

Spermatogenesis

Spermatogenesis is a sequence of events by which spermatogonia are transformed into mature sperms. The process begins at puberty.

Site: Seminiferous tubules of testis.

Duration: 64 days.

Stages: 1) Spermatocytosis, 2) Meiosis, 3) Spermiogenesis.

Type A spermatogonia represent the stem cells. They undergo mitosis to form type B spermatogonia.

Type B spermatogonia form primary spermatocytes.

Primary spermatocytes complete meiosis I, to form secondary spermatocytes (haploid).

Secondary spermatocytes undergo meiosis II, to form spermatids.

Four spermatids are produced from a primary spermatocyte.

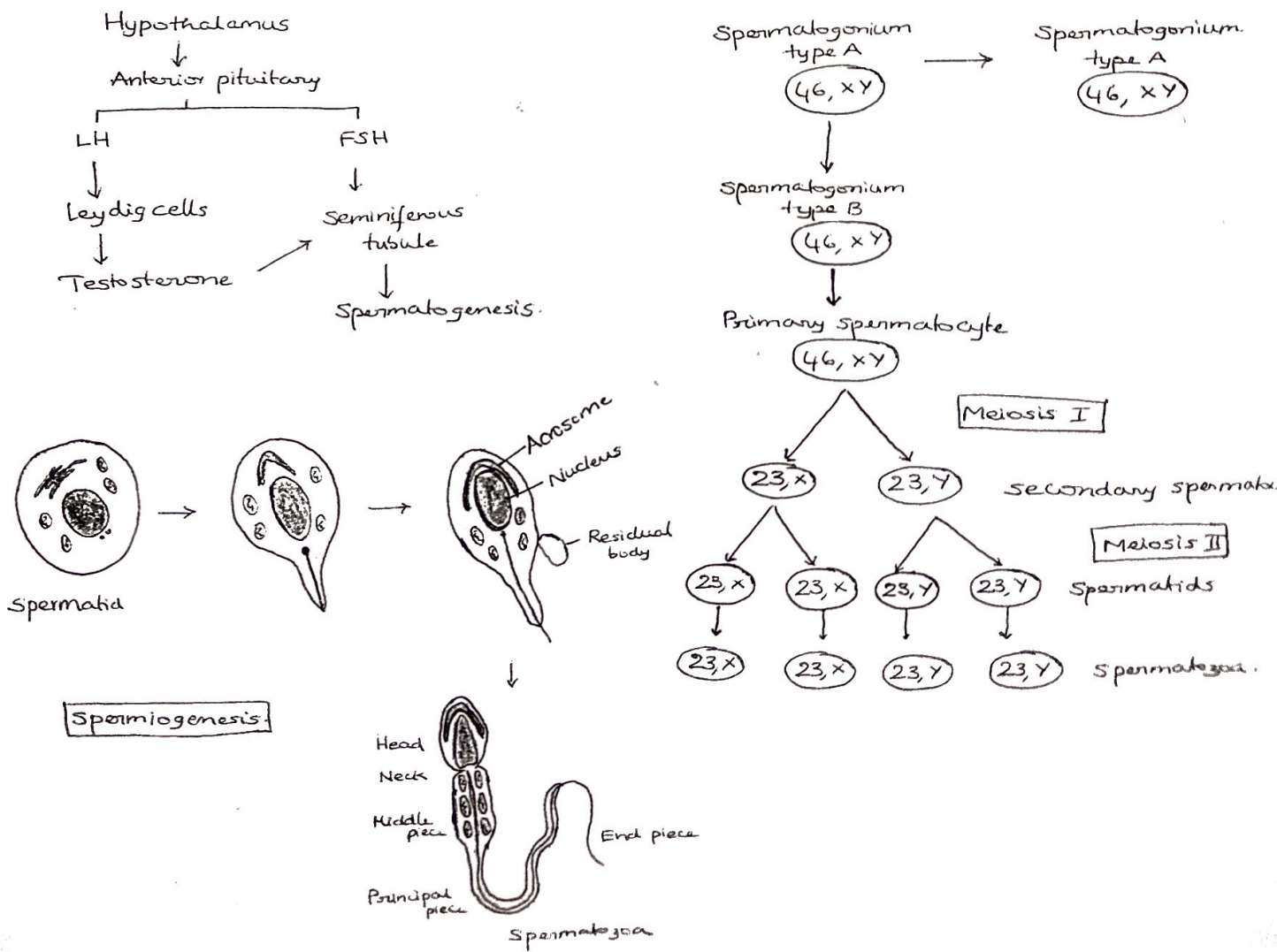
Spermatids do not divide further.

Spermiogenesis: The process of transformation of spermatids into spermatozoa is called spermiogenesis.

Changes during spermiogenesis:

- 1) Reduction in the size of nucleus.
- 2) Condensation of golgi apparatus to form acrosome.
- 3) Flagellum grows out.
- 4) Remainder cytoplasm (residual body) moves away from the nucleus.

Hormonal effect on spermatogenesis:



Oogenesis

It is the sequence of events by which the oogonium is transformed into mature ovum.

It begins before birth and is completed with fertilization. Oogenesis continues upto menopause.

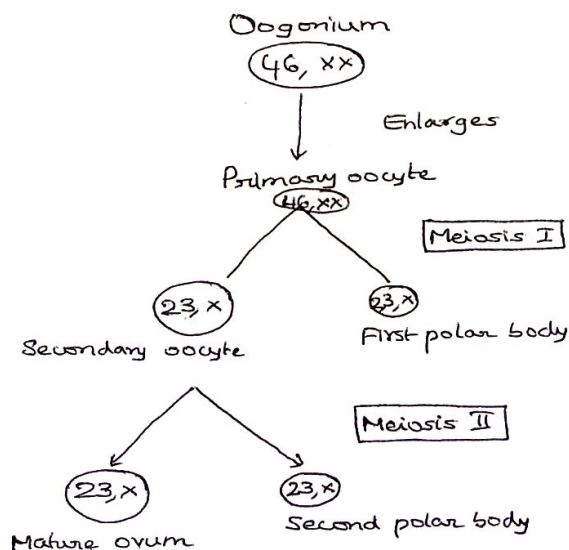
The oogonium enlarges to form primary oocyte. Roughly 2 million primary oocytes are present at birth.

In the late fetal period, the primary oocyte enter meiosis I. In the early months after birth, meiosis I is arrested in diplotene stage. All the primary oocytes remain arrested in diplotene stage of meiosis I until puberty.

During reproductive years, small number of primary oocytes completes meiosis I with each menstrual cycle and develops further. Shortly before ovulation, meiosis I is completed resulting in large secondary oocyte and small first polar body.

The secondary oocyte enters meiosis II. This is blocked in metaphase. The stimulus for the release of this block is fertilization.

Unfertilized ovum fails to complete meiosis II. If the fertilization occurs, meiosis II is completed resulting in mature ovum and second polar body.



Graffian follicle

Formation: In the embryo, the oogonia are naked. After meiosis begins, stromal cells of the ovary partially surround the primary oocytes to form **Primordial follicle**.

At birth, primary oocytes are surrounded by two complete layers of follicular cells, forming **Primary follicle**.

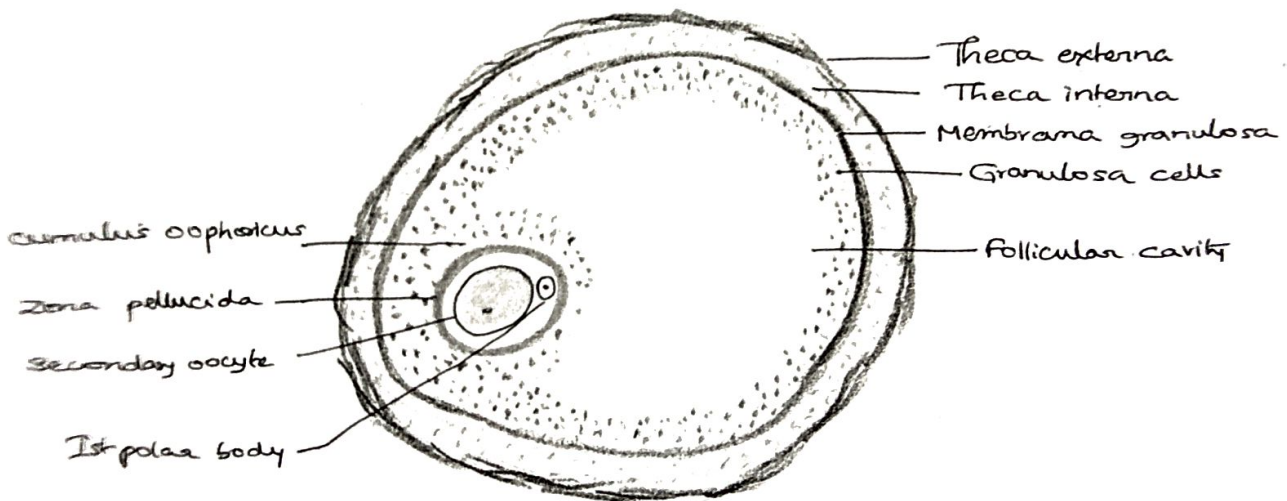
As puberty approaches, under the influence of FSH, follicular cells proliferate rapidly resulting in the formation of numerous fluid filled spaces. These spaces coalesce to form follicular antrum filled with follicular fluid. This is called **Secondary follicle**.

Just before ovulation, meiosis II is completed resulting in the formation of secondary oocyte. A mature follicle containing secondary oocyte and first polar body is known as **Graffian follicle**.

Structure: Secondary oocyte and first polar body are surrounded by zona pellucida. The follicular cells, with the formation of the cavity are separated into two layers – outer layer of granulosa cells and inner layer of cumulus oophorus.

Out side membrane granulosa, the stromal cells of the ovary are organized to form theca folliculi. Theca externa is fibrous. Theca interna is vascular and cellular. It produces oestrogen.

Fate of graffian follicle: On 14th day of the cycle, graffian follicle ruptures (Ovulation). The secondary oocyte and first polar body with zona pellucida and cumulus oophorus are shed into peritoneal cavity. Rest of the follicle forms corpus luteum.



Corpus luteum

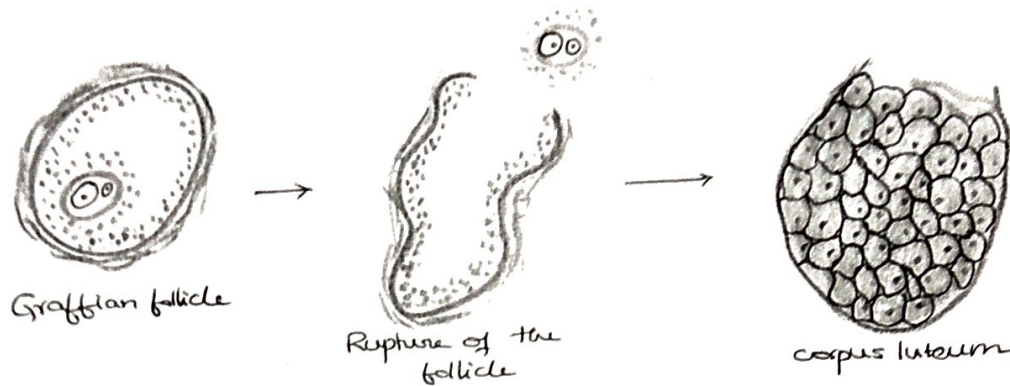
Ovulation occurs on 14th day of menstrual cycle. Secondary oocyte and first polar body surrounded by zona pellucid and cumulus oophorus are shed into the peritoneal cavity. The wall of the ovarian follicle and theca folliculi collapse and are thrown into folds.

Under the influence of LH, follicular cells enlarge. Their cytoplasm is filled with yellowish pigment called Lutein. These cells are called **Granulosa lutein cells**. Some cells of theca interna form **Theca lutein cells**. The corpus luteum produces progesterone and small amount of oestrogen.

Blood vessels of theca interna invade corpus luteum. This is called **Corpus hemorrhagicum**.

Fate: 1) If the fertilization occurs, it enlarges to form *corpus luteum of pregnancy* under the influence of HCG produced by syncytiotrophoblast. It remains active for first 20 weeks of pregnancy and later regresses.

2) If fertilization does not occur, the corpus luteum involutes and degenerates 10 – 12 days after ovulation. It is called *corpus luteum of menstruation*. Later it is transformed into a white scar – *Corpus albicans*.



FERTILIZATION

Fertilization can be defined as fusion of two mature gametes, ovum and spermatozoon to form the zygote.

Site of fertilization: Ampulla of uterine tube

Duration: The process takes place approximately 24 hours.

Phases of Fertilization:

Fertilization is a sequence of coordinated events which is preceded by acrosomal reaction of sperm. Just before approaching the oocyte, the capacitated sperm head establishes multiple contacts between the plasma membrane and outer membrane of acrosomal cap, and discharges the chemical substances. This process is called acrosomal reaction.

The sperm has to overcome three barriers.

1. Passage of a sperm through corona radiata:

The follicular cells of the corona radiata are dispersed by the action of hyaluronidase released from the acrosome of the sperm.

2. Penetration of zona pellucida:

Now the zona pellucida is exposed. The enzymes released from the acrosome - Acrosin, Esterases and Neuraminidase cause lysis of the zona pellucida. The most important of these enzymes is acrosin, a proteolytic enzyme.

Once the sperm penetrates the zona pellucida, a change occurs in the properties of the zona, that makes it impermeable to other sperms. This is called zona reaction.

3. Fusion of plasma membrane of the oocyte and sperm:

The plasma membrane or cell membranes of the oocyte and sperm fuse and break down at the area of fusion. The head of the sperm enters the cytoplasm of the oocyte. The tail degenerates. As soon as the sperm enters the oocyte a Ca^{+2} wave appears in the cytoplasm of oocyte.

4. Completion of the second meiosis:

Penetration of the oocyte by a sperm, activates the oocyte to complete meiosis II resulting in the formation of mature ovum and second polar body.

5. Formation of pronuclei:

The nucleus of the mature oocyte becomes the female pronucleus.

The nucleus of the sperm enlarges to form the male pronucleus.

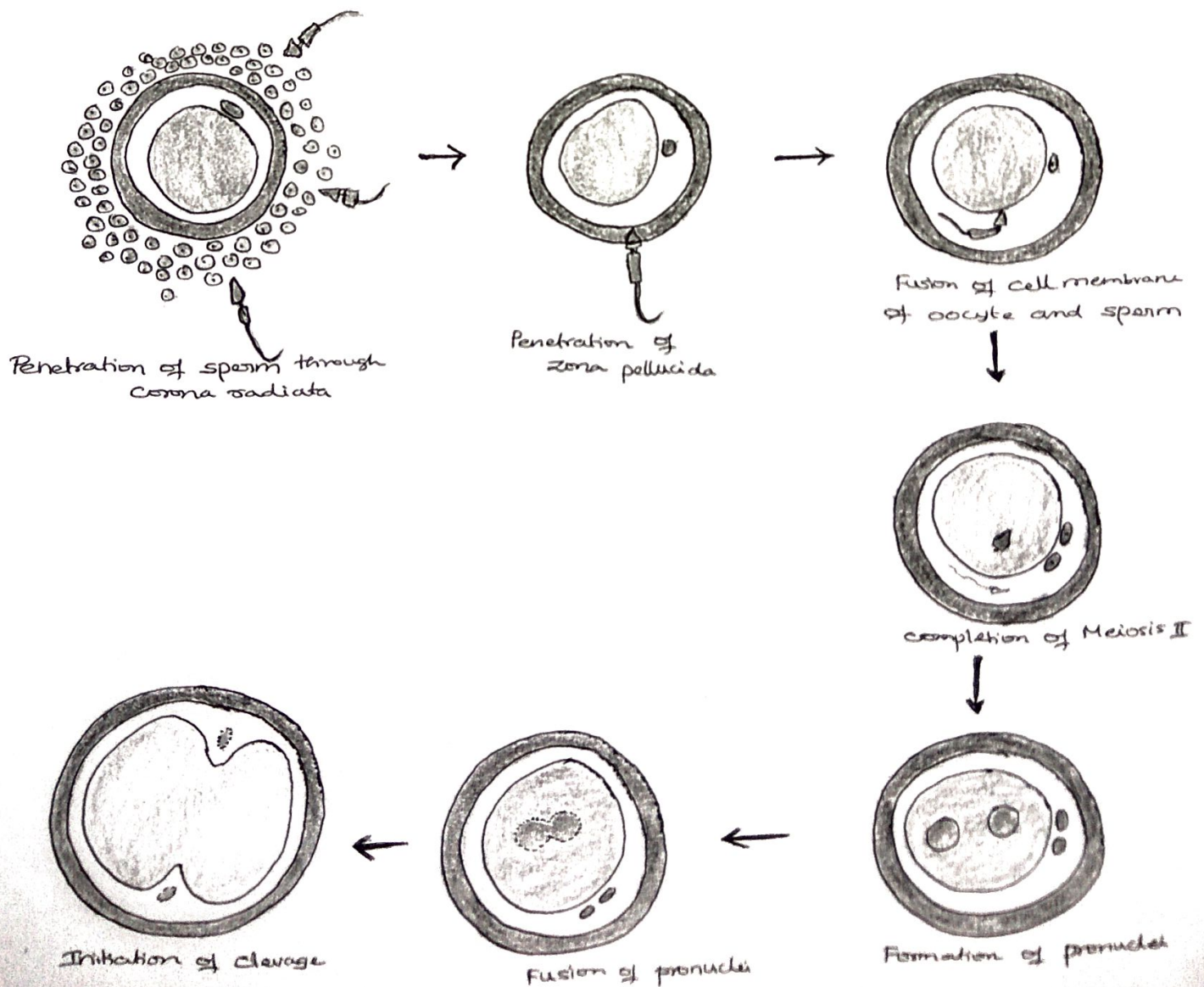
The oocyte containing two haploid pronuclei is called an ootid.

6. Fusion of pronuclei:

The pronuclei fuse into a single diploid aggregation of chromosomes. The ootid becomes a zygote.

Effects of Fertilization:

1. Fertilization stimulates the penetrated oocyte to complete second meiotic division.
2. Restoration of normal diploid no. of chromosomes in the zygote.
3. Determination of chromosomal sex of the embryo.
4. Results in variation of the human species through mingling of maternal and paternal chromosomes.
5. Initiation of cleavage of the zygote.



Invitro fertilization

External fertilization of oocytes and transfer of the cleaving zygotes into the uterus is called invitro fertilization.

Indication: Bilateral occlusion of uterine tubes.

Procedure: 1) Stimulation of growth and maturation of ovarian follicles by administration of clomiphene citrate.

2) Aspiration of mature oocytes from ovarian follicles during laparoscopy.

3) The oocytes are placed in special culture medium with capacitated sperms.

4) Fertilization of oocytes and cleavage of zygote are monitored microscopically for 3 – 5 days.

5) One or two embryos (4 – 8 cell stage) are transferred to uterus.

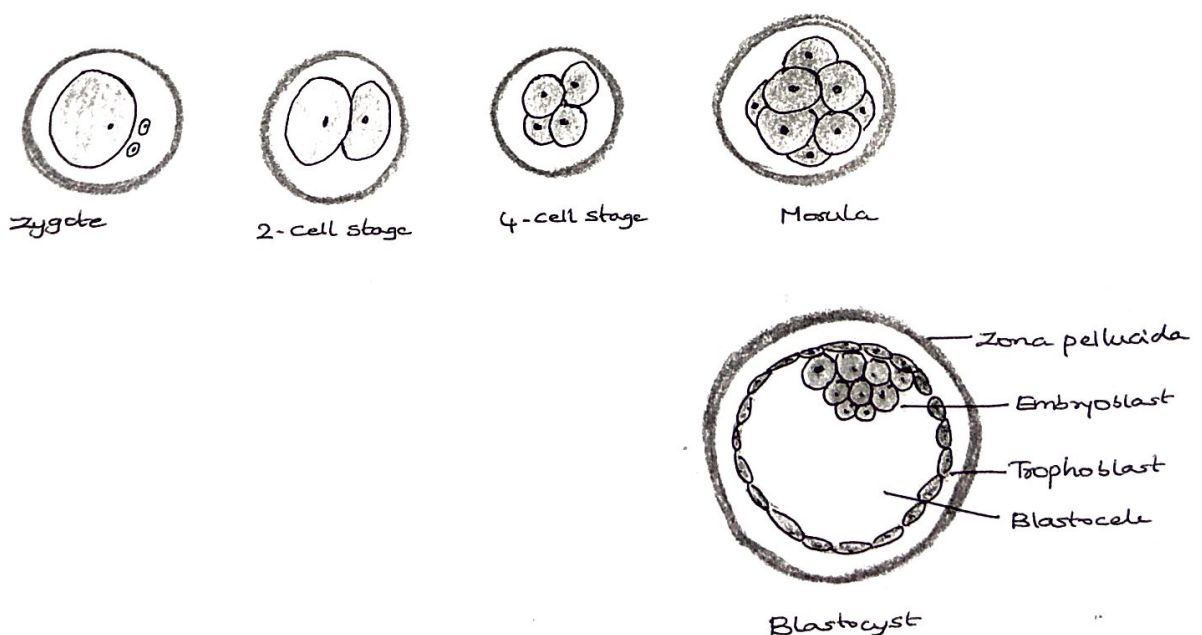
Blastocyst

Formation: When there are 12 – 32 blastomeres, the mass of cells is called morula. 4 days after fertilization, morula enters the uterus. The fluid from uterine lumen passes through zona pellucid and appears in the intercellular spaces. These spaces coalesce to form a single large cavity called blastocele. This stage is called blastocyst.

Structure: *Trophoblast* – It is a thin outer cell layer forming the wall of the blastocyst. It gives rise to embryonic part of placenta. The trophoblast covering the embryonic pole is called *polar trophoblast*. Rest of the trophoblast covering the abembryonic pole is called *mural trophoblast*.

Embryoblast – It is a clump of cells attached to one pole of the blastocyst. It gives rise to embryo.

Blastocele – It is the cavity of blastocyst.



Implantation

The process of embedding of the blastocyst in the endometrium of the uterus is called implantation.

It takes place on the 6th day after fertilization.

Process: On 5th day after fertilization, zona pellucid disappears. The hatched blastocyst increases in size rapidly. The polar trophoblast attaches to endometrial epithelium. At the site of attachment, the trophoblast differentiates into two layers – cytotrophoblast and syncytiotrophoblast.

Syncytiotrophoblast produces the enzymes that erode the maternal tissues, enabling the blastocyst to burrow into the endometrium. The cells of syncytiotrophoblast displace the endometrial cells at the implantation site.

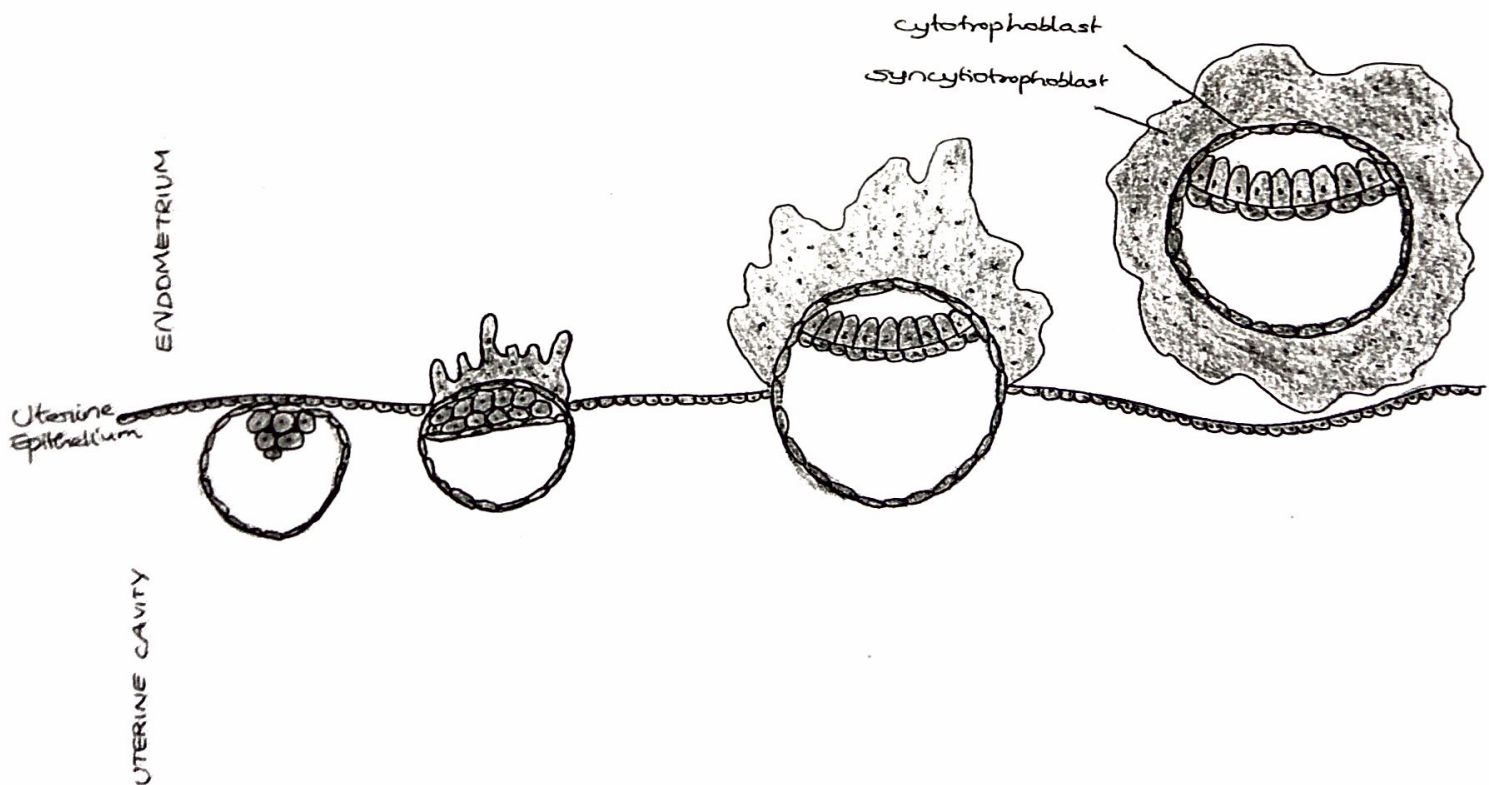
By about 10 – 12 days after fertilization, implantation is completed. The site of initial penetration is sealed by migrating uterine epithelial cells.

Type of implantation: Interstitial

Site of implantation: At the junction of fundus and posterior wall of the body of uterus.

Abnormal implantation: Implantation in areas other than normal site is called abnormal implantation.

- Intra uterine** – Implantation in the lower part of uterine cavity. It results in placenta previa.
- Extra uterine** – Implantation in the ovary or abdominal cavity or uterine tube. It causes death of embryo.



Primitive streak

The first sign of gastrulation is appearance of primitive streak. It appears on 15th day of development.

Formation: The cells of the epiblast occupying the caudal part of the germ disc are pluripotent and undergo rapid differentiation to form linear opacity in the median plane known as primitive streak. Anterior end of the primitive streak proliferates to form primitive node or Hensen's node.

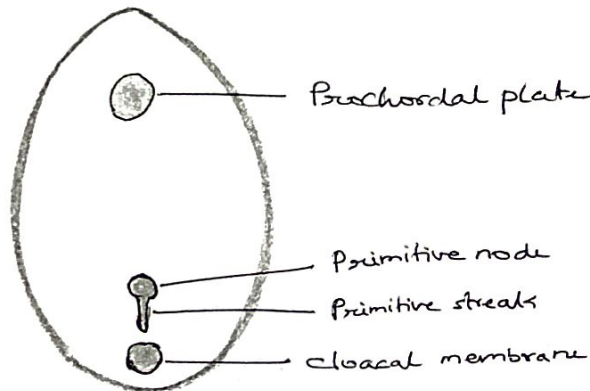
The cells of the epiblast converge in a well defined sequence in the region of primitive streak. The cells of epiblast on reaching it, pass through it, to form new layers beneath the epiblast. The movement of cells through the streak results in the formation of primitive groove. The groove is continuous with a small depression in the primitive node – the primitive pit.

Derivatives of primitive streak:

- 1) Formation of three germ layers – definitive ectoderm, definitive endoderm and intraembryonic mesoderm.
- 2) It induces the differentiation of notochord.

Fate of primitive streak:

By the end of 4th week it degenerates and become insignificant. Remnants of primitive streak may persist and give rise to sacrococcygeal teratoma.



Prochordal plate

At one end of embryonic disc, a rounded area becomes thicker than rest of the disc. This rounded area is called prochordal plate. In this region, the cuboidal hypoblast cells become columnar. With the development of prochordal plate, the cranial and caudal ends of the embryo are determined. The prochordal plate determines the central axis of the embryo.

Notochord

Formation: Some of the mesenchymal cells migrate cranially from the primitive node, forming a median cellular cord called the *notochordal process*.

The notochordal process grows cranially between ectoderm and endoderm until it reaches the prechordal plate.

The center of the primitive node presents a depression called primitive pit. This pit extends into the notochordal process forming a *notochordal canal*. The floor of the canal fuses with the underlying endoderm. The fused layers undergo degeneration. As a result a temporary *neurenteric canal* is formed which communicates amniotic and yolk sac cavities.

Now the notochordal plate folds along the long axis and gradually separates from the roof of the yolk sac. Later, a solid flexible cord of cells known as *definitive notochord* is formed.

Functions: 1) It defines the primordial longitudinal axis of the embryo. It gives rigidity to the germ disc.

2) It provides signals for the development of nervous and musculoskeletal system.

3) It contributes to the intervertebral discs.

Fate of notochord: Notochord degenerates with the formation of vertebrae. But small portion of it may persist as a) Nucleus pulposus of the intervertebral disc and

b) Apical ligament of dens.

Neural tube

As the notochord develops it induces the overlying ectoderm to thicken to form *neural plate*. The neural plate invaginates along its central axis to form a longitudinal *neural groove*.

The neural groove has *neural folds* on each side. The neural folds move together and fuse, converting the neural plate into *neural tube*.

Fusion of neural folds takes place first in the cervical region and then extends in both directions until two openings appear temporarily. The cephalic and caudal openings are called anterior and posterior neuropores which close in the 4th week.

Now a completely sealed neural tube is formed. Entire CNS is developed from it.

Derivatives of neural crest

As the notochord develops it induces the overlying ectoderm to thicken to form neural plate. The neural plate invaginates along its central axis to form longitudinal neural groove. The groove has neural folds on each side. As the neural folds fuse to form the neural tube, some of the neuroectodermal cells lying on the inner margin of the neural folds detach. As the neural tube separates from the ectoderm, the detached cells form flat irregular mass called neural crest. Later it separates into right and left masses and shift to dorsolateral aspect of neural tube.

Derivatives: 1) Dorsal root ganglia of spinal nerves

2) Sensory ganglia of cranial nerves

3) Ganglia of autonomic nervous system

4) Schwann cells of peripheral nerves

5) Adrenal medulla

6) Parafollicular cells of thyroid

7) Melanoblasts of skin

8) Conotruncal septum

9) Connective tissue of head and neck.

Intraembryonic mesoderm

Some of the cells of the primitive streak migrate laterally and forwards between the ectodermal and endodermal layers of the germ disc. This newly developed intermediate layer is known as intraembryonic mesoderm.

It spreads over the whole embryonic area except in the region of oropharyngeal membrane and cloacal membrane. At the periphery of the germ disc, intraembryonic mesoderm is continuous with extraembryonic mesoderm.

Intraembryonic mesoderm is subdivided into three parts.

- 1) **Paraxial mesoderm:** It is the longitudinal column of cells on each side of notochord.
 - Pre otic part --- unsegmented
 - Basal part of skull
 - Striated muscle of head and neck
 - Post otic part --- segmented. Each segment is called somite.
 - Somite
 - Sclerotome ----- Primitive vertebrae & Ribs
 - Dermomyotome ----- Dermis & Skeletal muscle
- 2) **Intermediate mesoderm:** It contributes to kidneys and gonads.
- 3) **Lateral plate mesoderm:** With the formation of intraembryonic coelom it is divided into
 - Somatopleuric / Parietal layer --- forms parietal layer of body wall
 - Splanchnopleuric / Visceral layer --- forms visceral layer of body cavities.

Somites

The paraxial mesoderm is a thick longitudinal column of intraembryonic mesoderm extending cranially from the primitive streak to the prechordal plate. The paraxial mesoderm is divided into

- Pre otic part --- unsegmented
 - Basal part of skull
 - Striated muscle of head and neck
- Post otic part --- segmented.

The post otic part of paraxial mesoderm is subdivided into cubical blocks called somites or metameres.

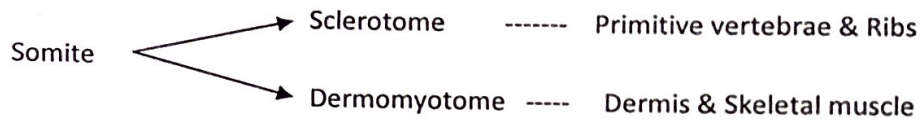
Segmentation extends in cranio caudal direction. Somites appear between 20th and 30th day of development.

Number of somites: By the end of 5th week 44 pairs of somites are present.

4 – Occipital 8 – Cervical 12 – Thoracic 5 – Lumbar 5 – Sacral 8-10 – Coccygeal

Each somite contains a cavity called myocele which is later obliterated.

Differentiation of somites:



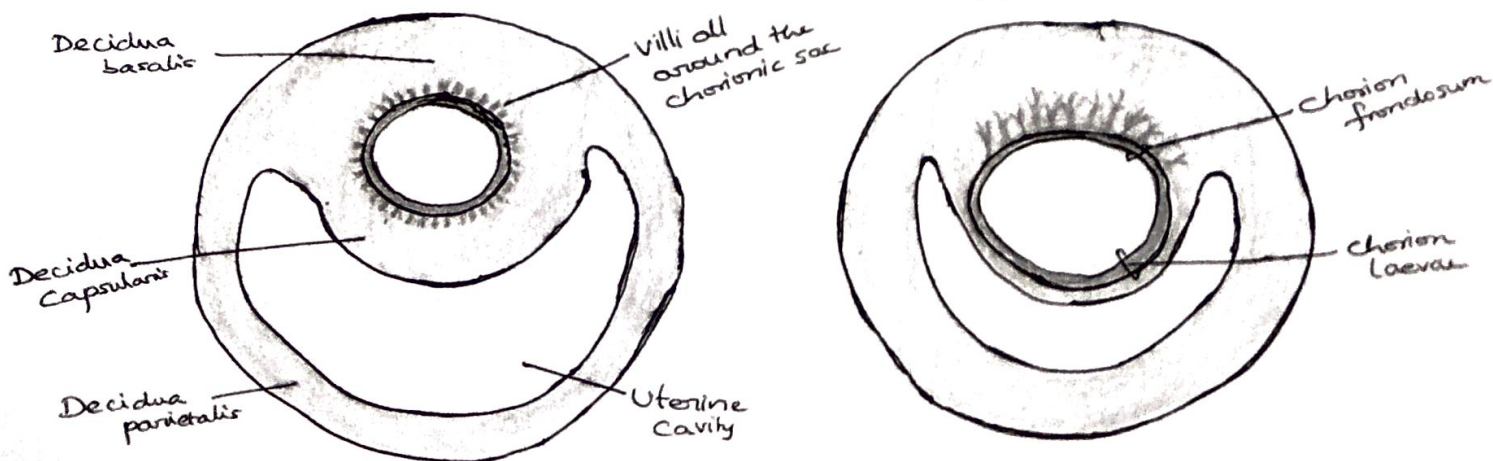
Chorion

The trophoblast together with somatopleuric layer of extraembryonic mesoderm is known as chorion.

Formation: With the formation of extraembryonic coelom, the extraembryonic mesoderm is divided into somatopleuric and splanchnopleuric layers. The somatopleuric layer with overlying trophoblast forms chorion.

During the development of placenta small finger like projections arise from chorion. Initially chorionic villi are formed all round the chorionic sac.

Later the villi in relation to decidua capsularis degenerate and this part of chorion becomes smooth and is called *chorion laeve*. The villi in relation to decidua basalis grow extensively and this part is called *chorion frondosum*. Chorion frondosum contributes to fetal portion of placenta.



Amnion

It is a thin extraembryonic membrane

It is made up of an outer layer of somatopleuric layer of extraembryonic mesoderm and inner layer of amniogenic cells. It forms the roof of amniotic cavity. When the amniotic cavity increases in size it fuses with chorion to form choria amniotic membrane.

Functions: 1) It contributes to amniotic fluid.

2) Protection – Amnion prevents ascending uterine infection.

Amniotic fluid

It is the fluid present in the amniotic cavity. It plays a major role in fetal growth and development.

Source: 1) Most of the fluid is derived as a transudate from maternal serum.

2) Some fluid is secreted by amnion.

3) Urine excreted by fetus.

Volume: 30ml – 10th week; 350ml – 20th week; 1000ml – 37th week.

Composition: Water – 99%, desquamated fetal epithelial cells, salts.

Circulation: Fluid is swallowed by the fetus and absorbed by the fetal digestive tract. Fluid passes into the fetal blood stream and the waste products present in it cross the placental membrane and enter the maternal blood. Excess water in the fetal blood is excreted by fetal kidneys and returned to amniotic sac through fetal urinary tract.

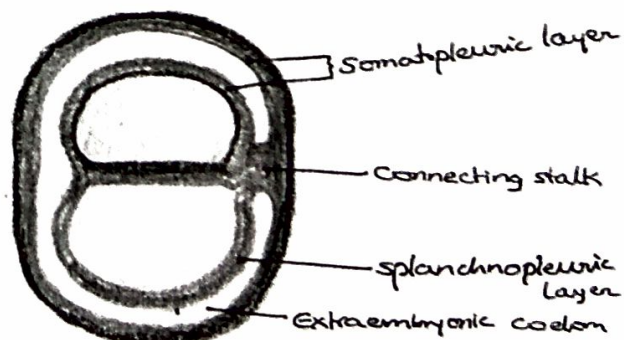
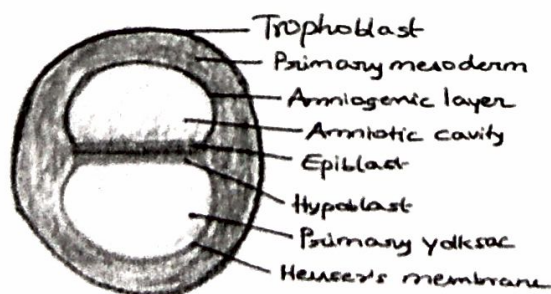
Functions: 1) It permits symmetrical external growth of the embryo. 2) It serves as a cushion.

3) Helps to control body temperature of the embryo.

4) Acts as a barrier to infection.

Disorders: Oligohydramnios – Low volume of the fluid (<400ml) Ex: Renal agenesis

Polyhydramnios – High volume of the fluid (>2000ml) Ex: Anencephaly, Oesophageal atresia.



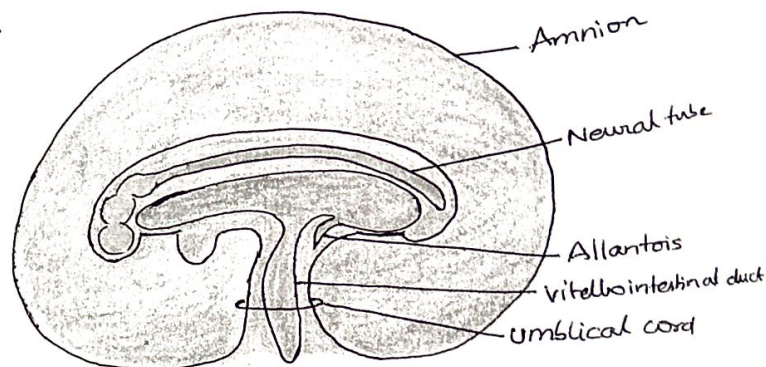
Allantois

Allantois is a sausage shaped diverticulum from the caudal wall of yolk sac that extends into the connecting stalk. It appears on the 16th day. After the formation of tail fold, it appears on the ventral side of the hind gut along with the connecting stalk.

In reptiles and birds, it has respiratory function and acts as reservoir of urine.

Derivatives: 1) Proximal part of allantois is absorbed into the urinary bladder.

2) Distal part forms a fibrous band urachus extending from apex of urinary bladder to the umbilicus. In adults it is represented as median umbilical ligament.



Decidua

Endometrium of the uterus after implantation is called decidua.

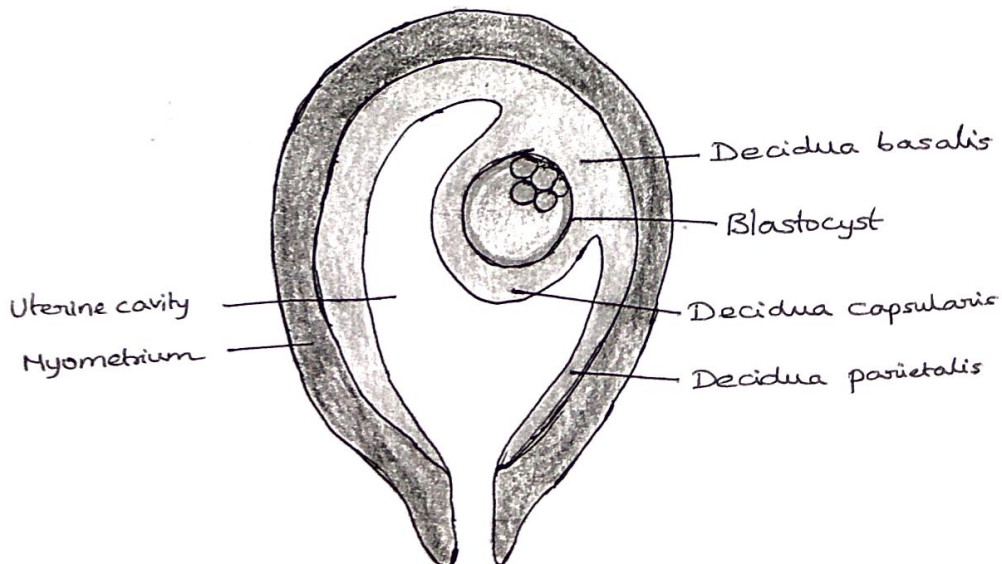
When the morula reaches the uterine cavity, the endometrium is in secretory phase. After implantation, the features of endometrium seen in secretory phase are intensified. The stromal cells become enlarged, vacuolated and store glycogen and lipids. This change in stromal cells is called **decidual reaction**.

Parts: *Decidua basalis*: It is the part of deciduas at the embryonic pole of the blastocyst. It is firmly anchored to chorion.

Deciduas capsularis: It is the part of deciduas covering the abembryonic pole.

Decidua parietalis: It is the part of deciduas lining the rest of uterine cavity.

Fate of decidua: At the end of pregnancy it is shed off along with fetal membranes and placenta.



Placenta

Placenta is a discoid, chorio-decidual organ which connects the fetus with the uterine wall of the mother.

At full term, its diameter is 15 – 20 cm, thickness is 3 cm, and weight is 500 gm.

Features: Fetal surface: It is smooth and covered by amnion. Umbilical cord is attached to this surface close to the centre. Beneath the amnion umbilical vessels radiate from the cord.

Maternal surface: It is rough. It presents 15 – 30 polygonal areas known as cotyledons which are limited by fissures.

Peripheral margin: It is continuous with fetal membrane.

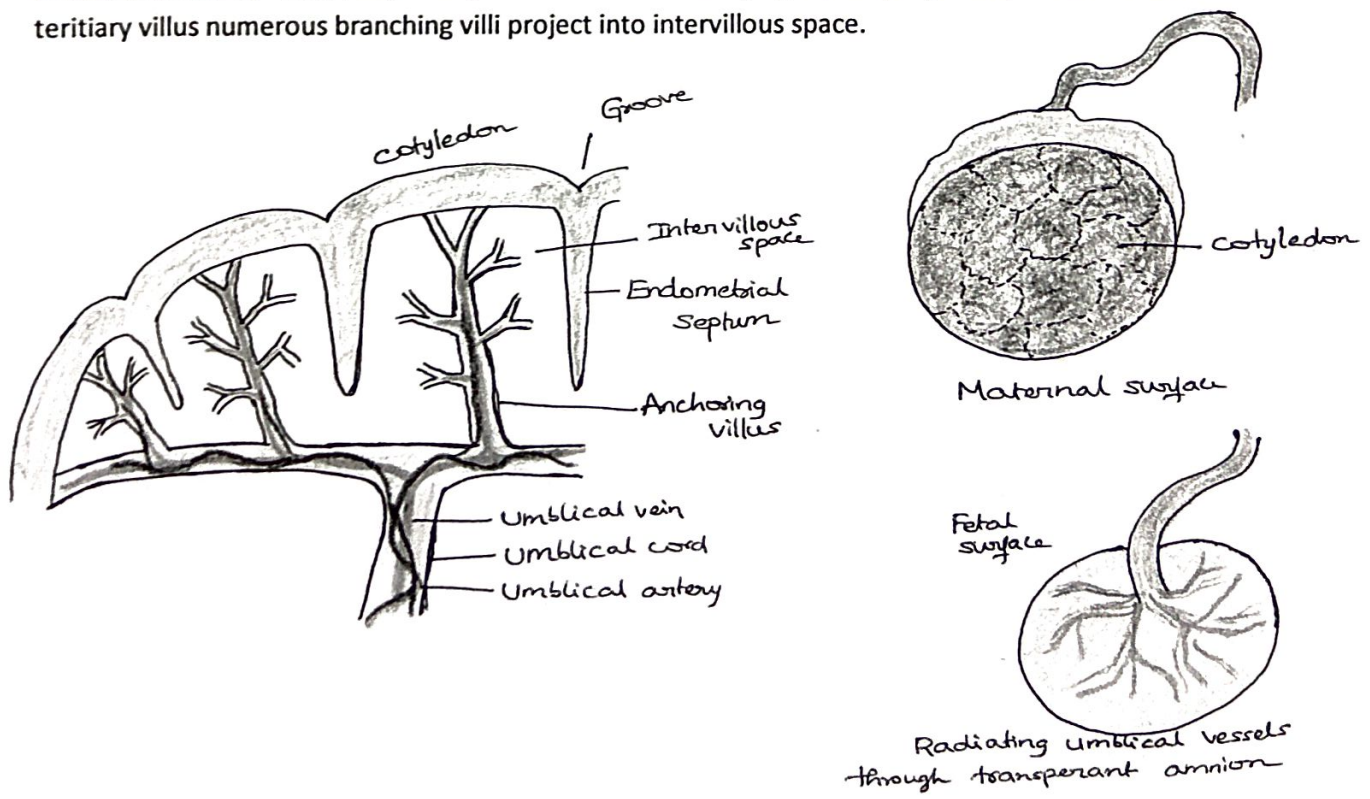
Development: It is developed from two sources. Fetal portion develops from *chorion frondosum* and maternal portion from *decidua basalis*.

Structure: The placenta consists of chorionic plate on the fetal side, basal plate on the maternal side, stem villi extending between the plates and the intervillous space between the stem villi filled with maternal blood.

Chorionic plate: It is covered by amnion. It is composed of a) Primary mesoderm containing umbilical vessels, b) Cytotrophoblast and c) Syncytiotrophoblast.

Basal plate: It is composed of a) Decidua basalis containing maternal blood vessels, b) outer layer of syncytiotrophoblast (Nitabuch's membrane), c) Outer shell of cytotrophoblast and d) Inner layer of syncytiotrophoblast (Rohr's fibrinoid striae).

Stem villi: They connect chorionic and basal plates. Three types of villi develop in succession. a) **Primary villi** – contain central core of cytotrophoblast covered by syncytiotrophoblast. b) **Secondary villi** – contain central core of primary mesoderm covered by cyto and syncytiotrophoblast. c) **Tertiary villus** – contain fetal blood vessels in primary mesoderm covered by cyto and syncytiotrophoblast. From tertiary villus numerous branching villi project into intervillous space.

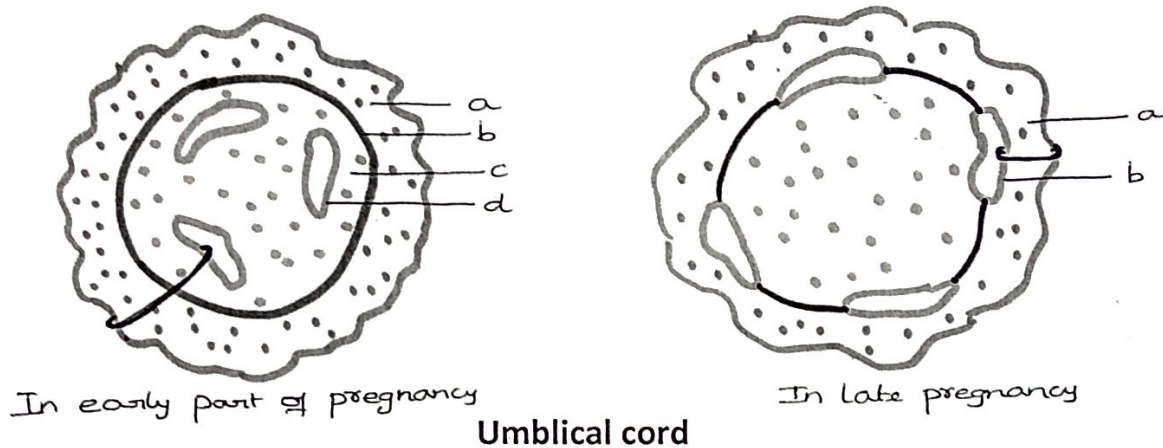


Placental barrier / Placental membrane

The placental membrane separates maternal blood in intervillous space from fetal blood in blood vessels present in villi.

Layers of placental membrane in early part of pregnancy: a) Syncytiotrophoblast, b) Cytotrophoblast, c) Primary mesoderm and d) Endothelium of fetal blood vessels.

Layers of placental membrane in ^{Late} early part of pregnancy: a) Thin syncytiotrophoblast, and b) Endothelium of fetal blood vessels



It is a tubular cord enveloped by the glistening membrane, amnion.

Attachments: One end of the cord is attached to the centre of anterior abdominal wall of fetus. The other end is attached to fetal surface of placenta.

Length: 45 – 50 cm **Width:** 2 cm

Characteristics: The cord is twisted presenting false knots.

Formation: The connecting stalk surrounded by a sleeve of amnion is converted into umbilical cord.

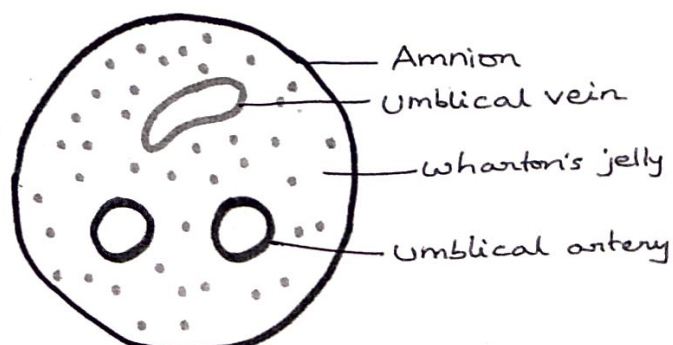
Contents: a) **Umbilical arteries** – 2 in number. They carry deoxygenated blood from fetus to placenta.

b) **Umbilical vein** – Right vein disappears. Left vein persists and it carries oxygenated blood.

c) **Wharton's jelly** – Formed by mucoid degeneration of primary mesoderm.

d) **Distal part of allantois**

e) **Vitellointestinal duct.**



Classification / Anomalies of placenta

Anomalies in shape:

Bilobed or Multi lobed placenta: The placenta consists of two or more lobes.

Diffuse placenta: The placenta is thin due to persistence of chorionic villi all around the blastocyst.

Placenta succenturiata: A small part of the placenta is separated from the main part but remains connect through fetal blood vessels and membranes.

Placenta fenestrata: A hole is present in the placenta.

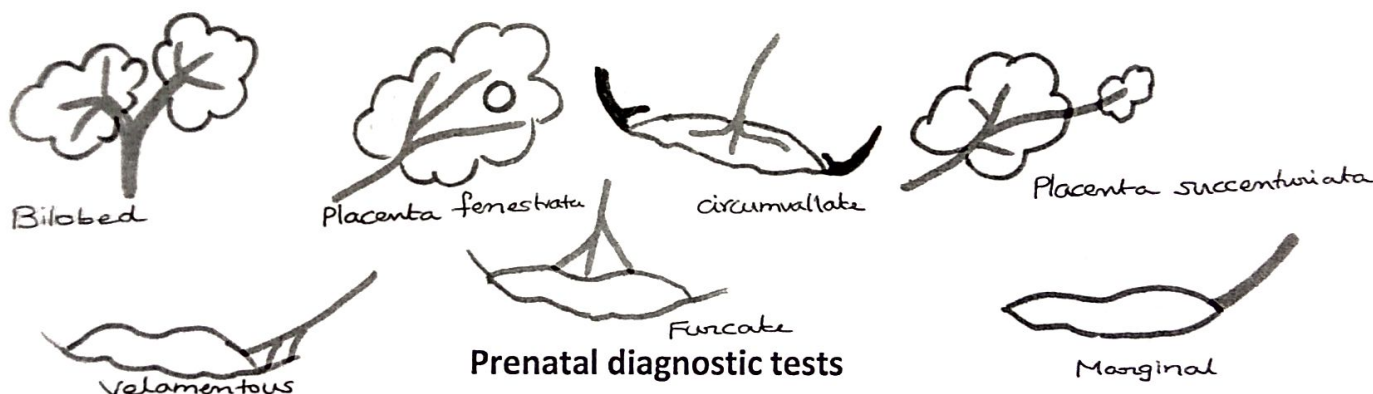
Circumvallate placenta: The peripheral margin of the placenta is covered by circular fold of decidua.

Anomalies in attachment of umbilical cord:

Marginal / Battle dore placenta: Umbilical cord is attached to the margin of placenta.

Furcate placenta: Blood vessels of umbilical cord divide before reaching the placenta.

Velamentous placenta: Umbilical cord is attached to the fetal membrane (amnion).



I. **Ultrasonography:** It is commonly used to evaluate the fetus because of low cost, wide availability and lack of adverse effects. Abnormalities of placenta, abnormal presentations, multiple births, etc can be determined.

II. **Amniocentesis:** It is a procedure in which a needle is inserted into the amniotic cavity through the anterior abdominal wall under ultrasound guidance. About 10 – 15 ml of fluid is withdrawn. It is performed at 14 – 16 weeks of gestation.

Uses	
Diagnostic	Therapeutic
Chromosomal / genetic disorders	Induction of labour
Inborn errors of metabolism	Acute hydramnios
Neural tube defects	

III. **Alfa feto protein assay:** It is a glycoprotein synthesized by fetal liver.

↑ AFP – CNS defects

↓ AFP – Down syndrome

IV. **Chorion villus sampling:** It is carried out between 10 – 12 weeks of gestation. It is used for detecting chromosomal abnormalities.

V. **Fetoscopy:** Used to scan congenital anomalies.

VI. **Percutaneous umbilical cord blood sampling:** Used for diagnosis of infection or anemia.

VII. **CT / MRI Scan:** MRI is safe due to non-ionising radiation.

Twins

When a mother gives birth to two young individuals in a single pregnancy, it is known as twinning.

Dizygotic (Fraternal) twins: They develop from two different zygotes which are formed as a result of fertilization of two oocytes. Approximately 2/3rds of twins are dizygotic. They are genetically different. They may be of same or different sex.

Monozygotic / Identical twins: They develop from one zygote which is formed as a result of fertilization of one oocyte. They are of same sex and genetically identical.

Types of monozygotic twins:

- Monozygotic bichorionic (25 – 30%):*** At two cell stage, each blastomere develop into two separate zygotes. So they possess separate placentae and chorions.
- Monozygotic biamniotic (70 – 75%):*** At the blastocyst stage, the inner cell mass is separated into two equal parts which develop into two embryos. So they possess single placenta, common chorion and separate amnion.
- Monochorionic monoamniotic (1 – 2%):*** In the bilaminar germ disc, two separate organizing centres appear and the disc gives rise to two separate embryos. They lie in single chorion and single amnion.

When the embryos are incompletely separated they are called **conjoint (Siamese) twins** (Craniopagus / Thoracopagus / Pygopagus).

When one of the conjoined twins remains rudimentary due to diminished blood supply it is called **parasitic twin**.

Pharyngeal apparatus

Derivatives of First Pharyngeal (Mandibular) Arch

- I. **Cartilage:** The cartilage of first arch is called Meckel's cartilage.
 - Dorsal part – Malleus, Incus
 - Middle part – Anterior ligament of malleus, Sphenomandibular ligament
 - Ventral part – Body of mandible from mandibular foramen to mental foramen.
- II. **Muscles:** Muscles of mastication (Masseter, Temporalis, Lateral pterygoid, medial pterygoid)
 - Tensor veli palatine
 - Tensor tympani
 - Anterior belly of digastric
 - Mylohyoid
- III. **Nerve:** Mandibular nerve
 - Chorda tympani nerve (pre trematic branch)
- IV. **Artery:** Most of the first arch artery regresses except a small part which forms part of maxillary artery.

First arch (Mandibular arch) syndrome:

Abnormal development of first pharyngeal arch results in various congenital anomalies.

- a) *Treacher Collins syndrome (Mandibulo facial dysostosis)* – Malar hypoplasia, Mandibular hypoplasia, down slanting palpebral fissure, deformities of ear.
- b) *Pierre Robin syndrome* – Micrognathia, cleft palate, glossoptosis.

Derivatives of Second Pharyngeal (Hyoid) Arch

- I. **Cartilage:** The cartilage of second arch is called Reichert's cartilage.
 - Dorsal part – Stapes, Styloid process of temporal bone
 - Middle part – Stylohyoid ligament
 - Ventral part – Superior cornua and superior part of body of hyoid bone.
- II. **Muscle:** Stapedius
 - Stylohyoid
 - Posterior belly of digastric
 - Muscles of facial expression, Platysma, Auricular muscles.
- III. **Nerve:** Facial nerve
- IV. **Artery:** Most of the second arch artery regresses except a small part which forms stapedial artery.

Derivatives of Third Pharyngeal Arch

- I. **Cartilage:** Dorsal part – disappears
 Ventral part – Greater cornua and inferior part of body of hyoid bone.
- II. **Muscle:** Stylopharyngeus.
- III. **Nerve:** Glossopharyngeal nerve
- IV. **Artery:** Ventral part – Common carotid artery
 Dorsal part – Internal carotid artery

Derivatives of Fourth and Sixth Pharyngeal Arches

	Fourth	Sixth
Cartilage	Dorsal part – disappear Ventral part – Thyroid cartilage	Dorsal part – disappear Ventral part – Cricoid and arytenoid cartilages
Muscle	Cricothyroid Levator veli palatine Constrictors of pharynx	Intrinsic muscles of larynx except cricothyroid
Nerve	Superior laryngeal nerve	Recurrent laryngeal nerve
Artery	Right side – Right subclavian artery Left side – Arch of aorta	Right side: Ventral part – Right pulmonary artery; Dorsal part – disappear Left side: Ventral part – Left pulmonary artery; Dorsal part – Ductus arteriosus

Cervical sinus/Branchial sinus

Cervical cyst/ Branchial cyst

The embryo exhibit four ectodermal pharyngeal grooves or clefts. The mesenchyme of second pharyngeal arch rapidly grows downwards and overlaps the second, third and fourth pharyngeal clefts. The intervening space lined by ectoderm is called cervical or branchial sinus.

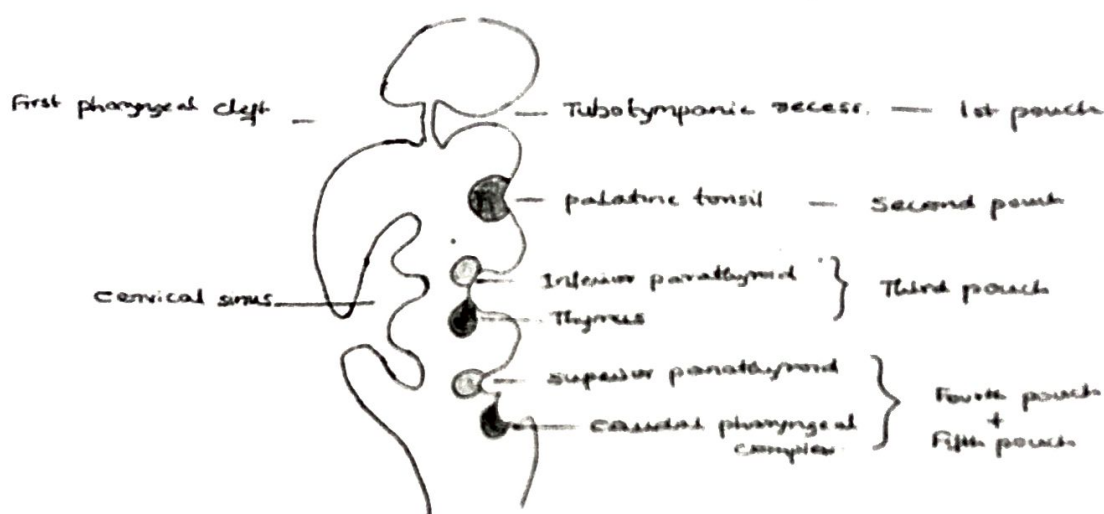
Boundaries of cervical sinus: Cranially by the overgrowing hyoid arch and caudally by epipericardial ridge.

The cervical sinus is obliterated by gradual approximation of its walls from within outwards. The second arch takes a greater share in the closure of the cervical sinus and this probably accounts for caudal migration of platysma.

Branchial cyst: Remnants of cervical sinus may persist and form a spherical or elongated cyst. They lie anywhere along the anterior border of the sternocleidomastoid, but more commonly inferior to angle of the mandible.

Derivatives of Pharyngeal / Endodermal pouches

- I. First Pharyngeal pouch: It elongates to form a diverticulum called tubotympanic recess. Distal part of the recess expands and forms mucosa of tympanic cavity and mastoid antrum. Proximal part is tubular and forms mucosa of auditory tube.
- II. Second pharyngeal pouch: Palatine tonsil
- III. Third Pharyngeal pouch: Inferior parathyroid and Thymus.
- IV. Fourth pharyngeal pouch: Superior parathyroid and Caudal pharyngeal complex. The neural crest cells which migrate into this complex form parafollicular cells of thyroid gland.



Development of Palatine Tonsil

The endoderm of second pharyngeal pouch proliferates and grows into underlying mesenchyme as tonsillar buds. The central parts of these buds break down to form tonsillar crypts. The endoderm of the pouch forms the surface epithelium and the lining of the crypts. The mesenchyme around the crypts differentiates into lymphoid tissue which soon organizes into lymphatic nodules. Most of the second pharyngeal pouch is obliterated, a part of it persists as tonsillar sinus or intra tonsillar cleft.

Development of Parathyroid Glands

The endoderm of third pharyngeal pouch proliferates into parathyroid III (inferior). The endoderm of fourth pharyngeal pouch proliferates into parathyroid IV (superior). The third pouch also gives origin to thymus. This organ is closely related to parathyroid III. The descent of the heart allows caudal migration of thymus and parathyroid III. Hence the parathyroid III sweeps along the dorsal surface of lateral lobe of thyroid and finally gets disconnected from thymus. As a result parathyroid III is caudal to parathyroid IV.

Superior parathyroids are relatively constant in position. But inferior parathyroids may descend into lower part of neck or even into anterior mediastinum.

Development of Tongue

I. Mucous membrane:

Its development is divided into ventral $2/3^{\text{rd}}$ (oral part) & dorsal $1/3^{\text{rd}}$ (Pharyngeal part).

A pair of **lingual swellings** appears at the ventral ends of the first arches. An unpaired median elevation, **tuberculum impar** appear caudal to the lingual swellings. The lingual swellings grow forwards and fuse with each other across the midline and subsequently join with tuberculum impar. The combined mass forms ventral $2/3^{\text{rd}}$ of tongue.

Just behind the tuberculum impar, the **thyroid diverticulum** extends caudally through the substance of tongue as thyroglossal duct. Later, most of the duct disappears but its commencement persists as foramen caecum.

Hypobranchial eminence develops in the ventral parts of third and fourth pairs of pharyngeal arches.

Rostral part forms posterior $1/3^{\text{rd}}$ of tongue and the caudal part forms epiglottis.

The rostral part of hypobranchial eminence overgrows the second arch and fuses with anterior $2/3^{\text{rd}}$ of tongue. The line of fusion is indicated by sulcus terminalis.

II. Muscles of tongue:

They are derived from myoblasts that migrate from **occipital myotomes**. The hypoglossal nerve accompanies the myoblasts.

III. Fibro arcolar stroma: Derived from the mesenchyme.

Nerve supply :(Evidence)

	Anterior $2/3^{\text{rd}}$	Posterior $1/3^{\text{rd}}$	Posterior most part
General sense	Lingual nerve (branch of Mandibular nerve – 1 st arch)	Glossopharyngeal nerve – Nerve of third arch	Superior laryngeal nerve – Nerve of fourth arch
Taste	Chorda tympani nerve (Pretrematic nerve – 1 st arch)		

Anomalies of tongue development:

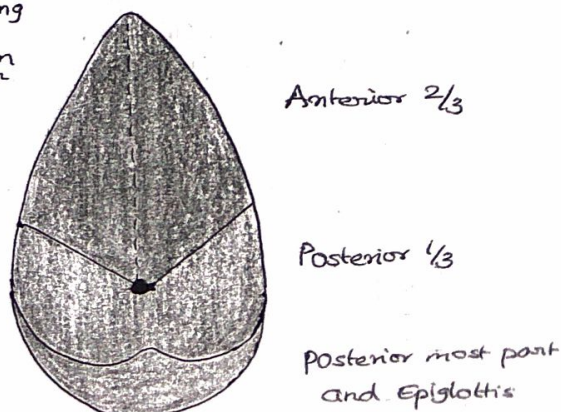
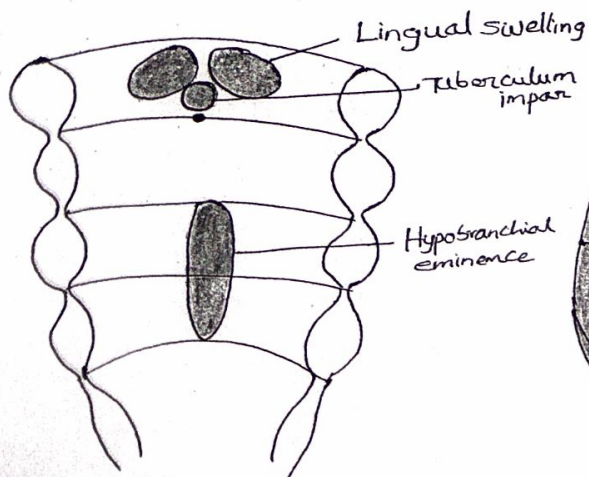
Aglossia – Absence of tongue

Macroglossia – Large tongue

Microglossia – small tongue

Ankyloglossia – Frenulum is short

Bifid tongue – Due to incomplete fusion of lingual swellings.



Development of Thyroid Gland

Thyroid gland is the first endocrine to develop in the embryo (approx. after 24 days of fertilization).

Thyroglossal duct:

Before the fusion of rudiments of tongue, the endodermal cells dorsal to the tuberculum impar proliferate to form a surface elevation – median thyroid rudiment. Thereafter the cells evaginate caudally through the substance of the tongue and form the thyroglossal duct. The thyroglossal duct descends in the neck, passing ventral to developing hyoid bone and laryngeal cartilages.

When the duct reaches ventral to the trachea, it divides into bilobed mass, which forms the primordium of isthmus and lateral lobes of thyroid.

The lateral thyroid rudiments, derived from *caudal pharyngeal complex* (fourth pouch + rudimentary 5th pouch) fuse with the bilobed mass and arrest the further caudal migration. The neural crest cells which migrate into this complex form parafollicular cells of thyroid gland.

Subsequently the thyroglossal duct disappear. The commencement of the duct persists as a small depression in the dorsum of the tongue – the foramen caecum.

Anomalies:

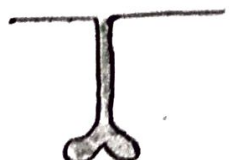
1. **Agnesis of Thyroid** – complete absence of the gland. One or both lobes may be absent. Isthmus may be absent.
2. **Thyroglossal cyst:** Abnormal persistence of thyroglossal duct forms the cyst.
3. **Ectopic thyroid:** It is common as lingual thyroid which is due to arrest of caudal growth of thyroglossal duct.



Median thyroid rudiment



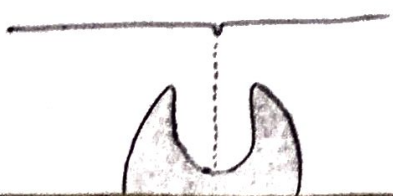
Thyroglossal duct



Bifid lower end of
Thyroglossal duct



Bilobed mass fuses with
Lateral thyroid rudiments



Regression of rest of
thyroglossal duct

Development of Face

Five facial primordia appear around the stomodeum.

One frontonasal prominence, A pair of maxillary prominences and a pair of mandibular prominences.

I Frontonasal prominence:

The mesenchyme which covers the caudal surface of fore brain vesicle proliferates, and this together with overlying surface ectoderm forms the frontonasal process.

The frontal part of this prominence forms the fore head.

On the infero lateral part of fronto nasal prominence, the surface ectoderm thickens to form **nasal placodes**. The mesenchyme in the margins of the placodes proliferates to form medial and lateral nasal processes. As a result the nasal placodes lie at the depression called nasal pit.

Lateral nasal process forms the ala of nose.

Median nasal process forms philtrum of upper lip, primitive palate and nasal septum.

II Maxillary prominences:

They develop from mandibular arches. They grow ventromedially and fuse with lateral nasal process along a line-naso-lacrima groove. A solid epithelial cord is formed as a result of thickening of ectoderm in the floor of the groove. Later it sinks into the mesenchyme and gets canalized to form nasolacrimal duct.

Maxillary processes grow further medially below the nasal pits and fuse with globular swellings of median nasal process.

III Mandibular prominences: They are formed from mandibular arches.

Lower lip: Fusion of mandibular prominences.

Upper lip: Fusion of two maxillary prominences with globular swelling of median nasal prominence.

Nose: External nares are formed from nasal pits. Ala of nose from lateral nasal process. Nasal septum from median nasal process.

Cheeks: Progressive fusion of maxillary and mandibular prominences.

Development of Upper Lip

The lateral part of the upper lip is formed by maxillary prominence.

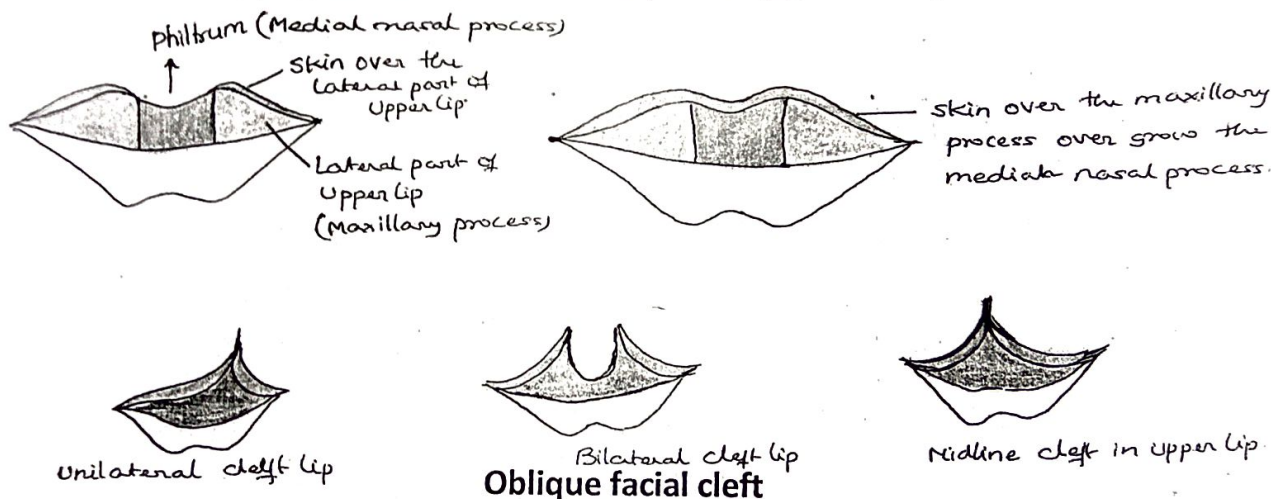
The median part (philtrum) of the upper lip is formed by globular swellings of median nasal process.

The ectoderm maxillary prominence overgrows the median nasal process in the midline. As a result skin of entire upper lip is innervated by maxillary nerve.

Cleft lip:

Incidence: 1 in 1000 births. Common in male infants

1. **Unilateral cleft in upper lip:** Failure of fusion of maxillary prominence with globular swellings of median nasal process on one side.
2. **Bilateral cleft lip (hare lip):** Failure of fusion of maxillary prominence with globular swellings of median nasal process on both sides.
3. **Midline cleft upper lip:** Due to defective development of lower part of frontonasal process.
4. **Cleft in lower lip:** Failure of fusion of mandibular prominences.



Failure of fusion of maxillary prominence with lateral nasal process gives rise to a cleft running from the medial angle of eye to the mouth. The nasolacrimal duct is not formed. Nasolacrimal grooves are persistent.

Development of Palate

Palatogenesis begins in the 6th week and is completed by 12th week.

- The palate develops from –
1. Primitive palate
 2. Secondary palate

Primitive palate: It is formed from globular swellings of median nasal process of frontonasal process. It ossifies to form premaxilla.

Secondary palate: Two mesenchymal projections (palatine shelves) extend from the inner aspect of maxillary prominences. Initially they project inferomedially on each side of the tongue. Later they become horizontal above the tongue. This is facilitated by release of hyaluronic acid by the mesenchyme. These palatine processes fuse with each other to form secondary palate. Posterior part of secondary palate remains unossified to form soft palate.

Cleft palate:

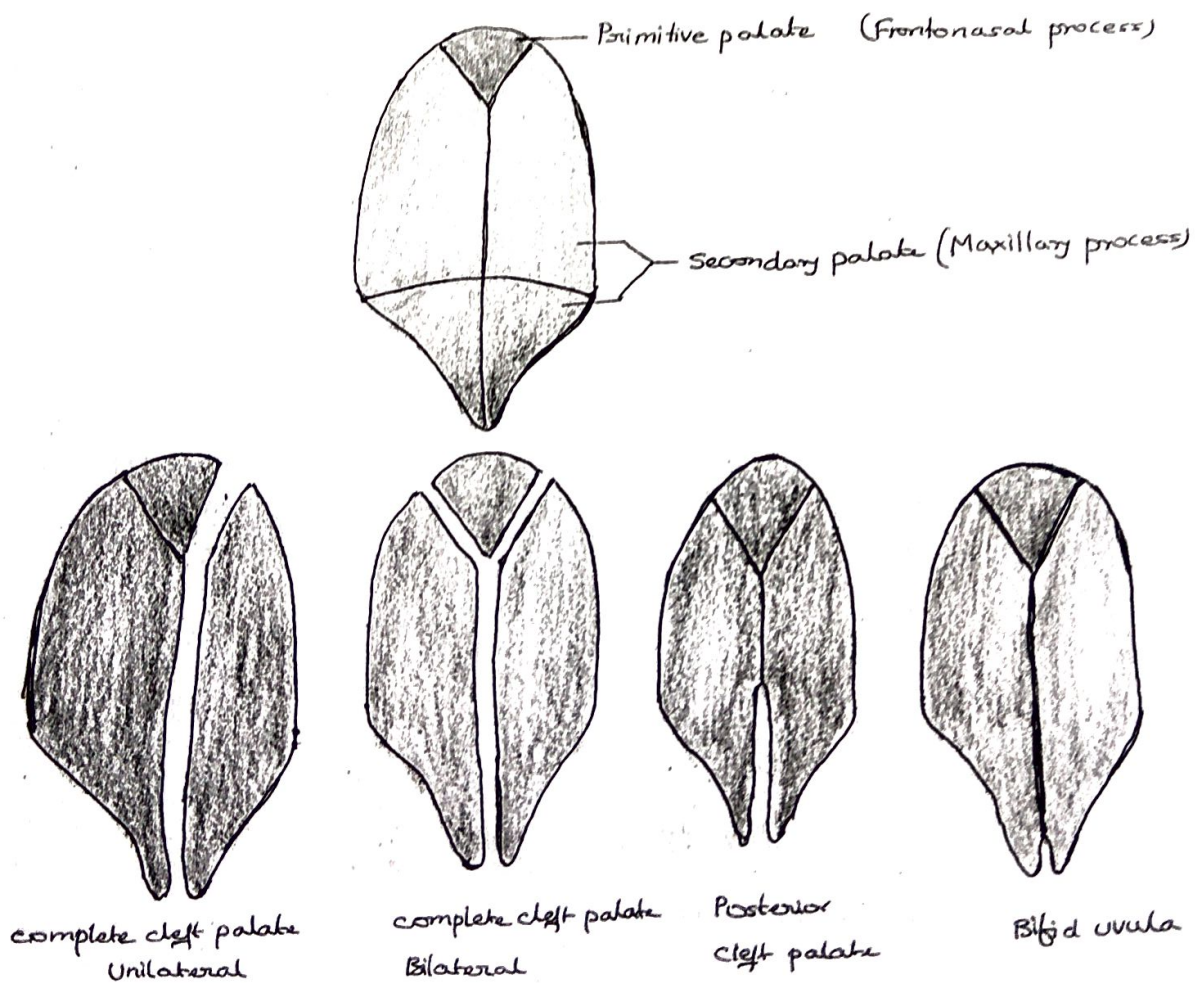
Incidence: 1 in 2500 births. Common in females.

Defective fusion of the various components of the palate gives rise to clefts in the palate. Clefts in the palate result in anomalous communication between mouth and the nose.

They may be unilateral or bilateral

1) **Clefts in anterior palate:** Failure of fusion of primitive palate with palatine processes of maxilla.

2) **Clefts in the posterior palate:** Failure of fusion of two palatine processes of maxillae. Depending on degree of fusion, the cleft may be confined to hard palate and soft palate (or) only soft palate (or) only uvula.



DIGESTIVE SYSTEM

Derivatives of foregut

Foregut is the part of the yolk sac which is incorporated into the head fold of the embryo.

Caudally, foregut is continuous with the midgut at the anterior intestinal portal, which in the adults corresponds to the termination of bile duct in the 2nd part of duodenum.

Ventrally, the foregut presents a median laryngotracheal groove, which bulges forwards and then caudally.

Foregut is divided into - Pre laryngeal part and Post laryngeal part.

Derivatives:

Prelaryngeal part	Postlaryngeal part
Floor of the mouth	Oesophagus
Tongue	Stomach
Pharynx	Duodenum up to the opening of bile duct
Derivatives of endodermal pouches	Liver and biliary apparatus
Thyroid gland	Pancreas
Lower respiratory tract	

Derivatives of midgut

Midgut is the part of yolk sac incorporated the lateral folds of the embryo.

Anteriorly, it communicates with the foregut at the anterior intestinal portal which corresponds to the opening of bile duct into the 2nd part of duodenum.

Posteriorly it communicates with the hindgut at the posterior intestinal portal which corresponds to the junction of right 2/3 and left 1/3 of transverse colon. Ventrally it communicates with the extra embryonic part of yolk sac through vitello intestinal duct.

A small diverticulum called caecal bud arises from the midgut loop close to the apex. It divides midgut into pre caecal and post caecal parts.

Derivatives:

Precaecal part	Postcaecal part
Duodenum, distal to the opening of bile duct	Caecum
Jejunum	Vermiform appendix
Ileum	Ascending colon
	Right 2/3 rd transverse colon

Houston

Derivatives of hindgut

Hind gut is the part of yolk sac which is incorporated into the tail fold of the embryo.

Anteriorly it communicates with the midgut at the posterior intestinal portal which corresponds to the junction between the hindgut and the midgut.

The ventral wall of hindgut presents allantoic diverticulum which extends up to the fetal end of umbilical cord. The hindgut is divided into pre allantoic and post allantoic parts.

The dilated post allantoic part of hindgut is called the endodermal cloaca. It is divided by urorectal septum into dorsal part - primitive rectum and ventral part - primitive urogenital sinus.

Derivatives of hindgut:

Preallantoic part	Post allantoic part	
Left 1/3 rd of transverse colon. Descending colon Sigmoid colon Rectum above <u>Houston's 3rd valve</u>	Primitive rectum	Primitive urogenital sinus
	Rectum below Houston's 3 rd valve <u>Anal canal above pectinate line</u>	Mucosa of urinary bladder <u>Most of urethra</u>

Development of Duodenum

Duodenum is developed from two sources –

- Above hepato pancreatic ampulla – from the foregut.
- Below hepato pancreatic ampulla – from midgut.

The dual development of duodenum is represented by its blood supply. Duodenum is supplied by anastomoses between superior pancreatico duodenal artery (branch of coeliac trunk – artery of foregut) and inferior pancreatico duodenal artery (branch of superior mesenteric artery – artery of midgut).

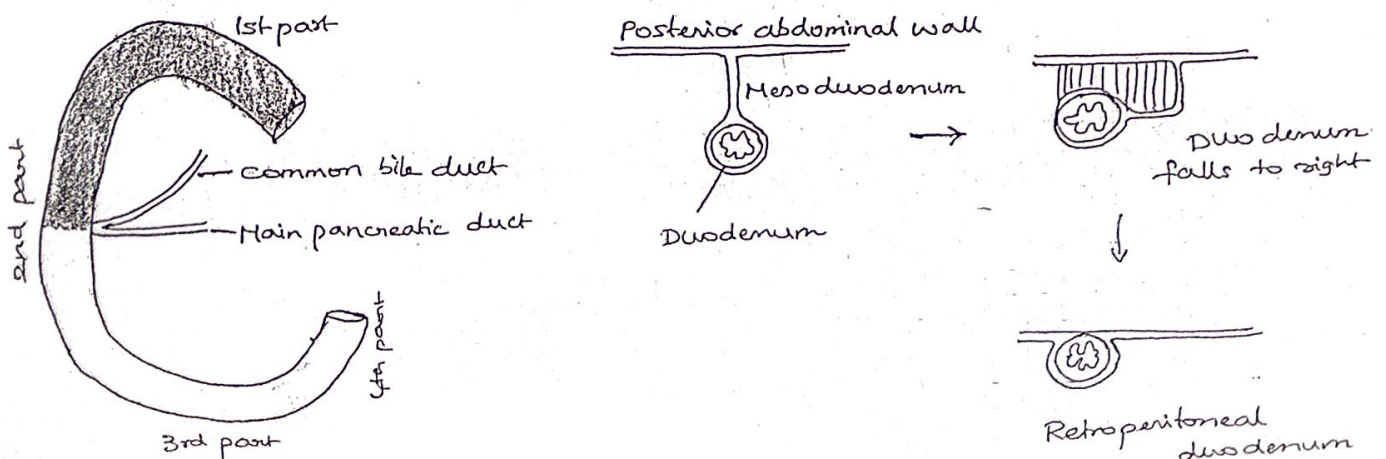
Rotation: The part of the gut that gives rise to the duodenum forms a loop attached to posterior abdominal wall by mesoduodenum. Later, this loop falls to the right.

Fixation: The mesoduodenum then fuses with peritoneum of posterior abdominal wall, with the result most of the duodenum becomes retroperitoneal.

Anomalies of duodenum:

Duodenal stenosis – Partial occlusion of the duodenal lumen. It is due to incomplete recanalization.

Duodenal atresia – complete occlusion of lumen of duodenum.



Rotation of midgut

As the midgut elongates, it projects into the extra embryonic coelom in the proximal part of the umbilical cord (physiological umbilical herniation). It occurs at the 6th week.

The loop is suspended by dorsal mesentry containing superior mesenteric artery. So the midgut loop presents a pre arterial segment and post arterial segment. The loop lies in sagittal plane.

Stage I: The pre arterial segment is subjected to downward pressure by the liver. Eventually, the pre arterial segment moves to the right and post arterial segment to the left. (90° rotation anti clock wise)

Stage II: Pre arterial segment (right) elongates rapidly to form coils of jejunum and ileum. Post arterial (left) segment presents cecal bud.

Expansion of abdominal cavity and progressive reduction in size of liver allow the midgut to reenter the abdomen. The small intestine (right) segment is reduced first passing dorsal to superior mesenteric artery.

Later, the left segment returns the abdomen and finds that dorsal part of the abdomen is full of coils of small intestine. So, it rotates upwards and to the right around the axis of superior mesenteric artery and pass successively through the left iliac, umbilical and subhepatic regions.

Rotation of midgut explains why transverse colon lies ventral to superior mesenteric artery, and why third part of duodenum lies dorsal to the artery.

Stage III: From sub hepatic region, caecum and appendix grow caudally through right lumbar, into right iliac fossa.

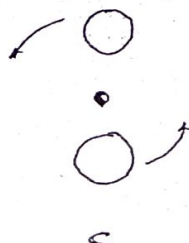
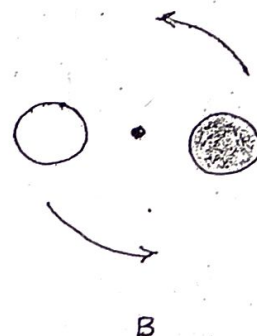
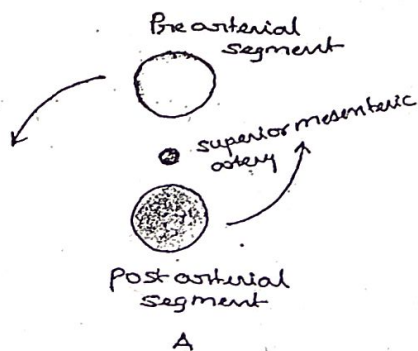
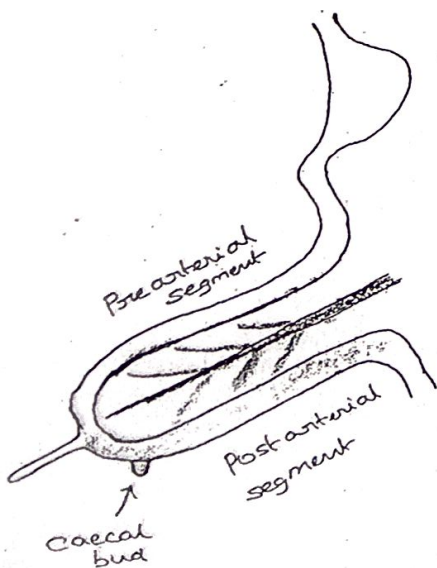
Total range of rotation around the axis of superior mesenteric artery is 270°. (90° within physiological umbilical hernia and 180° as the loop is reduced)

Anomalies:

Non rotation: Midgut fails to rotate as a result small intestine lies on right side and large intestine on the left side of the abdominal cavity.

Reverse rotation: Midgut loop sometimes rotates in clock wise direction. As a result, duodenum lies anterior to superior mesenteric artery and transverse colon lies posterior to the artery.

Exomphalos/ Omphalocele: Coils of small intestine fail to return into the abdominal cavity from their physiological herniation.



Development of Pancreas

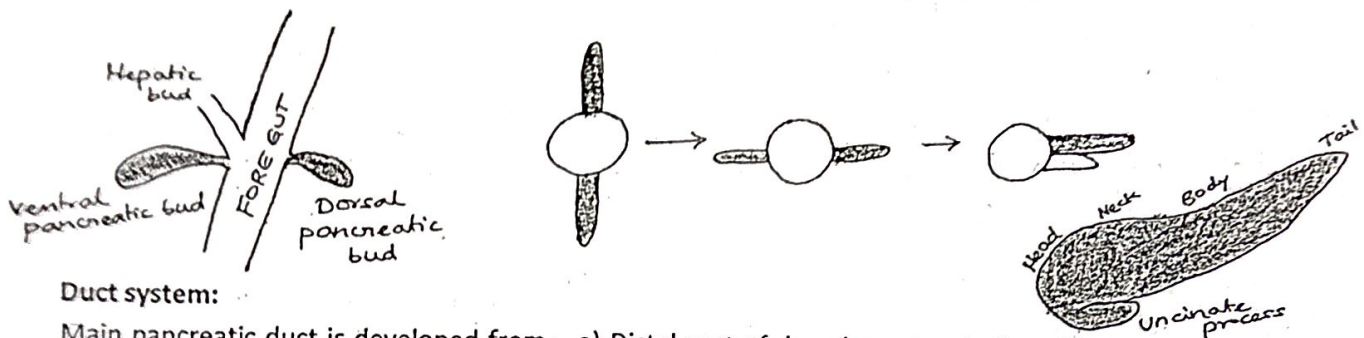
Pancreas develops from dorsal and ventral pancreatic buds, which arise from the caudal part of foregut.
Dorsal pancreatic bud: It grows rapidly between the layers of dorsal mesoduodenum and mesogastrium.

Ventral pancreatic bud: It arises from hepatopancreatic bud. It grows between the layers of ventral mesoduodenum.

When the duodenal loop falls to the right, the ventral bud points to the right and dorsal bud to the left. Thereafter due to the differential growth of the wall of the duodenum, ventral bud shifts to the left side. Pancreas is formed with fusion of two buds.

Ventral pancreatic bud forms uncinete process and lower part of head of pancreas.

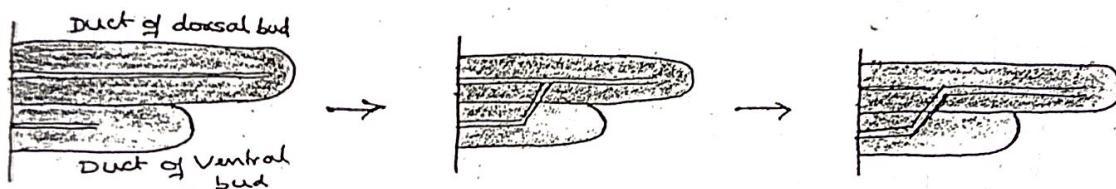
Dorsal pancreatic bud forms upper part of head, neck, body and tail of pancreas.



Duct system:

Main pancreatic duct is developed from – a) Distal part of dorsal pancreatic duct, b) Cross connection between the two ducts and c) Proximal part of ventral pancreatic duct.

Accessory pancreatic duct develops from proximal part of dorsal pancreatic duct.

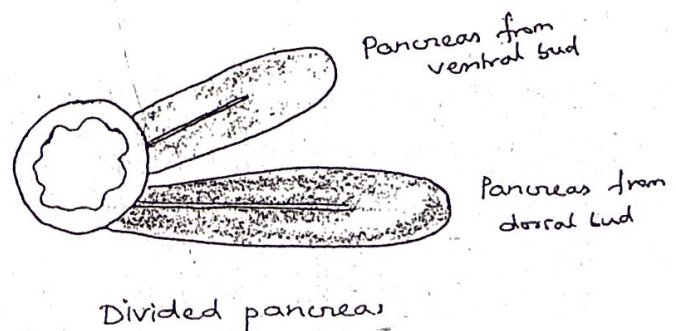
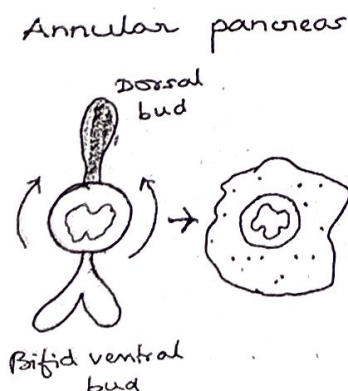


Anomalies:

Annular pancreas: It is due to the growth of bifid ventral bud around the duodenum. It may cause duodenal obstruction.

Accessory pancreas: May be found in the wall of stomach or duodenum or Meckel's diverticulum.

Divided pancreas: Due to failure of fusion of dorsal and ventral pancreatic buds.



Development of Liver and Biliary apparatus



A hepato pancreatic bud arises from the ventral wall of caudal part of the foregut. It divides into hepatic bud and ventral pancreatic bud.

The hepatic bud extends into ventral mesogastrium and into septum transversum. It soon divides into a large cranial part – pars hepatica and small caudal part – pars cystica.

Pars hepatica divides into right and left parts. The proliferating endodermal cells give rise to cords of hepatocytes and epithelium of intrahepatic biliary apparatus.

The fibrous tissue, hemopoietic tissue and kupffer cells of the liver are derived from mesenchyme of septum transversum.

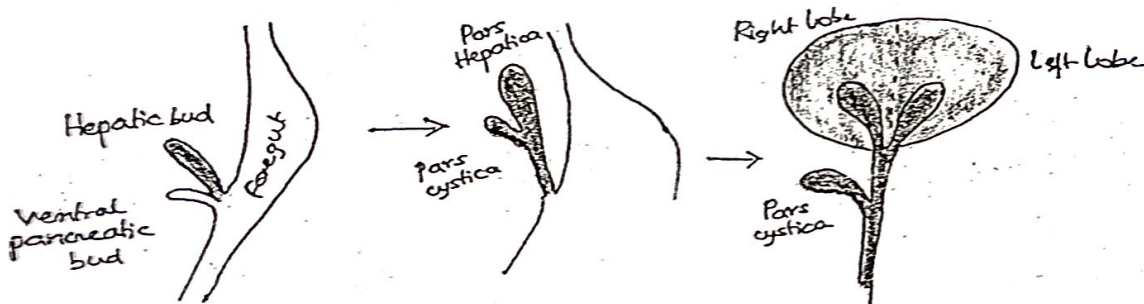
The growth of hepatic cords within the septum transversum disturbs the longitudinal course of vitelline and umbilical veins. These vessels break up into the sinusoids.

Pars cystica forms Gall bladder and cystic duct.

Part of hepatic bud proximal to pars cystica form the bile duct.

Anomalies:

1. Riedel's lobe: It is a tongue like extension from right lobe of the liver.
2. Gall bladder - a) agenesis, b) Phrygian cap, c) Hartmann's pouch, d) Septate bladder
3. Floating gall bladder – Gall bladder is completely covered by peritoneum on all sides.



Development of Spleen

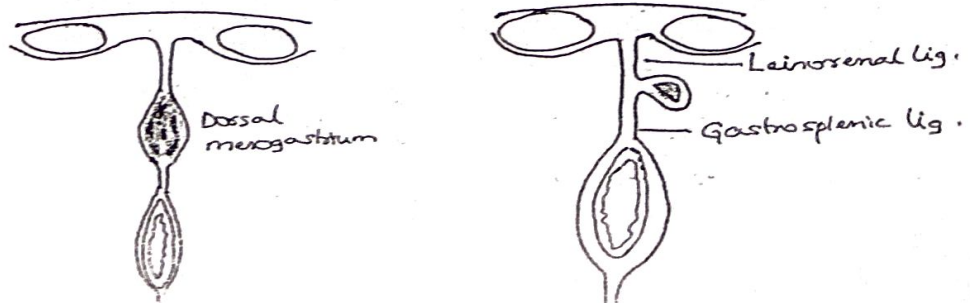
Spleen is developed from a mass of mesenchymal cells (mesoderm) between the layers of the dorsal mesogastrium during 5th week.

It appears as a number of lobules (Spleniculi), which fuse to form a single mass. The notches in the superior border of adult spleen indicate the lobulated development.

With the appearance of spleen, the dorsal mesogastrium is divided into gastrosplenic and lienorenal ligaments.

Anomalies:

Polysplenia / Accessory spleen: one or more splenic masses may exist in the hilum of spleen, gastrosplenic ligament, tail of pancreas etc.



Vitello intestinal duct

The midgut communicates ventrally with the extra embryonic part of yolk sac through vitello intestinal duct. It disappears completely. If it persists, the following anomalies are produced.

Meckel's / Ileal diverticulum:

It is an out pouching of ileum.

It is due to abnormal persistence of proximal part of vitello intestinal duct.

It occurs in 2% of individuals.

2 times more common in males.

2 inches in length.

Attached 2 feet proximal to ileo caecal junction.

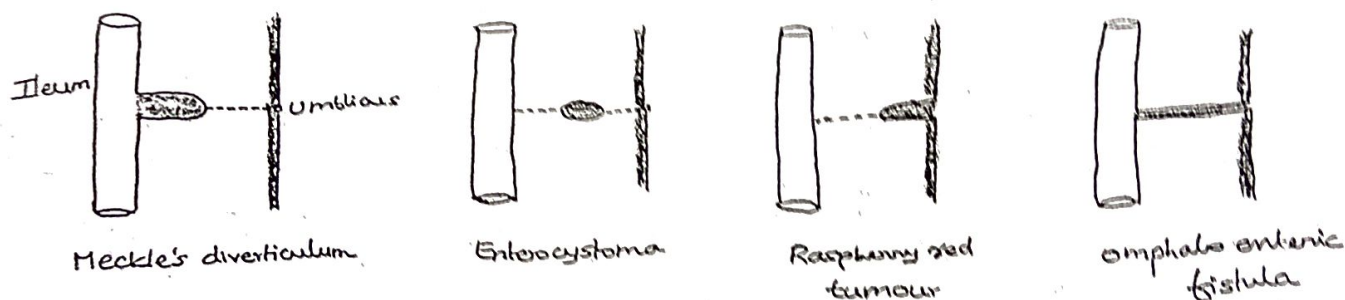
Inflammation – Meckel's diverticulitis. Symptoms mimics appendicitis.

Entero cystoma :

Vitello intestinal duct is closed at both ends, but remain patent in the middle.

Raspberry tumour at umbilicus: It is due to persistence of distal part of the duct.

Omphalo enteric fistula: Vitello intestinal duct remains completely patent.



Development of Rectum and anal canal

Development of rectum:

Above Houston's 3rd valve – from pre allantoic part of hindgut

Below third valve – from dorsal part of endodermal cloaca.

Anal canal:

Pectinate line indicates the former site of anal membrane.

	Above Pectinate line	Below Pectinate line
Development	endodermal cloaca	Ectodermal proctodeum
Arterial supply	Superior rectal artery	Inferior rectal artery
Venous drainage	Superior rectal vein	Inferior rectal vein
(Portocaval anastomosis)		
Lymphatic drainage	Inferior mesenteric nodes	Superficial inguinal nodes
Nerve supply	Autonomic	Inferior rectal nerve (somatic)

Respiratory System

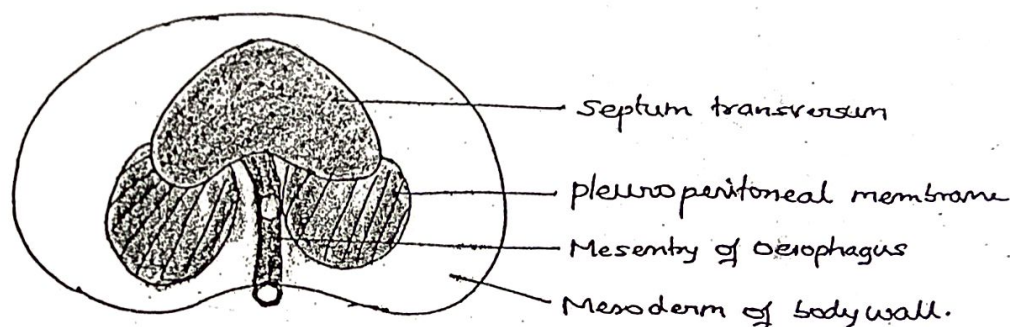
Development of Diaphragm

Diaphragm develops from four components.

- a) Septum transversum – forms the central tendon of diaphragm
- b) Pleuroperitoneal membranes – forms posterolateral part of diaphragm
- c) Dorsal mesentery of oesophagus – forms the crura of the diaphragm
- d) Mesoderm of body wall – forms the large peripheral part of the diaphragm.

Nerve supply:

When the septum transversum is present in the cervical region, it is supplied by C3, C4, C5 spinal segments. Later as it descends it carries its nerve supply, the phrenic nerve. Since the peripheral part is developed from mesoderm of body wall it receives sensory innervations from lower intercostals nerves.



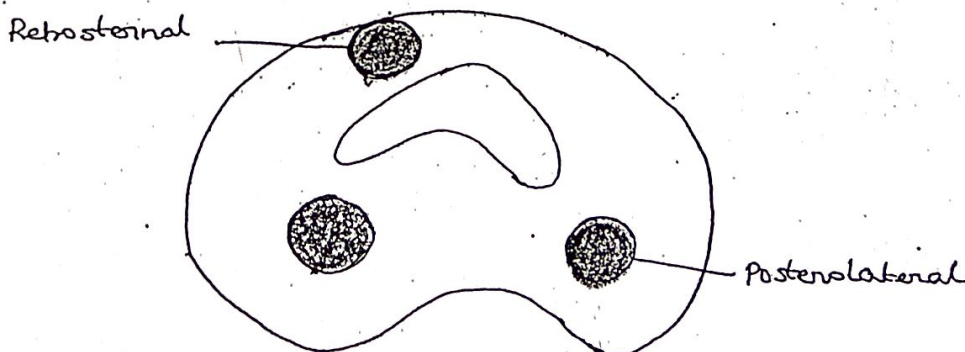
Anomalies:

Congenital diaphragmatic hernia: It is herniation of abdominal contents into thoracic cavity through a defect in the diaphragm.

Foramen of Bochdalek – Failure of development of pleuroperitoneal membrane.

Retrosternal hernia – Large gap between sterna and costal slips of diaphragm.

Hiatus hernia – Herniation of part of stomach through large oesophageal opening.



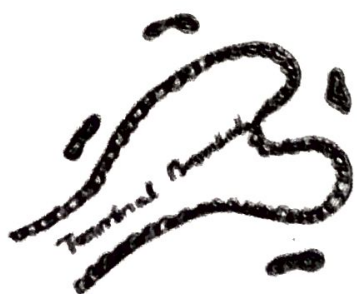
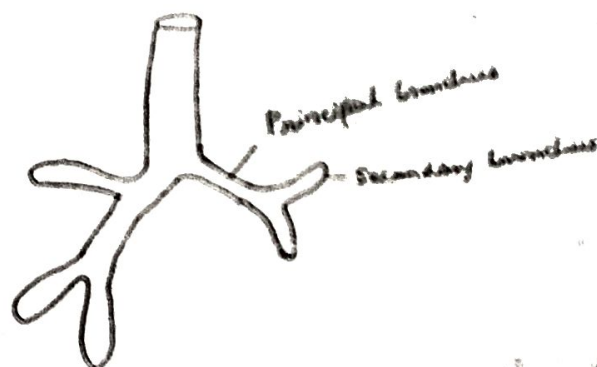
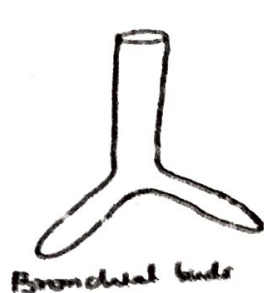
Development of lung

The laryngotracheal diverticulum (from the foregut) divides into two bronchial buds. Each bronchial bud develops into a principal bronchus. The principal bronchi subdivide into secondary bronchi which further subdivide.

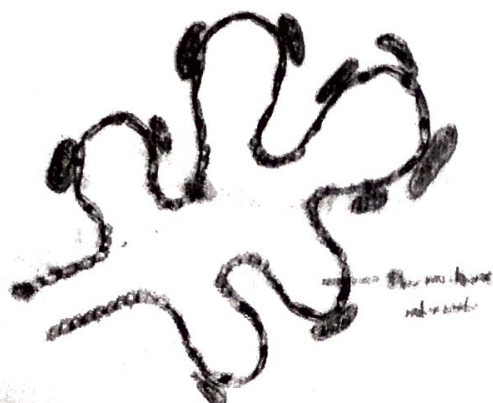
The endoderm of the laryngotracheal diverticulum gives rise to lining epithelium of the bronchial tree. The cartilages, smooth muscle and connective tissue components are derived from splanchnic mesoderm.

Maturation of lungs: It is divided into four stages.

- Pseudoglandular stage (5 - 16 weeks):** Bronchial tree is formed up to terminal bronchioles. Respiration is not possible.
- Canalicular stage (16 - 26 weeks):** Respiratory bronchioles and alveolar ducts are formed. Vascularity increases.
- Terminal sac stage (26 weeks - birth):** Large number of terminal sacs lined by many type I pneumocytes and few type II pneumocytes. Capillaries bulge into the sacs. They permit gas exchange.
- Alveolar stage (birth - 8 years):** Mature alveoli develop.



① Pseudoglandular stage



Cardiovascular system

Inter atrial septum

Septum primum, a sickle shaped fold arise from the roof of primitive atrium. It grows towards septum intermedium. The gap between the septum primum and septum intermedium is called foramen primum.

Progressive growth of septum primum closes the foramen primum. Before complete closure of foramen primum, another opening, the foramen secundum appears in the upper part of septum primum.

Septum secundum, is a thick muscular partition arises from the roof of primitive atrium, to the right of septum primum.

The caudal edge of septum secundum overlaps the cephalic free margin of septum primum. The valvular foramen formed between the two, is called foramen ovale.

In the fetal life, as the right atrial pressure more, blood form the right atrium passes to the left atrium through foramen ovale. After birth, left atrium receives blood from the lungs and left atrial pressure increases. Septum primum is pushed towards septum secundum and is plastered to it. Thus foramen ovale is closed structurally and functionally.

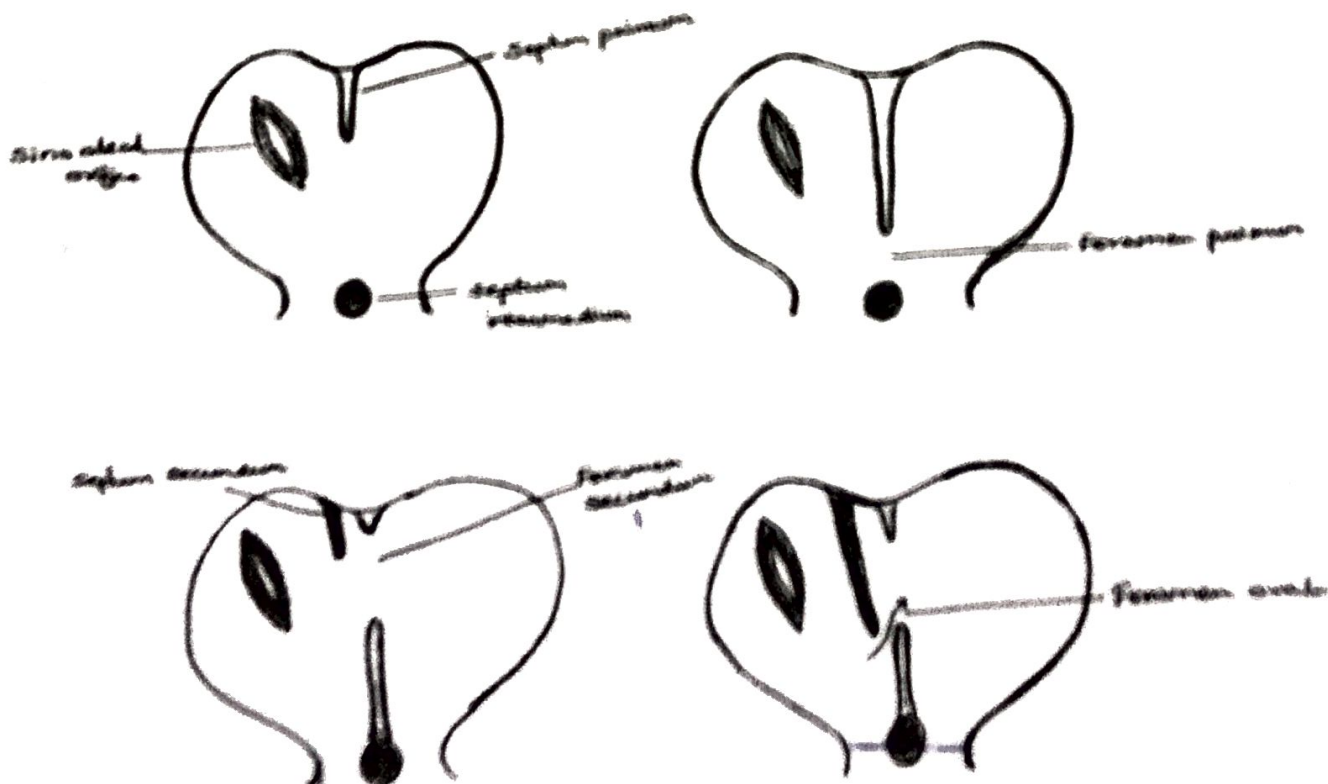
Caudal edge of septum secundum – Limbus fossa ovalis.

Septum primum – floor of fossa ovalis.

Anomalies:

Atrial septal defects (ASD): Common type of congenital heart disease.

- 1) **Patent foramen ovale:** The patency is significant only if there is shunt of blood through it.
- 2) **Ostium primum ASD:** Septum primum fails to fuse with endocardial cushion.
- 3) **Ostium secundum ASD:** Septum secundum may fail to develop – larges foramen secundum.
- 4) **Cortriloculare biventriculare / Common atrium** – Complete absence of septum.



Development of Right atrium

Posterior smooth part (sinus venarum) behind the crista terminalis is developed from the absorption of the right horn of sinus venosus.

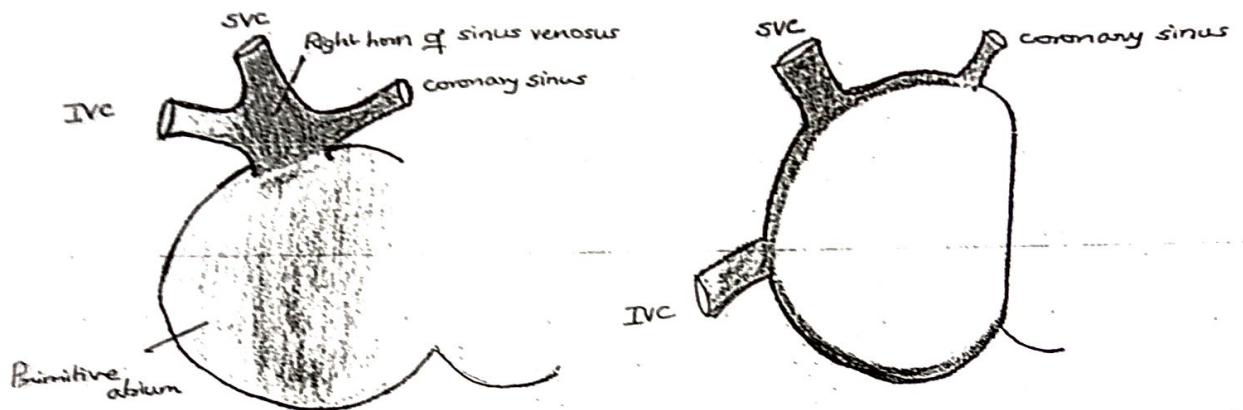
Rough part (atrium proper) in front of crista terminalis is developed from the right half of primitive atrium.

Most ventral smooth part is derived from the right half of atrio ventricular canal.

Dorsal wall of primitive atrium receives sino atrial orifice. It is guarded by right and left venous valves.

Left venous valve is incorporated into inter atrial septum.

Right venous valve forms – *crista terminalis*, *valve of IVC* and *valve of coronary sinus*.



Development of interventricular septum

A median ridge – the muscular inter ventricular septum grows from the floor of primitive ventricle. The growth of this septum takes place passively by the dilatation of the bulbo ventricular cavity on each side of the septum.

Right and left bulbar ridges fuse to form bulbar septum in bulbus cordis.

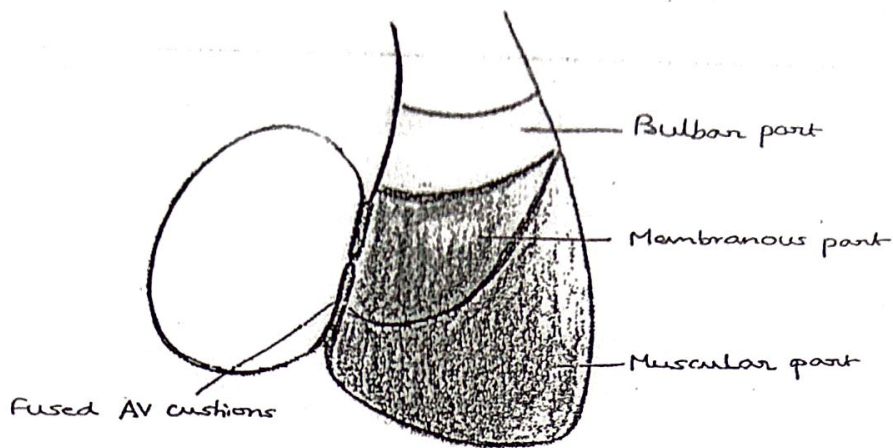
A ventricular foramen appears between upper margin of muscular IV septum and the lower margin of bulbar septum.

Inter ventricular foramen is closed by the proliferation of tissue from the atrioventricular cushions (membranous part)

Anomalies:

Ventricular septal defect (VSD) – More frequent in males

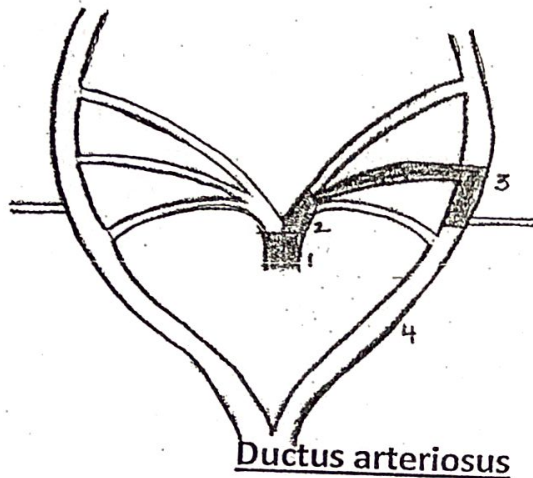
- 1) **Membranous VSD** – Membranous part of septum is deficient due to failure of proliferation from endocardial cushions.
- 2) **Muscular VSD** – Less common. It occurs due to excess cavitation of myocardial tissue during the formation of ventricular walls.
- 3) **Absence of IV Septum** - Cor triiloculare – bi atrium.



Development of Arch of aorta

Arch of aorta is developed from

- 1) **Aortic sac**
- 2) **Left horn of aortic sac:** This forms the part of arch between branchio cephalic trunk and left common carotid artery.
- 3) **Left fourth aortic arch and the part of left dorsal aorta between ductus caroticus and 7th intersegmental artery:** This forms the part of arch between left common carotid and left subclavian arteries.
- 4) **Left dorsal aorta distal to 7th intersegmental artery** – forms the rest of the arch.



Ductus arteriosus

On the right side, the portion of sixth arch artery between the artery to lung bud and dorsal aorta, disappear.

On the left side, it persists. This is called ducts arteriosus. It conveys most of the blood from left pulmonary artery to the dorsal aorta. After birth it is obliterated, as the blood from the right ventricle enters the lungs. It is then fibrosed and forms ligmentum ateriosum.

Anomalies:

Patent ductus arteriosus – Persistence of ductus arteriosus after birth.

Common cardinal vein

The anterior cardinal vein (drain the cranial part of the embryo) and the posterior cardinal vein (drain the caudal part of the embryo) on each side join to form the common cardinal vein. It is also known as duct of Cuvier. Each common cardinal vein opens into the corresponding horn of sinus venosus.

- a) Right common cardinal vein – forms the part of superior vena cava
- b) Left common cardinal vein – Proximal part forms part of coronary sinus and distal part – oblique vein of left atrium

Development of portal vein

Two vitelline veins are interconnected by three transverse anastomoses – cranial ventral, middle dorsal and caudal ventral.

Superior mesenteric and splenic veins join the left vitelline vein, slightly caudal to the dorsal anastomoses.

Portal vein is formed from

1. Left vitelline vein between the entry of superior mesenteric and splenic veins and the dorsal anastomosis.
2. Dorsal anastomosis
3. Right vitelline vein between dorsal anastomosis and cranial ventral anastomosis.
4. Cranial ventral anastomosis and part of left vitelline vein cranial to it forms left branch.
5. Right vitelline vein cranial to the ventral anastomosis forms right branch.

Development of Inferior vena cava

Inferior vena cava is formed from

- a) Right posterior cardinal vein
- b) Right supracardinal vein
- c) Right supracardinal – subcardinal anastomosis
- d) Right subcardinal vein
- e) Right subcardinal – right hepatocardiac anastomosis
- f) Right hepatocardiac channel.

Ductus venosus

Ductus venosus connects the left branch of portal vein to the primitive inferior vena cava (right hepatocardiac channel). The left umbilical vein is connected to left branch of portal vein.

Most of the blood from left umbilical vein bypasses the sinusoids of liver by passing through ductus venosus. After birth it is obliterated to form *ligamentum venosum*.

Excretory system

Development of Kidney

Kidneys develop from two sources.

a) **Excretory part:** It is developed from metanephric blastema. The ureteric bud invades metanephros and divides dichotomously. The distal ends are capped by solid clump of cells called metanephric cap. Soon it is converted into metanephric vesicle. Metanephric vesicle is pear shaped first and later forms s-shaped primitive renal tubule. **Bowman's capsule, proximal convoluted tubule, loop of Henle and distal convoluted tubule** are developed from primitive renal tubule.

b) **Collecting part:** Ureteric bud is derived from mesonephric duct. It divides dichotomously as it invades metanephros. It contributes to **collecting tubules, collecting duct, minor calyces and major calyces**.

Ascent of Kidney: Due to differential growth of posterior abdominal wall and reduction of fetal curvature the kidney ascends from sacral to lumbar region.

Rotation of kidney: During ascent the kidney rotates 90° medially so that hilum is directed medially.

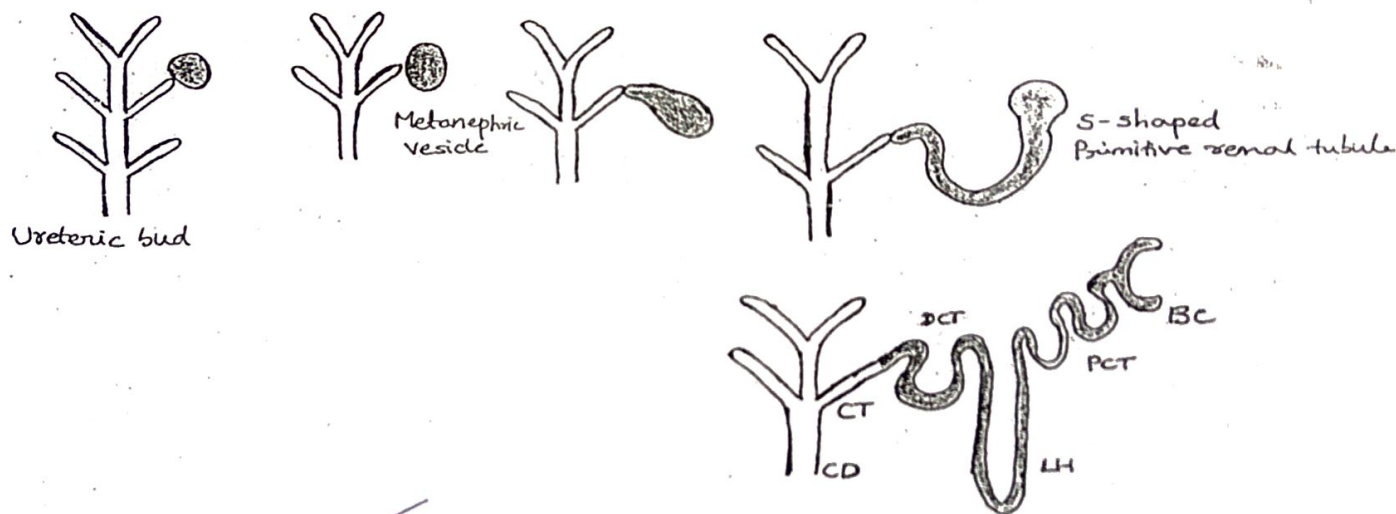
Anomalies:

a) **Renal agenesis** – Absence of kidney. It occurs when the ureteric bud fails to develop.

b) **Congenital polycystic kidney** – Numerous cysts filled with urine are present.

c) **Pelvic kidney** – Due to failure of ascent of kidney.

d) **Horse shoe kidney** – Inferior poles of two kidneys are fused.



Development of Urinary bladder

Mucosa – The epithelium of entire urinary bladder is derived from endodermal vesicourethral canal except the trigone, which is mesodermal derived from absorption of mesonephric ducts. Apex of the bladder is derived from proximal part of allantois.

Muscular and serous coats – Derived from splanchnopleuric intraembryonic mesoderm.

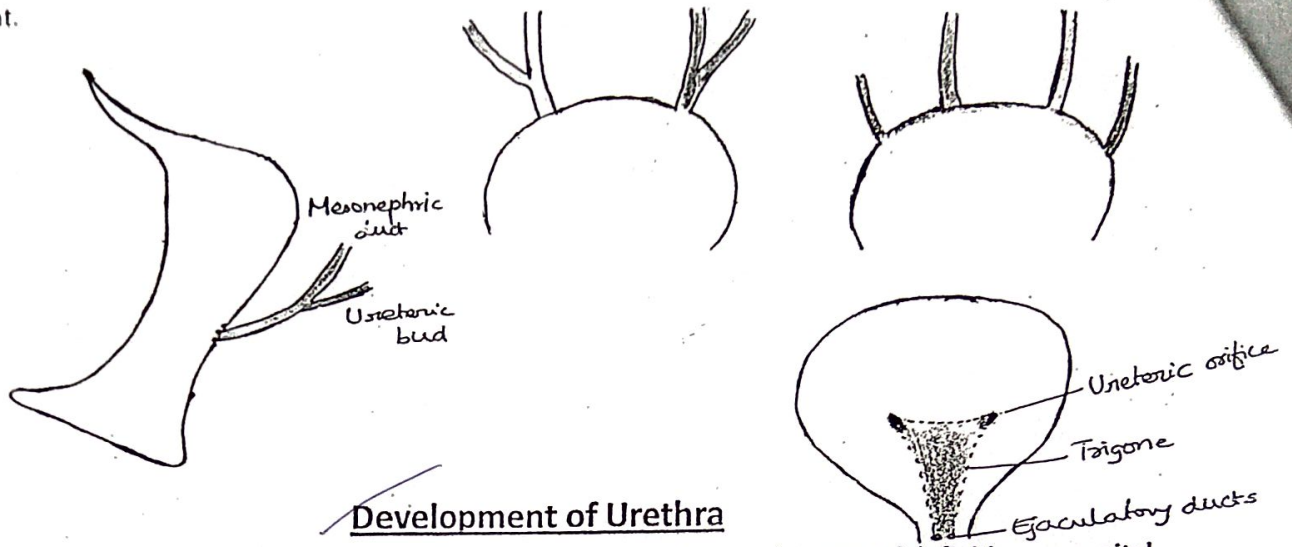
Anomalies:

Urachal sinus – Persistence of distal part of allantois.

Urachal fistula – Persistence of entire allantois.

Urachal cyst – Persistence of small intermediate part of allantois.

Ectopia vesicae – Anterior wall of the bladder and infraumbilical part of anterior abdominal wall are absent.

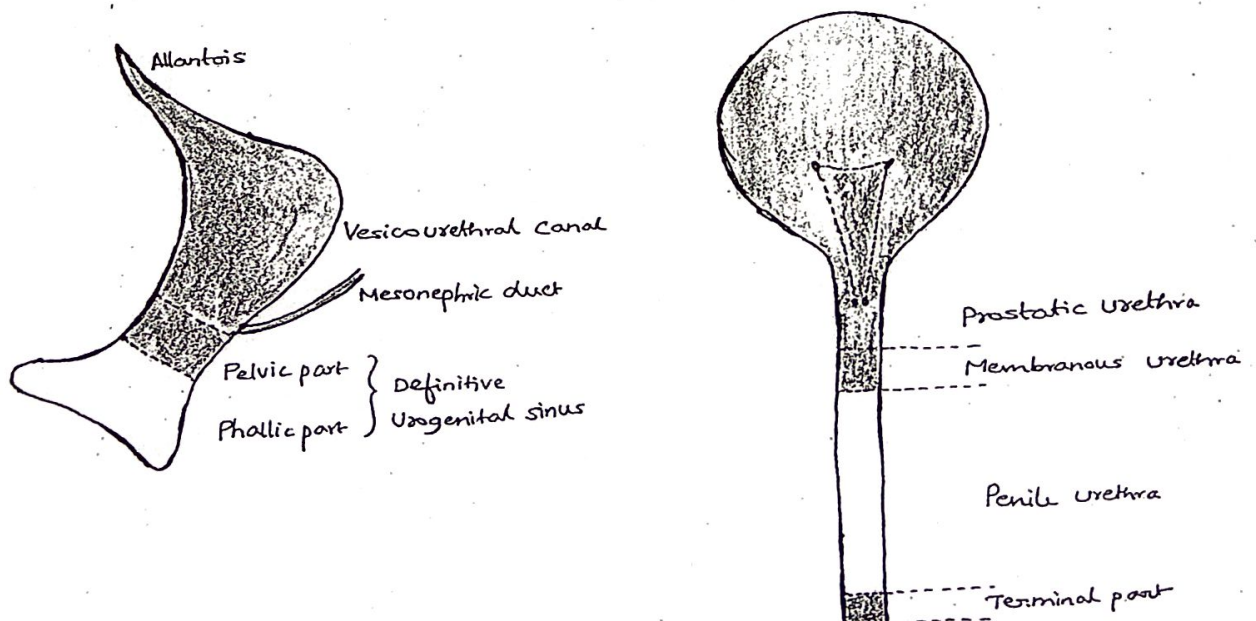


Development of Urethra

Female urethra: Derived from caudal part of vesicourethral canal and pelvic part of definitive urogenital sinus.

Male urethra:

- 1) Prostatic part – Above the level of opening of ejaculatory ducts is developed from caudal part of vesicourethral canal except posterior wall which is derived from absorption of mesonephric ducts. Below the level of opening of ejaculatory ducts is developed from pelvic part of definitive urogenital sinus.
- 2) Membranous part – Derived from pelvic part of definitive urogenital sinus.
- 3) Penile part – Derived from phallic part of definitive urogenital sinus.
- 4) Terminal part (in the glans penis) – Derived from surface ectoderm



Embryology – Genital system

Development of testis

Genital ridge is formed by the proliferation of coelomic epithelium on the medial side of mesonephric ridge. On the arrival of primordial germ cells, the cells of genital ridge proliferate and extend into the underlying mesenchyme as primitive sex cords. This stage is called indifferent gonad.

If the primordial germ cells carry Y chromosome, under the influence of SRY gene which codes for testis determining factor, the sex cords in the cortex regress and sex cords in the medulla become canalized to form seminiferous tubules. Cells of sex cord form Sertoli cells. Primordial germ cells form spermatogonia. Mesoderm around seminiferous tubules forms interstitial cells.

Descent of testis

Testis is developed in lumbar region. It descends into scrotum at birth.

Stages of descent

- | | |
|---|--|
| 1) 3 rd month – Iliac fossa | 2) 6 th month – Deep inguinal ring |
| 3) 7 th month – traverses inguinal canal | 4) 8 th month – superficial inguinal ring |
| 5) End of 9 th month – scrotum | |

Factors responsible for descent

- 1) Differential growth of posterior abdominal wall
- 2) Formation of inguinal bursa – out pouching of various layers of abdominal wall towards the scrotum
- 3) Processus vaginalis – A diverticulum of peritoneum that extends into the inguinal canal and scrotum
- 4) Gubernaculum testis – A mesenchymal band from lower pole of testis to bottom of scrotum
- 5) Increase in intraabdominal pressure.

Anomalies:

Cryptorchidism – Undescended testis – causes infertility.

Ectopic testis – Presence of testis else where, apart from expected path of descent. Ex: at root of penis, medial side of thigh, perineum etc.

Derivatives of mesonephric duct

In males	In Females
1) Ureteric bud – Collecting tubules, Collecting ducts, Minor calyces, Major calyces, Ureter, Trigone of the bladder, Posterior wall of prostatic urethra up to the opening of ejaculatory ducts, Mesodermal part of prostate.	1) Ureteric bud – Collecting tubules, Collecting ducts, Minor calyces, Major calyces, Ureter, Trigone of the bladder, Posterior wall of female urethra
2) Appendix of Epididymis	2) Gartner's duct
3) Epididymis	
4) Vas deferens	
5) Seminal vesicles	
6) Ejaculatory ducts	3) Mesonephric tubules – Epoophoron,
7) Mesonephric tubules – efferent ductules	Paraophoron

Development of Uterus

The paramesonephric ducts are formed by the invagination of coelomic epithelium. When traced caudally they cross the front of mesonephric ducts from lateral to medial side and come close to each other in the midline. The caudal vertical parts of two paramesonephric ducts fuse to form **uterovaginal canal**.

Uterus is developed from **upper part of uterovaginal canal**. Myometrium is formed from surrounding mesoderm.

Congenital anomalies:

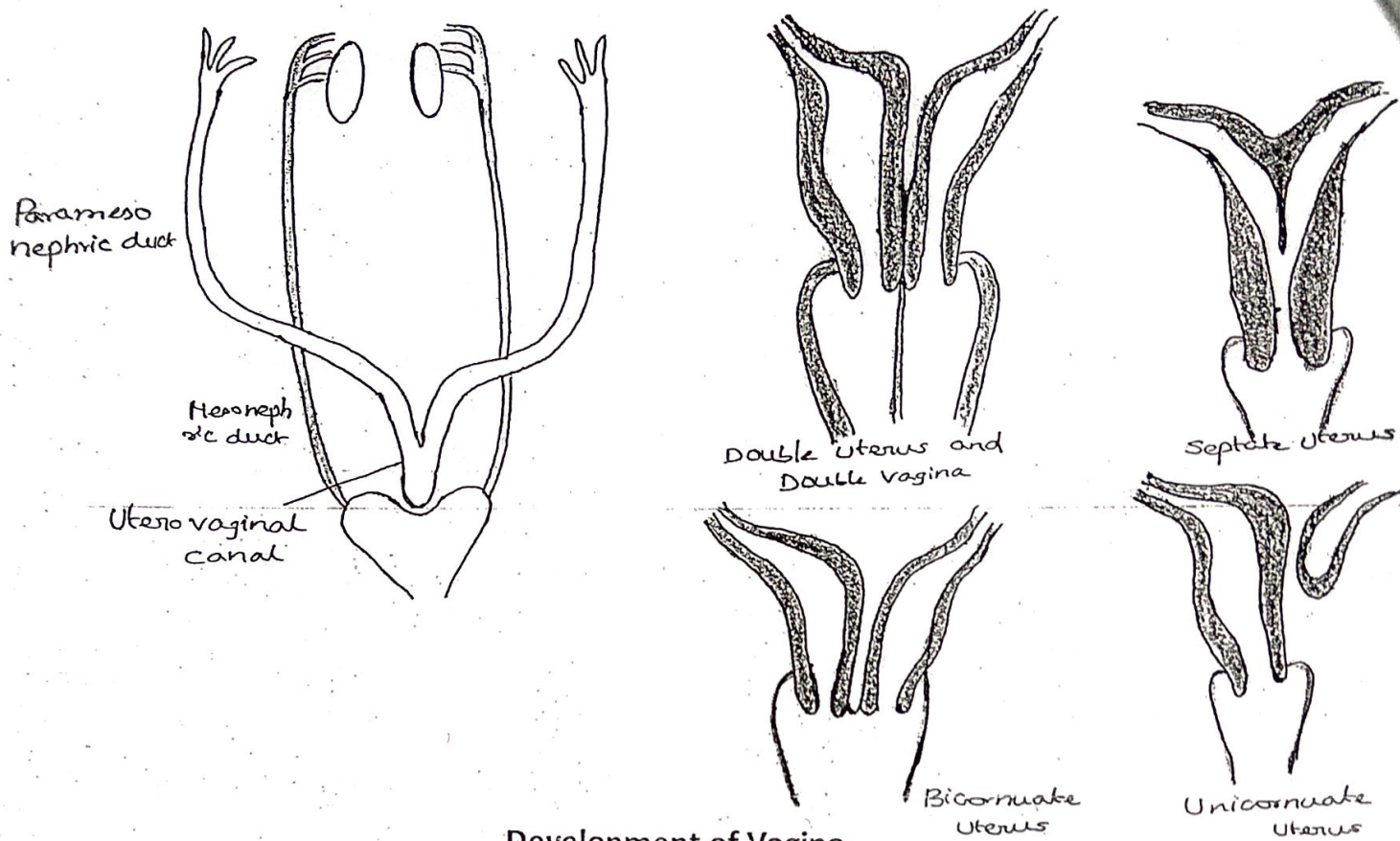
Double uterus (Uterus didelphys) – Due to failure of fusion of two paramesonephric ducts.

Bicornuate uterus – The paramesonephric ducts fuse in the lower part and upper parts remain unfused resulting in one cervix and the body is duplicated.

Septate uterus – The two paramesonephric ducts fuse but the septum separating them does not disintegrates.

Unicornuate uterus – One paramesonephric duct degenerates resulting in one horn of uterus with one fallopian tube.

Agenesis of uterus – Due to failure of development of paramesonephric ducts.



Development of Vagina

The paramesonephric ducts are formed by the invagination of coelomic epithelium. When traced caudally they cross the front of mesonephric ducts from lateral to medial side and come close to each other in the midline. The caudal vertical parts of two paramesonephric ducts fuse to form **uterovaginal canal**.

The uterovaginal canal comes in contact with dorsal wall of pelvic part of definitive urogenital sinus. This induces the formation of **sinovaginal bulbs** from definitive urogenital sinus. The sinovaginal bulbs fuse to form **vaginal plate**.

Vagina is developed from following sources.

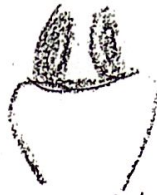
Upper part of vagina including fornices – Lower part of uterovaginal canal.

Lower part of vagina – Canalisation of vaginal plate.

Vestibule of vagina (below hymen) – Phallic part of definitive urogenital sinus.

Uterovaginal
canalUrogenital
sinus

sinovaginal bulbs



Vaginal plate



Vagina

Derivatives of paramesonephric (Mullerian) ducts

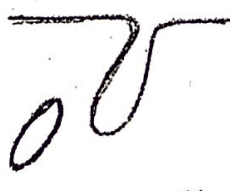
In Males	In Females
Appendix of testis	Uterine tubes
Prostatic utricle	<u>Uterus</u>
	<u>Upper part of vagina</u>

Development of Pituitary gland (Hypophysis cerebri)

Adenohypophysis is developed from Rathke's pouch (an evagination from the ectoderm lining the roof of stomodeum). Later the pouch is detached from the stomodeum. Anterior wall of Rathke's pouch proliferates to form pars anterior. Posterior wall proliferates to form pars intermedia. Cavity of the pouch persists as intraglandular cleft.

Neurohypophysis is developed as a diverticulum from the floor of third ventricle.

Neurectodermal diverticulum

Rathke's pouch from
stomodeum

Rathke's pouch cut off



Development of Suprarenal / Adrenal gland

Adrenal cortex is mesodermal in origin. It is developed from the coelomic epithelium between gonadal ridge and mesentery.

Adrenal medulla is developed from neural crest cells.

Development of Mammary gland

On the ventral aspect of the embryo, the surface ectoderm is thickened along the line extending from axilla to inguinal region to form mammary ridge or milk line. Later the ridge disappears except in pectoral region. In the pectoral region, the mammary bud develops as a solid down growth of epidermis. The bud presents a surface depression called mammary pit.

15 – 20 epithelial cords grow inwards from the bottom of the pit. At the end of fetal life, the epithelial cords are canalized to form lactiferous ducts. After birth the pit is evaginated by the growth of underlying mesoderm.

Anomalies:

Amastia – Absence of breast.

Athelia – Absence of nipple.

Polymastia – Accessory breasts.

Polythelia – Supernumerary nipples.