Embryology

Sheet Slide

number	1
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*We will discuss the development of the gut that is composed of three parts:

1- Foregut: esophagus, stomach, 1st part of duodenum, liver, gallbladder, pancreas and spleen.
2- Midgut: duodenum (distal half of 2nd part), jejunum...to the proximal 2/3 of transverse colon.
3- Hindgut: from the distal 3rd of transverse colon to the proximal 2/3 of the anal canal.

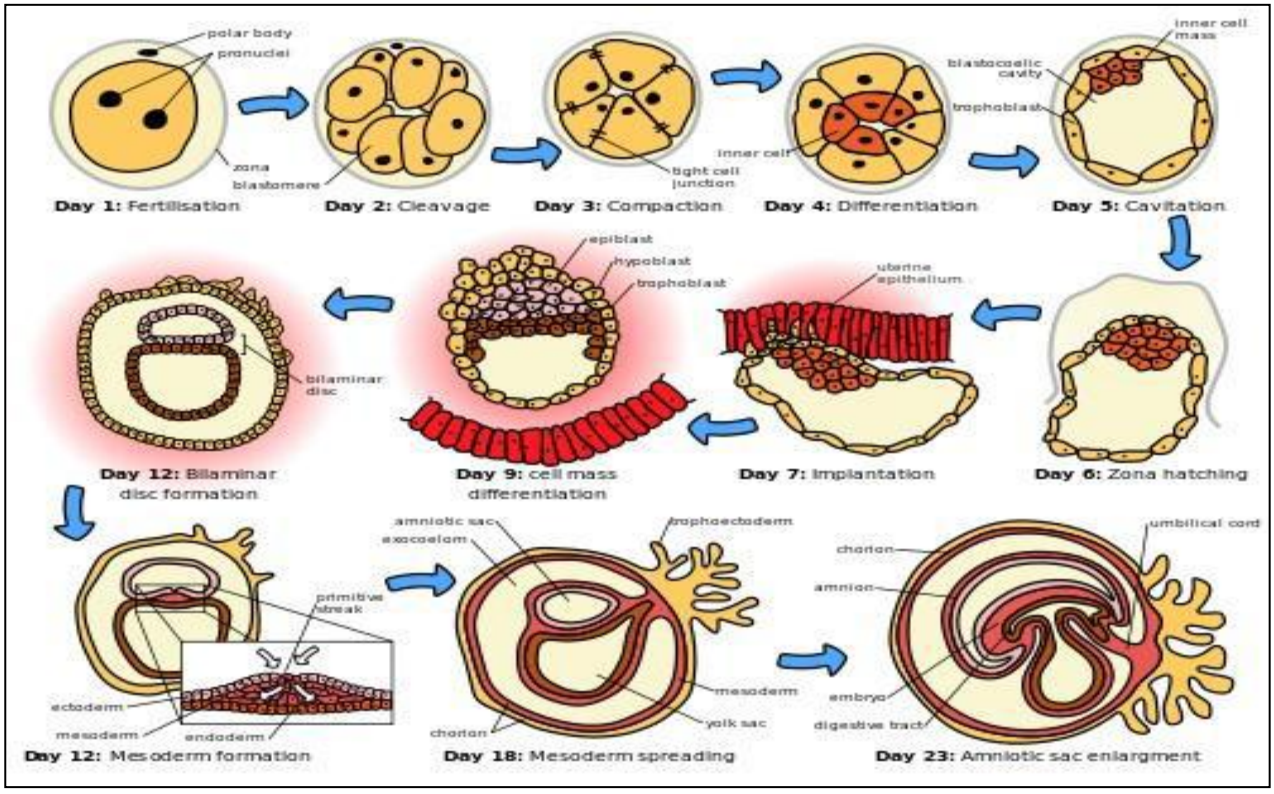
in this lecture we will talk about ***the foregut*.

The clinical orientation related to the GI development generally is the symptoms that appear which are:

1-vomiting 2-constipation 3-jaundice 4-abdominal distention

**the picture below describes the general embryology that we took before:

Two-cell level→ morula→ epiblast & hypoblast→ bilaminar disk→ trilaminar disc→ migration of mesoderm→ development of organs



Embryo folding starts in the first month, which produces cephalo-caudal folding, where the different organs form.

00:00-10:00

GI tract origin

*What comes from the same origin have the same blood supply, nerve supply and lymphatic supply.

Comes from two layers:

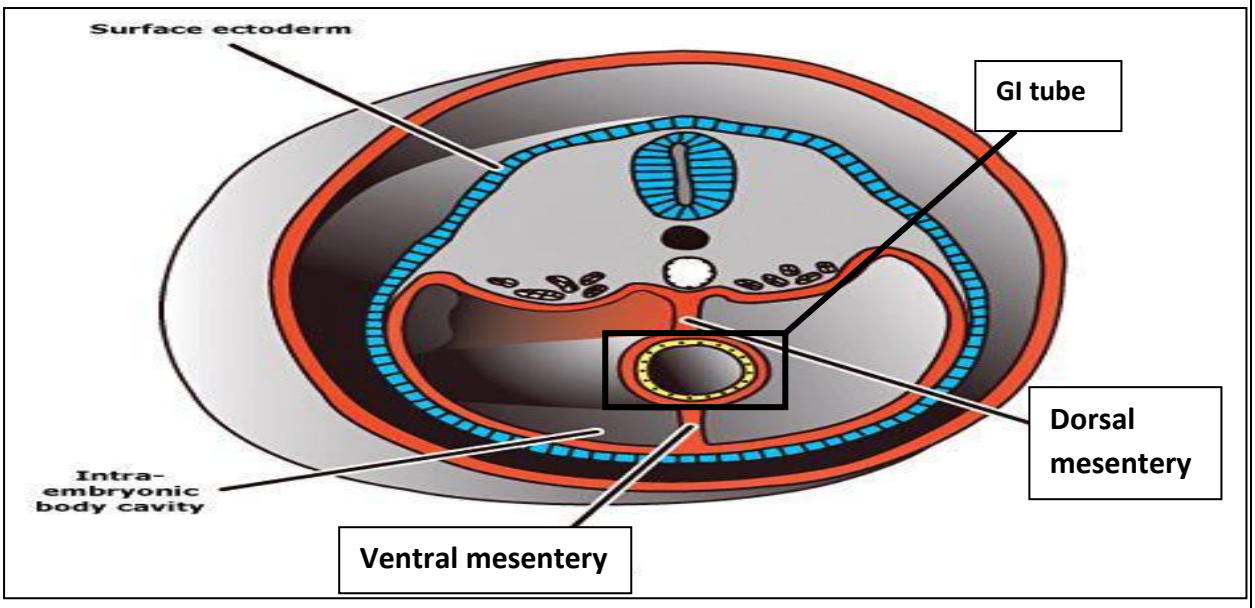
1. Endoderm, which give rise to

- Epithelial lining of GI tract.
- Organ parenchyma: hepatocytes and pancreas glands.

2. Mesoderm, which gives rise to:

- Stroma (connective tissue) of the GI glands.
- Muscles, CT tissue, and gut peritoneum.
- The spleen: the only organ that is completely formed from the mesoderm.

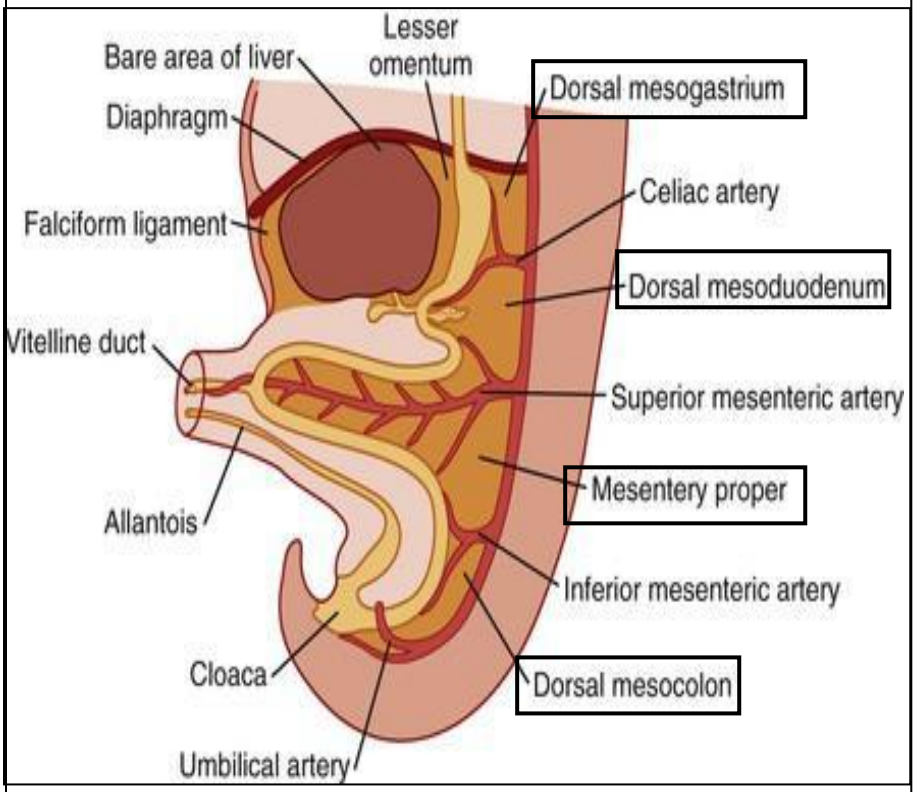
**let's look at the picture below, which is a cross section in the embryo and we look at it from the top. It shows the GI tube and the abdominal cavity. The GI tube is attached to a dorsal mesentery posteriorly and a ventral mesentery anteriorly (those mesenteries/ligaments attach the GI tract to the anterior and posterior abdominal walls)



The mesenteries are Double layer of peritoneum, they **function** in:

- Suspend the gut tube in abdominal cavity.
- Provide pathway for nerves, blood vessels, and lymphatics to pass to the organs.

- **Dorsal mesentery:** from esophagus to the lower hind gut.
- **Ventral mesentery:** esophagus to upper duodenum only. It's called septum transversum.

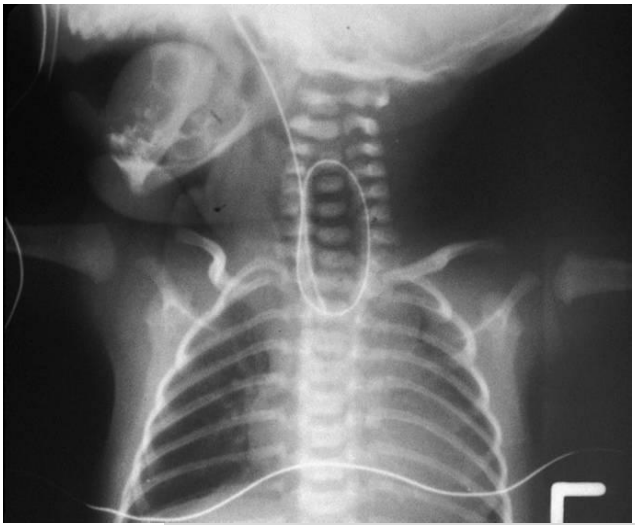


- The yellow parts resemble the GI tract, pay attention to the GI guts.
- Identify the blood vessels that supply the GIT on the picture.
- As you notice, the dorsal mesentery is subdivided relating to the organs it is related to. ex:
  - behind the stomach it's named dorsal mesogastrium
  - behind the duodenum: dorsal mesoduodenum
  - behind the small bowel: mesentery proper
  - behind the colon: dorsal mesocolon

** Clinical GI embryology

Case 1:

After delivering the baby and when the mother starts to breastfeed him, the baby starts to vomit everything even his saliva. So doctors make an X-ray for him and it appears like the picture below:

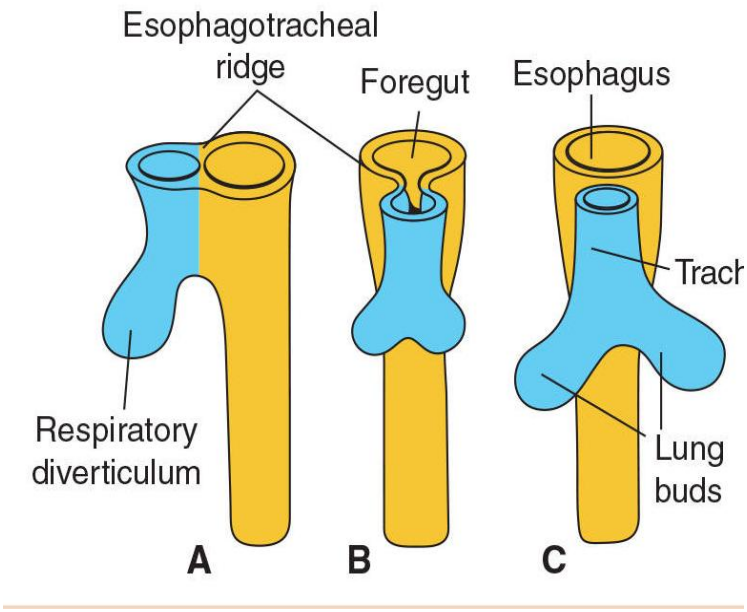


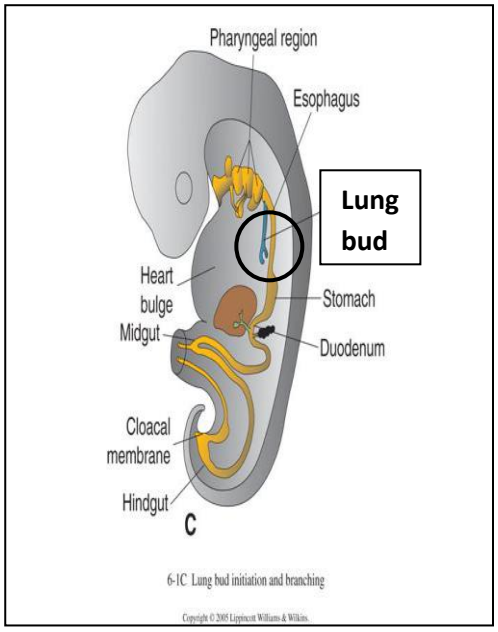
You will notice something in the baby's esophagus, this is a nasogastric tube where the doctor pushes it to the baby's esophagus through his nose and it sticks in this area circling on its self. This means that the esophagus is closed and the tube can't pass through. The same happens with milk and salvia (that's why he keeps vomiting), so this baby is diagnosed with *esophageal atresia*.

Esophageal atresia is an abnormal non-formed esophagus. This complication happens due to congenital abnormalities in the growth of the esophagus.

So let's talk about the **esophagus development**, in order to understand these abnormalities:

- When the embryo is 4 weeks (1 month) old, the respiratory diverticulum (lung bud) appears at the ventral wall of the foregut that develops later to lungs.





- The lung bud initially is in direct communication with the foregut, the two are opened to each other. Then a septum develops which is named the tracheoesophageal septum, which means that this septum will divide the foregut into:
  - The dorsal portion which is the esophagus
  - the ventral portion which is the respiratory primordium (future trachea and lungs)

  Then this septum starts narrowing until the two parts separate.

- The respiratory primordium maintains its communication with the pharynx through the laryngeal orifice.

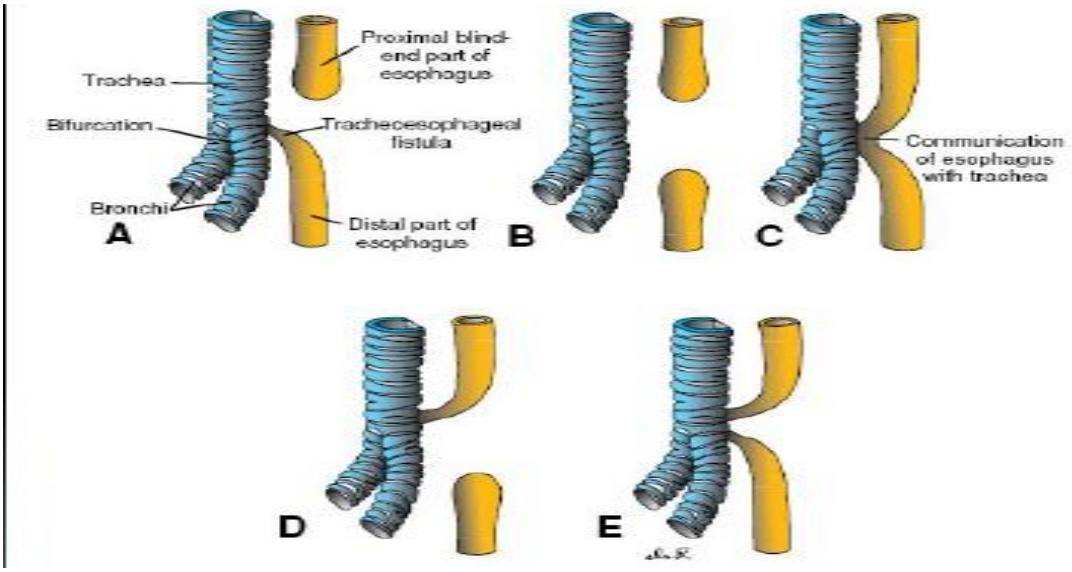
- At first the esophagus is short but with descent of the heart and lungs it lengthens rapidly.

Esophageal abnormalities:

Esophageal atresia or tracheoesophageal fistula

**so how does esophageal abnormalities develop?

- A posterior deviation of the septum may occur, leading to different types of atresia.
- Or from some mechanical factor pushing the dorsal wall of the foregut anteriorly.



10:00-20:00

**so what are the most common forms of these abnormalities (Atresia): (in the figure)

1) **A**: The most common type, where the proximal part of the esophagus ends as a blind sac and the distal part is connected to the trachea by a narrow canal (fistula) just above the bifurcation. It causes vomiting early in life (as soon as he starts breastfeeding).

2) **B:** like case 1; both ends of the esophagus are closed with no communication with the trachea.

3) **C:** *H-type fistula*, both ends are open in the trachea. Patients with this type usually don't suffer from vomiting. Rather, they suffer from aspiration leading to pneumonia.

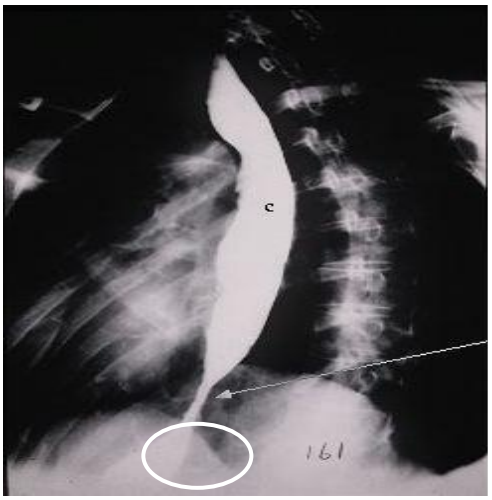
4) **B, C, D, and E**: are other types of defect in this region, they occur much less frequently.

- Atresia of the esophagus through the embryonic life prevents normal passage of amniotic fluid into the intestinal tract, this called polyhydramnios.

- Be attention that we diagnose it early in the first hour of life because the vomiting starts directly after breastfeeding.

Other causes for vomiting:

By making the patient swallow coloring material for diagnostic reasons for the esophagus like barium or gastrografin. If something is abnormal it will be detected.



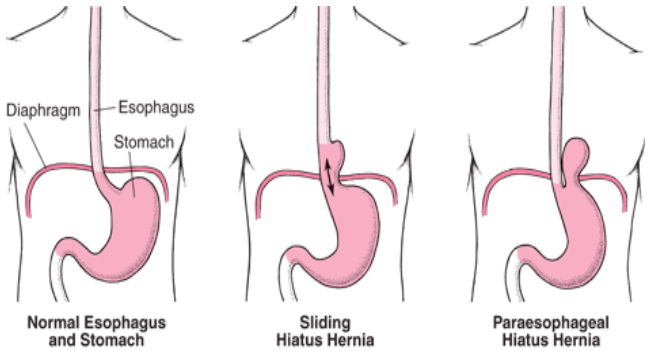
- So if the patient's image looked like this picture, it's mean that he has **esophageal stenosis**. It is an abnormality that affects the muscles of the lower esophagus causing narrowing.

- pay attention to the narrowing of the lower part of the esophagus, this may be caused by:
  1-incomplete recanalization
  2- Vascular abnormalities /accidents: compromise blood flow

Congenital hiatal hernia:

1- The esophagus fails to lengthen sufficiently.
2- The stomach is pulled up into the esophageal hiatus through the diaphragm.
It can be:

1. **Sliding hernia:** the stomach as a whole is pulled upward.
2. **Para-esophageal:** like a tube, next to the esophagus.



$$ a student asked a question: is esophagus atresia always congenital??
Most of the time it's congenital, but there is another type that occurs in the adult called secondary atresia (stricture) due to gastroesophageal reflux. It leads to fibrosis and narrowing in the third part of the esophagus leading to this complication.

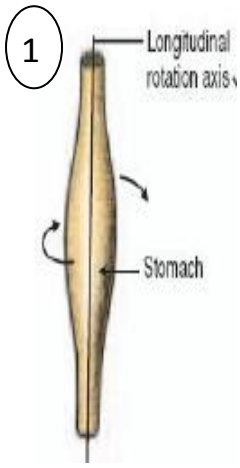
** Esophagus muscle layers:

Formed by surrounding splanchnic mesenchyme
-Upper 2/3: striated (skeletal) and innervated by the vagus nerve.
-lower third: smooth and is innervated by the splanchnic plexus.

Stomach

The stomach appears as a fusiform dilation of the foregut in the fourth week of development. During the following weeks, its appearance and position change greatly because of the different rates of growth in various region of its wall and the changes in position of surrounding organs. The positional changes of the stomach are most easily explained in the fact that it rotates around the longitudinal and anteroposterior axis.

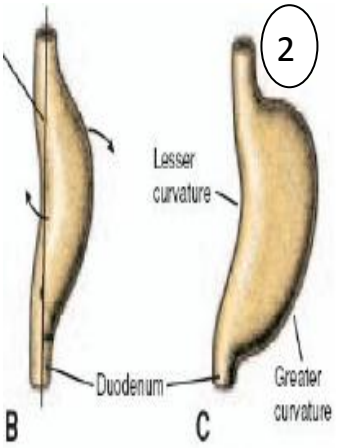
**Follow these steps:



- It rotates 90° clockwise around the axis, making its right side to face posteriorly and left anterior.

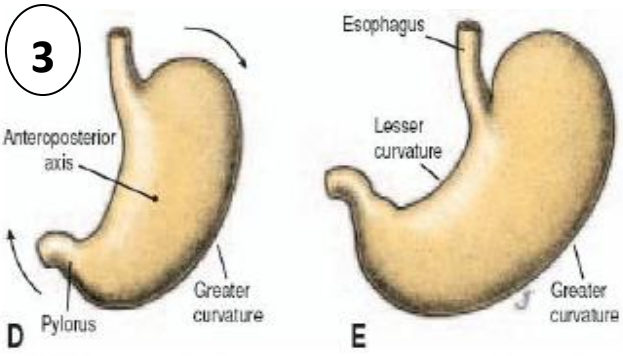
- So that makes the left vagus nerve (that was on the left side) innervate the stomach anteriorly, and the right innervate it posteriorly.

- During this rotation the original posterior wall of the stomach grows faster than the anterior portion, forming the greater and lesser curvatures.

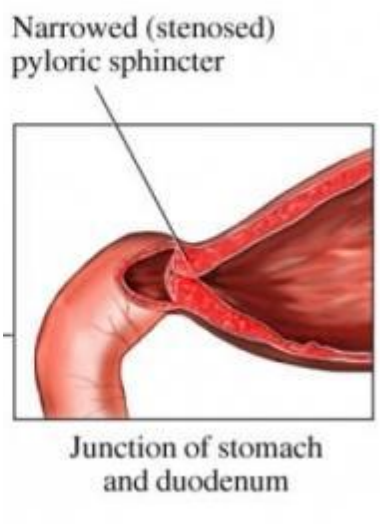


The lower part is developing faster than the upper part making the greater curvature.

And finally it completes its development



**<u>Congenital abnormalities in the stomach:</u>



-One of the most common abnormalities of the stomach in infants is **pyloric stenosis.** It occurs due to hypertrophy and thickening of the pylorus muscles, it develops during fetal life (3-6) weeks not immediately after birth.

-keep in mind that the vomiting that is characterized in this condition is non-bilious (no bile). you know that the bile open in the duodenum not the stomach.

-it's more common in boys than girls.

-treated through pyloroplasty/myotomy (surgery).

Stomach attachments

We will describe the fate of the ventral and dorsal mesenteries that we talked about and their relation with the rotation of the stomach:

Let's imagine that the mesenteries like a curtain that surround the GI tube; they move with the GI tube. The posterior abdominal wall is fixed and all the movements occur on it (acts like an axis). So the <u>dorsal mesogastrium</u> is related to the stomach on its dorsal wall (posterior), and the <u>ventral mesogastrium</u> to its ventral wall (anterior).

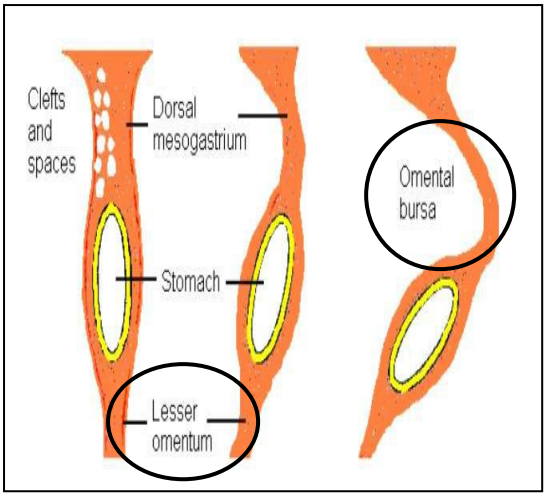
So with stomach rotation, it alters the position of these mesenteries leading to the following:

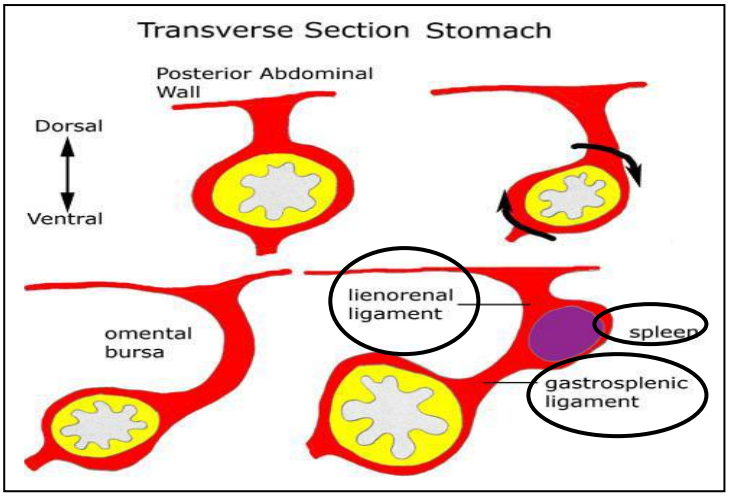
1- Rotation about the longitudinal axis pulls the dorsal mesogastrium to the left, creating a space behind the stomach called the <u>omental bursa</u> (lesser peritoneal sac).

2- The dorsal mesogastrium bulges down, it continues to grow down and forms a double-layered sac over the transverse colon and small intestinal loops called <u>greater omentum</u> (the policeman of the abdomen).

3- This rotation also pulls the ventral mesogastrium to the right and become above the stomach making the <u>lesser omentum</u>.

20:00-30:00





4- Through this rotation the formation of **the spleen** occurs:

- Spleen primordium appears in the fifth week.
- Originates from the mesenchyme (that originates from the mesoderm).
- located between the two leaves of the dorsal mesogastrium and it's an intraperitoneal structure.

5- Formation of **the pancreas** through buds/out-pouches from the gut while the stomach rotates. We will take about it at the end of the lecture.

6- The remnants of the dorsal mesogastrium posteriorly form ligaments; <u>lienorenal ligament</u> (between the left kidney and the spleen) and <u>gastrosplenic ligament</u> (between the stomach and spleen).

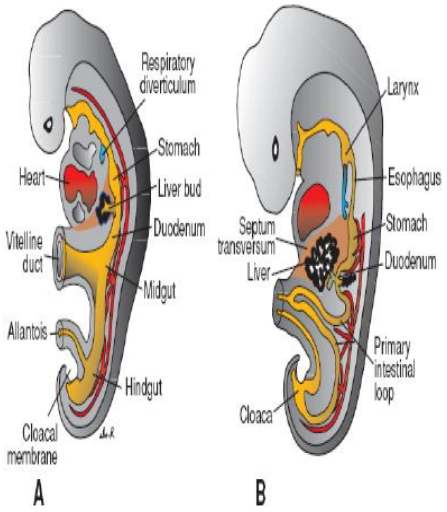
**clinical GI, Case 2:

- The baby is delivered normal, then he presented to you with yellow skin color (Jaundice) and acholic stools (colorless, not pigmented). So you as a doctor you will diagnose the baby with the congenital abnormality ***biliary atresia***. This disease is caused by the closure of the bile ducts.

Be attention: when you see acholic stools don't miss diagnose it with steatorrhea. Acholic stool is just a grey or white stool that happens due to an obstruction in the biliary duct. While the Steatorrhea is related to the consistency of the stool rather than the color; it's bulky, oily and pale due to the presence of fats. Biliary atresia may lead to steatorrhea (malabsorption of fat, you know that bile acids are needed for fat digestion).

-to understand the occurrence of this abnormality, lets discuss the development of the liver and the gallbladder.

Liver and gallbladder



-In the middle of the third week a <u>hepatic diverticulum</u> (liver bud, dorsal mesogastrium is posterior to it) appears at the ventral aspect of the foregut. This bud out grows and penetrates the septum transversum (ventral mesentery) anteriorly.

- A connection between the hepatic diverticulum and the foregut (duodenum) narrows, forming the bile duct.

- A small ventral outgrowth is formed by the bile duct to give: gallbladder and the cystic duct.

**liver parenchyma:

1- The hepatocytes originate mainly from the endoderm (hepatic bud). you know that the foregut mainly comes from the endoderm layer.

2- Blood vessels originate from the mesoderm; from septum transversum in front of it.

3- Hepatic sinusoids: combination from epithelial liver cords and umbilical veins and vitelline ducts.

4- Hematopoietic cells, Kupffer cells, and connective tissue cells are derived from mesoderm of the septum transversum.

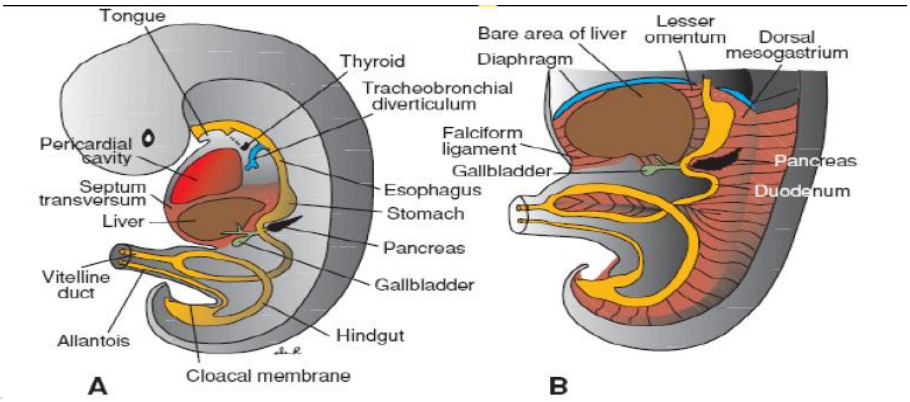
5- The hepatic bud communicates with the septum transversum forming the liver.

6- Finally the septum transversum also gives rise to:

a. Between the liver and the anterior abdominal wall it gives rise to <u>falciform ligament</u>.

b. Between the liver and foregut it gives rise to <u>lesser omentum</u>.

-don't get confused: the septum transversum is the same as ventral mesentery.



7- The free margin of the falciform ligament contains the umbilical vein. The umbilical vein is obliterated after birth to form the round ligament of the liver : Liagmentum teres hepatis.

**let's mention some information about lesser omentum that you already know:

1- The free margin of the lesser omentum connects duodenum and liver (hepatoduodenal ligament).

2-on its free margin it contains the bile duct, portal vein, and hepatic artery (portal triad).

3-This free margin forms the roof of the epiploic foramen (foramen of Winslow) which is an opening that connects the omental bursa (lesser sac) with the rest of the peritoneal cavity (greater sac).

NOTE: the septum transversum gives rise to the lesser omentum at first then the liver and finally the falciform ligament.

$$ let's go back to our case (biliary atresia). It occurs by obstruction of biliary, cystic, right and left hepatic ducts. So the bile accumulates in the liver (where it's produced) when it's highly produced with no clearance, leading to its escape to the serum. So it appears as yellow color on the skin of the patient. It causes hepatomegaly, portal hypertension….

30:00-40:00

-you know that the bile and pancreatic ducts form the ampulla of Vater and open in the 2nd part of the duodenum.

- The causes of biliary atresia are not well understood (no etiology).

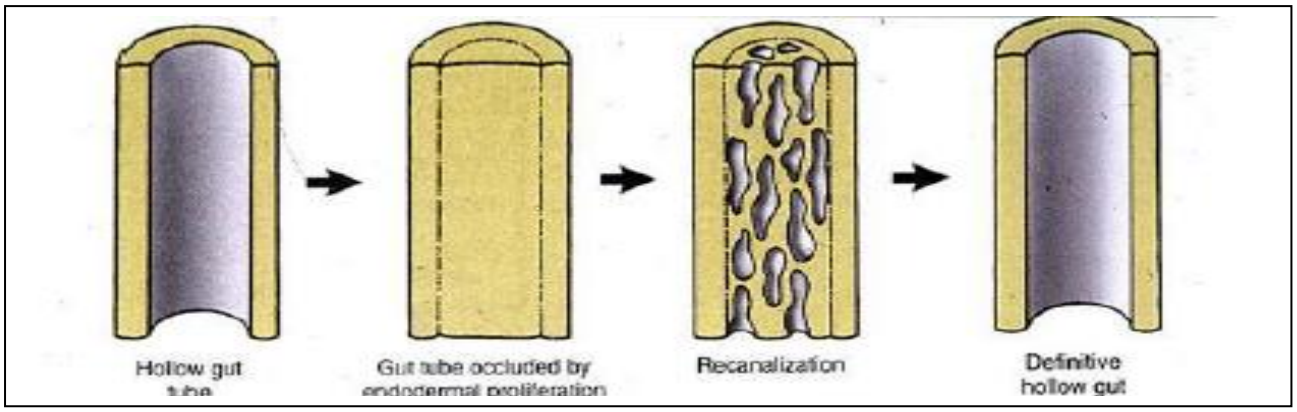
-The doctor performs a surgery to treat it. Some patient may need liver transplant.

Duodenum

-1st part is from the foregut.

-it looks like a tube, and then during the second month, the lumen of the duodenum is obliterated by proliferation of cells in its wall. Then it's recanalized shortly thereafter.

**the picture below shows this process:



-this process happens with the help of some cells, proteins and molecules.

-The duodenum originates from the terminal part of the foregut and the cephalic part of the mid gut. The junction of the two parts (terminal and cephalic) is distal to the origin of the liver bud.

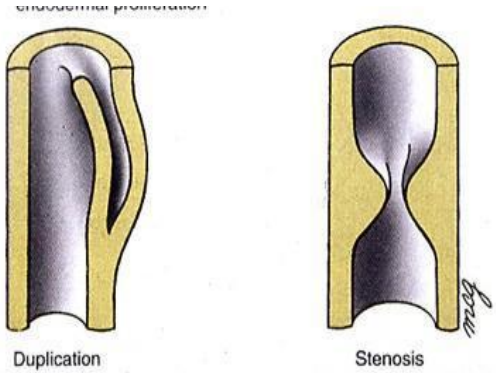
-As the stomach rotates, the duodenum takes on the form of a C-shaped loop and rotates to the right.

-Its retroperitoneal except the duodenal cap.

-amazingly this process keep repeats itself in the person, and with the same mechanical in all the populations (very regulated process).

$$ Failure to recanalize→ stenosis of the gut tube or ***duodenal atresia*** occurs:

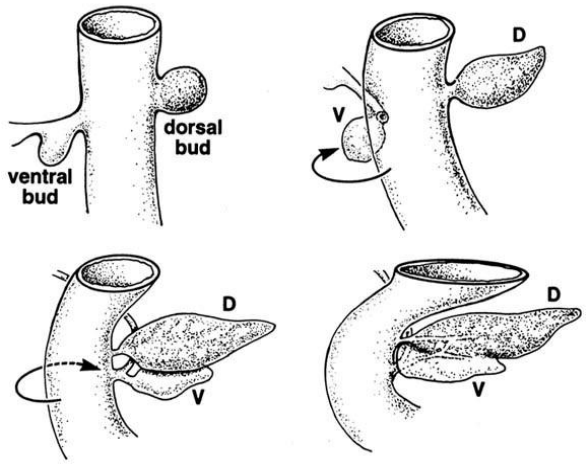
- The duodenum maybe completely closed or the lumen of it appears like a web (partial obstruction)
- One of its symptoms is **bilious vomiting**. Treatment is by surgery.

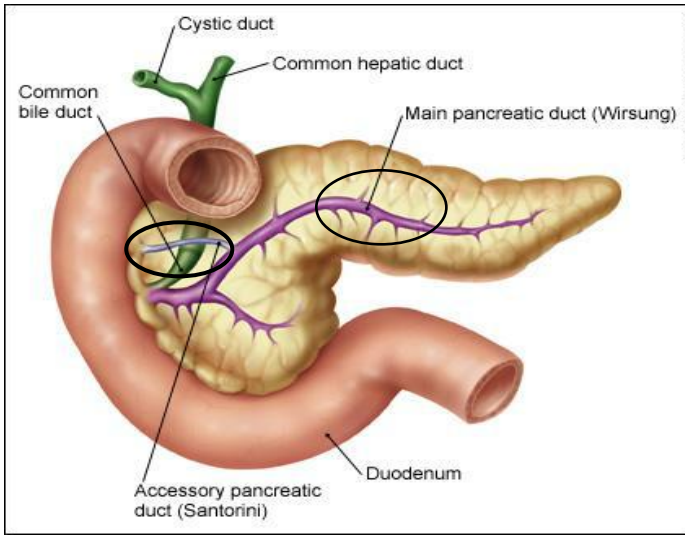


Pancreas

The pancreas is formed by two buds from the endodermal lining of the duodenum; ventral pancreatic bud (close to the bile duct) and dorsal pancreatic bud (in dorsal mesentery).

When the duodenum rotates to the right and becomes C-shaped, the ventral pancreatic bud rotates dorsally along with the bile duct, and then it fuses with the dorsal bud.





Notice that the big bud is the dorsal bud and the small one is the ventral bud.

The ventral bud forms the uncinate process and inferior part of the head of the pancreas, and the remaining part of the gland is derived from the dorsal bud.

The main pancreatic duct (of Wirsung) is formed by the distal part of the dorsal pancreatic bud and the entire ventral pancreatic bud.

The proximal part of the dorsal pancreatic bud either is obliterated or persists as a small channel, the accessory pancreatic duct (of Santorini).

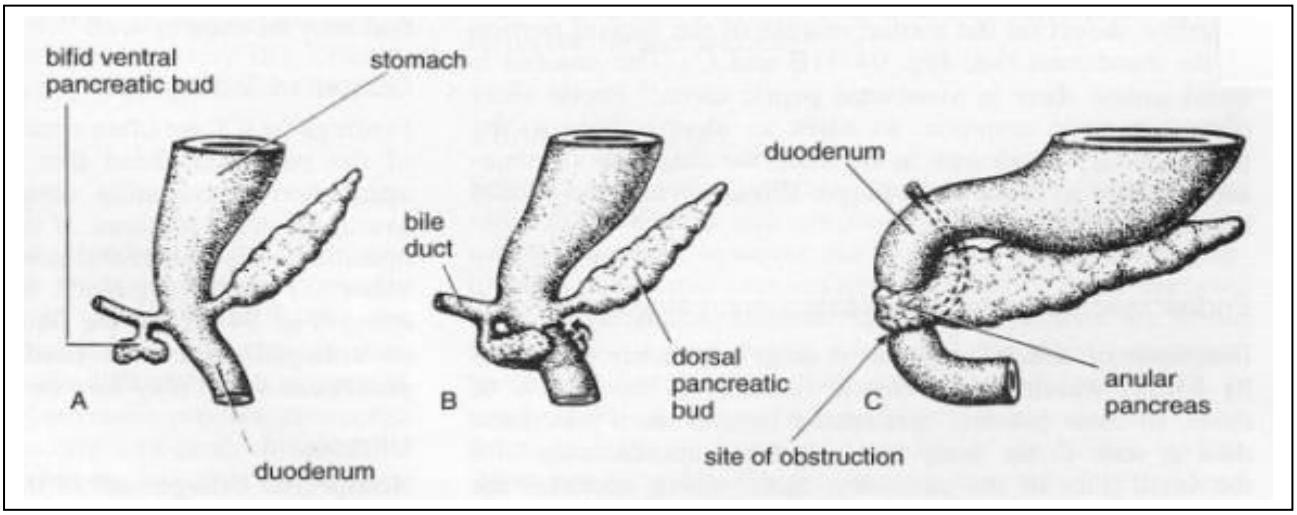
$$Pancreatic Abnormalities

Annular pancreas

-the right portion of the ventral bud migrates along its normal route, but the left migrates in the opposite direction.

-the duodenum is therefore surrounded by pancreatic tissue which constricts the duodenum and causes complete obstruction.

-One of its symptoms is the **Bilious vomiting.**



** Development of the glands

Epithelial cells proliferate to project into the underlying connective tissue.

1-EXOCRINE GLANDS

-retain their continuity with the surface via a duct.

2-ENDOCRINE GLANDS

- lose direct continuity with the surface (ducts degenerate).

- They are either arranged in cords or follicles.

** Pancreas hormones

1- **Insulin** secretion begins at approximately the fifth month.

2-**Glucagon**- and **somatostatin**-secreting cells also develop from parenchymal cells.

3-Splanchnic mesoderm surrounding the pancreatic buds forms the pancreatic connective tissue.

NOTE: there is no need to refer to the slides I wrote all the information, please try to watch the video that is uploaded on the website, it's really helpful.