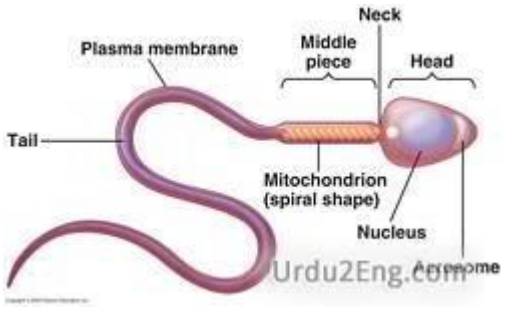
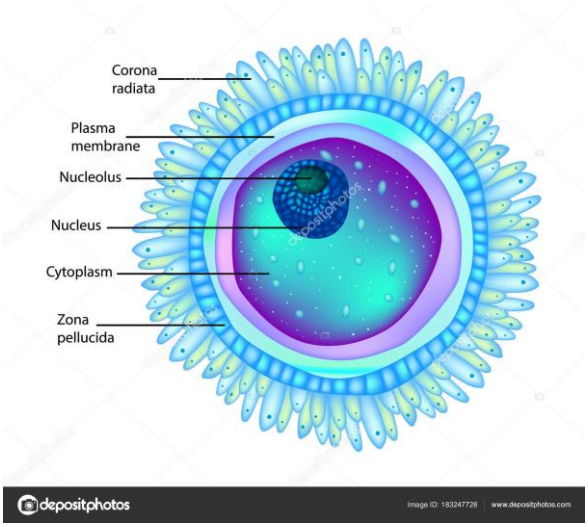
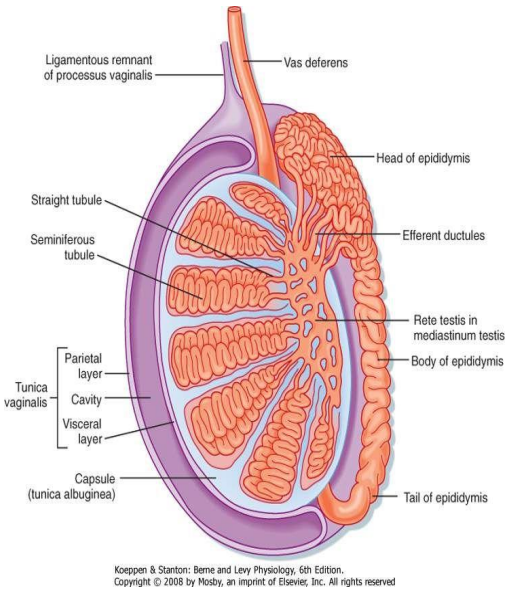
Gametogenesis

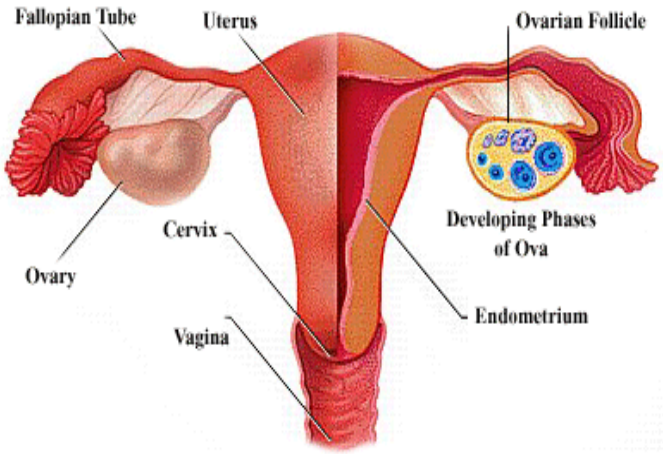
★ **Definition:** It is the processes of ***production mature gametes*** (sperms in males and ova in females) .





★**Site** : It takes place in the ***gonads*** (testes and ovary) .





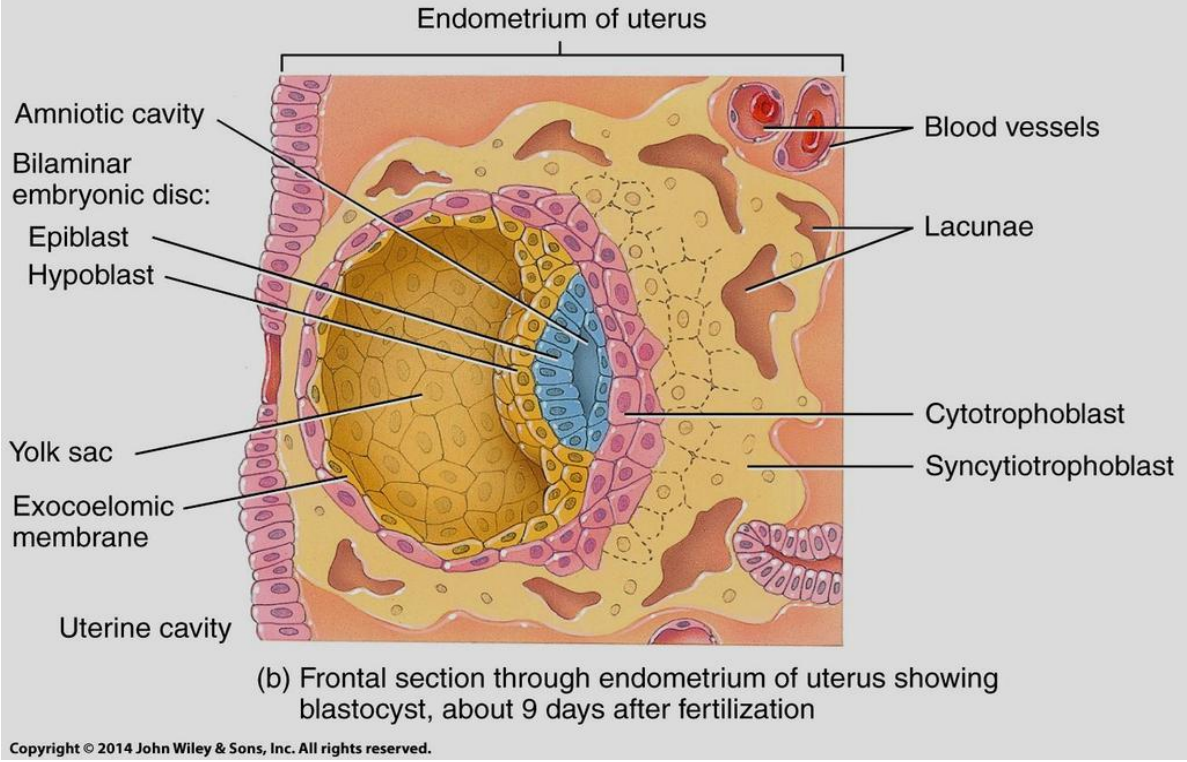
★**Mechanism :** Conversion of the primordial germ cells (spermatogonia and oogonia) into mature male or female gametes includes changes in :

a. ***Cytoplasm*** : is greatly increased in the ova but decreased in the sperms .

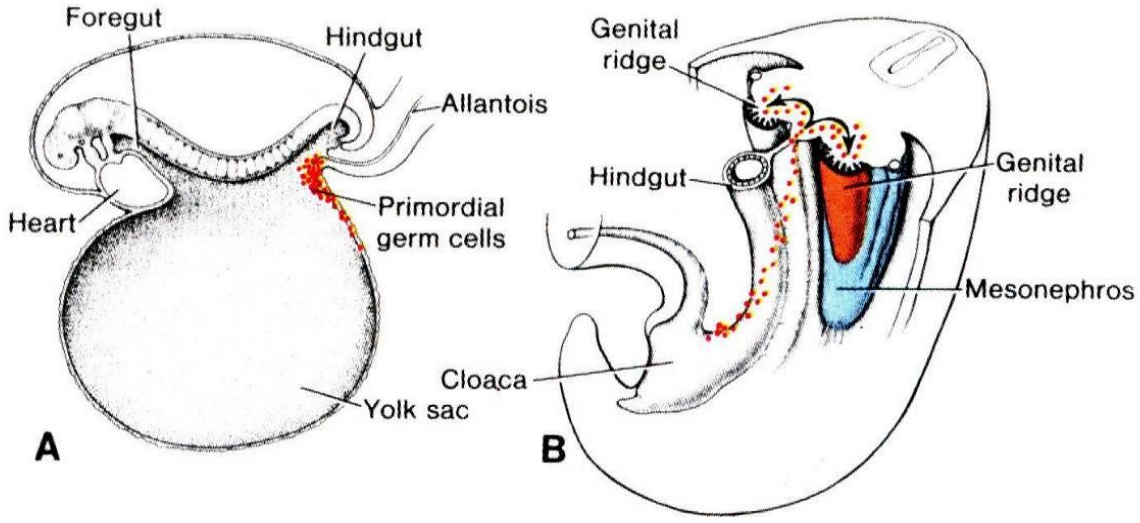
b. ***Nucleus*** : undergoes meiotic division (reduction division) to **reduce** the diploid number of chromosomes (46) to haploid number (23) .

★ **The primordial germ cell :**

- At the **2nd week**, it develops from the **epiblast** and migrates to the wall of the ***yolk sac.***
- At the **5th week**, the germ cells **migrate** from the wall of the yolk sac to reach the ***developing gonads*** (testis in males and ovary in females).



(b) Frontal section through endometrium of uterus showing blastocyst, about 9 days after fertilization



Migration of the germ cells from the wall of the yolk sac to reach the developing gonads .

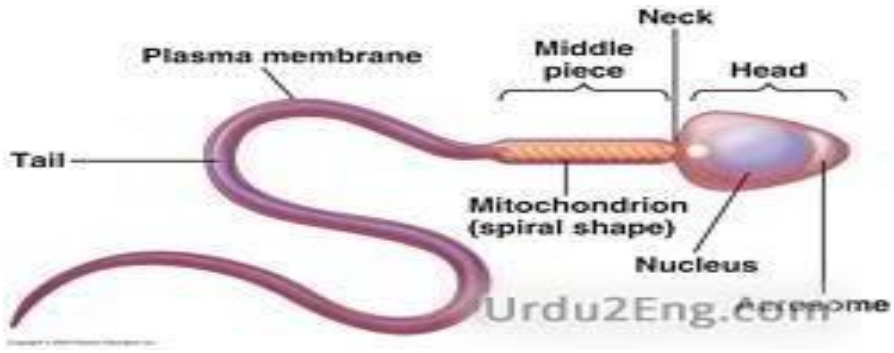
★ Gametogenesis is **divided into**:

a. spermatogenesis in the male .

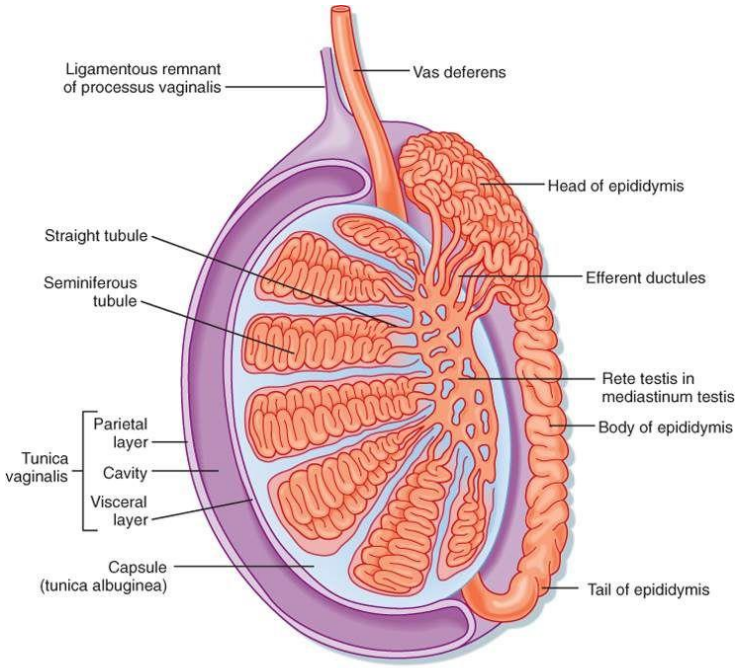
b. Oogenesis in the female.

Spermatogenesis

★**Definition:** It is the processes of ***production of sperms*** from the male primordial germ cells.



★**Site :** ***seminiferous tubules*** which are the structural unit of the testis .



★ **Age incidence :** It occurs from **puberty** (12 – 14 years) **to old age** .

★ **Condition :** low temperature (33^{o}C)**,** so the testes lie outside the body .

★ **Hormonal control :** Follicular stimulating hormone (FSH) secreted by pituitary gland .

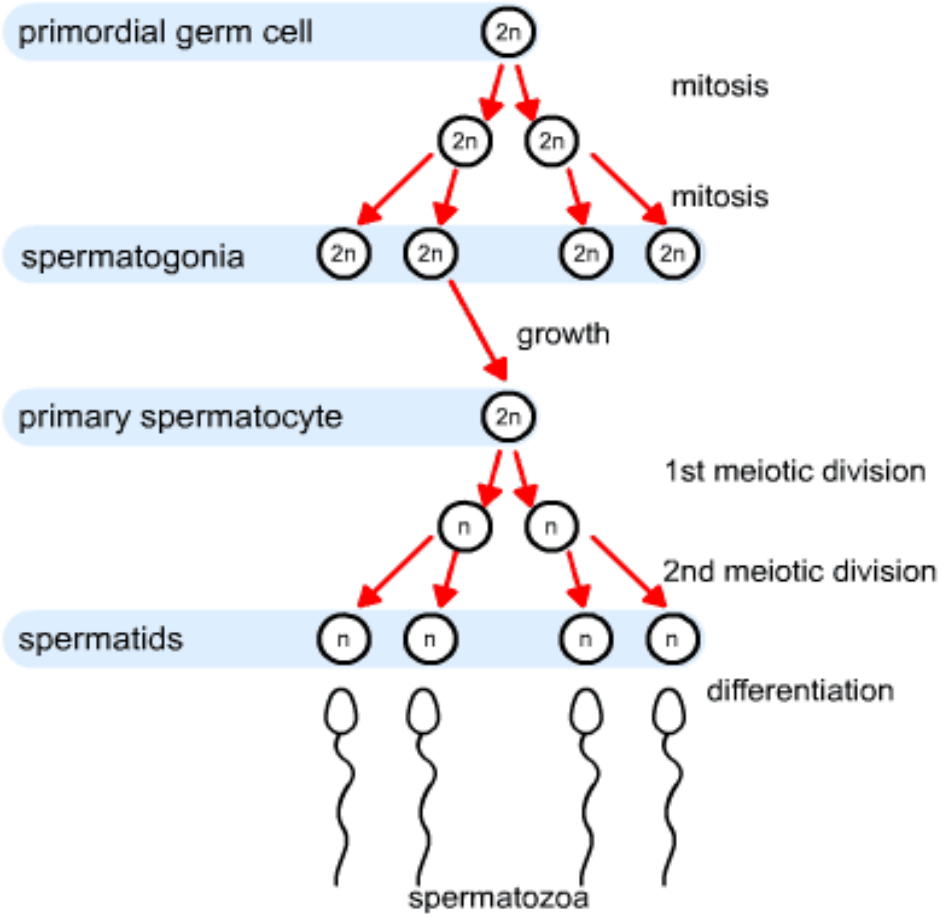
★ **Aim :**

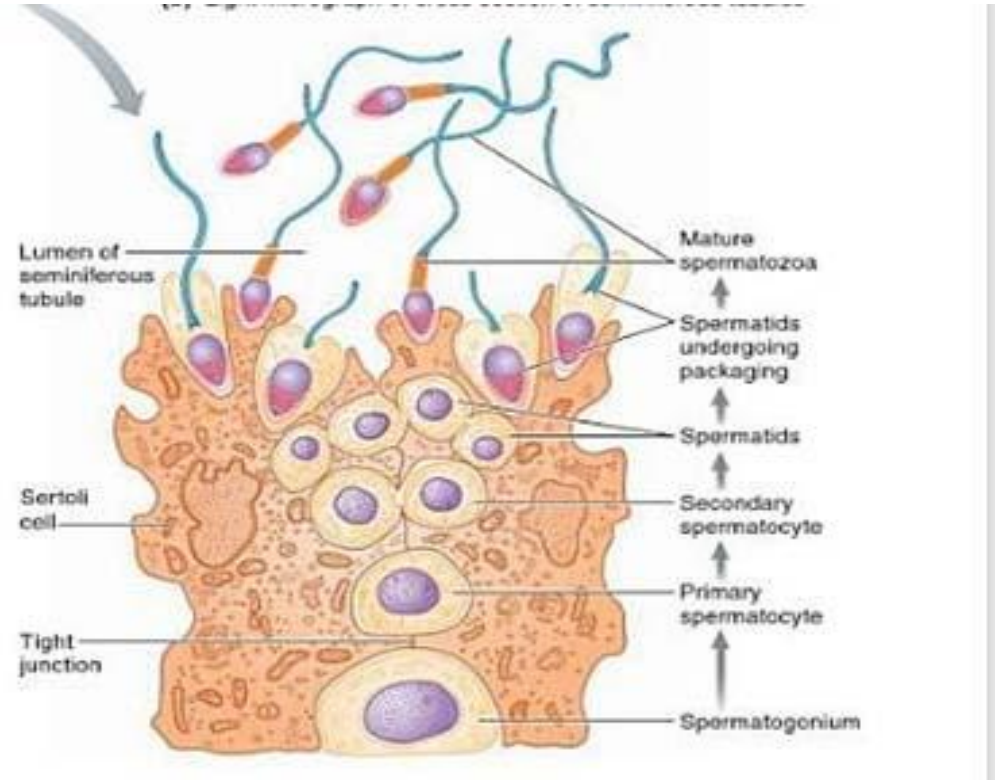
1. **Reduction** of the diploid number of chromosomes (46) to haploid number (23) by meiotic division .
2. **Morphological** changes in male primordial germ cell to produce sperm ready for fertilization of the ovum .
3. **Increase number** of cells so that each spermatogonium produce 8 - 16 sperms .
4. Determination of **sex of sperms.**

★ STAGES OF SPERMATOGENESIS:

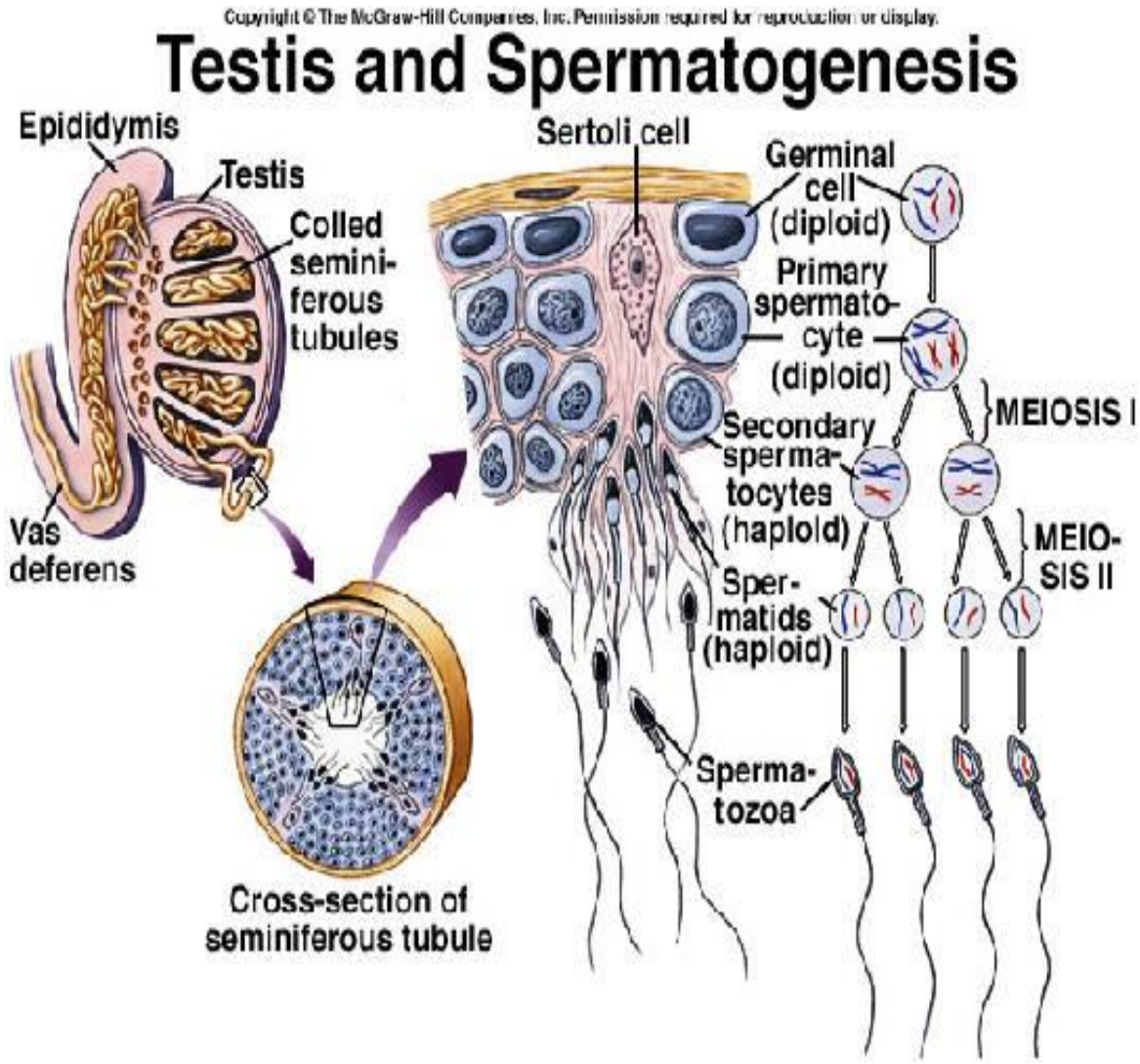
1-Spermatocytogenesis

- It is the process of transformation of the male primordial germ cells to ***spermatids*** **.**
- At **puberty , under the effect of FSH ,** the male **primordial germ cells** differentiate to ***spermatogonial stem cells*** which divide by **mitosis** (to increase their number of cells) **to** produce 2 **daughter type A spermatogonia**.
- The latter cells divide by mitosis to produce 4 **daughter type B spermatogonia**.
- Type B spermatogonia **grow** to form **primary spermatocytes** which are larger in size containing diploid number of chromosomes (44 autosomes and 2 sex chromosomes XY) .
- The primary spermatocytes undergo **1st meiotic** (reduction) division and give rise to **secondary spermatocytes** which have the haploid number of chromosomes (22 autosomes and 1 sex chromosomes which may be X or Y)
- The **secondary spermatocytes** rapidly complete the **second meiotic** division to form **spermatids** which have the haploid number of chromosomes (22 autosomes and 1 sex chromosomes which may be X or Y).





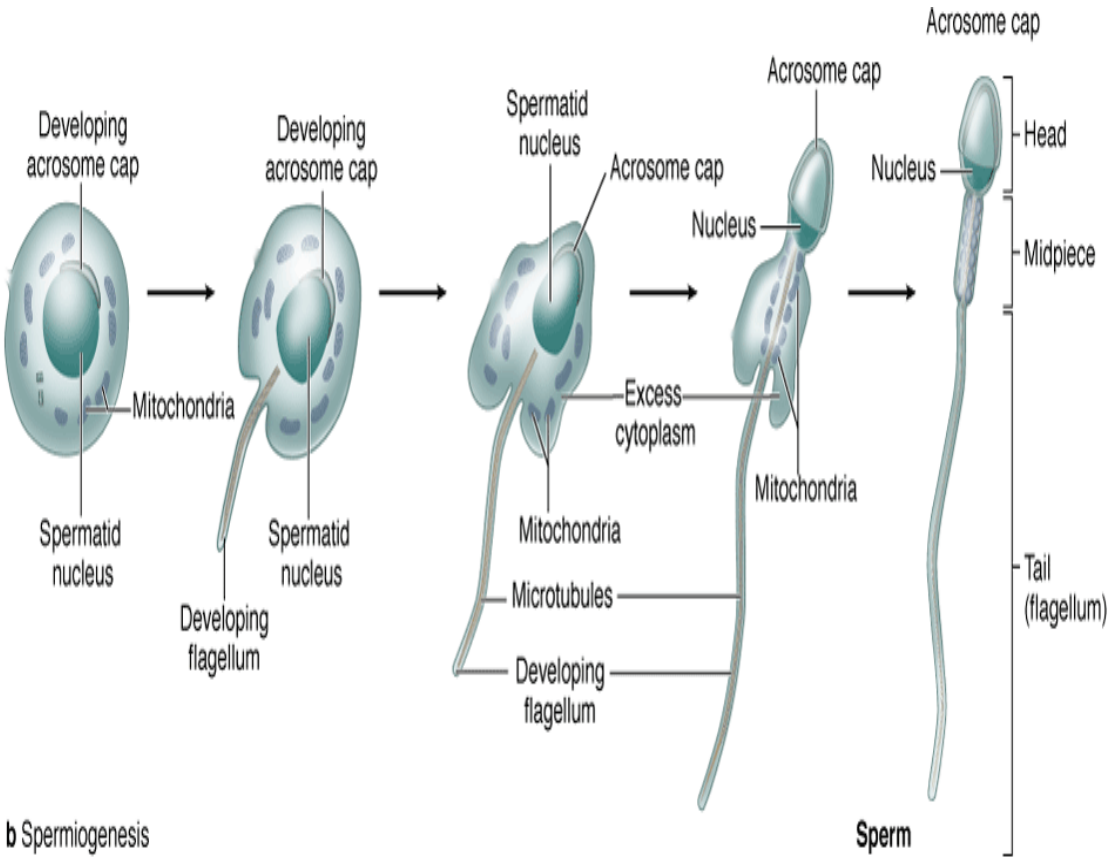
SPERMATOGENESIS

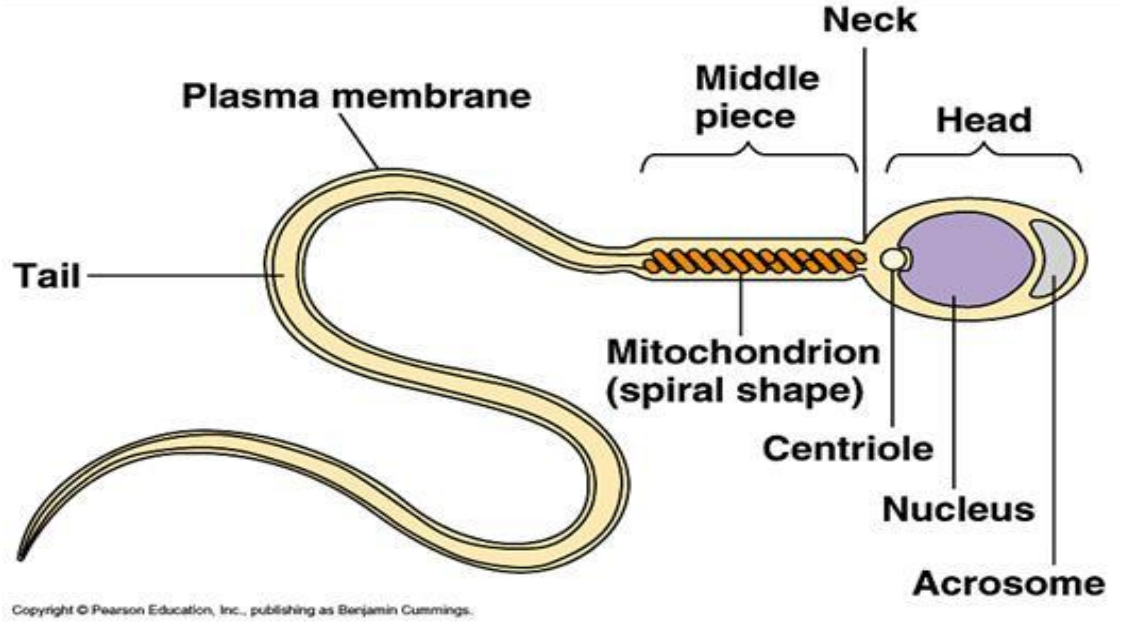


2-Spermiogenesis

- It is the process of transformation of a **spermatid** to a **sperm.**
- The time required for spermiogenesis in man is **74 days**.
- The spermatid changes **morphologically** to be able to fertilize the ovum as follows :
  - Formation of ***acrosomal cap*** , which covers 1/2 of the nuclear surface , which contain enzymes to penetrate the coverings of the ovum .
  - Condensation of the nucleus, carrying genetic informations , in one end called the ***head***.

- Formation of the ***neck***, ***middle piece*** (contain mitochondria give energy to the sperm) , and ***tail or flagellum*** (used for locomotion) .
- Shedding of most of the ***cytoplasm***.





- **Abnormalities of the sperms:**

1.Abnormalities in ***shape*** of the sperms (double heads,large head , pin head , taper head , double tails , dwarf sperm).

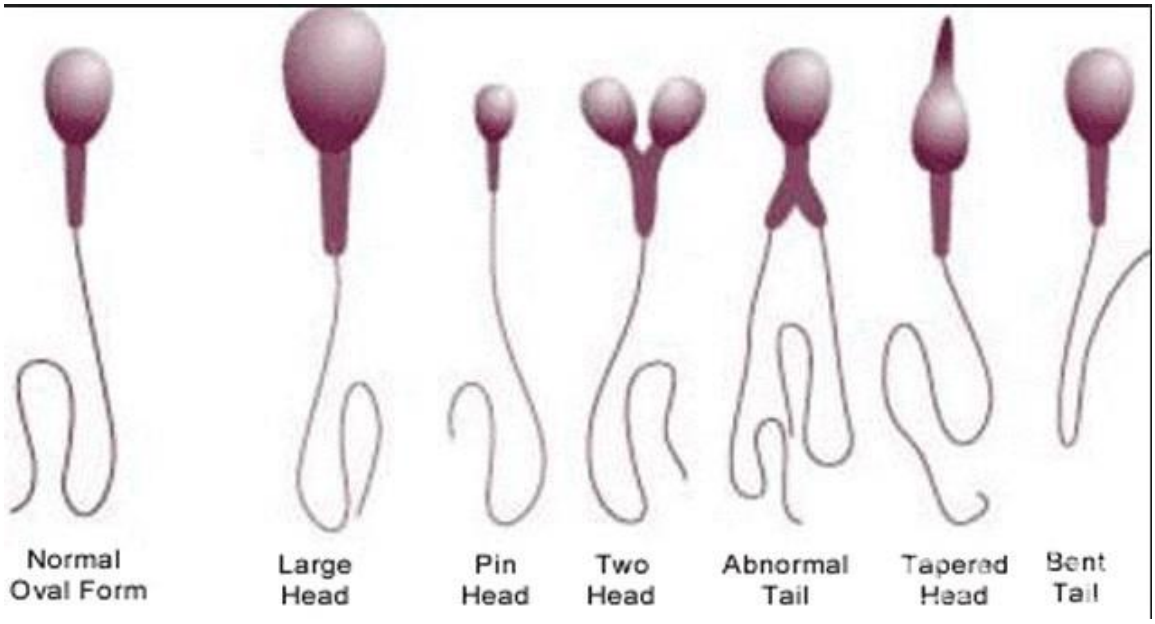
2.Abnormalities in the ***motility*** (normally it is actively motile).

3.Abnormal sperm ***count*** :

- ***Oligospermia*** : less than 20 million/ml
- ***Azospermia***: complete absence of sperms in the semen .

4.*Necrospermia* : dead sperms in the semen .

Abnormalities of sperms



Semen

(Seminal fluid)

★ **Definition** : It is the fluid containing the sperms suspended in the secretions of seminal vesicles , prostate and bulbo-urethral glands .

★ **Characters** : thick , opaque , white , alkaline fluid which has characteristic odour .

★ **Volume** : 3-5 c.c per ejaculation .

★ **Number of sperms** : 200 -300 millions per ejaculation .

★ **Motility** : normally 60-70 % of sperms are motile .

★ Normally , **abnormal forms** of sperms do not exceed 10% of total sperm count (if more than 25 % fertility is impaired)

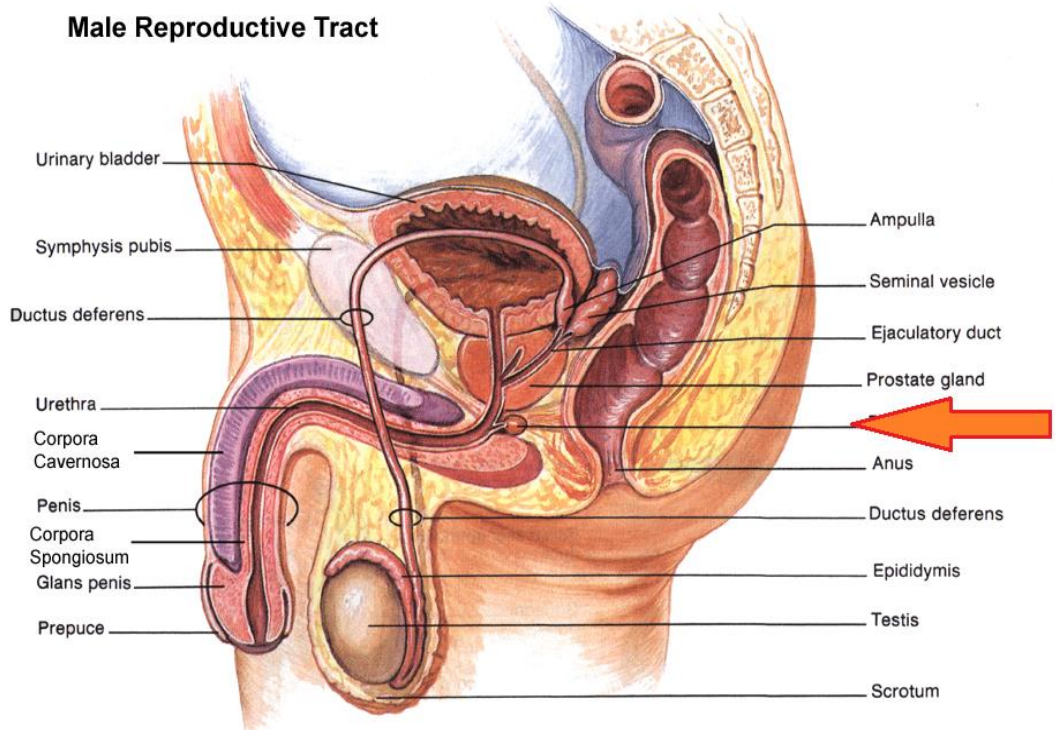
Transport and Fate of Sperms

★ The sperms leave the **testis** to reach the **epididymis** (for physiological maturation) then pass through the **vas deferens** to be **stored** in the **ampulla** of vas waiting for ejaculation .

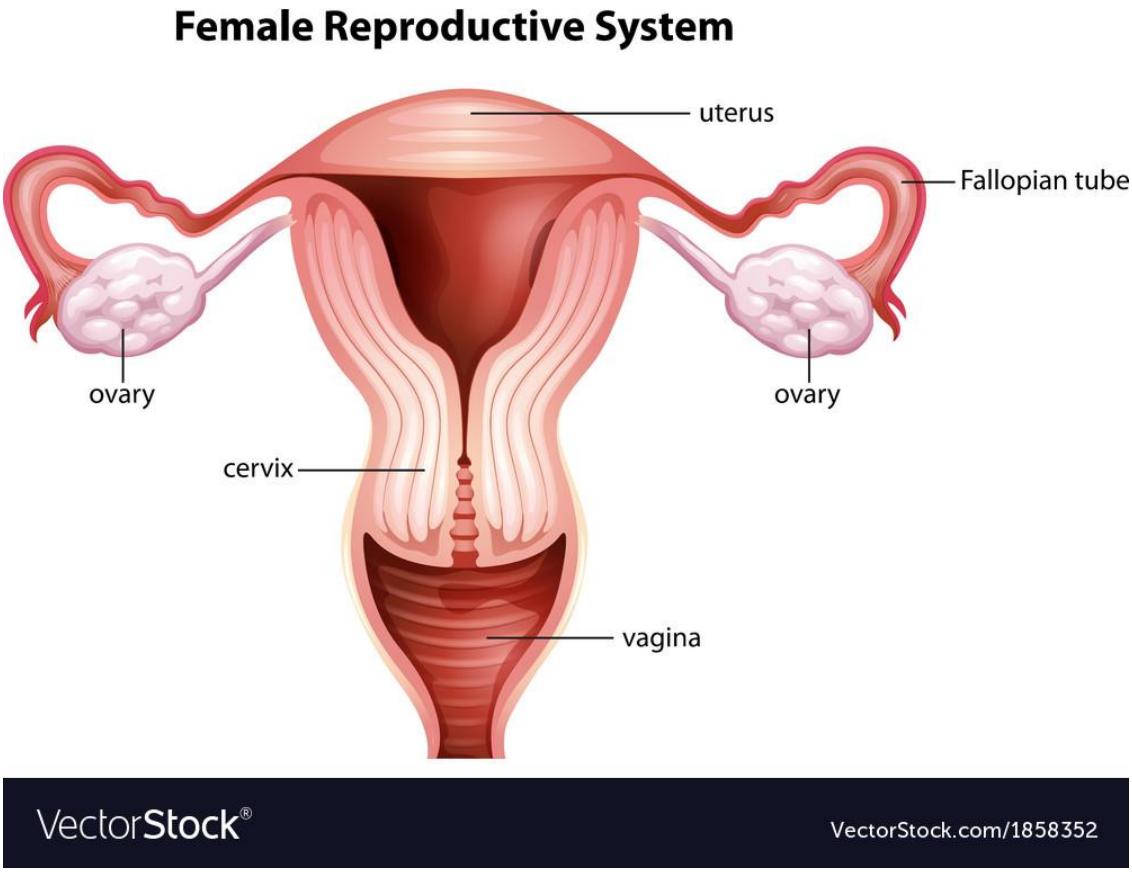
★ If **ejaculation does not occur** , the stored sperms die and becomes absorbed .

★ When **ejaculation occurs** the semen pass through the ejaculatory ducts and **urethra** and become deposited in the **vagina** .Then the sperms ascend through the **cervix** to the **uterine cavity** to enter the **uterine tube** to reach its lateral 1/3 .

- If ***ovum*** is found in the uterine tube , fertilization may occur .
- If ***no ovum*** is found , the fertilizing power of sperms is lost about 48 hours after ejaculation .



Modified from Van De Graaff, *Human Anatomy,* Wm. C. Brown: Dubuque, IA, 1988.



Oogenesis

★ **Definition** : It is the process of production of **mature ovum** from the female primordial germ cell.

★ **Site** : It takes place mainly in the **cortex of the ovary** and **completed after fertilization** ,in the lateral 1/3 of uterine tube .

★ **Age incidence** :

- Oogenesis **start** during **intrauterine** life .
- Oogenesis occurs mainly **from puberty** (12-14 years) and ends at **menopause** (45- 50 years).
- During this fertility period , **one secondary oocyte** successes to develop from right or left ovary **every 28 days** .

- Oogenesis is only **completed after fertilization** , in the lateral 1/3 of uterine tube , when the second meiosis occur in the secondary oocyte to form mature ovum .

★ **Condition :** normal body temperature .

★ **Hormonal control :** Follicular stimulating hormone (FSH) secreted by pituitary gland .

★ **Aim :**

1-Reduction of the diploid number of chromosomes (46) to haploid number (23) by meiotic division .

2-Increase size of the ovum from 30 to 120 micron in diameter .

★ **Stages of oogenesis:**

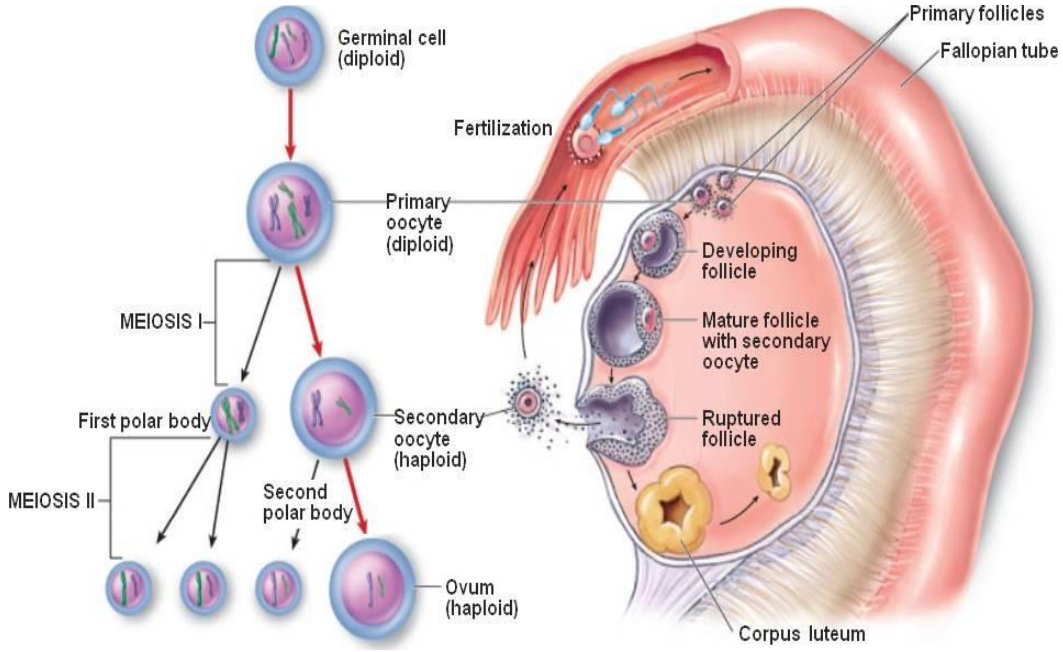
I- During intrauterine life :

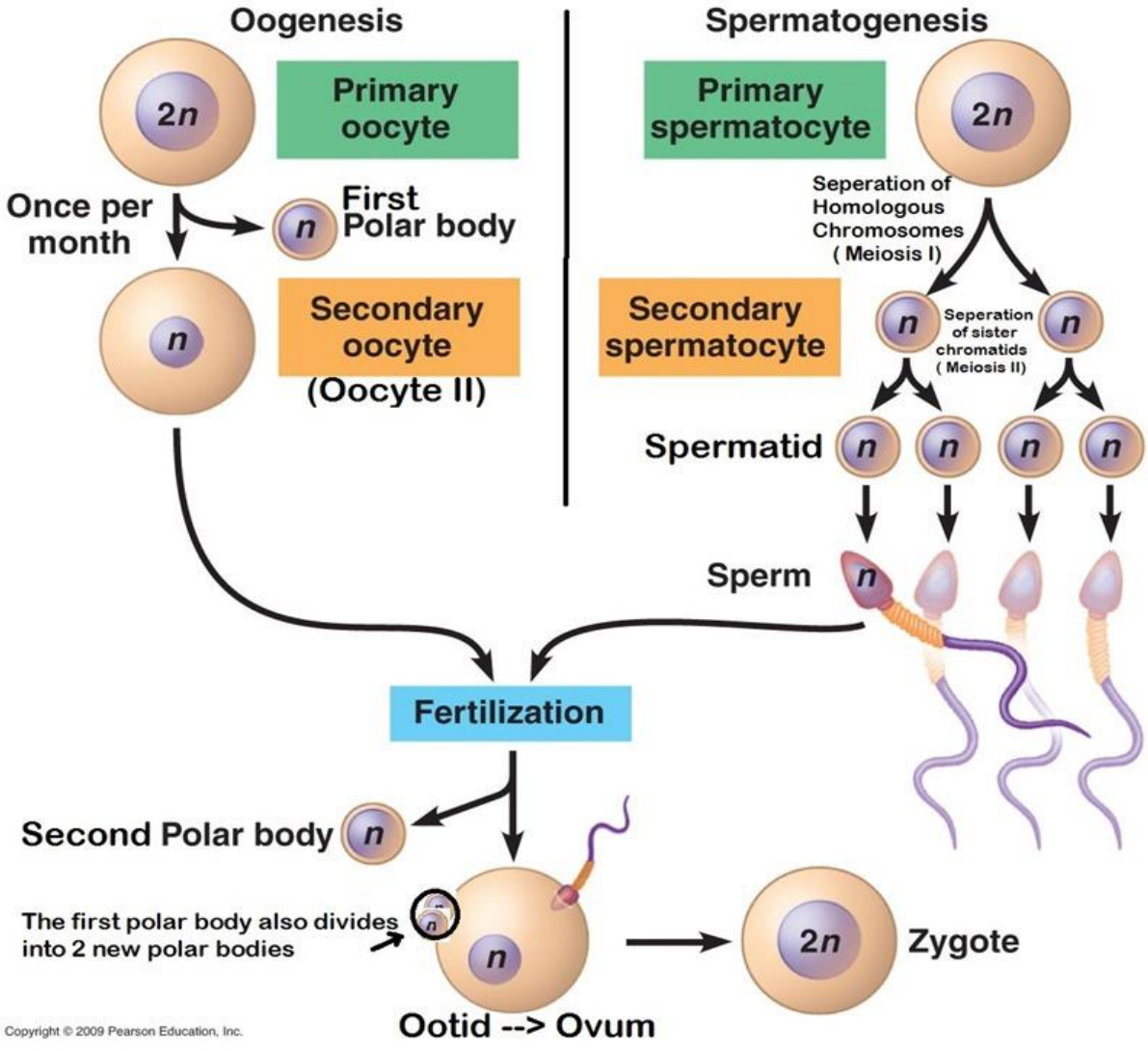
- The female ***primordial germ*** cells differentiate and proliferate by **mitotic** division (to increase their number) to form **oogonia & daughter oogonia** containing **diploid** number of chromosomes (44 autosomes and 2 sex chromosomes XX) .
- The daughter oogonia grow and enter **incomplete 1st meiosis** , during **3rd month** of fetal life , forming **primary oocytes** (containing 44 autosomes and 2 sex chromosomes XX) which **remain dormant till puberty**.
- Each primary oocyte is surrounded by one layer of flat **follicular cells** to form the **primordial follicle**.
- **At birth** there may be around **700,000 primordial follicles** present in the 2 ovaries .
- The number of follicles **diminish with age** so that about **40,000** present at puberty .

II- From puberty to menopause :

- Under the effect of follicular stimulating hormone (**FSH**) secreted by pituitary gland , **the ovarian cycle begins** .
- With **each cycle** , many follicles in both ovaries start to develop , but **only one follicle** successes to **reach full maturity** while the remaining follicles degenerate (called atretic follicle) .
- Thererore only ***one primary oocyte/month*** **completes its 1st meiosis few hours before ovulation** .
- **RESULTS OF FIRST MEIOSIS:**

1. **Two cells** are developed, one large cell called **secondary oocyte** , and another small one called **1st polar body**.
2. Each cell contains the **haploid** number of chromosomes (22+X).
3. Both cells enter the **second meiosis** till the metaphase stage at which ovulation occurs & the ***secondary oocyte*** which pass from the surface of the ovary to the lateral 1/3 of **uterine tube waiting for fertilization .**
4. The second meiosis is completed only if the **secondary oocyte is fertilized** leading to formation of mature ovum and one 2nd polar body.
5. The **first polar body** undergoes 2nd meiosis and gives two **2nd polar bodies**.
6. The three 2nd. polar bodies **degenerate** later on.


Germinal cell
(diploid)
Primary
oocyte
(diploid)
MEIOSIS I
First polar body
Secondary
oocyte
(haploid)
MEIOSIS II
Second
polar body
Ovum
(haploid)
Fertilization
Primary follicles
Fallopian tube
Developing
follicle
Mature follicle
with secondary
oocyte
Ruptured
follicle
Corpus luteum


Oogenesis
Spermatogenesis
2n
Primary
oocyte
Once per
month
n
First
Polar body
n
Secondary
oocyte
(Oocyte II)
Primary
spermatocyte
2n
Seperation of
Homologous
Chromosomes
(Meiosis I)
Secondary
spermatocyte
n
n
Seperation
of sister
chromatids
(Meiosis II)
Spermatid
n
n
n
n
Sperm
n
Fertilization
Second Polar body
n
The first polar body also divides
into 2 new polar bodies
n
n
2n
Zygote
Ootid --> Ovum
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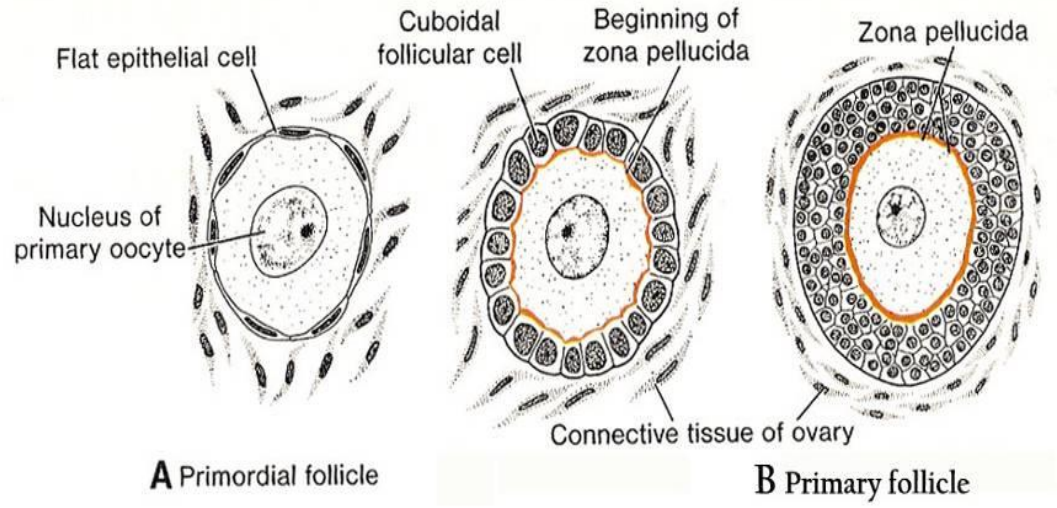
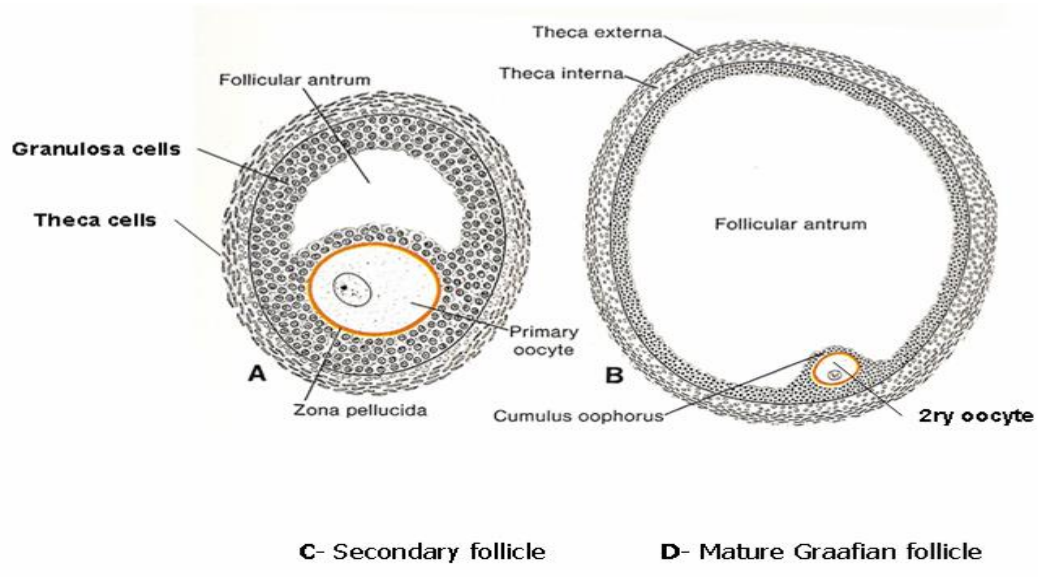
Development of the follicular cells & Formation of Graffian follicle

- **Aim :** protection of developing ovum & production of hormones .
- **During intrauterine life** : Each primary oocyte becomes surrounded by one layer of flat **follicular cells** to form the **primordial follicle**.
- **At puberty *:*** Under the effect of **FSH** secreted by pituitary gland , the following changes occur :
  - **The** single layer of flat **follicular cells** around the primary oocyte change to **cubical** cells which **proliferate** forming many layers of ***granulosa cells*** around the primary oocyte ***.***
  - The granulosa cells secret***e*** ***Zona pellucida*** (glycoprotein shell) around the primary oocyte .
  - ***Theca folliculi*** cells develop around the primary follicle from the surrounding stromal cells of the ovary.
  - The primordial follicle is changed now to the **primary follicle .**

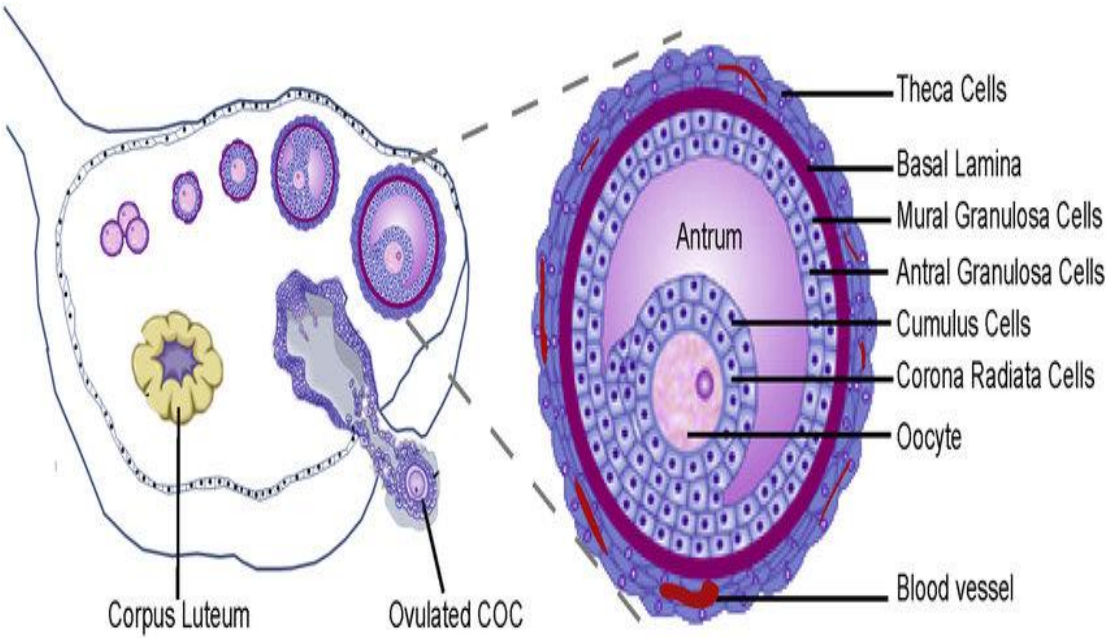


DEVELOPMENT OF THE FOLLICLE

- Small irregular ***spaces***, appear between granulosa cells , containing fluid secreted by granulose cells .
- These spaces later **coalesce** to form a single cavity called ***follicular antrum*** which filled with fluid , ***liquor folliculi*** , containing estrogen hormone secreted by granulosa cells .
- The appearance of follicular ***antrum*** with the theca cells differentiate into ***theca interna*** (cellular vascular layer) and ***theca externa*** (fibrous layer), change the primary follicle into **secondary follicle**.
- **Enlargement** of the secondary follicle changes it to mature **Graafian follicle which is :**
  - **10 mm spherical vesicle** lies bulge on the surface of the ovary
  - Its wall is formed of **membrana granulosa** (lining the antrum) , **theca interna** and theca **externa**.
  - **Cumulus oophrus** are the granulosa cells surrounding the oocyst which having **eccentric** position .

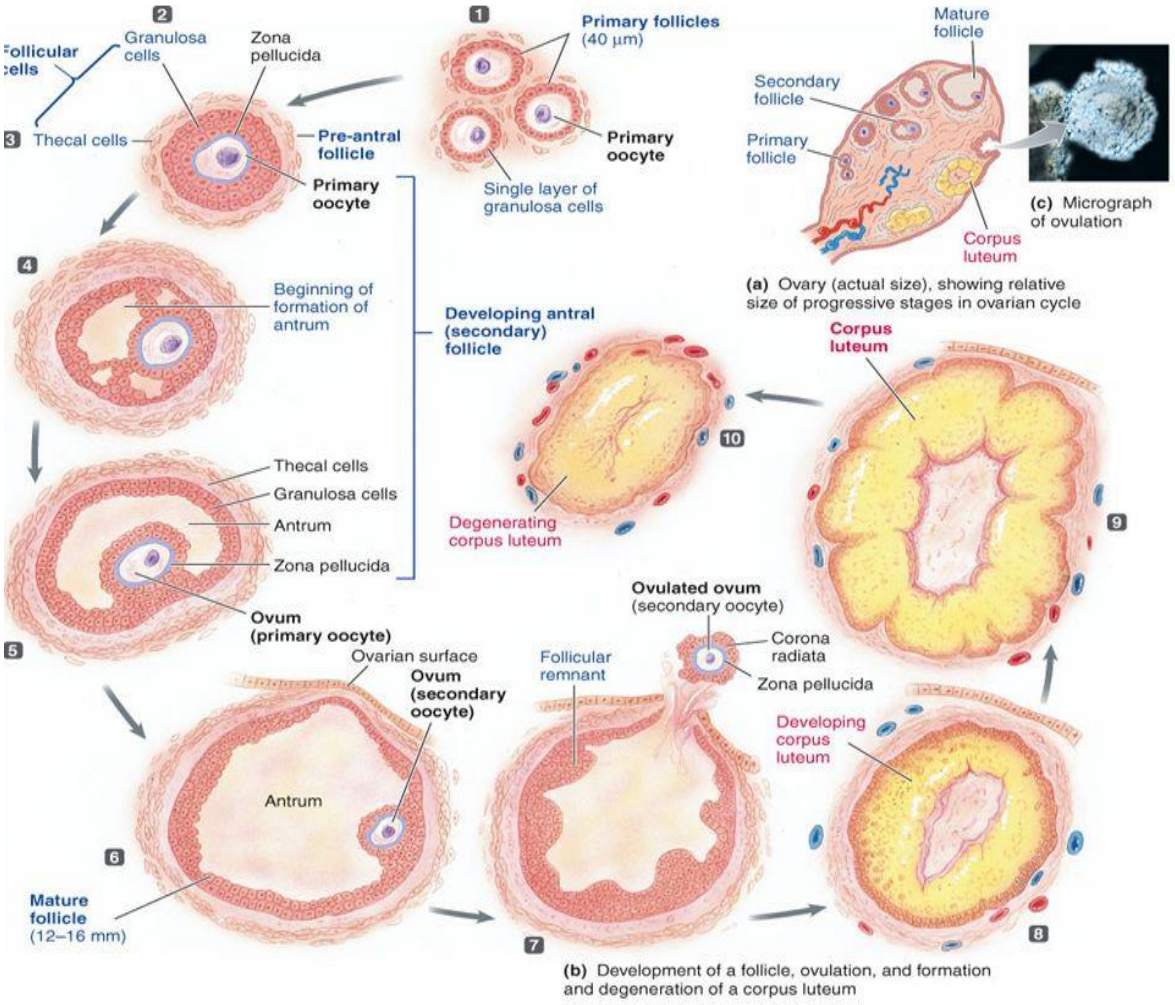


Mature Graafian follicle

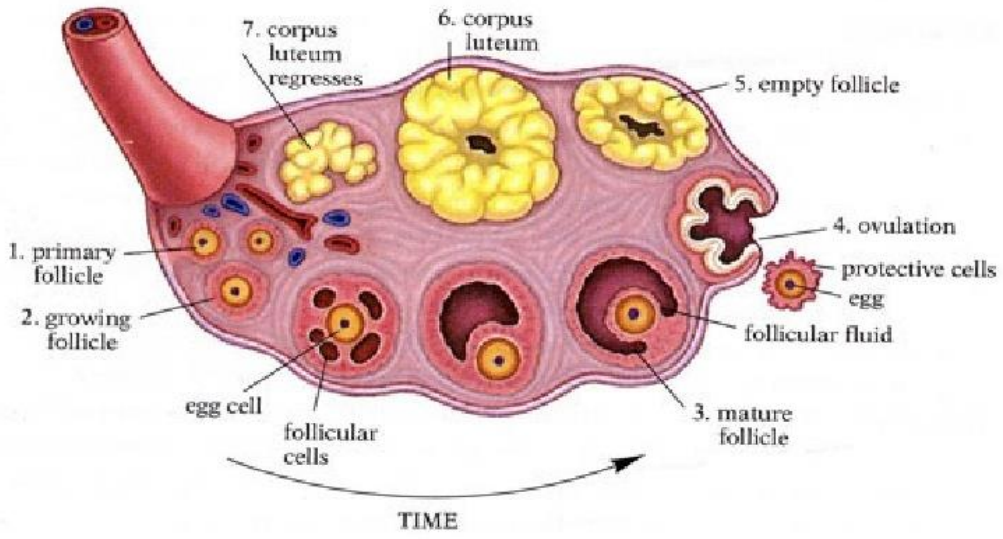


- With **each cycle** , many follicles in both ovaries start to develop , but **only one follicle** successes to reach full maturity , while the remainder becomes **atretic follicles** .
- **At ovulation** , the mature graafian follicle **ruptures** releasing the secondary oocyte , surrounded by the **zona pellucida** & **corona radiata** (cells from the cumulus oophorus) , which is sucked by uterine tube where it lies in its later 1/3 waiting for fertilization .
- **If fertilization occurs** , **second meiosis** is completed in the secondary oocyte with formation of **mature ovum** and a **zygote** is formed.
- **If no fertilization occurs ,** secondary oocyte **dies after 24 – 36 hours** .
- The ruptured Graffian follicle is transformed to a yellow body called **corpus luteum** , the fate of which depends on whether fertilization occurs or not .

Development of the Follicle, Ovulation, and Formation and Degeneration of the Corpus Luteum



Follicle developement



Cyclic Changes in the Female

- These are **periodic changes** which occur every **lunar month** (28 days) during the **fertile** period of the **non pregnant** female.
- It starts at puberty (12-14 years) and stops at menopause (45-50 years).
- These changes are **controlled by** the hypothalamus and the pituitary gland.
- They affect the **ovaries** and the **uterus**.

HYPOTHALAMUS

↓

Gonadotropin releasing hormone

↓

PITUITARY GLAND

↓

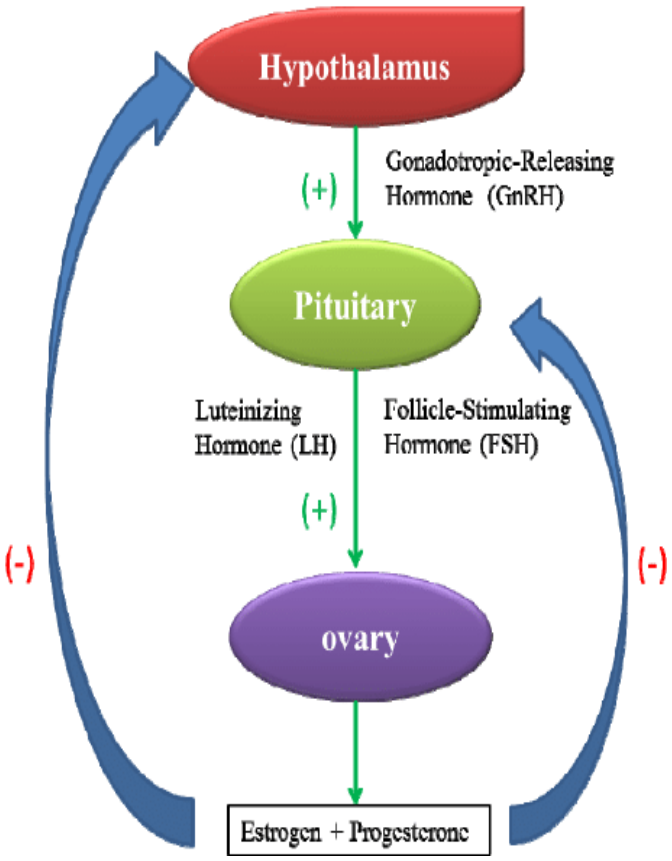
Gonadotropins (FSH – LH)

↓

Ovary

↓

Ovarian hormones
which affect the endometrium



The Ovarian Cycle

- These are ***periodic changes*** which occur in the ***ovary*** every lunar month (28 days) during the ***fertile period*** of the ***non pregnant*** female.
- **The ovarian cycle is divided into three phases:**
  - ***Preovulatory*** (follicular) phase.
  - ***Ovulation***.
  - ***Postovulatory*** (Luteal phase).

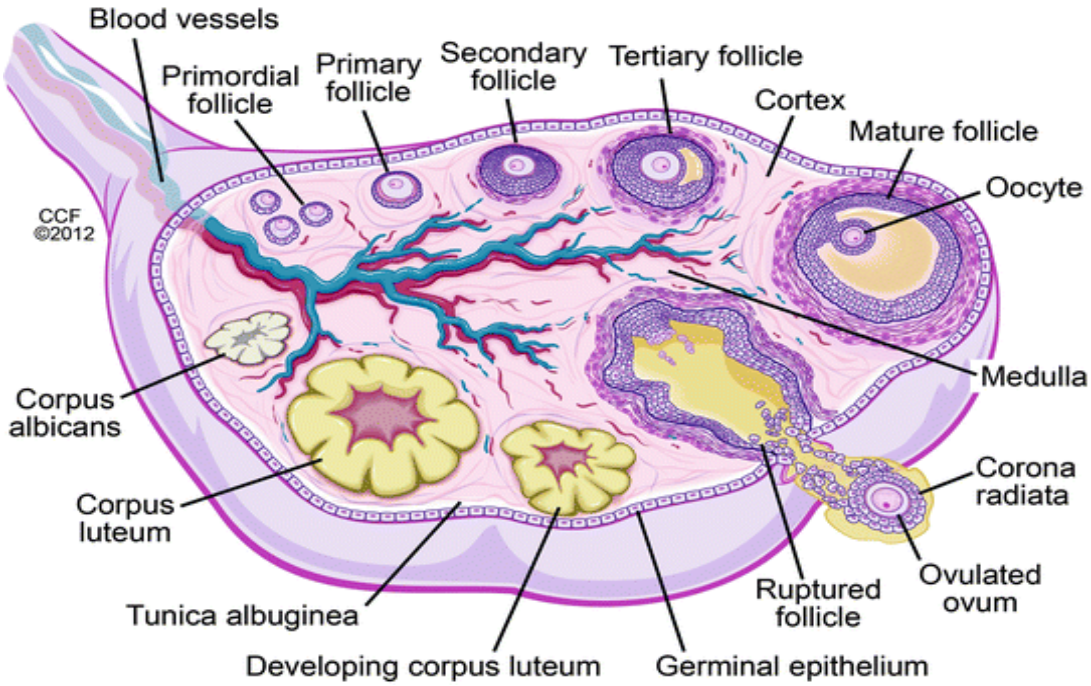
I- PREOVULATORY (FOLLICULAR) PHASE: (1St half of the cycle)

- At the **beginning** of each ovarian cycle , the anterior lobe of pituitary gland secretes **FSH** which stimulates a number of **primordial follicles** to develop .
- **Only one follicle** reaches maturity and **secretes estrogen** which **inhibit** secretion of FSH by pituitary gland (and stimulate secretion of luteinizing hormone) leading to **degeneration** of the remaining follicles which become **atretic follicles** .
- The estrogen secreted in this phase is responsible for the **proliferative phase of the uterine cycle .**

II- OVULATION :

- Luteinizing hormone (***LH):***
  1. Stimulates **collagenase** activity resulting in digestion of collagen fibers surrounding the mature Graafian follicle.
  2. Increases **prostaglandin** activity resulting in **ovarian contraction**.
- Secondary oocyte together with the corona radiata and the zona pellucida release due to **rupture of the mature Graafian follicle** on the surface of the ovary.

- At the time of ovulation the body **temperature** is slightly elevated and the female feel **pain** in the iliac fossa (mid-cycle pain) . If this pain occurs on the right side , it may be miss diagnosed as **acute appendicitis** .
- Ovulation occur **once every lunar month** , approximately **14 days** (plus or minus one day) before the beginning of next menstruation .
- Ovulation does **not occur** during pregnancy and occurs to **less extend** during lactation .



III- POST OVULATORY (LUTEAL) PHASE:

- **After ovulation** , Under the effect of **luteinizing hormone** , the cells of **membrana granulosa** and **theca interna** cells are changed to the ***luteal cells*** to form the **corpus luteum .**
- **Corpus luteum** secrets **progesterone** hormone responsible for **secretory phase of uterine cycle** and **inhibit** pituitary LH .

- **Fate of the corpus luteum *:***
  - **If fertilization does not occurs** , the corpus luteum **degenerate** , after **9 days** from ovulation , and becomes a fibrous body called ***corpus albicans*** . Degeneration of corpus luteum leads to **decrease progesterone** level in the blood .
  - **If fertilization occurs** the corpus luteum changes to ***corpus luteum of pregnancy*** (which is maintained till the **4th month** of pregnancy by the human ***chorionic gonadotropin hormone*** secreted from the embryo). After that, the formed **placenta** will secrete progesterone till labor.

Uterine (Menstrual) Cycle

- These are ***periodic changes*** which occur in the ***endometrium*** (mucous membrane of the uterus) every lunar month (28 days) during the ***fertile period*** of the ***non pregnant*** female.
- It is affected by the ovarian cycle and the ovarian hormones.
- ***It passes through three phases :***

I. Menstrual phase : (3-5 days)

- It corresponds to the **beginning** of the **pre-ovulatory phase** of the ovarian cycle.
- **Cause** :It is mainly due to **decreased** progesterone level & estrogen level to less extent (at the end of the previous luteal phase of ovarian cycle) , leading to **constriction of spiral arteries** supplying the superficial part of endometrium .

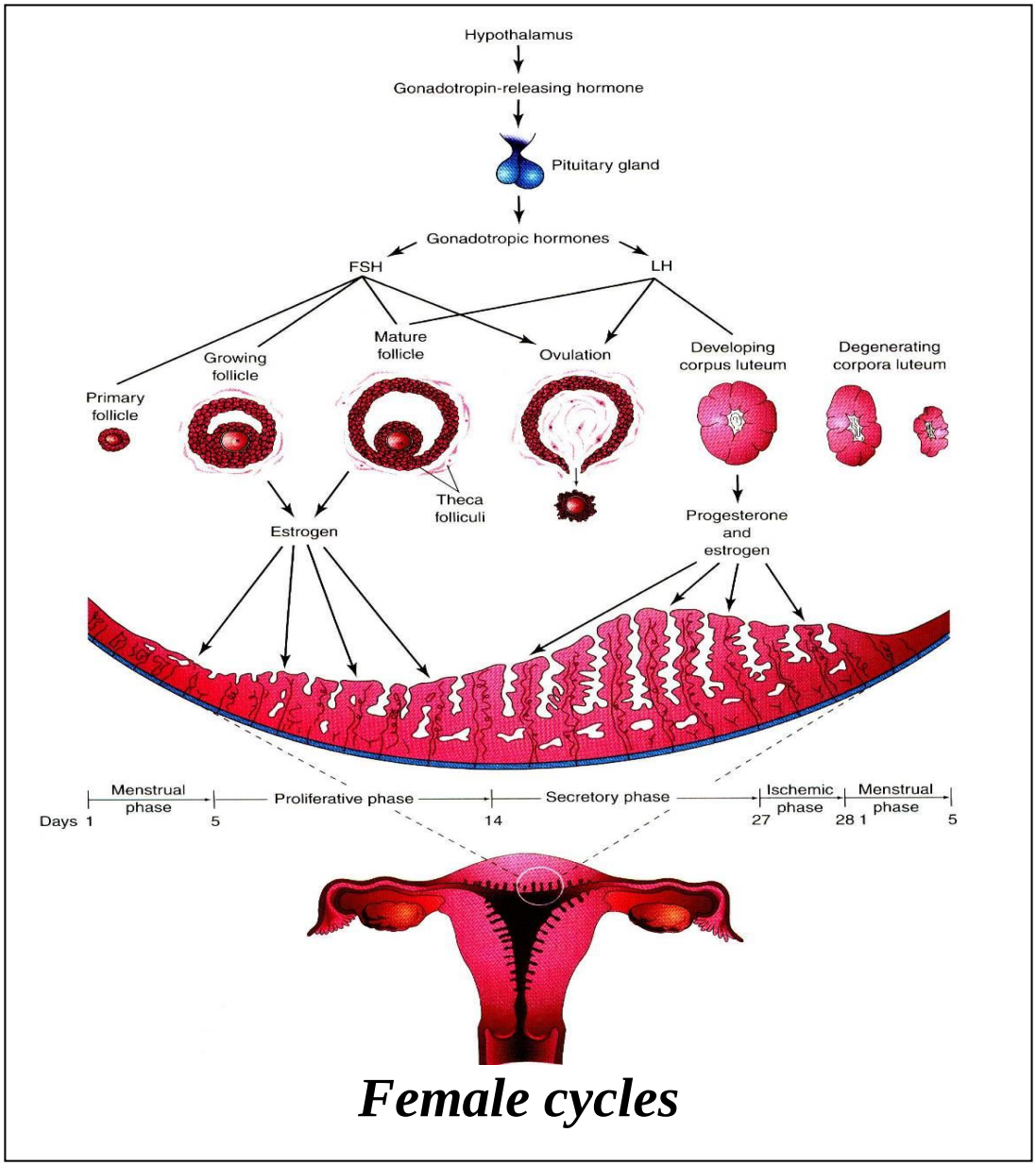
- The superficial part of **endometrium** degenerates and expelled with **mucous** & **50-60 cc of unclotted blood** (due to presence of proteolytic enzymes) from the ulcerated uterus .
- At the end of this phase the endometrium is reduced to **1/5 to 1/10** its maximal thickness .
- The **basal layer** of the endometrium is not affected.

II. Proliferative (estrogenic or postmenstrual) phase : (10 days)

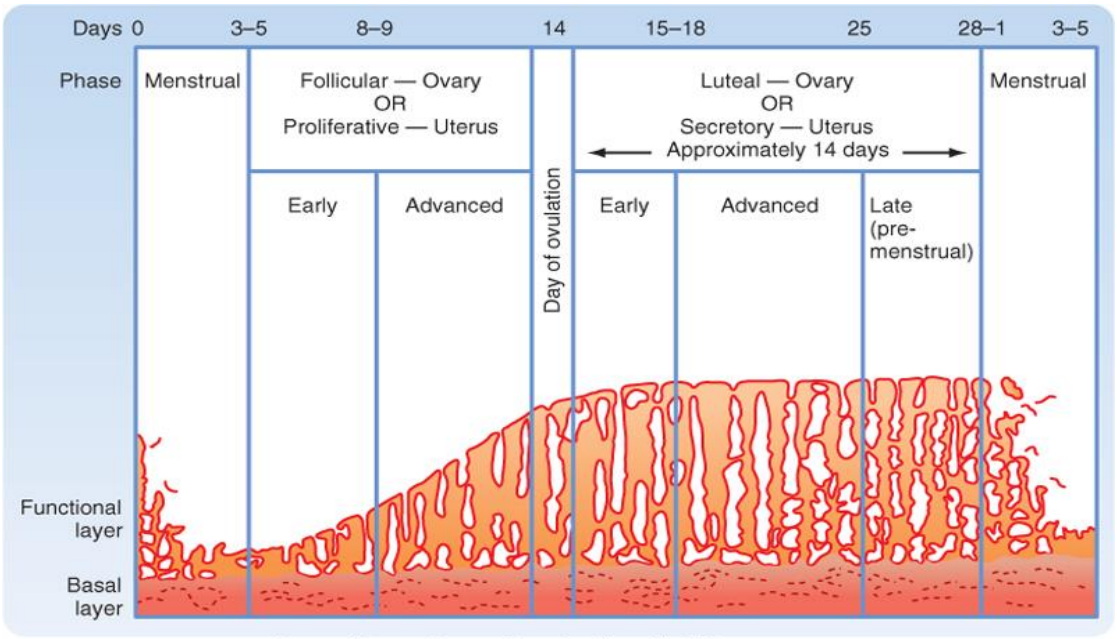
- It corresponds to the **last 10 days** of the **pre-ovulatory** phase of the ovarian cycle.
- It is under the effect of **estrogen** hormone secreted by developing follicle.
- The **endometrium** gradually thickens; its blood supply increases and its mucous glands enlarge.

III. Secretory (premenstrual or progestational) phase : (last 14 days)

- It corresponds to the **postovulatory** phase of the ovarian cycle.
- It is under the effect of **progesterone** hormone mainly (from corpus luteum) & estrogen to less extent .
- The thickness of the **endometrium** is markedly increased. The **arteries** become spiral and the **mucous glands** become long , tortuous & distended with secretion .
- These changes in the endometrium can be regarded as the **preparation of the endometrium** for the reception and nourishment of the suspected blastocyst if fertilization occur .



Female cycles



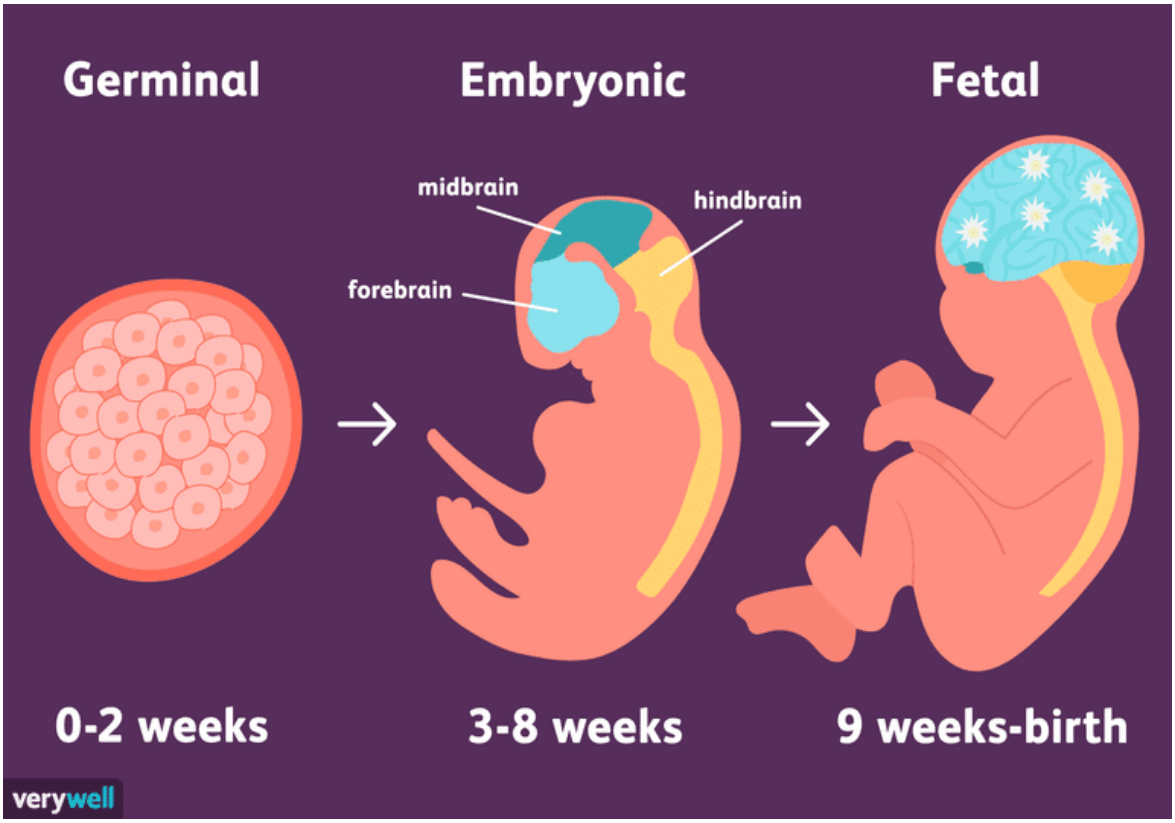
The Intra-Uterine Life

★ It is the time between **fertilization** and **birth** of a new individual .

★ It is about **10 lunar months** (280 days)

★ The intra-uterine life is **divided into** 3 periods :

	1-Germinal period	**2-Embryonic period**	**3-Fetal period**
Duration	- **1st 2 weeks** .	- **3-8 weeks .**	-From beginning of **9th. week** to **birth .**
Characters	-Formation of 2 **germ layers** (ectoderm & endoderm)	- Formation of mesoderm -**Differentiation** of 3 germ layers to organs & systems (**organogenesis**) .	- **Growth** of organs & systems . - Appearance of **external features** of the fetus .
Congenital anomalies	-**More** liable to occur during the germinal and embryonic periods .		-**Less** liable to occur .



First Week of Development

★ The 1st week of pregnancy is characterized by 4 processes :

1- **Fertilization .**
2- **Cleavage .**
3- **Migration .**
4- **Implantation .**

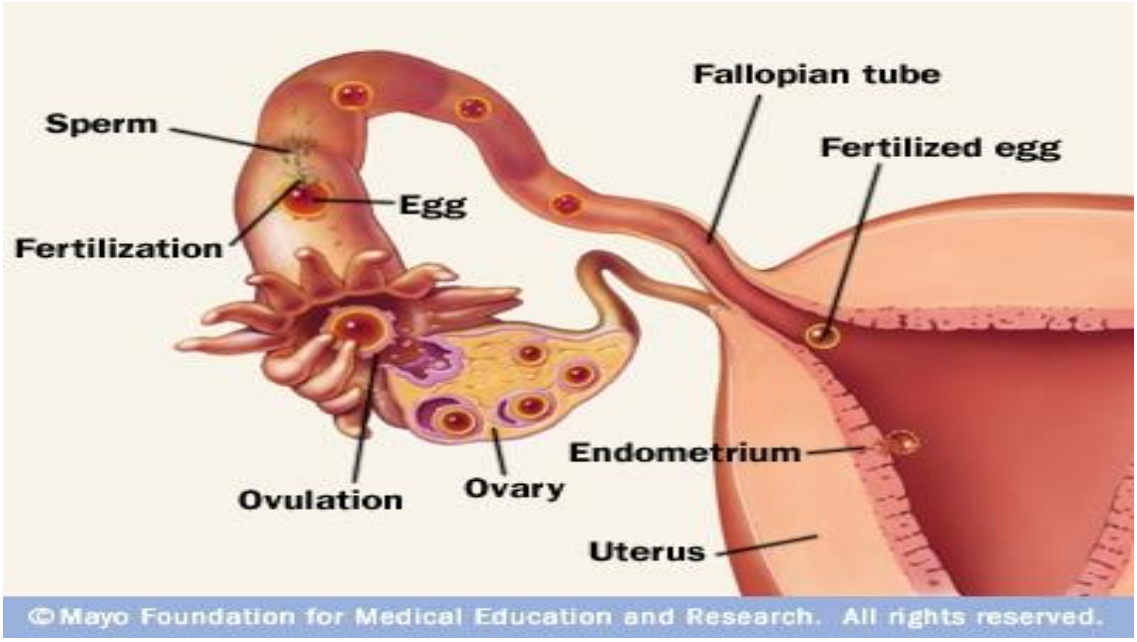
Fertilization

★ Fertilization is the **union of the sperm** and the mature **ovum** to form the zygote.

★ **Site**: in the lateral 1/3 of the uterine tube.

★ **200 -300** millions sperms , are deposited into the vagina , swim through the cervix then muscular contraction of the uterus direct them to the uterine tube . Only **200-500** sperms can reach the site of fertilization .

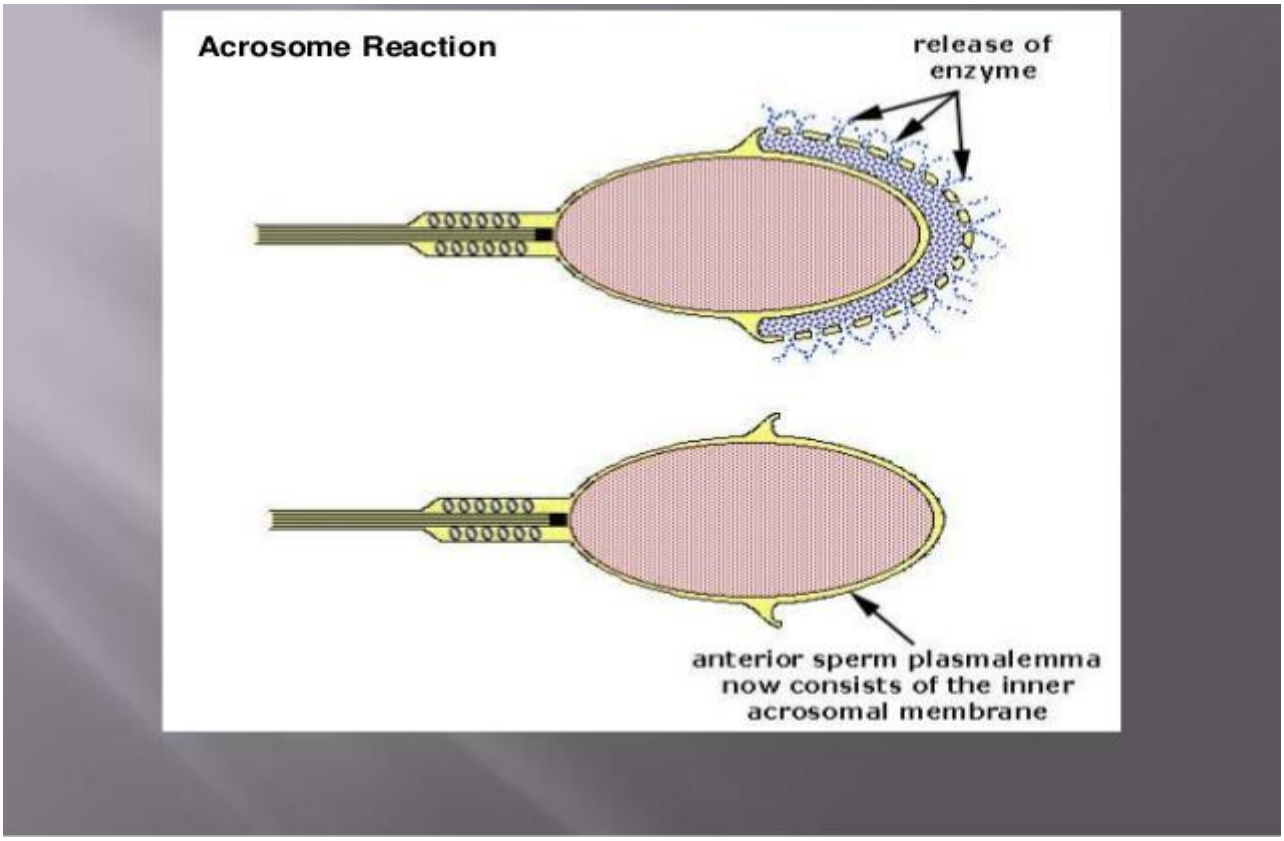
★ Only **one** sperm can fertilize the ovum and called the **fertilizing sperm** . The **other sperms help** the fertilizing sperm by their enzymes to **detach** the cells of **corona radiata** and to **penetrate the zona pellucida**.



★ **Mechanism**:

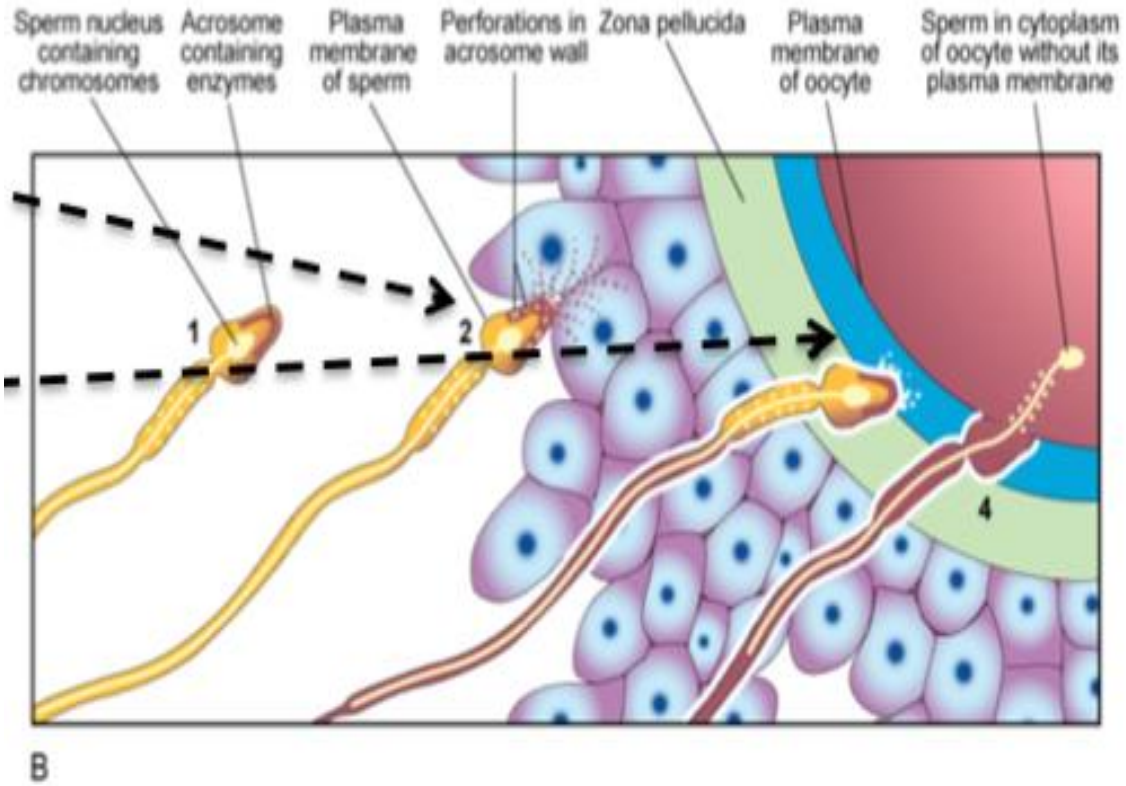
1- Capacitation and Hyperactivation of the sperms: (7 hours)

- Freshly ejaculated human **sperm** are not capable of fertilization.
- A period of time in the female reproductive tract is necessary before **sperm** can fertilize secondary oocyte. Thus, during their journey, **sperm** gain the ability to fertilize an egg (a process called **sperm capacitation**).
- It is the process of **clearing of the acrosomal cap** of the sperms from the glycoprotein coat and the plasma membrane.
- The sperms becomes **hyperactive** , their tail move frequently and their heads moves laterally .



2-Penetration of the zona pellucida:

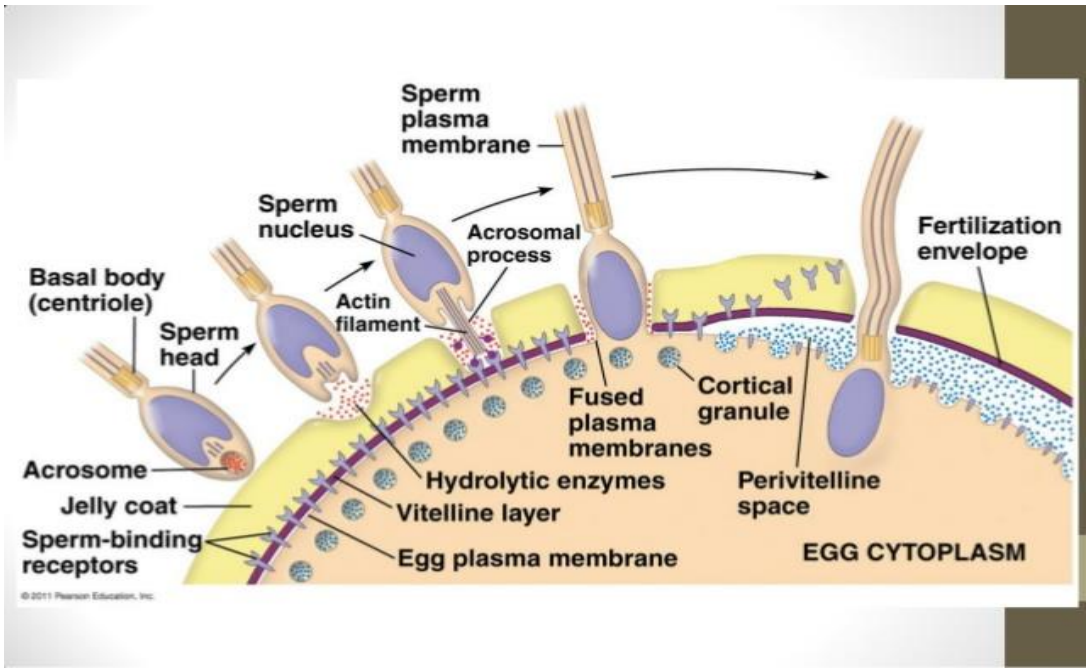
a. The capacitated sperms **pass through corona** radiate to reach and **bind to the zona** pellucida at specific **binding sites**.
b. They start secreting **acrozomal enzymes** that allow only **one** sperm to **penetrate** the zona pellucida (***acrosomal reaction***).
c. The head of that sperm **reaches the plasma membrane** of the secondary oocyte.
d. The plasma membrane of the head **fuses** with that of the 2nd oocyte.
e. The **contents of the sperm** (head, neck, middle piece and tail) **enter** the cytoplasm of the secondary oocyte, **leaving its cell membrane outside**.



3. Cortical and zona reactions:

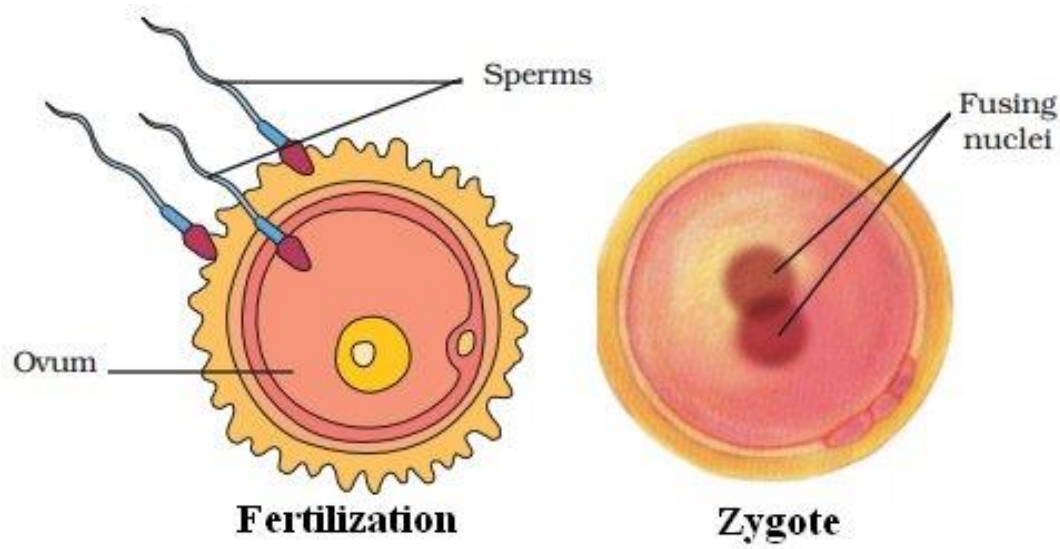
- The secondary oocyte releases enzymes from the cortical granules lining its plasma membrane. These enzymes cause:

- Changing of the **sperm binding sites** at the **zona pellucida** preventing entry of more sperms.
- Changing the **plasma membrane** to become **impermeable** to other sperms.



4. Completion of the 2nd meiosis: The 2nd oocyte changes to a mature ovum.

5. Fusion of the and nuclei to form the nucleus of the zygote.



★ **Results of Fertilization :**

- Formation of the **zygote**.
- Restoration of the **diploid** number of chromosomes.
- Determination of the **sex** of the new individual (by union of X chromosome of the ovum with X or Y chromosome of the sperm).

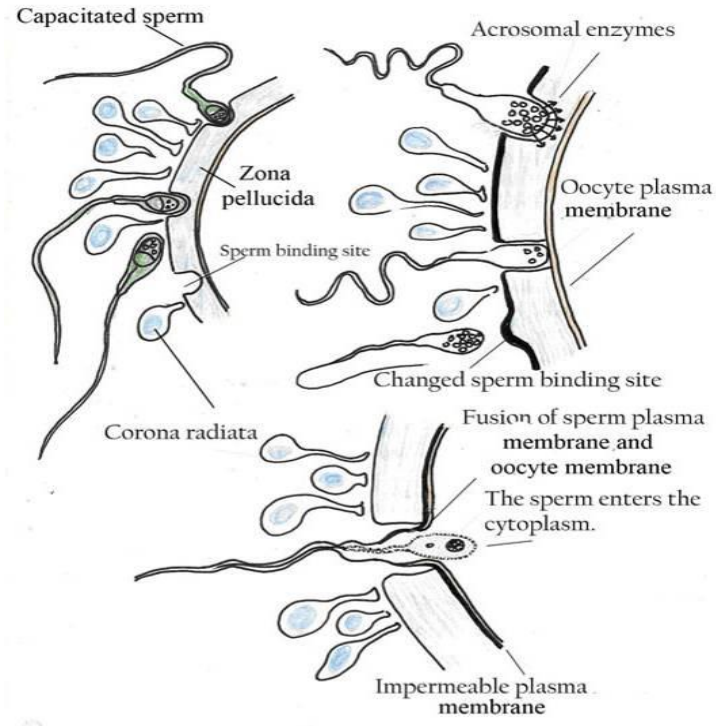
★ **Artificial Fertilization:**

1. In vitro fertilization :

- Done by stimulation of follicular growth by **gonadotropins**.
- Withdrawal of the **oocyte** just before ovulation.
- Addition of the **sperms** to the **ovum** in a special **culture** medium.
- **Implantation** of the fertilized egg into the uterus as it reaches the **8 cell stage**.

2. Intracytoplasmic sperm injection :

- Injection of a single sperm into the cytoplasm of the oocyte to cause fertilization



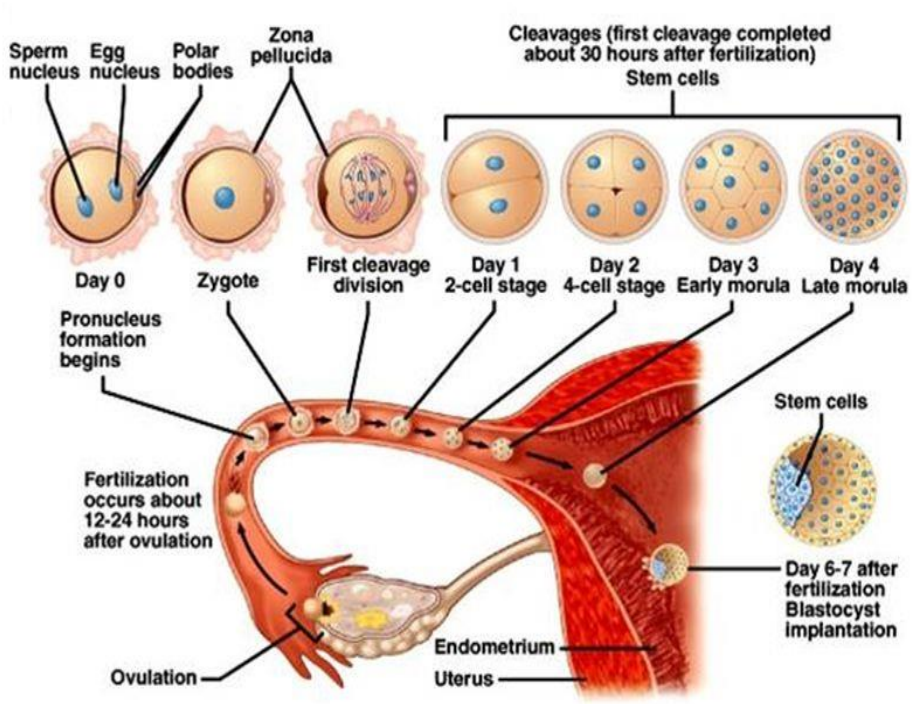
Sammary of the process of fertilization

★ **N.B : Please see this excellent video .**

https://www.youtube.com/watch?v=7G2rL5Cutd4

MIGRATION

- The ***transport*** of the zygote from the lateral 1/3 of the uterine tube to the ***uterine cavity*** takes place by 3 mechanisms:
  1. Muscular ***peristalsis*** of the uterine tube.
  2. The motion of the ***cilia*** of mucosa linning the tube.
  3. ***Secretion*** of mm provide a fluid vehicle & nourishment for the dividing zygote .



- Cleavage occurs as the zygote passes along the uterine tube toward the uterus.
- During cleavage, zygote lies within the thick zona pellucida.

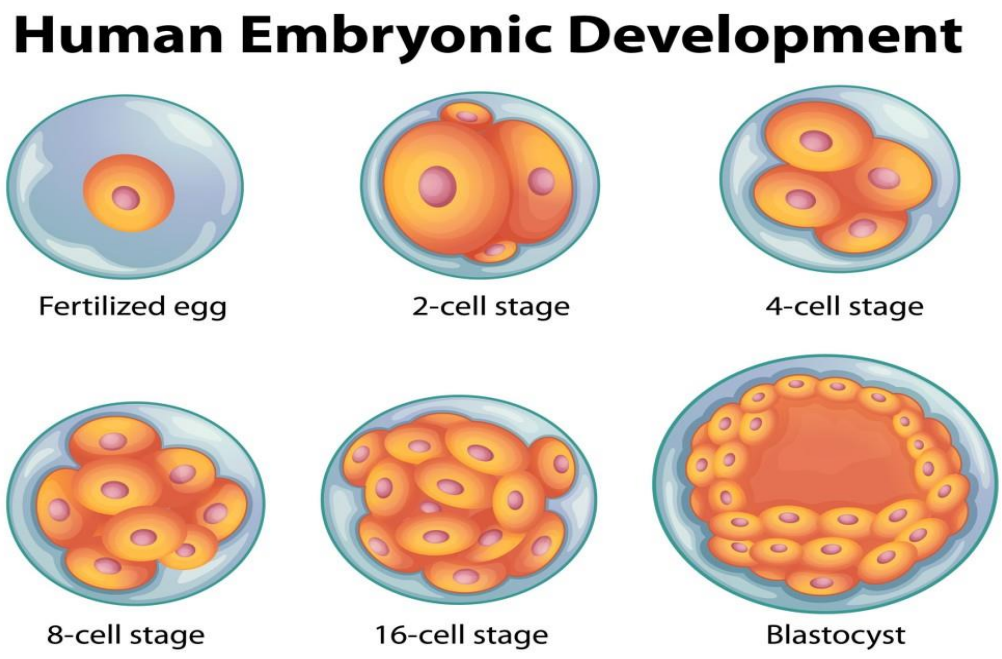
CLEAVAGE

★ It is a **series of mitotic** divisions occurring in the **zygote** as it passes in the **uterine tube** .

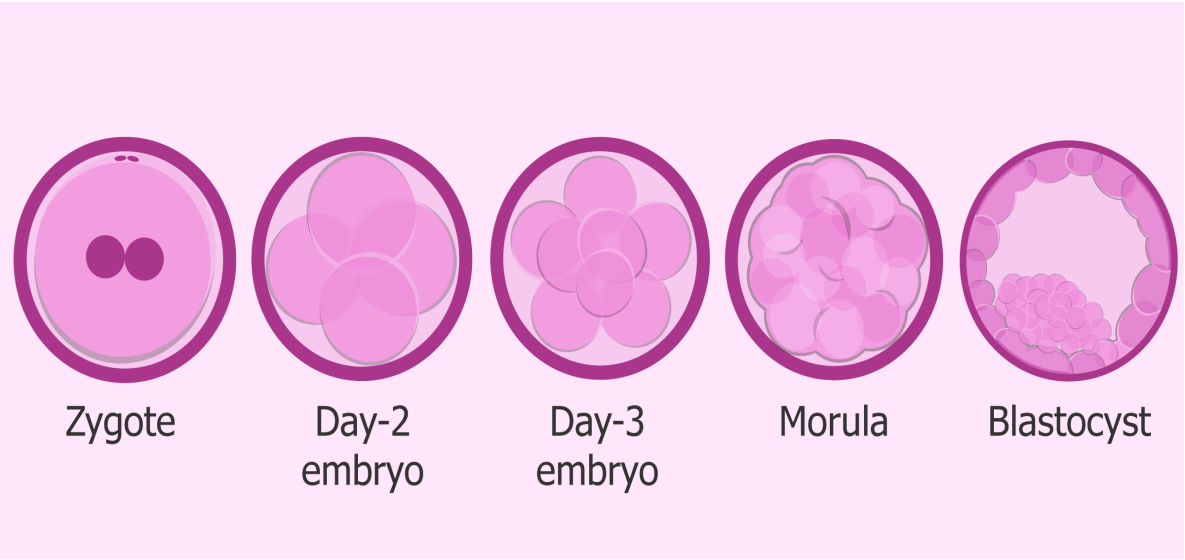
★ Each cell resulting from cleavage is called **blastomere**

★ ***BY mitosis the zygote gives*** **:-**

- **Two cell stage** : occur about 24 hours after fertilization .
- **Four cell stage** : occur about 48 hours after fertilization.
- **16 cell stage** :(called **morula**) occur about 3 days after fertilization.
  - The total size of the morula has **not significantly increased** within the zona pellucida , since at each cell division the blastomeres were reduced in size (i.e no new protoplasm has been formed) .
  - The morula reaches the **uterine cavity** at the **4th day** after fertilization.
  - The **zona pellucida disappears** at the end of the **5th day** after fertilization.



- **Formation of the blastocyst:**
  - As the morula enters the uterine cavity, **uterine fluid** begins to penetrate through the zona pellucida into the intercellular spaces .
  - Gradually, the intercellular spaces become coalesce , and finally, a single cavity called ***blastocele*** forms.
  - At this time, the morula becomes a **blastocyst** which has an inner cell mass , called the **embryoblast** (will form the embryo) and the outer cell mass (shell) , is called the **trophoblast** (will form the fetal membranes).
  - The pole of the blastocyst at the embryoblast is called the **embryonic pole** while the opposite pole is called the **abembryonic pole** .



★ **N.B : Please see these excellent videos .**

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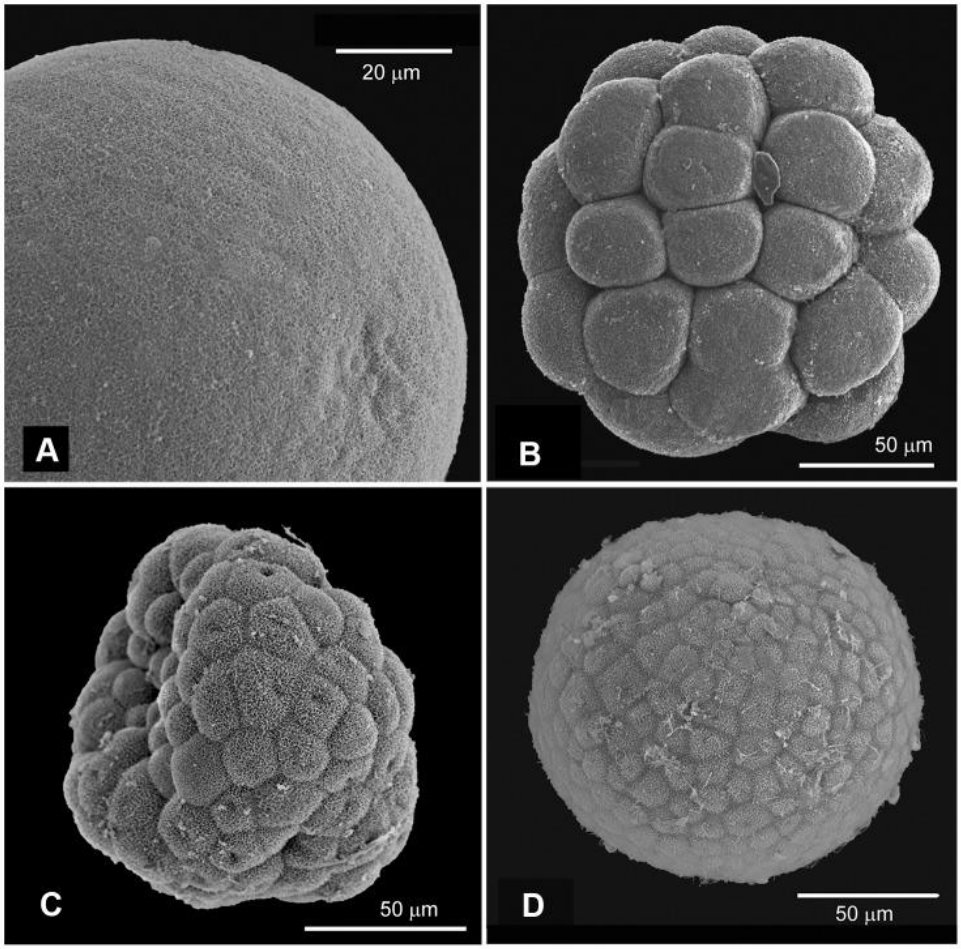
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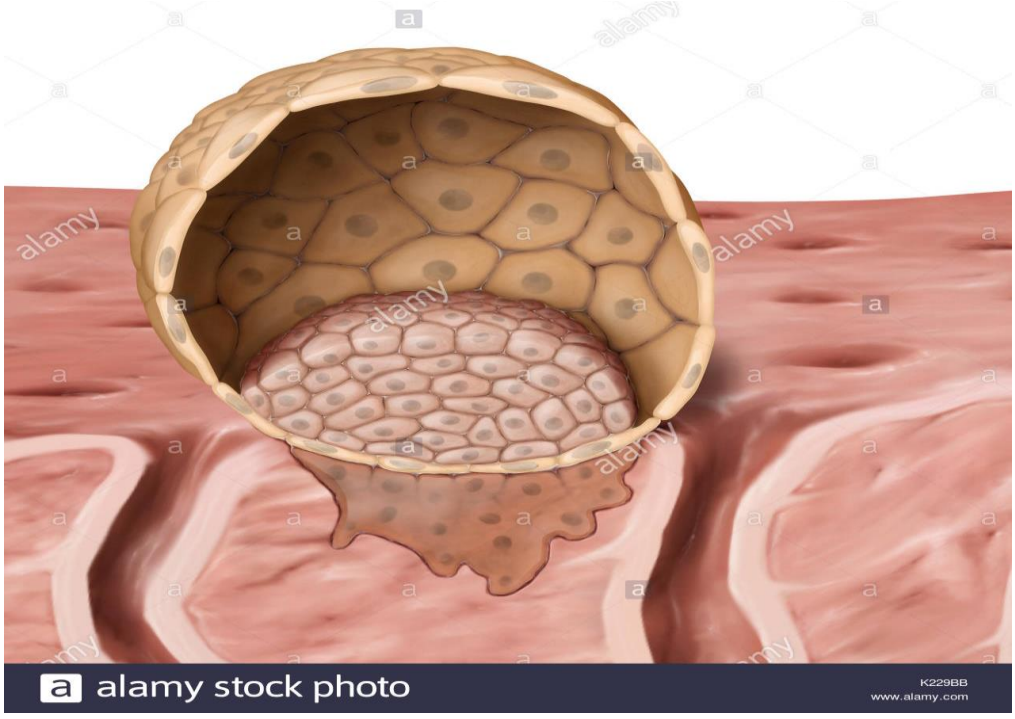
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Blastocyst

Implantation

★ **Definition:** It is the process of **penetration of** the superficial layer of the endometrium by the **blastocyst**.

★ **Time: starts** at the 6^{th} or 7^{th} day and is **completed** at the 11^{th} or 12^{th} day after fertilization.

★ **Site:** upper part of the posterior wall of the **body** of the uterus .

★ **Mechanism *:***

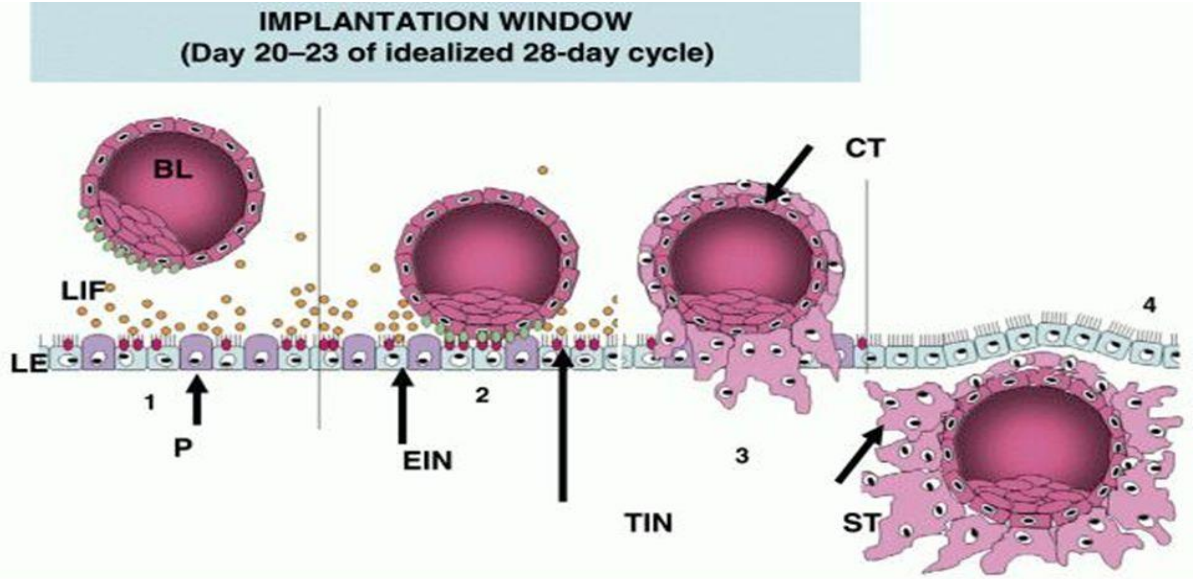
1-The blastocyst comes in contact and **attaches** to the endometrium by its **embryonic pole** .

2- Erosion of the mucosa , by **enzymes** secreted by the trophoblast at the embryonic pole of the blastocyst , **forming defect** in the endometrium .

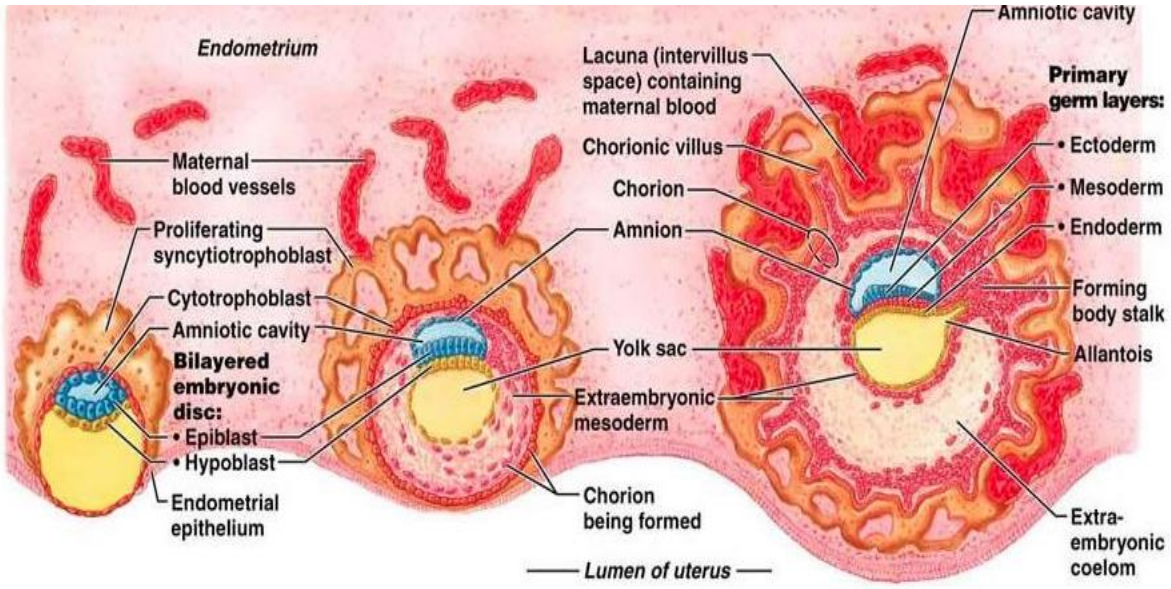
3- The blastocyst **enter** the endometrium , through the defect , by its **embryonic pole** .

4- **After complete embedding** of the blastocyst into the endometrium , the defect in the endometrium is **closed** first by **blood clot** and later by proliferation of surrounding surface **epithelium** .

★ **Implantation bleeding** is of clinical importance , as it may simulate menstrual bleeding which is expected about this time , may result in an erroneous calculation of the duration of pregnancy .



- **Implantation**
  - Blastocyst embeds itself into the uterine wall
  - Trophoblastic shell forms connection with maternal blood supply



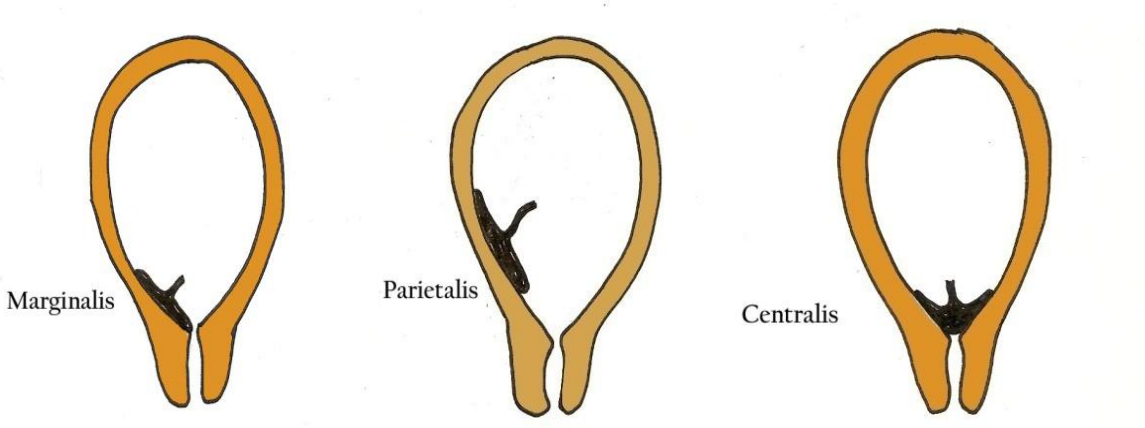
(a) 7½-day implanting blastocyst (b) 12-day implanted blastocyst (c) 16-day embryo

★ **ABNORMAL SITES OF IMPLANTATION :**

a. ***Intrauterine :*** resulting in **placenta previa**

- **Definition:** implantation occurs in the **lower segment** of uterus.
- **Types of placenta previa**:

- ***Placenta previa parietalis,*** the margin of the placenta does not reach the internal os of the uterus.
- ***Placenta previa marginalis,*** the margin of the placenta reaches the internal os.
- ***Placenta previa centralis,*** the center of the placenta overlies the internal os.

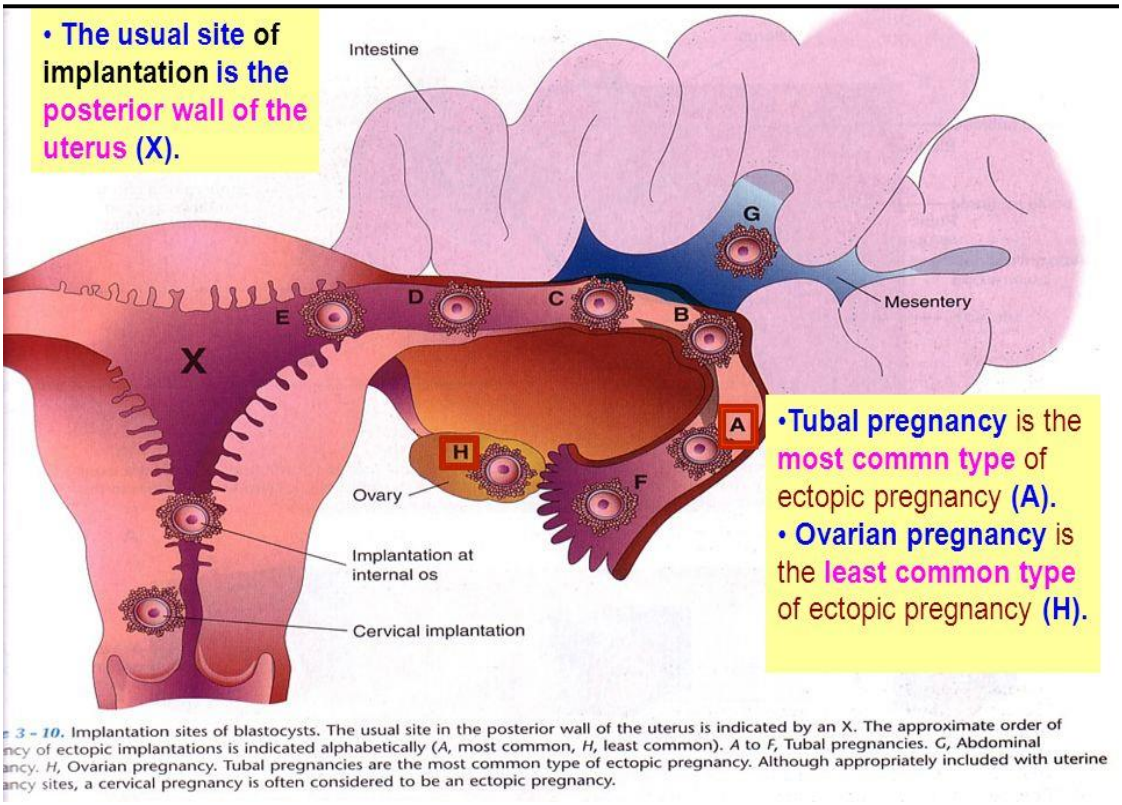


b. ***Extrauterine :*** resulting in **ectopic pregnancy*.***

- **Sites of ectopic pregnancy**

1. ***Tubal*** (in the uterine tube).This is the **commonest** site of ectopic pregnancy which usually rupture in the 2nd month leading to acute abdominal **pain** and internal **hemorrhage** . If this pain occurs on the right side , it will be miss diagnosed as **acute appendicitis** .
2. ***Ovarian*** (in the ovary).
3. ***Abdominal*** (in the peritoneum of the mother).

Ectopic Implantation (Pregnancy)



3 - 10. Implantation sites of blastocysts. The usual site in the posterior wall of the uterus is indicated by an X. The approximate order of ncy of ectopic implantations is indicated alphabetically (*A*, most common, *H*, least common). *A* to *F*, Tubal pregnancies. *G*, Abdominal ancy. *H*, Ovarian pregnancy. Tubal pregnancies are the most common type of ectopic pregnancy. Although appropriately included with uterine ancy sites, a cervical pregnancy is often considered to be an ectopic pregnancy.

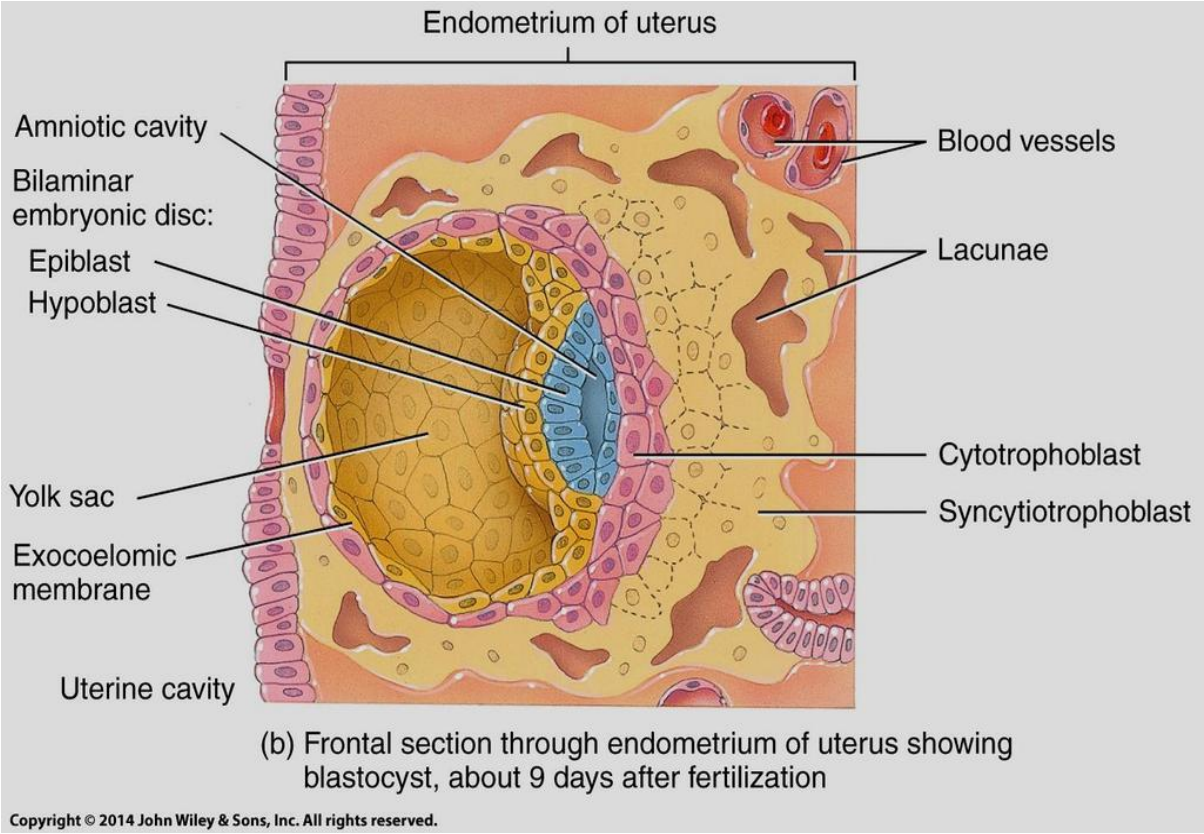
Second Week of Development

★ The following changes occur during 2nd week of pregnancy :

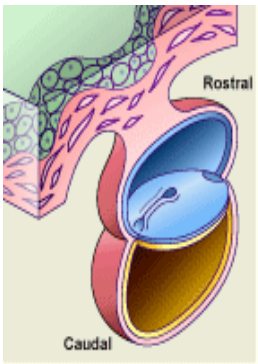
1- **Completion of implantation** by 11th or 12th day

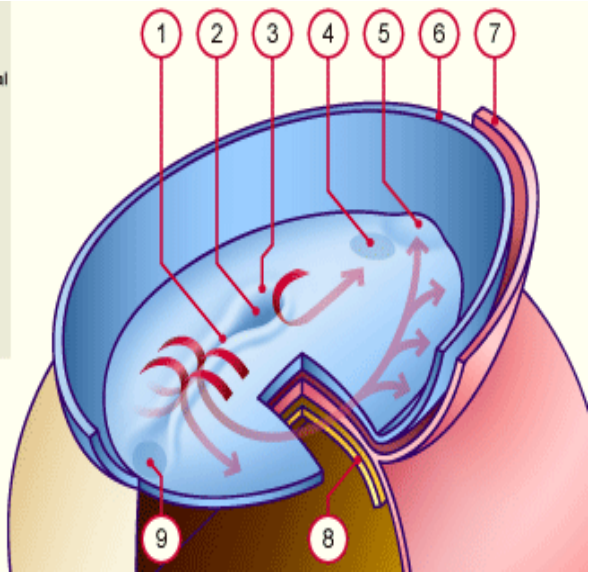
2- Changes in the embryoblast :

- Formation of the **bilaminar germ disc** (***Epiblast*** adjacent to the trophoblast and ***Hypoblast*** adjacent to the blastocele).
- The germ disc is **rounded or oval** in shape .



1.Primitive groove
2.Primitive pit
3.Primitive node
4.Oropharyngeal membrane
5.Cardiogenic plate
6.Sectional edge of amniotic membrane
7.Mesoderm
8.Endoderm
9.Future cloacal membrane
1+2+3 = primitive streak

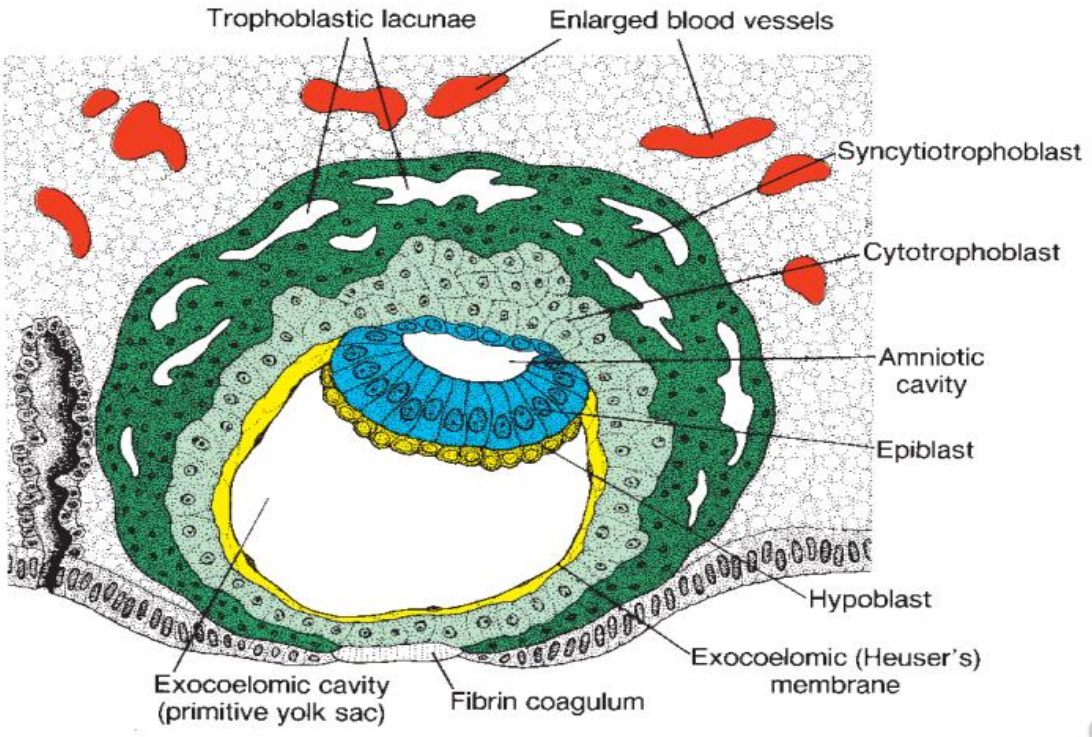




3- Changes in the trophoblast :

- During 2nd. week ,the trophoblast shows **rapid rate of development** as compared to the slow rate of development of the bilaminar germ disc
- The trophoblast is **differentiate** into an outer ***syncytiotrophoblast*** and an inner ***cytotrophoblast.***

- ***Syncytiotrophoblast:***
  - It is formed of a **multinucleated** zone **without** distinct cell **boundaries**.
  - **Small spaces** appear & coalesce (at the 9th day) in the syncytiotrophoblast , at the **embryonic pole** first then spread all over the syncytiotrophoblast , to form **trophoblastic lacunae** (**lacunar stage**).
  - At the 11th & 12th days, the syncytiotrophoblast **erodes the maternal sinusoids** and its lacunae are filled with maternal blood & uterine secretions which begins to flow through the trophoblastic lacunae establishing the **utero-placental circulation** which allow nourishment of the germ disc & change of gases & metabolites.
  - At the end of 2nd week , **1ry. Chrionic villi** appears at the embryonic pole .
- ***Cytotrophoblast:*** Its cells maintain their cell walls. They divide externally to produce more syncytiotrophoblast.



4 – Formation of 2 cavities :

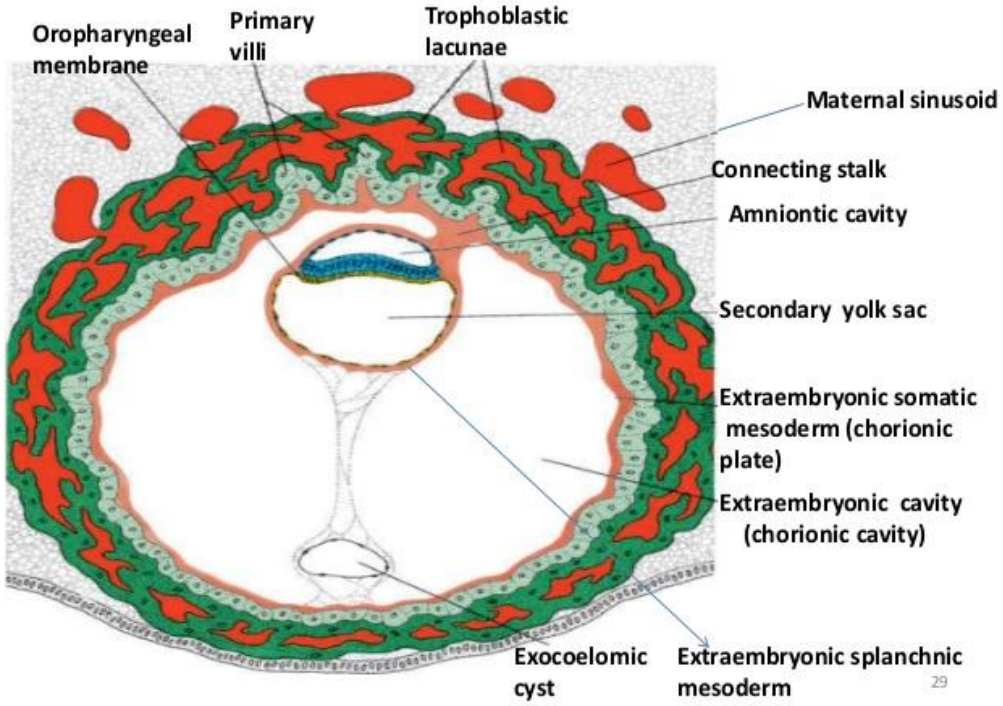
a) ***Amniotic cavity*** : (8th day)

- It is a **space appears between** the epiblast and the cytotrophoblast
- The epiblast cells form a layer of flat cells called **amnioblasts** which form the **roof** of the amniotic cavity while its **floor** is formed by the epiblast .

b) ***Primary yolk sac*** : (9th day)

- The **hypoblast cells** form a layer of flat cells to form a membrane , which line the blastocele , called **Hauser's membrane**.
- The **space between** the hypoblast and the Hauser's membrane

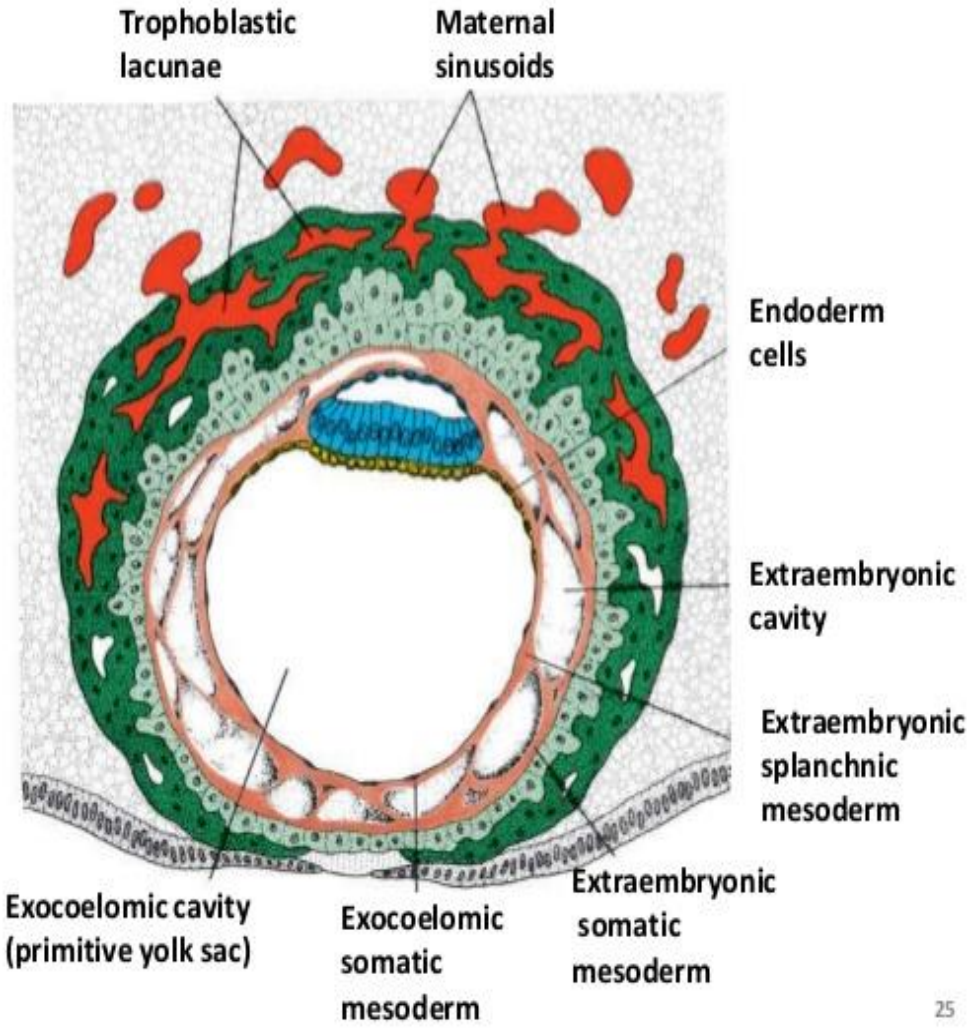
is called the **1ry yolk sac** , which replaces the blastocele , with its **roof** is the hypoblast and the remaining part of its **wall** is formed of Hauser's membrane .



- The hypoblast produces additional **cells that migrate inside** the Heuser's membrane. These cells proliferate and gradually form a new cavity known as the **secondary yolk sac** (day 13).

5-Extraembryonic mesoderm:

- These are cells **derived from** the yolk sac cells appear and form very loose tissues **between** the **cytotrophoblast** externally and the the **yolk sac** internally.
- **Cavities appear** & coalesce , in the extra-embryonic mesoderm , forming a single large C shape cavity called the **extra-embryonic coelom** (or **chorionic cavity**).



- The extra-embryonic mesoderm is **divided** by the extra-embryonic coelom (chorionic cavity) into:
  a. ***Extraembryonic somatopleuric mesoderm*** which line the cytotrophoblast .
  b. ***Extraembryonic splanchnopleuric mesoderm*** which cover the yolk sac.
  c. ***Connecting stalk :*** (future umbilical cord) It is the extra-embryonic mesoderm **connecting** the roof of amniotic cavity with the over lying cytotrophoblas . It is found **dorsal to the amniotic cavity**.
- The cytotrophoblast +Syncytiotrophoblast + Extraembryonic somatopleuric mesoderm are called **Chorion .** The blastocyst is now called the ***Chorionic vesicle*** (at the 12th day).

★ **N.B : Please see these excellent videos .**

https://www.youtube.com/watch?v=bIdJOiXpp9g

https://www.youtube.com/watch?v=4XcBHuGwzNQ

Third Week of Development

★ The following changes occur during 3rd. week of pregnancy **:**

A) Changes in the embryonic disc :

I. Changes in shape : During 3rd. week the embryonic disc becomes **pear shape** because the cranial part grows at a higher rate than the caudal part .

II. Gastrulation : (15-20 day) It includes the followings :

1. Formation of the ***primitive streak*** (15 days)
2. ***Invagination***

3. Formation and beginning of differentiation of the ***intra-embryonic mesoderm .***

III. Formation of notochord .

IV. Neurulation (formation of neural tube) .

V. Beginning of folding of the embryonic disc (end of 3rd. week).

B) Changes in the trophoblast (chrion) :

- 3 types of chorionic villi (primary , secondary & tertiary) develop and cover the whole surface of chorionic vesicle .

★ Gastrulation :

- It is the process of transformation of the bilaminar embryonic disc to form a **trilaminar germ disc** as follows :

1. Formation of the primitive streak: (15 days)

- The **primitive streak** is formed in the median region of the embryonic disc near its caudal end due to migration of the cells of epiblast in the caudal part of embryonic disc to the middle line .
- It appears as a narrow groove called **primitive groove** with slightly bulging regions on either side.
- Its cephalic end forms a bulge called **primitive node** which has a central depression called **primitive pit** .

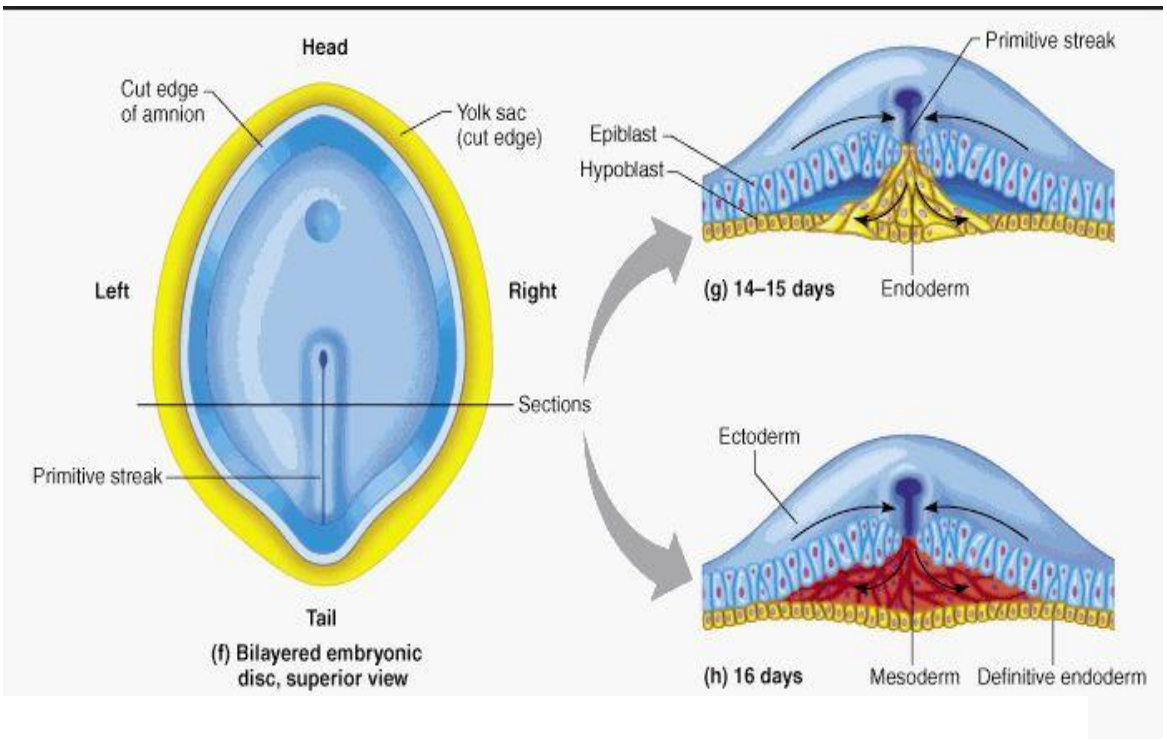
2. Invagination :

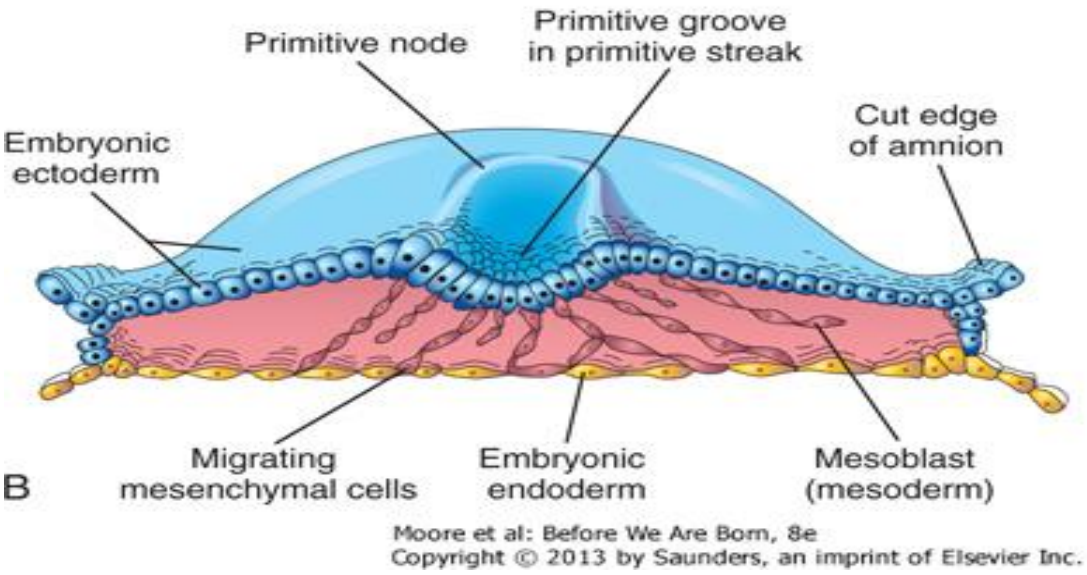
- The cells of epiblast migrates towards the primitive streak , detach from the epiblast and slip beneath it into the interior of the embryonic disc to :

  a) Invade and replaces the hypoblast to form the ***endoderm***.

b) The remaining part of the epiblast forms the ***ectoderm***; it is attached to the amnioblast at the **amnio-ectodermal junction**.

c) Some of the invaginated epiblast cells remain and migrate in all directions in between the ectoderm and the endoderm to form ***intra-embryonic mesoderm .***





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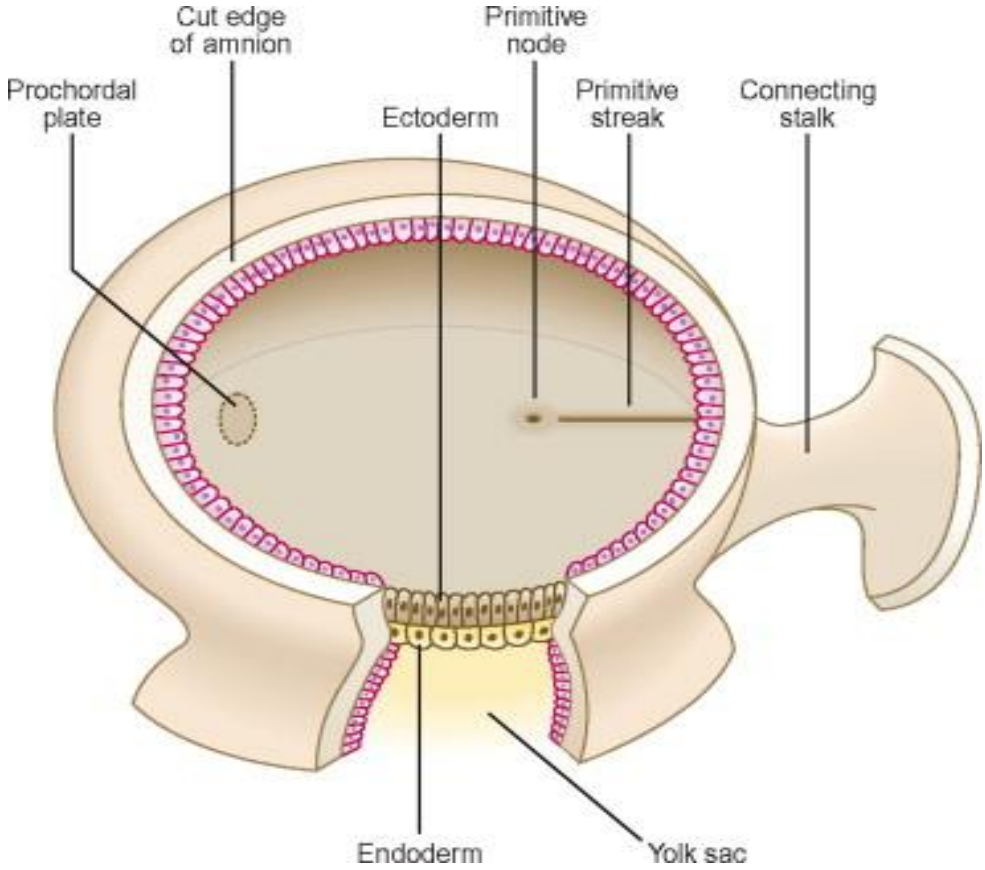
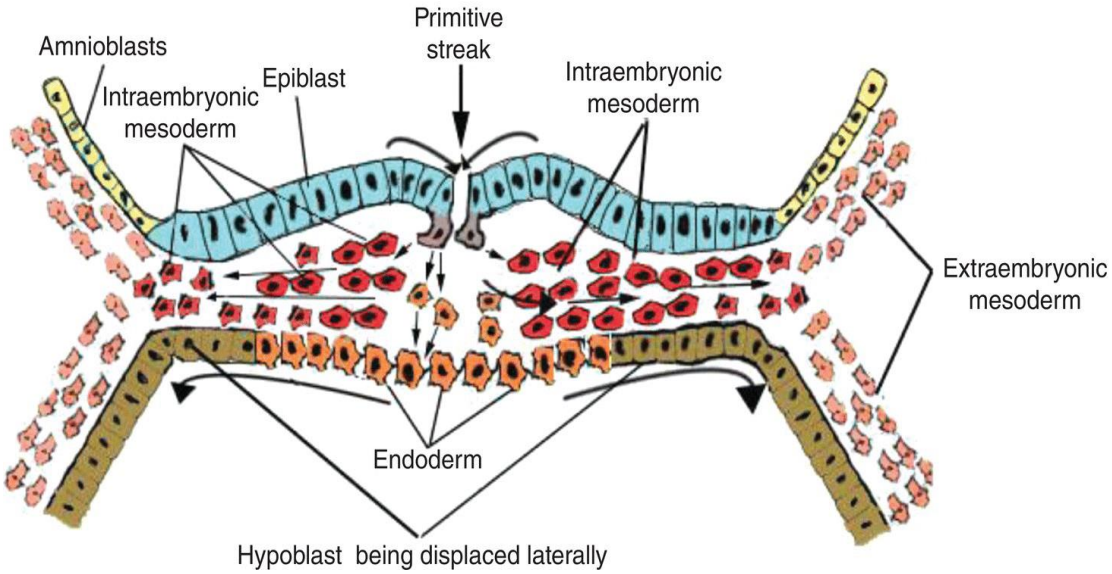
https://www.youtube.com/watch?v=3AOoikTEfeo



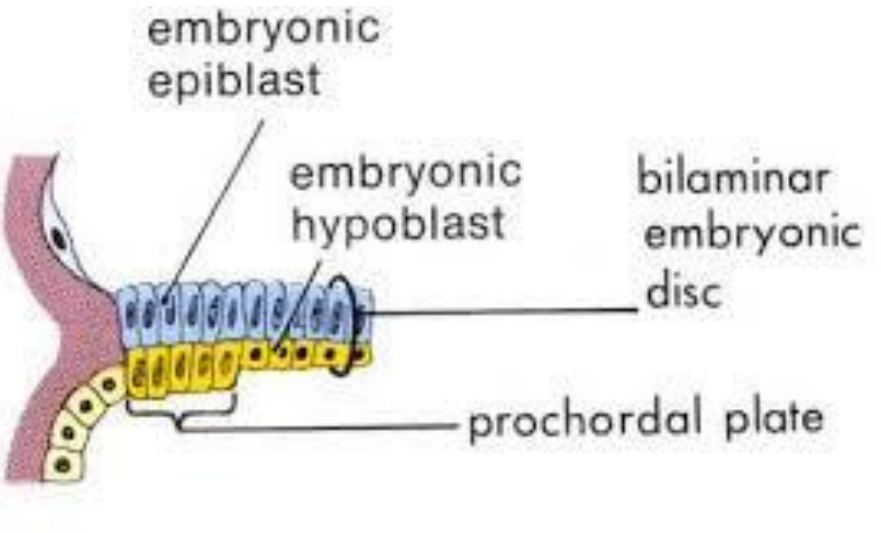


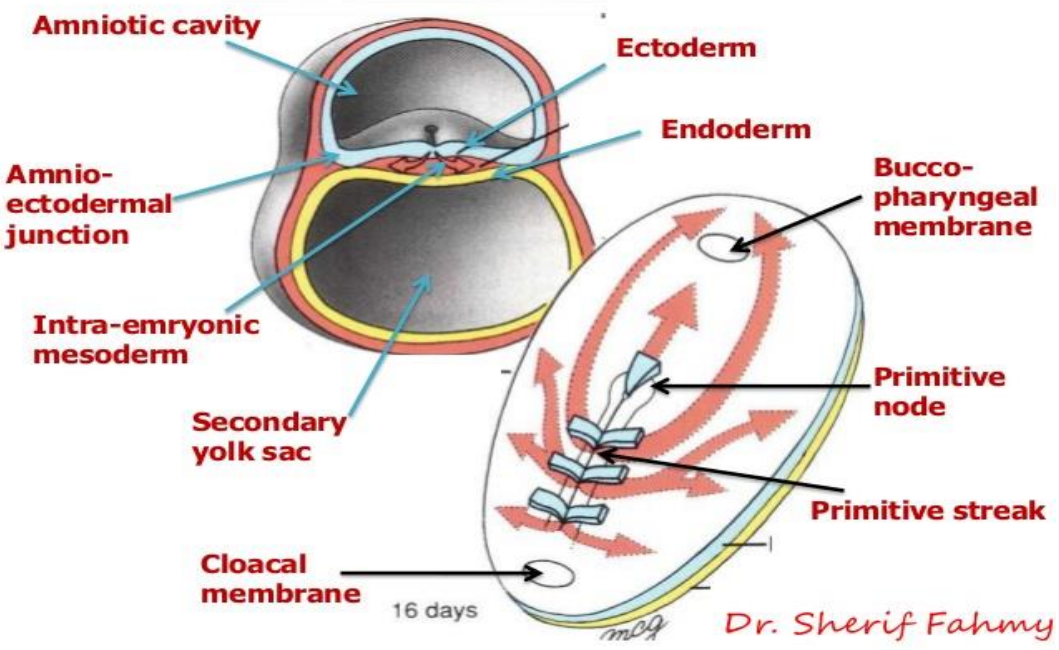
★ **N.B : Please see this excellent video .**

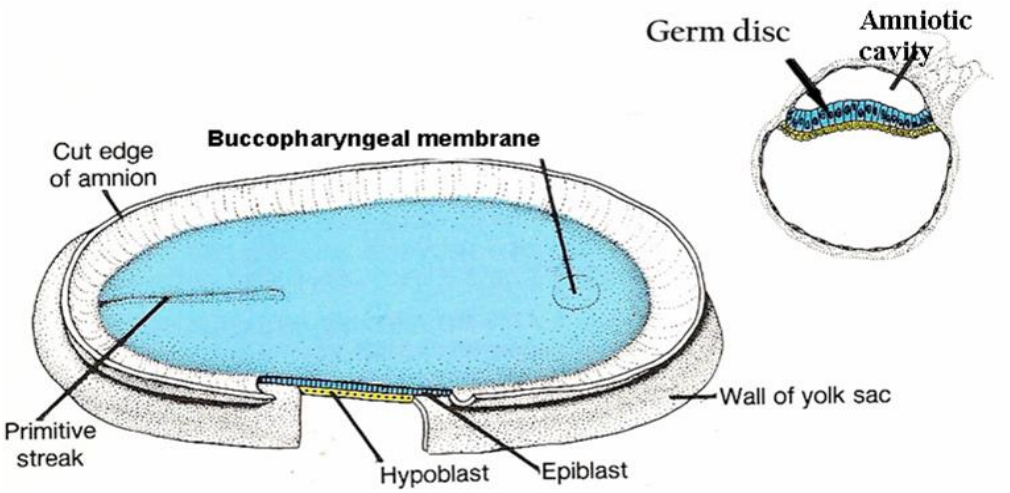
https://www.youtube.com/watch?v=3AOoikTEfeo

★ N.B : The embryonic disc remain bilaminar i.e ectoderm and endoderm with no intervening mesoderm in 3 sites :

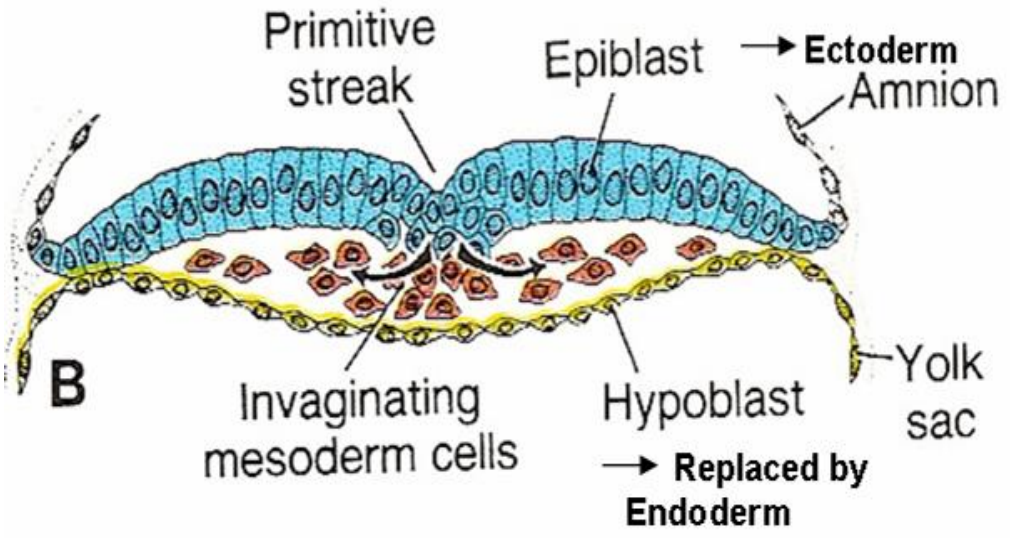
1) ***Prochordal plate*** : near the cephalic end of the embryonic disc . The prochordal plate later on will become the oro-pharyngeal membrane .
2) ***Cloacal membrane*** : immediately behind the caudal end of the primitive streak .
3) ***Midlian region*** of the embryonic disc between primitive node and Prochordal plate.



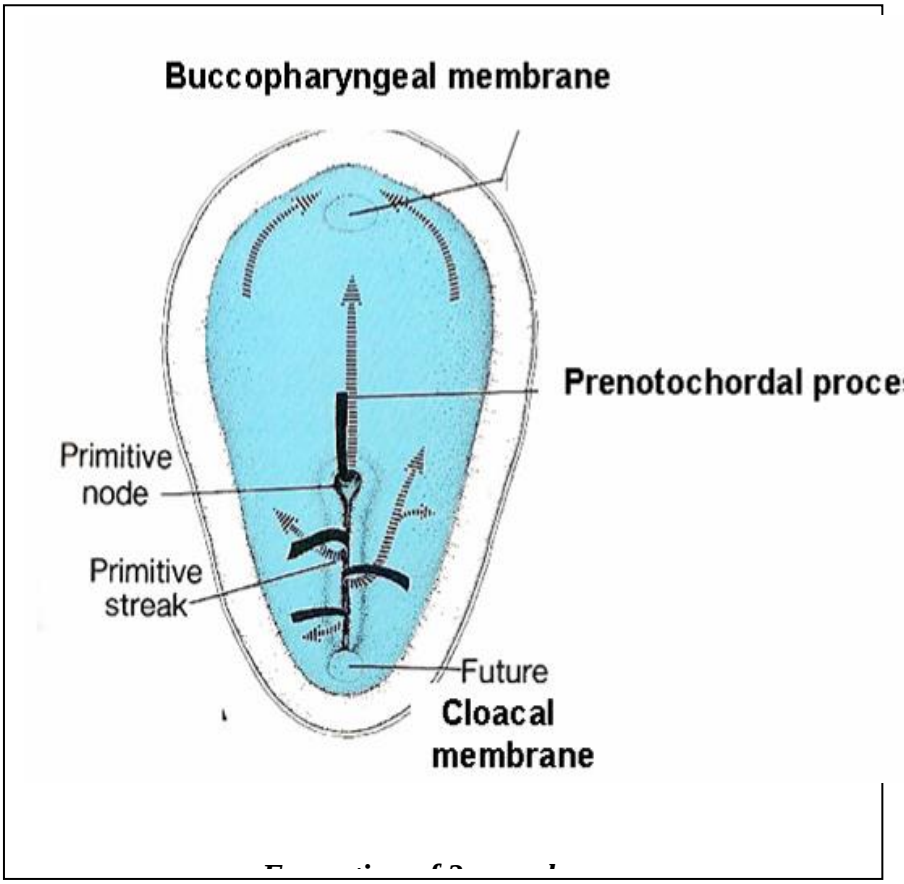


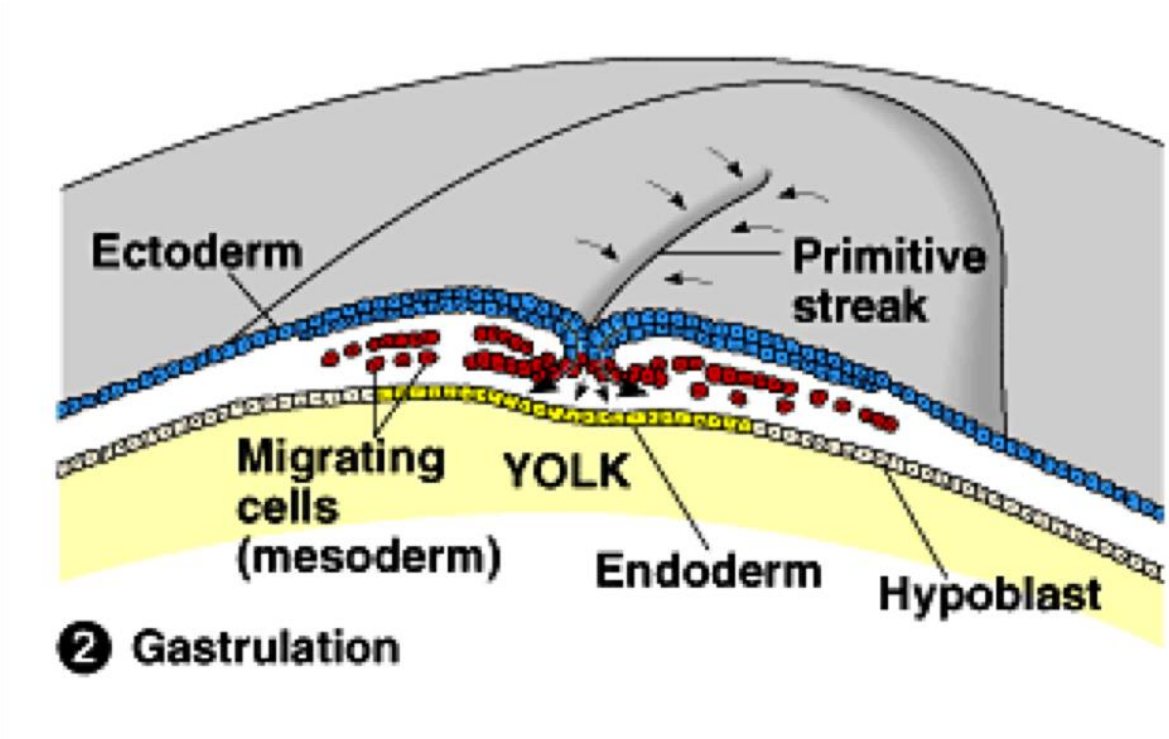


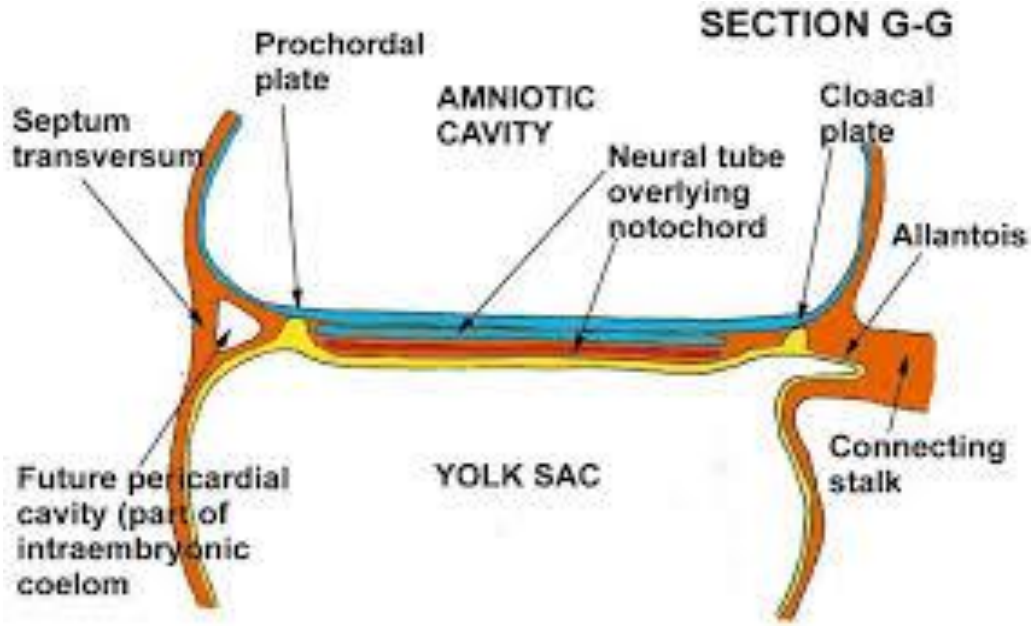
Formation of the primitive streak



Invagination


Buccopharyngeal membrane
Prenotochordal process
Primitive node
Primitive streak
Future Cloacal membrane


Ectoderm
Primitive streak
Migrating cells (mesoderm)
YOLK
Endoderm
Hypoblast
2 Gastrulation



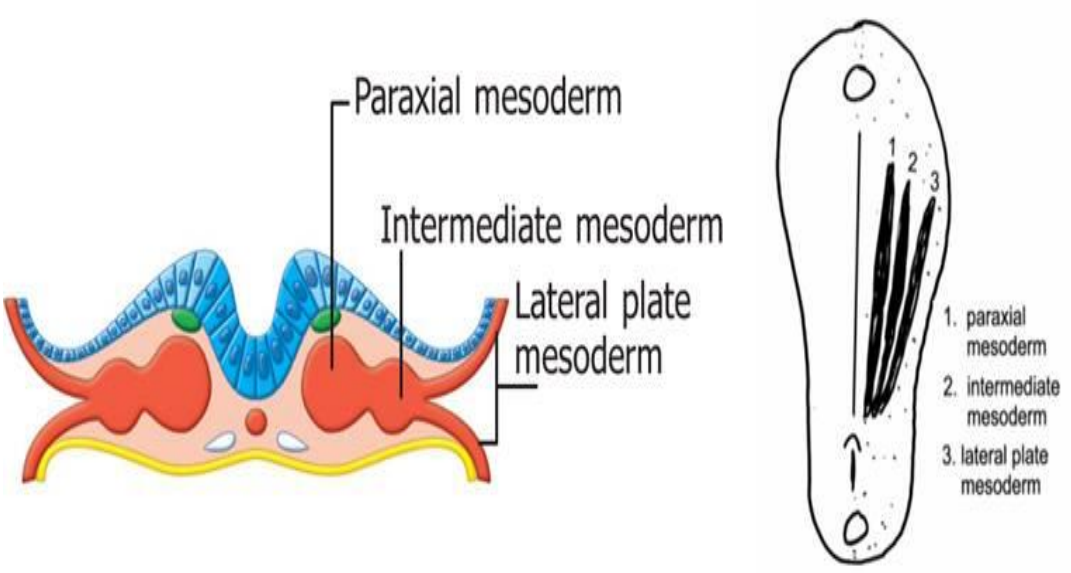
3. Formation & beginning of differentiation of the **intra-embryonic mesoderm :**

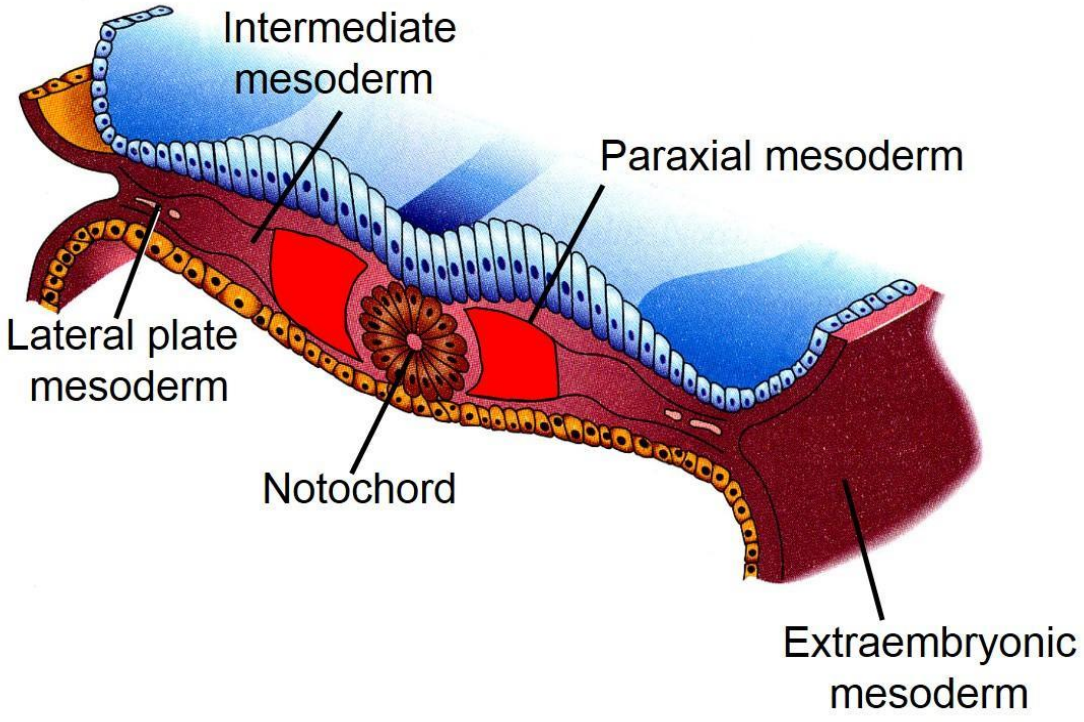
- It **migrates & spreads between** the ectoderm and endoderm **except** in three region:
  1. ***Prochordal plate*** cranially.
  2. ***Cloacal membrane*** caudally.
  3. ***Medlian region*** of the germ disc between primitive node and Prochordal plate .
- At the **17th day** , the intra-embryonic mesoderm is formed as a sheet of loose tissue between the ectoderm and endoderm on either side of the notochord (except in the previous 3 areas) .
- It establishes **contact** with the **extra-embryonic mesoderm** at the **margins** of the embryonic disc.
- As development proceeds , 2 longitudinal grooves appear in the ***intra-embryonic mesoderm*** on either sides of the notochord dividing it into 3 parts :

a) ***Paraxial mesoderm*** : on each sides and parallel to the notochord

b) ***Intermediate mesoderm*** lateral to the paraxial mesoderm.

c) ***Lateral plate mesoderm*** most laterally near the edge of the embryonic disc and it extends in the cephalic region of the disc cranial to the buccopharyngeal membrane.





★ **Formation of the notochord :**

- Formation of the **prenotochordal process** by invagination of cells in the ***primitive node*** . These cells grow cranially in the median plane between endoderm & ectoderm until they reach the buccopharyngeal membrane.
- A fine canal develops , starts from the ***primitive pit*** then extends cranially into the prenotochordal process , transforming it to **prenotochordal canal .**
- **Notochordal-endodermal fusion**: The ***floor*** of prenotochordal canal is adherent to the undelying endoderm .
- The floor of the prenotochordal tube ***degenerates*** together with the underlying endoderm , forming a ***Neurenteric canal*** that temporarily ***connects*** the yolk sac with the amniotic cavity.
- **Notochordal plate** is formed by fusion of the **roof** of the prenotochordal canal with the surrounding endoderm.
- **Definitive notochord** formed by ***folding*** of the notochordal ***plate*** along its longitudinal axis to form a solid cord of cells ***extending*** from the primitive pit to the buccopharyngeal membrane.
- . The ***endoderm*** on each side of the notochordal plate fuse together to ***resume its continuity***.
- **Significance of notochord** : it acts as **temporary axial skeleton** for the embryo being **replaced later** on by the vertebral column which is the permenant axial skeleton .

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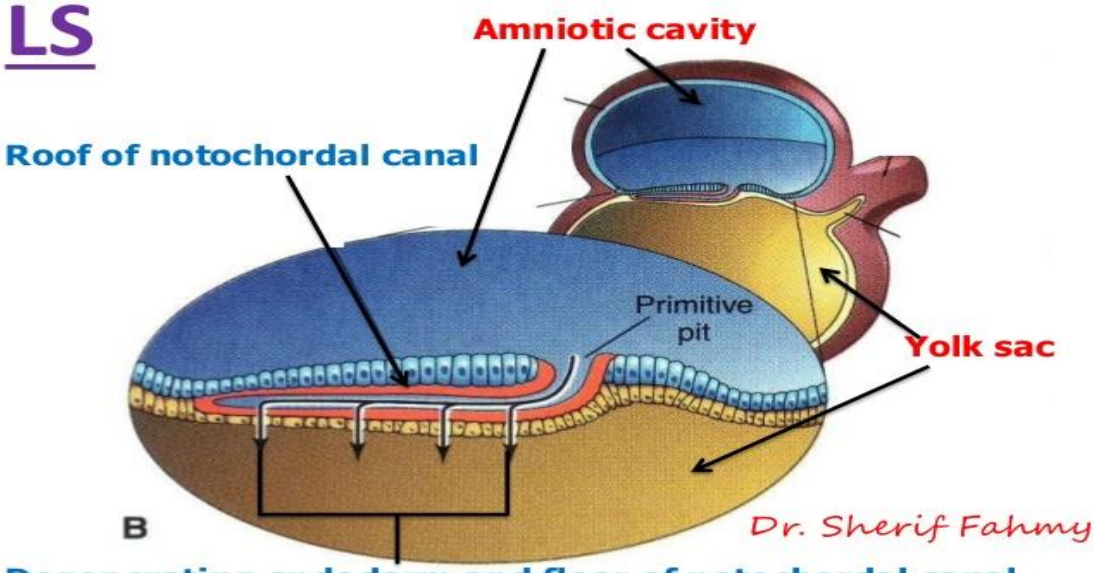
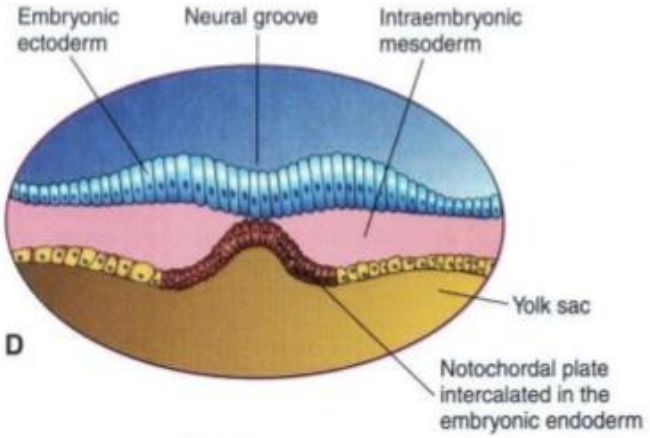
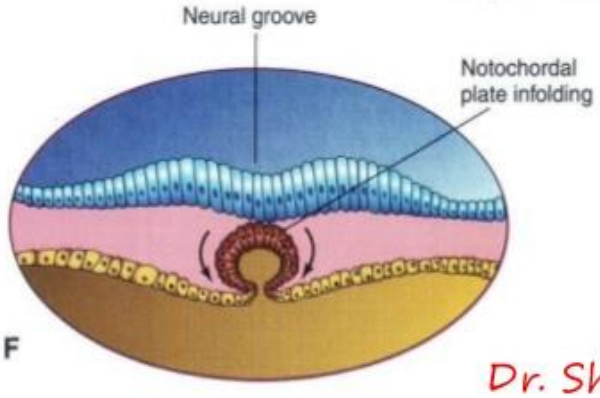


Dr. Sherif Fahmy

Degenerating endoderm and floor of notochordal canal





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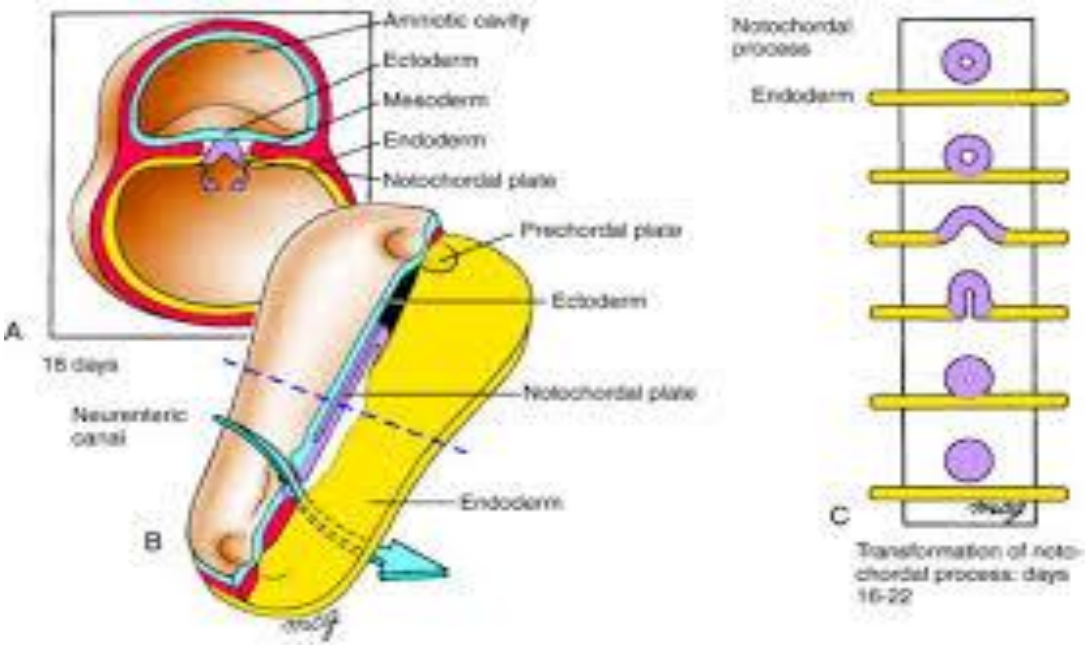
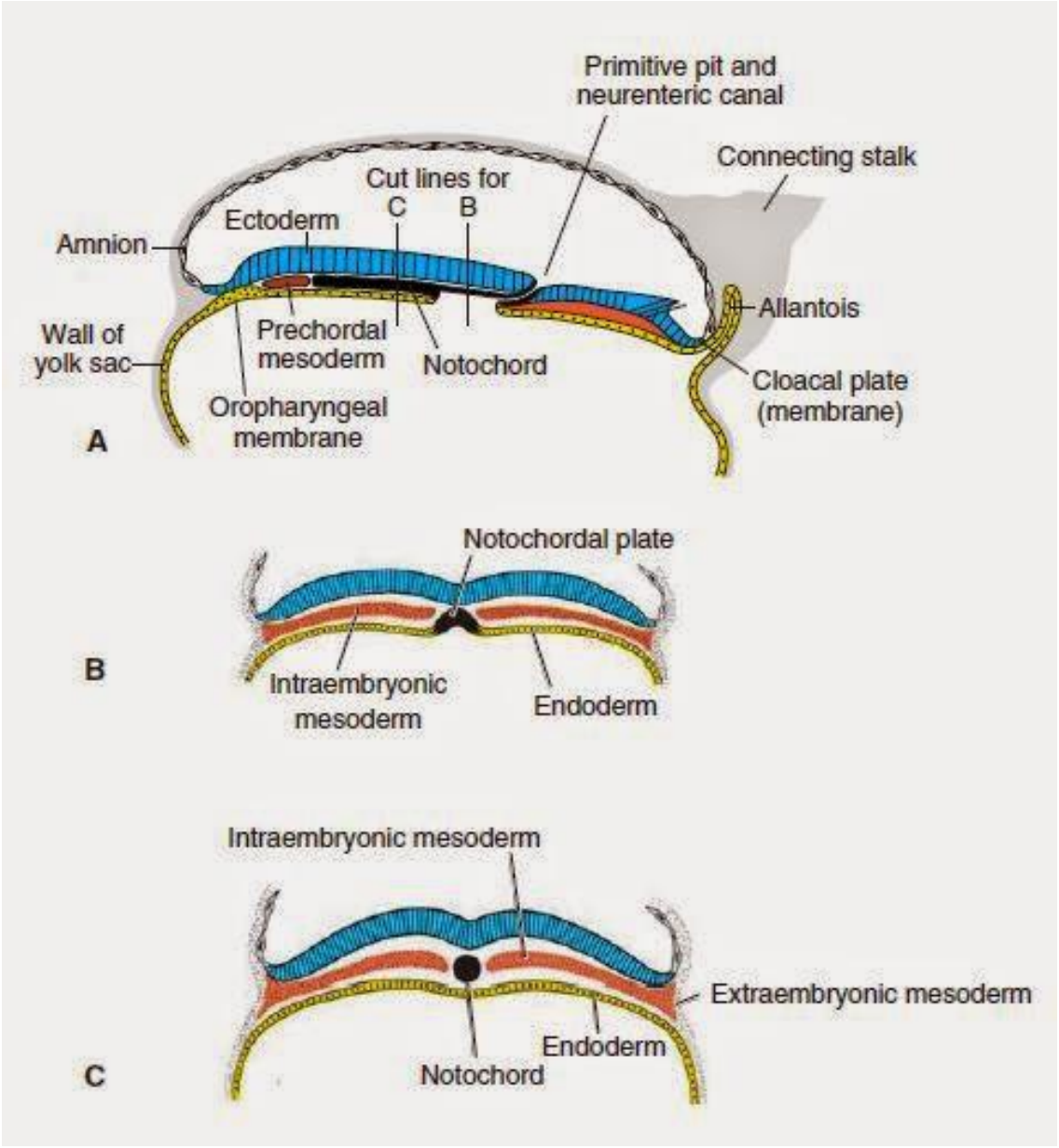
Dr. Sherif Fahmy

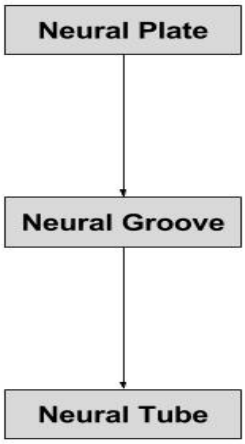

Amniotic cavity
Ectoderm
Mesoderm
Endoderm
Notochordal plate
Prechordal plate
Ectoderm
A
15 days
Notochordal plate
Neurenteric canal
Endoderm
B
Notochordal process
Endoderm
C
Transformation of notochordal process: days 16-22

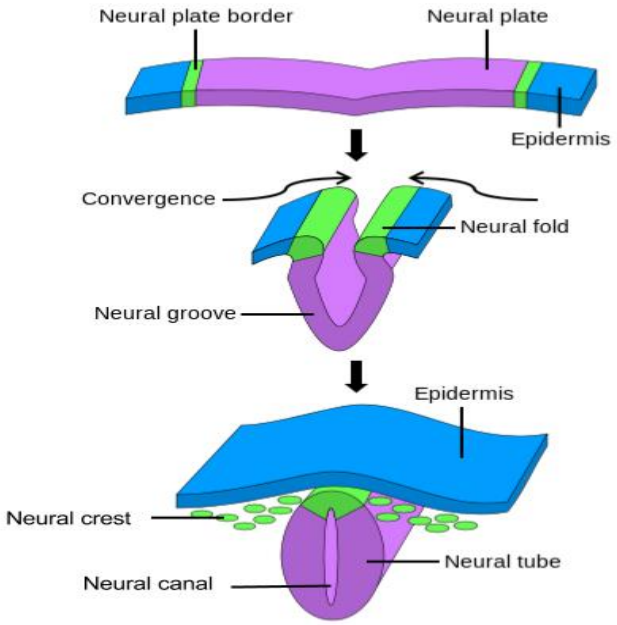

Primitive pit and neurenteric canal
Connecting stalk
Cut lines for
C
B
Ectoderm
Amnion
Allantois
Wall of yolk sac
Prechordal mesoderm
Notochord
Cloacal plate (membrane)
Oropharyngeal membrane
A
Notochordal plate
B
Intraembryonic mesoderm
Endoderm
Intraembryonic mesoderm
Extraembryonic mesoderm
Endoderm
Notochord
C

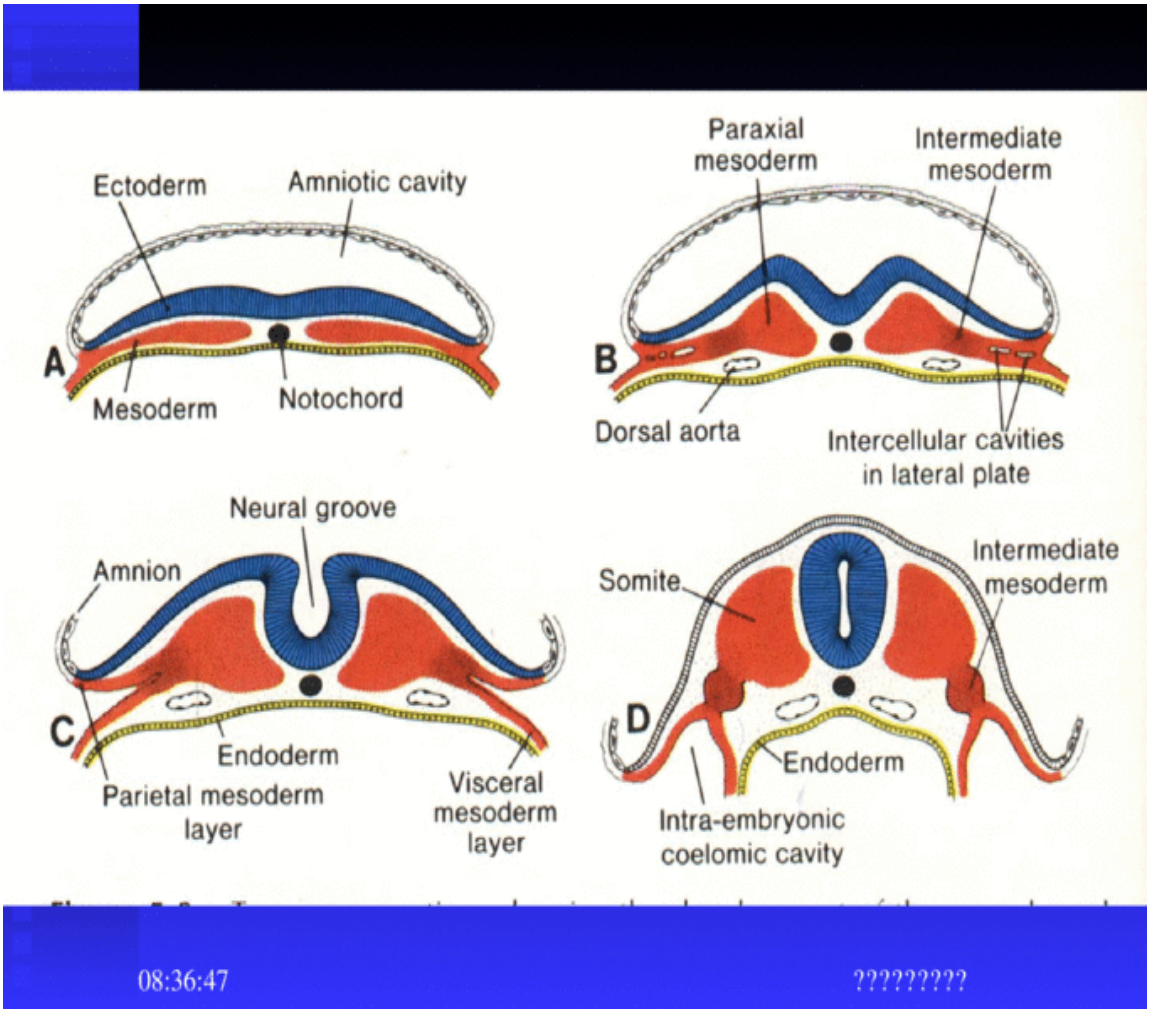
★ **Neurulation :**

- It is the **beginning** of development of the central nervous system by **formation of the neural tube** as follows :

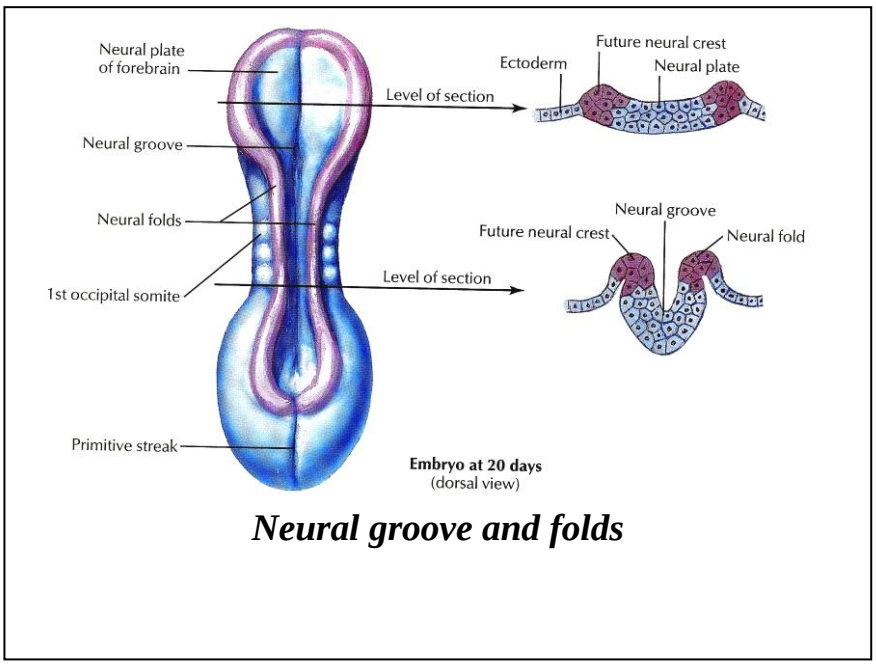
1. At the beginning of 3rd. week , the notochord stimulates proliferation of the overlying ectoderm leading to formation of the **neural plate** .
2. Formation of the **neural groove** & its raised edges form **neural folds**.
3. **Fusion** of the neural folds , **starts** in the middle of the embyo and **proceeds** in a cranial and caudal directions , with formation of **neural tub .**
4. The surface **ectoderm regains its continuity** again.
5. The **fusion** of the folds is **absent** at the anterior & posterior **end**s of the tube leaving 2 openings on the surface ectoderm called **the anterior & posterior neuropores**.
7. Anterior neuropore closes at 23rd day while posterior neuropore **closed** at 25th day.
8. The closed neural tube develops into the **brain and spinal cord**.



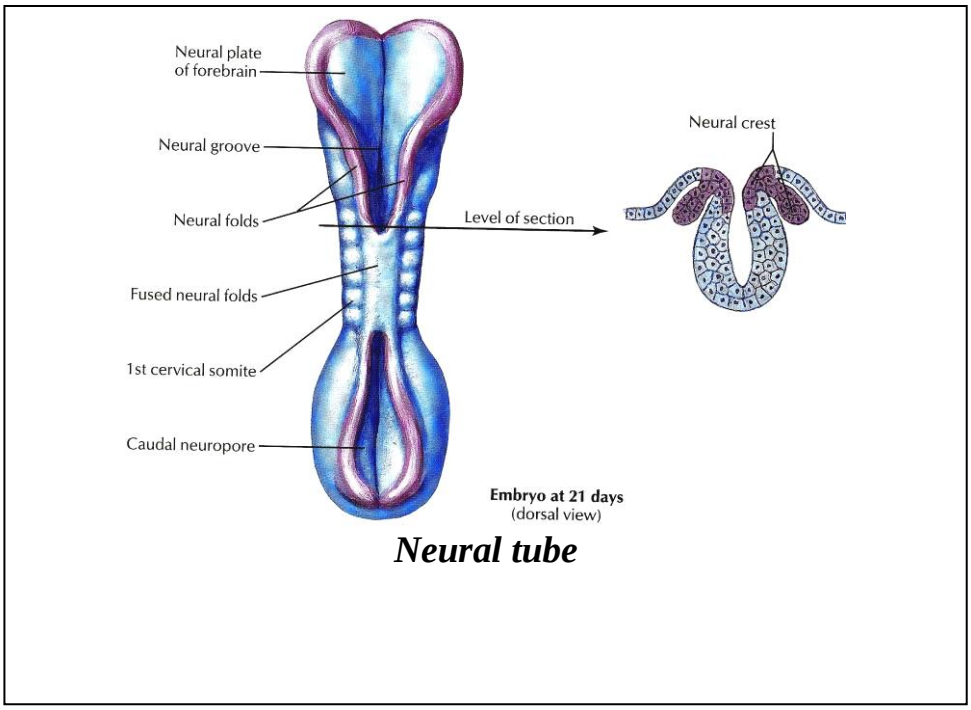




★ **Dorsal View to the Embryo at the beginning of 3rd. Week**



Neural groove and folds



Neural tube

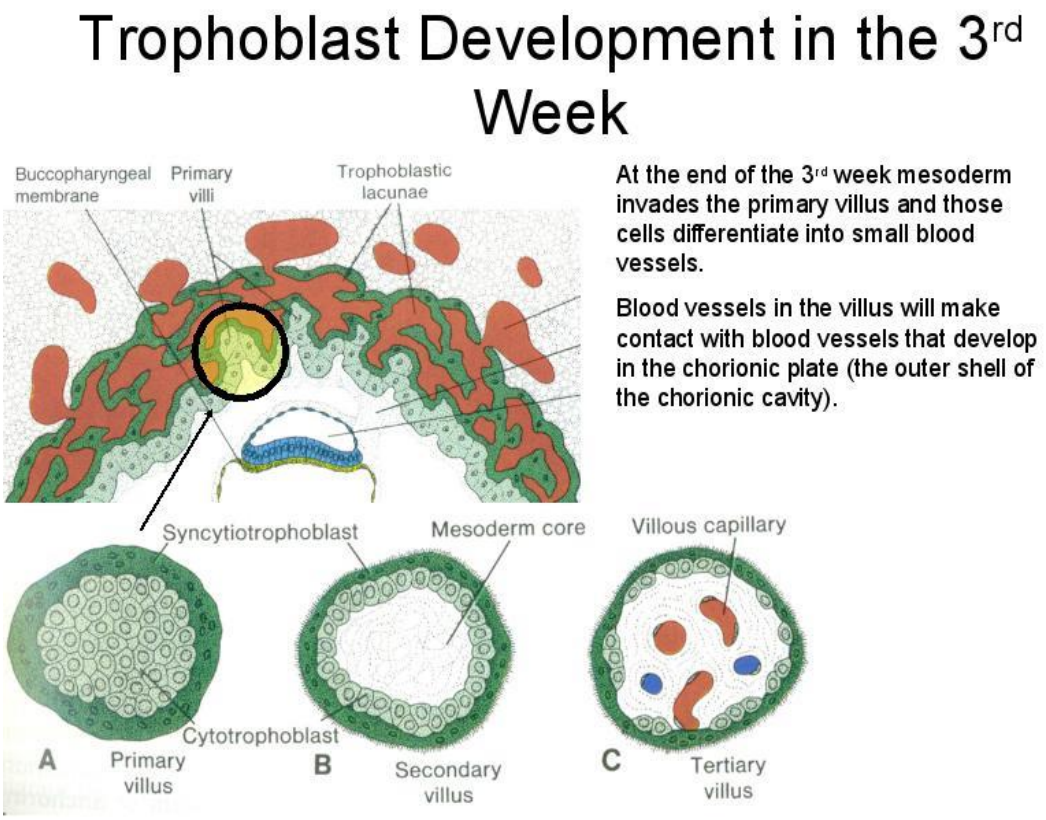
★ **Please see this excellent video for neurulation :**

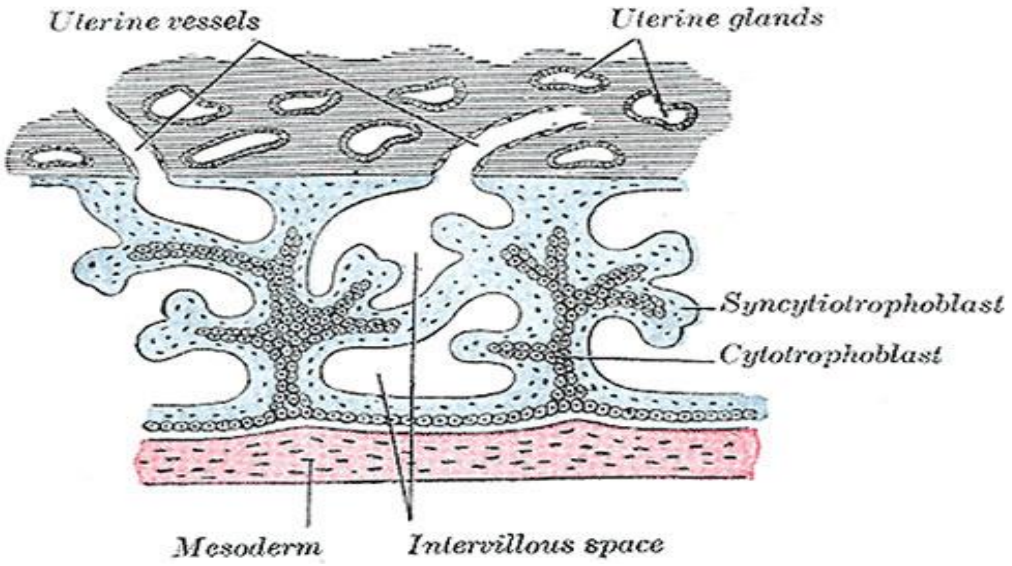
https://www.youtube.com/watch?v=lGLexQR9xGs

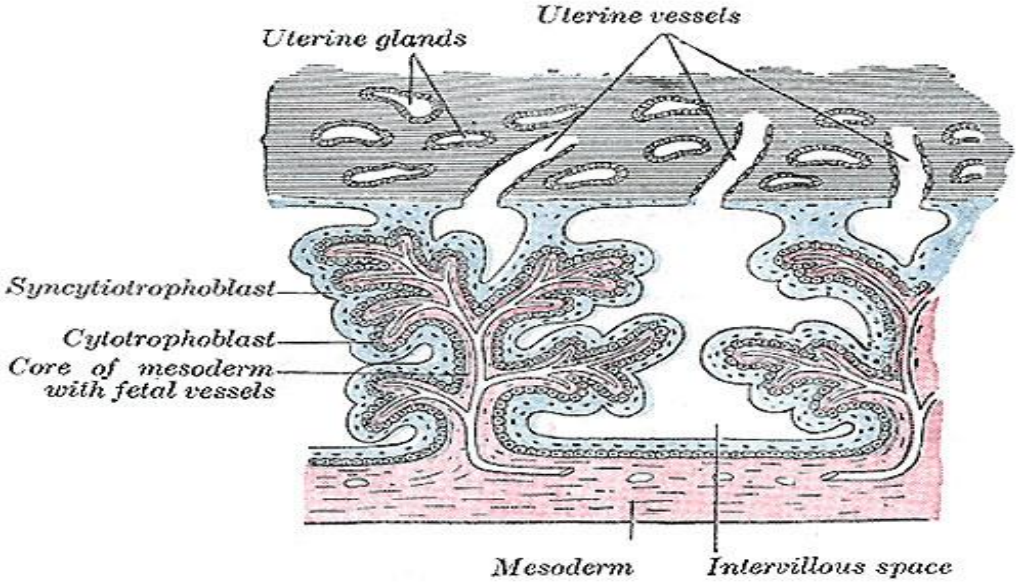
★ ***Development of the trophoblast during 3rd. week :***

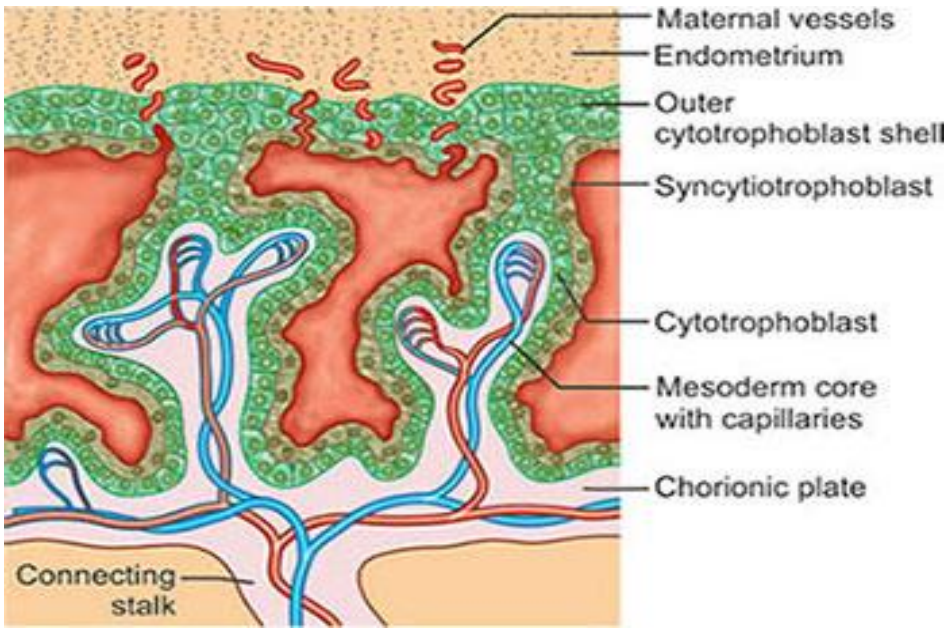
- The trophoblastic lacunae are surrounded by **trophoblastic (chorionic) villi** as following:
- ***The primary villi :*** (syncytiotrophoblast + cytotrophoblast) the cytotrophoblast penetrates into the syncytiotrophoblast in between the lacunae to form the primary villi .
- ***The secondary villi :*** (cytotrophoblast + syncytiotrophoblast + core of mesoderm***):*** a core of extraembryonic mesoderm which lines the cytotrophoblast enters into the primary villi to form the secondary villi .
- ***The tertiary or definitive villi:*** (syncytiotrophoblast + cytotrophoblast + core of mesoderm + blood capillaries)
  - Blood capillaries are formed in the extraembryonic mesoderm of the secondary villi to change them into tertiary villi.

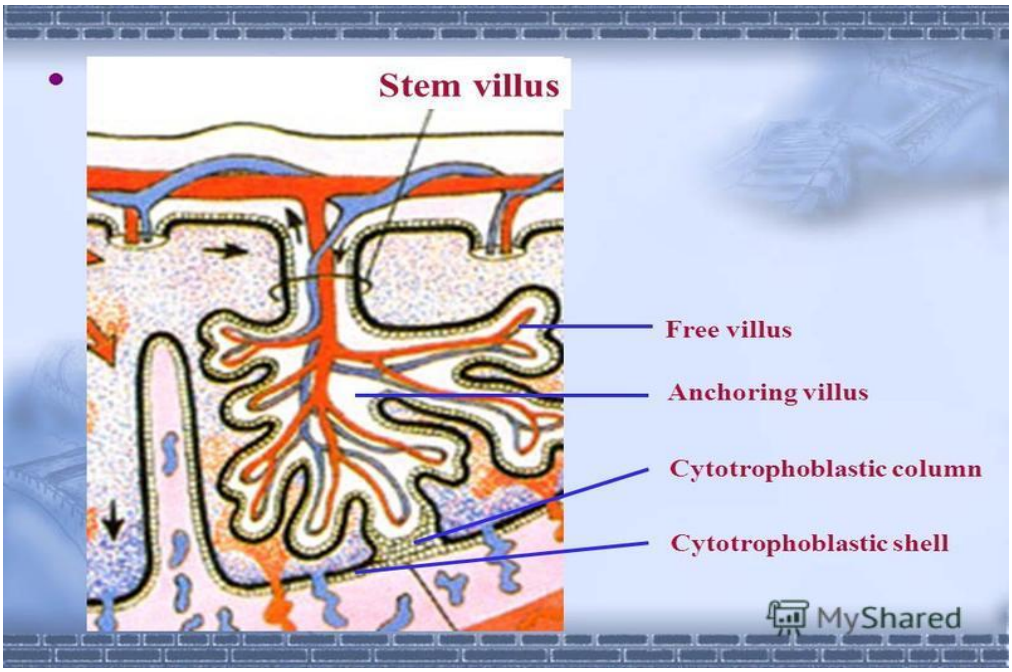
- These capillaries will be connected to the vessels in the chorionic plate and connecting stalk thus will be connected to umbilical vessels
- ***Outer cytotrophoblastic shell*** is formed by penetration of the cytotrophblast into the overlying syncytium until it reaches the maternal endometrium . The cytotrophoblastic cells of one villous establish contact with similar extensions of the neighboring villi forming the cytotrophoblastic shell.
- ***Stem villi*** are those attached to the chorionic plate .
- ***Anchoring villi*** are those which extend to the ***decidua basalis*** (endometrium forming the maternal part of the placenta) to fix the chorionic vesicle to the uterine wall .
- ***Free , floating or absorbing villi*** :
  - Those are the side branches from the stem villi and float freely within maternal blood in the intervellous spaces .
  - At these villi exchange of nutrients and other factors will occur.

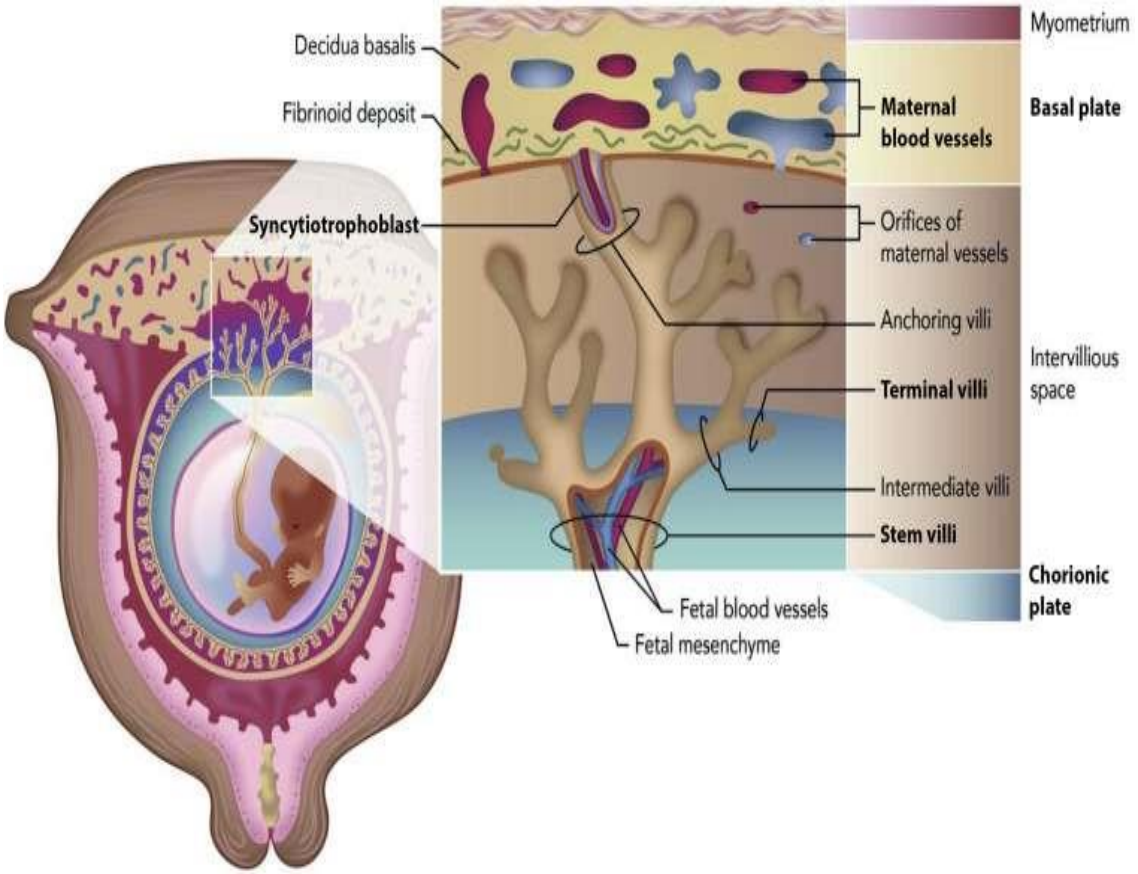



Uterine vessels
Uterine glands
Syncytiotrophoblast
Cytotrophoblast
Mesoderm
Intervillous space


Uterine glands
Uterine vessels
Syncytiotrophoblast
Cytotrophoblast
Core of mesoderm with fetal vessels
Mesoderm
Intervillous space

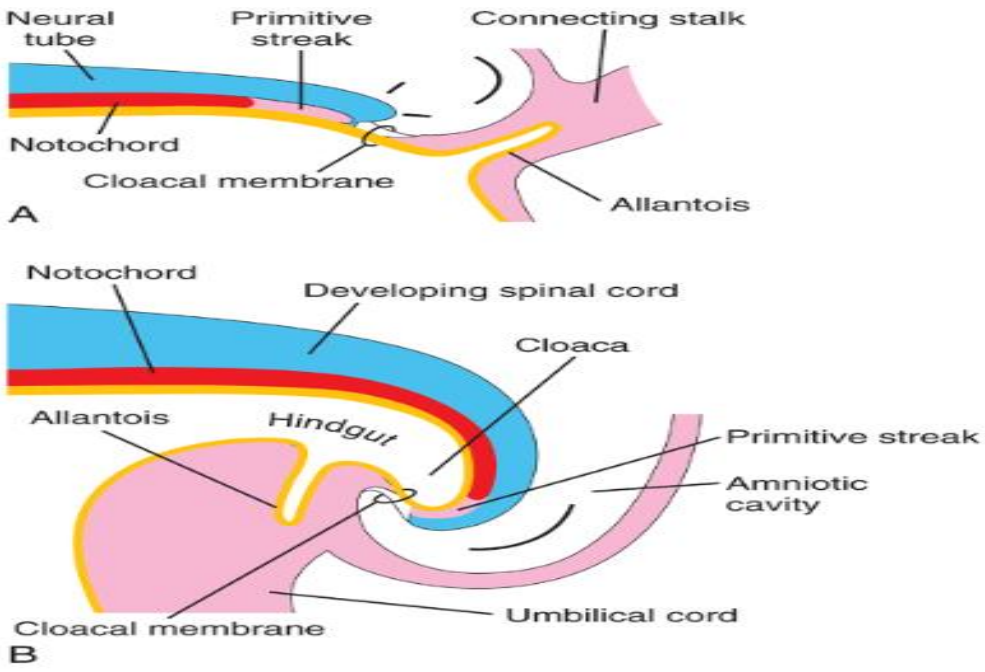

Maternal vessels
Endometrium
Outer cytotrophoblast shell
Syncytiotrophoblast
Cytotrophoblast
Mesoderm core with capillaries
Chorionic plate
Connecting stalk


Stem villus
Free villus
Anchoring villus
Cytotrophoblastic column
Cytotrophoblastic shell
MyShared


Decidua basalis
Fibrinoid deposit
Syncytiotrophoblast
Myometrium
Basal plate
Maternal blood vessels
Orifices of maternal vessels
Anchoring villi
Intervillious space
Terminal villi
Intermediate villi
Stem villi
Chorionic plate
Fetal blood vessels
Fetal mesenchyme

Allantois

- It is a tubular evagination of the dorsi-caudal part of the yolk sac into the connecting stalk .
- **Development :**
  - During 3rd. week , the allantois develops as a tubular projection from the dorsi-caudal part of the 2nd. Yolk sac into the connecting stalk .
- **Parts and fate : It is formed of 2 parts :**
  - **Intra-embryonic part :**
    - **The proximal part :** form the apex of urinary bladder .
    - **The distal part , called urachus** connect the urinary bladder to the yolk sac , is obliterated forming **median umnilical ligament** which extends from the apex of the bladder to the umbilicus .
  - **Extra-embryonic part ,** inside the umbilical cord , become **obliterated .**
  - **Allantoic vessels** form the **umbilical vessels .**



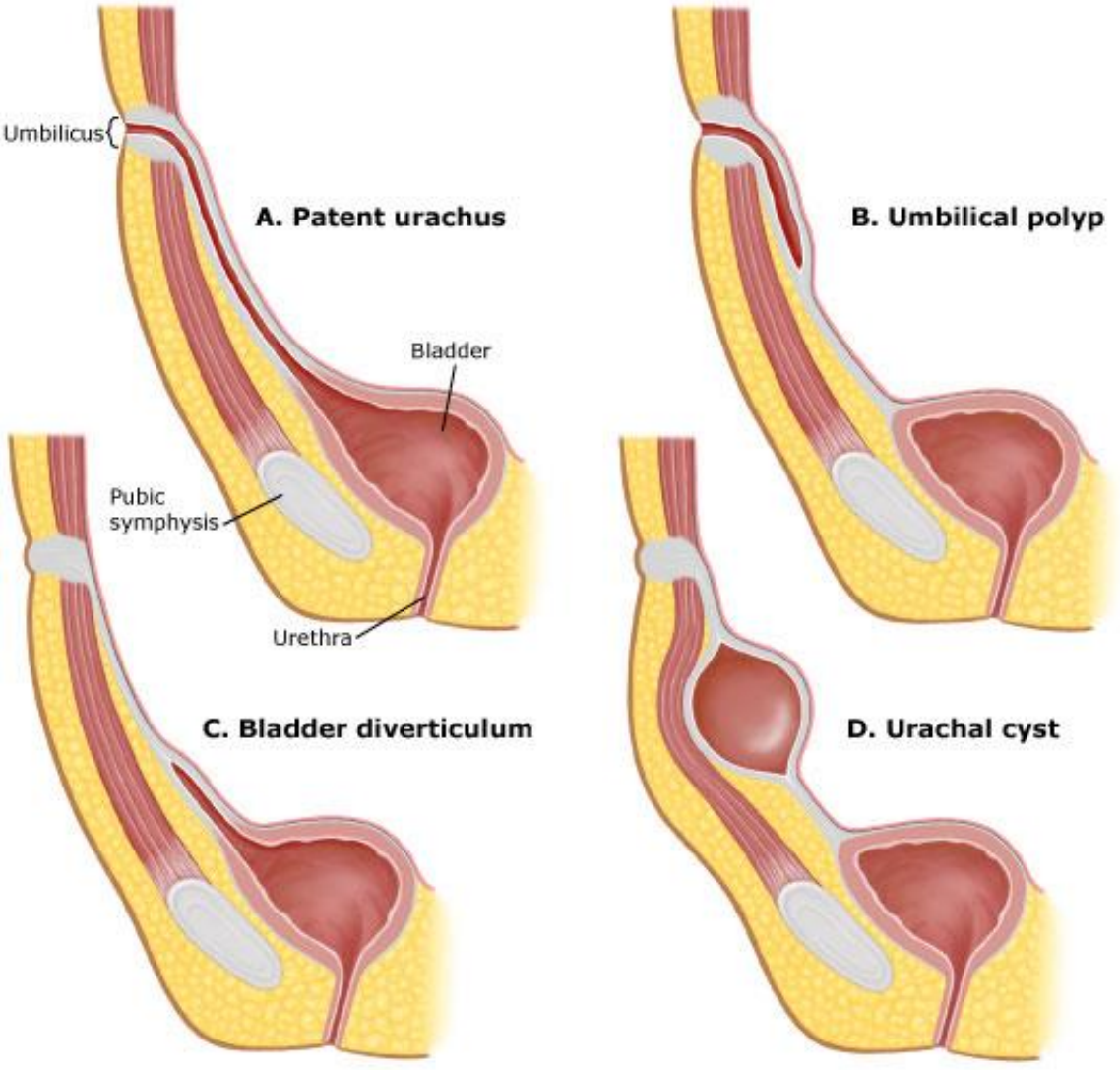
- **Anomalies of urachus :**

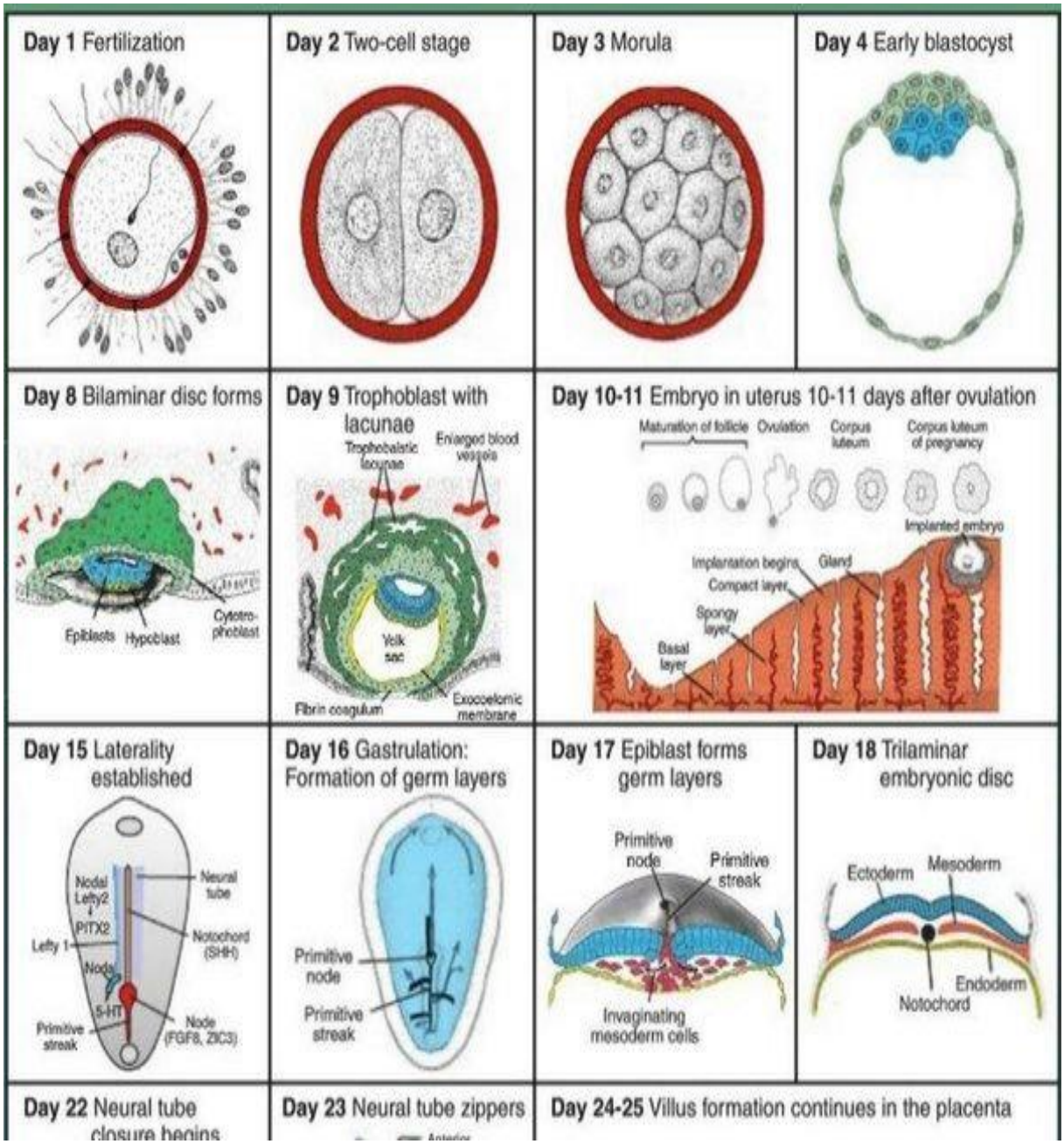
1- Persistence patency of whole length of urachus leads to **fistula** between the urinary bladder and umbilicus .

2- **Umbilical polyp :** due to persistence patency of thedistal part of the urachus .

3- **Bladder diverticulum** due to persistence patency of proximal part of the urachus .

4- **Urachal cyst :** due to persistence patency of central part of the urachus .





Summary of first 3 weeks of pregnancy

4th – 8th Weeks of EMBRYONIC PERIOD

(Period of organogenesis)

★ This part of embryonic period is characterized by **2 events :**

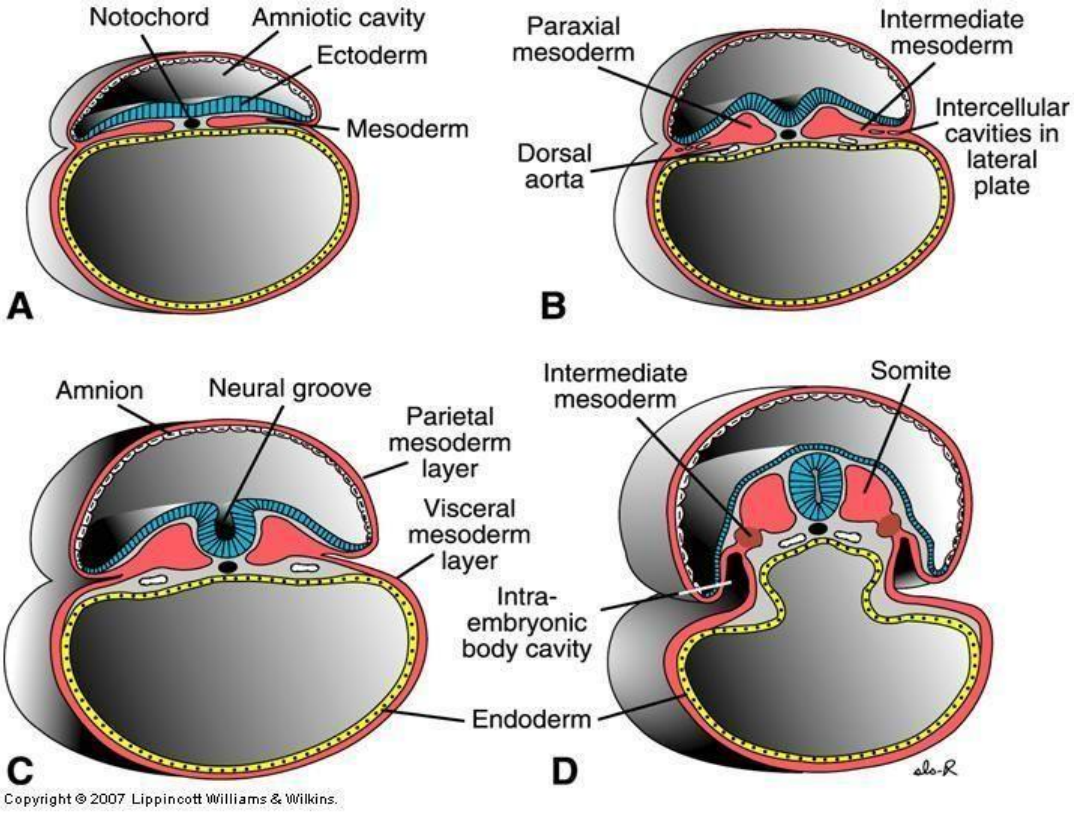
I. **Organogenesis :** is formation of all organs from the 3 germ layers .

II. **Morphogenesis :** formation of the shape of the embryo by folding and exchange of the external features .

I- Organogenesis by development of the three germ layers :

a) Development of the ectoderm :

- **Early ,** the ectoderm forms the **dorsal** layer of the germ disc and forms the **floor** of the amniotic cavity .
- **After folding ,** the ectoderm becomes the outer layer of the embryo.



- The ectoderm germ layer differentiates into the following structures :

1- ***The epidermis of the skin*** including skin glands ,hair & nails

2-***Nervous system :***

- ***The neural tube*** gives brain , spinal cord , retina and posterior lobe of pituitary gland .
- Peripheral nerves.
- ***Pia & arachnoid mater .***
- ***Sensory*** epithelium of sensory organs eg. Olfactory epithelium and taste buds .

3-**Ear :** external auditory meatus & outer layer of ear drum .

4-**Respiratory** system : nasal epithelium .

5- **GIT** : anterior part of oral cavity and lower ½ of anal canal .

6-**Glands** : suprarenal medulla and pituitary glands .

7-**Urinary** tract : terminal part of male urethra.

b) Development of the endoderm :

- **Early ,** the endoderm forms the **ventral** layer of the germ disc and forms the **roof** of the yolk sac .
- **After folding ,** the upper part of yolk sac becomes incorporated into the embryo , forming the **primitive gut** which differentiates into the following structures :

1- Epithelium lining of:

- ***Digestive system*** except anterior part of oral cavity and lower ½ of anal canal .
- ***Respiratory tract*** except nasal mucosa .
- ***Urinary bladder*** except trigone and **urethra** except its terminal part .

- The ***middle ear*** cavity and the ***Eustachian tube***.

2- Parenchyma of Palatine tonsils , thyroid , parathyroid glands ,thymus , Liver & pancreas .

c) Development of the intraembryonic mesoderm :

1- Paraxial mesoderm:

- It is segmented in the head region to form 7 ***somitomeres*** which gives skeletal muscles of face , jaws and throat .
- It is segmented from the occipital region caudally to form the ***somites***.

Somites

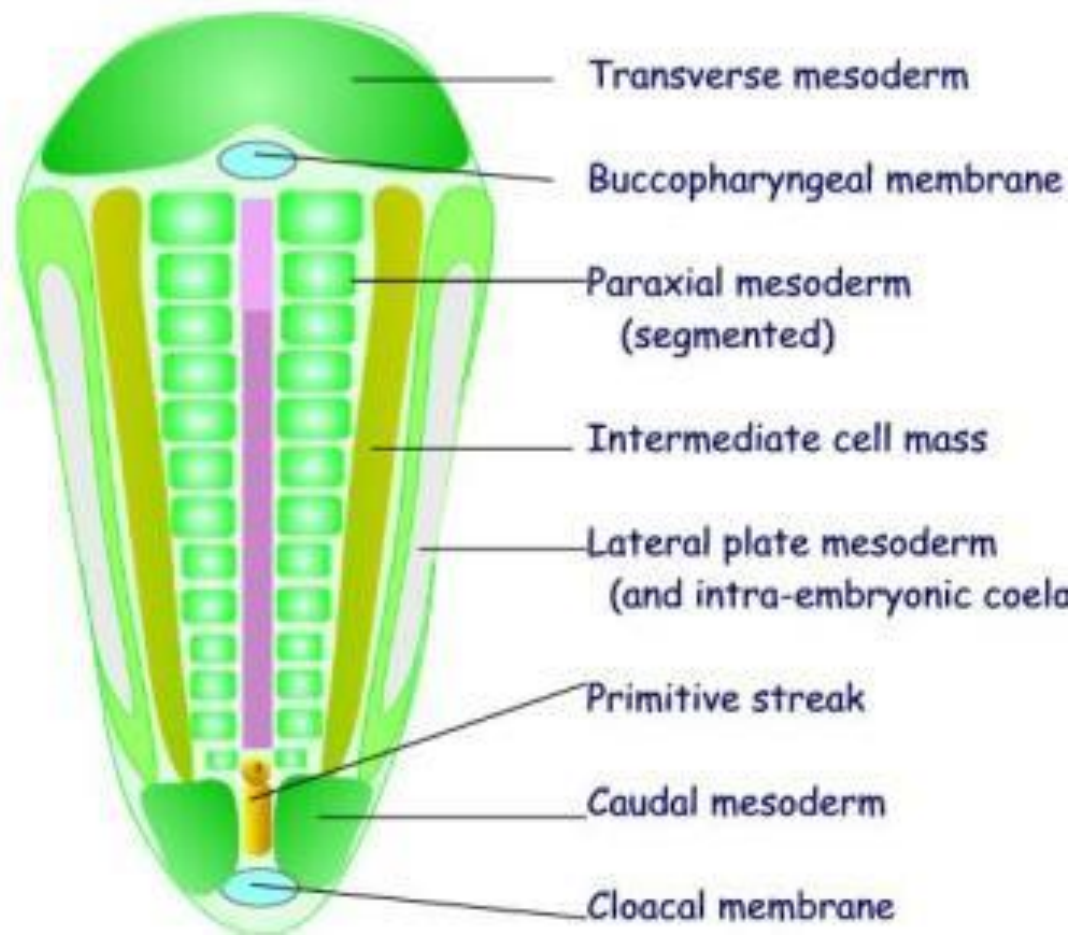
- **Organization** of the somites:
  - The **first** pair appears in the **occipital** region at the **20th day**.
  - **Three somites** appear **every day** appear from the **20th** day till the **30th** day .
  - They **continue** to appear till the **35 or 40th** day but at a **slower** rate.
  - The period from the 20th to the 30th day is called the **somite period**.
- The **age of the embryo** could be calculated in the somite period as follows = (number of somites - 1)/3 + 20

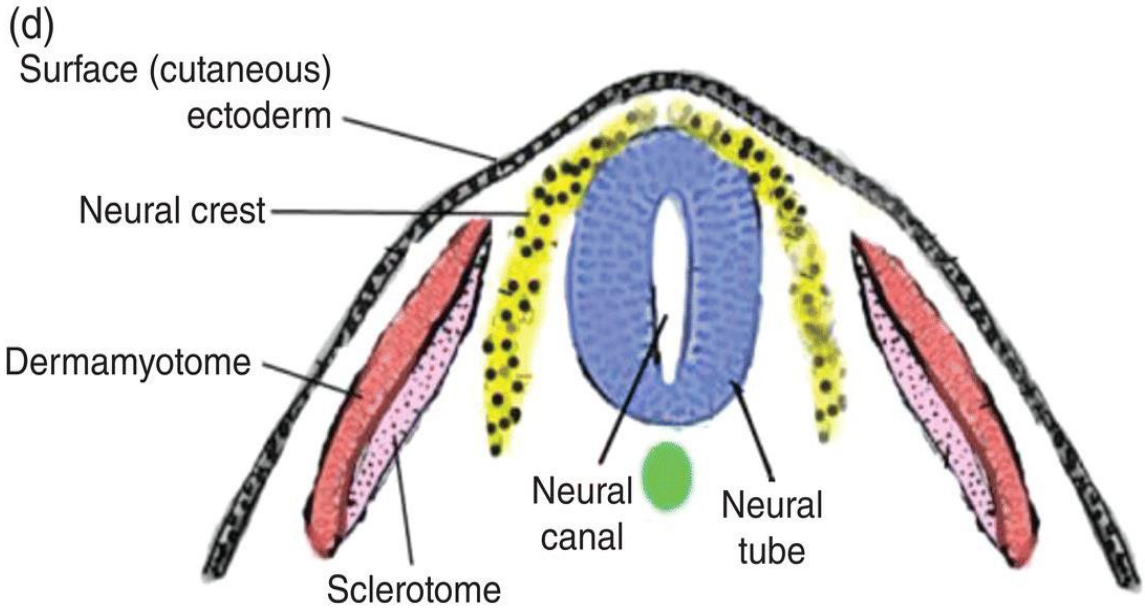
Age in days	20	21	22	23	24	25	26	27	28	29	30
Number of somites	1	4	7	10	13	16	19	22	25	28	31

- **Total number** of somites formed are **42 – 44** classified as follows :
  - 4 occipital, 8 cervical, 12 thoracic, 5 lumbar, 5 sacral & 8 – 10 coccygeal.

- The first occipital and last 7 coccygeal somites disappears .

- **Derivatives of somites** :Each somite **divides obliquely** into :
  - A ventro-medial part called the ***sclerotome*** which surround the neural tube & notochord to form the **vertebral column**.
  - A dorso-lateral part called the ***dermo-myotome*** which divides into ***dermatome*** which form the dermis of skin and ***myotome*** which form the striated muscles .





2- Development of the intermediate mesoderm :

- It forms the cortex of suprarenal gland , nephrons of the kidneys, ureter and parts of genital system.

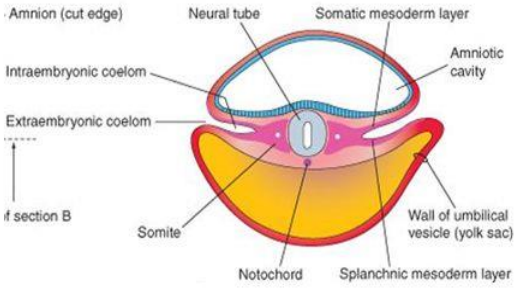
3- Development of the lateral plate mesoderm :

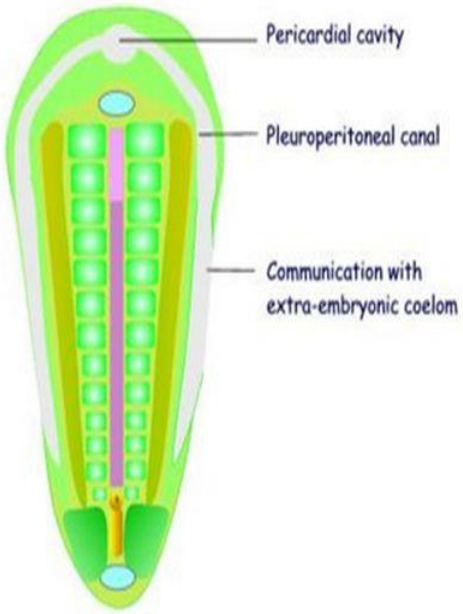
- Small spaces , appear in the lateral plate of mesoderm , which coalesce to form a cavity in this plate called the **intraembryonic coelomic** cavity which has the following characteristics:
  - It is in the form of an **inverted U** with a central part in cephalic to the buccopharyngeal membrane and 2 limbs on the sides of embry.
  - The central part will form the **pericardial cavity**.
  - The cranial part of the 2 limbs will form the **2 pleural cavity**.
  - The caudal part of the 2 limbs will form the **peritoneal cavity** .
  - The mass of mesoderm cephalic to the pericardial cavity is called the **septum transversum** which will form the **diaphragm**.
  - The limbs of the intraembryonic coelomic cavity are open at the periphery of the embryonic disc and are **connected** to the

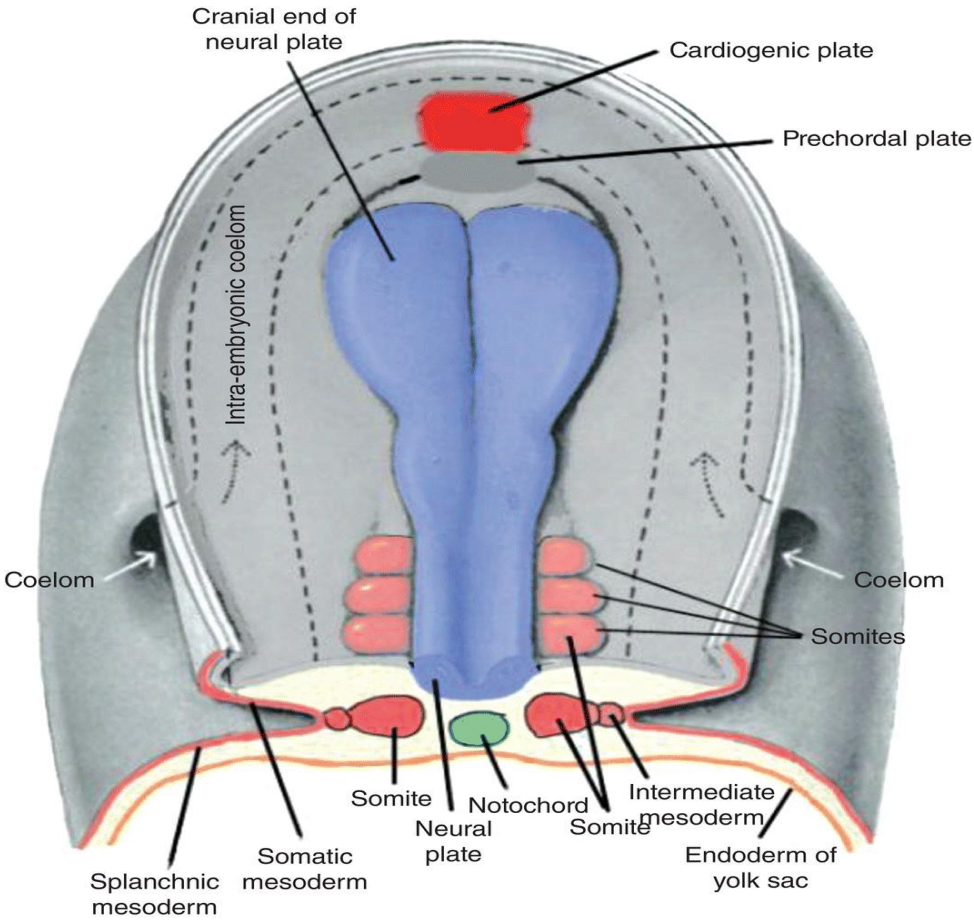
extraembryonic coelom but this connection is closed at the 10 week .

INTRA EMBRYONIC CEOLOM

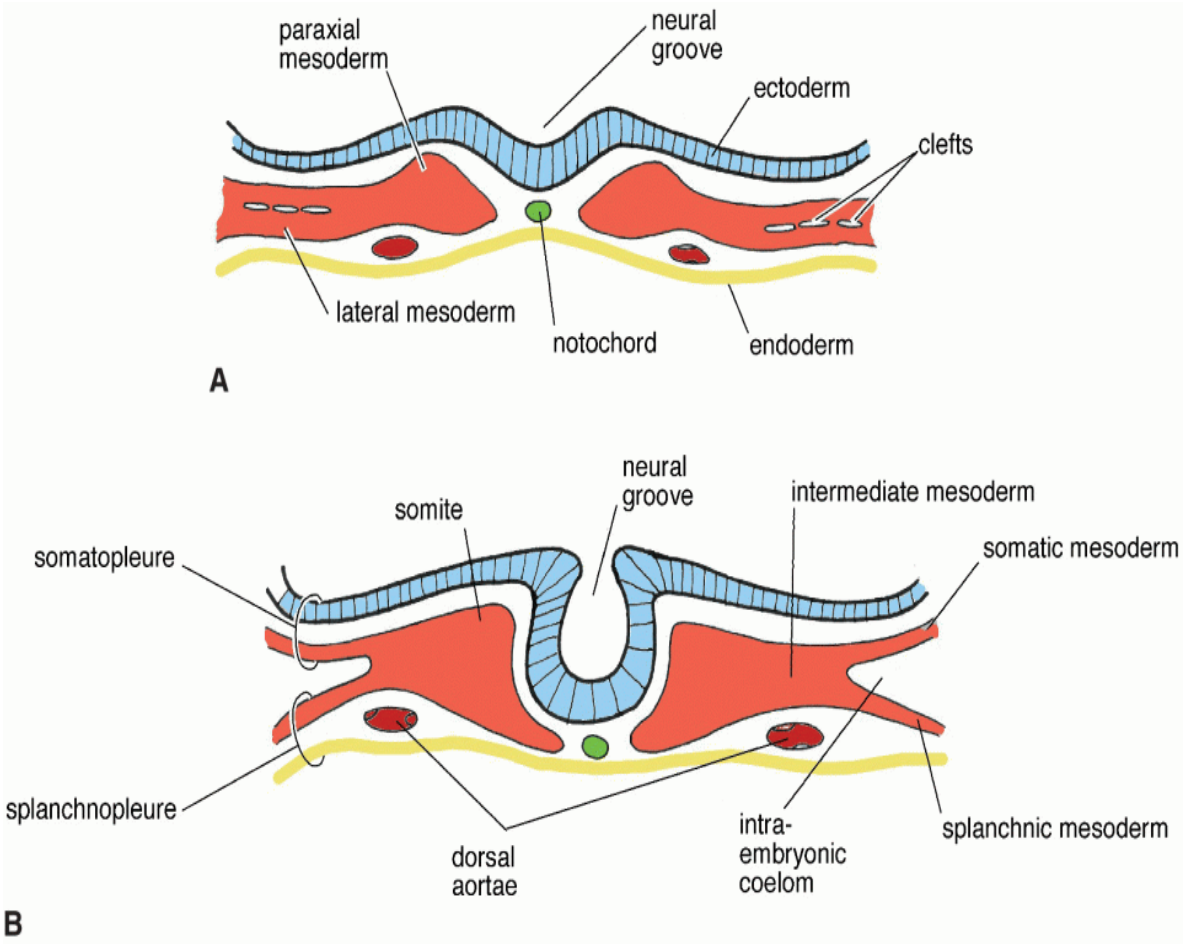
- Intraembryonic coelom extends to caudal wall of the yolk sac.
- Distal part of each limb communicates with the **extraembryonic coelom** from 4th somite.
- Connection closes during the 10th week







- **The intraembryonic coelomic** cavity **divides the lateral plate mesoderm** into:
  - **The somatic mesoderm:**
    - It becomes adherent to ectoderm to forms the striated muscles and connective tissue of the **lateral & ventral aspect of body wall** .
    - Parietal layers of **serous membranes**.
  - **The splanchnic mesoderm:**
    - It becomes adherent to endoderm to forms the smooth muscles and connective tissue of the **gut & respiratory system .**
    - **Cardiac muscles** .
    - visceral layer of **serous membranes**.



Morphogenesis of the Embryo

I. Folding of the embryonic disc :

★ At the **end of 3rd. week** , the flat embryonic disc starts to **fold** and **bulges** into the amniotic cavity .

★ **Two types of folding:**

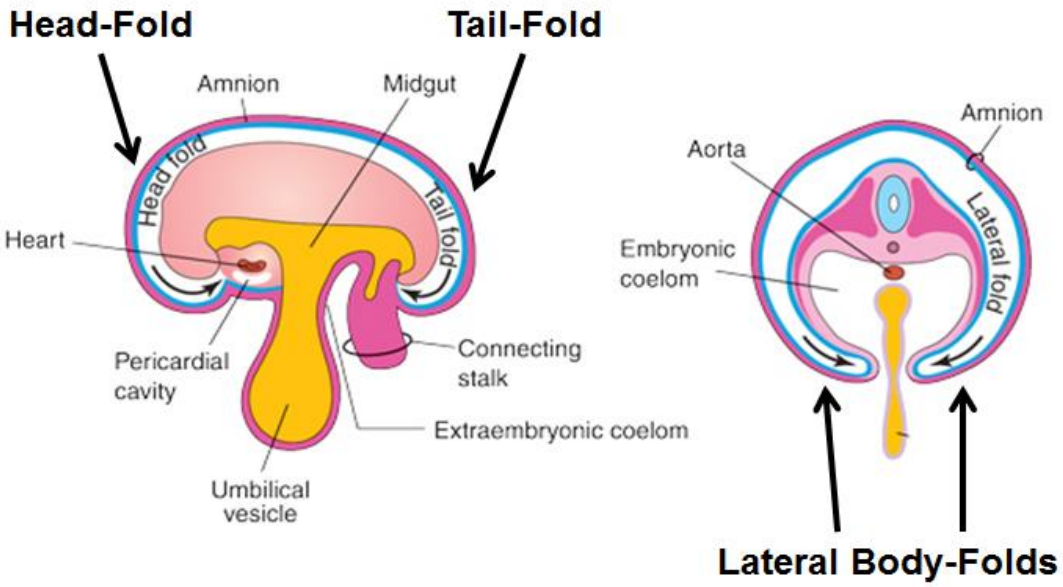
- The embryonic disc becomes folded in 2 directions simultaneously

1-Cephalo-caudal folding :

- It is due to growth of the **central nervous** system.
- It leads to formation of **head and tail folds** .

2- ***Lateral folding*** :

- It due to the rapid growth of the **somites**.
- It leads to formation of **lateral folds** .



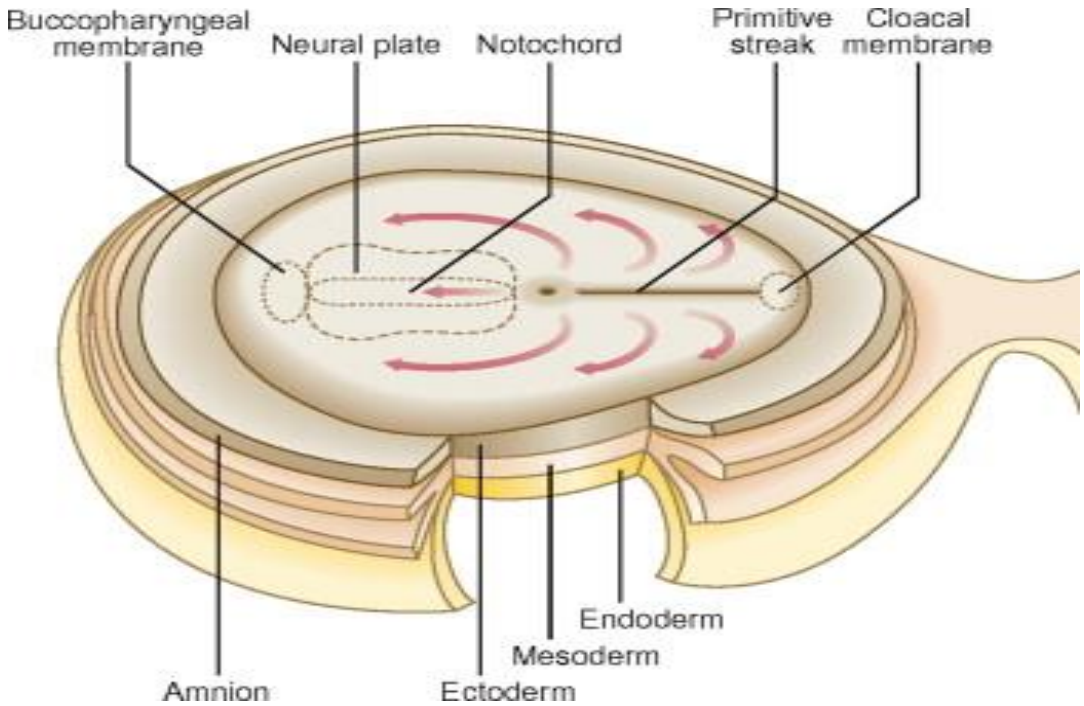
★ **Causes of folding :**

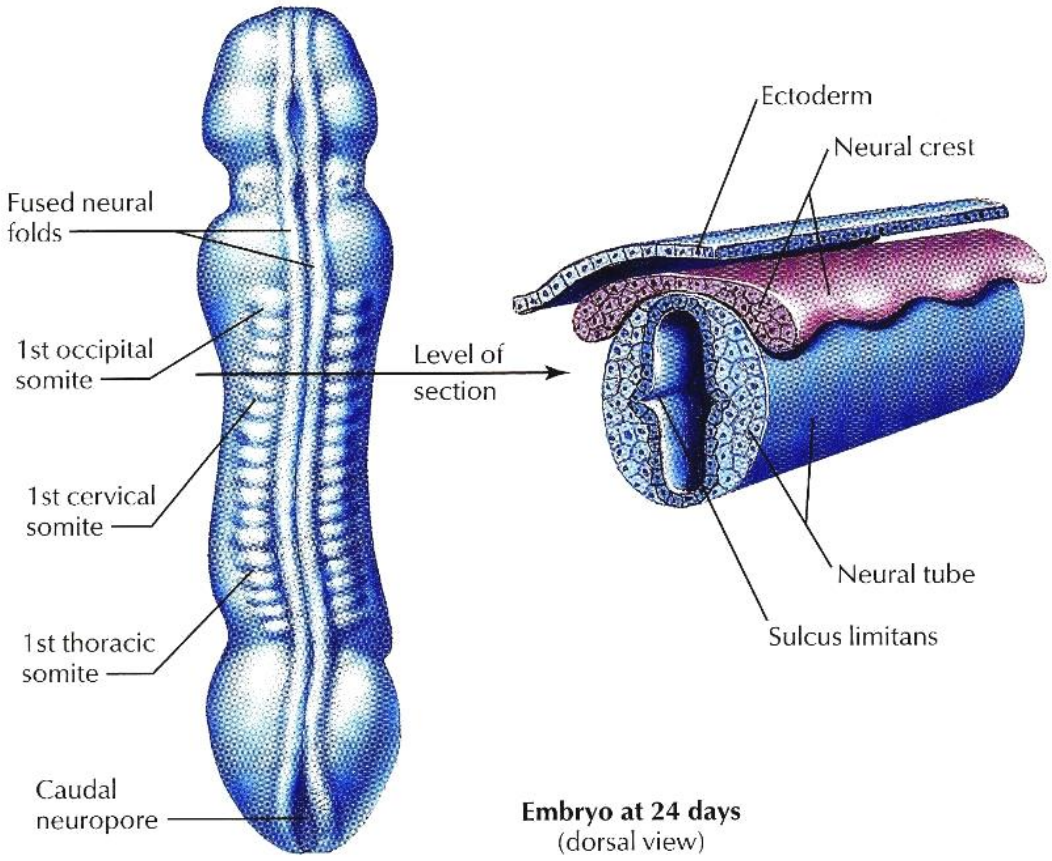
1- ***Rapid growth*** of embryonic disc in the cenrtral part of the disc (neural tube) more the its peripheral parts .

2- Progressive expansion of the ***amniotic cavity*** .

★**Results of folding:**

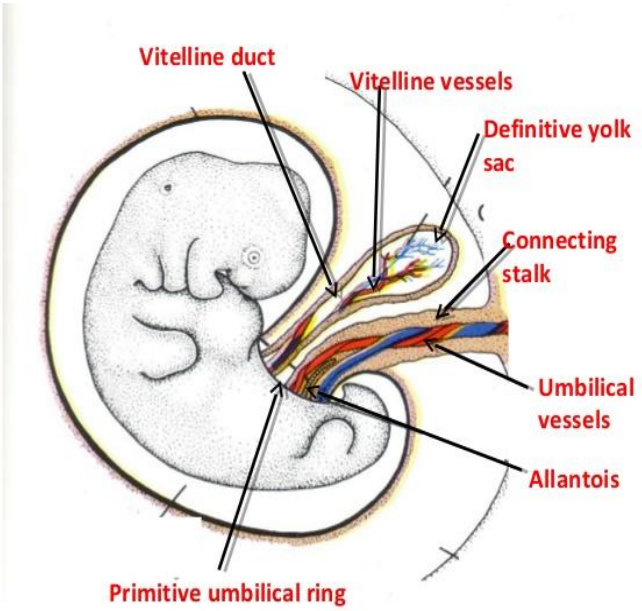
1-The flat shaped **embryonic disc** changes to the ***cylindrical*** appearance with formation of **body cavity**.





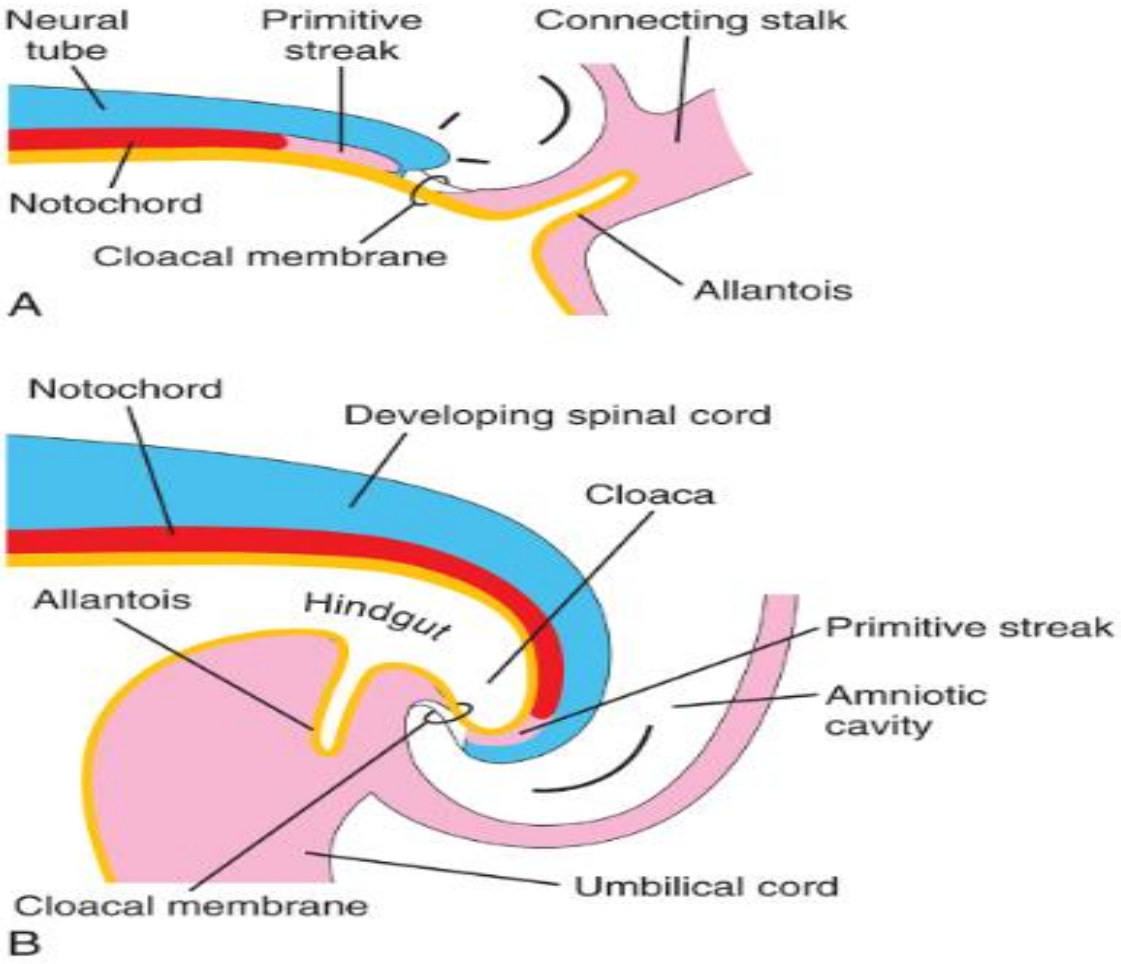
2- The **amniotic cavity** which was dorsal to the embryonic disc , now surrounds the embryo almost completely .

3-The **amnio-ectodermal junction** shifts to the ventral aspect of the body to form the **primitive umbilical ring** which is bounded by the 4 folds. Thus the ventral aspect of the embryo shows a wide umbilical ring .



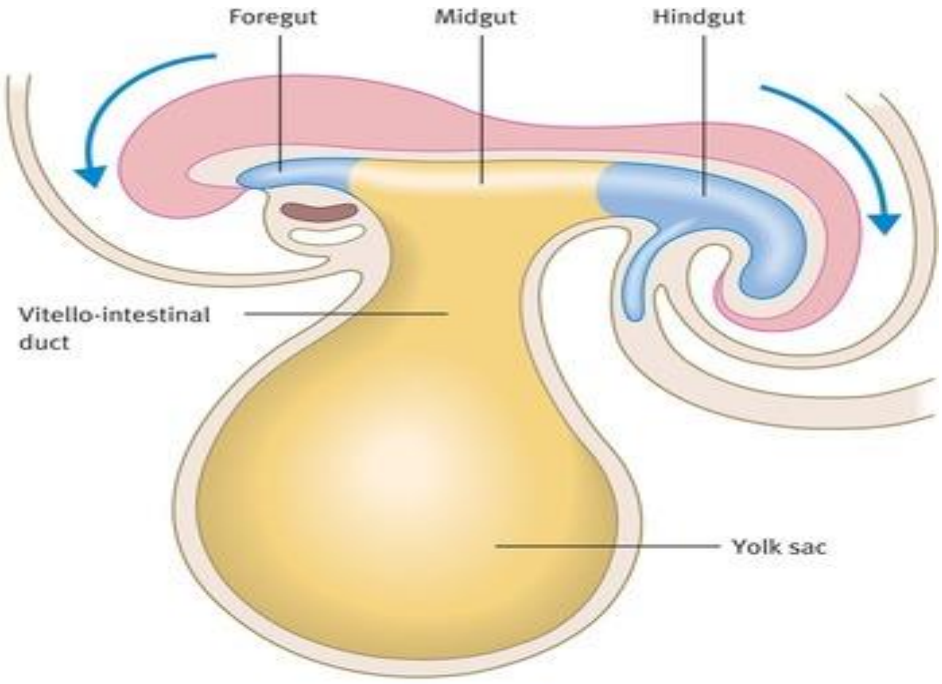
4-The **connecting stalk** which was attached to the caudal end of the embryonic disc , shifts to the ventral side of the body.

5-The **allantois** (projection from the yolk sac) which lie inside the connecting stalk , shift to the ventral side of the body with the connecting stalk into the **primitive umbilical ring** .



5- A large part of the cavity of the **secondary yolk sac** is incorporated into the body of the embryo forming the **primitive gut** which is lined by endoderm.

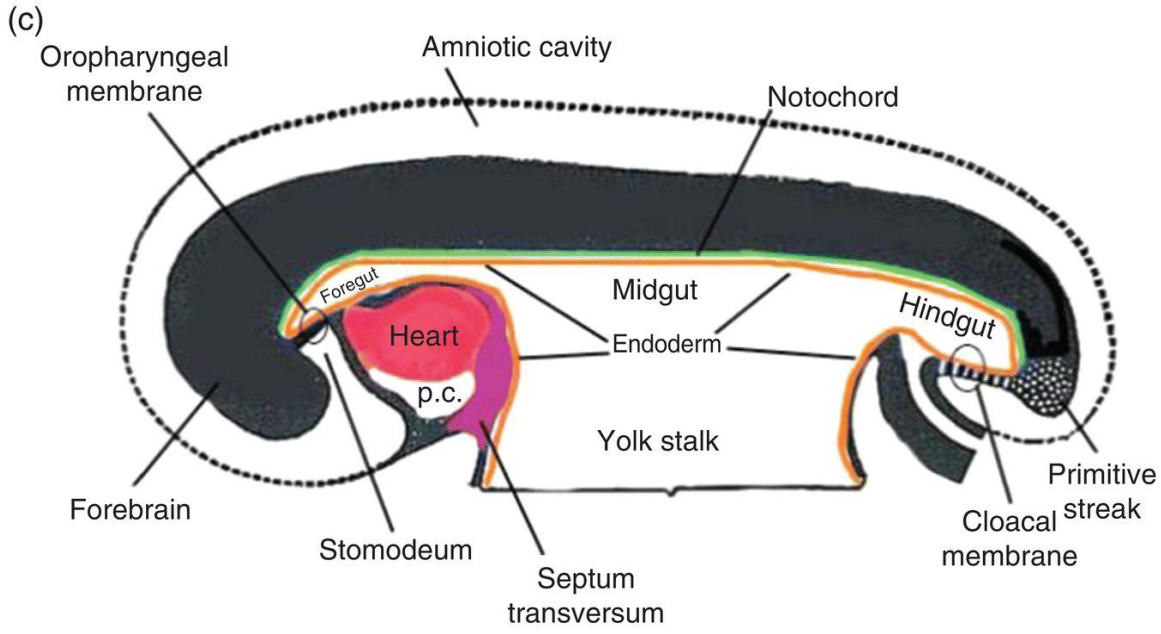
6-The remaining part of the yolk sac outside the embryo is called the **definitive yolk sac** which is connected to the midgut by the **vitello-intestinal duct .**



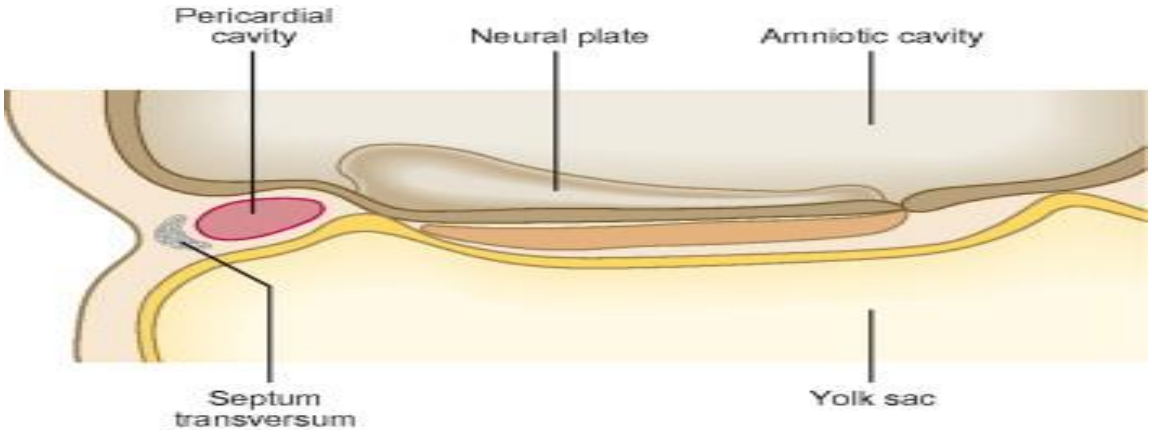
Arrows indicate the formation of head and tail folds.

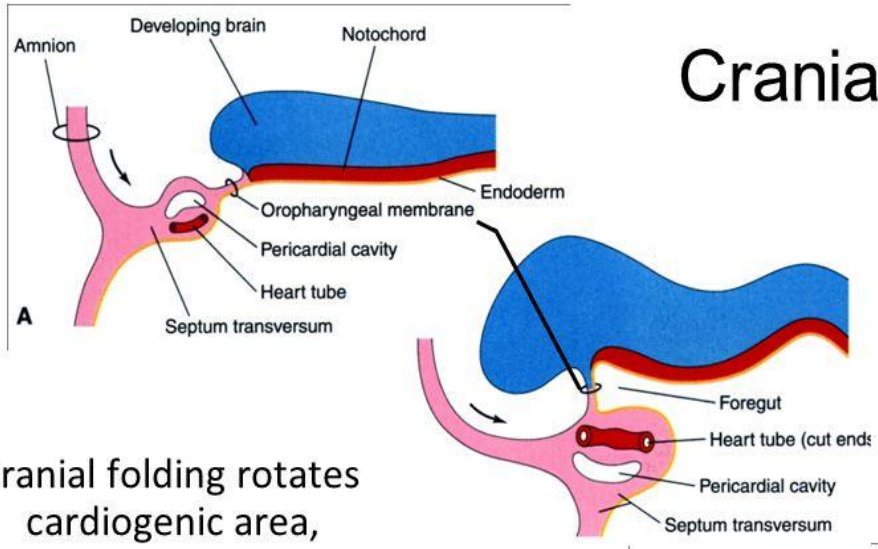
7-The part of the gut found in the **head fold** is called the **foregut**, the part found in the **tail fold** is called the **hind gut**, whereas the part in between within the **lateral folds** is called the **midgut .**

8-The buccopharyngeal lie at the **cranial ends** of the gut and cloacal membranes lie at **caudal ends** of the gut.



7-The **septum transversum** as well as the **pericardial cavity & heart** which was at the cephalic end of the embryo become shifted to the ventral side of the body ventral to the foregut , and **the brain** becomes in the **most cephalic** region of the embryo.

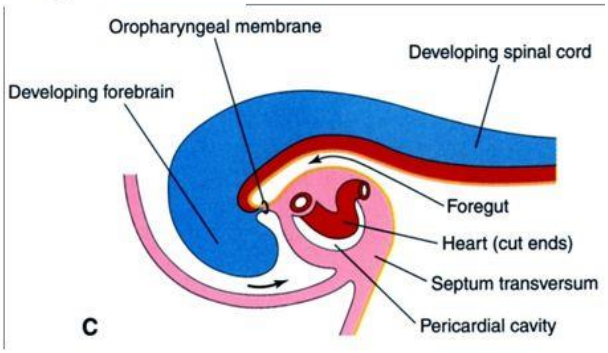




Cranial folding

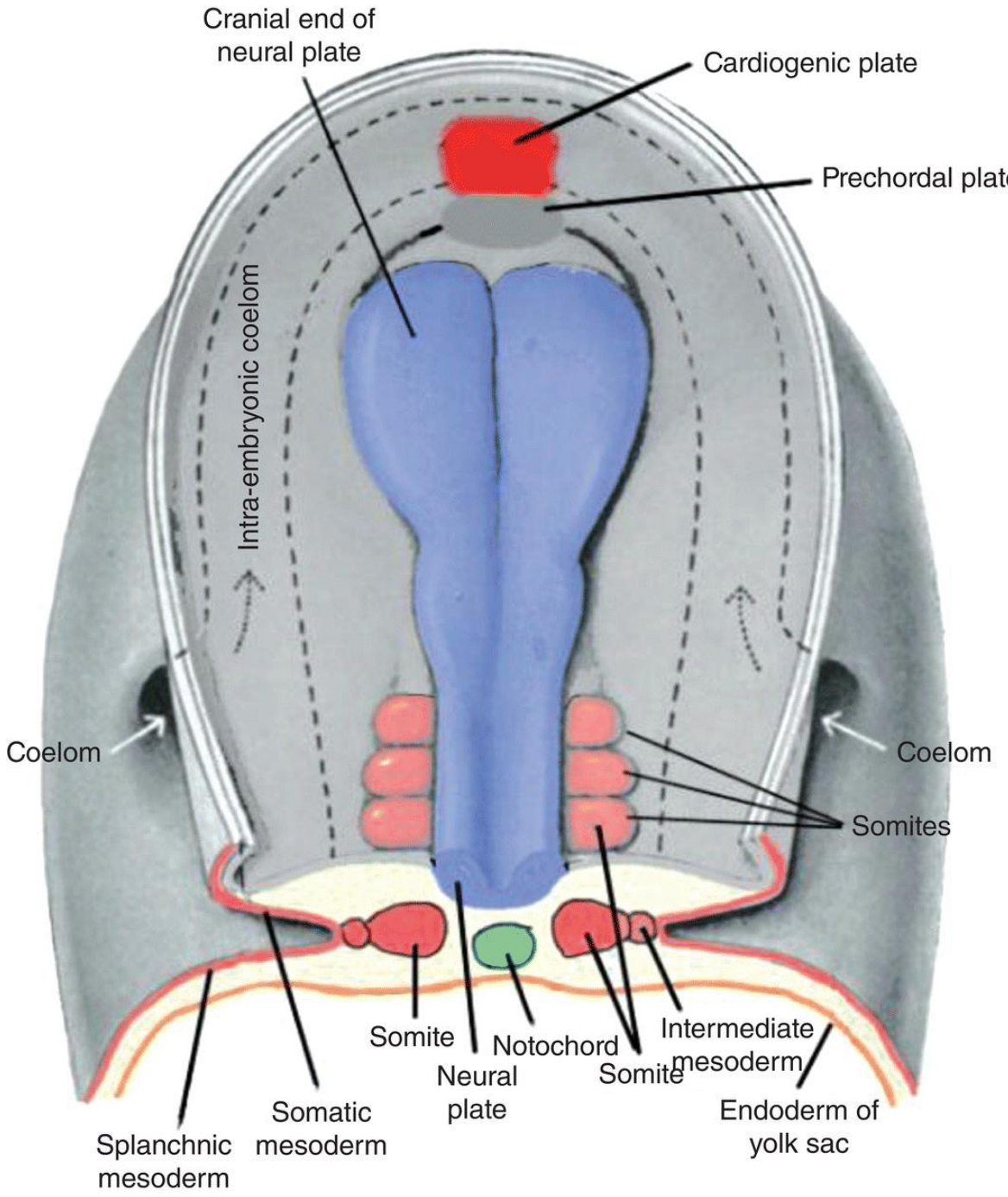
Cranial folding rotates cardiogenic area,

moves it ventrally and caudally, and orients **heart tube** and **pericardial cavity**



Moore & Persaud fig 13-9

8-The **initial relation** of the septum transversum , the pericardial cavity and the buccopharyngeal membrane to each other **is reversed**, so after folding the **buccopharyngeal membrane** becomes the **most cephalic**, and the **septum** transversum becomes the **most cauda**l, while the pericardial cavity and heart remain in between.



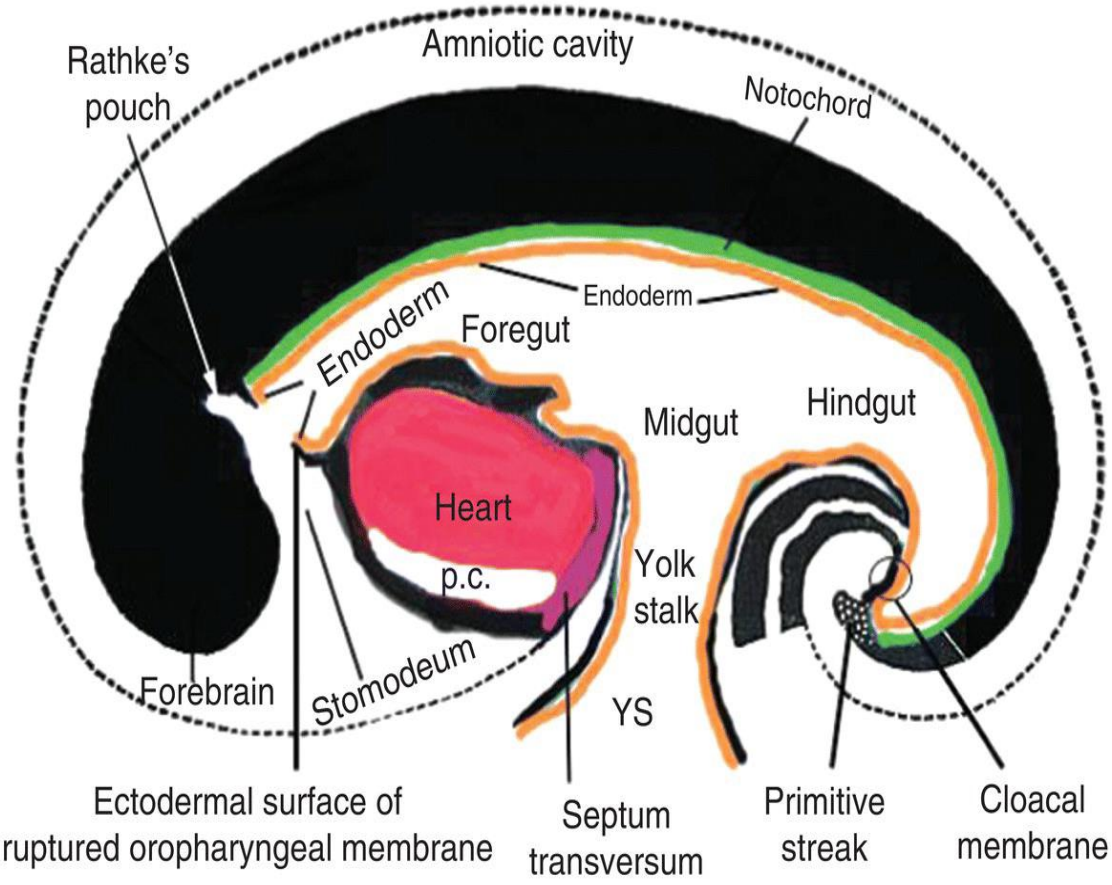
9- The **cranial end** of the folded embryonic disc shows the followings :

a) **Forebrain swelling** produced by the developing forebrain .

b) **pericardial swelling** produced by the developing heart .

c) Depression between the previous 2 swellings called **stomatodeum** .

(d)



★ Please see the following videos :

https://www.youtube.com/watch?v=yXUv4MPuNTA
https://www.youtube.com/watch?v=qMnpxP6EeIY

II. External appearance of the embryo :

1- The head, buttocks, anterior and posterior body walls could be identified.

2- The **head** is large in proportion with the body

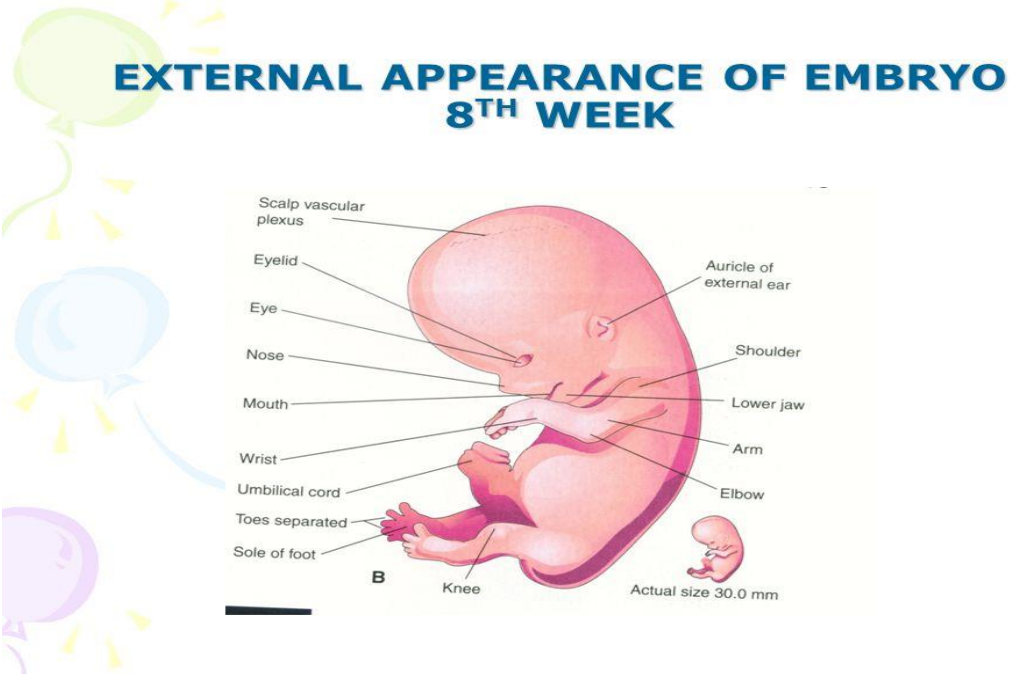
3- The **face** is formed with the eyes, nose and ears are easily identified.

4- The **forelimb** buds appear as small buds at the 5th week at a level from 4th. cervical to 1st. thoracic somites .

5- The **hind limb** buds appear as small buds at the 6th week at a level of lumbar and upper sacral somites .

6- The **age** of the embryo is estimated from the 5th – 8th weeks by the crown-rump (CR) length (the measurement from the vertex of the skull to the point between the apices of the buttocks) .

CR length in mm	Age of embryo in weeks
5 – 8	5
10 – 14	6
17 – 22	7
28 – 30	8



(From 9th week till birth)

1. Growth in length :

- ***CR length***:
  - At the end of 3rd month = 5 – 8 cm.
  - At the end of 5th month = 18 cm.
  - At birth = 36 cm.
- ***Crown heel length (from the vertex of the skull to the heel).***
  - CH length at birth is 50 cm.

2. Relative size of head to body :

- At the beginning of 3rd month the head is ½ the CR length.
- At the beginning of 5th month the head is 1/3 the CH length.
- At birth the head is ¼ the CH length.

3. Weight growth :

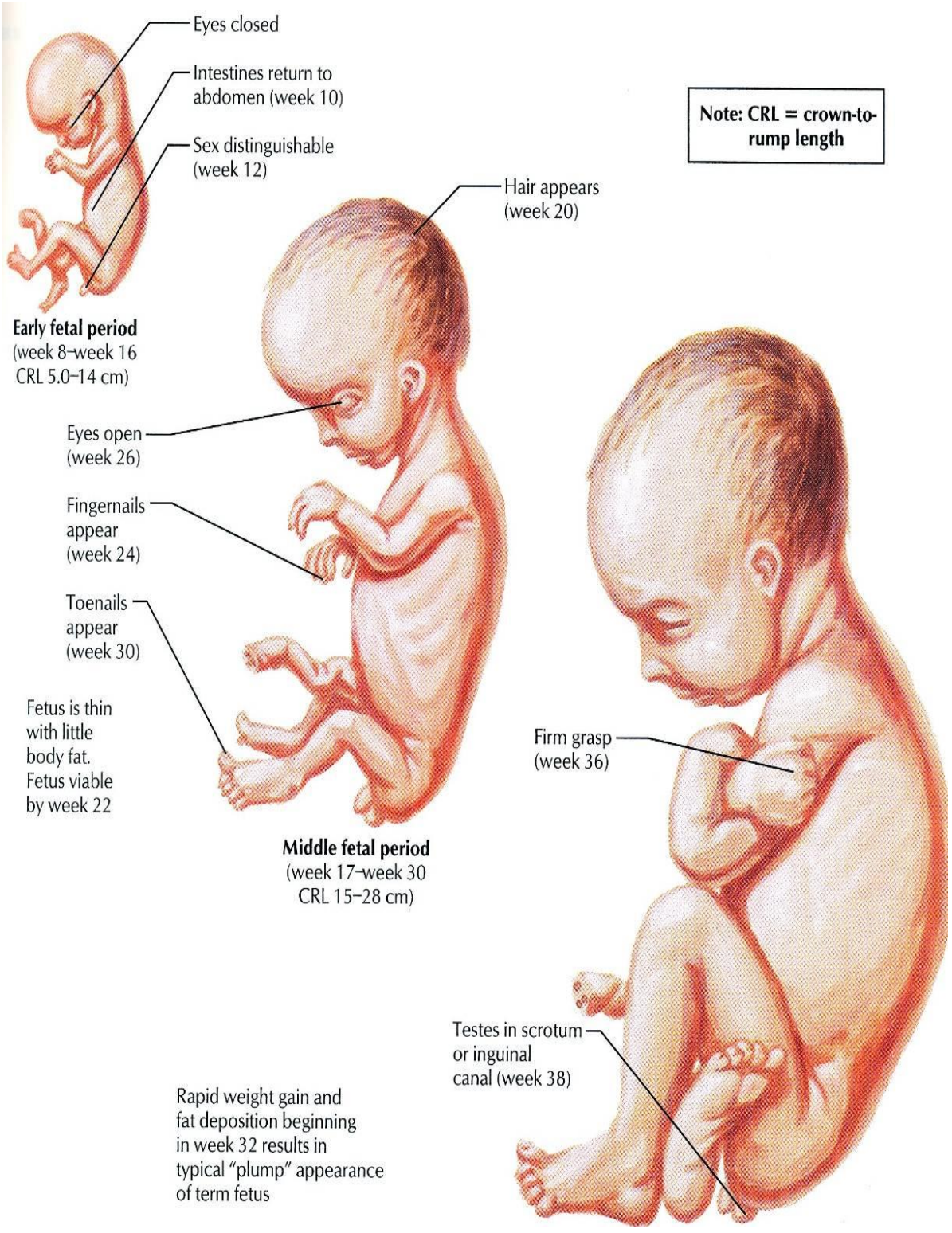
- At the end of the 5th month the fetal weight is ½ kg.
- At the 7th month the weight is 1.75 kg.
- At full term the weight is 3.5 kg.

4. Changes of the external features of the body :

- **Face** becomes **human** looking.
- **Limbs** reach the relative **length** in relation to the body.
- The **external genitalia** are differentiated at the **12th week**.
- The **testes** descend to the scrotum just before birth.
- **Lanugo hair** covers the fetus since the 4th month.
- The **skin is wrinkled** till the end of **6th** months then disappear due to deposition of s.c fat .
- The **skin** is covered by fatty substance called **vernix caseosa**.

5. Fetal movements :

- It is clearly recognized since the **5th month.**



Fetal period

Decidua

★ **Definition:** It is the ***endometrium of gravid uterus*** after complete implantation of the blastocyst.

★ **Parts of the Decidua**

1. Decidua basalis

- It is the part of the decidua which coversto the **embryonic pole** of the chorionic vesicle.
- It forms the **maternal** component of the **placenta.**

2. Decidua capsularis

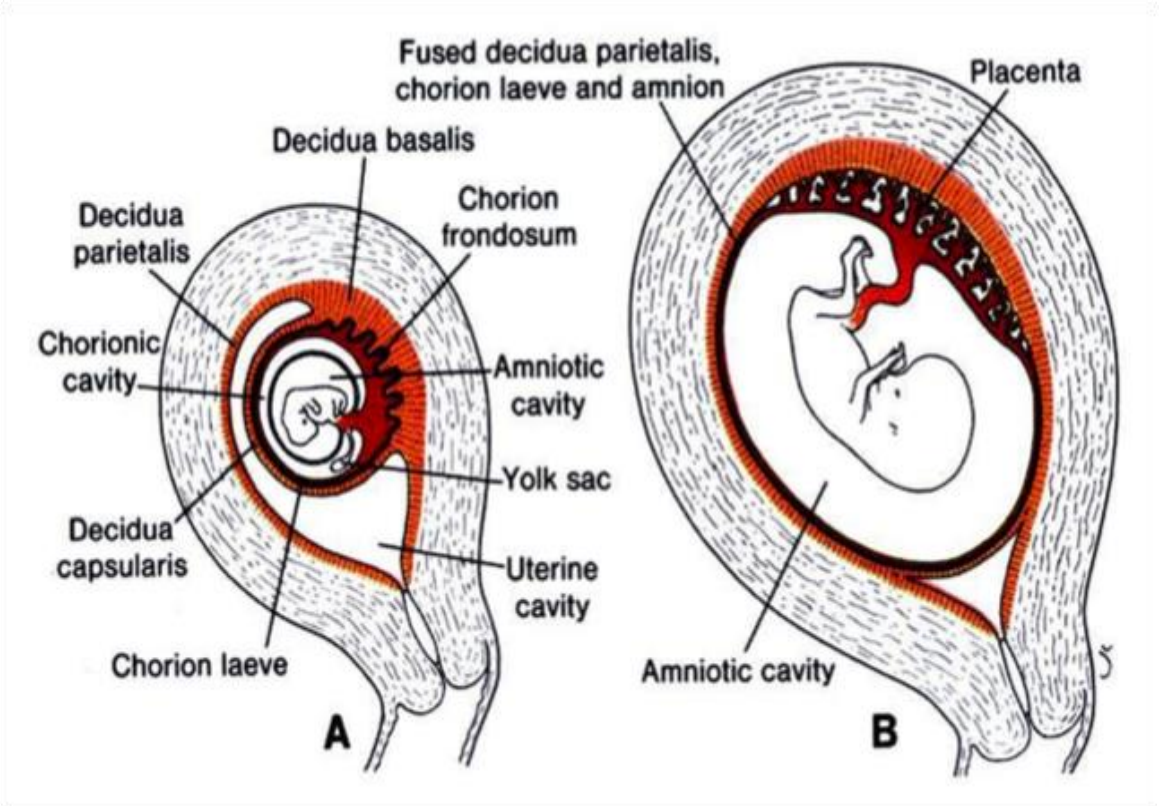
- It is the part of the decidua which covers the chorionic vesicle , **except the embryonic pole .**

3. Decidua parietalis

- It is the part of the decidua which lines the uterine cavity.

★ **Fate of the decidua**

- ***Decidua basalis*** markedly **develops** and is invaded by the chorionic villi and to form the **maternal part of the placenta**.
- ***Deciduae capsularis and parietalis*** come in **contact** obliterating the uterine cavity. Finally they **degenerate** .



Decidua

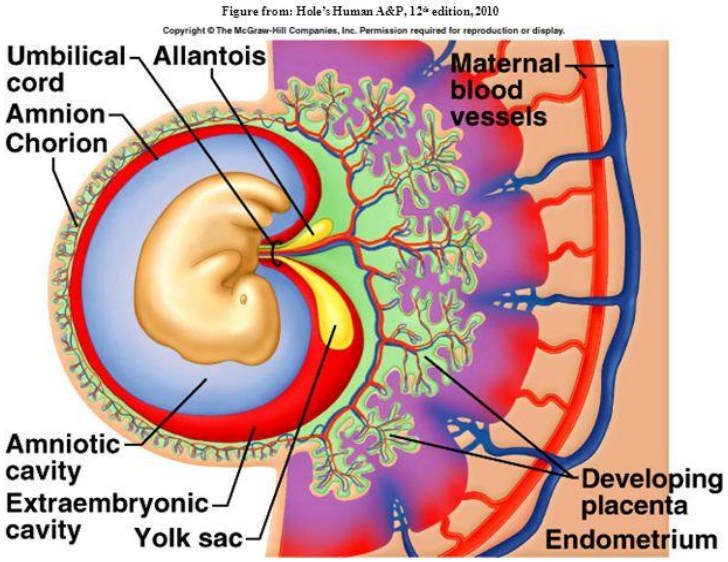
FETAL MEMBRANES

★ ***Definition:*** All the structures that are derived from the zygote and do not share in the formation of the body of the embryo. They are:

1. Chorion.
2. Amnion.
3. Umbilical cord
4. Yolk sac.

Embryonic Membranes

As amnion develops, it surrounds the embryo, and the umbilical cord begins to form from structures in the connecting stalk



16

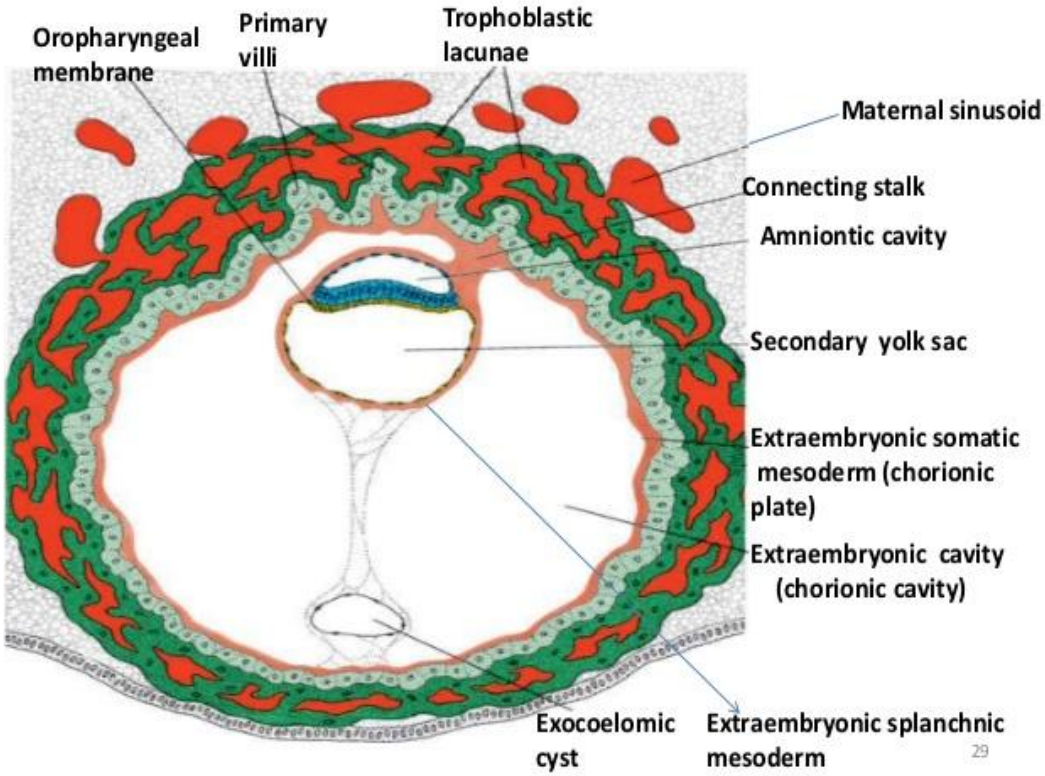
CHORION

★ At the 12th day the trophoblast + the linning extraembryonic somatopleuric mesoderm are called the **Chorion.** The blastocyst is called the ***Chorionic vesicle.***

★ **Structure** :The Chorion is composed of three layers:

- Syncytiotrophoblast :**outer** layer
- Cytotrophoblast: **middle** layer
- Extraembryonic mesoderm: **inner** layer

Formation of chorion



★ The Chorion is formed of two parts:

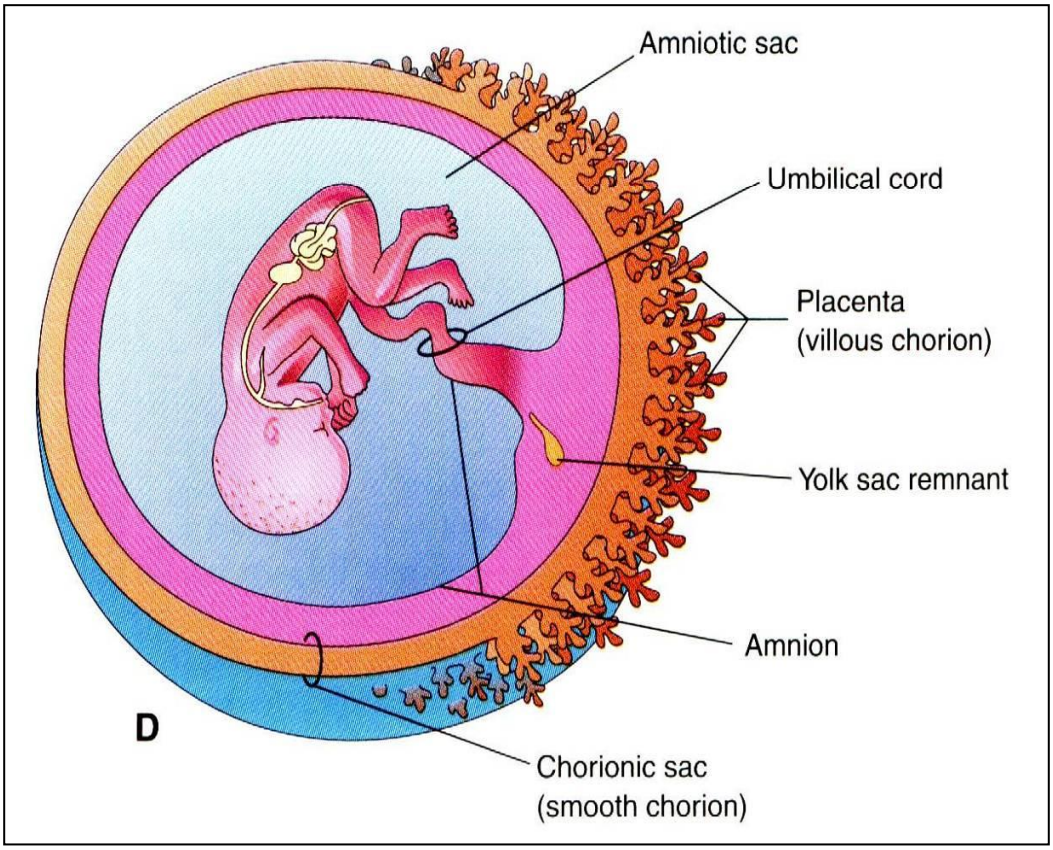
1) Chorion frondosum :

- It is the part of the chorion which cover the **embryonic pole** of the chorionic vesicle.
- The villi in this part develop , **enlarge and branch** (tertiary , stem ,free and anchoring villi) to form the **fetal part of the placenta**.

2)Chorion leave :

- It is the part of the Chorion which cover the chorionic vesicle **except embryonic pole** .
- The villi in this part **degenerate** and the surface of the chorionic vesicle appears smooth.

★ Mention **types and development of chrionic villi** : (as before)



Parts of Chorion

THE PLACENTA

★ It is the **vital organ** which is the respiratory , nutritive , excretory , protective and endocrinal organ **for the fetus** .

★ **MORPHOLOGY *:***

- **Shape**: discoid
- **Diameter**: 15–25 cm
- **Thickness**: 3 cm in the center but thinner at the periphery .
- **Weight**: 500–600 gram.
- It covers about 15–30% of the internal surface of the uterus.

★ **Surfaces*:***

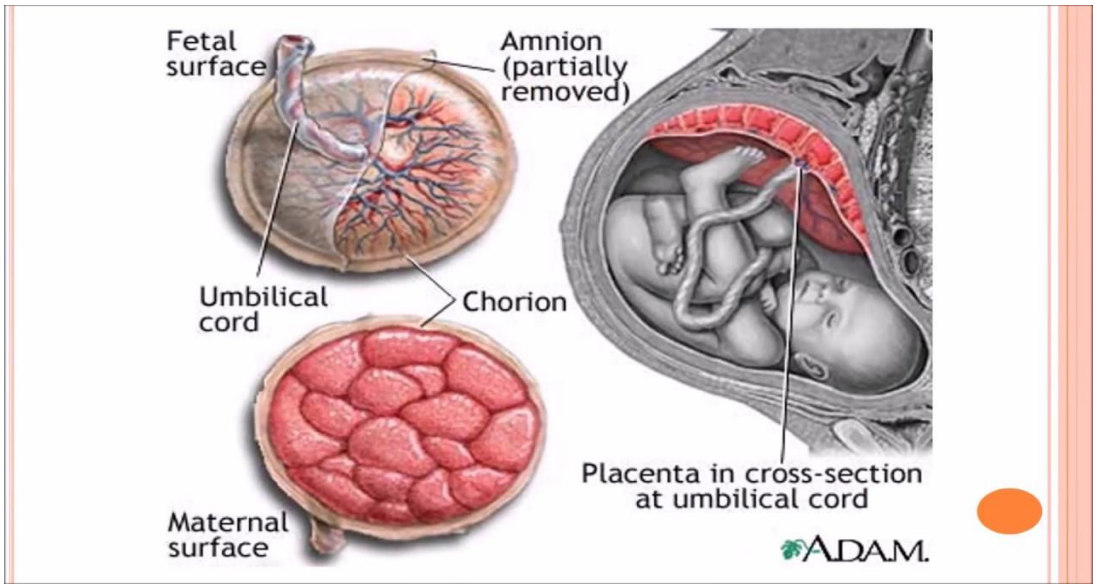
a. ***Fetal* surface** is **flat** , **smooth**, covered by **amnion** and shows the attachment of the umbilical **cord** near its center.

b. ***Maternal* surface** which was attached to the **uterine wall**.

- It is **convex** divided by **grooves** formed by **decidual septa** into areas called **cotyledons.**

★ ***Components of the placenta :***

1. **Maternal component**: Decidua basalis
2. **Fetal component**: Chorion frondosum



★ **Structure of the placenta :**

1. **Chorionic plate**:
   - It is the area of chorion to which the **chorionic villi are attached** .
   - It is **formed of** :
     a. Amnion.
     b. Extra-embryonic mesoderm.
     c. Cytotrophoblast.

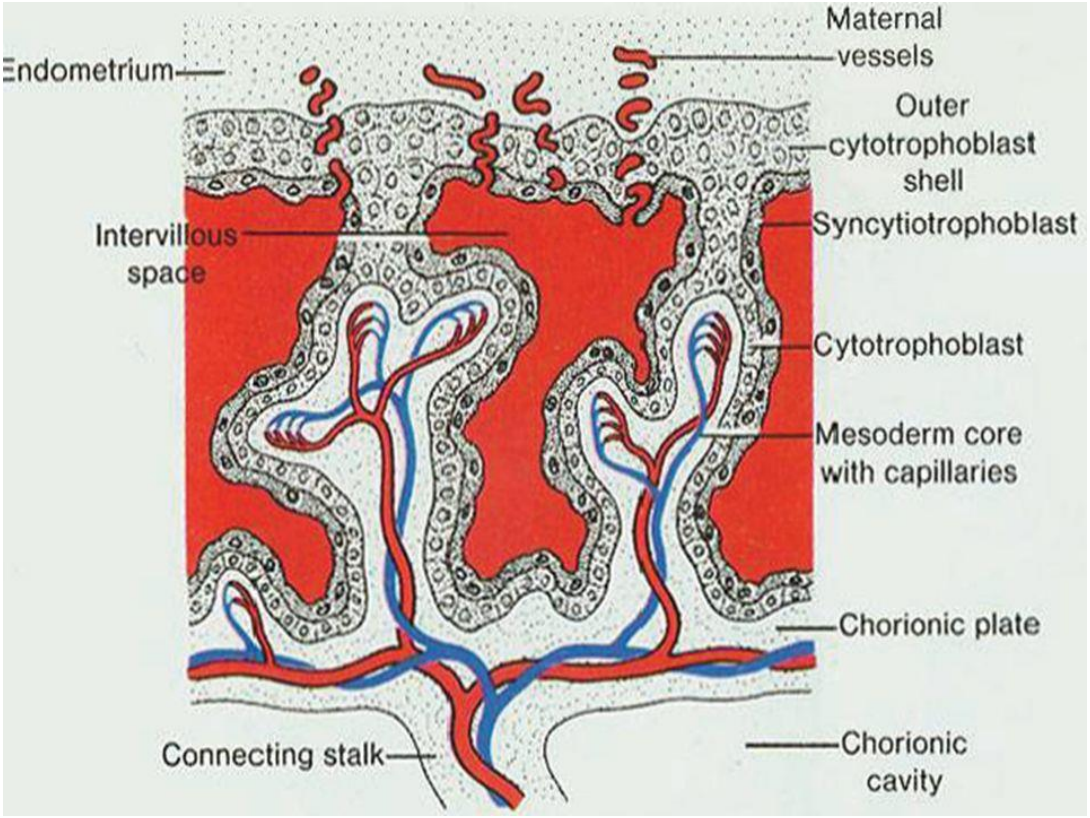
d. Syncytiotrophoblast

2. **Decidual plate: formed of**

a. Syncytiotrophoblast lining the intervillous space.

b. Outer cytotrophoblastic shell.

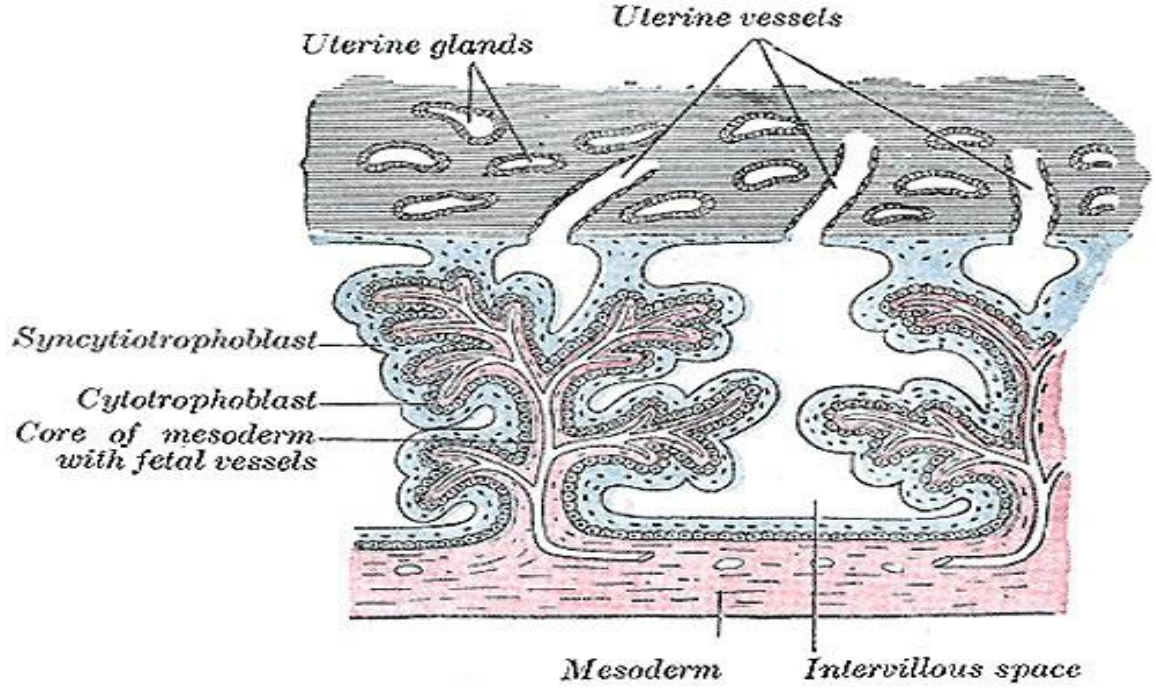
c. Maternal decidua basalis.



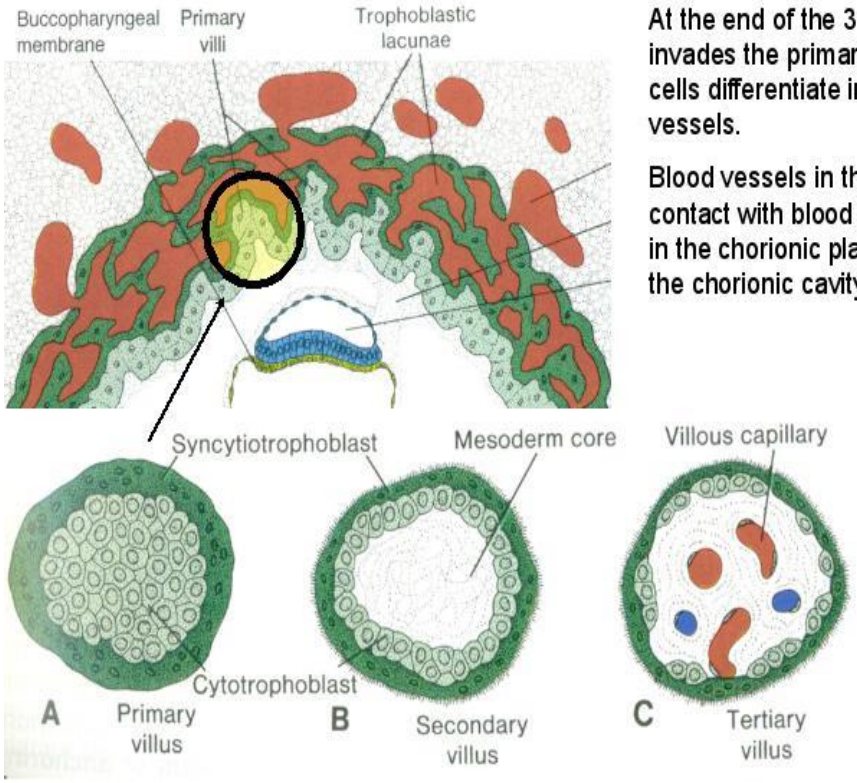
3. **Chorionic villi** (mentioned before in the 3rd. week of pregnancy)

- ***The tertiary or definitive villi:*** (syncytiotrophoblast + cytotrophoblast + core of mesoderm + blood capillaries)
  - Blood capillaries are formed in the extraembryonic mesoderm of the secondary villi to change them into tertiary villi.
  - These capillaries will be connected to the **chorionic vessels** , in the chorionic plate , which are branches of **umbilical vessels** .

- ***Outer cytotrophoblastic shell*** is formed by penetration of the cytotrophblast into the overlying syncytium until it reaches the maternal endometrium . The cytotrophoblastic cells of one villous establish contact with similar extensions of the neighboring villi forming the cytotrophoblastic shell.
- ***Stem villi*** are those **attached** to the chorionic plate .
- ***Anchoring villi*** are those which extend to the ***decidua basalis*** (endometrium forming the maternal part of the placenta) to **fix** the chorionic vesicle to the uterine wall .
- ***Free , floating or absorbing villi*** :
  - Those are the side branches from the stem villi and float freely within maternal blood in the intervellous spaces .
  - At these villi exchange of nutrients and other factors will occur.

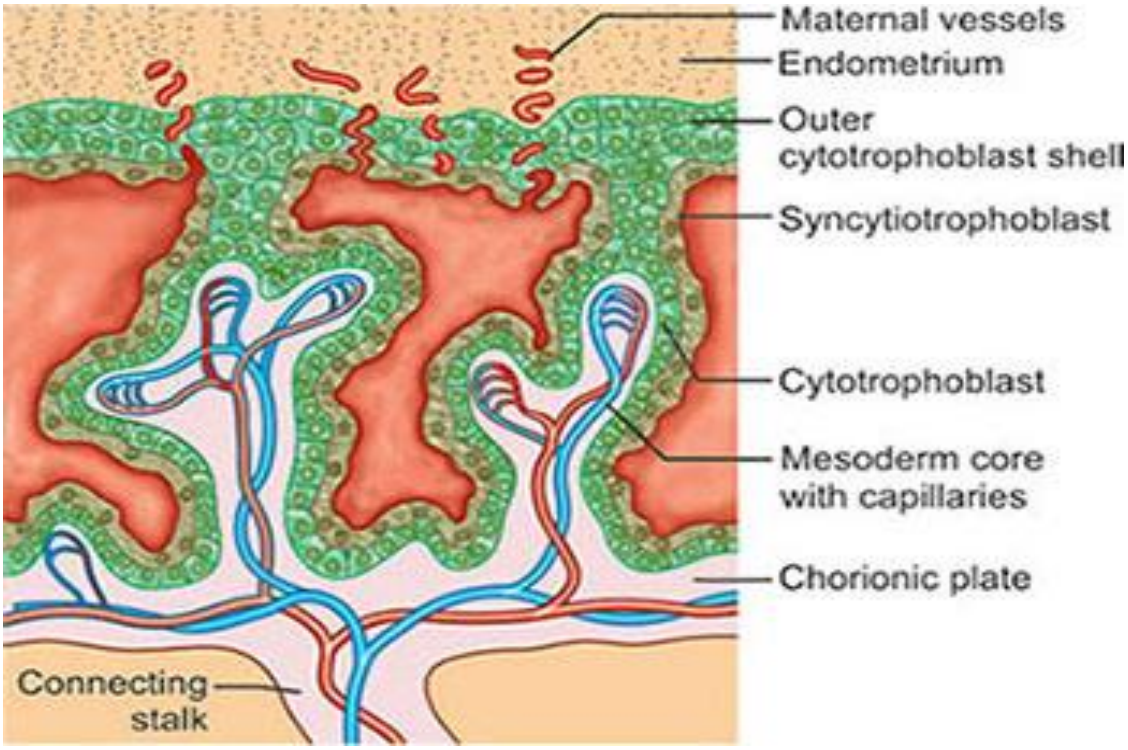


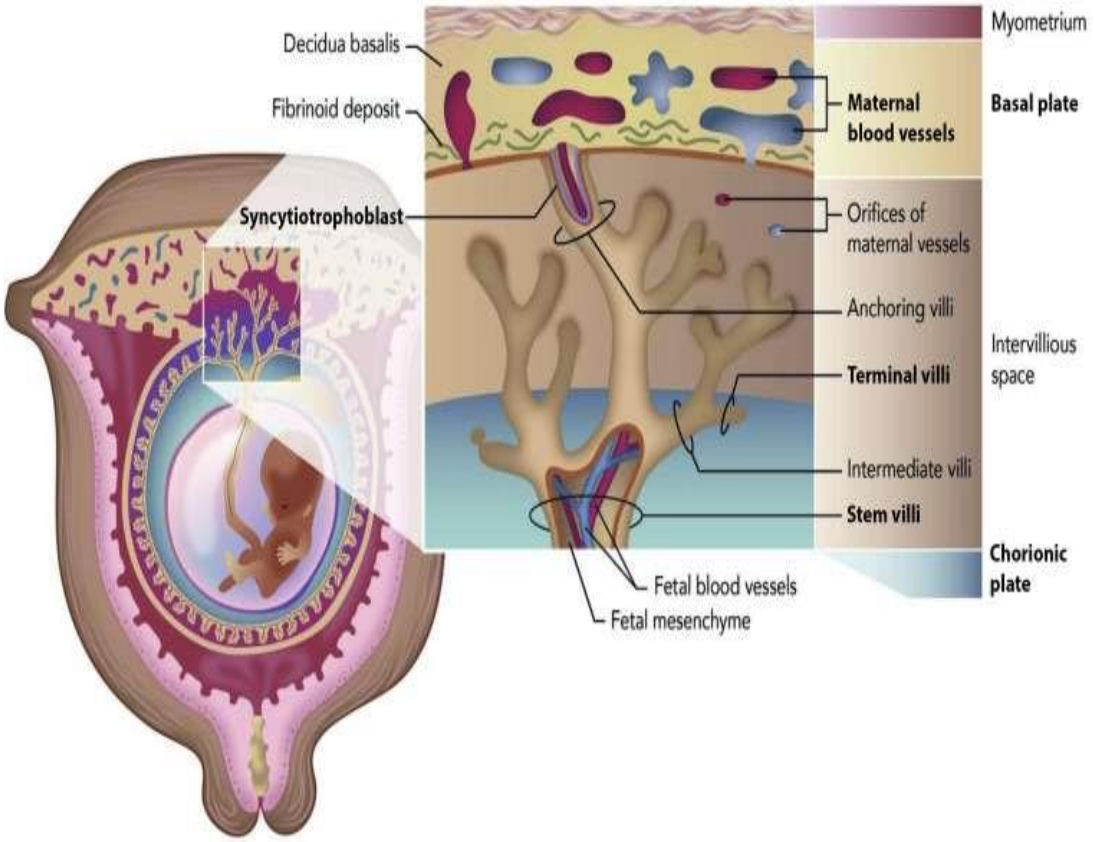
Trophoblast Development in the 3rd Week



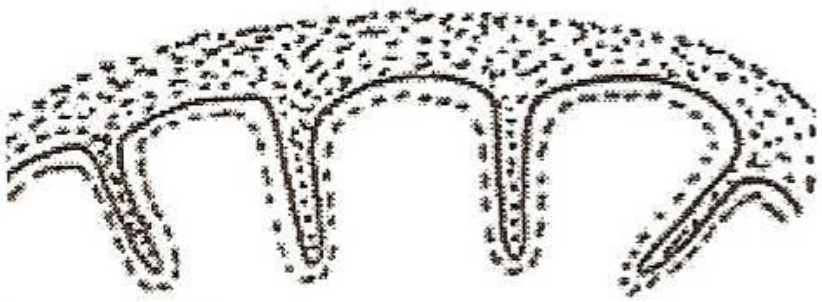
At the end of the 3rd week mesoderm invades the primary villus and those cells differentiate into small blood vessels.

Blood vessels in the villus will make contact with blood vessels that develop in the chorionic plate (the outer shell of the chorionic cavity).

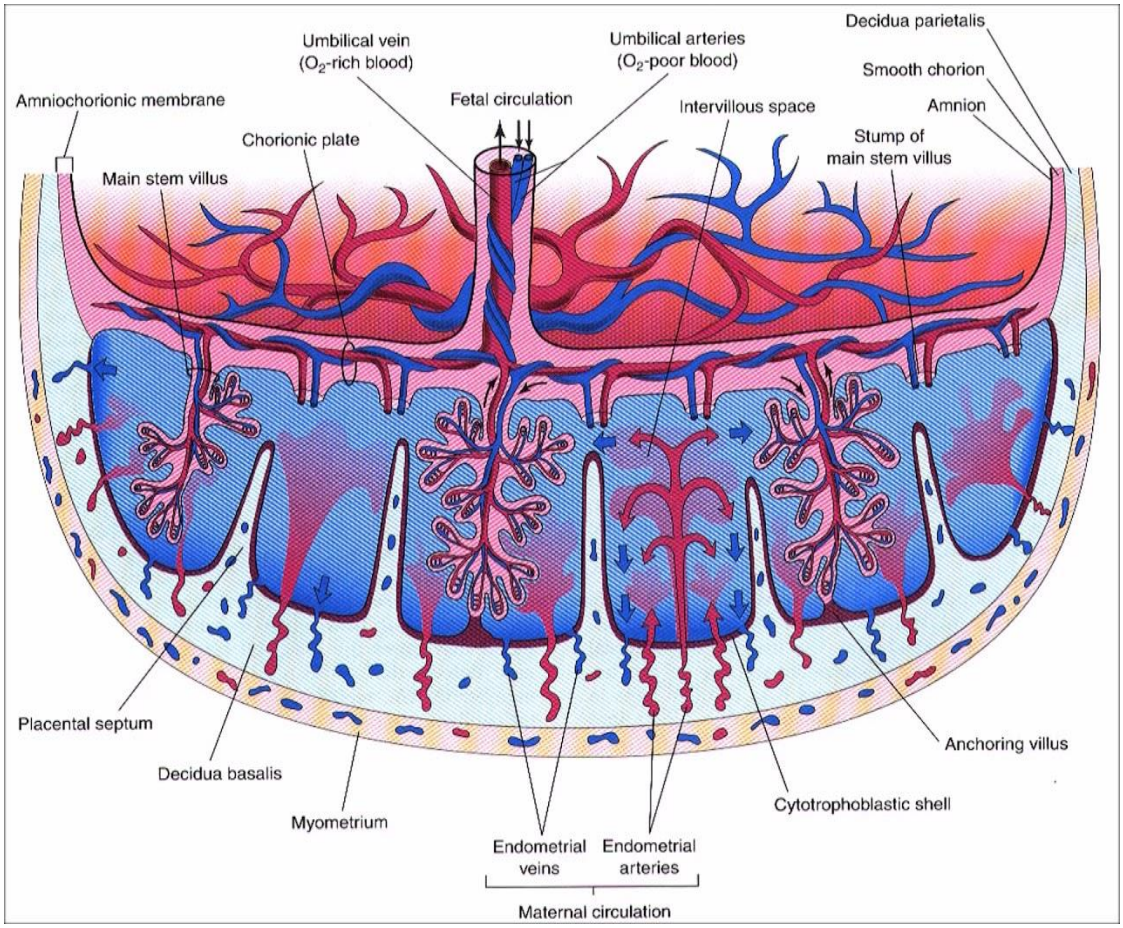


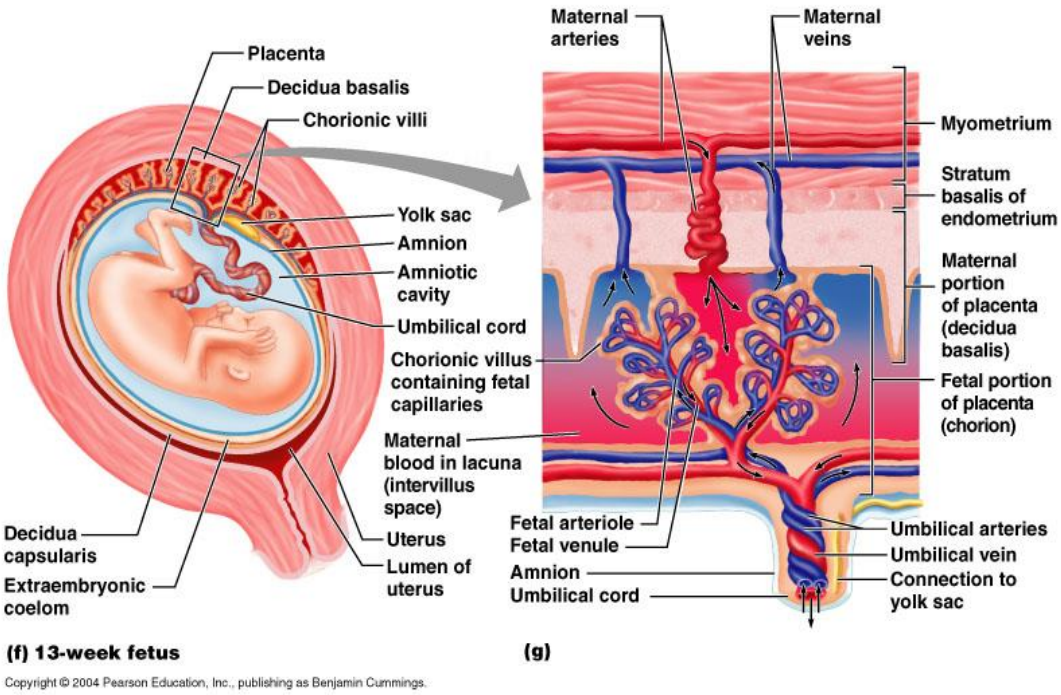


4. **Intervillous spaces :**
   - Due to enlargement of trophoblastic **lacunae** , intervillous spaces appear **between** the chorionic villi , with the chorionic plate forming their **floor** and decidual plate forming their **roof** .
   - They are filled with **maternal blood** .
5. **Decidual (placental) septa :**
   - These septa are formed by the **decidua basalis** during the 4th and 5th month .
   - They **project** into the intervillous spaces but do not reach the chorionic plate.
   - They have a core of **maternal** tissue and covered by **syncytial** cells.
   - They result in dividing the **dividing** the maternal surface of the placenta into a number of compartments called **cotyledons**.



Decidual septa



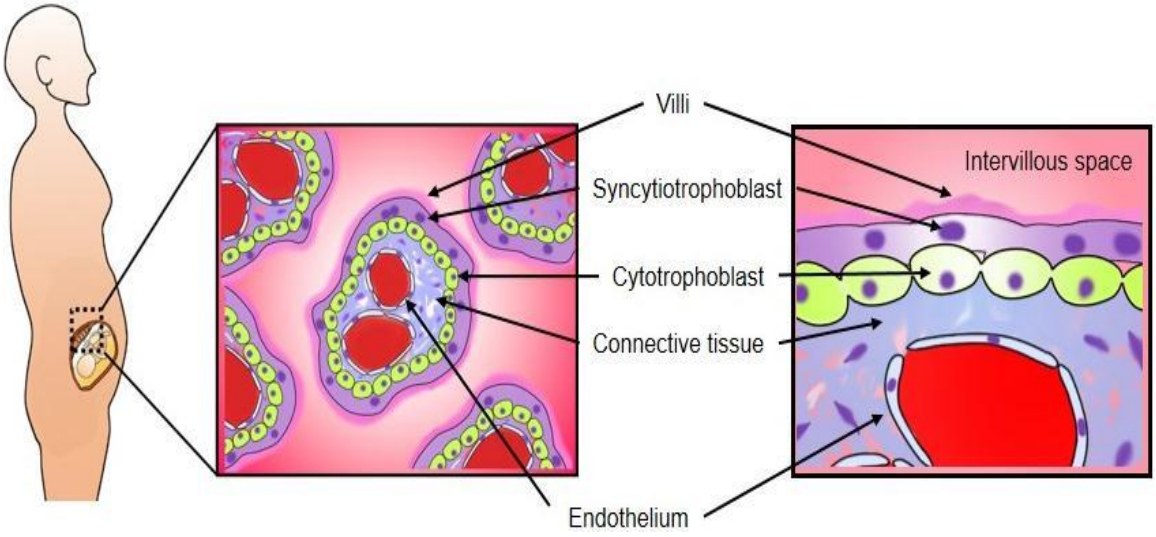


★ **Placental membrane (placental barrier):**

- ***It is a membrane formed by the tissues which separate the maternal from the fetal blood.***
- ***Early placental membrane***: It is formed of:
  1. The endothelium of the fetal vessels.
  2. The extraembryonic mesoderm of the villous.
  3. The cytotrophoblast.
  4. The syncytiotrophoblast.
- ***Late placental membrane*** (from the 4th month):
  - ***It becomes thinner to facilitate more exchange between fetus and mother.***
  - It is formed of:
    1. The endothelium of the fetal vessels.
    2. The syncytiotrophoblast.

- ***Functions:***

1. Permits gaseous , metabolites and nutritive **exchange** between the blood of the fetus and the blood of the mother.
2. **Separates** maternal from fetal blood.
3. **Prevents** transport most of (not all) **bacteria** and **viruses** from the mother to the baby.
4. Prevents transport of **damaging factors** and most of the **maternal hormones** from mother to fetus .
   - Some **synthetic hormones** like progestins and diethylstilbestrol can cross the placental barrier and cause **serious** effects on the embryo .

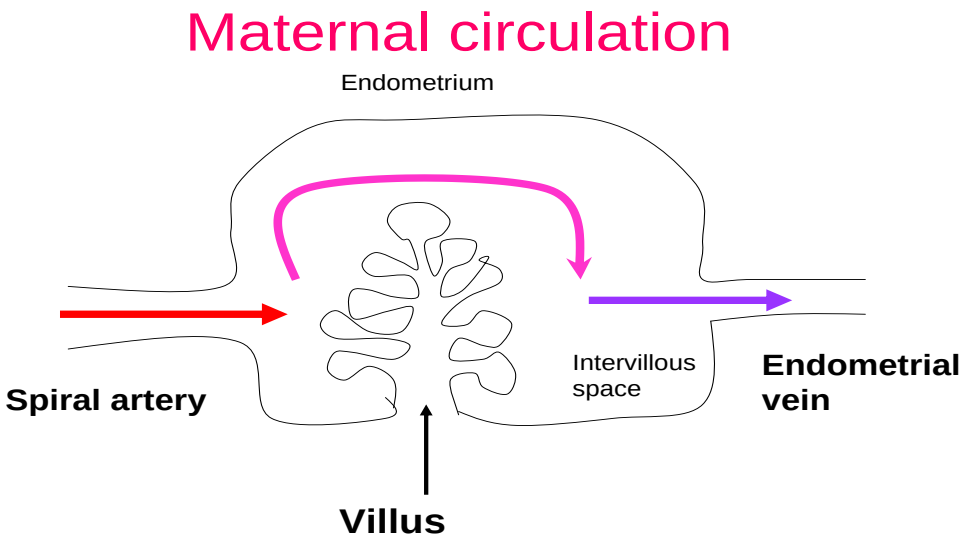


★ Placental circulation :

1)Maternal part:

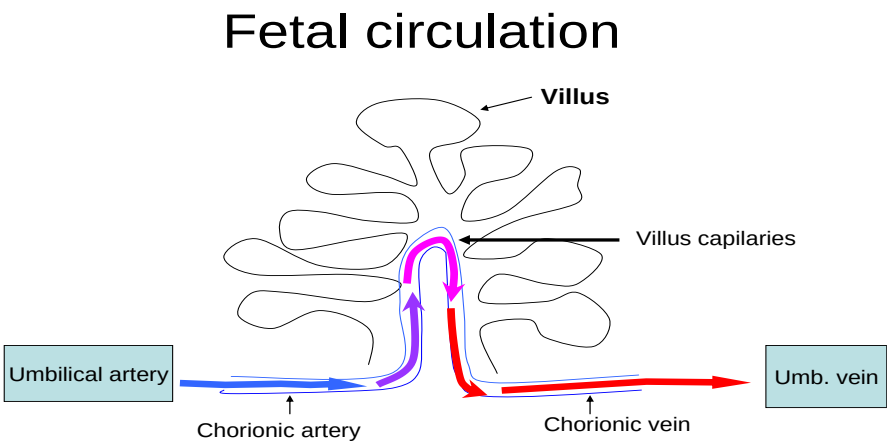
- Oxygenated maternal blood flows from the **spiral arterioles** of the decidua basalis (80 – 100 in each cotyledon) into the **intervillous spaces**.
- The **free villi** of the villous tree are floating in the oxygenated blood and **exchange** takes place.

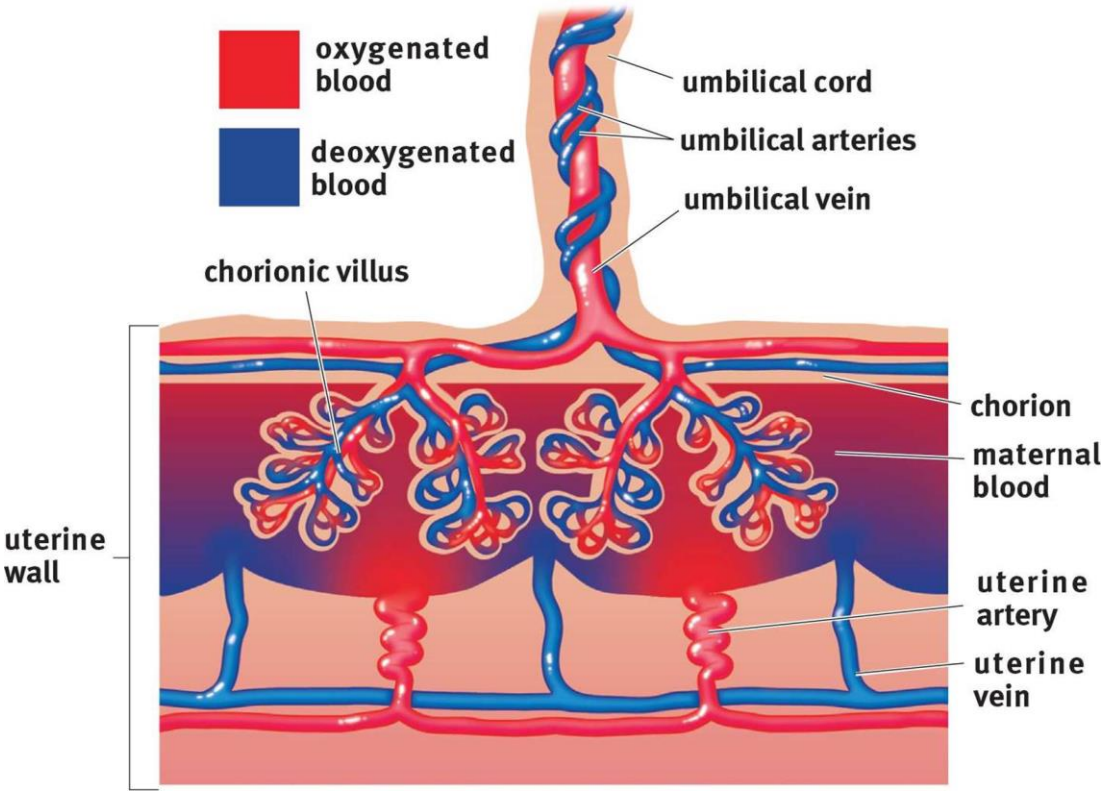
- The **deoxygenated** blood **flows back** from the chorionic plate towards the decidua basalis where it enters the **decidual veins** to reach the maternal circulation.

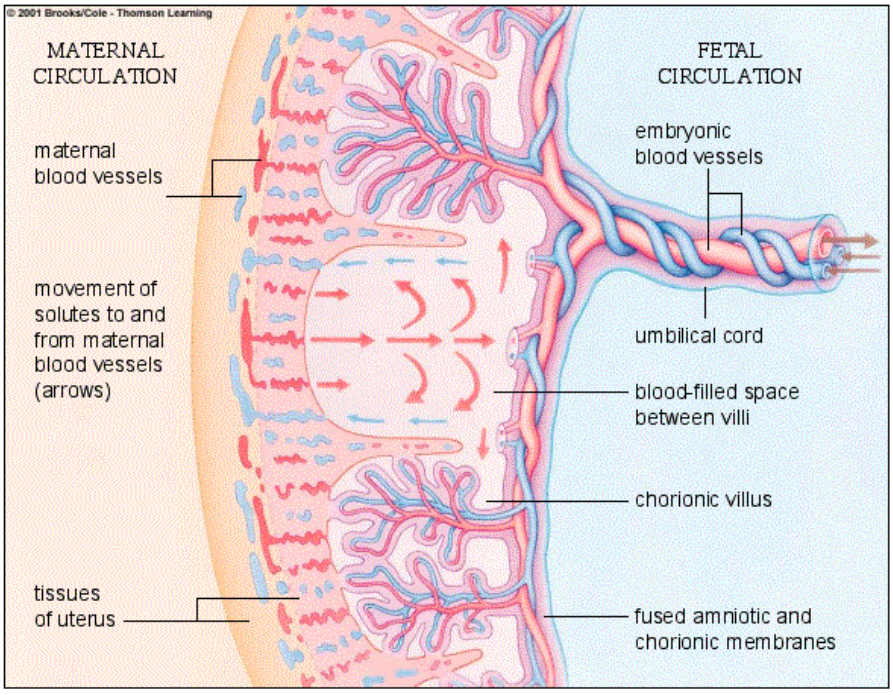


2)*Fetal part:*

- The **umbilical arteries** carry the deoxygenated venous blood from the fetus to the **chorionic vessels** and finally blood passes in the **villous capillaries** where exchange takes place.
- Oxygenated blood is drained back from the villi to the **chorionic veins** which are connected with the **umbilical vein.**




oxygenated blood
deoxygenated blood
umbilical cord
umbilical arteries
umbilical vein
chorionic villus
chorion
maternal blood
uterine wall
uterine artery
uterine vein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MATERNAL CIRCULATION
FETAL CIRCULATION
maternal blood vessels
embryonic blood vessels
movement of solutes to and from maternal blood vessels (arrows)
umbilical cord
blood-filled space between villi
chorionic villus
tissues of uterus
fused amniotic and chorionic membranes

★ **Functions of the placenta*:***

1. **Respiratory and excretory** functions : It allows exchange of metabolites and gases between maternal and fetal blood.
2. **Nutrition** : It allows passage of glucose , nutrient substances , vitamins & minerals from the maternal blood to the fetal blood .
3. **Protective function** :
   - Transmission of maternal antibodies so the fetus gains passive immunity against many infectious diseases since the 14th week.
   - Prevent passage of most (not all) micro-organisms to the fetus .
   - Certain viruses (eg. HIV & german measeles , rubella, cytomegalovirus, Coxackie, variola, varicella, & poliomyelitis) and bacteria (eg. Syphilis) can pass the placental barrier and infect the fetus .
4. **Production of hormones** as:
   - ***Progesterone*** is secreted from the end of 4th. month and it is essential to **maintain** pregnancy.
   - ***Estrogen*** : which stimulates **uterine growth** and development of the **mammary gland**. It increase sensitivity of uterus to **oxytocin** hormone at the end of pregnancy .
   - ***Human chorionic gonadotropins*** (HCG) which stimulate **corpus luteum of pregnancy** in the first 4 months of pregnancy and pass in urine (principle of **pregnancy test**) .
   - ***Melanin spreading hormone*** responsible for pigmentation of skin in pregnant females .
   - ***Somatomammotropin*** : a hormone that gives the fetus priority on maternal blood **glucose** .

★ **Abnormalities of the placenta:**

I- Abnormalities in position of the placenta :**(Placenta previa)**

- **Normal implantation** occurs in the upper part of posterior wall of the body or fundus of the uterus .
- If implantation occur in the lower segment of the uterus , the placenta develops in the lower uterine segment and called **Placenta previa** which may be one of the following:

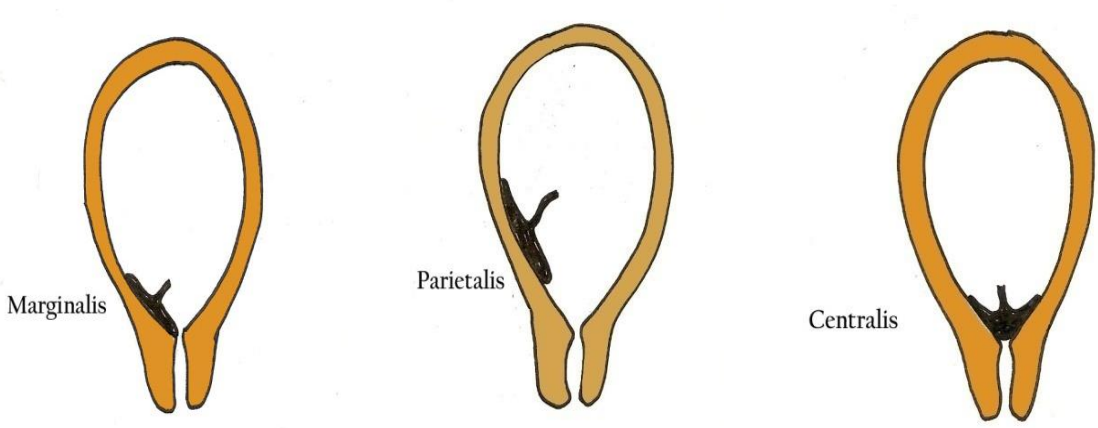
a) ***Placenta previa parietalis,*** the margin of the placenta does not reach the internal os of the uterus.

b) ***Placenta previa marginalis,*** the margin of the placenta reaches the internal os.

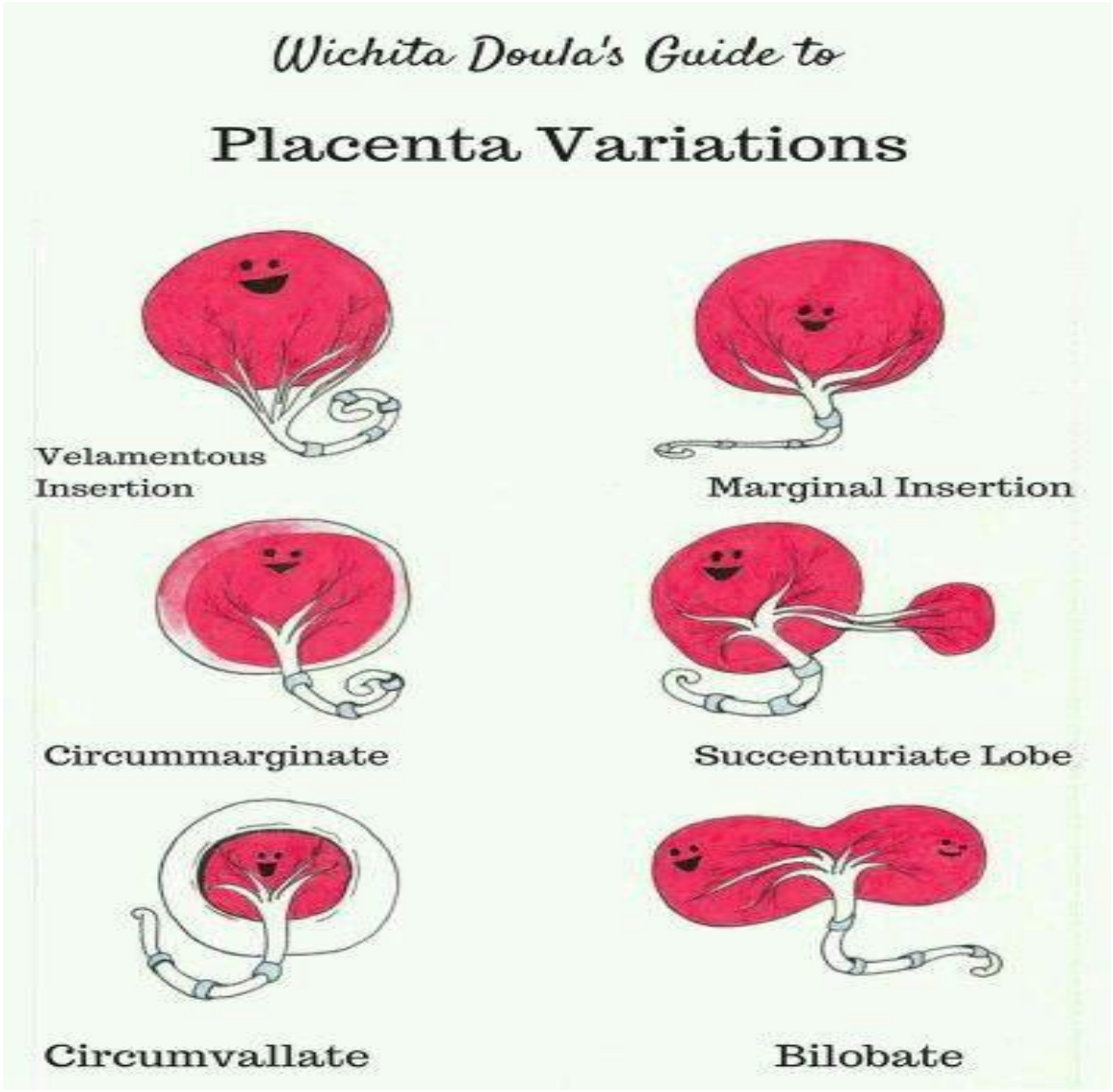
c) ***Placenta previa centralis,*** the center of the placenta overlies the internal os.

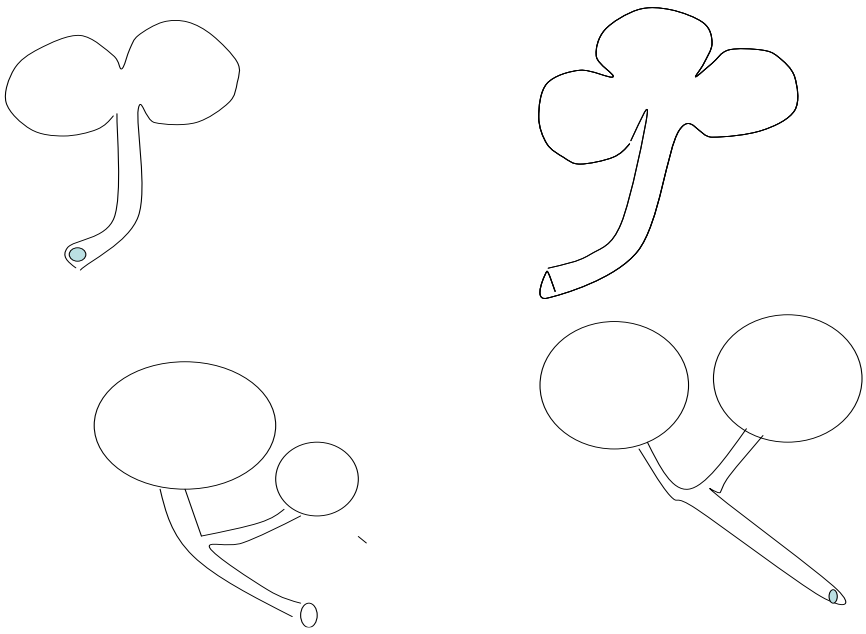
- Placenta previa is a **dangerous** condition leading to premature separation of the placenta from uterine wall before labor and hemorrhage .

Placenta Previa



II- Abnormalities in shape : The placenta may be bilobed or trilobed.





III- Abnormalities in number

- ***Twin placenta:*** A condition in which two identical placentae are attached to the umbilical cord.
- ***Accessory placenta****:* a condition in which an additional small placenta is attached to the cord.

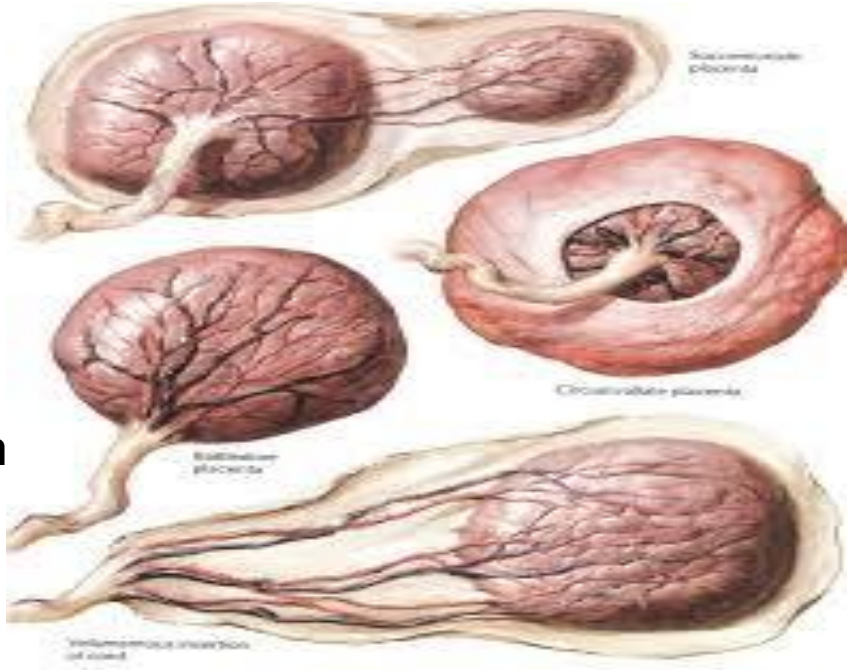
IV- Abnormal attachment of the placenta to the uterus :

- If the decidua basalis is poorly developed the chorionic villi may reach the myometrium (**placenta accreta**) or invade the myometrium (**placenta increta**) .

V. Abnormalities in the attachment of the umbilical cord to the placenta

- Usually the cord is central and occasionally near the margin.
- Abnormally it is attached to the placenta through **a membrane in** which the vessels run to the placenta (***velamentous attachment***)
- It may be attached to the **placental margin** ***(Battle door placenta).***

Abnormalities of the Placenta



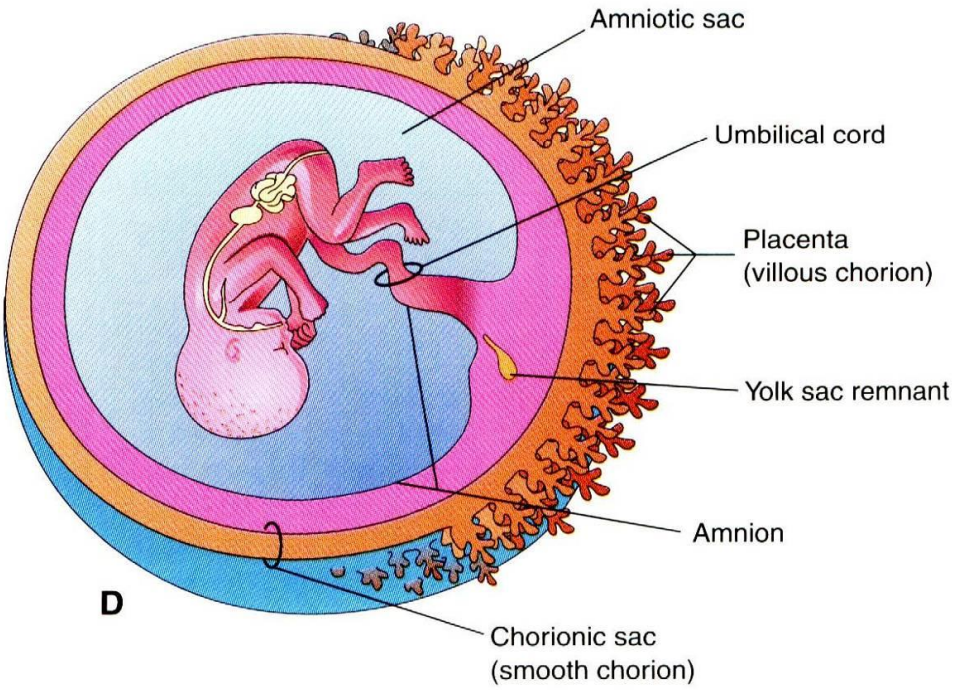
★ **Please see this excellent video:**

https://www.youtube.com/watch?v=bped-RVWsLk

AMNION

★ Is a large sac containing **amniotic fluid** in which the fetus is **suspended** by its umbilical cord.

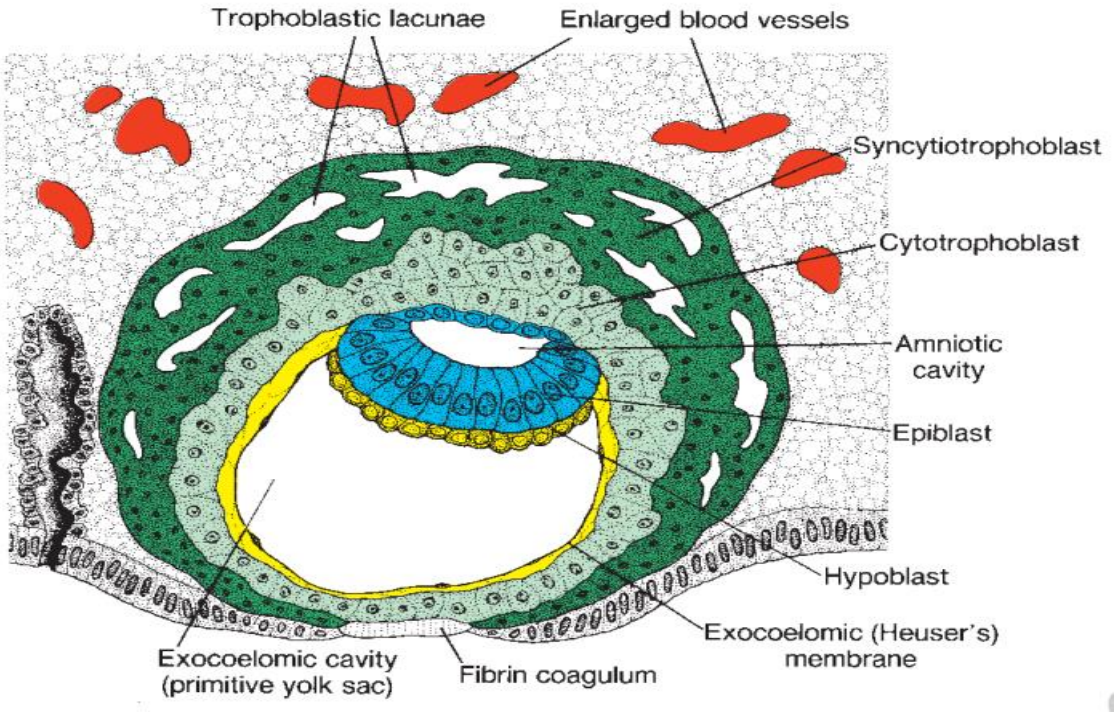
★ The cavity of this sac is called **amniotic cavity** .



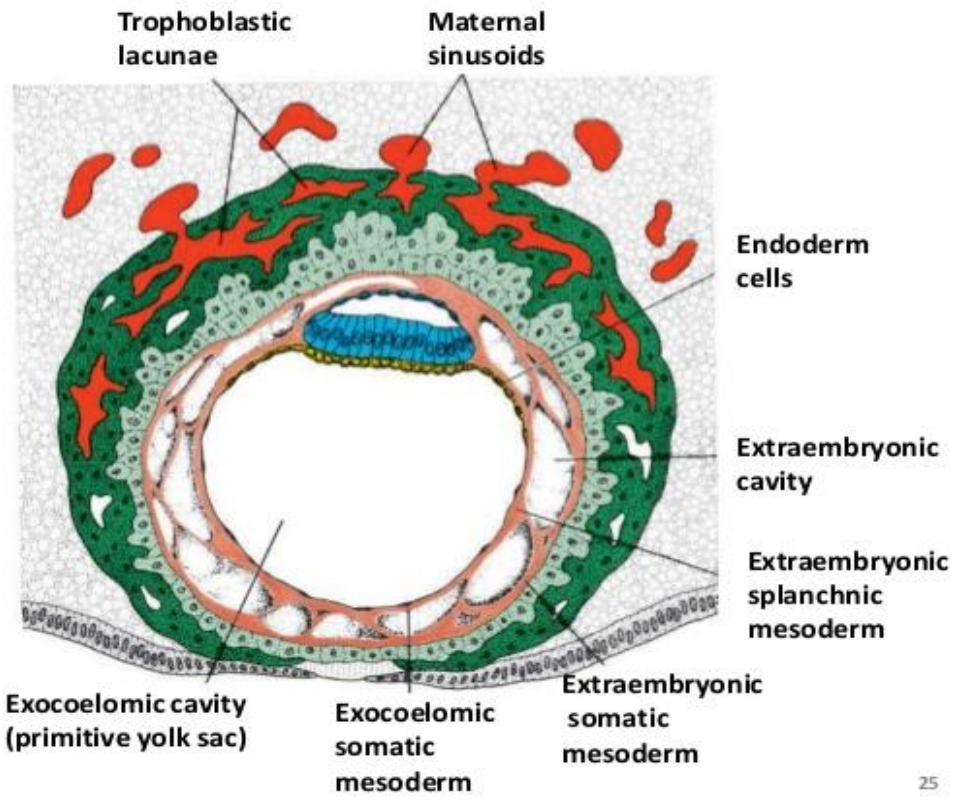
Amnion and amniotic fluid

★ **Formation** :

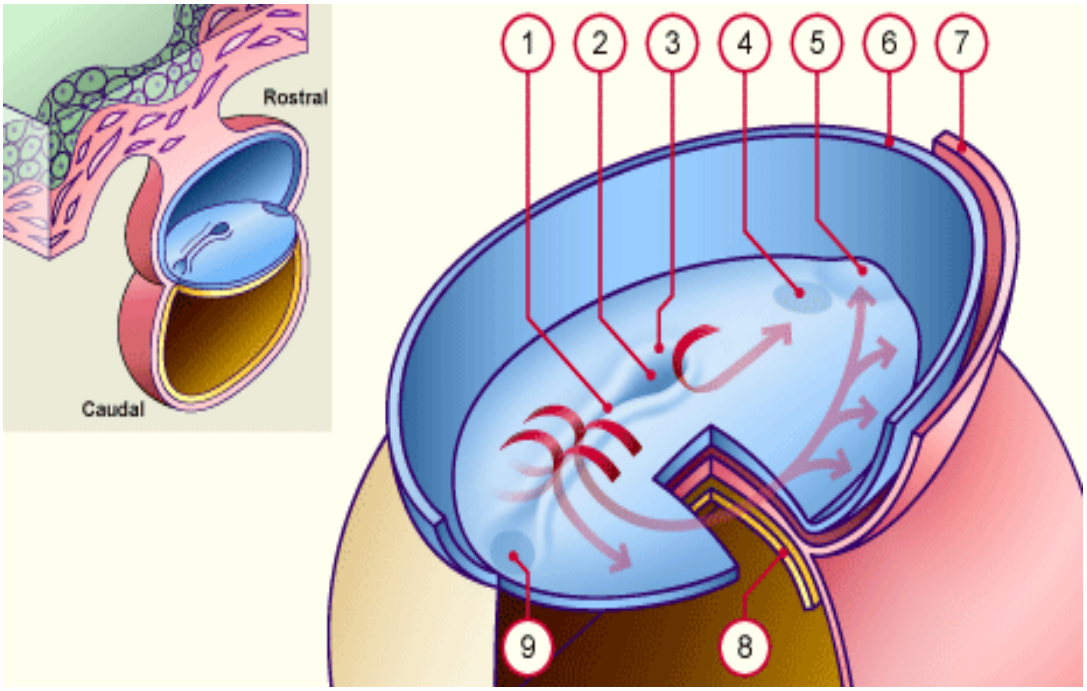
- It is the **first cavity** start to develop in the blastocyst (at the 8th day)
- It starts as **small spaces** , between the epiblast and the over lying trophoplast , which **coalesce** to form a cavity the called the amniotic cavity.



- The epiblast cells form a layer of flat cells called **amnioblasts** which form the **roof** of the amniotic cavity while its **floor** is formed by the epiblast .
- After development of **extra-embryonic mesoderm** and extr-embryonic coelom , the roof of the amniotic cavity becomes separated from the overlying trophoblast by a mass of extra-embryonic mesoderm called the **connecting stalk** (future umbilical cord).
- The amniotic cavity is now bounded by a membrane called the **amnion** , formed of **amnioblasts** and extra-embryonic **mesoderm**
- The line of **meeting** between the amnioblasts and the ectoderm , at the margine of the embryonic disc is called the **amnio-ectodermal junction.**

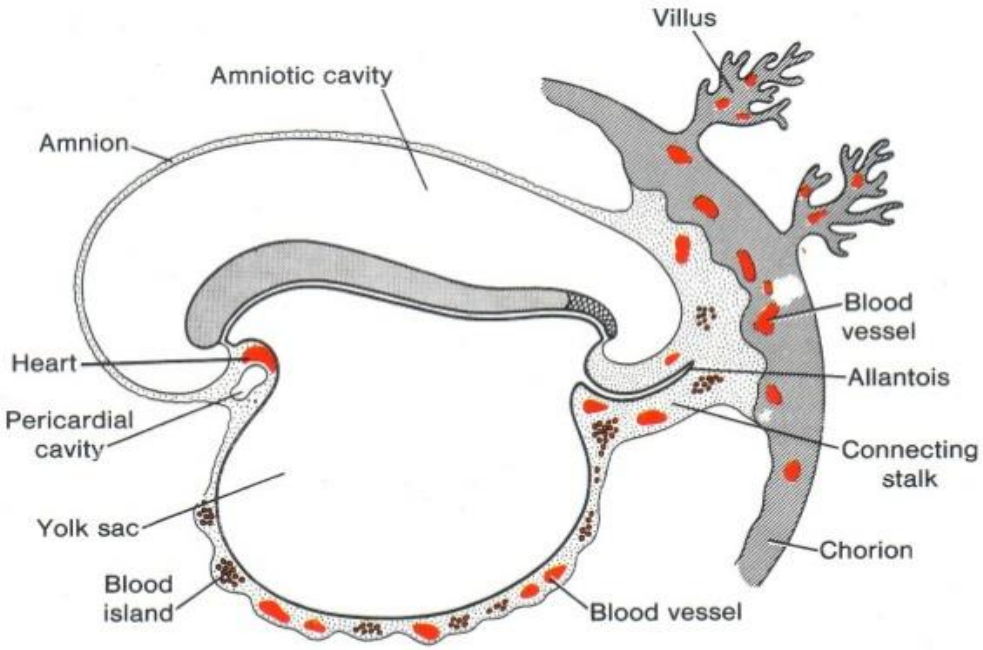


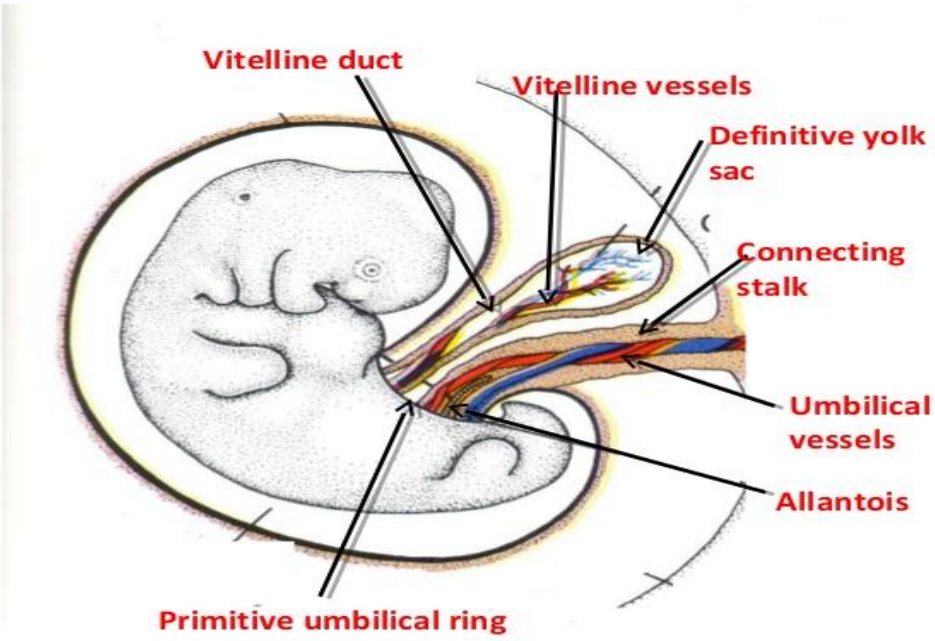
Amnio-ectodermal junction.



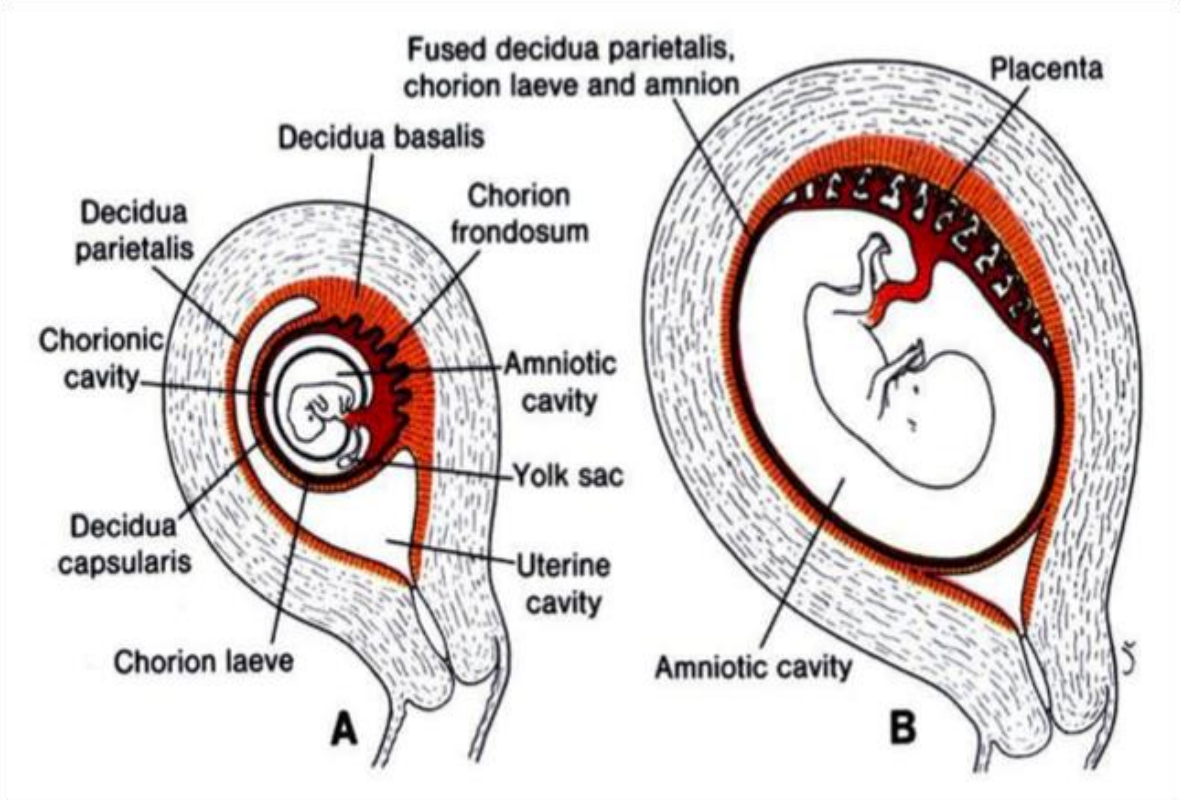
1.Primitive groove
2.Primitive pit
3.Primitive node
4.Oropharyngeal membrane
5.Cardiogenic plate
6.Sectional edge of amniotic membrane
7.Mesoderm
8.Endoderm
9.Future cloacal membrane
1+2+3 = primitive streak

- As a result of **folding** , the embryo bulges inside the amniotic cavity, and the amnio-ectodermal junction is **shifted** toward the ventral side of the body to form of a ring called the **primitive umbilical ring.**
- With excessive bulging of the embryo inside the amniotic cavity, the primitive umbilical ring is **narrowed and elongated** to form the **primitive umbilical cord** which is covered by a layer of amnion .





- At the end of **3rd month** the amniotic cavity **surrounds** the embryo almost completely (except umbilicus) and comes in contact with the chorion (obliterating chorionic cavity) to form the **amnio-chorionic membrane ,** (covered with the decidua capsularis) , which comes in contact with the decidua parietalis, thus the uterine cavity is obliterated and the amnion occupies the inside of the uterus.



★ ***The amniotic fluid:***

- ***Definition***: It is a clear watery sterile fluid secreted by the amnioblast and fills the amniotic cavity .
- ***Amount:*** 1 – 1.5 liters at the end of pregnancy .
- **Functions of amniotic fluid:**

I. At early pregnancy

1. It **absorbs** external jolts.

2. It prevents adherence of the embryo to the amniotic membrane.
3. It **prevents adherence** of the fetal parts (limbs or fingers).
4. It acts as a **heat insulator** so protects the embryo against high temperature if the mother is feverish.

II. At late pregnancy

1. It gives a space for **fetal movements** to develop its **muscles**.
2. It gives a space for accumulation of **urine**.
3. From the beginning of the 5th month, the fetus **swallows** the amniotic fluid. By this swallowing the fetus learns the **suckling** which **develops** the musculature of the gut and its digestive glands.

III. During labor

1. It **protects** the baby from strong uterine contractions.
2. It helps **dilatation of the cervix** of the uterus by formation of the fore bag of water which has a high hydrostatic pressure.
3. The sterile amniotic fluid **washes the vagina** just before delivery after rupture of the amniotic membrane.
4. Rupture of the fore bag of water is a sure **sign of start of labor**.

★ **Abnormalities of the amniotic fluid:**

1. Polyhydramnios :

- **Increased** amount of amniotic fluid (more than 2 liters) may occur at the last weeks of pregnancy.
- It is idiopathic in 35% of cases but may be due to:

a. Maternal diabetes.

b. Congenital malformations .

2. Oligohydramnios :

- **Decreased** amount of amniotic fluid (may reach less than 1/2 liter) may occur at the last weeks of pregnancy.
- It may result from renal agenesis.

3. Premature rupture of the amniotic membrane:

- It is usually idiopathic. It is the commonest cause of preterm labor.

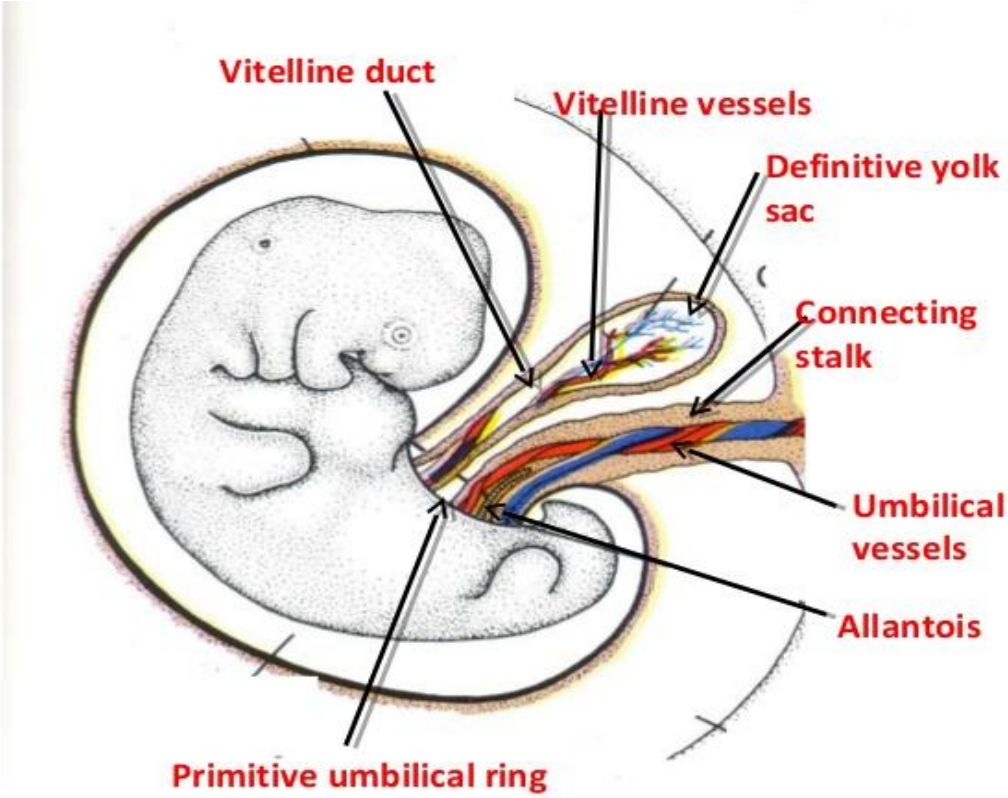
UMBILICAL CORD

★ It is a bundle of vessels , enclosed within a tubular sheath of amnion , which extends from the placenta to the umbilicus of the fetus .

★ **Development:**

***1. Primitive umbilical ring* :**

- The amnioblast covering the amniotic cavity is attached to the ectoderm along the margin of the germ disc by the **amnio-ectodermal junction.**
- As a result of folding , and the amnio-ectodermal junction also **shifts** towards the ventral aspect of the embryo to form the **primitive umbilical ring** which is bounded by the 4 embryonic fold .
- At the 5th week of development the following structures **pass through the ring:**
  - **a.** The **connecting stalk** containing the **allantois** and the vessels of the later will forms **umbilical vessels.**
  - b. **Vitellio-intestinal duct** and the **vitelline vessels**.
  - c. The **canal** connecting the intraembryonic to the extraembryonic coelomic cavities.



2. Primitive umbilical cord :

- With further development, the **amniotic cavity enlarges** rapidly causing **narrowing** & **elongation** of the primitive umbilical ring to form the **primitive umbilical cord** which includes :
- **Distally** the yolk sac and connecting stalk with their vessels.
- **More proximally** the cord contains an intestinal loop and the remnant of the allantois.
- By the **6th week**, intestinal loops protrude in the umbilical cord (**physiological umbilical hernia**).

3. Definitive umbilical cord :

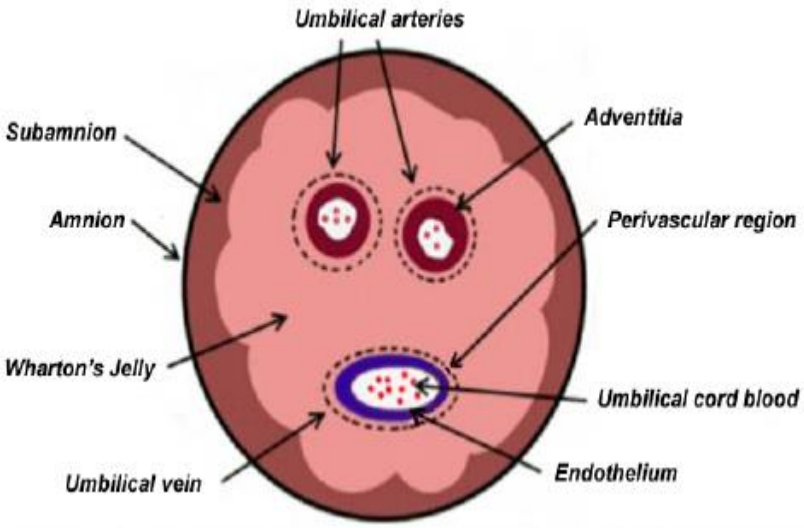
- At end of 3rd month , the physiological umbilical **hernia** is **reduced** into the body of the embryo , the **coelomic** cavity in the cord is **obliterated**.

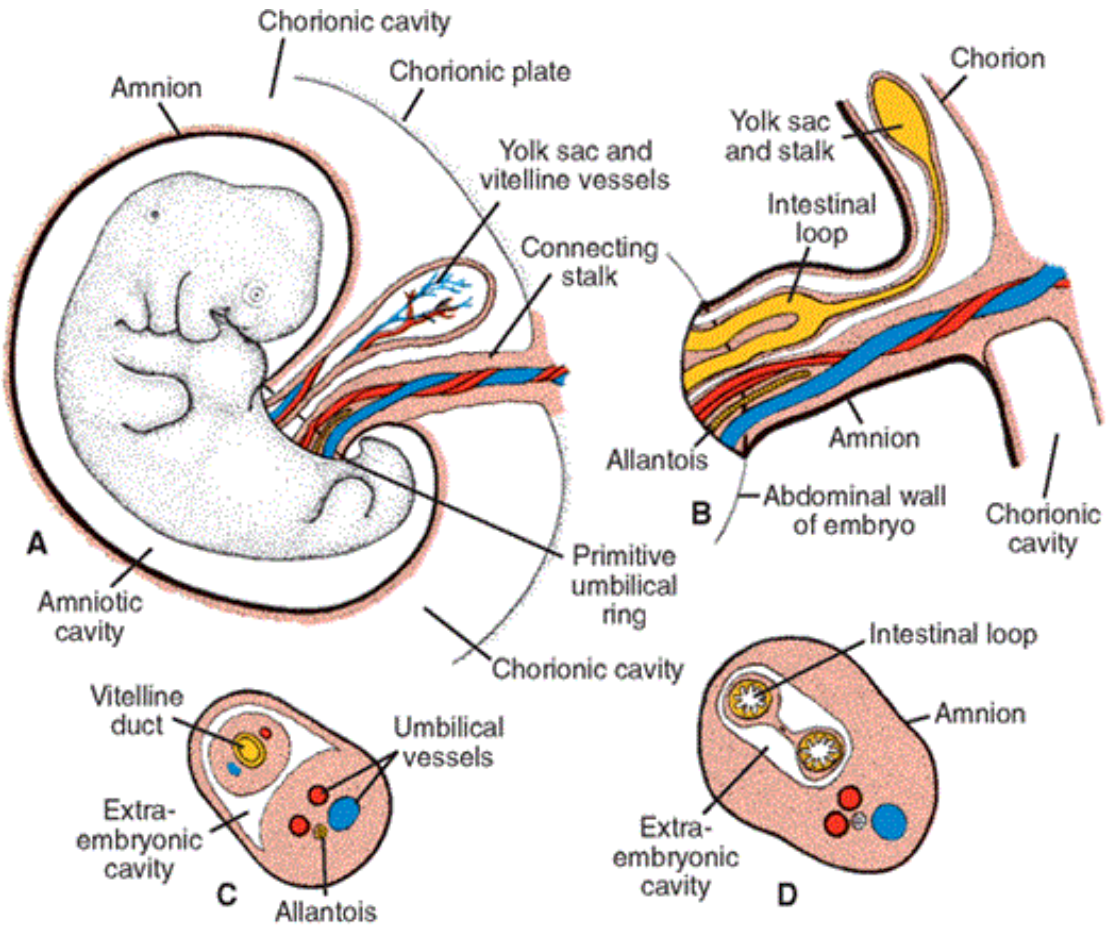
- The **connecting stalk** changes to mucoid material called **Wharton's jelly** which form the main bulk of the cord .
- The **allantois** is **obliterated** but its **vessel** is persist to form the **umbilical vessels** .
- The **yolk sac** and **vitellio-intestinal** duct are obliterated but intra-embryonic part of vetilline vessels develop many embryonic vessels.
- The **definitive umbilical cord** is now formed of the umbilical vessels (2 arteries and one vein) and the Wharton's jelly surrounded by a tube of amnion .

★ **Morphology of the umbilical cord:**

- **Length:** 50 – 60 cm.
- **Diameter:** 2 cm.
- **Shape:** tortuous, showing false knots.
- **Contents:** two arteries and one vein enclosed in Wharton's jelly and surrounded by amniotic membrane.

T.S. in umbilical cord

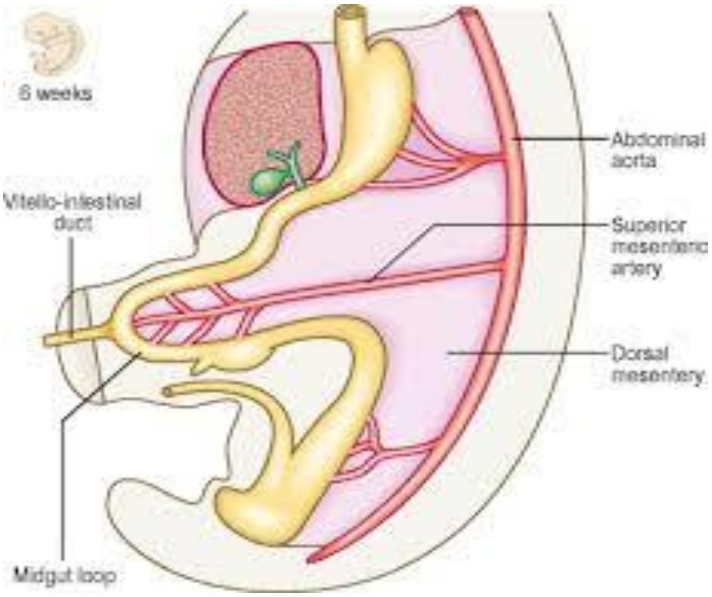




★ **Abnormalities of the umbilical cord:**

1. Extremely ***long*** cord:may ***encircle*** a part of the baby causing damage or forms ***true knots*** which result in occlusion of its vessels .
2. Extremely ***short*** cord which may result in premature ***separation*** of the ***placenta*** by pulling it from its attachments in the uterus.
3. Abnormal ***attachment*** to the placenta (marginal or velamentous)
4. Presence of ***one umbilical artery*** only.
5. ***Omphalocele:*** the presence of intestinal loops in the proximal part of the cord due to persistent and failure of reduction of physiological umbilical hernia.

Physiological umbilical hernia



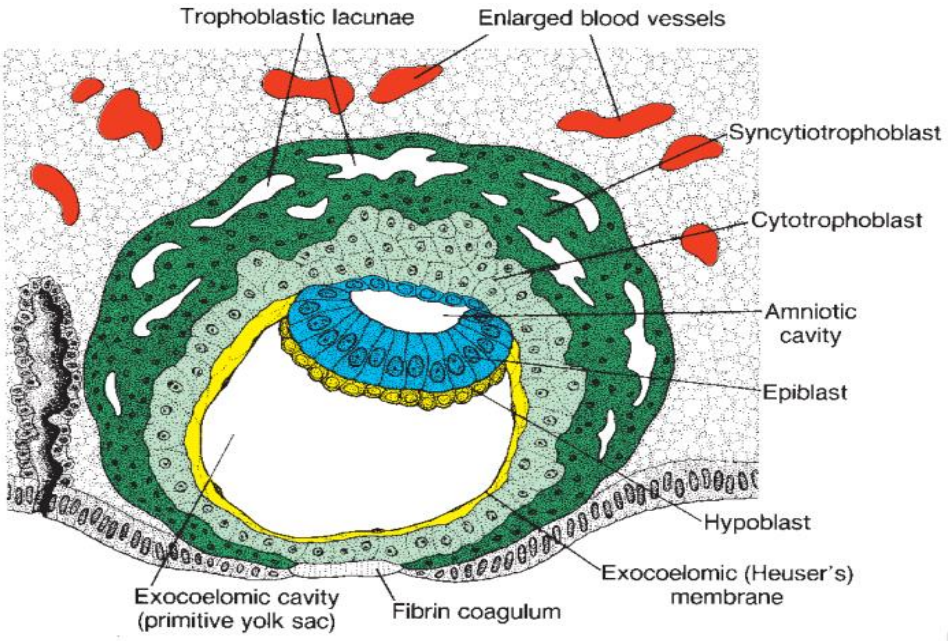
YOLK SAC

★ It is the cavity develops on the ventral aspect of the embryonic disc.

★ **Development:**

1. Primary yolk sac:

- It appears at the **9th** and 10th days.
- Flat cells from the hypoblast form **Heuser's membrane** which lines the inner surface of the blastocele .
- The original blastocele is now called the primary yolk sac.



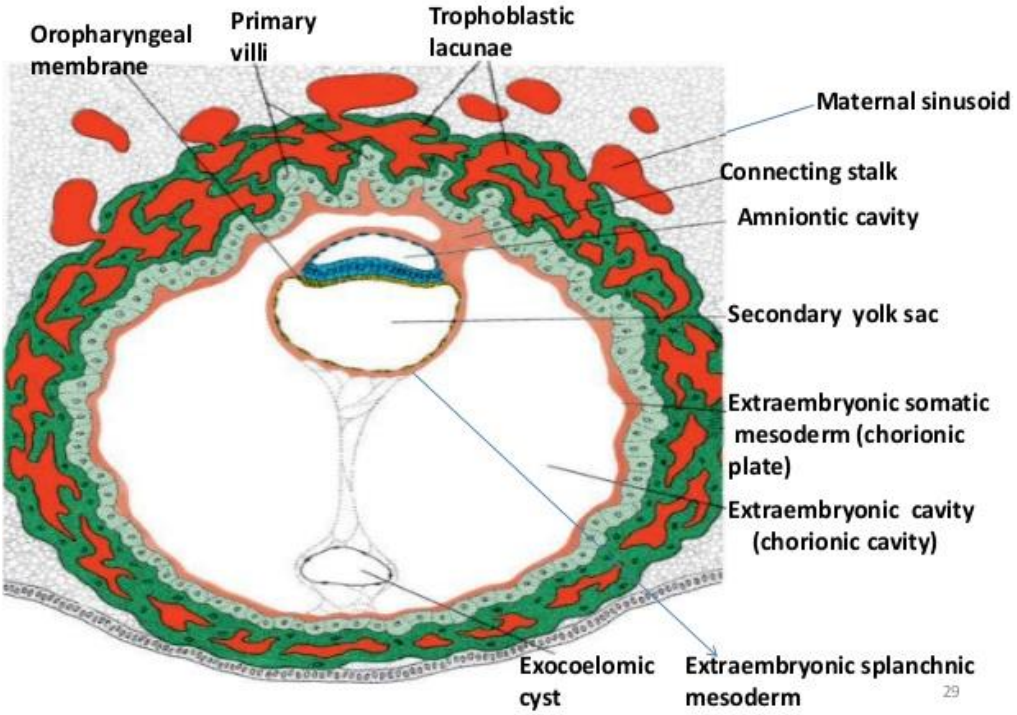
2. Secondary yolk sac:

- The hypoblast at the end of the 2nd week produces cells that migrate inside of Heuser's membrane to form a smaller cavity within the primary yolk sac known as the secondary yolk sac.

3. Definitive yolk sac:

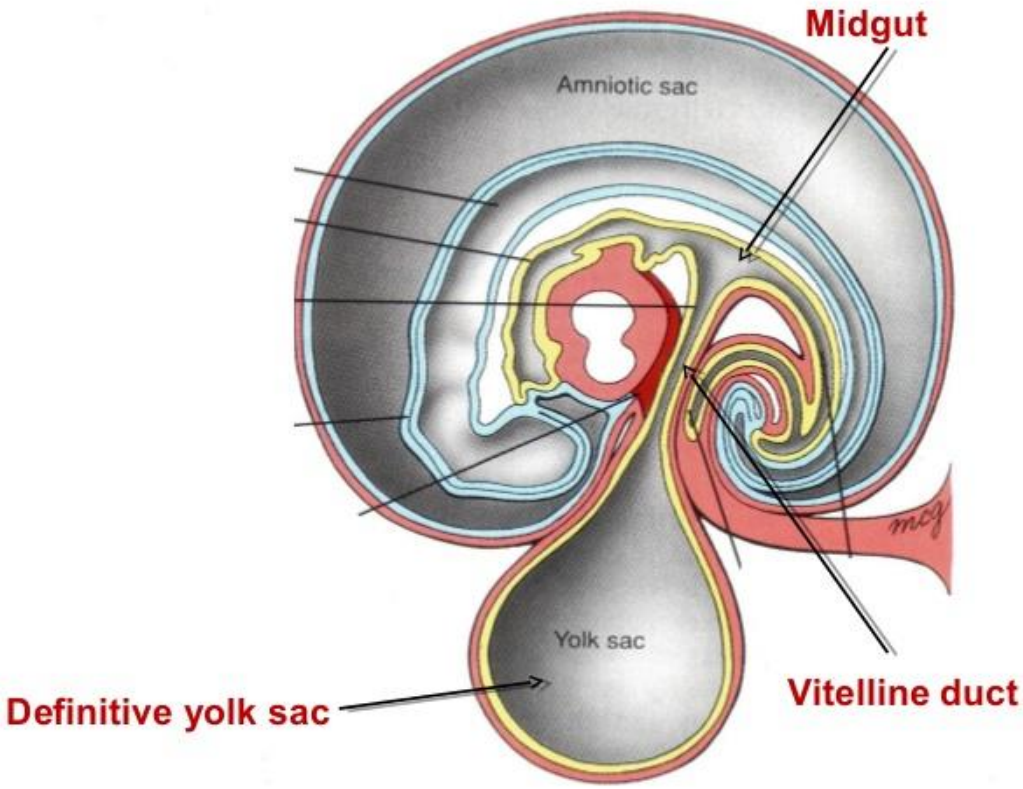
- During the **3rd week** the hypoblast is replaced by the **endoderm** which forms the roof of the yolk sac .
- As a result of **folding** , the secondary yolk sac is divided into :
  1- **The gut** :The upper part inside the embryo .
  2- **Definitive yolk sa**c : The lower part outside the embryo inside the primitive umbilical cord .
  3- **vitallo-intestinal duct** (yolk sac stalk) which present in the primitive umbilical cord and connects the midgut with the definitive yolk sac.

★ **Fate:** the definitive yolk sac and vitallo-intestinal duct are gradually disappear.



★ **Functions of the yolk sac**

1. Formation of the ***gut.***
2. From its caudal wall migrate the ***primordial germ cells*** to the developing gonad .
3. The **mesoderm covering** the wall of the yolk sac forms the ***blood cells*** (3-6 week of embryonic life) and the ***vitelline vessels***.
4. The intra-embryonic parts of the **vitelline vessels** form the single branches of the abdominal aorta, the portal and hepatic veins and the liver sinusoids.



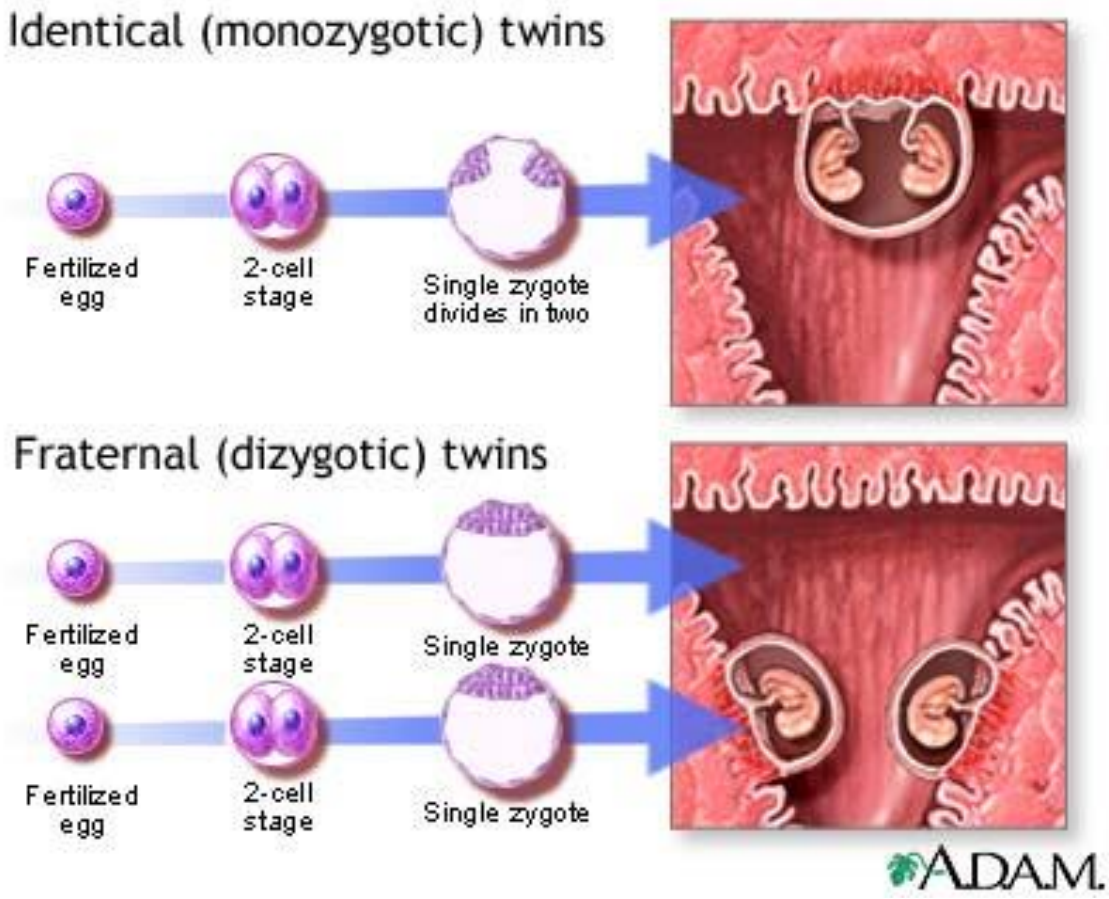
TWINS

★ **Definition:** Giving birth to more than one baby.

★ **Types of twining:**

I- Dizygotic (Fraternal) twins:

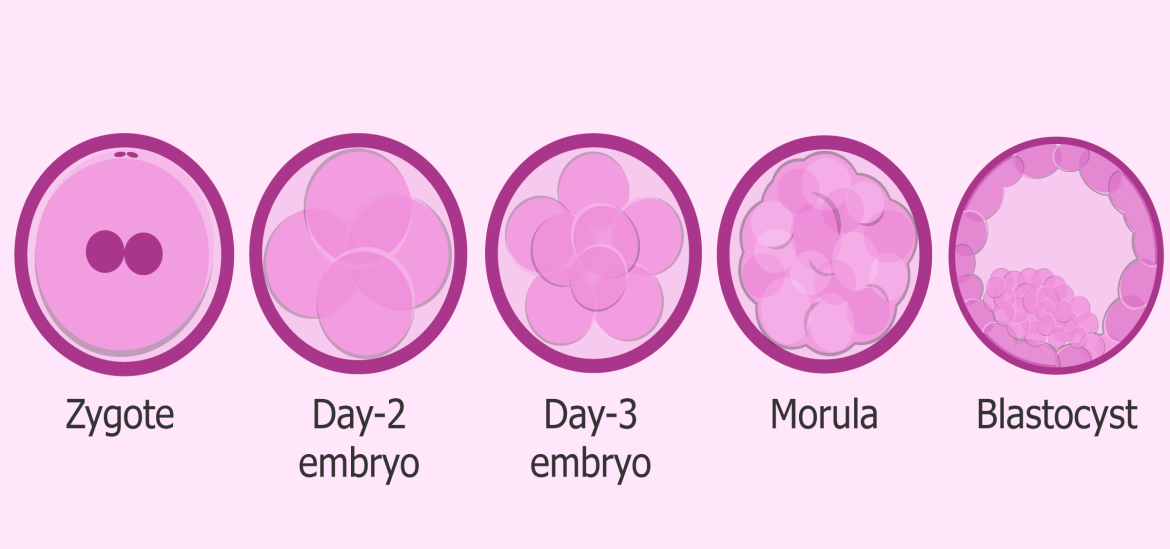
- This is the ***most common*** type of twins. Approximately ***two-thirds*** of twins are dizygotic, and their incidence is ***7-11 per 1000*** births.
- They result from simultaneous production of ***two oocytes*** and their fertilization by ***two different sperms***.
- ***Both zygotes implant individually*** in the uterus and each develops its own ***separate*** amnion, chorionic sac and placenta.
- Since both zygotes have a totally ***different genetic*** constitution, the off springs have ***different features*** .
- They may or may not have the same sex.



II- Monozygotic (Identical) twins:

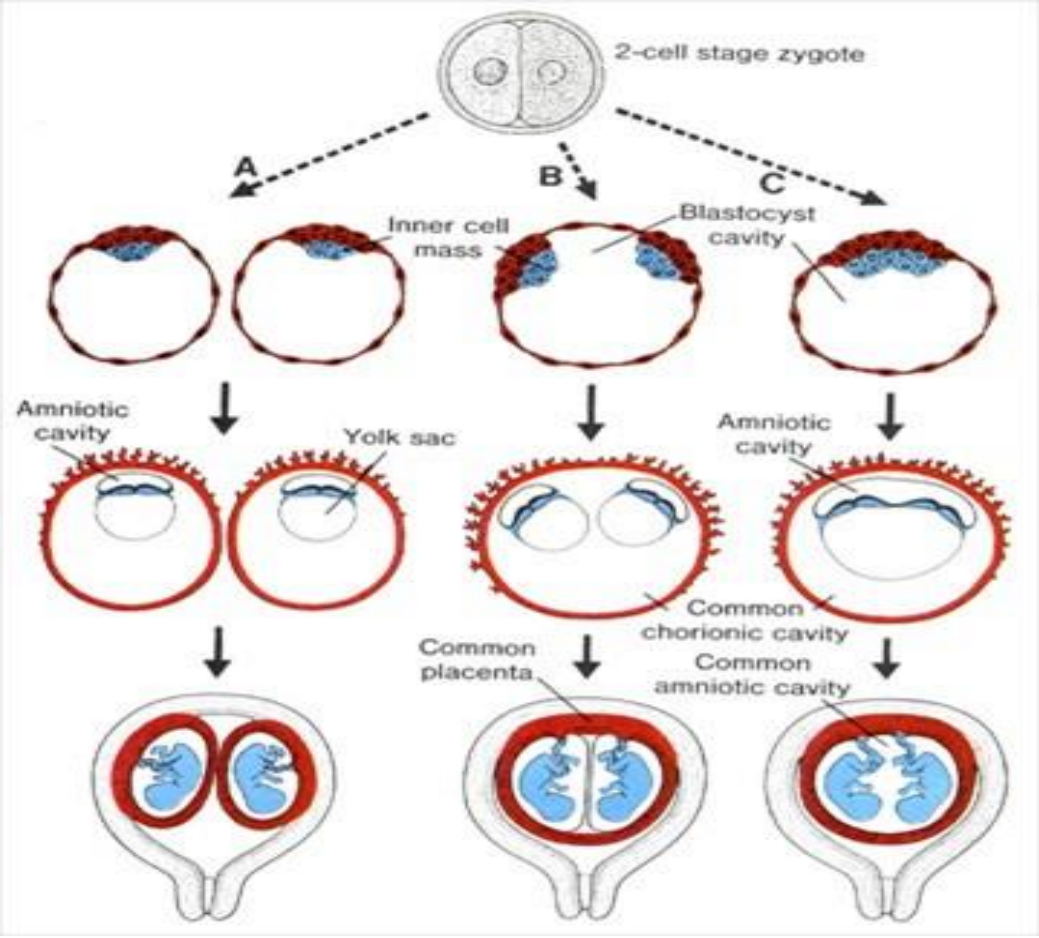
- Their incidence is 3-4 per 1000 births.
- They develop from a ***single fertilized ovum*** but the resulting ***zygote splits*** into two. This splitting occurs at ***various stages*** of the zygote development.
- Since the monozygotic twins arise from one ovum and one sperm, they have the ***same genetic*** constitution , they are of the same ***sex*** and they are identical in their ***external features***.
- **Mechanisms of formation of identical twins**:

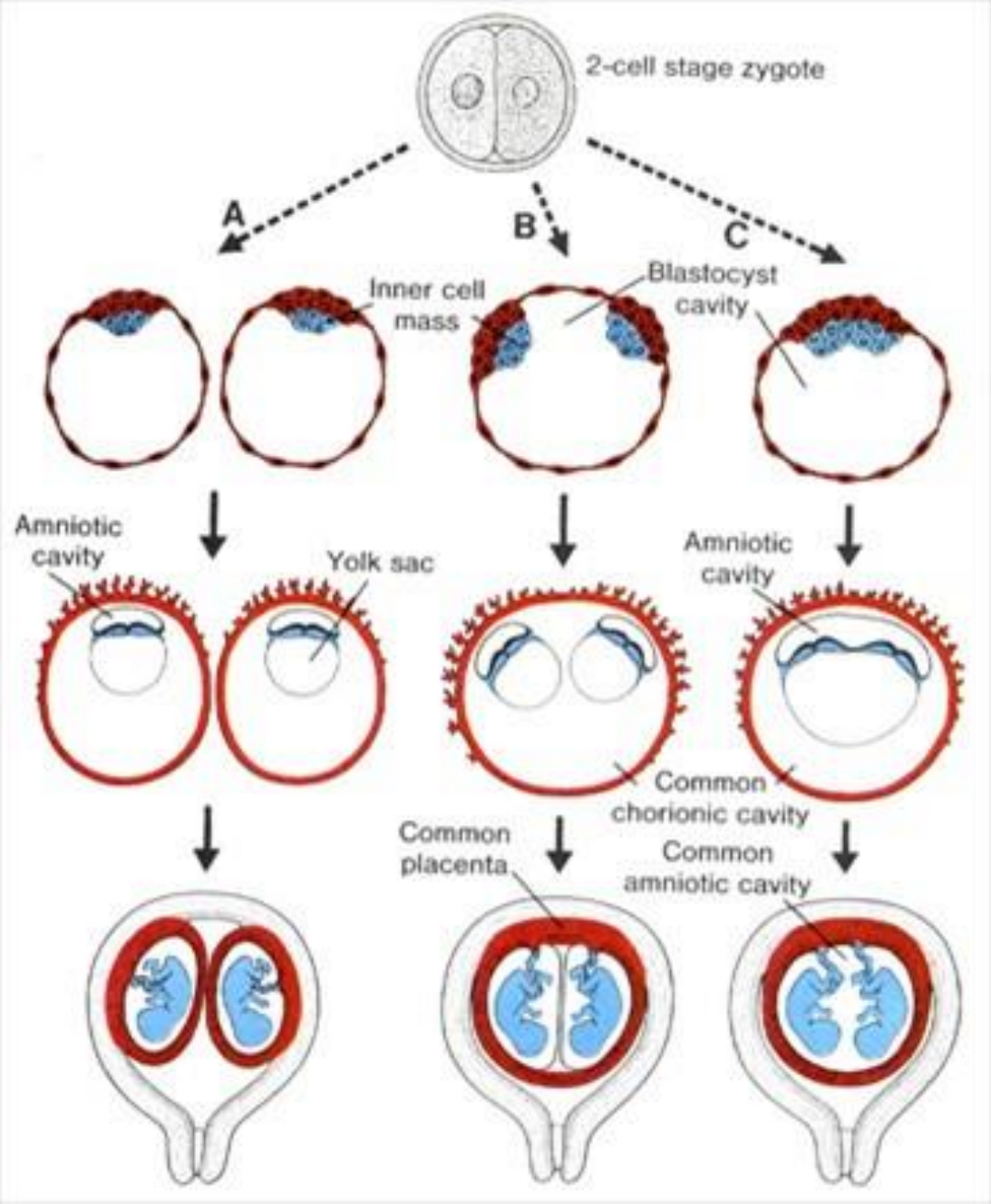
1. ***Very early separation of the morula:***
   - The ***morula divides*** into two and each develops into a blastocyst.
   - The 2 blastocysts ***implant separately*** in the uterus and each develops a ***separate*** amnion, chorionic sac and placenta as the case of dizygotic twins.
2. ***Separation of the inner cell mass of an early blastocyst:***
   - The two embryos have a common placenta and a common chorionic cavity, but each of them has **separate amniot**ic cavity.
3. ***Separation of the bilaminar germ disc of a late blastocyst :***
   - The two embryos have a ***common*** placenta, a common chorionic cavity and a common amniotic cavity.
   - ***Incomplete separation*** of the bilaminar germ disc results in ***conjoined (Siamese)*** twins. Several cases of such conjoined twins have been successfully separated by surgical procedures.



★**Twin defects**:

1. A tendency towards prematurity. Approximately 12% of premature infants are twins.
2. Low birth weight
3. A high incidence of prenatal mortality.





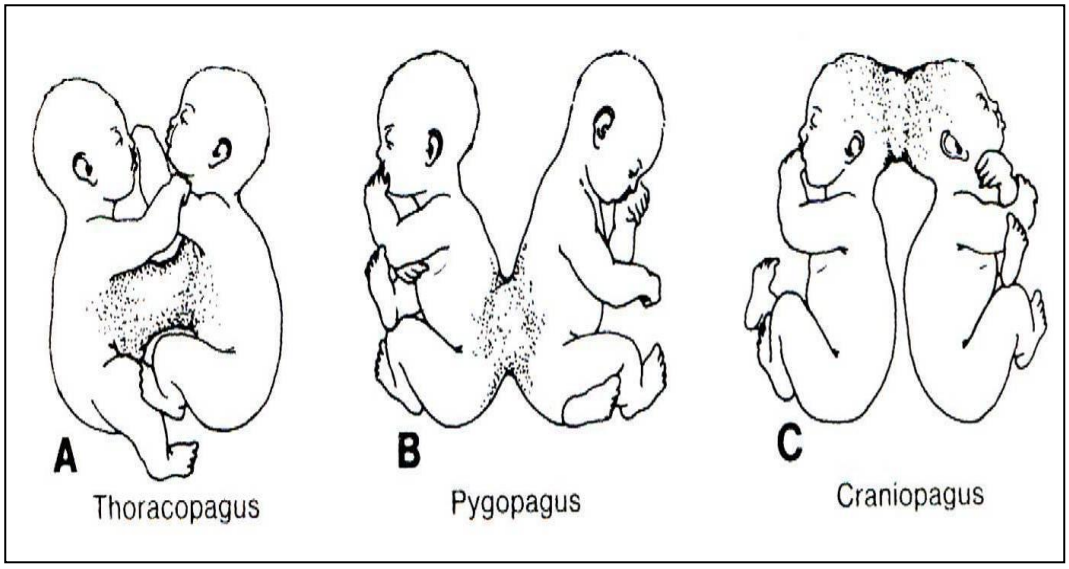
BIRTH DEFECTS

⋆ FACTORS RESPONSIBLE FOR BIRTH DEFECTS

A- Environmental factors

- Many environmental factors (teratogens) can cause birth defects as fetal death, congenital malformations, growth retardation or functional disorders. The effect of the teratogens varies according to:

1. The developmental stage at the time of exposure to the teratogens. The most sensitive period for inducing birth defects is the 3rd to 8th weeks of pregnancy which is the period of embryogenesis.
2. The dose and duration of exposure to the teratogens.



- The environmental teratogens include:

I) Infectious agents

1- Viruses:

- The most dangerous viruses having definite teratogenic effects are: German measles, cytomegalovirus, herpes simplex, varicella and human immunodeficiency virus (HIV).

2- Bacteria as syphilis.

3- Parasites as toxoplasmosis.

4-Radiations : X-rays, gamma rays , ionizing radiations have a teratogenic effect because:

a- They kill the rapidly proliferating cells.

b- They lead to genetic alterations of the germ cells with subsequent malformations.

II) Drugs and chemicals

- Most of the drugs have teratogenic effects of the commonly ingested chemicals; alcohol and nicotine have a definite teratogenic effect.

III) Maternal diabetes

- The risk of congenital malformations in children of diabetic mothers is 3 or 4 times that in the offspring's of non diabetic mothers; it has been reported to be as high as 80% in the offspring of mothers with long-standing diabetes.

B- Chromosomal abnormalities

- The chromosomal abnormalities may be either numerical or structural.

I) Numerical chromosomal abnormalities :

a- Autosomal abnormalities

1*. Trisomy 21 (Down syndrome) (Mongolism):*

- Each cell of the body of this individual contains an extra copy of the chromosome 21, so the chromosomal number of the cell is 47 (45+XX or 45+XY).
- It results usually from non-disjunction of homologous chromosomes 21 during the formation of the oocyte resulting in an ovum of 24 chromosomes with an extra copy of the chromosome 21.
- The incidence of Down syndrome is approximately 1 in 2000 pregnancies for women under age 25. This risk increases with maternal age to 1 in 300 at age 35 and 1 in 100 at age 40.

2. Trisomies 13, 15, 17, and 18 are less common than Trisomy 21. The infants of these syndromes are mentally retarded with many congenital malformations and usually die by the age of two months.

b- Sex chromosomal abnormalities

1- Klinefelter syndrome:

- This syndrome is 47 (44+XXY).
- It usually results usually from non-disjunction of the two X chromosomes during the formation of the oocyte thus giving an ovum of 24 chromosomes with an extra copy of the X chromosome. When this ovum is fertilized by a normal sperm containing Y chromosome, the genotype of the offspring will be 44 + XXY.

2- Turner syndrome:

- This syndrome affects females where each cell of the body of this affected individual contains one X chromosome only, so the chromosomal number of the cell is 45 (44+XO). It results from non-disjunction of the sex chromosomes during formation of either male or female gametes.

II)Structural chromosomal abnormalities :

- The chromosomes are liable to break due to many environmental factors as viruses, radiations and drugs.
- Examples of chromosomal deletion:

a. **Cri-du-chat syndrome**: It is a well-known syndrome, caused by partial deletion of the short arm of chromosome 5.

Such children have a cat-like cry, microcephaly, mental retardation and congenital heart disease.

b. **Angelman syndrome**: It results from deletion of a short segment of the long arm of chromosome 15. Such children are mentally retarded, cannot speak, exhibit poor motor development, and are prone to unprovoked and prolonged periods of laughter.