يسم الله الرحمن الرحيم



# FINAL | Lecture 2 GI Embryology (أَمَنْنَاكُمْ الْمَنَاكُمُ الْمَنْكَكُمُ الْمَنْكَكُمُ الْمَنْكَكُمُ الْمَنْكَكُمُ الْمَنْكَكُمُ الْمُتَعَالَقُوا الْمَنْكَكُمُ اللَّهُ اللَّهُ الْمُتَعَالَقُوا الْمُنْكَكُمُ اللَّهُ الْمُ اللَّهُ اللَّهُ اللَّهُ اللَّهُ اللَّهُ الْمُ الْمُولُا الْحُلْلُكُولُ الْمُ الْحُلُولُ الْحُلْمُ الْمُ الْحُلُلُلُلُلُلُلُلُلُلُلُلُلُولُ الْمُ الْمُ الْمُ الْمُ الْمُ الْمُ الْمُ لَالْمُ لَلْمُ لَلْمُ الْمُ لَالْمُ الْمُ لَلْمُ لَلْمُ لَالْمُ لَلْحُلُلُ لَالْلُ لَالْلُلُلُ لَالْلُلُلُ لَالْلُلُلْلُ الْلُلْلُلُلُ الْمُ لَلْلُلُلُ لُلُ

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EMBRYOLOGY

**Reviewed by:** Sara Masadeh



# Some parts of the lecture is supported with external short animations, whenever you see the logo of <u>Osmosis.org</u>, click on it . (Unsponsored) GI empryology 2

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# 1-The normal development of the esophagus

Recall that we ended the last lecture by lung budding from the foregut; hence, we can say that the respiratory system arises from the gastrointestinal tract.

- ✓ As we know, the foregut includes the esophagus, the stomach, and the duodenum down to the major duodenal papilla.
- ✓ The picture A shows a ridge between esophagus and trachea.
- $\checkmark\,$  In picture B , tracheoesophageal septum begins to form.
- ✓ In picture c, the trachea and the esophagus are fully separated.
- However, abnormalities during the esophagus development can occur, resulting in many conditions which will be discussed in the next slide including: Esophageal atresia +/ - tracheoesophageal fistula, Hiatal hernia, stenosis.



**FIGURE 15.6** Successive stages in development of the respiratory diverticulum and esophagus through partitioning of the foregut. **A.** At the end of the third week (lateral view). **B,C.** During the fourth week (ventral view).

Check me! OSMOSIS.org 2:10->3:00 3

- ✓ If the tracheoesophageal septum fails to separate, the fetus will develop esophageal abnormalities, which can manifest as atresia (an uncanalized tube=a blind-ended sac), fistula (a connection between the esophagus and the respiratory tract-most common at the site of trachea bifurcation ), or both.
- A) **Proximal** Esophageal **Atresia** with **distal** Tracheoesophageal **Fistula** occurs in 90% of cases (most common).\*
- B) Double Blind end sac both **proximal and distal** esophageal **atresia** (no communication, no fistula) (in 4% of the cases).
- C) H-shaped fistula, Fistula only a communication between the trachea and esophagus without atresia. (In 4% of the cases) \**Editor's Note: We know that the doc*



\*Editor's Note: We know that the doctor mentioned the case A to be only in 4% of the cases in the recorded lecture on JU medicine ; however, this year's lecture in sections other than the one in which it was recorded, the textbook, as well as the last year's modified says it's as common as 90%, so don't worry, the editor has got your back!

أحمديثه

D) Distal atresia with proximal fistula. (In 1% of the cases)E) Double fistula with no atresia. (In 1% of the cases)



Figure 13.7 Variations of esophageal atresia and/or tracheoesophageal fistula in order of their frequency of appearance: A, 90%; B, 4%; C, 4%; D, 1%; and E, 1%.

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 The clinical consequences of esophageal abnormalities: we will take case A in which there is a proximal atresia and distal fistula (the most common case scenario): Soon after birth you can notice (postnatal manifestations):
 1) During breastfeeding, instead of swallowing the milk into its normal route from the mouth to the stomach passing through the esophagus, the swallowed milk will face a dead end where the esophagus is closed (blind end pouch = proximal atresia), so what goes in, comes back out into the mouth.

2) As a result of the **fistula**, air enters the stomach, so every time the baby cries, the baby's belly **becomes bloated as the stomach is filled** with air.

3) The **fistula** may also cause **gastric contents regurgitation into the lungs** causing acute **pneumonia** which can develop into chronic pneumonia if left untreated.

Extra figure

- ✓ You may ask yourself: Can't we detect this congenital abnormality before birth? The answer is yes, we absolutely can.(Prenatal manifestation) During routine fetal development checks, the obstetrician measures the amount of amniotic fluid in the amniotic sac surrounding the fetus. The fetus urinates into the amniotic fluid, swallows it, and then urinates again into the amniotic fluid creating a continuous cycle. The level of amniotic fluid should remain within a normal range. If the amount increases beyond normal, the condition is called **polyhydramnios**. 4)One of the causes of polyhydramnios is proximal esophageal atresia with distal tracheoesophageal fistula, in which the total pool of the amniotic fluid is in the amniotic sac (unlike in normal cases in which the fluid is divided between the amniotic sac and the fetus ).
- ✓ Treatment: surgical correction after birth of the esophageal abnormality as soon as possible.

- ✓ Since the esophagus is a narrow tube that descends downward toward the stomach as a result of the crowding in the chest cavity that contains the pericardium, the heart, and the lungs, all of these structures applies pressure on the esophagus, pushing it downward further and causing the esophagus to elongate downward into the abdomen.
- ✓ Sometimes stenosis occurs, especially in the lower third of the esophagus (abdominal esophagus) where it perforates the diaphragm in its way to the stomach , so when the patient eats, most of the food is regurgitated and only a small fraction reaches the stomach, fortunately, a minor outpatient procedure can be applied to relieve (dilate) the stenosed area.



- ✓ The third esophageal abnormality is the congenital hiatal hernia.
- $\checkmark$  The hiatal hernia can be either classified as :
- 1) Sliding hiatal hernia (a portion of the stomach protrudes upward through the diaphragm (through the esophageal hiatus).
- 2) Paraesophageal hiatal hernia which involves the upper part of the stomach bulging alongside -parallel to - the esophagus.



# **3- Stomach Embryogenesis**

- ✓ The stomach is considered a fusiform\* shaped with proximal and distal openings in the early embryonic stages.
- ✓ To ease the learning process, we will study the transformation of the fusiform stomach to the mature one (the stomach which has 2 surfaces, 2 boarders and 2 curvatures) around 2 axes, a vertical axis (crosses the 2 openings of the fusiform) and an anteroposterior axis.
- ✓ During the following weeks, its appearance and position change greatly as a result of the different rates of growth in various regions of its wall and the changes in position of surrounding organs.

\* The term "fusiform" describes something shaped like a spindle, meaning wide in the middle and tapering towards the ends



Figure 13.8 A, B, and C. Rotation of the stomach along its longitudinal axis as seen anteriorly. D and E. Rotation of the stomach around the anteroposterior axis. Note the change in position of the pylorus and cardia.

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# **3- Stomach Embryogenesis**

- ✓ During the stomach development, 90 degrees clockwise rotation occurs around the longitudinal axis, this causes the original left side becomes anterior and the right side becomes posterior.
- ✓ As a result, the left vagus nerve will innervate the anterior wall of the stomach and the right vagus nerve will innervate the posterior wall.
- ✓ The posterior surface (which will shift to the left after the rotation) exhibits rapid growth in contrast to the anterior one, forming the greater curvature, while the slower growing anterior side (which will shift to the right ) forms the lesser curvature.



## **3- Stomach Embryogenesis**

- ✓ The cephalic (cardiac portion) and caudal (pyloric portion) ends of the stomach are originally located in the midline (both are crossed by the longitudinal axis in the fusiform stage).
- ✓ However, during development, the stomach rotates around anteroposterior axis such that the cardiac part moves downward and to the left while the pyloric part moves upward and to the right, decreasing the distance between the two ends .



### **4-Stomach Abnormalities**

Pyloric stenosis (pyloric hypertrophy)

 occurs when there is a thickening of the inner layer of
 the smooth muscle of the pyloric sphincter causing it to
 close. As a result, the baby experiences projectile
 vomiting (vomiting with force), fortunately, it can be
 surgically corrected.



# 5- The dorsal and Ventral Mesentery

- ✓ Initially the foregut, midgut, and hindgut are in broad contact with the mesenchyme of the posterior abdominal wall .
- ✓ By the fifth week however, the connecting tissue bridge has narrowed, and the caudal part of the foregut, the midgut, and a major part of the hindgut are suspended from the abdominal wall by the dorsal mesentery the dorsal mesentery extends from the lower end of the esophagus to the cloacal region of the hindgut.
- ✓ In the region of the stomach it forms the dorsal mesogastrium or greater omentum; in the region of the duodenum it forms the dorsal mesoduodenum; and in the region of the colon it forms the dorsal mesocolon.



**FIGURE 15.12 A.** Derivatives of the dorsal mesentery at the end of the third month. The dorsal mesogastrium bulges out on the left side of the stomach, where it forms part of the border of the omental bursa. **B.** The greater omentum hangs down from the greater curvature of the stomach in front of the transverse colon.

# 5- The dorsal and <u>Ventral</u> Mesentery

- Ventral mesentery, which includes the lesser omentum (including the hepatodoudenal and hepatogastric ligaments) as well as other liver ligaments (falciform ligament, coronary ligaments as well as the triangular ligaments of the liver) forms from the ventral mesogastrium, which itself is derived from mesoderm of the septum transversum.
- Notice that all the ligaments of the liver arises from the ventral mesogastrium, except ligamentum teres which results from the obliteration of the umbilical vein.



# 6- Mesogastrium Formation

- ✓ The stomach is attached **posteriorly** to the dorsal body wall by the **dorsal mesogastrium** and **anteriorly** to the ventral body wall by the **ventral mesogastrium** (in the fusiform stage).
- ✓ Rotation around the longitudinal axis pulls the dorsal mesogastrium to the left (12 to 3 o'clock rotation), creating a space behind the stomach called the omental bursa (lesser peritoneal sac).
- $\checkmark$  This rotation also pulls the ventral mesogastrium to the right (6 to 9 o'clock rotation).



**FIGURE 15.9 A.** Transverse section through a 4-week embryo showing intercellular clefts appearing in the dorsal mesogastrium. **B,C.** The clefts have fused, and the omental bursa is formed as an extension of the right side of the intraembryonic cavity behind the stomach.



**FIGURE 15.10 A.** The positions of the spleen, stomach, and pancreas at the end of the fifth week. Note the position of the spleen and pancreas in the dorsal mesogastrium. **B.** Position of spleen and stomach at the 11th week. Note formation of the omental bursa [lesser peritoneal sac].

✓ As we see in the picture, when the stomach rotates, the lesser sac is formed behind the stomach.

# 6- Mesogastrium Formation

- ✓ The dorsal mesogastrium lengthens to the left, forming:
  - 1) The spleen.
  - 2) Gastrosplenic (Gastrolienal) ligament.
  - 3) Lienoranal ligament.



**FIGURE 15.11** Transverse sections through the region of the stomach, liver, and spleen, showing formation of the omental bursa (lesser peritoneal sac), rotation of the stomach, and position of the spleen and tail of the pancreas between the two leaves of the dorsal mesogastrium. With further development, the pancreas attaches to the posterior body wall.



## 7-Some notes regarding the 3 germ layers

- ✓ An intraembryonic mesoderm on each side of the midline differentiates into a paraxial portion, an intermediate portion, and a lateral plate.
- ✓ When intercellular clefts appear in the lateral mesoderm, the plates are divided into two layers: the somatic mesoderm layer which forms the parietal peritoneum and the splanchnic mesoderm layer which forms the visceral layer of the peritoneum, the latter is continuous with mesoderm of the wall of the yolk sac.
- ✓ As illustrated in the image, the peritoneal cavity is initially open and later it closes.





\*Editor's Note 2: This slide is not directly related to the scope of our lecture

# **8**-Liver Development

- ✓ In embryology, the **duodenum** is divided into upper and lower halves:
- The **upper** half is derived from the **foregut**
- The lower half originates from the midgut
- ✓ Liver bud (hepatic diverticulum):
- Originates as an outgrowth of **endodermal epithelium** of the duodenum.
- Appears at the **junction** between the **upper** and **lower** halves of the **duodenum**.
- This outgrowth consists of **rapidly proliferating cells** that penetrate the **septum transversum** (which is a mesenchymal mesoderm), lies between the **pericardial** and the **yolk sac** (the liver forms inside the septum transversum).



### **8**-Liver Development

#### Do you remember this slide from V0?

- ✓ The doctor explained the parenchyma formation of the liver as follows : "The parenchyma of the liver, which is derived from the mesenchyme of the septum transversum, forms the hepatocytes, the blood sinusoids, capsule of the liver as well as Kupffer cells (with connective tissue origin)."
- \*However, directly quoting from the Langman's Medical Embryology textbook :

   "Endoderm forms the epithelial lining of the digestive tract and gives rise to the specific cells (the parenchyma) of glands, such as hepatocytes and the exocrine and endocrine cells of the pancreas." Page 231, chapter 15, 14th edition.

2) "Hematopoietic cells, Kupffer cells, and connective tissue cells are derived from mesoderm of the septum transversum." Page 241, chapter 15, 14th edition.

✓ The umbilical vessels (arteries and veins) together with the vitelline vessels contribute to the formation of the blood sinusoids

\*Editor's Note 3: We will check the embryonic origins and the details of this portion of the lecture from the doctor and inform you with the results in V1 inshallah.

Good to know: One of the embryology past papers questions indicates that the liver develops from all of the following: endoderm of the gut, umbilical vein sinuses, vitelline venous sinuses as well as septum transversum.

Editor's Note: After emailing the doctor about this confusion regarding the embryonic development of the liver tissue, he replied by: "All originated from the mesenchyme of septum (including Kupffer cells and connective tissue) except the hepatocytes endodermal in origin". Without any further explanation. (5:20->6:45)

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# 9 - Gallbladder Development

#### Bile duct development:

- ✓ While hepatic cells continue to penetrate the septum, the connection between the hepatic diverticulum and the foregut (duodenum) narrows, forming the bile duct .
- ✓ The liver is a **mixed** gland, its **exocrine** part includes the **bile duct**.
- ✓ The first to develop is the common bile duct, which initially forms as a solid column of proliferating cells and later goes through canalization.
- ✓ As it extends into the developing liver tissue, it gives rise to the hepatic ducts..
- From the **right hepatic duct**: cell proliferation forms the cystic duct.
- At the end of the cystic duct: the wall of the gallbladder begins to develop.



Extra figure

# **10-Liver and Gallbladder Abnormalities**

- ✓ Liver and gallbladder, like any other organ, can exhibit congenital abnormalities, including:
  - 1) Accessory hepatic duct. (Usually asymptomatic)
  - 2) Duplication of the gallbladder (B).(Usually asymptomatic)
  - 3) Extrahepatic biliary atresia (blind end --> closed biliary duct lumen --> we have to open it to enable the bile to reach its destination). (Happens because of failure of duct recanalization after its solid stage)
  - 4) Intrahepatic biliary duct atresia (requires treatment ).



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Figure 13.20 A. Obliteration of the bile duct resulting in distention of the gallbladder and hepatic ducts distal to the obliteration. B. Duplication of the gallbladder.

✓ Treatment: If there are no complications associated with the abnormality, the patient doesn't require any intervention, and the condition is left as it is. However, if complications present, like stenosis of the duct (which results in a decrease in the amount of bile "bile insufficiency"), here intervention must be done to treat the underlying problem.

## **10-Liver and Gallbladder Abnormalities**

✓ Notice in the image how the rotation facilitates the common bile duct to reach its anatomical position (posteromedial to the second part of the duodenum). It rotates behind the duodenum deep to the pancreas, then it opens.



Enjoy the illustration of the accessory hepatic duct *Extra figure* 



### **11-Duodenum Development**

- ✓ The duodenum lies distal to the stomach . Initially, the stomach is fusiform in shape, while the duodenum is an elongated duct (finger-like shape). As the stomach rotates to the right in a clockwise direction , the duodenum rotates along with it correspondingly to the right . the dorsal mesogastrium pulls the duodenum backwards and to the left, resulting in the concavity (its C- shaped loop) of the duodenum facing left.
- ✓ During this rotation, the common bile duct, which originally lies to the right of the duodenum, also shifts and comes to lie on the left side of the duodenum.



**FIGURE 15.17** Transverse sections through the region of the duodenum at various stages of development. At first, the duodenum and head of the pancreas are located in the median plane **(A)**, but later, they swing to the right and become attached to the posterior abdominal wall **(B)**.

### **11-Duodenum Development**

- ✓ The dorsal mesogastrium that moves the duodenum is composed of two layers : anterior and posterior .
- ✓ The posterior layer disappears, while the anterior layer covers the anterior surface of the duodenum and the pancreas, thus making the duodenum and pancreas retroperitoneal organs. They rest on the posterior abdominal wall with no peritoneum behind them.
- ✓ However, the first and last inches of the duodenum remain intraperitoneal. The first inch, located immediately after the pylorus, is called the 'duodenal cap' and is completely covered by peritoneum.



**FIGURE 15.17** Transverse sections through the region of the duodenum at various stages of development. At first, the duodenum and head of the pancreas are located in the median plane **(A)**, but later, they swing to the right and become attached to the posterior abdominal wall **(B)**.

### **12-Duodenal Abnormalities**



**FIGURE 15.18** Upper portion of the duodenum showing the solid stage **(A)** and cavity formation **(B)** produced by recanalization.

✓ In a similar fashion of biliary duct development, the development of the duodenum starts with the proliferation of cells, leading to temporary complete closure of its lumen. Then, the proliferated cells are absorbed, leading to the recanalization of the duodenum and the formation of a clear lumen.

✓ One of the abnormalities in the duodenum is its obliteration, where it becomes filled with proliferated cells (failure of recanalization). This causes an obstruction, preventing food from passing through, so surgical correction is needed to reopen the passage.

# **13-Pancreas Development**

The pancreas develops from two buds: the dorsal and the ventral pancreatic buds.
 The ventral bud is initially located below the common bile duct (Fig 15.19). As the stomach and duodenum rotate clockwise, the ventral bud rotates posteriorly and clockwise, shifting to lie below the dorsal bud (Fig 15.20).

- Recall the shifting position of the opening of the **common bile duct** (both **the ventral bud** as well as the bile duct shift in a similar manner).





**FIGURE 15.19** Stages in development of the pancreas. **A.** 30 days (approximately 5 mm). **B.** 35 days (approximately 7 mm). Initially, the ventral pancreatic bud lies close to the liver bud, but later, it moves posteriorly around the duodenum toward the dorsal pancreatic bud.

**FIGURE 15.20 A.** Pancreas during the sixth week of development. The ventral pancreatic bud is in close contact with the dorsal pancreatic bud. **B.** Fusion of the pancreatic ducts. The main pancreatic duct enters the duodenum in combination with the bile duct at the major papilla. The accessory pancreatic duct (when present) enters the duodenum at the minor papilla.

# **13-Pancreas Development**

#### ✓ The ventral bud forms:

- 1) The inferior part (the lower half) of the head of the pancreas.
- 2) The uncinate process.

#### ✓ The dorsal bud forms:

- 1) The remaining part of the pancreas (most of the pancreas is formed by **the dorsal bud**).
- ✓ Formation of **the pancreatic ducts**:

-The main pancreatic duct (of Wirsung) is formed by the distal part of <u>the dorsal</u> <u>pancreatic duct</u> and the entire <u>ventral pancreatic duct</u>.

-The proximal part of <u>the dorsal pancreatic duct</u> either is obliterated or persists as a small channel, the accessory pancreatic duct (of Santorini).



الله أكبر

# **13-Pancreas Development**

✓ The **parenchyma** of the pancreas :

The pancreas is a **mixed** gland; the **endocrine** part is the **pancreatic islets** (of **Langerhans**), which are cells present in the pancreatic tissue and are able to **proliferate**.

- ✓ Insulin secretion begins at approximately the fifth month (of gestation).
- ✓ Glucagon- and somatostatin-secreting cells also develop from parenchymal cells.
- ✓ Splanchnic mesoderm surrounding the pancreatic buds forms the pancreatic connective tissue.

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# **14-Pancreatic Abnormalities**

- ✓ One of the abnormalities of the pancreas is 1)ectopic pancreas (Accessory pancreatic tissue), which refers to the presence of pancreatic tissue in locations other than its normal site.
- A more serious abnormality is 2)annular pancreas, in which the ventral pancreatic bud abnormally rotates around the duodenum and obstructs it, leading to duodenal blockage (complete obstruction) instead of moving to its normal position below the dorsal bud, in this case, surgical intervention must be done.

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**FIGURE 15.23** Annular pancreas. The ventral pancreas splits and forms a ring around the duodenum, occasionally resulting in duodenal stenosis.





# For any feedback, scan the code or click on it.

#### Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	11	Shifting to the Right and left were opposed	Corrected
	15	ligamentum trees	ligamentum teres
	20	The liver development	The indicated information was checked from the doctor
	4+5	Case E is said to be known as the H-shaped fistula.	Case C is the H-shaped fistula (Based on scientific references, modified slides of the previous batches + approved by Dr Al-Muhtaseb)
V1 → V2			

رسالة من الفريق العلمي:

#### Reference Used:

- 1. Langman's Medical embryology, Fourteenth Edition
- 2. Nutter's Atlas for Embryology

إِنَّ الله تعالى يُحِبُّ إذا عمِلَ أحدُكم عملًا أَنْ يُتقِنَهُ الراوي : عائشة أم المؤمنين | المحدث : الألباني | المصدر : صحيح الجامع

> ذو العَقلِ يَشقى في النّعيم بعَقلِهِ وَأَخُو الْجَهَالَةِ فِي الْشَقَاوَةِ يَنْعَمُ وَ الناسُ قَد نَبَذو ا الْحِفاظَ فَمُطْلَقٌ يَنسى الّذي يولى وَعافٍ يَندَمُ لا بَخدَعَنَّكَ مِن عَدُق دَمعُهُ وَارِحَم شَبابَكَ مِن عَدُقٍ تَرِحَمُ لا يَسلَمُ الشَرَفُ الرَفيعُ مِنَ الأَذي حَتّى يُراقَ عَلى جَوانِبهِ الدَمُ يُؤذى القَليلُ مِنَ اللِئام بطبعهِ مَن لا يَقِلُ كَما يَقِلُ وَيَلُؤُمُ الظُلمُ مِن شِيَم النُفوسِ فَإِن تَجِد ذا عِفَّة فَلِعِلَّةٍ لا يَظْلِمُ