Summary of first week.

- Fertilization and formation of the zygote (30 hours).
- Cleavage of the zygote into 12 to 16 blastomere- the Morula (day 2 and 3).
- Formation of the blastocyst (day 5-8).

FirstRanker.com Summary of second week.

Bilaminar germ disc.

- Complete implantation or alorine wall.
- Trophoplast Differentiated into two layers.
- Two cavities formed Amniotic cavity and
 - Extra embryonic coelomic cavity (Chorionic Cavity)
- Two layers of extra embryonic mesoderm -Somatopleuric and Splanchnopleuric.
- Beginning of Uteroplacental Circulation.



3rd week of development

Host characteristic event occurring during the third week is gastrulation, which begins with the appearance of the **primitive** streak, which has at its cephalic end the primitive node. In the region of the node and streak, epiblast cells move inward (invaginate) to form new cell layers, endoderm and mesoderm.

Cells that do not migrate through the streak but remain in the epiblast form **ectoderm.** Hence, epiblast gives rise to all three **germ layers** in the embryo, **ectoderm**, **mesoderm**, and **endoderm**, and these layers form all of the tissues and organs .



R 3rd week of embryonic development is characterized by :

- 1. Appearance of primitive streak
- 2. Development of notochord
- 3. Differentiation of three germ layers

Gastrulation:

This is the formation of 3 germ layers in embryos.
During gastrulation, the bilaminar embryonic disc is converted into a trilaminar embryonic disc.

Extensive cell shape changes, rearrangement, movement, and changes in adhesive properties contribute to the process of gastrulation

•Gastrulation is the beginning of morphogenesis (development of body form) and is the significant event occurring during the 3rd week

Ist morphologic sign of gastrulation begins with formation of the primitive streak on the surface of the epiblast of the embryonic disc
During this period, the embryo may be referred to as a gastrula
the 3 germ layers are

- ✓ Ectoderm
- ✓ Mesoderm
- \checkmark and endoderm
- Each of these layers gives rise to specific tissues and organs
 Embryonic ectoderm: gives rise to the epidermis, central and peripheral nervous systems(CNS & PNS), the eye, and inner ear, neural crest cells
- **Embryonic mesoderm** gives rise to all skeletal muscles, blood cells and the lining of blood vessels, all visceral smooth muscular coats, the serosal linings of all body cavities, the ducts and organs of the reproductive and excretory systems, and most of the cardiovascular system

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- In the trunk, it is the source of all connective tissues, including cartilage, bones, tendons, ligaments, dermis, and stroma of internal organs.

•Embryonic endoderm gives rise to the epithelial linings of the respiratory and alimentary (digestive) tracts, including the glands opening into the gastrointestinal tract and the glandular cells of associated organs such as the liver and paneteas.

> Primitive streak

The <u>first sign</u> of gastrulation is the <u>appearance of the primitive</u> <u>streak</u>

The primitive streak results from the proliferation and movement of cells of the epiblast to the median plane of the embryonic disc
At the beginning of the 3rd week, the primitive streak appears caudally (tail end) in the median plane of the dorsal (posterior) aspect of the embryonic disc .

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Www.FirstRanker.com www.FirstRanker.com With formation of the primitive streak, several axes of an embryo get defined.

- Craniocaudal (anteroposterior) axis: As the primitive streak is present in the posterior half of the embryo, the craniocaudal axis of the embryo gets defined
- Medial and lateral axes: Since the primitive streak is present in the median plane of the embryonic disk, anything away from the median plane becomes lateral to the median plane.
- Right and left axes: As the primitive streak lies in the median plane, while visualizing the germ disk from the amniotic cavity, the right half of the germ disk represents the right side and the left half of the germ disk represents the left half.
- Dorsal-ventral axis: At this stage, the dorsal-ventral axis gets vaguely defined. The ectoderm is
 dorsal and endoderm is ventral. This axis gets well defined after folding of the embryo

There are five subdivisions of Embryonic mesoderm: So Paraxial mesoderm Intermediate mesoderm Lat plate mesoderm Cardiogenic mesoderm So In median plate Prechordal plate and Notochord.



development of Vertebrate animals, the prechordal plate is a "uniquely thickened portion" of the endoderm that is in contact with ectoderm immediately rostral to the cephalic tip of the notochord. It is the most likely origin of the rostral cranial mesoderm





Caudal end



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View of dorsal surface of bilaminar embryonic disc through sectioned amnion and yolk sac. Inset at upper left shows relation of the embryo to the wall of the chorionic cavity. The primitive streak, now 1 day old, occupies 50% of the length of the embryonic disc. The future positions of oropharyngeal and cloacal membranes are indicated.

Fination of the primitive streak also defines all major body axes. The primitive streak forms in the caudal midline of the embryonic disc, thus defining the cranial-caudal axis and medial-lateral axis (with the primitive streak forming in the midline, that is, most medially).

- The Primitive streak
- consists of:
- 1. primitive groove.
- 2. Primitive node.
- 3. Primitive pit.

After primitive streak formation, the embryo has:

- 1. Craniocuadal axis.
- 2. Dorsal &ventral surfaces.
- 3. Right & left sides.

By the end of 4th week the primitive streak shows regressive changes, rapidly shrinks and soon DISAPPEARS.



As the *primitive streak elongates* by addition of cells to its caudal end, its cranial end proliferates to form a **primitive node**.

Concurrently, a narrow groove called the **primitive groove** develops in the primitive streak .This '<u>primitive groove</u>' is continuous with a small depression in the primitive node called the **primitive pit**.

Shortly after the primitive streak appears, cells leave its deep surface and form mesenchyme (a tissue consisting of leosely arranged cells suspended in a gelatinous matrix).

Mesenchymal cells are ameboid and actively phagocytic. Mesenchyme forms the supporting tissues of the embryo, such as most of the connective tissues of the body and the connective tissue framework of glands

Firstranker's choice Events in Gastrulation:

Cell proliferation:

Formation of the primitive streak heralds the beginning of gastrulation. During gastrulation, epiblast cells move toward the primitive streak, enter the primitive streak, and then migrate away from the primitive streak as individual cells. The movement of cells through the primitive streak and into the interior of the embryo is called ingression



Gastrulation:

The main event that occurs during the third week of development is the formation of the trilaminar embryo from bilaminar germ disc. This process is called gastrulation.

The first sign of gastrulation is the formation of the primitive streak in the epiblast.

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Because formation of the primitive streak occurs in the midline, when the epiblast is viewed looking down at it from inside the amniotic cavity, what lies to the right of the primitive streak represents the right side of the embryo and what lies to the left represents its left side.

Formation of Definitive Endoderm

On day 16, epiblast cells lateral to the primitive streak begin to move into the primitive streak where they undergo an epithelial-to-mesen chymal transformation (EMT).



This collective movement of cells through the primitive streak and into the interior of the embryo to form the three primary germ layers constitutes gastrulation .



T7



(b) TranswerserseRaiokerfdoitaminar embryonic disc, about 16 days after fertilization



Gastrulation — Mammal





Some mesenchyme forms mesoblast (undifferentiated mesoderm), which forms the *intraembryonic or embryonic mesoderm*. Cells from the epiblast, as well as from the primitive node and other parts of the primitive streak migrate in order to displace the hypoblast This inward movement is known as invagination.

Cell migration and specification are controlled by fibroblast growth factor 8 (FGF8), which is synthesized by streak cells themselves

Once the cells have invaginated, some displace the hypoblast, creating the embryonic **endoderm**, and others come to lie between the epiblast and newly created endoderm to form **mesoderm**. Cells remaining in the epiblast then form **ectoderm**

In summary, cells of the epiblast, through the process of gastrulation, give rise to all 3 germ layers in the embryo, the primordia of all its tissues and organs.

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The primitive streak actively forms mesoderm by the ingression of cells until the early part of the fourth week; thereafter, production of mesoderm slows down.

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

Clinical correlate: Sacrococcygeal Teratoma

Remnants of the primitive streak may persist and give rise to a **sacrococcygeal teratoma.** Because they are derived from pluripotent primitive streak cells, these tumors contain tissues derived from all three germ layers in incomplete stages of differentiation

Sacrococcygeal teratomas are the most common tumor in newborns and have an incidence of approximately one in 35,000. most affected infants (80%) are female. These are usually diagnosed on routine antenatal ultrasonography, and most tumors are benign. These tumors are usually surgically excised proppuy, and the prognosis is good.



Cell migration

by amoeboid movement – the costs insinuate themselves between the epiblast and hypotest

Cell determination:

- the cells arising from the primitive streak are determined to give rise to different tissues

Distriction of the germ disc showing the FirstRanker.com primitive streak and a fate map for epiblast cells Specific regions of the epiblast migrate through different parts of the node and streak to form mesoderm. Thus, cells migrating at the cranial most part of the node will form the **notochord**; those migrating more posteriorly through the node and cranial most aspect of the streak will form paraxial mesoderm (*pm*; somitomeres and somites); those migrating through the next portion of the streak will form intermediate mesoderm (*im*; urogenital system); those migrating through the more caudal part of the streak will form lateral plate mesoderm (*lpm;* body wall); and those migrating through the most caudal part will contribute to extraembryonic mesoderm (*eem;* chorion).





- 1. Ectoderm develops into CNS (induced by mesoderm and skin)
- 2. Endoderm forms the lining of the Alimentary System and Respiratory System.
- **3.** *Mesoderm* forms the CVS (induced by endoderm)



Conterne goes rise to all skeletal muscles, blood cells, the lining of blood vessels, all visceral smooth muscular coats, serosal linings of all body cavities, ducts and organs of the reproductive and excretory systems, and most of the cardiovascular system.

- In the body (trunk or torso), excluding the head and limbs, it is the source of all connective tissues, including cartilage, bones tendons, ligaments, dermis, and stroma (connective tissue) of internal organs.
- ✓ Head connective tissues is derived from Neural Crest cells.
- In Limb Intially, the limb bud mesenchyme consists exclusively of cells derived from the lateral plate mesoderm. These cells give rise to the skeleton, connective tissue, and some blood vessels. Mesenchymal cells derived from the somites migrate into the limb bud as precursors of muscle and endothelial cells.
 - Midline mesoderm forms notochord.
 - Paraxial mesoderm gives rise to myotomes (skeletal muscle); sclerotomes (vertebra); and dermatomes (dermis).

FirstRaNotoEnordal process and notochord

Notochordal process

• Some mesenchymal cells that have ingressed through the streak, acquired mesodermal cell and migrate cranially from the primitive node and pit, forming a median cellular cord, the **notochordal process**

This process soon acquires a lumen, the **notochordal canal**.

The notochordal process grows cranially between the ectoderm and endoderm until it reaches the **prechordal plate**, a small circular area of columnar endodermal cells where the ectoderm and endoderm are in contact. The prechordal plate is the

primordium of the **oropharyngeal membrane** located at the future site of the oral cavity. Caudal to the primitive streak there is a circular area-the **cloacal membrane**, which indicates the future site of the anus.





Cranially on each side of the notochordal process is a region of mesoderm called the cardiogenic region(area), This region lies **rostral** (*anterior/cranial*) to the prochordal plate, and it is where the primordium heart begins to develop at the end of the third week.

The embryonic disc remains **bilaminar** at the <u>cloaca</u> and <u>oropharyngeal</u> <u>membrane.</u>

Exprise because the ombryonic ectoderm and endoderm are fused at these sites, thereby preventing migration of mesenchymal cells (which form mesoderm) between them. By the middle of the 3rd week, intraembryonic mesoderm separates the ectoderm and endoderm everywhere except :-

- I. At the oropharyngeal membrane cranially.
- II. In the median plane cranial to the primitive node, where the notochordal process is located.
 III. at the cloacal
 - membrane caudally.



FirstRanker.com Notochord

Notochord is a rod of mesenchymal cells
 located in the midline
 extending *cranially* from the primitive node to the buccopharyngeal membrane.







FirstRanker.com Formation of the notochord

 The notochordal process elongates by invagination of cells from the primitive pit (fig 1a & b)





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2. FirstRanker.com 2. The primitive pit extends into the notochordal process, forming a notochordal canal (fig 2a & b)



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3 floor of the ontochordal process fuses with the underlying embryonic endoderm (fig 3a) The fused layers gradually undergo degeneration, resulting in the formation of openings in the floor of the notochordal process, which brings the notochordal canal into communication with the umbilical vesicle (fig 3b)



4 The openings rapidly become confluent and the floor of the notochordal canal disappears (fig 4)

6 **1** filloor of the tube and the underlying endoderm fuse and then break down, forming a **notochordal plate** The notochordal plate becomes continuous with the endodermal layer

And the yolk sac, termed the neurenteric canal

New Yordal place folds to form the notochord, which gets separated from the underlying endoderm



Functions as motocharac

Defines primordial axis of the embryo Provides rigidity to the embryo.

- Serves as a basis for the development of the axial skeleton Contributes to the intervertebral discs.
- Regulates differentiation of surrounding structures including the overlying ectoderm and the mesoderm.

FirstRanker.com Fate of notochord

Degenerates and disappears as the bodies of the vertebrae develop
The part that lies between the vertebral bodies persists as the nucleus pulposus of each intervertebral disc

FR

•Remnants of notochordal tissue give rise to tumors called Chordomas

•Approximately one third of chordomas occur at the base of the cranium and extend to the nasopharynx.





FirstRanker.com Differentiation of the Intraembryonic Mesoderm

•Induced by the notochord

•Differentiates into the:



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• The embryonic period, or period of organogenesis, occurs from the <u>third to the eighth weeks of development</u> and is the time <u>when each of the three germ layers</u>, <u>ectoderm</u>, <u>mesoderm</u>, and endoderm, gives rise to a number of specific <u>tissues and organs</u>

By the end of the embryonic period, the main organ systems have been established, rendering the major features of the external body form recognizable by the end of the second month.

It is the process by which the <u>neural tube</u> is formed
 During neurulation, the embryo may be referred to as a neurula

Neurulation

The stages of neurulation includes he formation of:
 Neural plate
 Neural groove
 Neural folds & their fusion
 Neural crest cells
 Neural tube

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Under the inducing effect of the developing notochord, the overlying ectodermal cells thickens to form the neural plate.



stRanker.com At first the neural <u>plate</u>: \checkmark cranial to the primitive node \checkmark dorsal(posterior) to the developing notochord & the mesoderm adjacent to it corresponds in length to the underlying notochord



er.com As the notochord forms & elongates: \checkmark The embryonic disc elongates and becomes club-shaped ✓ *The neural plate* broadens and extends cranially as far as the buccopharyngeal membrane, ✓ *later on grows* beyond the notochord



GR8th day: the neural plate invaginates to form <u>neural</u> <u>groove & neural folds</u>



rest cell

Neural fold

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- ALANA

Notochord

Events of 3rd week, the neural folds move to the midline and fuse to form the neural tube.







Reputation:Pormation of the Neural



The end of 3rd week, the neural folds move to the midline and fuse to form the **neural tube** The <u>neural tube separates from the surface ectoderm</u>, lies in the

midline, dorsal to the notochord.



FirstRanker.com \checkmark The cranial $\frac{1}{3}$ of the neural tube represent the future brain

 \checkmark The caudal $\frac{2}{3}$ represents the future spinal cord



Neural tube is open at both ends, communicating freely with the amniotic cavity

 ✓ The cranial opening, the <u>rostral</u> <u>neuropore closes</u> at about 25th day while the caudal neuropore closes at about the 27th day(2 days after)



FRure of the Neural Tube (Day 22)

Cut edge of amniotic membrane Somite 21 days Yolk sac-Pericardial bulge 22 days Somite Cranial neuropore Pericardial bulge 23 days Caudal neuropore Pharyngeal arches Pharyngeal bulge 24-25 days Yolk sac www.FirstRanker.com

FirstRanker.com Closure of the Neural Tube proceeds Bilaterally



FirstRanker.comCongenital anomalies

Disturbance of neurulation may result in severe abnormalities of the brain and the spinal cord. Most defects are the result of non-closure or defective closure of the neural tube:

1.In the brain region (e.g. anencephaly: total absence of the brain.

2.Meroencephaly (partial absence of the brain) is the most severe neural tube defect and is also the most common anomaly affecting the CNS.

3.In the spinal cord regions (e.g. spina bifida)

FirstRanker.com Maiformations of Neural Tube Closure (1 in 600 births)













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1. Surface ectoderm

2. Neuroectoderm

FirstRanker.com Surface Ectoderm Derivatives

- Epidermis of the skin
- Hair
- Nail
- Sweat & Sebaceous glands
- Mammary glands
- Enamel of the teeth
- Lens of eye
- Internal ear
- Anterior lobe of the pituitary gland



Neuroectoderm

Neural TubeNeural Crest Cells



- Central nervous system
- Peripheral nervous system
- Retina
- Sensory epithelia of nose & ear
- Pineal gland
- Posterior lobe of the pituitary gland

FirstRanker.com Neural Crest Cells Derivatives

- Sensory ganglia (cranial & spinal)
- Autonomic ganglia
- Meninges (Pia mater & Arachnoid mater) of the brain & spinal cord
- Schwann cells
- Satellite cells
- Melanoblasts
- Suprarenal medulla (chromaffin cells)
- Several skeletal & muscular components in the head (derived from pharyngeal arches)

FirstRan Seriçatives of mesodermal germ layer

- As the notochord & neural tube form, the *intraembryonic mesoderm* on each side of them proliferates to form:
- I. a thick, longitudinal column of *paraxial mesoderm*
- II. which is continuous with *intermediate mesoderm* which gradually thins into
- III. <u>lateral mesoderm</u>
- The lateral mesoderm is continuous with the <u>extraembryonic</u> <u>mesoderm</u> covering the yolk sac & amnion.



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- By the <u>beginning of the 3rd week</u>, paraxial mesoderm is organized into segments called *somitomeres*
- Somitomeres appear first in the cephalic region of the embryo, and their formation proceeds cephalocaudally (extra scranially and caudally /from head to tail or crown to rump)
- From the occipital region caudally, *somitomeres* further organize into *somites*
- Toward the end of the 3rd week (at approximately the <u>20th</u> <u>day</u> <u>of</u> <u>development</u>), the 1st pair of somites arises in the occipital region From here, new somites appear in craniocaudal sequence at a rate of approximately 3 pairs per day
- The somite period of human embryo development is from $\frac{days 20 30}{day 30}$ About <u>38 pairs of somites are present on $\frac{day 30}{day 30}$ </u>
- By the end of the 5th week, <u>42 to 44 pairs of somites are resent</u>

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- \checkmark 4 occipital,
- \checkmark 8 cervical,
- \checkmark 12 thoracic,
- $\checkmark 5$ lumbar,
- \checkmark 5 sacral,
- \checkmark and 8 to 10 coccygeal pairs
- The <u>1st occipital and the last 5-7 coccygeal somites later disappear</u>
- The remaining somites divide into:
- a. ventromedial part called *sclerotome* sclerotome gives rise to the bones, cartilages and ligaments of the vertebral column & ribs
 So, the somites give rise to most of the axial skeleton
- b. Middle part called *myotome* myotome gives rise to skeletal muscles of the chest and abdomen



c Russolateral part Called dermatome.

It gives rise to dermis and subcutaneous tissue of the skin → Because the somites are so prominent during the 4th and 5th weeks, they are used as one of several criteria for <u>determining an embryo's age</u>

<u>Intermediate mesoderm</u>

connects paraxial mesoderm with the lateral plate *differentiates into* <u>urogenital structures</u>. Excretory units of the urinary system (kidney) and the gonads (testis and ovary) develop from the intermediate mesoderm.

<u>Lateral mesoderm</u>

•is a thin plate of mesoderm located along the lateral sides of the embryo •Large spaces develop in the lateral mesoderm and coalesce to from the *intraembryonic coelom*
he intraembry one coelom divides the lateral mesoderm into 2 layers:

✓ somatic/ parietal layer of lateral mesoderm

✓ splanchnic or *visceral layer* of lateral mesoderm

somatic/parietal layer : is located before the the ectodermal epithelium and continuous with the extraembryonic resoderm covering the amnion
 splanchnic or visceral layer: is located adjacent to the endoderm and continuous with the extraembryonic mesoderm covering the umbilical vesicle (yolk sac).

The somatic mesoderm and overlying embryonic ectoderm form the embryonic body wall or somatopleure
whereas the splanchnic mesoderm and underlying embryonic endoderm form the embryonic gut or splanchnopleure

 Image: the second file.
 the intraembryonic coelom is divided into three body cavities:

 Pericardial cavity
 Somile

 Pleural cavities
 Neural blds about to

 Peritoneal cavity
 Somile

 Peritoneal cavity
 Image: the form neural blds



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Blood cells and blood vessels also arise from mesoderm

Blood vessels form in two ways:

✓ vasculogenesis: whereby vessels arise from blood islands and

✓ angiogenesis, which entails sprouting from existing vessels

A) Mesenchymal Vasculogenesis (blood vessels)

cells differentiate into endothelial precusors called angioblasts (vesselforming cells)

Angioblasts aggregate to form blood islands. Small cavities appear within the blood islands. Angioblasts flatten and arrange themselves around the cavities to form endothelial cells of blood vessels.

These endothelium – lined cavities soon fuse to form networks of endothelial channels.

B : Angiogenesis: entails sprouting from existing vessels

E A

eells iormation

- blood cells(hamatoblasts) develop from the endothelial cells of vessels develop on the umbilical vesicle(yolk sac) and allantois at the end of the 3rd week
- Blood formation (hematogenesis) does begin in the embryo until the fifth week.
- It occurs first along the aorta and then in various parts of the embryonic mesenchyme, mainly, the liver, and later in the spleen, bone marrow, and lymph nodes.



- Heart & great vessels develop from mesenchymal cells in the cardiogenic area.
- <u>Paired longitudinal endothelial lined channels</u> or endocardial heart tubes develop during the 3rd week.
- These tubes fuse to form the heart tube.
- The tubular heart joins with blood vessels in the embryo, connecting stalk, chorion and yolk sac to form a *primordial cardiovascular system*
- Heart begins to beat on 21-22 days and blood circulate
- CVS is the first organ system to reach a functional state



Endoderm gives rise to the epithelial lining of the gastrointestinal and respiratory tracts, parenchyma of the tonsils, thyroid and parathyroid glands, thymus, liver, and pancreas, epithelial lining of the urinary bladder and most of the urethra, and the epithelial lining of the tympanic cavity, tympanic antrum, and pharyngotympanic (auditory) tube

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Development of Somites:



The dermomyotome is the dorso-lateral part of the somite.

Cells from the dermomyotome migrate laterally and, as its name implies, gives rise to

(i) the dermis of the skin.(ii) skeletal muscle and

Each anatomical myotome is derived from the embryological dermomyotome that is innervated by a segmental nerve and forms a group of skeletal muscle cells and the dermis of the corresponding segment of ectoderm.



Remeanume, the trophoblast progresses rapidly. Primary villi obtain a mesenchymal core in which small capillaries arise. When these villous capillaries make contact with capillaries in the chorionic plate and connecting stalk, the villous system is ready to supply the embryo with its nutrients and oxygen.









Thanks to you all