

ANATOMY

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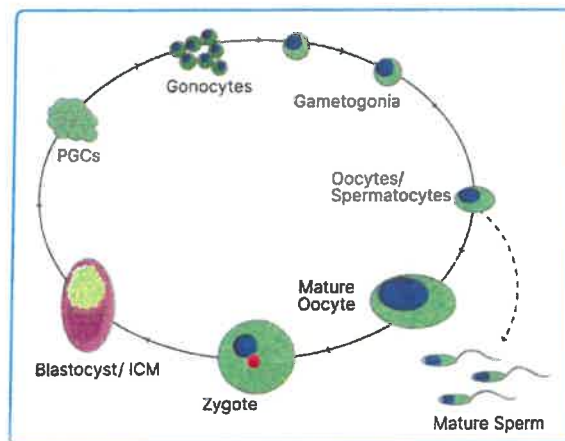
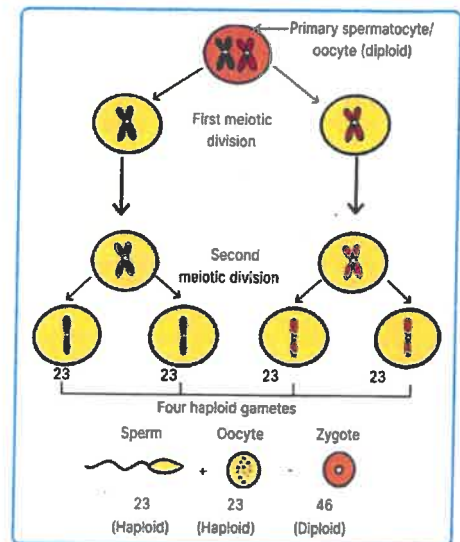
GENERAL EMBRYOLOGY



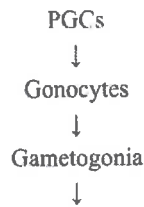
Gametogenesis

- The process of gametogenesis is same for males and females
- n in $2n$ represents the number of chromosomes
 - Diploid organisms
- 46 chromosomes are represented by $2n$
 - 23 chromosomes from mother and 23 from father
- 23 pair of homologous chromosomes = 46 chromosomes
- All cells in our body are in diploid status
- Primary oocyte and spermatocytes are in diploid status
- As the cell undergoes Meiosis, which is a two stage process (Meiosis 1 and 2)
- Meiosis 1 is the reduction division
 - It reduces the chromosome numbers to half (maternal and paternal chromosomes separate)
- Next cell is the secondary spermatocyte/secondary oocyte becomes haploid (n = number of centromeres)
- In Meiosis 2, sister chromatids will separate (there will be a break at the centromere)
 - Meiosis 2 doesn't change the chromosome number
 - Its like Mitosis
- Meiosis 1 is the reduction division that reduces chromosome number to half
- Meiosis 2 results in the formation of four gametes
- These gametes have 23 chromosomes each (n)
- They are ready for fertilization
- The sperm (haploid) meets with Oocyte (haploid) and undergoes fertilization to form Zygote ($2n$)
 - Thus diploid status is reestablished

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- The genetic make-up of a zygote is referred to as ($2n, 2N$)
- Zygote ($2n, 2N$) where n is the number of chromosomes and N is the number of DNA
- Zygote further divides and forms Blastocyst
- Blastocyst has an Inner Cell Mass (ICM).
- ICM has an epiblast cells. This epiblast forms Primordial Germ Cells (PGCs).
- PGCs are the 1st sex cells of the body
- The formation of gametocytes can be summarized as below



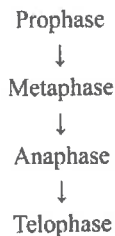
Primary & Secondary Gametocytes

- PGCs form male or female gametes (depending upon the presence or absence of Y chromosome)
- PGCs form sperms when Y chromosomes are present
- PGCs forms oocytes when Y chromosomes are absent
- Y chromosome is Acrocentric and a gene is present on the short arm called SRY gene (Sex region on the Y chromosome)
- In Males, PGC → Spermatogonia → Primary and secondary spermatocytes → Spermatids → Spermatozoa
- In Females, PGC → Oogonia → Primary and secondary oocytes → Mature oocyte (secondary oocyte)

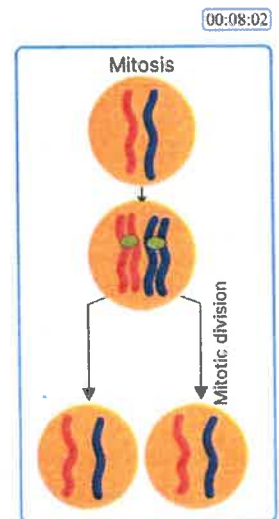
Mitosis and Meiosis

Mitosis

- It is also known as Equational division (because the chromosome number remains the same).
- It happens in somatic cells (e.g., skin cells, muscle cells, hair cells, blood cell) and gamete cells
- The daughter cells have the same chromosome pattern as the parental cells ($2n, 2N$)
- Before any cell division, DNA duplication occurs.
- DNA duplication occurs in the 'S phase' or the 'Synthesis phase' of the Interphase.
- This means that the cell changes from a ($2n, 2N$) to ($2n, 4N$)
- The cell remains diploid ($2n$) but the DNA amount is doubled ($4N$). The sister chromatids are available.
 - Each sister chromatid carry one unit of DNA
- Phases of Mitosis:

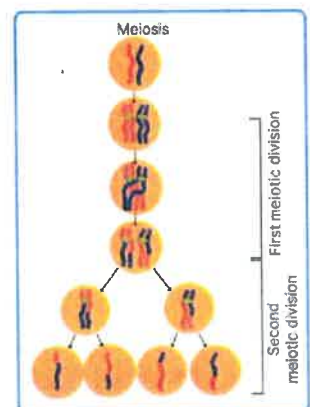


- During anaphase: Sister chromatids arranged at the equator break in the centromere
 - One sister chromatid from maternal and paternal side will move to the daughter cell
- Finally, 2 daughter cells are formed.
- The daughter cells have the same genetic make-up, that is ($2n, 2N$)



Meiosis

- It is a reduction division
- It is also known as → Reduction division (because the chromosome number is reduced to half).
- The gametes formed at the end of Meiosis is haploid
- Primary gametocyte can be primary spermatocyte and primary oocyte ($2n, 2N$)
- DNA duplication occurs in the 'S phase' or the 'Synthesis phase' of the Interphase.
- $2n, 2N$ of the cell becomes $2n, 4N$ (Amount of DNA doubles)
- Meiosis has 2 stages:
 - Meiosis I (Prophase I, Metaphase I, Anaphase I, Telophase I)
 - Meiosis II (Prophase II, Metaphase II, Anaphase II, Telophase II)
- Prophase I → further divided into 4 phases:
 - Leptotene

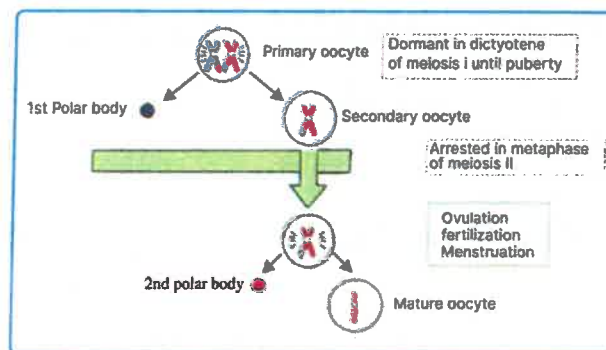
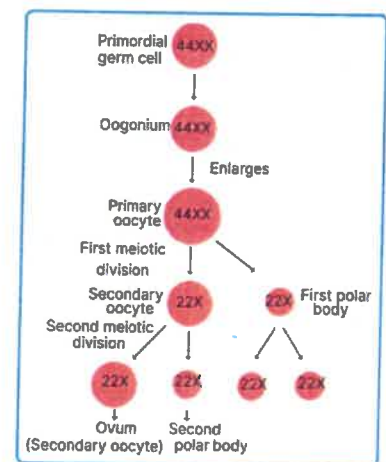


- Zygotene
- Pachytene
- Diplotene
- Tetrad stage (4 sister chromatids) and Chiasma formation occurs in the Pachytene stage. (mnemonic: PTC)
- Chiasma formation helps in exchange of genetic material between the maternal and paternal chromosome. This occurs during Pachytene
- Genetic Recombination due to chiasma formation is a characteristic of meiosis.
- By the end of Meiosis I, the maternal and paternal chromosomes separate and form Secondary gametocyte
- Secondary gametocyte can be Secondary spermatocyte/Secondary oocyte ($n, 2N$)
- In Meiosis II → only the sister chromatids are separated after break in the centromere
- Therefore, by the end of Meiosis II → Gametes (n, N) are formed
- Gametes are haploid
- This is needed because a gamete, sperm (n, N) fertilizes a oocyte (n, N) - Normal status ($2n, 2N$) is restored

Difference between Male and Female Gametogenesis

- In both sexes, primordial germ cells are present
- Primary germ cell is the cell in the beginning to form the gamete
- Primary germ cell gives the Oogonium which then gives the Oocyte
 - Until this, the cell division that occurs is Mitosis
- Primary oocyte enters Meiosis I as ($2n, 4N$).
- Primary oocyte is the first cell that undergoes Meiosis I
- Secondary oocyte undergoes Meiosis II to form gametes)
- Gametes are the mature oocytes that is ready for fertilization
- Other cells are polar bodies
 - First polar body and Second polar body
- These polar bodies undergo apoptosis and degenerate
- The ratio in a female is 1:1 (1 primary oocyte → 1 gamete)
- The ratio in a male is 1:4 (1 primary spermatocyte gives 4 sperms)
- The process of meiosis starts in utero in a female
- The primordial germ cells remain dormant until puberty
 - Till puberty, meiosis does not happen in a male
 - Spermatogenesis begins only after puberty
- Secondary oocyte completes Meiosis II only if it is fertilized by a sperm.

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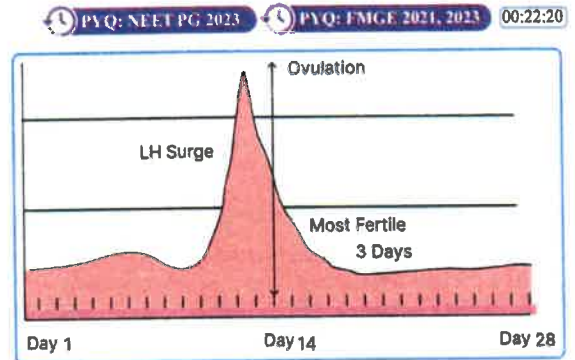


- Primary oocyte which has only entered meiosis before birth remains dormant in the Dictyotene (Diplotene) stage of Prophase I of Meiosis I
 - P - Primary oocyte
 - P1 - Prophase I
 - P - Puberty

- After puberty females will have LH surge
 - The primary oocyte forms secondary oocyte and 1st polar body
- Secondary oocyte gets arrested in metaphase 2 of meiosis 2 until fertilization
- If fertilization fails to happen then Secondary oocyte gets degenerated followed by menstruation
- If fertilization happens, it leads to the formation of mature oocyte and 2nd polar body.
- Second polar body is seen after fertilization
- First polar body is seen after LH surge but before Ovulation

Menstrual Cycle

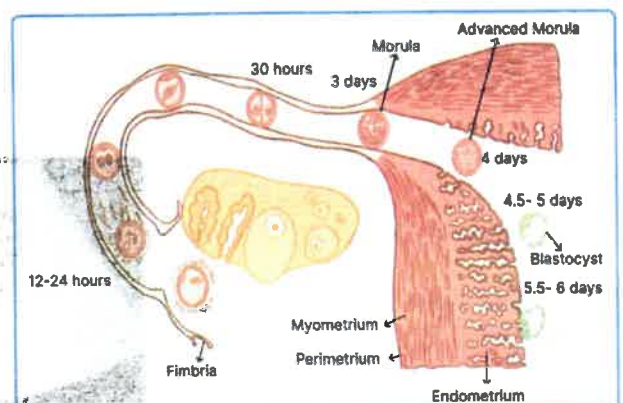
- Menstrual cycle is calculated from the 1st day of the last menstrual period (LMP).
- Normally, menstrual cycle duration is 28 days (average).
- If it is a 28-days cycle, then ovulation will occur on Day 14 (mid-cycle) of the menstrual cycle.
- LH Surge:
 - Rise in the concentration of LH (Luteinizing Hormone) before ovulation.
 - LH surge starts about 36 hours before ovulation.
- LH Peak:
 - When maximum concentration of LH is reached.
 - LH peak occurs about 12 hours before ovulation.
- 1st polar body is released when LH peak occurs (i.e., about 12 hours before ovulation).
- 2nd polar body → is released after fertilization.
- Fertilization should occur within 24 hours of ovulation for the zygote to form.
- If ovulation happens on day 14, zygote should be formed on day 15
 - Otherwise, the secondary oocyte will be degenerated and menstruated and she has to wait for the next cycle to be fertilized and get pregnant
- When the sperms are ejaculated, they are capable of fertilization
- Sperms only have the capacity to fertilize the ovum for about 2 days or 48 hours after ejaculation.
- Therefore, if sperms are ejaculated on/after day 12 to day 14, fertilization can occur, and the female can conceive.
- For a male, the fertile period following ejaculation is 48 hours
- For a female, the fertile period is 24 hours following ovulation
- Hence, most fertile period is 3 days (Day 12, 13 and 14) around the day of ovulation.
- If the sperms are ejaculated before day 12 or after 14, fertilization is not possible.
- If the sperms are ejaculated after that period, there is no chance of fertilization



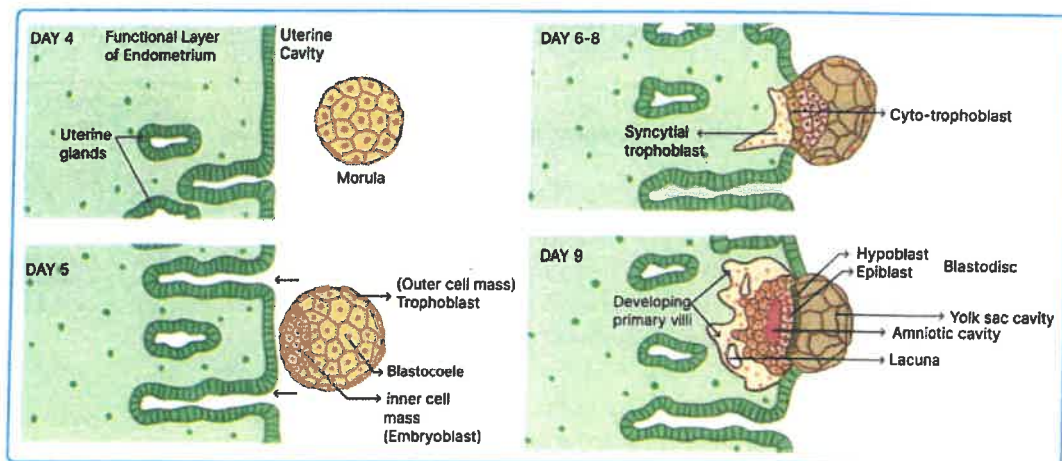
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Ovulation, Fertilization and Implantation

- Ovulation: Graafian follicle bursts and releases the secondary oocyte.
- The secondary oocyte is covered by a glycoprotein membrane called Zona Pellucida attracting the sperm
- The secondary oocyte attracts sperm and undergoes fertilization in the ampulla of the fallopian tube
- Once a single sperm nucleus is inside, it is the Zona pellucida that prevents Polyspermy
- Zona pellucida prevents abnormal implantation in the uterine tube
- Implantation occurs only in the uterus.
 - For this the Zona pellucida has to be lost

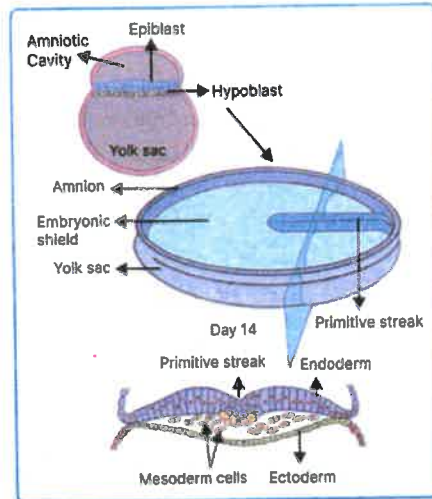


- Fertilization should occur within 24 hours of ovulation.
- Day 1 of fertilization: Zygote
- Day 2 of fertilization: 2-celled stage
- Day 3 of fertilization: Morula (12 / 16 / 32 / 58 celled stage) - Multicell stage
 - Morula is a 16 cell stage (If question is asked)
- Day 4 of fertilization: Advanced Morula (can have > 16-64 cells; enters the uterine cavity)
- Day 5 of fertilization: Blastocyst (blast cells and cyst like cavity) is still covered by zona pellucida
- After day 5, the blastocyst loses the zona pellucida and starts implantation
- Implantation is a week-long process.
- Implantation starts on day 5 and finishes by day 12.
- More precisely, **day 7-9 post-ovulation** or post-fertilization is the time when implantation occurs in the endometrium



- Day no: 5 Blastocyst has 2 types of cells:
 - Inner cell mass (a.k.a. embryoblast) forms the embryo
 - Outer cell mass (a.k.a. trophoblast) forms the placenta (which provides nutrition)
- On day 6-8/ week of 2
 - Week of 2 because there are 2 trophoblasts, 2 embryoblasts, 2 cavities
 - Embryoblast divides into Epiblast (top -columnar) and Hypoblast (bottom-cuboidal)
 - Trophoblast divides into Syncytiotrophoblast & Cytotrophoblast
 - Syncytiotrophoblast have lost their cell margins and helps in implantation
 - Cytotrophoblast has intact cell membranes and are towards the conceptus
 - Syncytiotrophoblast and Cytotrophoblast form finger like projections called villi
 - There is formation of villous: Primary, secondary and tertiary villi
- Trophoblasts are involved in placenta formation and embryoblasts are formed in Embro proper
- 2 cavities are formed - Amniotic cavity (dorsal) & Yolk-sac cavity (ventral)
- TVS - 2nd week shows "double bleb sign"
 - Suggestive of intra uterine pregnancy
 - Embryonic disc is present between the amniotic and yolk sac cavities



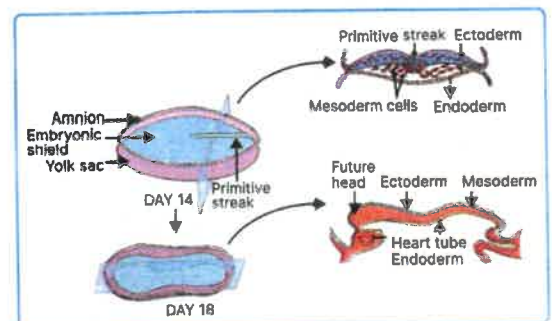


Week 2:

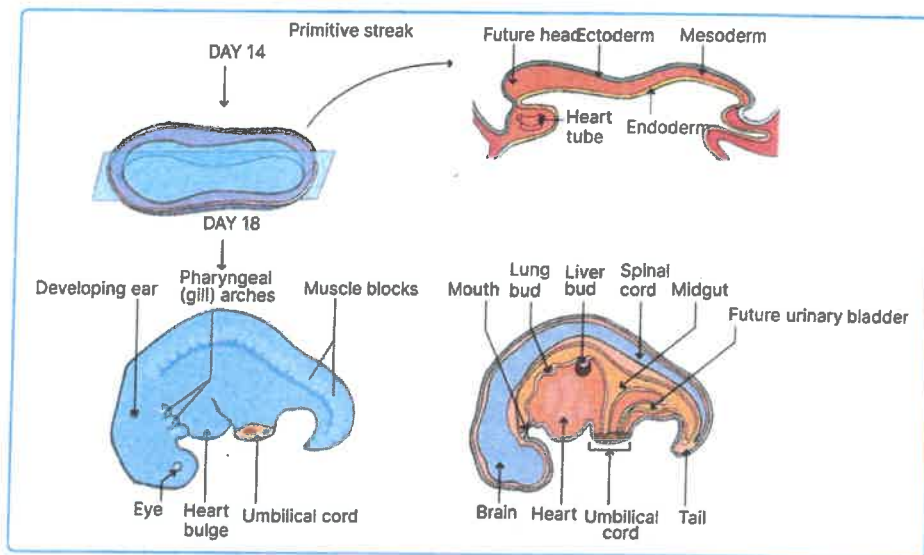
- There are two cavities and two cell types coming from Embryoblasts
- Embryoblasts has epiblasts (above) and hypoblasts (below)
- Epiblasts are made up of Columnar cells and Hypoblasts are made up of Cuboidal cells
- Two cavities - Dorsal amniotic cavity and Ventral yolk sac cavity
- At the roof of Yolk sac cavity - hypoblasts are present
- At the floor of the amniotic cavity, epiblasts are present
- Embryo develops from the epiblast cells and Hypoblast cells are removed from the baby
 - These would be replaced by the migratory cells - epiblast cells

Week 3/ By the end of day 14:

- Primitive streak is formed by the proliferation of epiblast cells.
- Primitive streak formation occurs in the caudo-cephalic direction.
 - This means it begins towards the tail end of the embryo (caudal end/posterior end) and progresses to the head end of the embryo (cephalic end/anterior end).
- This primitive streak forms a primitive pit
- The primitive pit, epiblasts cells move ventrally from dorsally
- This movement is called Ingression and replace the Hypoblast cells
- As they remove the hypoblast cells, they will form germ layers
- The first germ layer formed is Endoderm, which is formed by epiblast cells that removed the hypoblast cells
- Mesoderm is the second layer formed
- Ectoderm is the last layer formed
- Formation of three germ layers in the sequence is called gastrulation (week no:3)
- All Epiblast cells which were present in the floor of amniotic cavity have migrated downwards to form disc shaped structures.
- A single disc would be changed into three discs by epiblast cells
 - Dorsal disc: Made up of Ectoderm
 - Middle disc: Made up of Mesoderm
 - Lower disc: Made up of Endoderm
- Ectoderm is the dorsal most layer
- Mesoderm forms the cardiovascular tubes
- Ectoderm forms the neural tube - brain and spinal cord
- Endoderm (Ventral) forms the gut tube
- The head comes close to the tail end- Cephalocaudal folding
- Gut tube is divided into 3 parts:



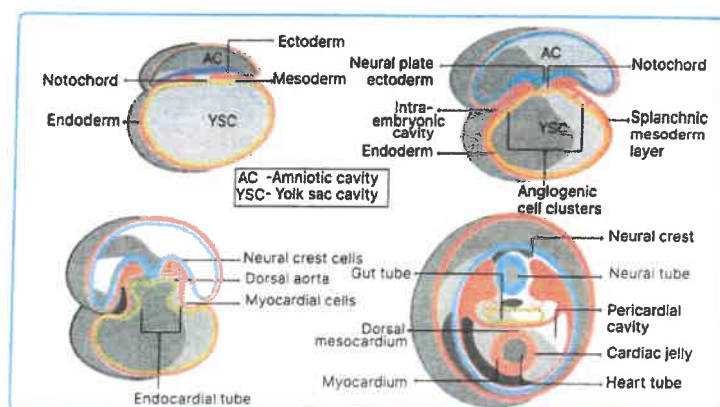
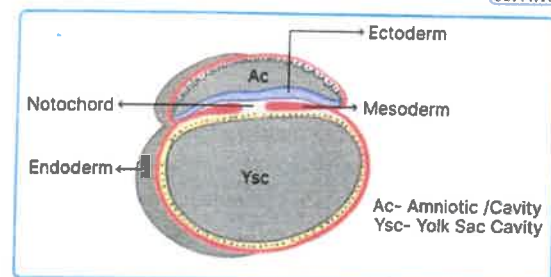
- Foregut
- Midgut
- Hindgut
- Mid gut gives a diverticulum called Vitellointestinal duct entering the umbilical cord region
- Hind gut diverticulum called Allantois entering the Umbilical cord region
- Vitellointestinal duct and Allantois form the content of Umbilical cord



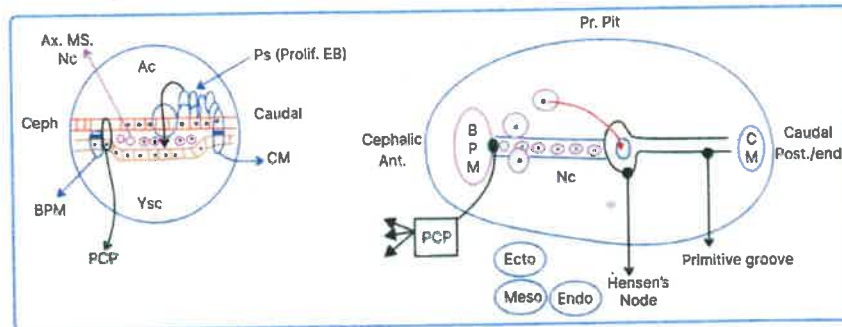
Intraembryonic Coelomic Cavity

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- Intra-embryonic cavity or the coelomic cavity develops laterally on either side, all around the embryo.
- The mesoderm here divides into two parts because of the intervening intra-embryonic coelomic cavity.
- Endoderm lines the roof of the yolk sac cavity
- Ectoderm lies at the floor of the amniotic cavity and forms the Neural tube
- Neural plate forms the Neural groove
- Neural groove then forms the Neural tube
- Neural tube then forms the Central Nervous System - Brain & Spinal Cord
- Mesoderm forms the Cardiovascular tube
- Endoderm forms the gut the gut tube



- Intraembryonic coelomic cavity splits the mesoderm laterally
 - Intra-embryonic cavity later develops to form 3 more cavities:
 - Pericardial cavity (Around heart)
 - Pleural cavity (Around the lung)
 - Peritoneal cavity (Around the abdominal contents)
 - The dorsal layer, Ectoderm meets with the ventral layer, Endoderm with no intervening Mesoderm layer
1. Buccopharyngeal membrane
 - Towards the cephalic (head) end, there will be formation of the bucco-pharyngeal membrane.
 - Future mouth
 2. Cloacal membrane.
 - Towards the caudal (tail) end, there will be formation of the cloacal membrane.
 - Future anus



- Primitive streak starts to form from the caudal end and moves towards the cephalic end.
- Primitive streak has 3 components:
 1. Primitive groove
 2. Blastopore (Primitive pit)
 3. Hensen's node (Primitive node)
- The cells in the primitive streak starts Ingression
- Some epiblast cells (columnar) jump into the primitive pit and move ventrally to replace the hypoblast and forms the first germ layer- endoderm.
- After forming the endoderm, these migrated epiblast cells also form the mesoderm
- The remaining epiblast cells proliferate to form the ectoderm (dorsal layer)
- The dorsal most disc will be Ectoderm
- On removing the ectodermal disc - Mesodermal disc is seen
- On removal of Mesodermal disc, Endoderm is seen
- Mesoderm is not present everywhere
- Endoderm fuses with the Ectoderm at the cephalic end to form the Buccopharyngeal membrane
- Towards the caudal (tail) end, there will be formation of the cloacal membrane.
- Towards the cephalic (head) end, there will be formation of the bucco-pharyngeal membrane.
- The cloacal membrane and the bucco-pharyngeal membrane have no intervening mesoderm.
- The ventral endoderm and the dorsal ectoderm directly fuse to form these membranes.
- Some epiblast cells ingress from the primitive pit towards the bucco-pharyngeal membrane to form the **axial mesoderm or the notochord**.
- The axial mesoderm or the notochord stimulates the overlying central ectoderm on the dorsal side to form the nervous system.
- Ventral to notochord, endoderm is present
- Notochord is dorsally lined by Ectoderm and ventrally lined by Endoderm
- Prochordal plate /Prechordal plate develop just Prior to notochord i.e. cephalic to notochord but caudally to Buccopharyngeal Membrane
- Have all three germ layer
- Prechordal plate has an intervening mesoderm
- It is sandwiched between the Notochord and the Buccopharyngeal membrane

Transverse Section of Embryo after Gastrulation

- Ectoderm is the most dorsal layer
- Middle layer is mesoderm
- The ventral layer is the Endoderm
- There are two cavities:
 - Dorsal amniotic cavity
 - Ventral yolk sac cavity
- The third cavity known as the Intraembryonic coelomic cavity is the lateral cavity
 - It gives the pericardial, pleural and peritoneal cavity.
- The axial mesoderm/Notochord stimulates the overlying ectoderm to form Neural plate ectoderm
- Ectoderm at the periphery is the Surface ectoderm
 - Any external opening in the body is lined by Surface ectoderm
- Oral cavity lined by Surface ectoderm forms some of the glands
 - Rathke's pouch at the roof of oral cavity
- Adenohypophysis comes from Surface ectoderm
- Parotid/ Submandibular/ Sublingual salivary glands come from Surface ectoderm
- Surface ectoderm forms skin epithelium and sweat glands, sebaceous glands
- Neural plate ectoderm in the central region forms the Neural tube
- Neural tube forms the Central nervous system
- Diencephalon part of the brain forms the Neurohypophysis (Posterior pituitary)
- Pituitary gland develops from the Ectoderm only
- Neural crest cells- It develop at the junction of the neuroectoderm and surface ectoderm
- Neural crest cells are thought to be derived from the Neural plate ectoderm
- Neural crest cells are the fourth germ layer derived from the Epiblast cells
 - These cells form peripheral nervous system, ganglia
- Neural crest cells form the secondary mesenchyme
 - It restricts to the anterior, lateral aspect of the head and neck region
 - Its lightly enroach on the thorax region
 - It forms most of the skull bones, eye ball, Pharyngeal arch bones (Mandible, Hyoid), Aorta pulmonary septum
- DiGeorge syndrome - Defect in neural crest cell migration
 - It results in mandible bone defects, skull defects, eye ball defects, pharyngeal arch defects (Small mandible- hyponathia) and Episeptum anomlaies (Tetralogy of Fallot, Persisting Truncus Arteriosus, Transposition of great vessels)
 - Episeptum anomalies cause death in these patients
- Primary mesenchyme forms the occipital bone
- All the skeletal muscles are formed from the Primary mesoderm (Pharyngeal arch muscles like Masseter)

