ANA 301H1
EMBRYOLOGY LECTURE # 3

THE THIRD AND FOURTH WEEKS OF DEVELOPMENT

Objectives:

- Describe the cells movements and significance of gastrulation, neurulation and the development of the foregut.
- Describe the formation and derivatives of the notochord, ectoderm, endoderm, intraembryonic coelom and intraembryonic somatic (parietal) and splanchnic (visceral) mesoderm.
- Distinguish between the ectoderm and the epiblast.
- Understand the general features of the embryonic and fetal periods of development.

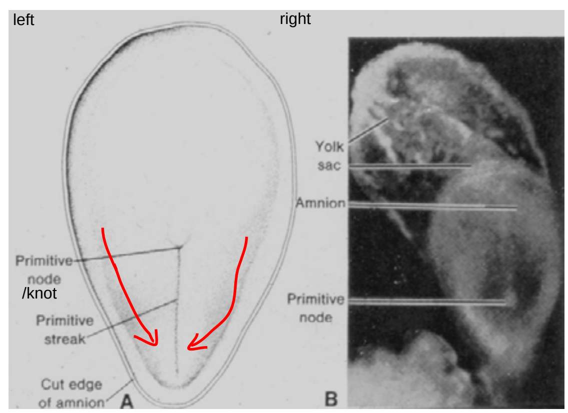
The third week of development is taken up with the process of gastrulation. During gastrulation, the appearance of a third tissue layer converts the bilaminar embryo to a trilaminar one. During the third and fourth weeks, the flat, two-dimensional embryonic disc begins to gain complex three-dimensional form and the process of organogenesis begins with the development of the neural tube and the primitive gut tube.

THE PRIMITIVE STREAK

- At 13 or 14 days following fertilization, proliferating epiblast cells begin to migrate medially and toward one end of the bilaminar disc. This end of the disc then defines the caudal part of the embryo. As they begin to pile up in the caudal midline, the cells produce a thickening of the epiblast layer, called the primitive streak.

- The cranial end of the primitive streak is called the primitive knot (Hensen's node).

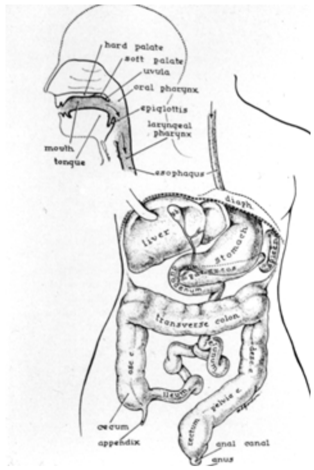
rostral



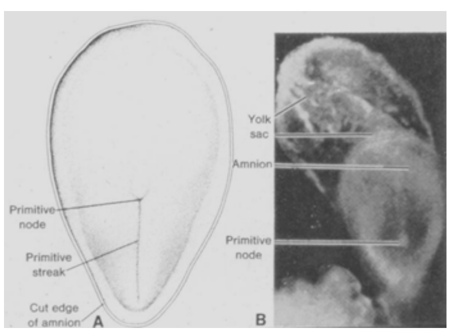
caudal

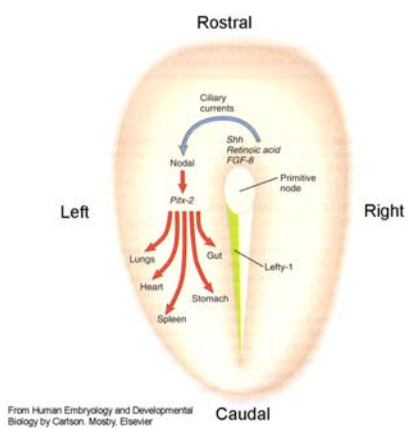
Asymmetries

of the body are set up at this point as well
- e.g. heart to left; liver to right; right lung has 3 lobes and left lung has 2 lobes; ascending colon; these asymmetries are all set up by the primitive streak



Sidedness seems a function of right to left ciliary sweep and the resulting distribution of signal molecules.





cilia on the streak beat R to L; push growth factors to the left

when cilia don't fxn properly, can lead to fertility problems; high incidence of situs inversus (= organs on abnormal side); resp infection
- 1' ciliary diskinesia
- immotile ciliary syndrome
- kartagener syndrome

Purpose of primitive streak is to drive gastrulation

- The epiblast cells ingress at the primitive knot (primitive pit) and along the primitive streak (primitive groove) and then begin to migrate rostrally and laterally.

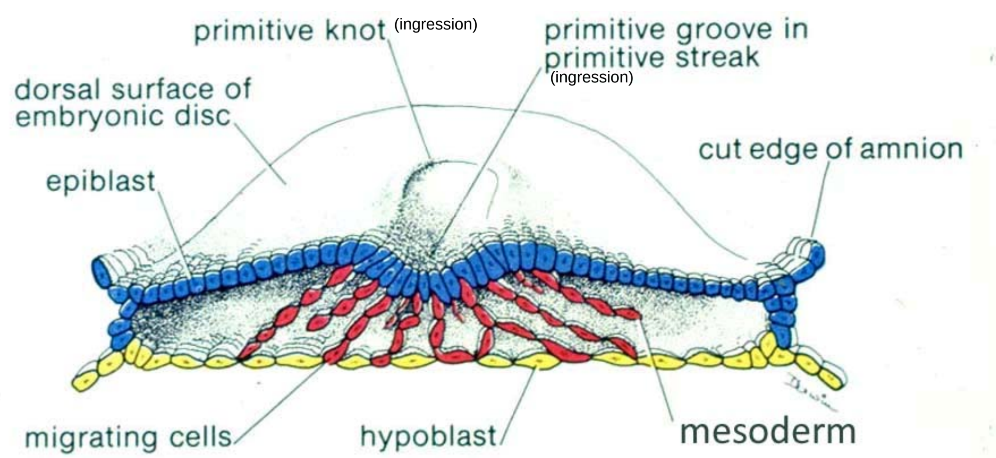
- Epiblast cells migrate between the endoderm and the epiblast to form a layer called the **mesoderm.**

- Some of the ingressing epiblast cells displace the hypoblast and form a single layer of cells called the embryonic **endoderm.**

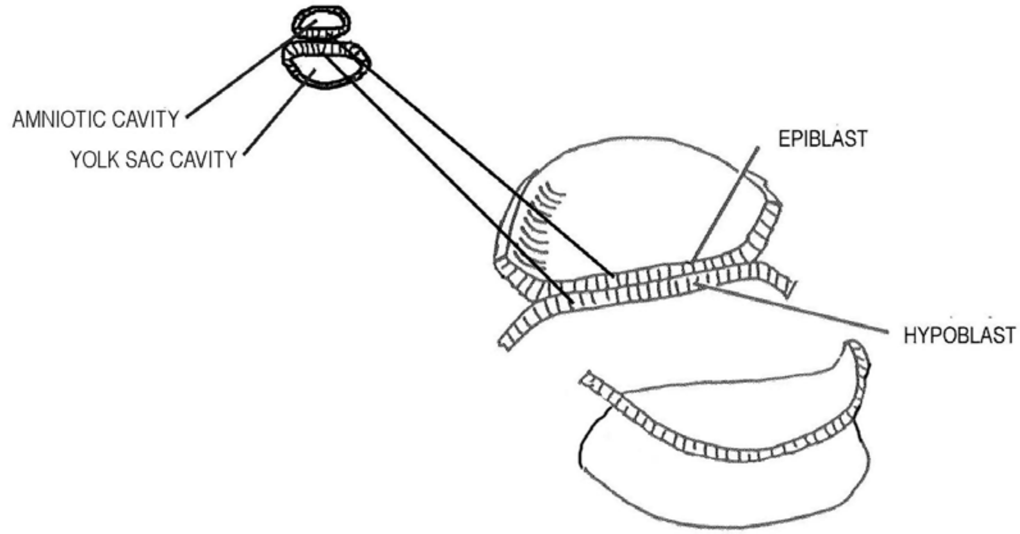
- With the appearance of the mesoderm, the overlying epiblast tissue that does not migrate through the streak and that remains on the surface of the embryo facing the amniotic cavity is then referred to as **ectoderm.**

- The primitive streak continues to form mesoderm through the third, fourth and fifth weeks. However, as the rest of the embryo grows in size, the streak becomes relatively smaller. At the time of its disappearance in the fifth week, it is situated in what will become the sacrococcygeal part of the trunk.

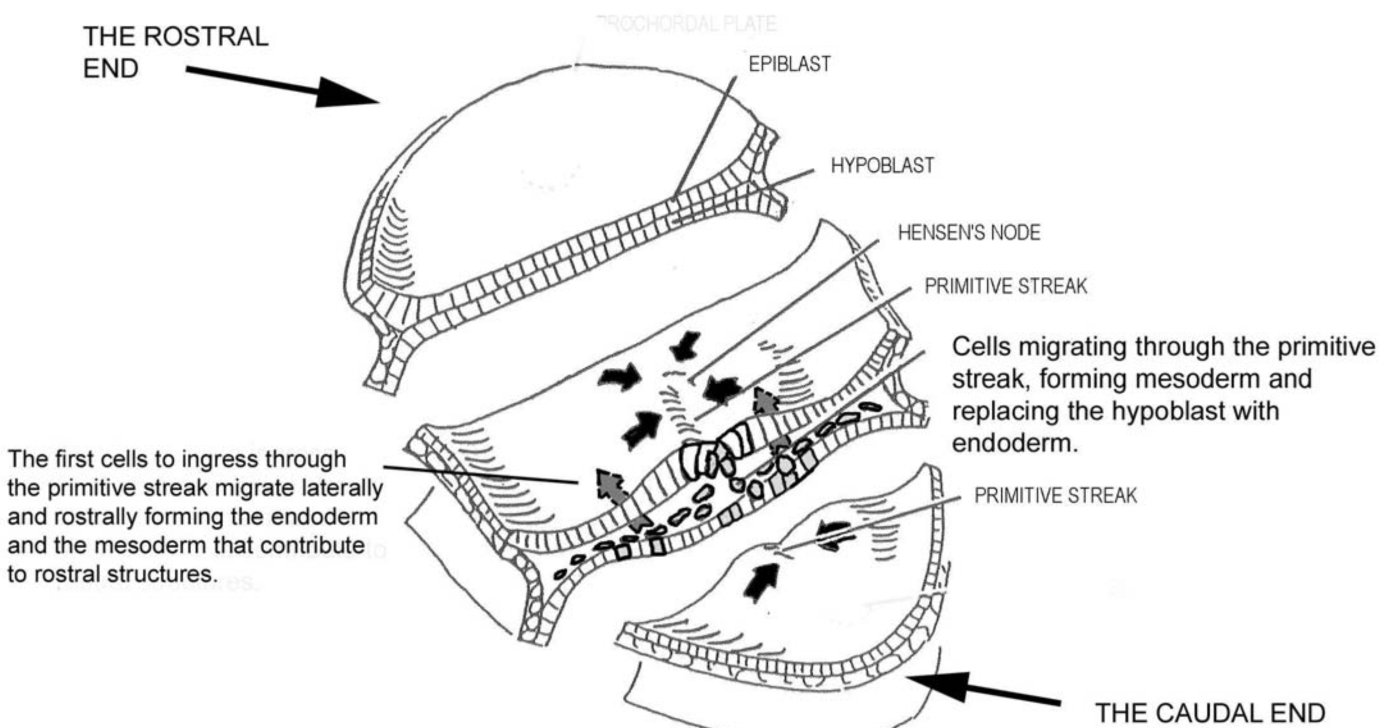
- The cells which are first to migrate through the primitive streak tend to migrate rostrally and form tissues that contribute to rostral structures. Those that migrate through later on in development form progressively more caudal structures. While the primitive streak is still forming mesoderm and endoderm for the caudal part of the embryo, the rostral tissues proceed with the business of growth, differentiation and organ formation. Thus there is a rostro - caudal gradient in developmental activity. That's why the more rostral structures of the embryo are typically more developmentally advanced than the caudal structures.

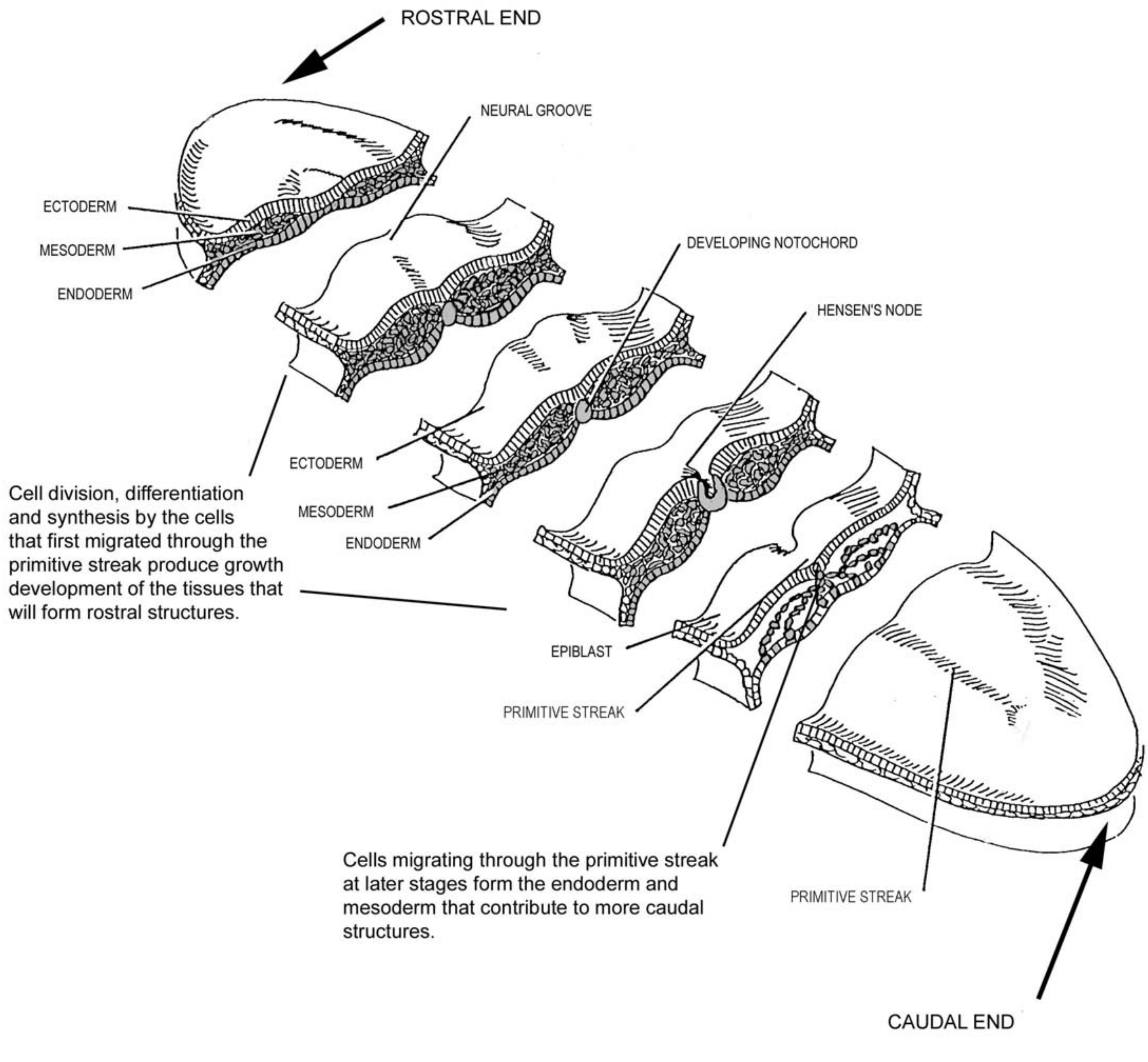


From Moore and Persaud. The Developing Human. B.C. Decker



THE BILAMINAR EMBRYONIC DISC



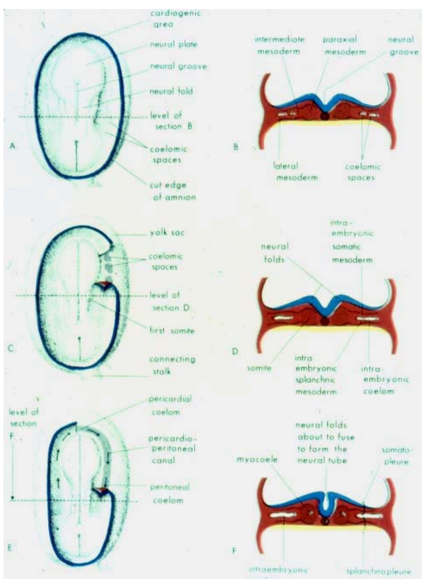

ROSTRAL END
NEURAL GROOVE
ECTODERM
MESODERM
ENDODERM
DEVELOPING NOTOCHORD
HENSEN'S NODE
ECTODERM
MESODERM
ENDODERM
Cell division, differentiation and synthesis by the cells that first migrated through the primitive streak produce growth development of the tissues that will form rostral structures.
EPIBLAST
PRIMITIVE STREAK
Cells migrating through the primitive streak at later stages form the endoderm and mesoderm that contribute to more caudal structures.
PRIMITIVE STREAK
CAUDAL END

The Notochord

The epiblast cells which ingress through Hensen's node migrate rostrally straight up the midline between the ectoderm and the endoderm and form a condensation of cells that develops into a rod-like structure called the notochord. The notochord serves as an important organizer in subsequent embryonic development.

Primitive Streak Activity

The primitive streak functions until the fifth week



- The first-formed tissues contribute to rostral structures. these don't wait for gastrulation to finish before developing (which is why rostral structures typically more developmentally advanced than caudal structures)
- Later-formed tissues contribute to more caudal structures.
- As development continues, the primitive streak regresses and disappears at 5 weeks.

finishes as sacral/coccygeal segments
- sacrococcygeal teratoma = when primitive streak remains active (no signals to organize its pattern of growth)

FATE OF THE ECTODERM

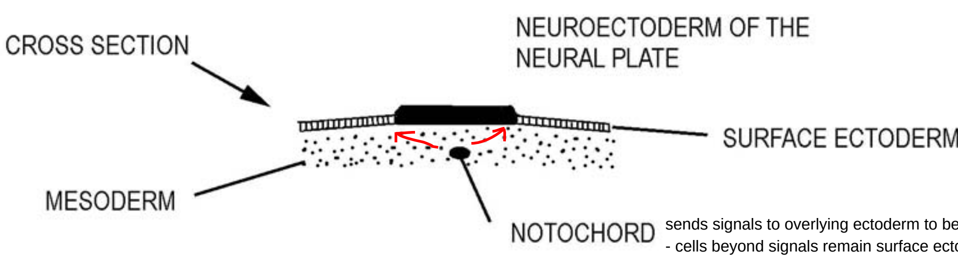
The ectoderm contributes to the formation of the nervous system, to the tissues that cover the body surface (epidermis, hair, nails) and to the glands that connect by ducts to the body surface (sweat and sebaceous glands).

Neurulation is the term given to the process by which the neural tube, the forerunner of the central nervous system, develops from the ectoderm. Neurulation involves:

ectoderm -> neural tube -> CNS

1. Induction of the Neural Plate.

- The notochordal process and adjacent paraxial mesoderm induce the overlying ectoderm to differentiate into a neural plate made up of neuroectoderm.

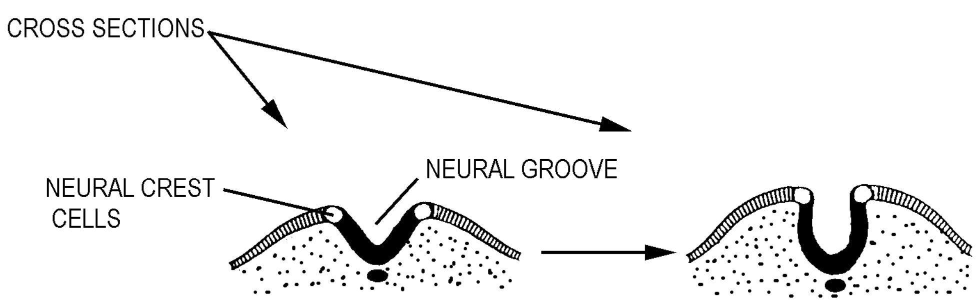


sends signals to overlying ectoderm to become neural plate made up of neuroectoderm
- cells beyond signals remain surface ectoderm

2. Elevation of the Neural Folds.

(move toward each other)

- The edges of the neural plate elevate, forming the neural folds. The neural folds have the neuroectoderm of the neural plate on their medial sides, non - neural (surface) ectoderm on their lateral sides and mesoderm in the core.

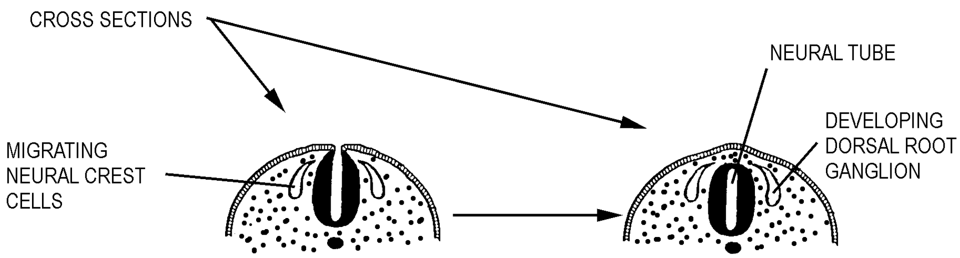


3. Apposition and Fusion of the Neural Folds

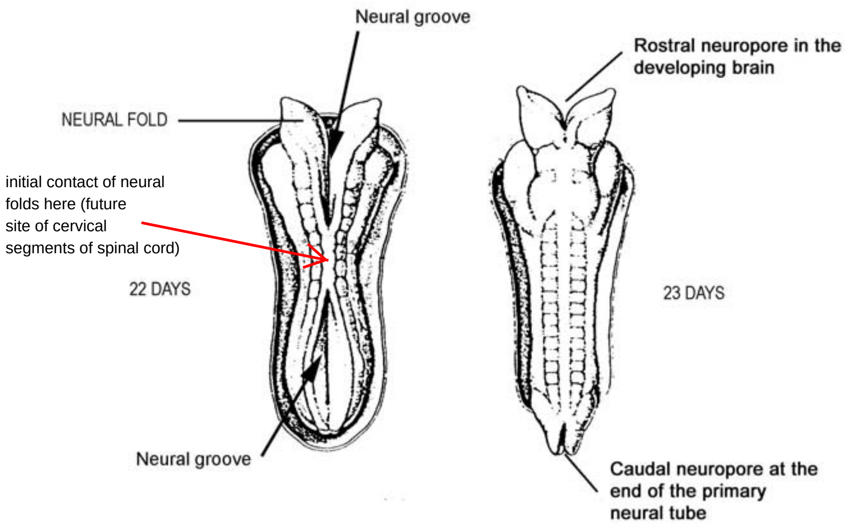
- The neural folds make contact with each other and join together to form the neural tube. The neural tube develops into the brain and the spinal cord.

- As the neural tube forms, the non - neural ectoderm, flanking the neural plate is able to come together sealing over the neural folds and allowing the tube to separate from the surface. The ectoderm will contribute to the skin covering the brain and spinal cord.

- Mesoderm can then migrate into the space between the neural tube and the ectoderm. This mesoderm will form the bones of the calvarium, covering the brain and the vertebrae covering the spinal cord.



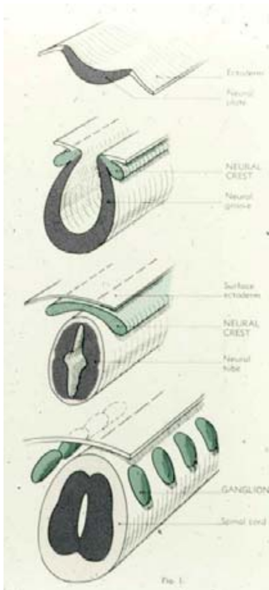
- Initial contact between the neural folds occurs at the site of the future cervical segments of the spinal cord. The fusion process proceeds cranially and caudally along the neural folds simultaneously.
- The last parts of the neural groove to close are called the rostral neuropore and the caudal neuropore.

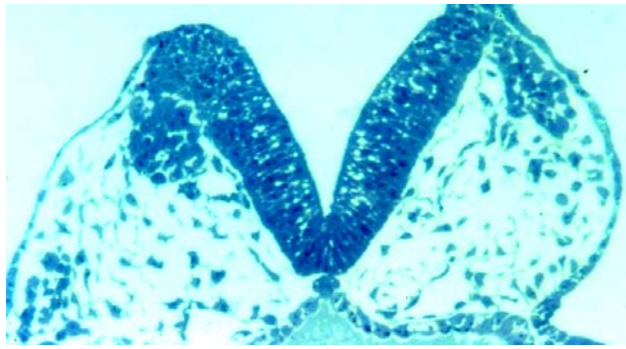


DORSAL VIEWS OF HUMAN EMBRYOS DURING THE FOURTH WEEK

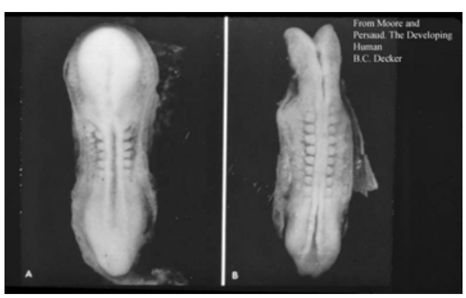
From Langman's Medical Embryology, by Sadler. Williams and Wilkins.

Neurulation





The last parts of the neural groove to close are the cranial and the caudal neuropores



DEFECTS OF NEURULATION

- Failure of the neural folds to close results in the neuroectoderm of the neural plate exposed on the body surface. Since the neural folds failed to make contact, there is no closure of the ectoderm and thus no skin cover for the defect. Moreover, since there is no separation of neural plate from the ectoderm, there can be no bony covering either.

- These 'open' defects of neurulation can occur anywhere along the neural axis but are most common in the vicinity of the rostral (*anencephaly)* and caudal (*myeloschisis)* neuropores

Anencephaly = open neural tube defect; rostral neuropore doesn't close -> skin can't develop -> skull bone can't develop over it

Myeloschisis = same defect but at caudal neuropore (didn't close properly); no skin or bone; spinal cord open to amniotic fluid and deteriorates
- at risk of developing hydrocephalus

In Utero Repair of NTD

- when surgery successful, these children tend to do better than children who get similar surgery after birth (less sensory and motor challenges and less susceptible to developing hydrocephalus)
- but this type of operation is high risk (infection; death etc)

THE NEURAL CRESTS

- A special population of cells that lie at the apices of the neural folds, where the surface ectoderm meets the neuroectoderm.

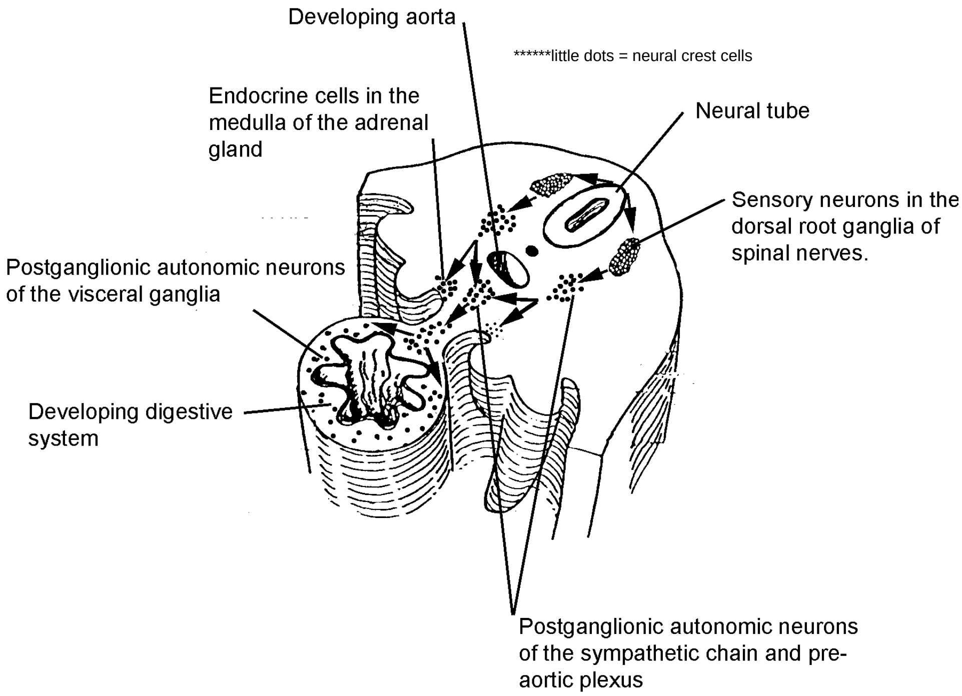
Neural Crest Cells

- As neurulation takes place, the neural crest cells migrate out of the neural folds and into the body forming a variety of structures which are related to the nervous system ~~and which you will encounter in the gross anatomy laboratory or in histology: eg)~~

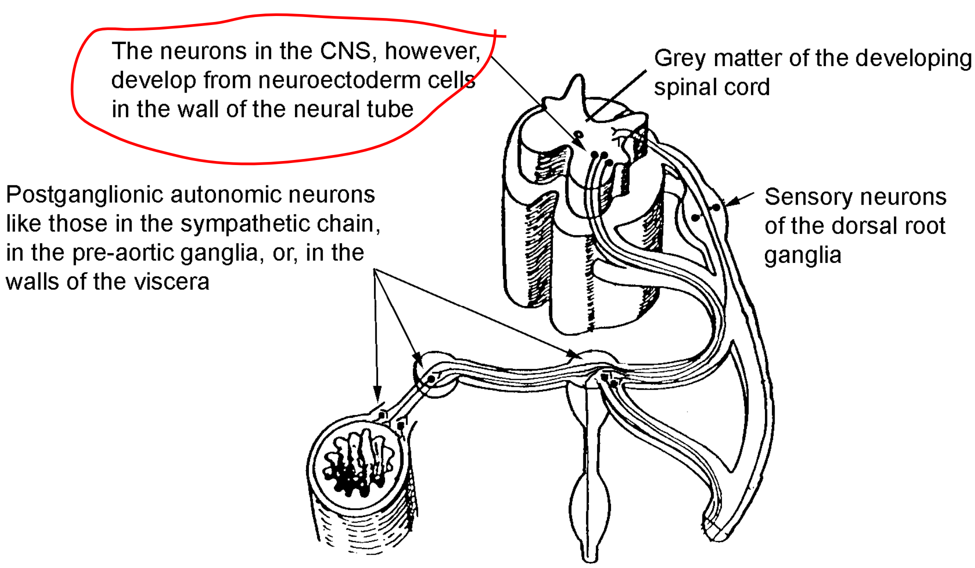
    - the sensory neurons of the dorsal root ganglia of spinal nerves
    - the postganglionic autonomic neurons in the ganglia of the sympathetic chain
    - the postganglionic autonomic neurons in the preaortic ganglia aka prevertebral ganglia
    - etc.
    - the postganglionic autonomic neurons of the visceral ganglia Auerbach's and Meissner's plexuses
    - the endocrine cells in the medulla of the adrenal gland
    - the Schwann cells of peripheral nerves
    - the melanocytes of the skin
    - etc.

- In addition, the neural crest cells that migrate out from the cranial end of the neural tube are also able to form a variety of cranial connective and skeletal tissues.
  - this is peculiar to neural crest cells that come out of the rostral end of neural tube

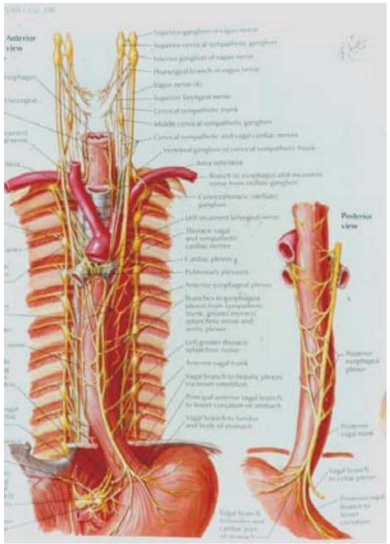
CROSS SECTION THROUGH THE DEVELOPING EMBRYO

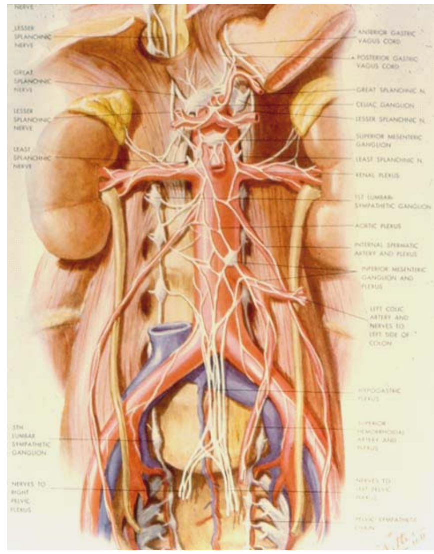


SPINAL CORD AND AUTONOMIC GANGLIA



Autonomic Ganglia





Treacher – Collins Syndrome

- Cranial neural crest cells contribute to the formation of the facial skeleton
- Treacher Collins syndrome, a condition characterized by maxillary hypoplasia, micrognathia, conductive hearing loss, and abnormalities of the pinna among other features is thought to be the result of faulty development of the cranial neural crest cells

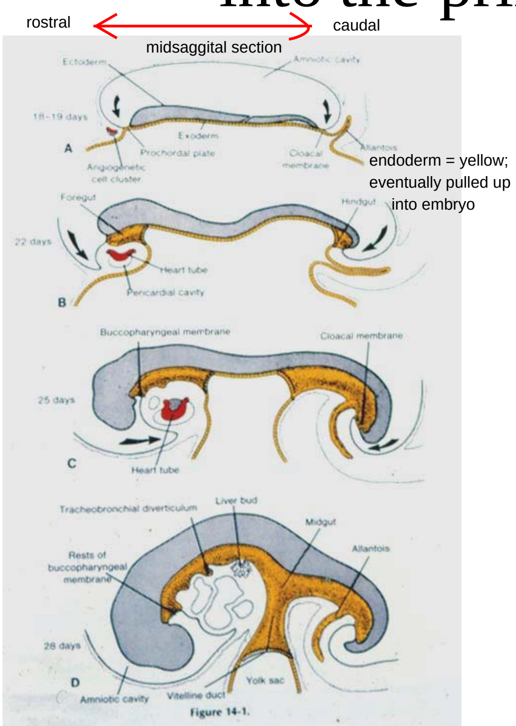
Treacher Collins Syndrome

FATE OF THE ENDODERM

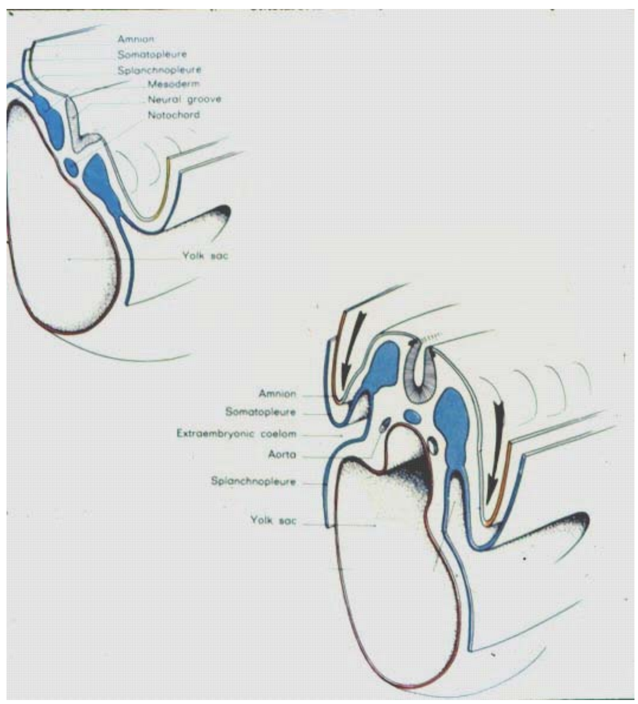
- The endoderm will form the lining tissue (epithelium) of the gastrointestinal tract. It also forms the secretory cells of the liver, gall bladder, and pancreas (which are all outgrowths of the gastrointestinal tract), the lining of the ducts of these organs, and the lining of the respiratory system – another outgrowth of the gastrointestinal tract.

- During the fourth week of development, different rates of growth in the tissues of the embryo cause it to buckle, or, fold.

Embryonic folding rolls the endoderm into the primitive gut tube



Longitudinal



Transverse

endoderm also folds transversely

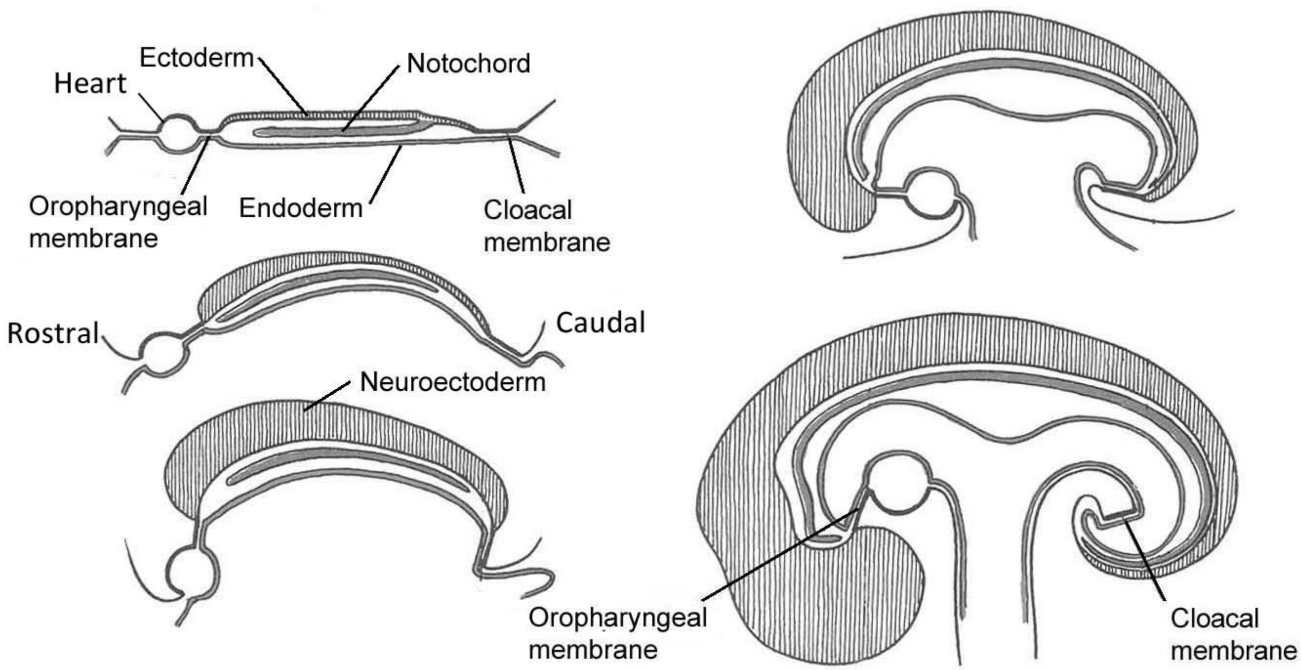
1. Folding in the Long Axis

- Rapid elongation of the neural tube and the notochord produce the head fold and the tail fold.

- As these folds develop, the endoderm is rolled into the primitive foregut and the primitive hindgut.

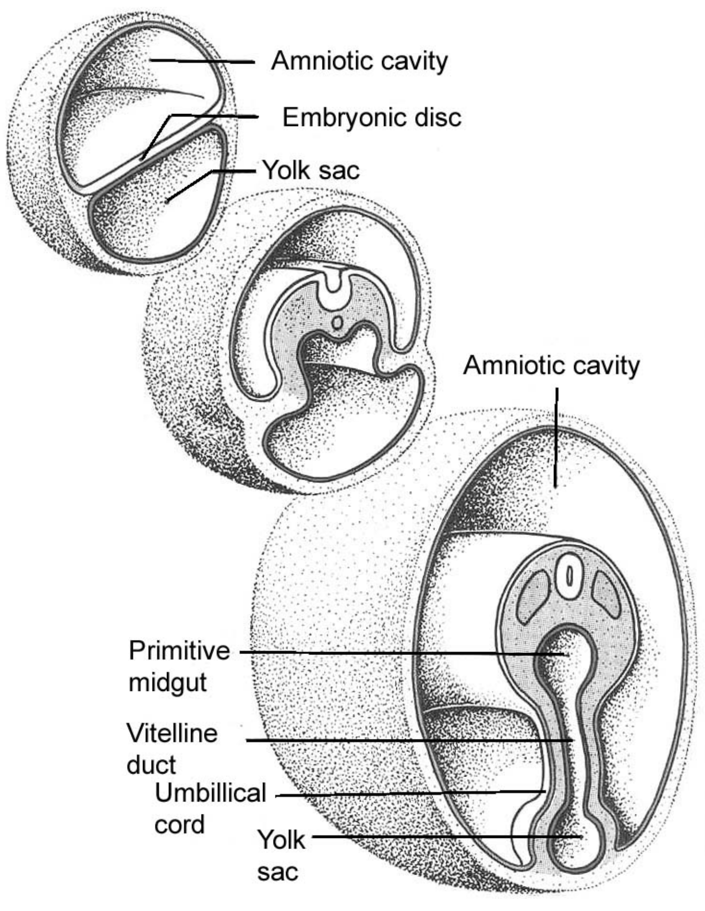
- The primitive foregut forms parts of the mouth, the esophagus, the stomach and the duodenum as far as the opening of the common bile duct. By outgrowth, the primitive foregut also forms the respiratory airways and lungs and the liver, gall bladder and pancreas.

- The primitive hindgut forms the large intestine from the distal part of the transverse colon to the anal canal as well as parts of the bladder and urethra.

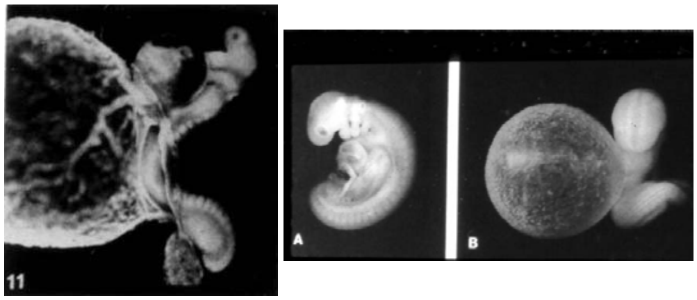


2. Folding in the Transverse Axis

- Enlargement of the somites causes the sides of the embryo to fold.
- During transverse folding, the endoderm is rolled into a primitive midgut.
- The primitive midgut remains connected to the remains of the yolk sac by the vitelline duct (yolk stalk).
- The primitive midgut forms the small intestine from the opening of the common bile duct to the ileocecal junction, and the large intestine from the caecum to the distal part of the transverse colon.



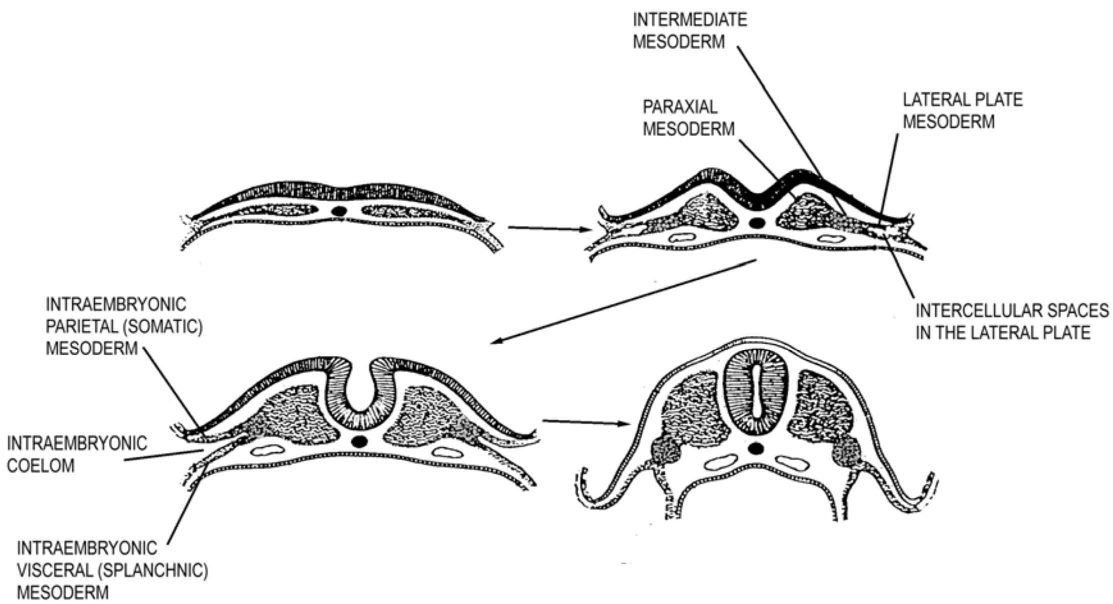
As the primitive gut forms the yolk sac is excluded



FATE OF THE MESODERM

The mesoderm forms most of the muscle and connective tissues in the embryo.

- ~~On each side of the developing neural tube and notochord, the~~ mesoderm becomes subdivided into regions running the length of the embryo – the paraxial, lateral plate and intermediate mesoderm.



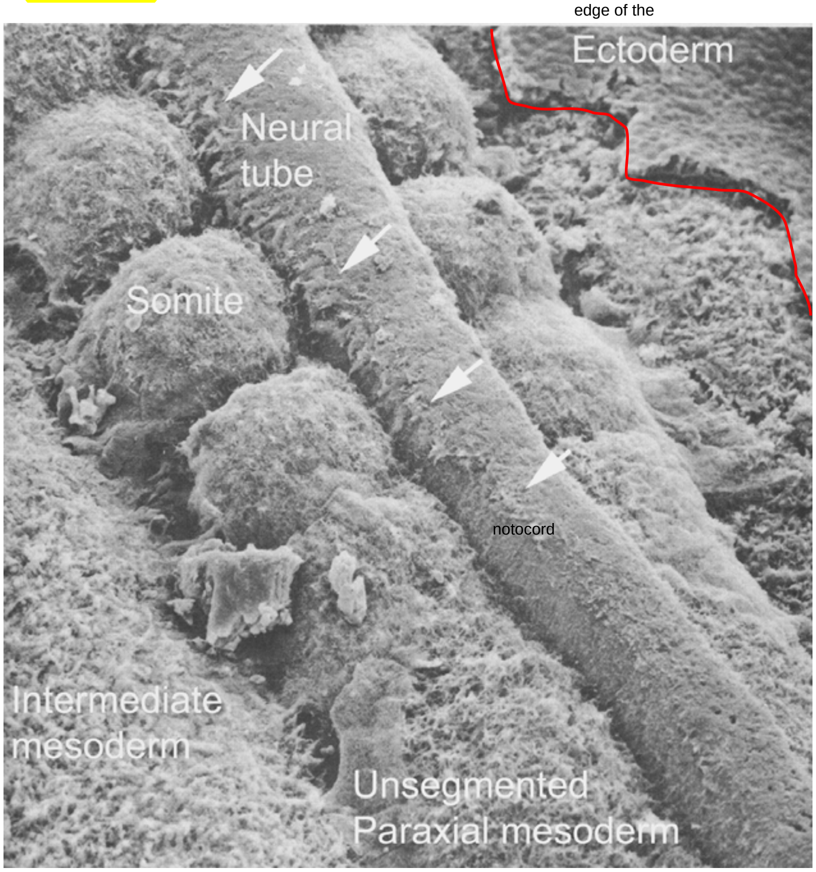
CROSS SECTIONS OF AN EMBRYO SHOWING THE SEPARATION OF THE MESODERM INTO PARAXIAL, LATERAL PLATE AND INTERMEDIATE REGIONS.

1. The Paraxial Mesoderm

- ~~This lies immediately on either side of the notochord.~~

- Somites form in a craniocaudal sequence as paired blocks of cells ~~in the paraxial mesoderm. The somites flank the notochord and neural tube~~

- The somites will develop into the vertebrae and intervertebral discs, the ribs, the skeletal muscles of the body wall and limbs and they will contribute to the connective tissues of the body wall.



human embryo
- counting the no. somites is better than chronology for determining developmental age (some embryos develop faster/slower than others)

Dorsal view of a somite stage embryo viewed by scanning electron microscopy. The surface ectoderm has been removed, exposing the neural tube and somites. The arrows indicate neural crest cells migrating from the neural tube.

2. The Lateral Plate Mesoderm

- ~~This lies at the periphery of the embryo.~~

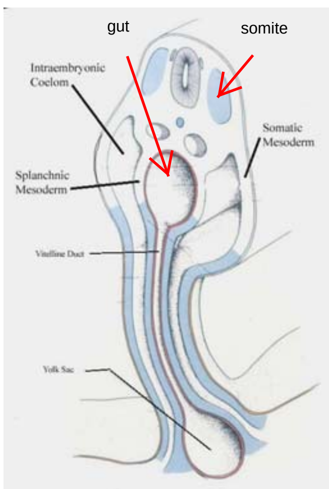
- ~~The appearance of a cavity (the intraembryonic coelom) in the lateral plate mesoderm divides it into the somatic (parietal) mesoderm supporting the ectoderm and the splanchnic (visceral) mesoderm supporting the endoderm~~.

- The somatic mesoderm contributes to the connective tissues, blood vessels and smooth muscle of the body wall and limbs.

- The splanchnic mesoderm contributes to the smooth muscle, blood vessels and connective tissue of the gastrointestinal tract and associated organs.

- the intraembryonic coelom develops into the main body cavities, i.e.) the pleural, pericardial and peritoneal cavities.

Lateral plate mesoderm forms connective tissues and smooth muscle



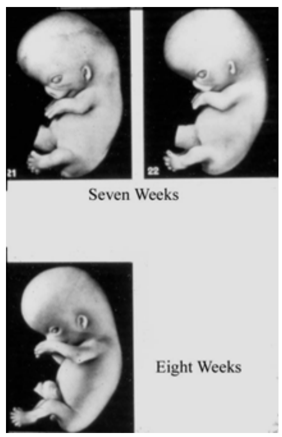
- Somatic mesoderm … along the body walls.
- Splanchnic mesoderm … along the primitive gut and its derivatives.
- Intraembryonic coelom forms the body cavities … pleural, peritoneal and serous pericardial

3. The Intermediate Mesoderm

- ~~Lies between the paraxial mesoderm and the lateral plate mesoderm~~.
- Contributes to the formation of the urinary and reproductive systems.

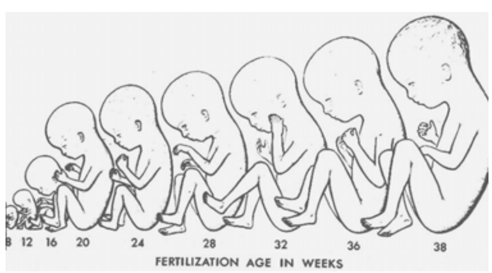
kidneys and gonads

look like a comma after 4th week



- Most structure is complete by the end of the eighth week after fertilization
  - fingers, organs

Periods of Development



- **<u>Embryonic period</u>** … 0 to 8 weeks
- ✓ First two weeks … transport and implantation.
- ✓ 3 to 8 weeks … morphogenesis/organogenesis
- **<u>Fetal period</u>** … 9 weeks to term
- ✓ Growth and physiological maturation.

Definitions

Fertilization age – the age from conception

Gestational age – the age from the first day of the last normal menstrual period

Embryo – the conceptus from fertilization to the end of the 8^{th} week of development (fertilization age, ie 10 weeks of gestational age)

Fetus – The conceptus from 9 weeks fertilization age to birth