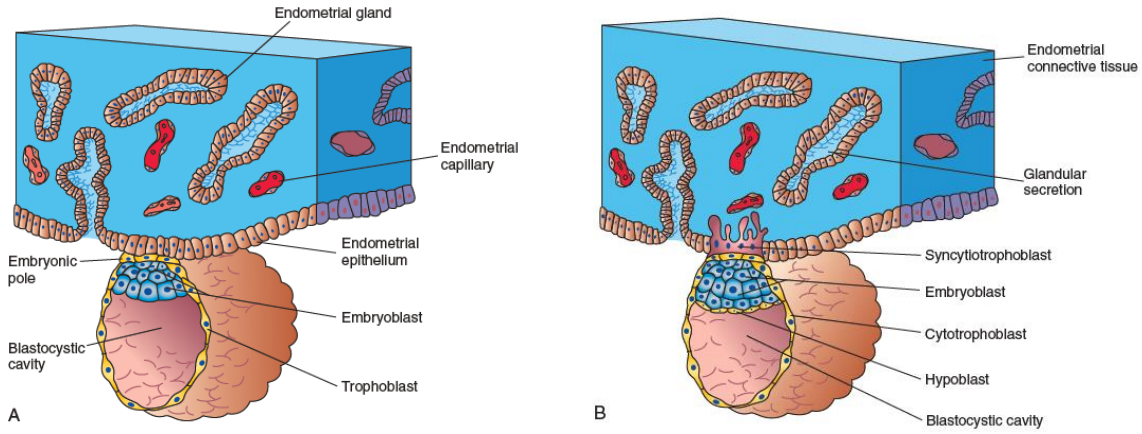
• at (Day 6), blastocyst attaches to endometrial epithelium, and as soon as it attaches, trophoblast starts to proliferate rapidly and differentiate into 2 layers:

A. **Cytotrophoblast**, the inner layer of cells
B. **Syncytiotrophoblast**, the outer layer of multinucleated protoplasmic mass of tissue; no cell boundaries

• the highly-invasive syncytiotrophoblast that rapidly expands adjacent to the embryoblast is called (**Embryonic pole**)
• at (Day 7), layer of cuboidal cells called (**Hypoblast**) appears in the surface of the embryoblast facing blastocystic cavity
• when implantation initiates:

- Syncytiotrophoblast produces proteolytic enzymes that erode (تنحت) the maternal tissue to enable the blastocyst to borrow into the endometrium
- later on week 2 (Day 13), syncytiotrophoblast will secrete (**HCG**) which stimulates 3 main actions:

① maintains the presence of Corpus Luteum (الجسم الأصفر) which will secrete Progesterone during the (**1st Trimester**)
② enters maternal blood in lacunae to stimulate the development of spiral arteries in myometrium
③ stimulates the formation of syncytiotrophoblast (**+ve feedback**)



• Function of progesterone → enriches the uterus with thick lining of blood vessels so that it can sustain the growing fetus

• **Pregnancy test** → **HCG** (**Human Chorionic Gonadotropin**) forms the basis for pregnancy tests; highly sensitive assays are available for detecting HCG at the end of the 2nd week even though the woman is probably unaware that she is pregnant. Concentration of HCG in the maternal blood and urine rises to a maximum levels by the 8th week of pregnancy

✪ Clinical correlation: Early spontaneous abortion

❖ Implantation is a critical stage that may fail to occur and result in Abortion

❖ **Reasons & Causes:**

① inadequate estrogen & progesterone secretion during early pregnancy
② chromosomal abnormalities that results in defects in dividing cells

❖ **Signs of early spontaneous abortion:**

① delayed menstrual cycle for several days
② unusual profuse flow

✪ Clinical correlation: Ectopic pregnancy (Extrauterine implantation)

❖ **Definition**: the implantation and development of the embryo outside uterus

❖ **Causes**: (scar, inflammation, abnormal anatomy), it is twice more frequent in smoking women; because Nicotine paralyzes the cilia that lines the epithelium

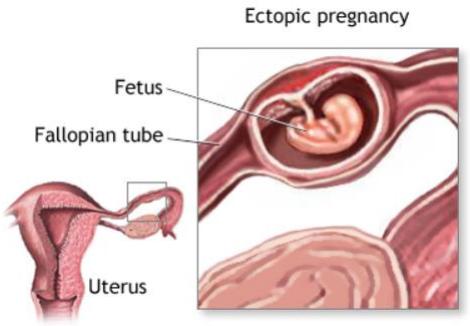
❖ **Location**: nearly 95% of ectopic pregnancy occurs in Ampulla or Isthmus of fallopian tube

❖ **Signs:**

① acute abnormal pain; due to distention/swelling
② abnormal bleeding
③ rupture of fallopian tube and internal bleeding

❖ **Treatment:**

① Surgical removal
② Anticancer drug (Methotrexate)



Second Week

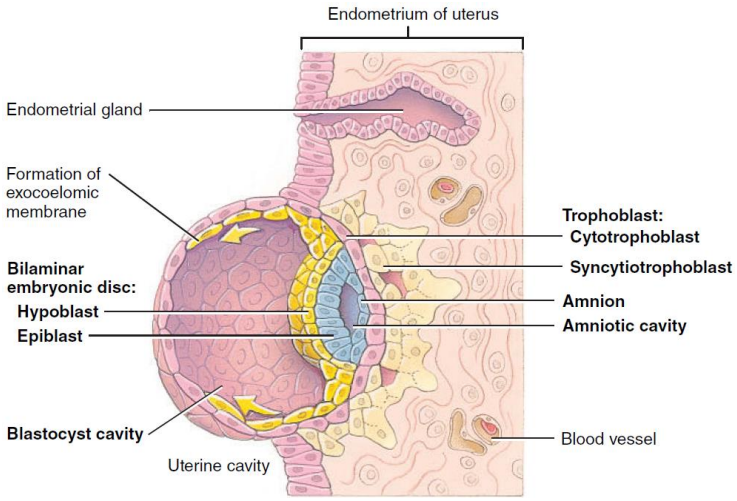
❖ Main event of the second week ❖

❶ **Completion of implantation of the blastocyst**
❷ **Formation of the Bilaminar embryonic disc**
❸ **Formation of the extraembryonic structures**

Now, we will discuss the development of the blastocyst By Days, not events

Day 8

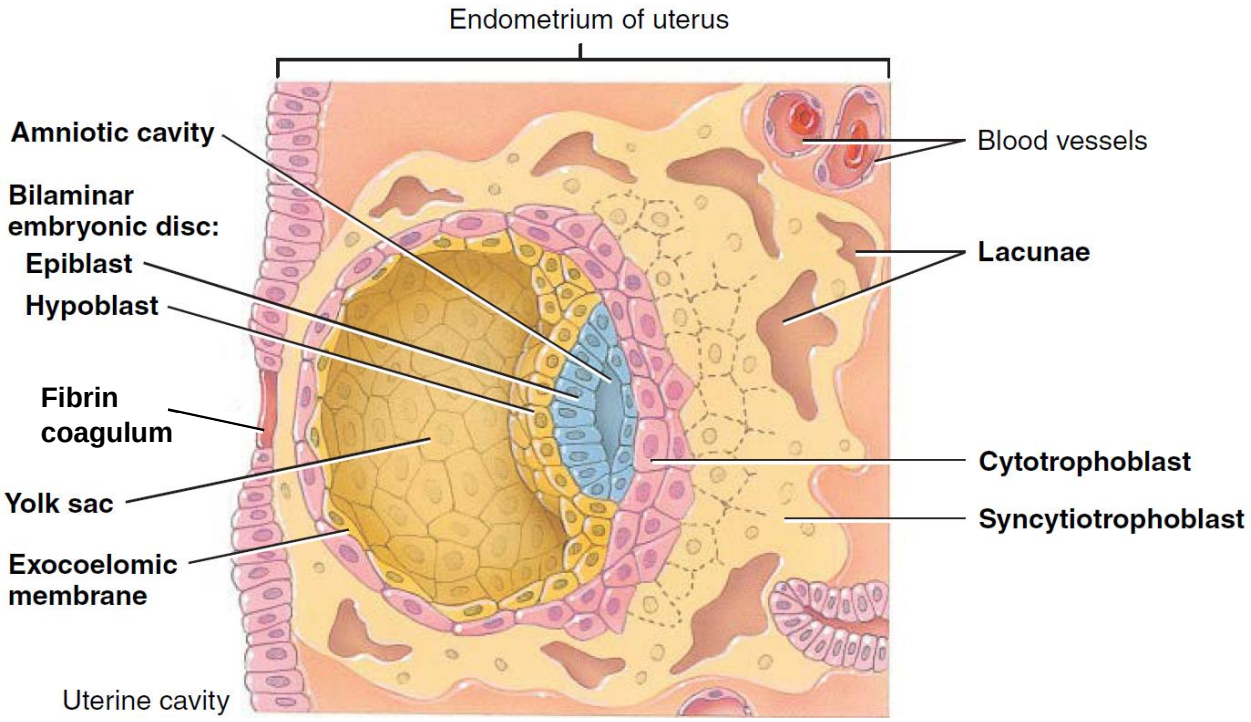
- Blastocyst is partially and slowly embedded in the endometrium, as the following:
  - more cytotrophoblast cells will divide and migrate into syncytiotrophoblast, then they fuse & lose their cell membrane
  - syncytiotrophoblast continues its invasion deeper in the endometrium; thereby eroding its blood vessels and glands; because the endometrium adjacent to the implantation site is edematous and highly vascular



- Embryoblasts differentiate into:
  - **Epiblast layer**, adjacent to amniotic cavity, made up of high columnar epithelium
  - **Hypoblast layer**, adjacent to blastocyst cavity, made up of small cuboidal epithelium
    - these 2 layers will form a flat ovoid disc called (**Bilaminar Embryonic disc**)
    - epiblast cells adjacent to the cytotrophoblast are called (**Amnioblasts**)
    - Amnioblasts + the rest of the epiblasts will line the amniotic cavity

Day 9

- Blastocyst is more deeply, but not completely, embedded in the endometrium, and many changes occurs there:
  - the penetration defect (الفتحة بالجدار) in the surface epithelium of uterus is closed by a clot called (**Fibrin coagulum**), and later it will be closed by epithelium
  - small vacuoles appear at the region of the syncytiotrophoblast, and they fuse to form larger lacunar network, this phase of trophoblast development is known as the (**Lacunar stage**)
- the cells of hypoblast adjacent to cytotrophoblast and lining its inner surface form a thin membrane called Exocoelomic membrane (**Heuser's membrane**), this membrane will form a cavity called (**Exocoelomic cavity**) or (**Primitive yolk sac**) or (**Primary umbilical vesicle**)



Day 10

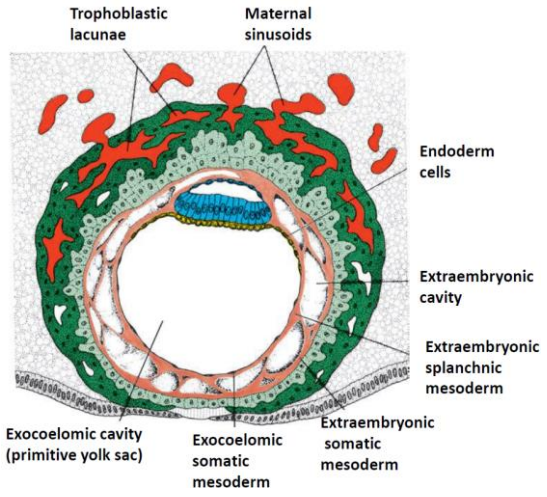
No major changes occur or take place in the 10th day of pregnancy

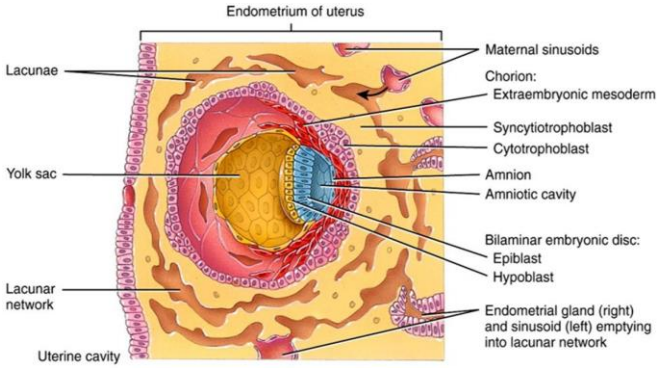
Day 11 & 12

- Blastocyst is completely embedded in the endometrium and will produce a slight protrusion into the lumen of uterus
- Fibrin that covers the defect in the endometrium is almost entirely, but not completely, covered with surface epithelium
- Syncytiotrophoblast cells penetrate deeper into the stroma [stroma = tissue] and erode 2 structures:

① some endometrial glands, will empty into the lacunar network
② Sinusoids, which are the endometrial capillaries

- syncytiotrophoblast erodes and ruptures the endothelial of the sinusoids
- lacunar network will communicate with these capillaries and maternal blood will enter the lacunae, and this establishes a blood circulation called (**Primordial Uteroplacental Circulation**) it is the very first fetal blood circulation
- when maternal blood flows into the lacunae, O_2 and nutrients will be available to the embryo





- a new population of cells derived from the yolk sac cells appears:
  - these cells are between: **Inner surface of cytotrophoblast & Outer surface of exocoelomic cavity**
  - these cells will form a fine, loose CT layer called (**Extraembryonic mesoderm**), has 2 types:

① **Extraembryonic SOMATIC mesoderm** → lines the cytotrophoblast
② **Extraembryonic SPLANCHNIC mesoderm** → covers the yolk sac

  - the extraembryonic mesoderm surrounds the whole space around yolk sac and amniotic cavity, **EXCEPT** where the embryonic disc is connected to the trophoblast by (**Connecting stalk**)
  - soon, large cavities will develop in the extraembryonic mesoderm, and when these cavities confluent/merge together they will form a new space called (**Extraembryonic cavity**) or (**Extraembryonic coelom**)

➢ **Conceptus** = (**Embryonic disc + All the structures surrounding it**), and after week 3 it will be called Embryo

- during the implantation of conceptus, the CT of endometrium undergoes a transformation called (**Decidual reaction**)
- the transformation includes the swelling of endometrial cells because of the accumulation of lipids and glycogen in their cytoplasm, these cell will be called (**Decidual cells**). The main function of the decidual reaction is to:

① provide nutrition for the early embryo
② provide an immunologically-privileged site for the conceptus

▪ **Embryotroph**: the fluid in the lacunae that passes to the embryonic disc by **Diffusion**

Day 13

- the fibrin that covers the defect in the endometrium is completely sealed with surface epithelium
- bleeding at the implantation site occasionally occurs as a result of increased blood flow in lacunae
- Cytotrophoblast cells proliferate locally and penetrate the syncytiotrophoblast forming cellular columns surrounded by syncytium, this whole structure is called (**Primary villi**)
- the extraembryonic cavity develops and becomes larger, this leads to many changes:

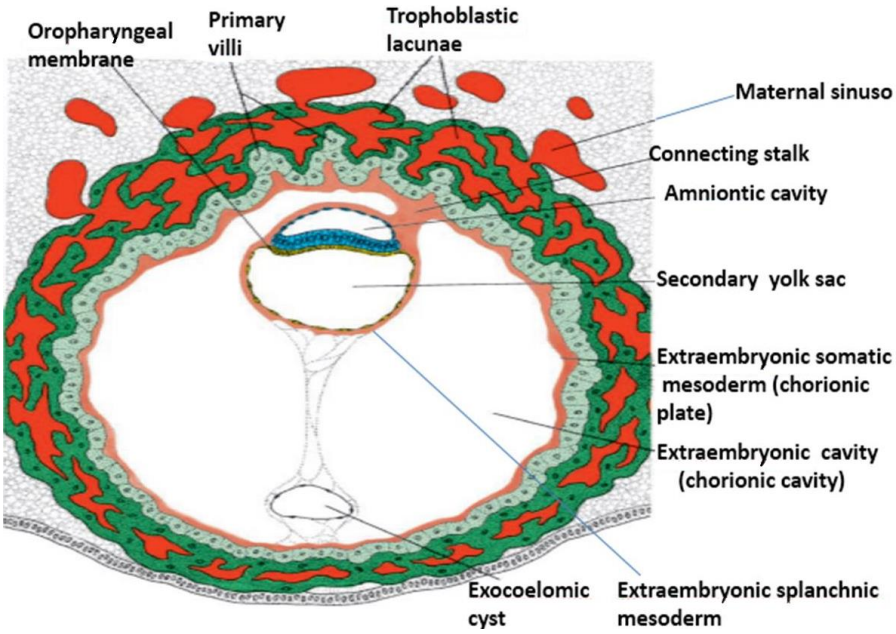
① the (**Exocoelomic cavity**) or (**Primitive yolk sac**) or (**Primary umbilical vesicle**) will decrease in size and forms the (**Definitive yolk sac**) or (**Secondary yolk sac**) or (**Secondary umbilical vesicle**), a much smaller sac

② large portions of the exocoelomic cavity are pinched off to form (**Exocoelomic cysts**) at the opposite pole of the conceptus in the extraembryonic cavity

③ the (**Extraembryonic cavity**) or (**Extraembryonic coelom**) will expand into a larger cavity called the (**Chorionic cavity**)

④ the **extraembryonic SOMATIC mesoderm** is then known as the (**Chorionic plate**), and the only place in the chorionic cavity where extraembryonic mesoderm traverses is the **Connecting stalk**

- **with development of blood vessels, the connecting stalk becomes the Umbilical cord (الحبل السُّري)**



Third Week

❖ Main event of the third week ❖

❶ Appearance of Primitive streak
❷ Development of Notochord
❸ Differentiation of the 3 germ layers (Gastrulation)

Now, we will discuss the development of the blastocyst By Structures, neither days nor events

Gastrulation

▪ **Gastrulation**: the formation of the 3 germ layers, and the conversion of the Bilaminar embryonic disc into the Trilaminar embryonic disc; from (**Epiblast & Hypoblast**) to (**Endoderm, Mesoderm, Ectoderm**)

- gastrulation is the beginning of (**Morphogenesis**); development of body form & shape, this occurs during extensive cell: (Shape changes, Rearrangement, Movement, Adhesion changes)
- during the period of gastrulation, the embryo may be referred to as a Gastrula
- gastrulation results in the formation of the 3 germ layers (**Primordia of all tissues and organs**), these layers are:

[1] Ectoderm, at this point, the ectoderm cells are distributed in:

A. Surface ectoderm, the original place at the epiblast before
B. Neuroectoderm, located in 2 regions:

① Neural tube ② Neural crest cells

[2] Mesoderm, as the notochord & neural tube form, the intraembryonic mesoderm on each side of them proliferates to form 3 sub-regions:

A. Paraxial mesoderm, thick longitudinal column
B. Intermediate mesoderm, continuous with the paraxial mesoderm and gradually thins into lateral mesoderm
C. Lateral mesoderm, continuous with the extraembryonic mesoderm that covers amniotic sac and yolk sac

[3] Endoderm, the innermost layer

▪ **Embryonic period** (**Period of Organogenesis**): the period when each of the 3 germ layers gives rise to a number of tissues and organs, occurs between (**3rd - 8th**) weeks. Major features of external body are recognizable by the 2nd month

Organogenesis

Ectoderm

Surface ectoderm	Neuroectoderm	
	Neural tube	Neural crest cells
- Sweat glands - Sebaceous glands - Hair & Nails - Enamel of the teeth - Lens of eye - Internal ear - Mammary glands - Pituitary gland, anterior lobe	- CNS & PNS - Pituitary gland, posterior lobe - Pineal gland - Sensory epithelial of nose and ear - Retina of eye	- Sensory ganglia - Autonomic ganglia - Meninges, Pia mater & Arachnoid mater - Schwann cells - Satellite cells - Melanoblasts - Suprarenal medulla, Chromaffin cells - Head muscles and bones

Mesoderm

- Most skeletal muscles
- Blood cells
- Lining of blood vessels
- Most of the CVS
- Visceral smooth muscular coats
- Serosal lining of all body cavities
- stroma of internal organs
- Ducts and organs of reproductive system and excretory system

- All CT of the trunk:
  - Bones
  - Cartilages
  - Ligaments
  - Tendons
  - Dermis of skin

Endoderm

- Epithelial lining of:
  - GI tract
  - Respiratory tract
  - Urinary bladder
  - Most of the urethra
  - Glands opening into GIT

- Parenchyma of:
  - Tonsils
  - Thyroid and parathyroid glands
  - Thymus
  - Liver
  - Pancreas

Primitive streak

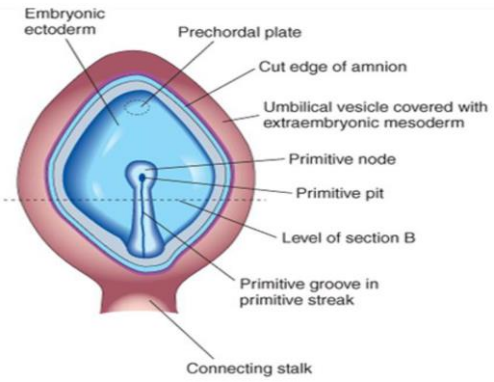
➢ Definition of Primitive streak

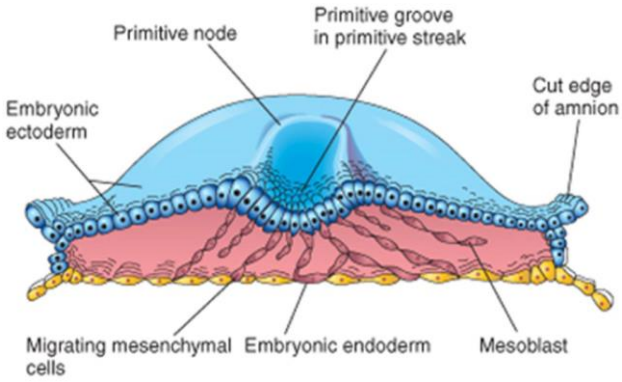
- Primitive streak a thickening streak of the epiblast cells
- appears at the beginning of week 3, it appears caudally in the median plane of posterior aspect of the embryonic disc
- the appearance of the primitive streak is the first morphological sign of Gastrulation
- results from proliferation & movement of cells of epiblast to the median plane of the embryonic disc

➢ Structure of Primitive streak

The primitive streak has 2 ends: **Caudal end** & **Cranial end**, and it elongates by the addition of cells to its Caudal end, and at the end it will have the following parts:

❶ **Primitive groove**, the narrow groove of the primitive streak, travels through the epiblast
❷ **Primitive node**, a node in the cranial end of the primitive streak, concurrently develops with the primitive groove
❸ **Primitive pit**, a small depression in the middle of the primitive node, it is continuous with the primitive groove





➢ Gastrulation steps through the primitive streak

- cells of primitive streak start to lose their adhesion and leave its deep surface downward to form the **Mesenchyme**, and a part of the mesenchyme will form (**Mesoblasts**); the undifferentiated mesoderm
- cells from (Epiblast, Primitive node, Other parts of primitive streak) migrate and accumulate in order to cause an inward displacement movement of the hypoblast, this process is called (**Invagination**)
- once the cells have invaginated, cells from the epiblast start constructing the 3 germ layers:

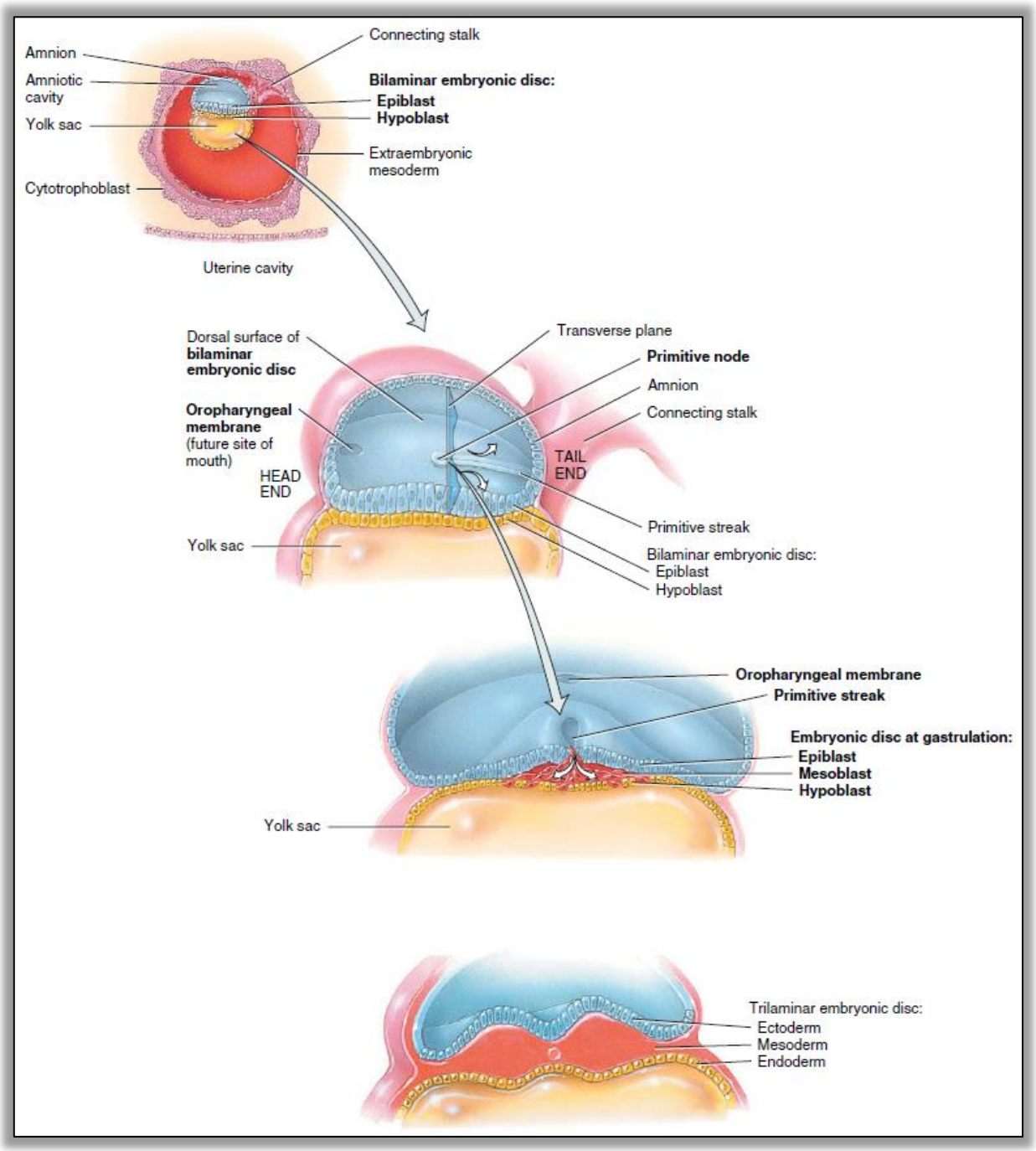
❶ Endoderm, mesoblasts will replace the cells of hypoblast and create the Endoderm, the hypoblast will be banished
❷ Mesoderm, other mesoblasts come to lie between the epiblast and the newly-created endoderm to form the Mesoderm. Mesoderm is also called (**intraembryonic mesoderm**)
❸ Ectoderm, the remaining cells in the epiblast form the Ectoderm

▪ **Mesenchyme**: a tissue of loosely arranged cells suspended in a gelatinous matrix

➢ Fate of the primitive streak

- The primitive streak actively forms mesoderm by the ingression (إدخال/تصدير) of cells until the early part of the 4th week, after that, production of mesoderm slows down.

- The primitive streak diminishes in relative size and becomes an insignificant structure in the sacrococcygeal region of the embryo and will undergo degenerative changes and disappears by the end of the 4th week.



✪ Clinical correlation: Sacrococcygeal Teratoma

❖ **Cause**: some remnants of the primitive streak may persist in the sacrococcygeal region and give rise to a (**Sacrococcygeal teratoma**)

❖ **Properties**: because teratomas are derived from pluripotent primitive streak cells, these tumors contain tissues derived from all three germ layers in incomplete stages of differentiation

❖ **Statistics**: Sacrococcygeal teratomas are the most common tumor in newborns and have an incidence of approximately 1 in 27,000, most affected infants are females (80%)

❖ **Diagnosis & Treatment**: Sacrococcygeal teratomas are usually diagnosed on routine antenatal ultrasonography, and most tumors are mild. These tumors are usually surgically excised promptly, and the prognosis is good

Notochord

➢ Definition of Notochord

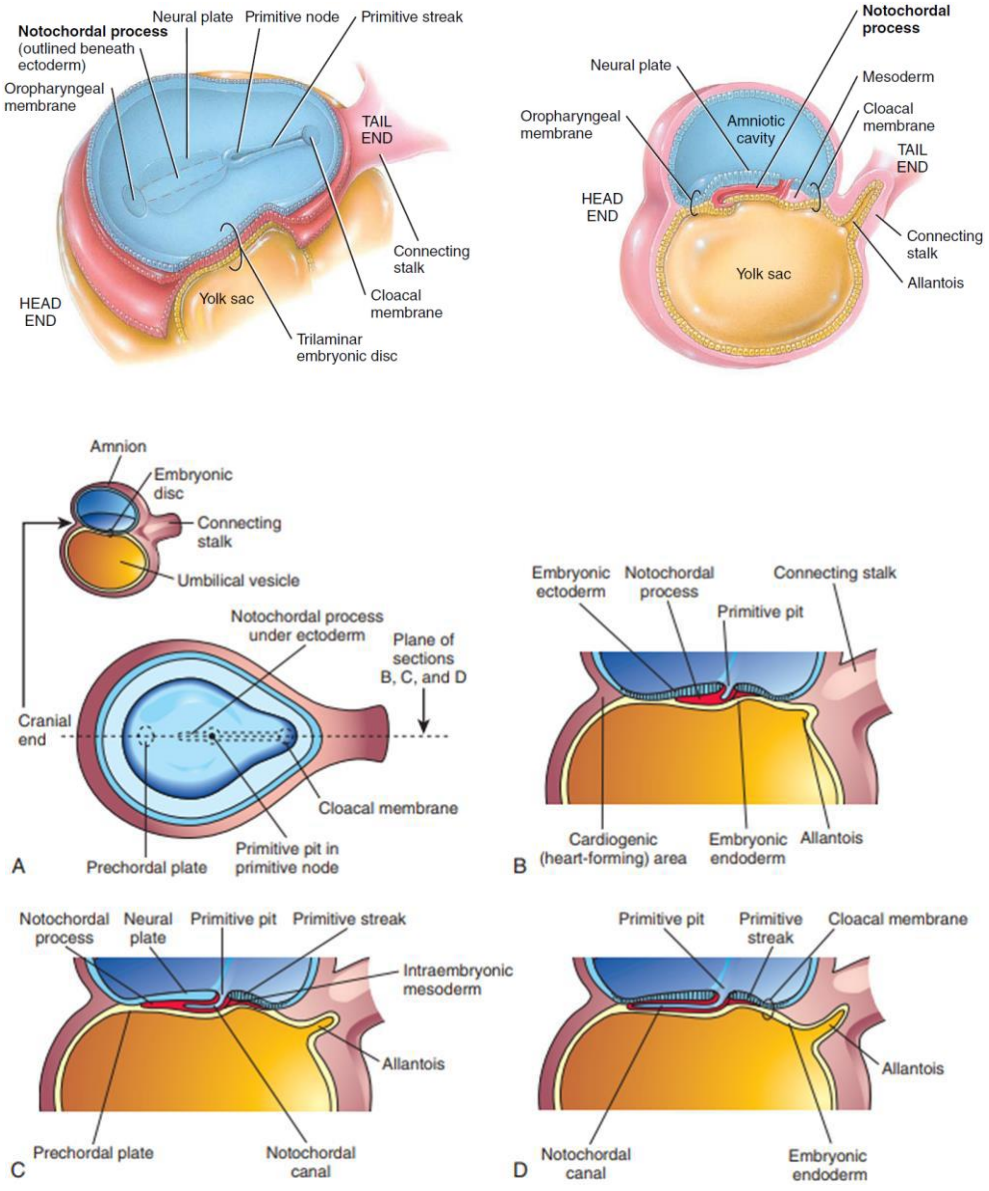
- Notochord is an embryonic midline cord that grows between ectoderm and endoderm from mesenchymal cells that migrate cranially from the primitive node
- it grows and extends there until it reaches the (**Prechordal plate**) and can't extend farther than that; because the prechordal plate is firmly attached to the ectoderm

✓ Notochord soon acquires a lumen called the (Notochordal canal)

▪ **Prechordal plate**: a small circular thickening of the endoderm, <u>there is no mesoderm in that area</u>

***Note**: All areas that are devoid of mesoderm are:

❶ **Prechordal plate/membrane**, located at the oropharyngeal membrane which is formed by the fused layers of ectoderm and endoderm, and it is the future site of the oral cavity
❷ **Cloacal membrane**, formed by the fused layers of ectoderm and endoderm, and it is the future site of the anus
❸ **Notochord**



➢ Functions of Notochord

1) further defines the axis of the embryo and gives it some rigidity
2) serves as the base for the development of the axial skeleton (skull & vertebral column)
3) indicates the future site of the vertebral bodies
4) induces the overlying embryonic ectoderm to thicken and form the Neural plate, the primordium of the CNS

***Notes**:

- Vertebral column forms around the notochord, which extends from the oropharyngeal membrane to the primitive node

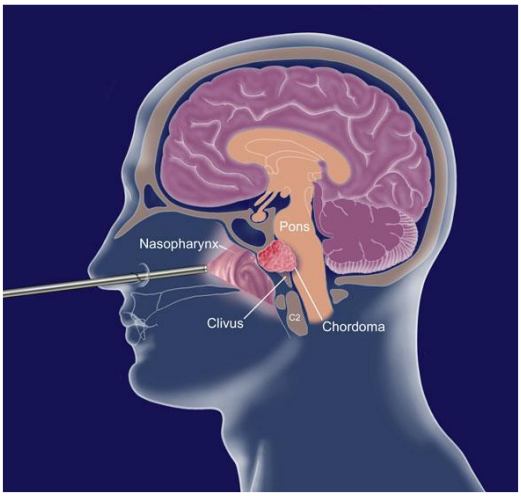
- Some cells from the primitive streak migrate cranially on each side of the notochordal process and around the prechordal plate, they meet cranially to form the (**Cardiogenic mesoderm**) in the cardiogenic area where the primordium of the heart begins to develop at the end of the 3rd week

➢ Fate of Notochord

• the notochord degenerates and disappears as the bodies of the vertebrae develop

• the part that lies between the vertebral bodies persists as the nucleus pulposus of intervertebral disc

• remnants of notochordal tissue give rise to tumors called (**Chordomas**), and approximately $^{1}/_{3}$ of chordomas occur at the base of the cranium and extend to the nasopharynx



Neurulation

➢ Definition of Neurulation

• Neurulation is the process by which the neural tube is formed
• during the period of neurulation, the embryo may be referred to as a Neurula
• located inferior to ectoderm, lying in the midline and posterior to the notochord

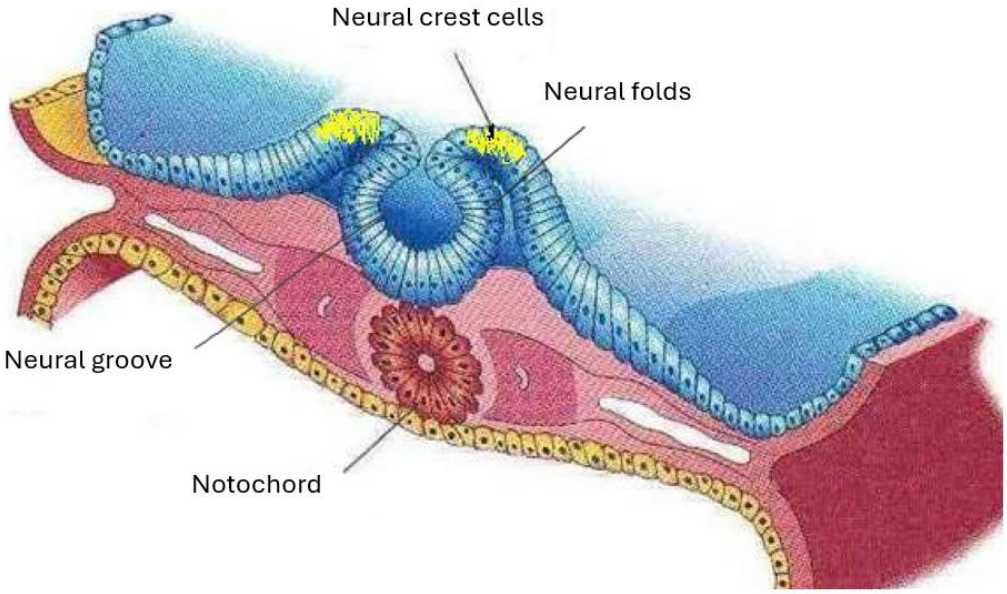
➢ Stages of Neurulation: (**Plate → Groove → Folds & Fusion → Crest → Tube**)

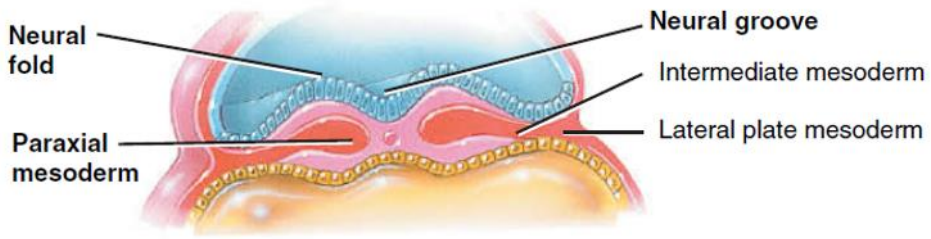
❶ the notochord, during its development, induces the overlying ectodermal cells to thicken and form the (**Neural plate**). The ectoderm of the neural plate is called (**Neuroectoderm**)

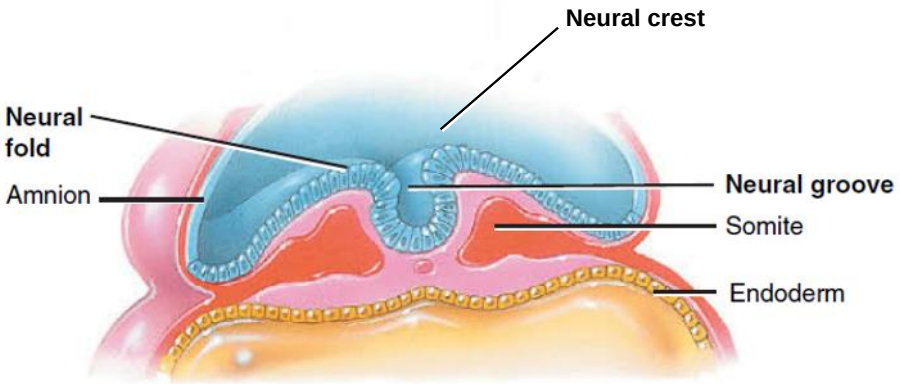
❷ the neural plate invaginates on Day 18 to form the (**Neural groove**) and (**Neural folds**), and some neuroectodermal cells on the neural fold differentiate into (**Neural crest**)

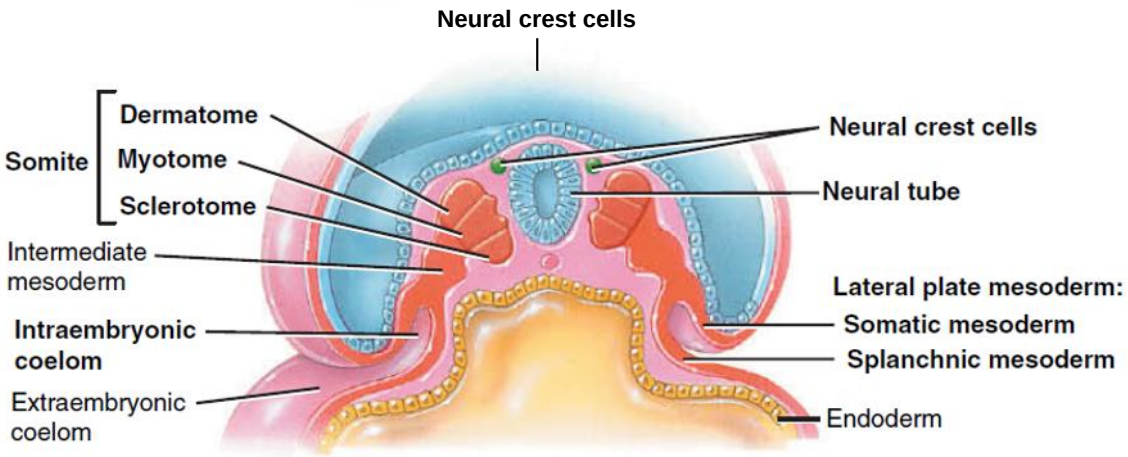
❸ the neural folds by the end of week 3 will move to the midline and **fuse** to form the (**Neural tube**)

❹ after the neural tube is formed, it will be separated from the ectoderm and the ectodermal cells above the neural tube are the (**Neural crest cells**)


Neural crest cells
Neural folds
Neural groove
Notochord

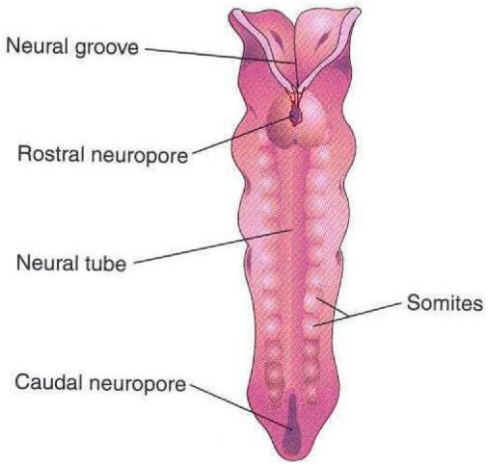

Neural fold
Neural groove
Intermediate mesoderm
Lateral plate mesoderm
Paraxial mesoderm


Neural crest
Neural fold
Amnion
Neural groove
Somite
Endoderm


Neural crest cells
Somite
Dermatome
Myotome
Sclerotome
Neural crest cells
Neural tube
Intermediate mesoderm
Lateral plate mesoderm:
Somatic mesoderm
Intraembryonic coelom
Splanchnic mesoderm
Extraembryonic coelom
Endoderm

➢ Parts of the Neural tube

- **Neural groove**
- **Somite**
- **Rostral neuropore**, the cranial opening that closes at Day 25
- **Caudal neuropore**, the caudal opening that closes at Day 27



- the cranial $^{1}/_{3}$ of the neural tube represents the future brain
- the caudal $^{2}/_{3}$ of the neural tube represents the future spinal cord

***Note**: Both neuropores directly communicate with the amniotic cavity

✪ Clinical correlation: Congenital anomalies

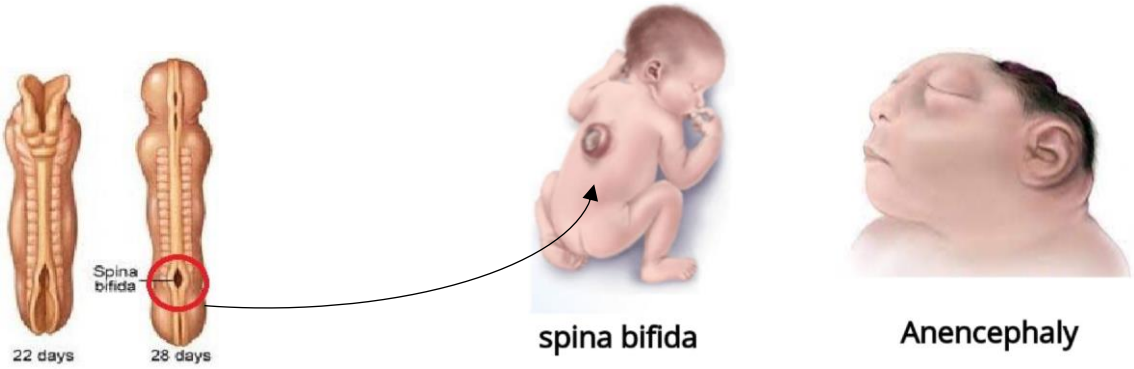
❖ **Definition**: disturbance of neurulation, it may result in severe abnormalities of the brain and the spinal cord.

❖ **Cause**: most defects are the result of non-closure or defective closure of the neural tube.

❖ **Examples in anomalies**:

❶ in the brain region: (**Microencephaly**) or (**Anencephaly**), the partial absence of the brain, it is the most severe neural tube defect and is also the most common anomaly affecting the CNS

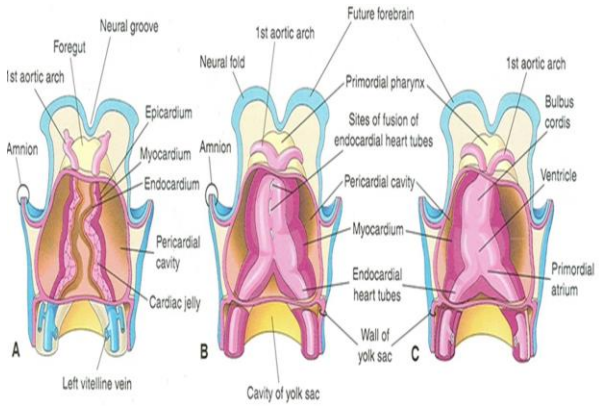
❷ in the spinal cord regions: (**Spina bifida**)



❁ Primordial CVS development:

① Heart & great vessels develop from mesenchymal cells in the cardiogenic area
② two (**Paired longitudinal endothelial lined channels**) or (**Endocardial heart tubes**) develop during week 3
③ these tubes fuse to form the heart tube
④CVS primordial will be formed by:

- Tubular heart
- Blood vessels
- Connecting stalk
- Chorion
- Yolk sac



➢ Facts about the CVS:

✓ Heart begins to beat and blood begins to circulate on Day 21 or Day 22
✓ CVS is the first organ system to reach a functional state

المطلوب من الصورة رح ينحكى بالفيديو

Chorionic villi

▪ **Chorion** (خملات الكوريون): a double-layered membrane, formed by: Trophoblast + Extraembryonic somatic mesoderm, and it will give rise to a part of the fetal placenta (placenta y3ni blood and blood vessels)

✓ the embryo, amniotic sac, and yolk sac are suspended in chorionic cavity by the connecting stalk

The system of chorionic villi is going to form a part of the **Placenta**, as the following:

(1) cytotrophoblast invades syncytiotrophoblast at the end of 2nd week to form the (**Primary chorionic villi**)

(2) mesenchyme grows into the primary villi and form a core of loose mesenchymal tissue at each villi, the forming of these cores switches primary villi into (**Secondary chorionic villi**) and the entire surface of each chorionic sac is covered

(3) some mesenchymal cells of the core in the villi soon differentiate into both capillaries & blood cells, and when capillaries are presented, the villi are called (**Tertiary chorionic villi**)

(4) capillaries in the chorionic villi fuse to form (**Arterio-capillary networks**) which soon connect with the embryonic heart through vessels that differentiate from the mesenchyme of the connecting stalk

(5) by the end of the 3rd week, embryonic blood begins to flow slowly through the capillaries [remember that fetal blood starts circulating at day 21 or day 22] in the chorionic villi

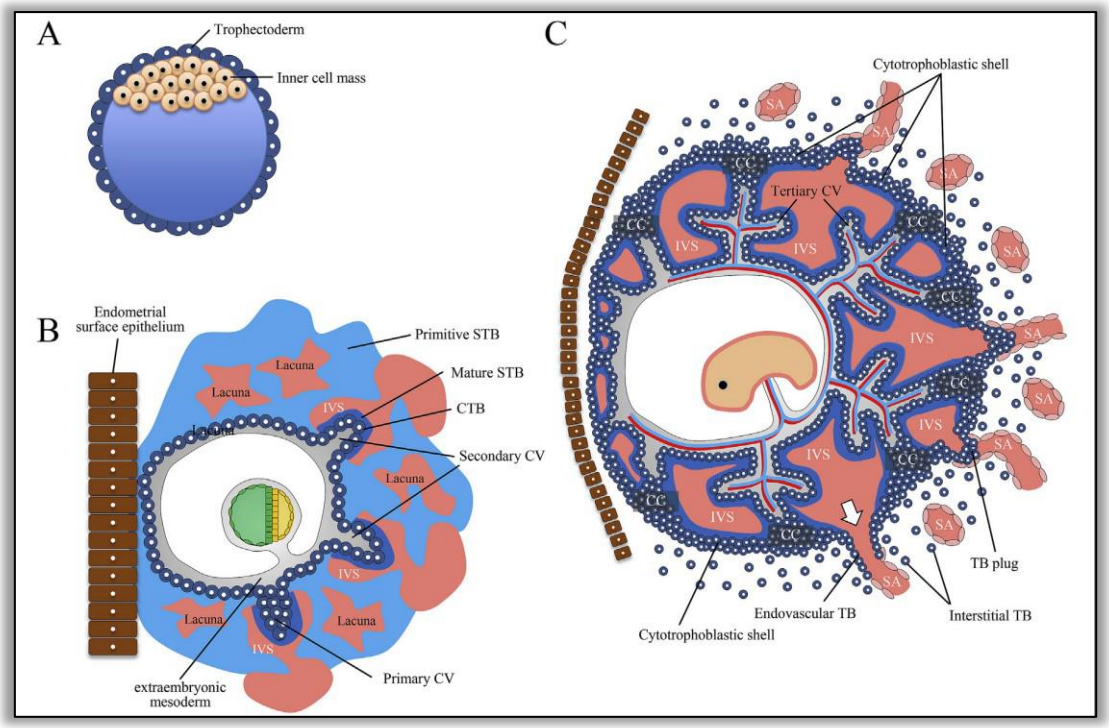
(6) O_2 & nutrients in maternal blood in the intervillous space diffuse through the walls of villi and enter embryo's blood

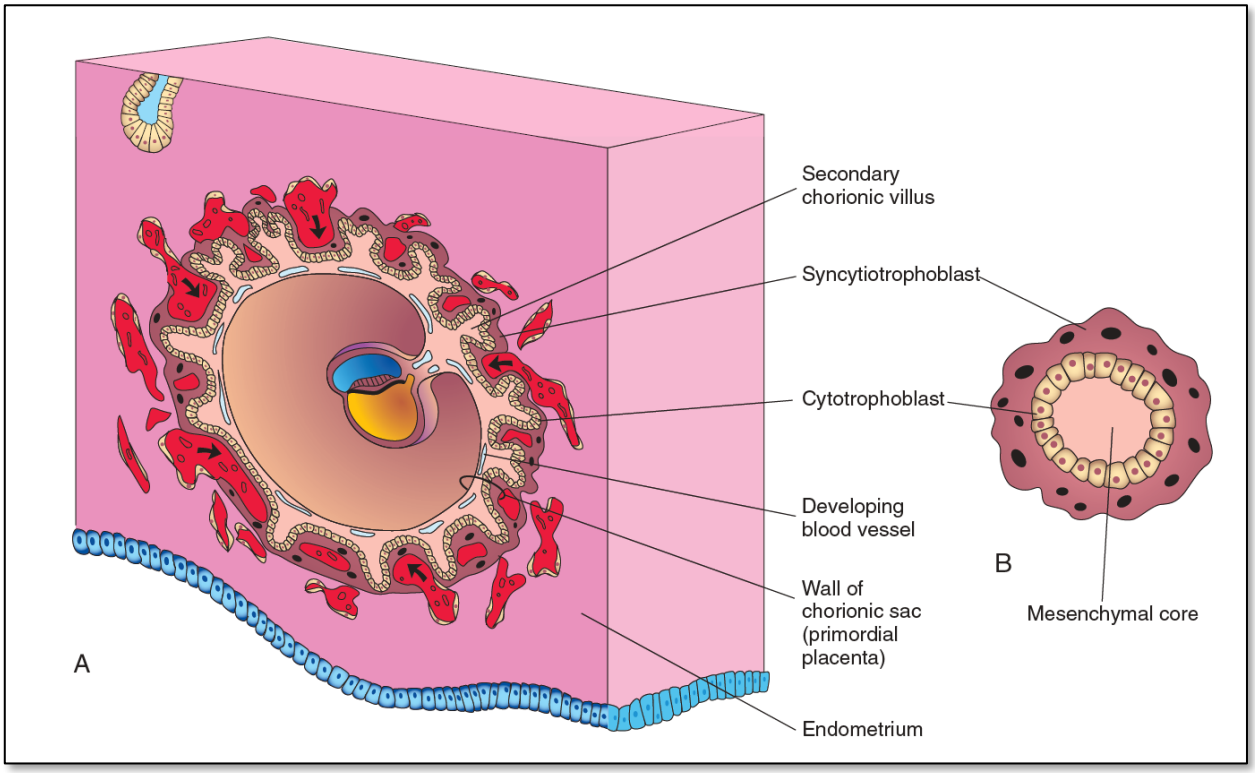
(7) CO_2 and wastes diffuse from blood in the fetal capillaries through the wall of the villi into the maternal blood

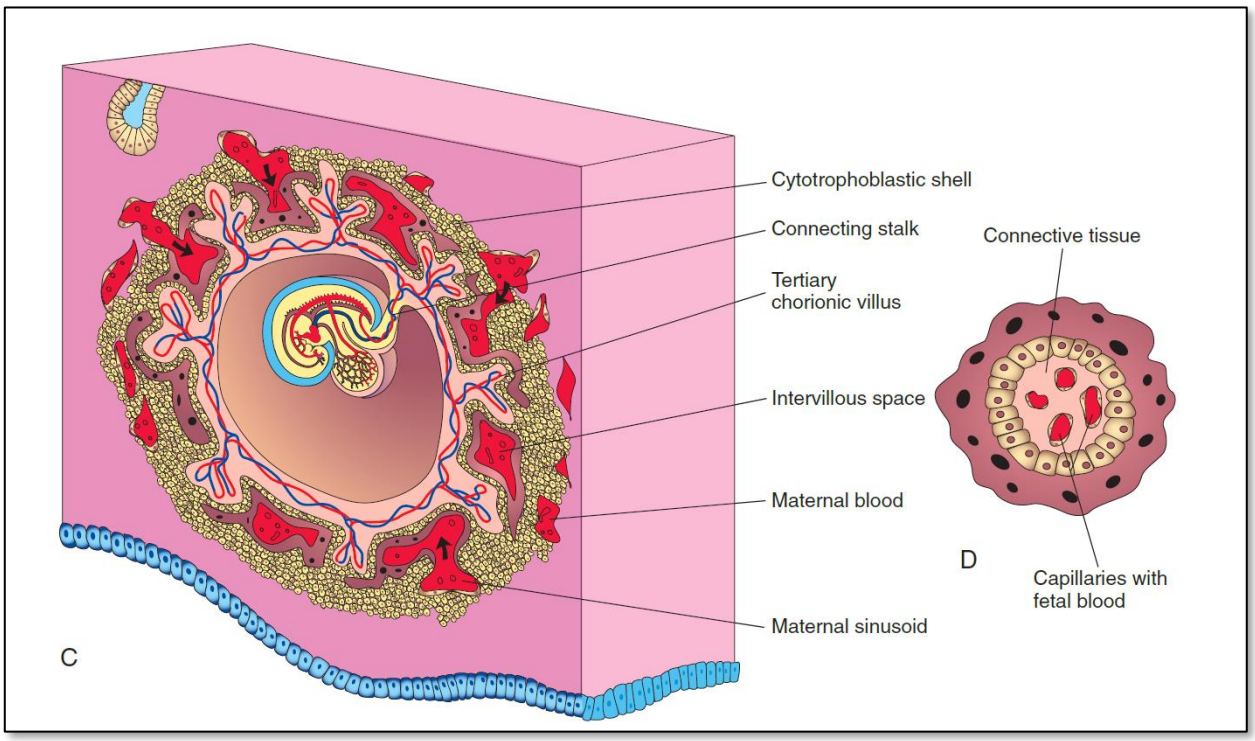
(8) simultaneously, cytotrophoblast cells of the chorionic villi proliferate and extend through the syncytiotrophoblast to form a cytotrophoblastic shell, which gradually surrounds the chorionic sac and attaches it to the endometrium

▪ Stem chorionic villi (Anchoring villi), villi that attach to the maternal tissues through the cytotrophoblastic shell

▪ Branch chorionic villi (Terminal villi), villi that grow from the sides of the stem chorionic villi, and through the walls of the branch villi the main exchange between the blood of the mother and the embryo takes place




Secondary chorionic villus
Syncytiotrophoblast
Cytotrophoblast
Developing blood vessel
Wall of chorionic sac (primordial placenta)
Endometrium
A
B
Mesenchymal core


Cytotrophoblastic shell
Connecting stalk
Tertiary chorionic villus
Intervillous space
Maternal blood
Maternal sinusoid
C
Connective tissue
D
Capillaries with fetal blood