Module 7

Organogenesis

After the three germ layers are established at the gastrula stage, it leads to **organogenesis**, the formation of organs. It is at this stage that process of pattern formation continues as specific structures of the organism are formed from the three germ layers.

The cells that remain on the outer surface of the gastrula is the **ectoderm** that will form the *epidermis of the skin, nervous system, sense organs and a few other cell types.* The **endoderm** gives rise to tissues that *line the digestive tract and organs that develop as outgrowths of the digestive tract (including the liver, pancreas, and lungs*). The remaining intermediate layer is the **mesoderm** that will give rise to the *skeletal, muscle tissues and circulatory, excretory and reproductive systems.*

Learning Objectives: At the end of this lesson, the student should be able to:

1. Explain how the different organs develop by induction through chemical signals from neighboring cells
2. Define organogenesis and summarize the fate of each of the germ layers.

Induction

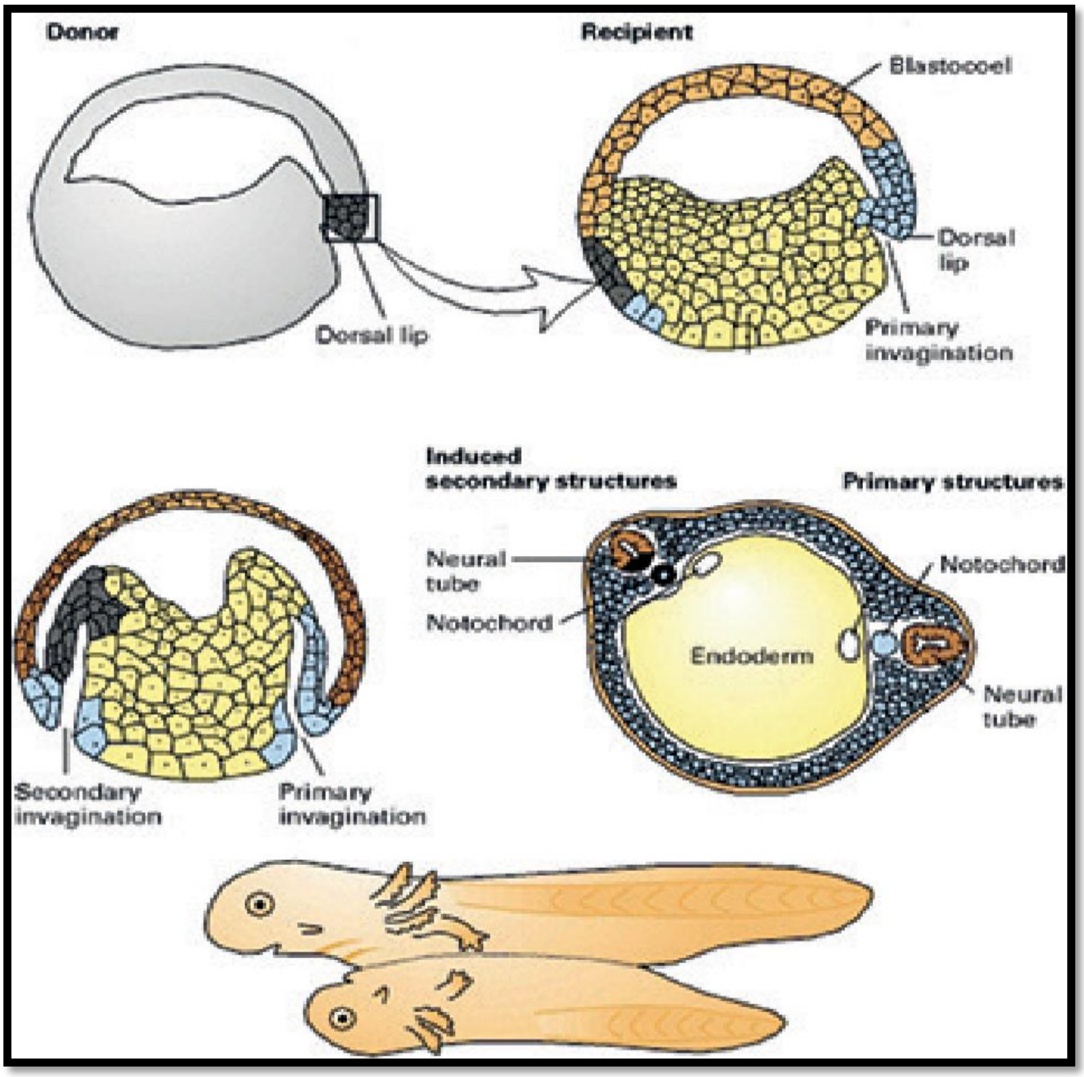
We have learned that even as early as in the fertilization stage, the anteroposterior and dorsoventral axes are already specified and established. By by the blastula stage of the amphibian embryo, the fates of the cells in different regions of the embryo are already specified. Then in the gastrula stage, the cells of the blastula undergo different kinds of movements to organize and establish the three germ layers from where the different organs of the animals will be derived from.

Genetic programs are also crucial in the formation of organs. Even before the egg is fertilized, genes that will encode for specific proteins essential for development are already in existence. But with the fertilization of the egg by the sperm, a new set of genetic programs (e.g. gene expression) for new set of proteins of development come into view. These proteins released by group of cells act as chemical signals to adjacent cells or tissues to to set in motion a different pathway of differentiation, leading to the morphogenesis of tissues or organs.

The response of these cells to the chemical signals released by adjacent cells is called **embryonic induction.** It is the process by which the identity of certain cells influences the developmental fate of surrounding cells (https://pdfs.semanticscholar.org/e607/829eea10d19dea04920ac2cb22c81c69cd35.pdf?_ga=2.66937582.158688425.1608142260-1842665231.1608142260)

Two scientists are recognized for this phenomenon of induction, and they are the German embryologist **Hans Spemann** and his student **Hilde Mangold**. They did several experiments by transplanting the cells of the **dorsal lip of the blastopore** (DLB) of salamanders to different sites of the recipient embryos. Based on the results of their experiments, the transplanted DLB results to the formation of a secondary axis, then to a second central nervous system (CNS), muscles and other axial organs in the recipient. What does this tell us? The DLB contains chemical signals that induces the neighboring cells to develop as what they are programmed to become.

The classic experiment of Spemann and Mangold is shown below.



https://www.semanticscholar.org/paper/Spemann-Mangold-Organizer-Mangold-Spemann/d0315ad858eaae42a8125d33cc555103e2d70561/figure/3

The transplantation experiment of Spemann and Mangold have shown that the cells in the DLB have an extraordinary role in the formation of the dorsal mesoderm, particularly the notochord and some pharyngeal endoderm.

The cells of the DLB have been referred to as the **Spemann organizer** since the cells here induces the formation of the CNS. One important chemical that was later known to be the cause of the induction of the CNS is **chordin** (encoded by the gene *chordin*). Before the CNS is induced to form, chordin is a protein that dorsalises early vertebrate embryonic tissues binds to **bone morphogenetic proteins (BMPs**) that may be involved also in organogenesis (Segen's Medical Dictionary, 2012). If you want to know more about embryonic induction, you can go to this link : https://doi.org/10.4161/org.28026. In other embryonic vertebrates with no DLB, the organizer will be embryonic shield (fishes) and the **Hensen's node** (amniotes).

Neurulation as the first induction event in animal development

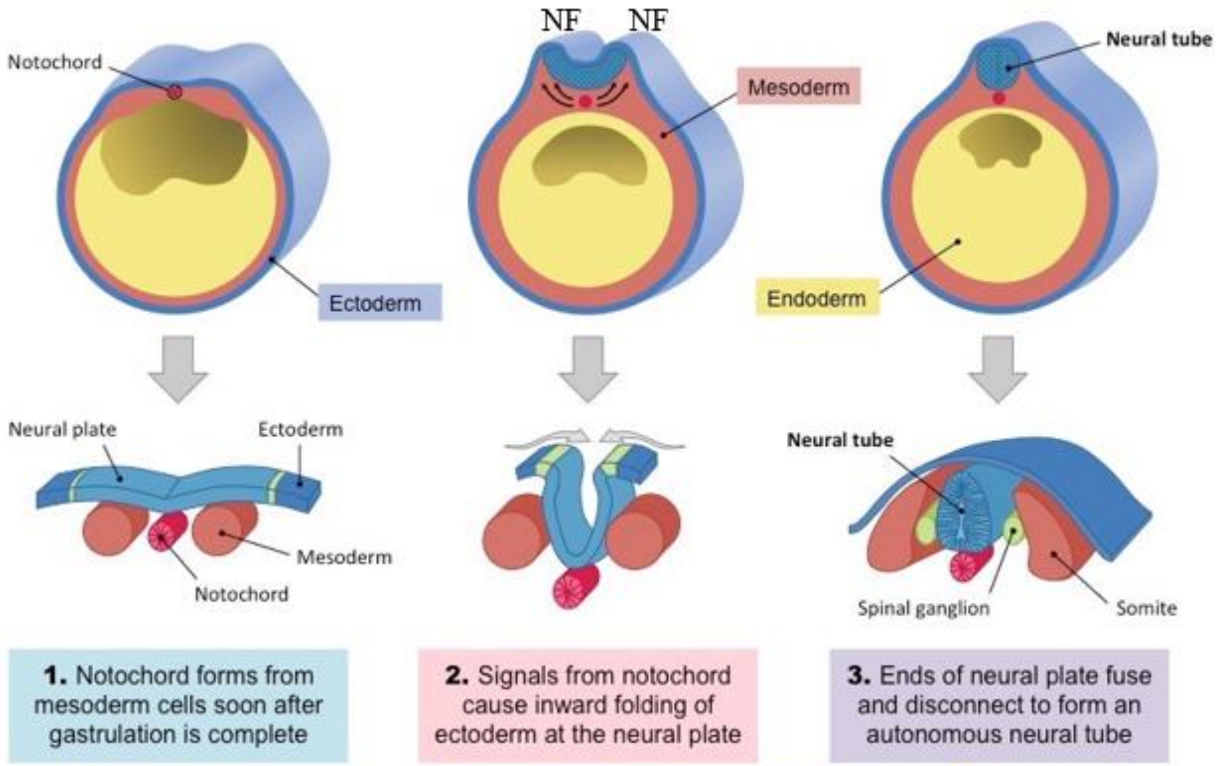
The organs first formed in the early vertebrate embryos are the notochord, brain and spinal cord. The notochord is first formed from the mesodermal cells of the DLB or the mesodermal cells of the **Hensen's node** of amniotes called the **chordamesoderm**.

But before we proceed further to induction, let us first understand more about the Hensen's node in amniotes, including humans. As mentioned in the previous module, a blastopore is not formed in amniote gastrulation because of the enormous amount of yolk. Instead a primitive streak is formed by the movement of the cells and later on a primitive groove is formed as the functional equivalent of the blastopore.

Further movement (by ingression) of the cells from the surface epiblast results to a thickened structure at the anterior end of the primitive streak called the **Hensen's node.** The aggregate of cells in this thickened knot are destined to form the **notochord.** Notochord, if you recall, is made of cartilage-like cells that serves as a flexible axial support in all chordate embryos. It grows forward along the length of the embryoas a cylindrical rod of cells. At this point, we can generalize that where the DLB in amphibians or the Hensen's node in amniotes, establishes the posterior end of the embryo since the notochord develops anterior to these structures.

How does the notochord play a role in the formation of the brain and spinal cord? Several experiments have been done by transplanting portions of the notochord mesoderm to other areas of the embryo. These experiments have established where first induction event happens in chordate embryos. The notochord releases chemical signals to the ectoderm above or dorsal to it. Note that the mesodermal cells are not in close contact with the overlying ectoderm. This tells us that the chemical signals, generally called as **morphogens,** diffuse to these neighboring cells and induce their differentiation.

Results of the experiments have shown that the notochord induces/causes the overlying ectoderm to thicken and differentiate to form the precursor of the central nervous system, and that is the **neural plate.** Later on, the cells of the neural plate undergo conformational changes that makes the the central cells of the neural plate to move downward forming a depression called the **neural groove (NG);** and the structures flanking this groove are called the **neural folds (NF).** Further changes in the shape of the cells of the neural folds cause them to move closer until the two folds meet and fuse to form the **neural tube.**



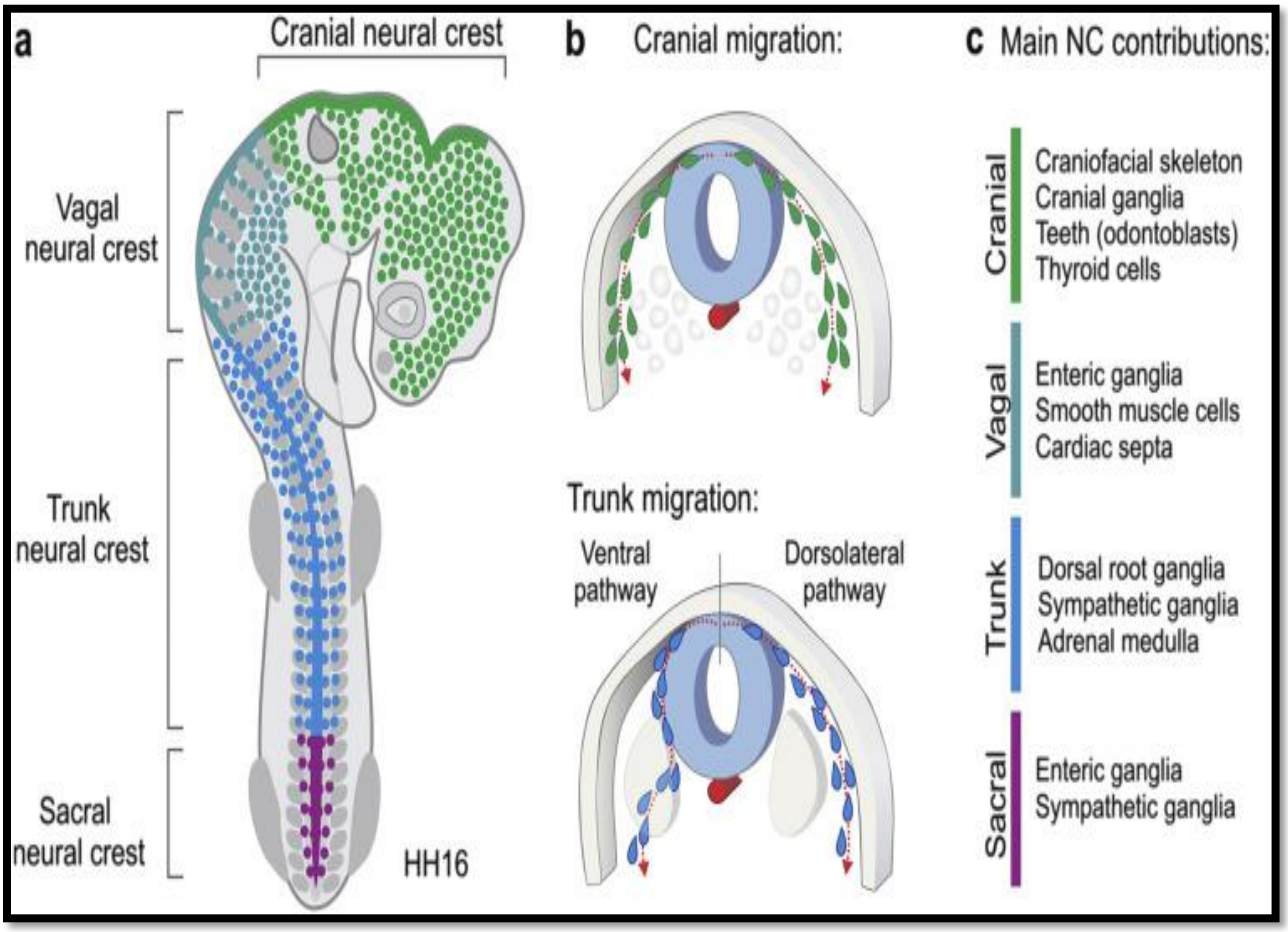
https://ib.bioninja.com.au/options/option-a-neurobiology-and/a1-neural-development/neurulation.html

Click this link for a 2 minute video on neurulation: https://youtu.be/Tp25wrm-AoA

Therefore, at the end of the neurulation event, the ectoderm that did not differentiate as neural tube will become the outer layer of the skin, the **epidermis.** Further growth and differentiation of the neural tube cause the anterior end to become the brain and the rest of the tube develops into the spinal cord. Recall that the neural tube encloses the former neural groove and as a result the neural tube is said to be hollow until the adult stage; the reminder of this embryonic beginnings as hollow strctures can be seen as the **ventricles of the adult brain** and the **central canal of the spinal cord.**

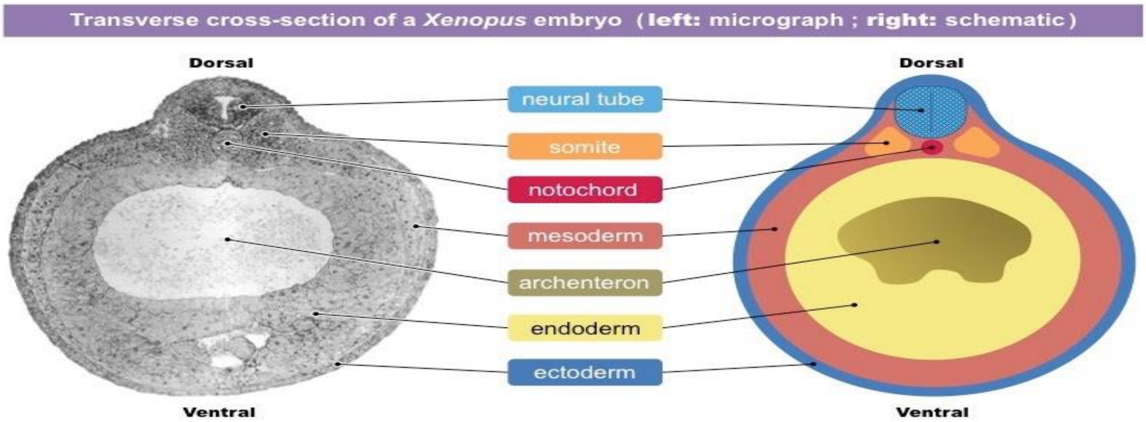
Go back to the figure above on neurulation. In the section of the neural plate, notice the small area colored green, that later increase in size at the neural tube stage. This green area indicates the location of cells that what we call the **neural crest.** So, these cells are also ectodermal cells that differentiate not as epidermis of the skin nor the neural tube. The neural crest cells migrate downward from their original position and form the the **dorsal root ganglia of the spinal nerves** and the **postganglionic sympathetic neurons.**

The figure below shows the migration of the neural crest cells from the anterior region of the body to the posterior end and what are their fates in these regions. The link given is where this figure was copied from and can also be read by you for mor more information and understanding about the neural crest cells. https://www.sciencedirect.com/science/article/pii/S0012160617305985#f0010



Formation of other organs

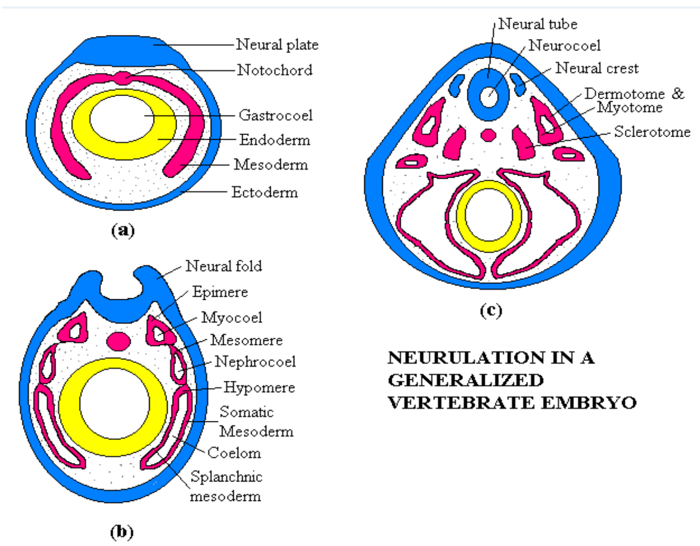
When the nervous system is developing thru neurulation, other organs also take shape (by morphogenesis, right?). Shown below is a cross-section of the frog neurula, the embryonic stage when the neural tube is forming and has formed already. We can see that blocks of **anterior mesoderm (or epimere)** called **somites** form on either side of the neural tube. Further differentiation of these somites will give rise to *vertebrae, muscles,* and *other parts of the body axis.* The cells of middle mesoderm **(intermediate mesoderm or mesomere)** gives rise to the prospective *kidneys* and *reproductive structures.*



https://ib.bioninja.com.au/options/option-a-neurobiology-and/a1-neural-development/neurulation.html

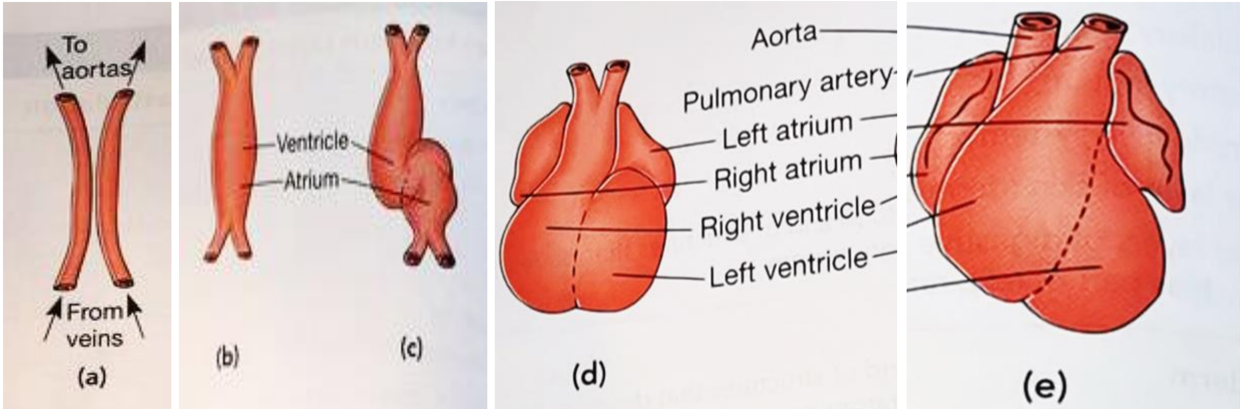
The ventrolateral mesoderm (**lateral plate mesoderm or hypomere)** splits into two layers : an outer layer that becomes associated with the ectoderm the **somatic mesoderm** layer and an inner layer that becomes associated with the endoderm, the **splanchnic mesoderm.** The splanchnic mesoderm covers the endoderm and eventually the gut that develops from it. There is a space that is formed between these two layers, it is called the **coelom.**

Other organs that develop very early too in development are the *heart and blood vessels* and function already while still developing.



http://palaeos.com/vertebrates/glossary/early_development.html

Another example of organogenesis is seen in the development of the four-chambered heart of birds and mammals. Lifting the figure from Solomon, Berg & Martin is the formation of heart in birds and mammals. We can see that heart forms from the fusion of two blood vessels (a) and that at first the end that receives blood from veins is at the bottom. The developing heart twists or loops in the very small space called the pericardial cavity, bringing the atrium to position above the ventricle, and the chambers then divide by septation to form the four-chambered heart.



If you are interested to know what can go wrong in the the development of the cardiovascular system, you can click this link https://radiologykey.com/embryology-of-the-cardiovascular-system/. Any mistake that happens in the development of organs while the mammal is still in the mother's womb is called **congenital deformities** or **diseases.**

The endoderm layer as we have said gives rise to organs of the digestive and respiratory systems. The digestive tract is formed as a separate foregut and hindgut as the body wall grows and folds. As the embryo grows, these tubes, which are lined by endoderm, grow and become greatly elongated.

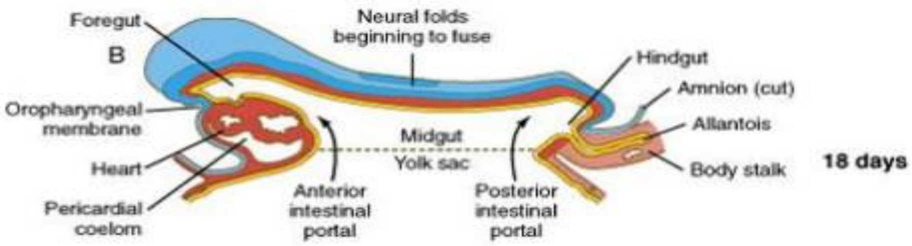
Lifted from the site https://web.duke.edu/anatomy/embryology/gi/gi.html, the formation of the primitive gut tube is as follows:

(a) The gut tube is formed from endoderm lining the yolk sac which is enveloped by the developing coelom as the result of cranial and caudal folding.
(b) During folding, somatic mesoderm is applied to the body wall to give rise to the parietal peritoneum.
(c) Visceral (or splanchnic) mesoderm is wraps around the gut tube to form the mesenteries that suspend the gut tube within the body cavity.
(d) The mesoderm immediately associated with the endodermal tube also contributes to most of the wall of the gut tube.
(e) Nerves and neurons found in the wall are derived from neural crest.
(f) Summary of germ layer contributions:

- endoderm: mucosal epithelium, mucosal glands, and submucosal glands of the GI tract.

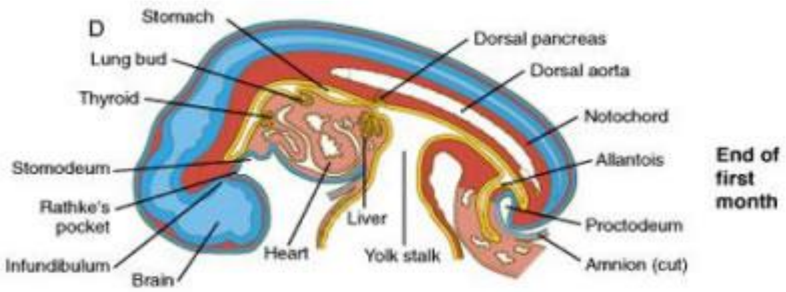
- mesoderm: lamina propria, muscularis mucosae, submucosal connective tissue and blood vessels, muscularis externa, and adventitia/serosa
- neural crest: neurons and nerves of the submucosal and myenteric plexus

Basic subdivisions of the gut tube



Cranio-caudal and lateral folding cause the opening of the gut tube to the yolk sac to draw closed (like a purse string) forming a pocket toward the head end of the embryo called the "anterior (or cranial) intestinal portal" and a "posterior (or caudal) intestinal portal" toward the tail of the embryo. These are the future foregut and hindgut, respectively. The midgut remains open to the yolk sac.

Further folding and growth of the embryo causes the communication of the gut with the yolk sac to continue to get smaller and the regions of the gut (foregut, midgut, and hindgut) to become further refined:



The derivatives of the gut regions are as follows:

FOREGUT	Trachea and respiratory tract, lungs, esophagus, stomach, liver, gallbladder and bile ducts, pancreas and upper duodenum
MIDGUT	Lower duodenum, jejunum, ileum, cecum, appendix, ascending colon, proximal 2/3 of descending colon
HINDGUT	Distal 1/3 of the transverse colon, descending and sigmoid colon, rectum, upper anal canal, urogenital sinus

The respiratory system develops from the ventral evagination of the foregut called the **lung buds.** The trachea grows downward from it and bifurcates into two lung buds, which develop into lungs. The anterior part of the foregut becomes the pharynx. A series of small outpocketings of the pharynx, the **pharyngeal pouches** bud out laterally. These pouches meet the **branchial grooves**, a corresponding set of inpocketings from the overlying ectoderm. The arches of tissue formed between the grooves are called **branchial arches**. They contain the rudimentary skeletal, neural, and vascular elements of the face, jaws and neck.

These are just some of the overview of organogenesis in vertebrate embryos. And do you need to memorize these derivatives from the three germ layers....YES.. kalimutan niyo na si Ma'am Meggie, wag lang ang mga germ layers and the organs derived from each ☺. Aside from these derivatives, Wilt & Hake (2004) said you should memorize also the characteristic arrangement of these germ layers since the basic body plan of all vertebrates have these as the foundation of the anatomical arrangements in the subphylum of vertebrates. Any deviation from this basic plan results to **anomalies, malformations, abnormalities** of the organs and this results to malfunctioning body parts.

There are still more to know about the development of animals, but for now, knowing and understanding the basic concepts and principles involved in transforming a fertilized egg into a new being or individual is commendable.

Have a wonderful semester/Christmas Break.

Let's be grateful to everything we can do and have despite the pandemic.

Thank you…Ma'am Meggie ☺

BOOK REFERENCES:

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3. Solomon EP, Berg LR and Martin DW. 2008. Biology. 8th ed. Thomson Brooks/Cole.
4. Wilt, F & S. Hake. 2004. Principles of Developmental Biology. W.W. Norton & Company.