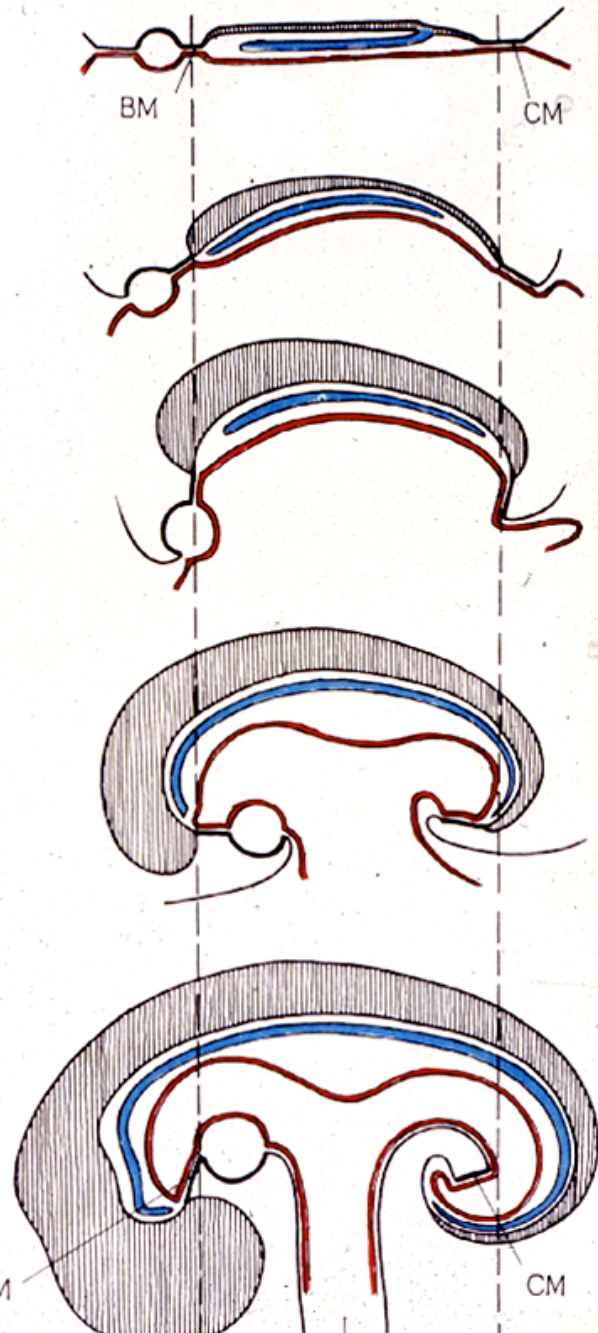




**Entodermal
derivatives: formation
of the gut, liver, and
pancreas**

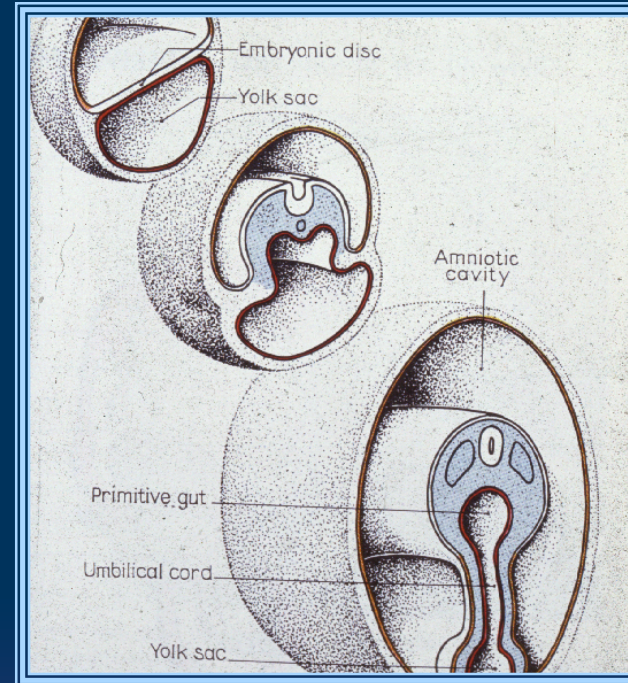
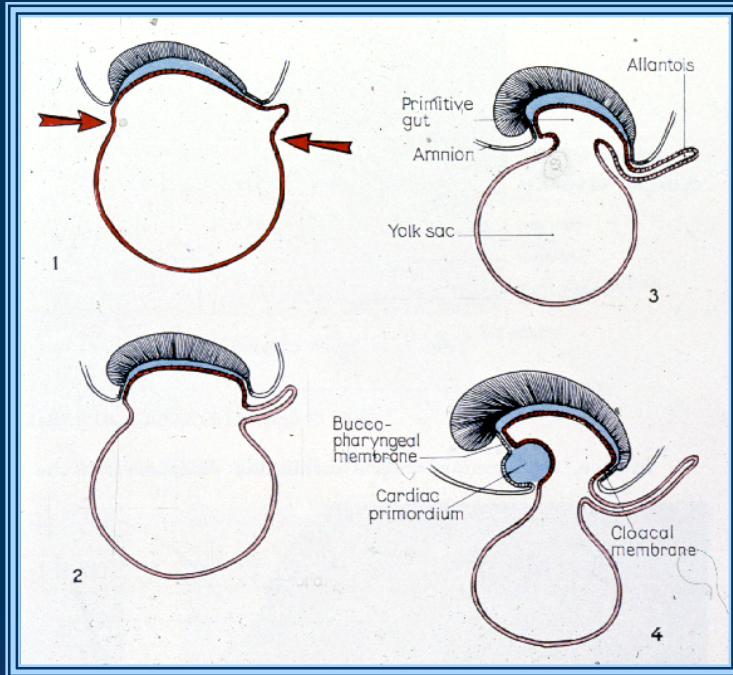
Mike Gershon

Folding forms the gut



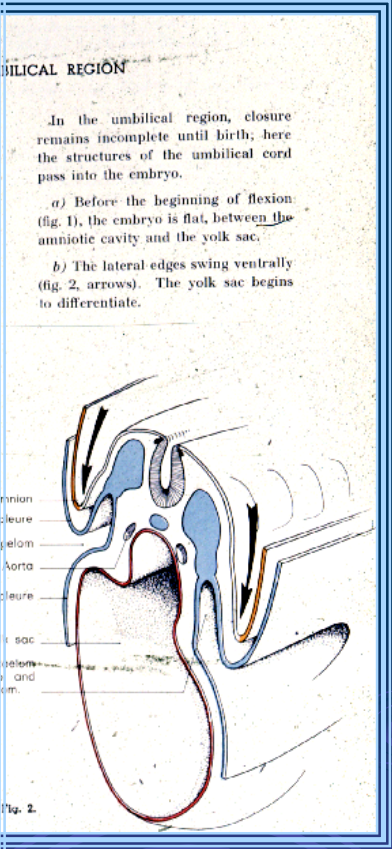
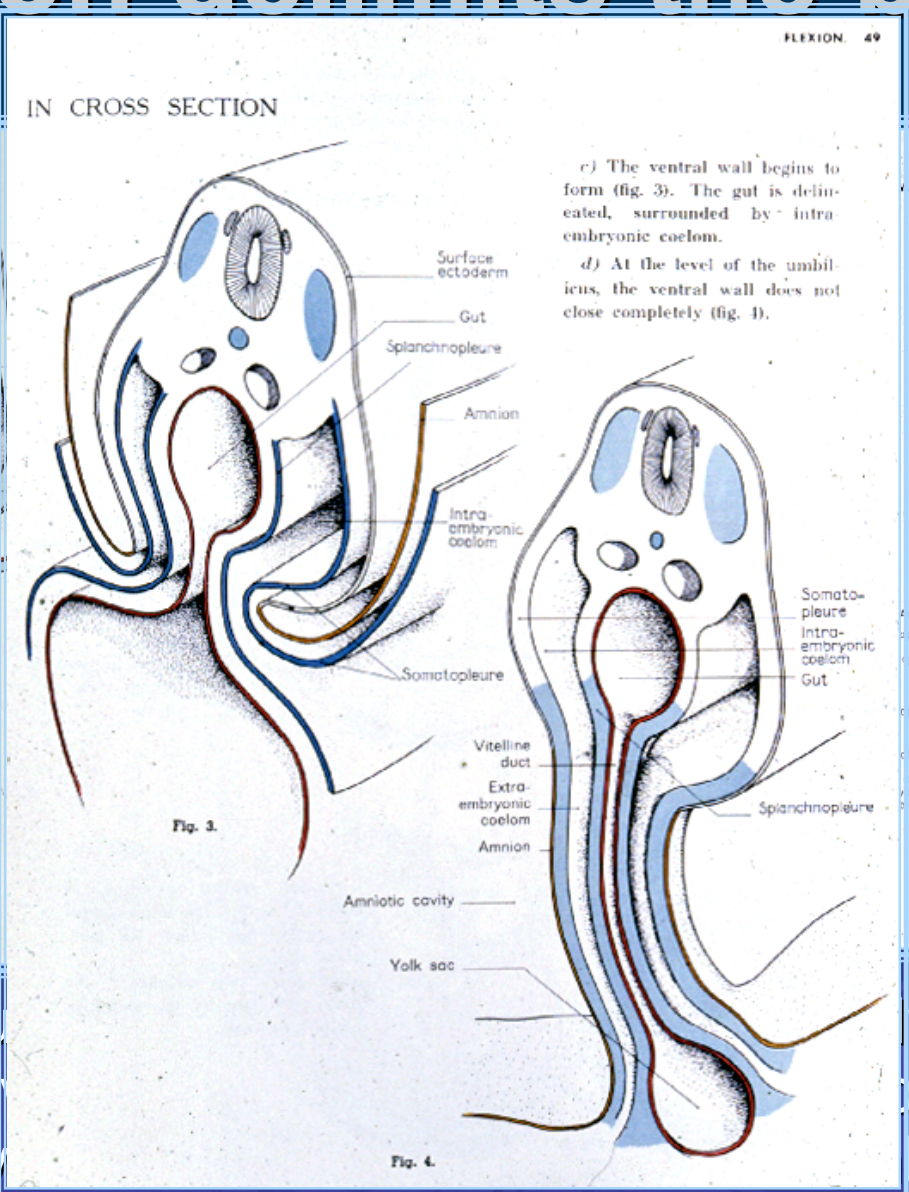
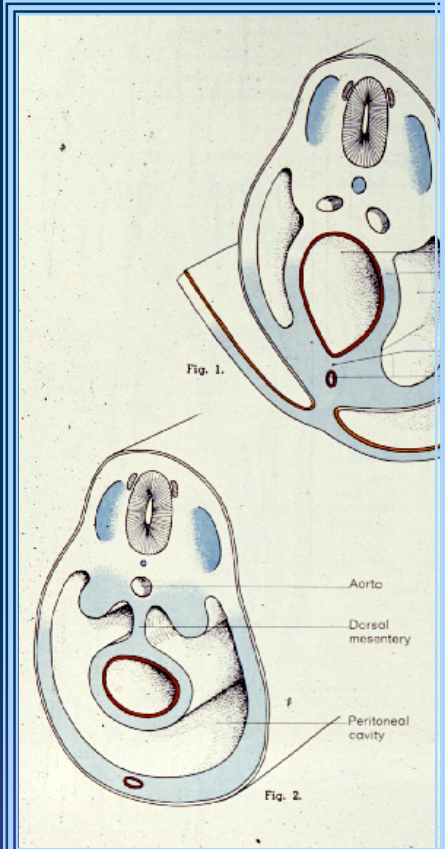
- Primitive gut extends from buccopharyngeal to cloacal membrane.
 - Move toward each other
- Cardiogenic mesenchyme is originally rostral, but folding brings it caudal to buccal membrane.
- Foregut and hindgut become recognizable
- Portion of yolk sac is incorporated into the embryo as bowel.
- Midgut remains open.

Cephalocaudal and lateral folding occur simultaneously



- Meeting and fusion of cranial, lateral, and caudal edges of the embryo create the primordial foregut and hindgut
 - Slow fusion of midgut-due to presence of yolk sac. Midgut remains open until week 6-connects to yolk sac via *vitelline duct*.
 - Buccopharyngeal membrane opens at 4 and cloacal membrane at 7 weeks

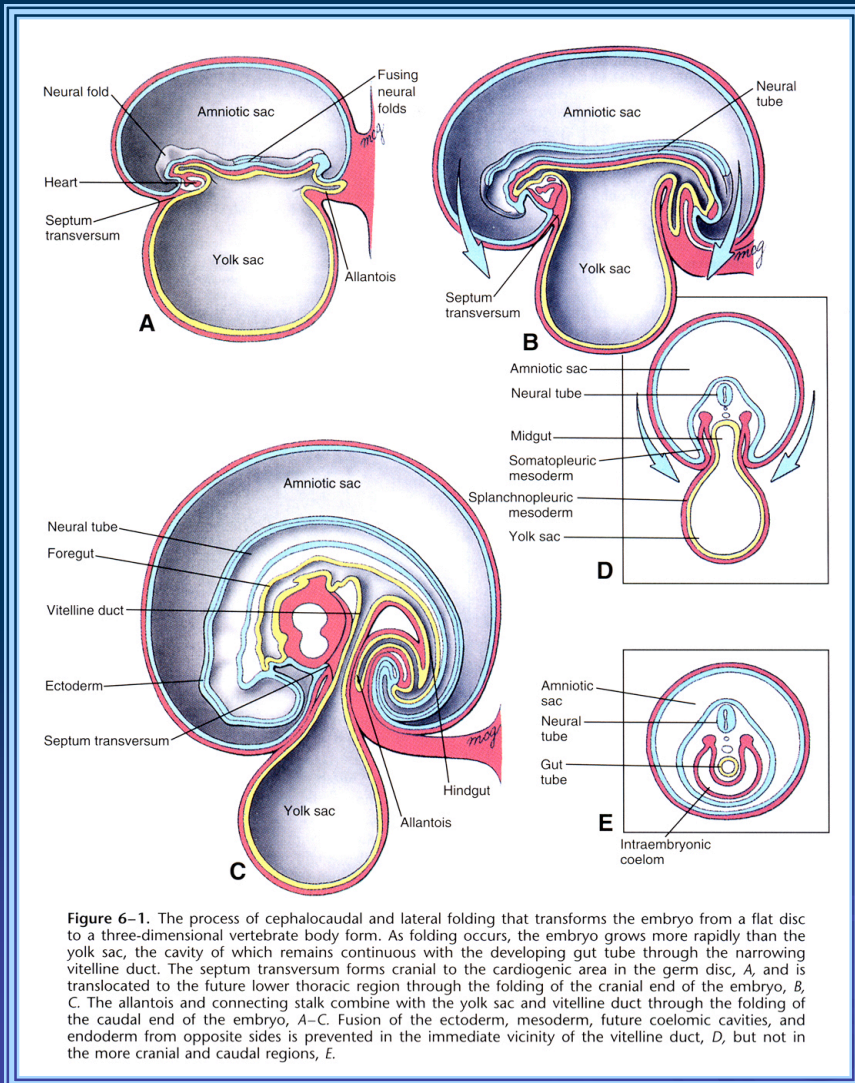
Flexion delimits the bowel



➤ After the gut is formed, the dorsal and ventral regions of the embryo are delimited by the

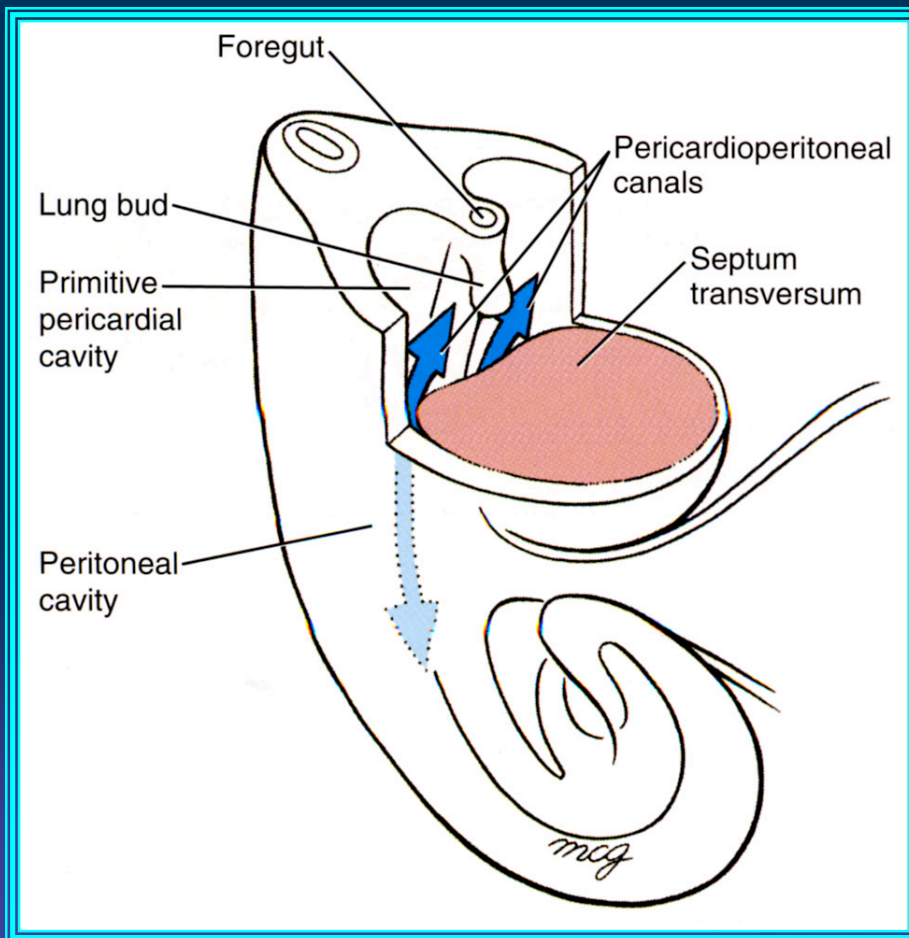
ventral wall by the closure of the gut tube, except in the umbilical cord.

Anterior-posterior and lateral folding form the primitive gut



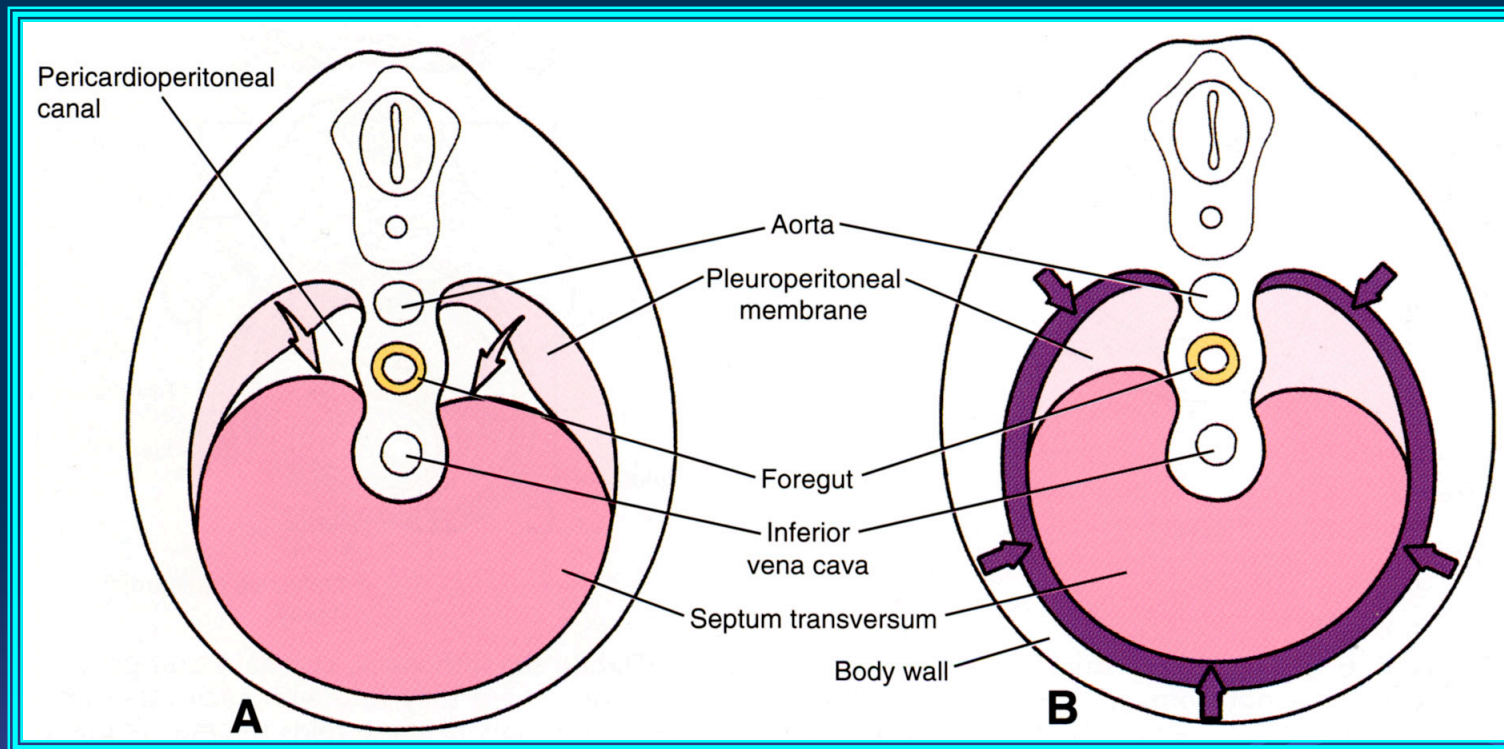
- Embryonic disc grows faster in length than the yolk sac causing the embryo to bend.
 - Dorsal surface grows more rapidly than the ventral
- Lateral folding
 - Fusion with apposing side except in the region of the yolk sac, and allantois
- Folding brings the heart and septum transversum caudal to buccopharyngeal membrane.

The septum transversum partially separates the thoracic and abdominal cavities



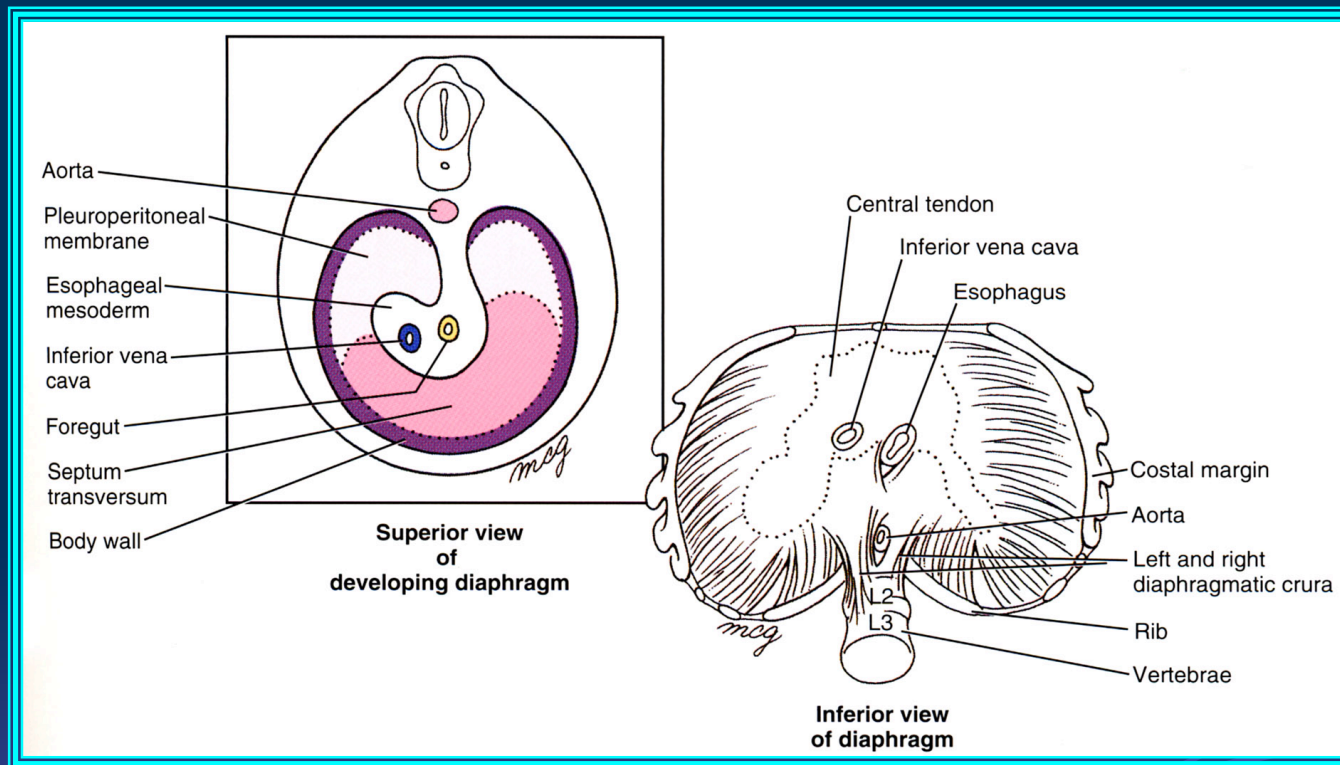
- The superior portion is the primitive pericardial cavity.
- **The inferior portion is the future peritoneal cavity.**
- The pericardial and peritoneal cavities communicate through the pericardioperitoneal canals

The pericardioperitoneal canals are closed by the formation of the pleuroperitoneal membranes



- The pleuroperitoneal membranes contribute muscle to the definitive diaphragm

The definitive diaphragm is a composite structure



- 1. Septum transversum
- 2. Pleuropericardial membranes
- 3. Paraxial mesoderm
- 4. Esophageal mesenchyme

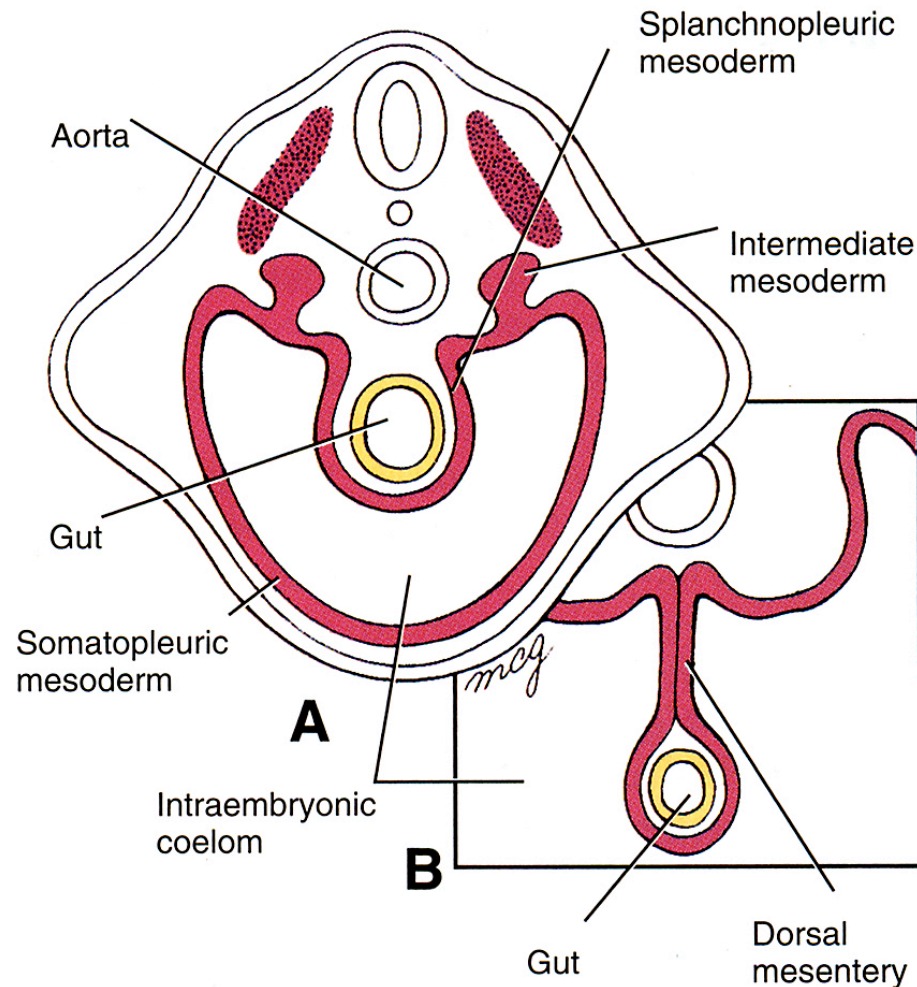
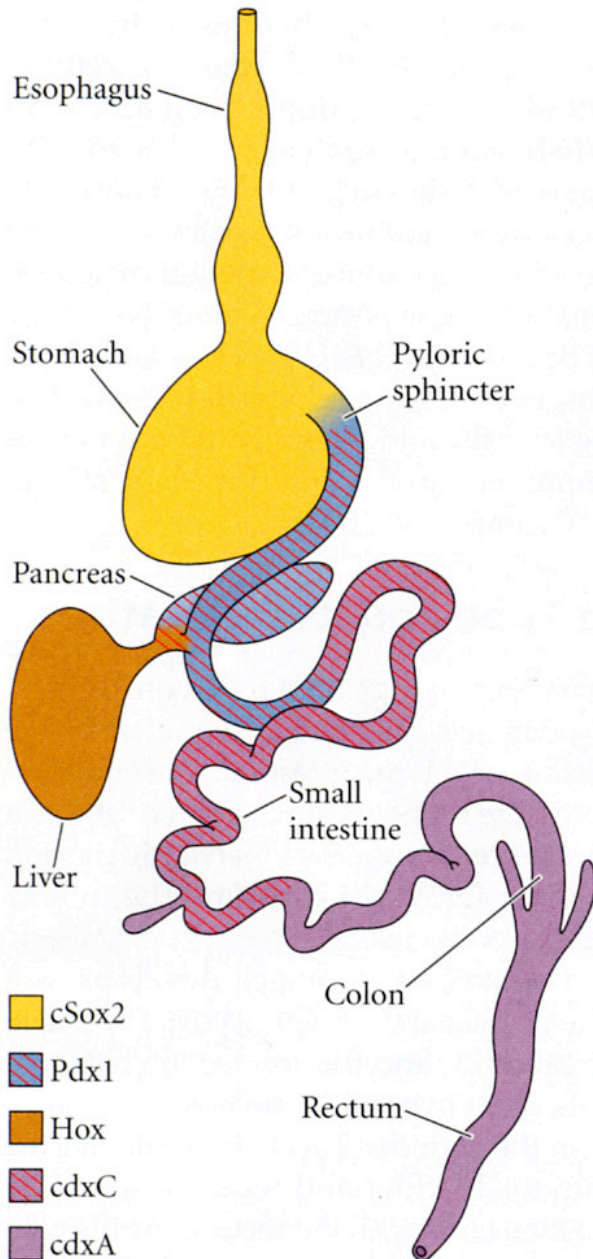


Figure 6–3. Formation of the dorsal mesentery. *A*, The primitive gut tube initially hangs from the posterior body wall by a broad bar of mesenchyme but, *B*, in regions inferior to the septum transversum this connection thins out to form a membranous dorsal mesentery composed of reflected peritoneum.

The dorsal mesentery thins to allow the gut to be flexibly suspended

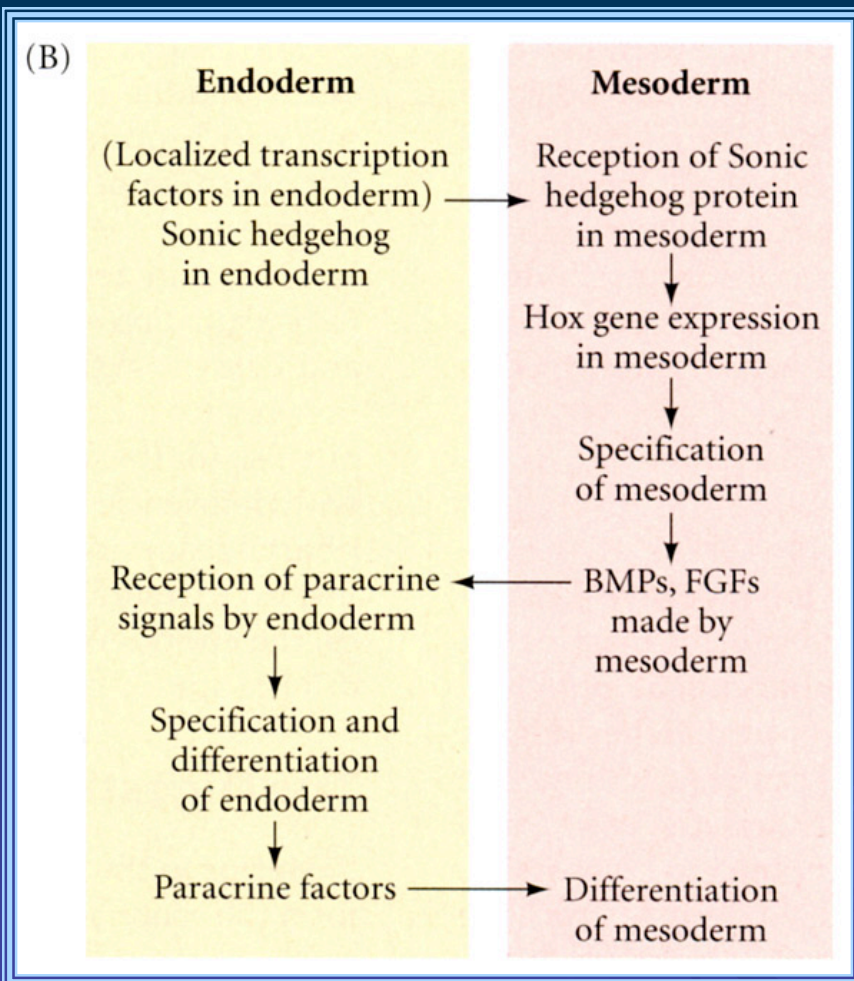
(A)



The gut is regionally specified early in development

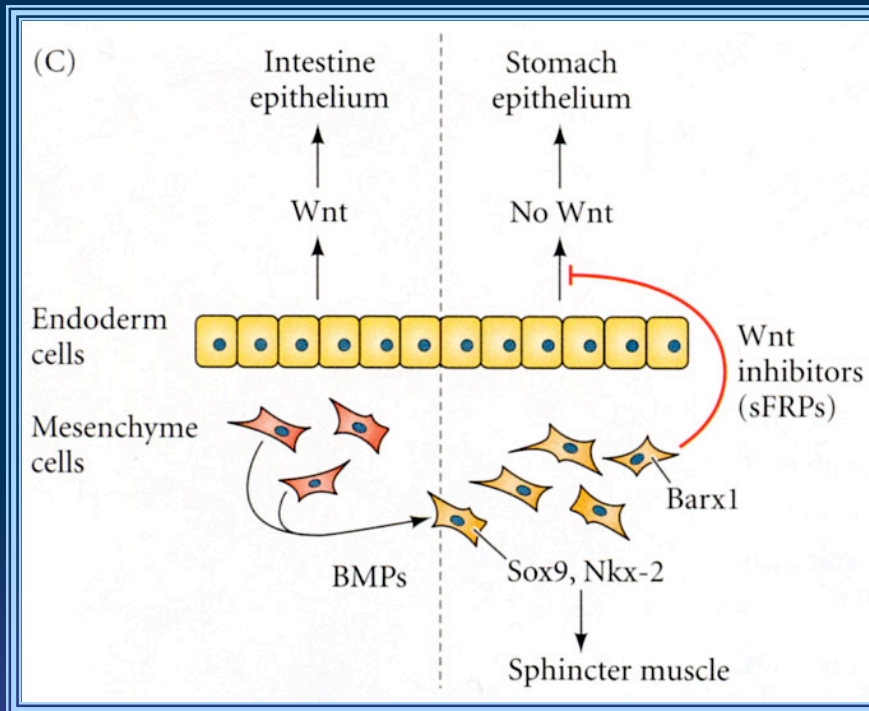
- Endoderm is specified before gut tube is complete.
- Specification is manifest as a series of regionally specific transcription factors.
- The boundaries between regions, however, are plastic and depend on interactions with mesoderm

The boundaries of GI regions are set by endodermal mesodermal cross-talk



- The language is paracrine secretion.
 - Secreted growth factors
 - Detected by appropriate receptors.
 - Coupled to transduction channels that affect transcription.
- Begins with Shh expression in posterior endoderm- spreads to whole gut
 - Induces series of Hox genes in mesoderm
 - Mesoderm then influences epithelial differentiation

Mesenchyme critically affects epithelial differentiation



➤ **Wnt signaling specifies intestinal epithelium.**

- Wnt = intestine
- No Wnt = stomach

➤ **Mesenchyme of stomach expresses Barx1 and secretes Wnt inhibitors (SFRP1, 2).**

➤ **Mesenchyme of intestine secretes BMP4**

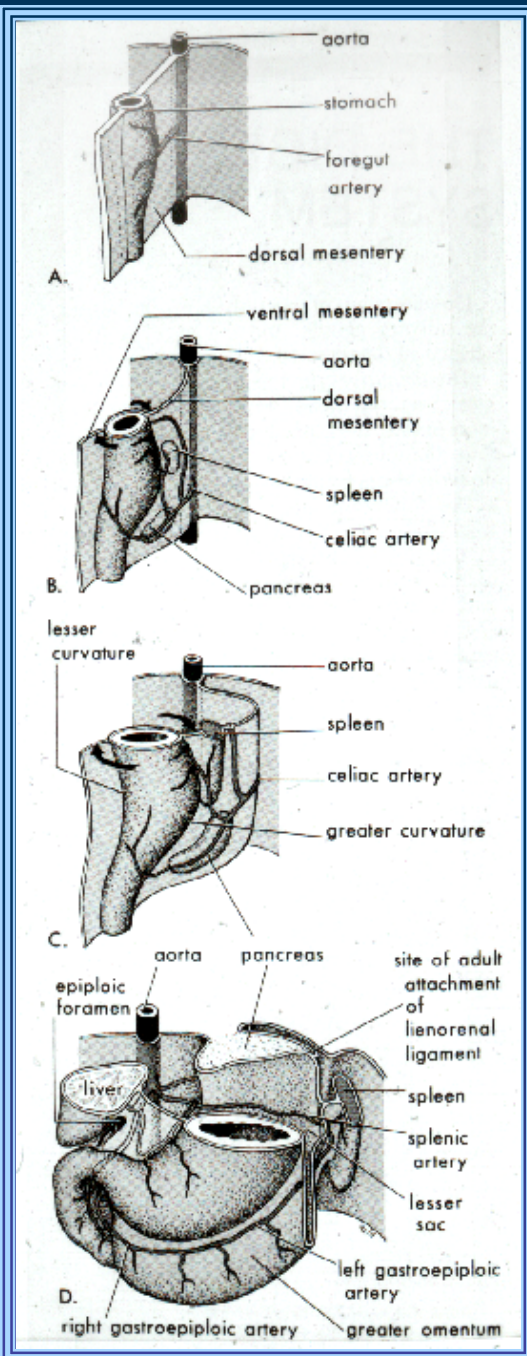
- Induces mesenchyme anterior to it to express Sox9 + Nkx-2
- Become pyloric sphincter

The foregut has many derivatives

- Pharynx and its derivatives
- Lower Respiratory tract
- Esophagus
- Stomach
- Duodenum proximal to ampulla of Vater
- Liver
- Biliary Apparatus
- Pancreas

From stomach to biliary apparatus, all are supplied by the celiac artery, “the artery of the foregut.”

Esophagus elongates rapidly



- Appears to grow faster at its cranial than caudal end.
- **Stomach does not descend but arises from a region just caudal to septum transversum that has been fated to be stomach.**
- **Epithelium obliterates lumen of esophagus and is recanalized by apoptosis (week 8).**
 - Failure causes polyhydramnios
 - Esophageal atresia or tracheo-esophageal fistula.
- Stomach enlarges and rotates

Obliteration of the lumen and recanalization occurs

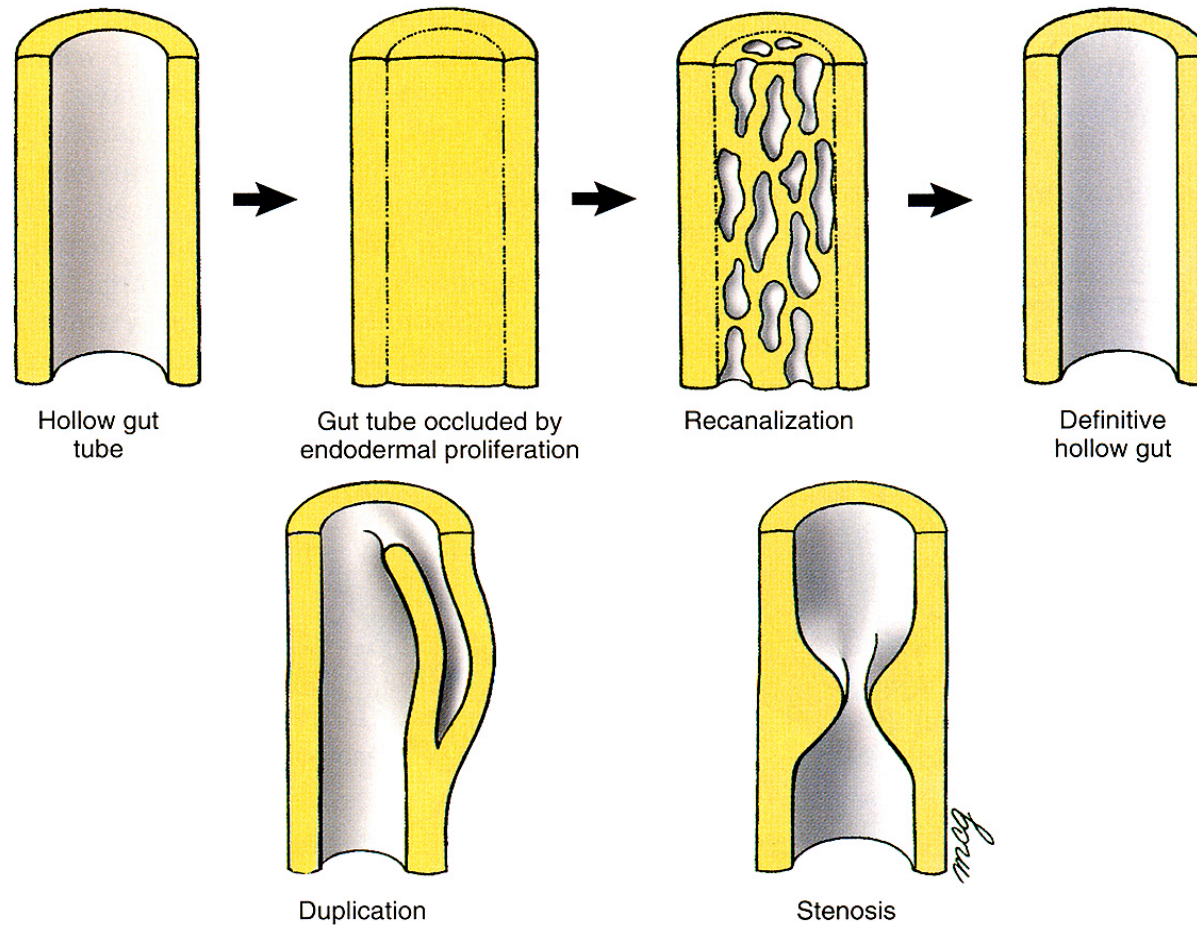
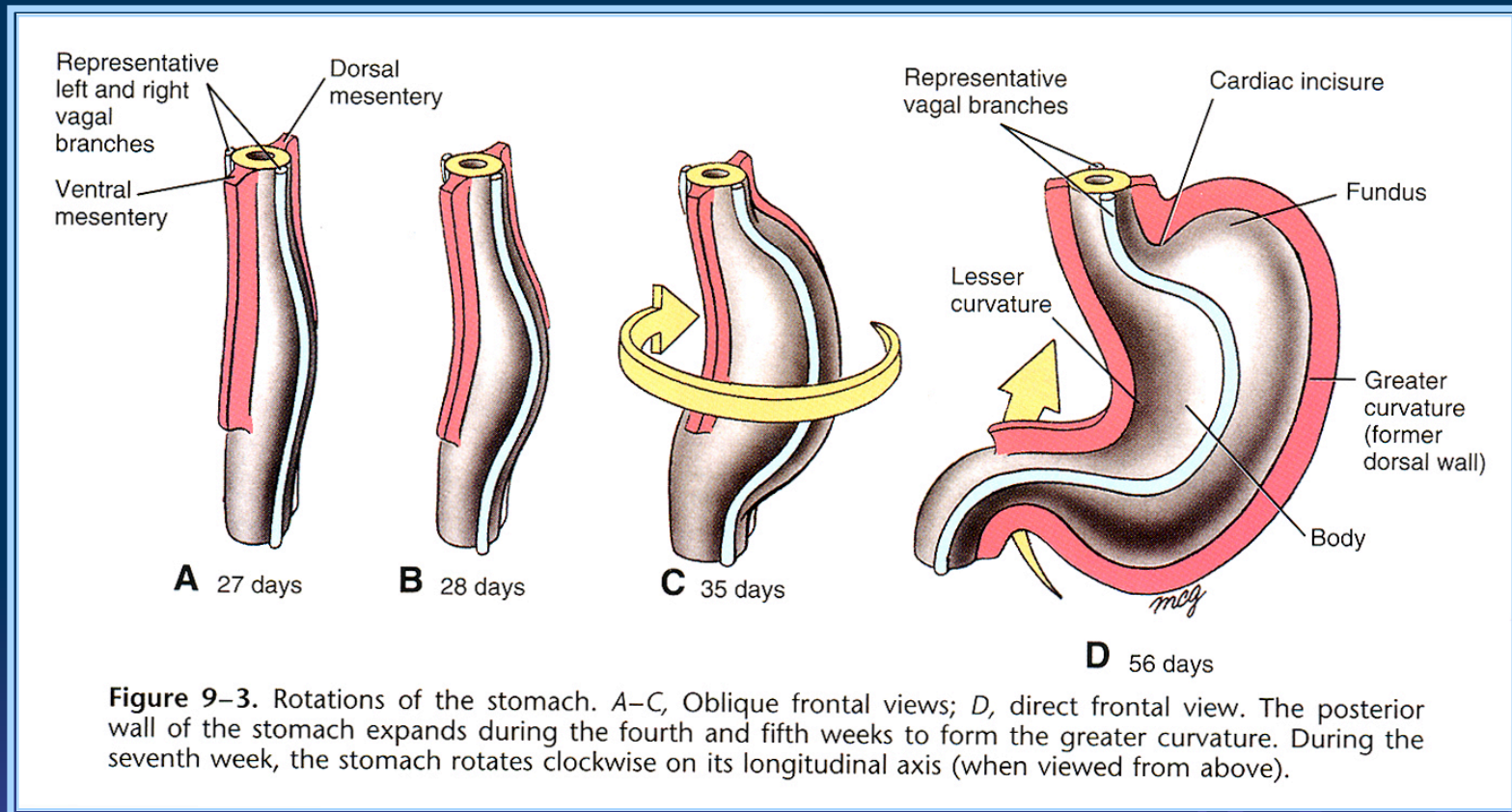


Figure 9-13. Formation of the definitive gut lumen. Proliferation of the endodermal lining completely occludes the gut tube during the sixth week. Recanalization is completed by week 9. Incomplete or abnormal recanalization may result in duplication of the lumen or stenosis of the gut tube.

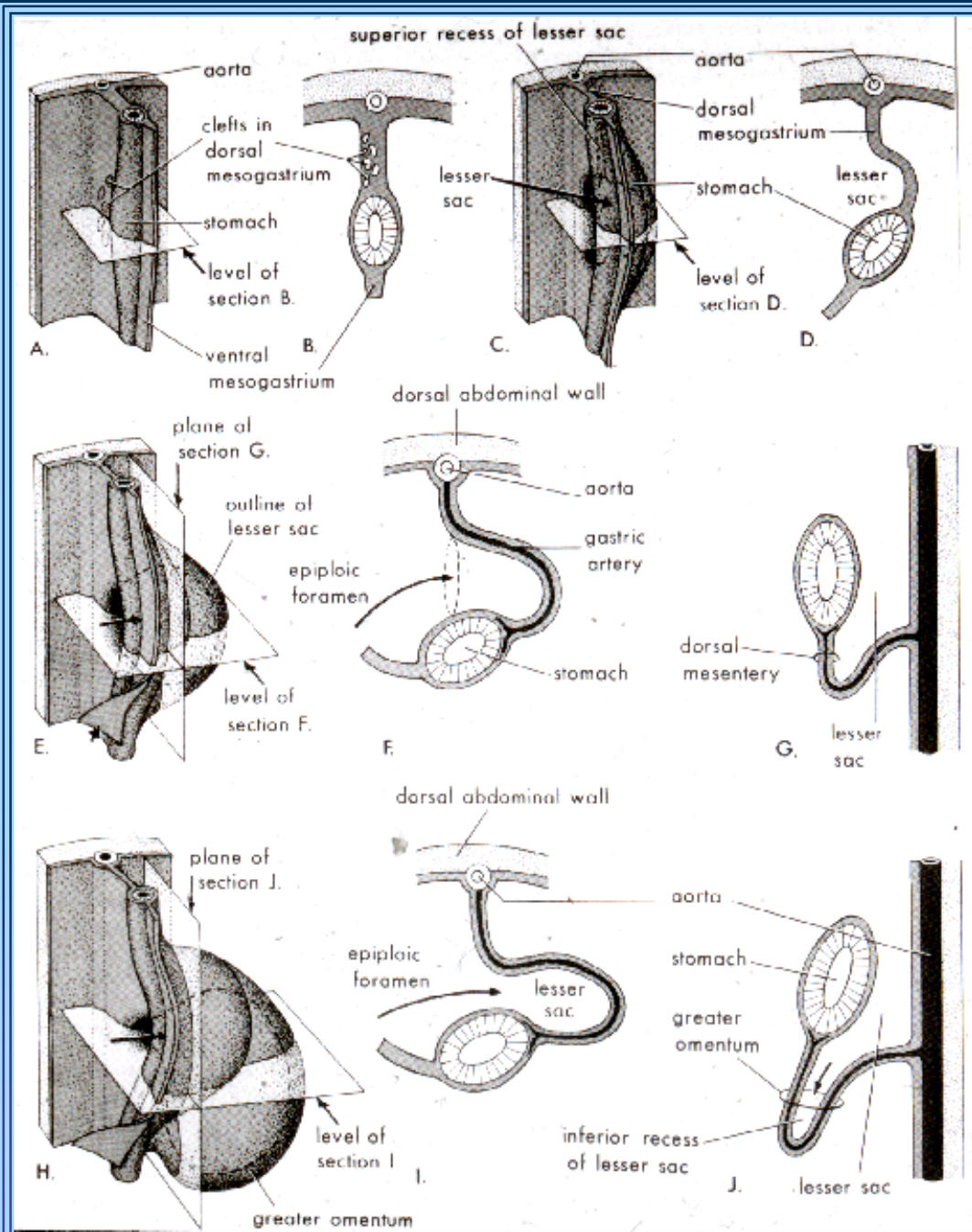
The stomach rotates 90° in a clockwise direction



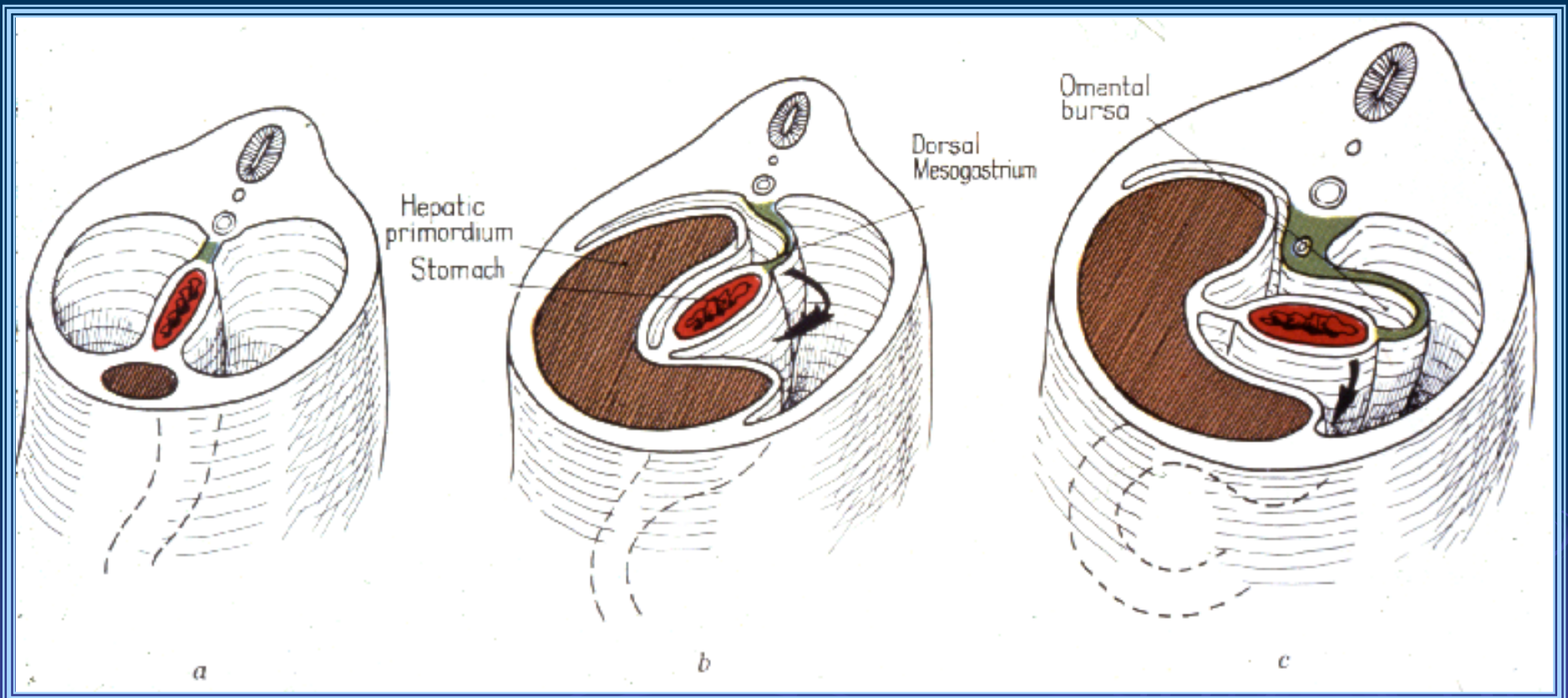
- Dorsal surface grows faster than the ventral to create the greater and lesser curvature. Acquires a transverse position

Rotation of the stomach creates the lesser sac

- Dorsal mesogastrium moves to left.
- **Ventral mesogastrium attaches to liver and body wall.**
- Inferior recess forms the greater omentum
 - Layers fuse to obliterate the lesser sac



Rotation of the stomach forms the omental bursa



Movements of the mesentery and stomach are made possible by vacuolization due to selective apoptosis

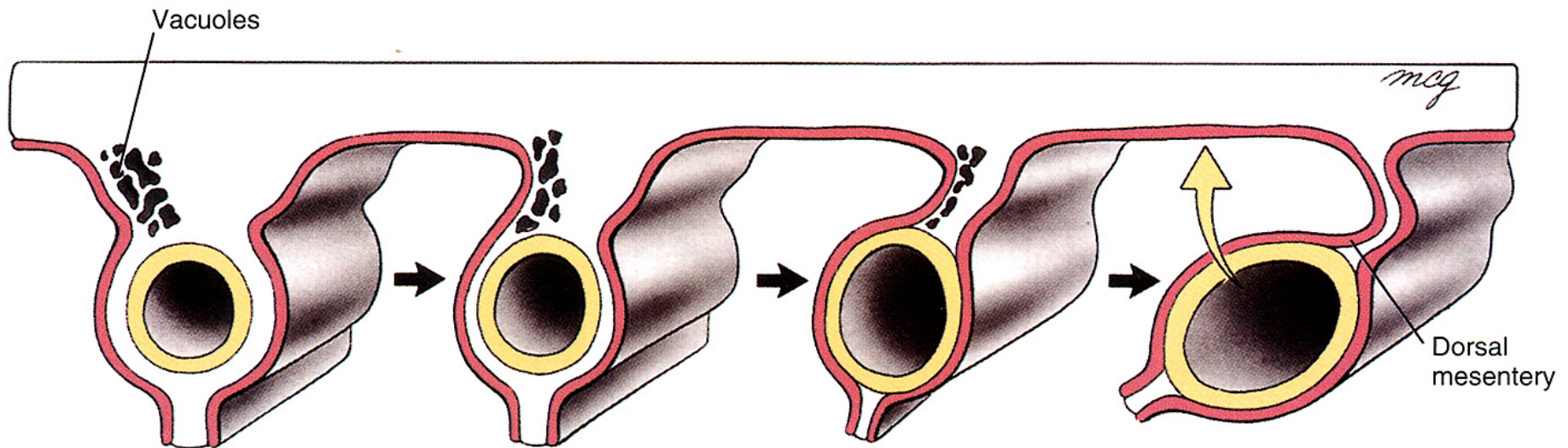


Figure 9-4. The rotation of the stomach around its longitudinal axis commences with vacuolization of the right side of the thick mesenchymal bar that initially suspends the stomach from the posterior body wall.

Liver, biliary system and pancreas arise from the duodenum

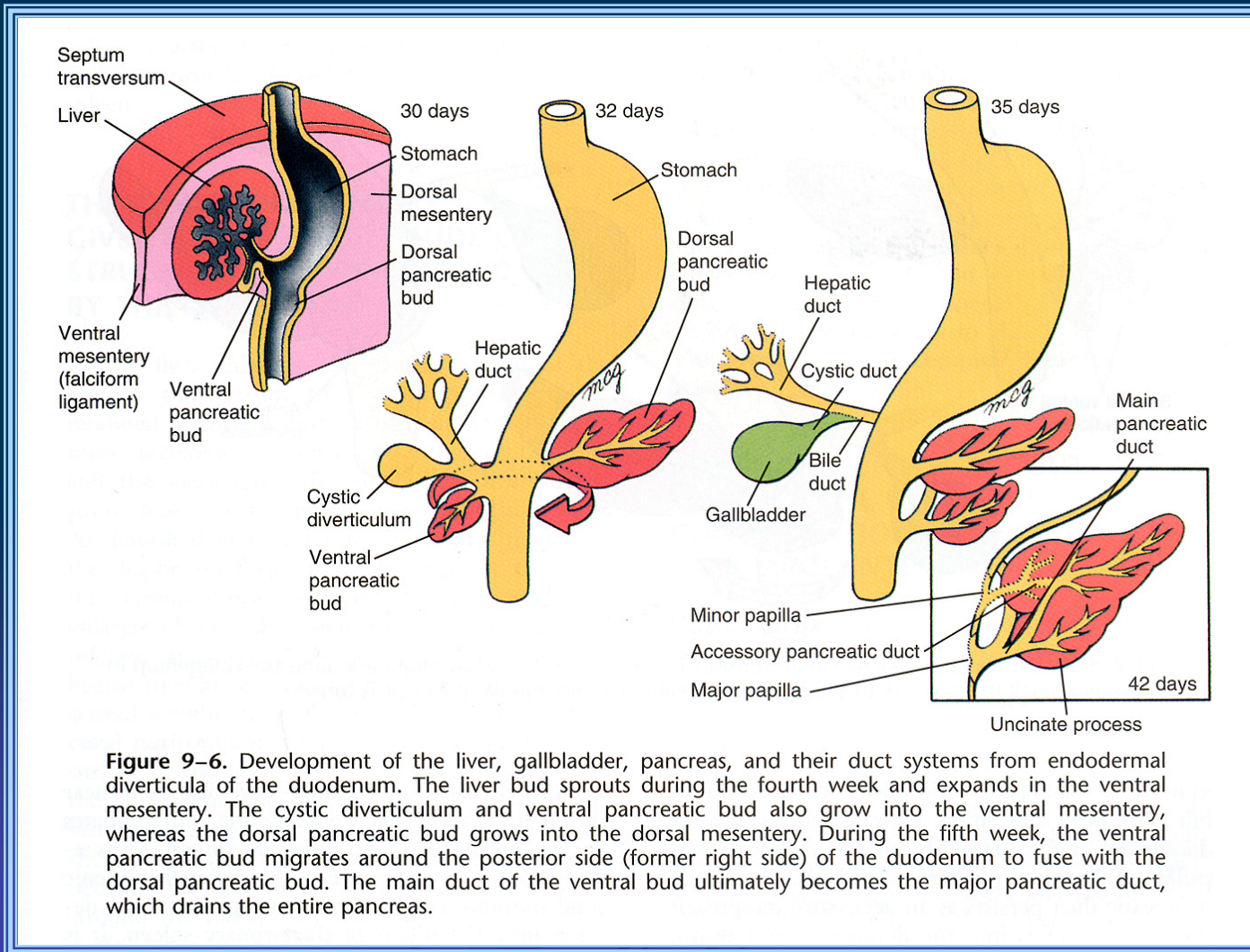
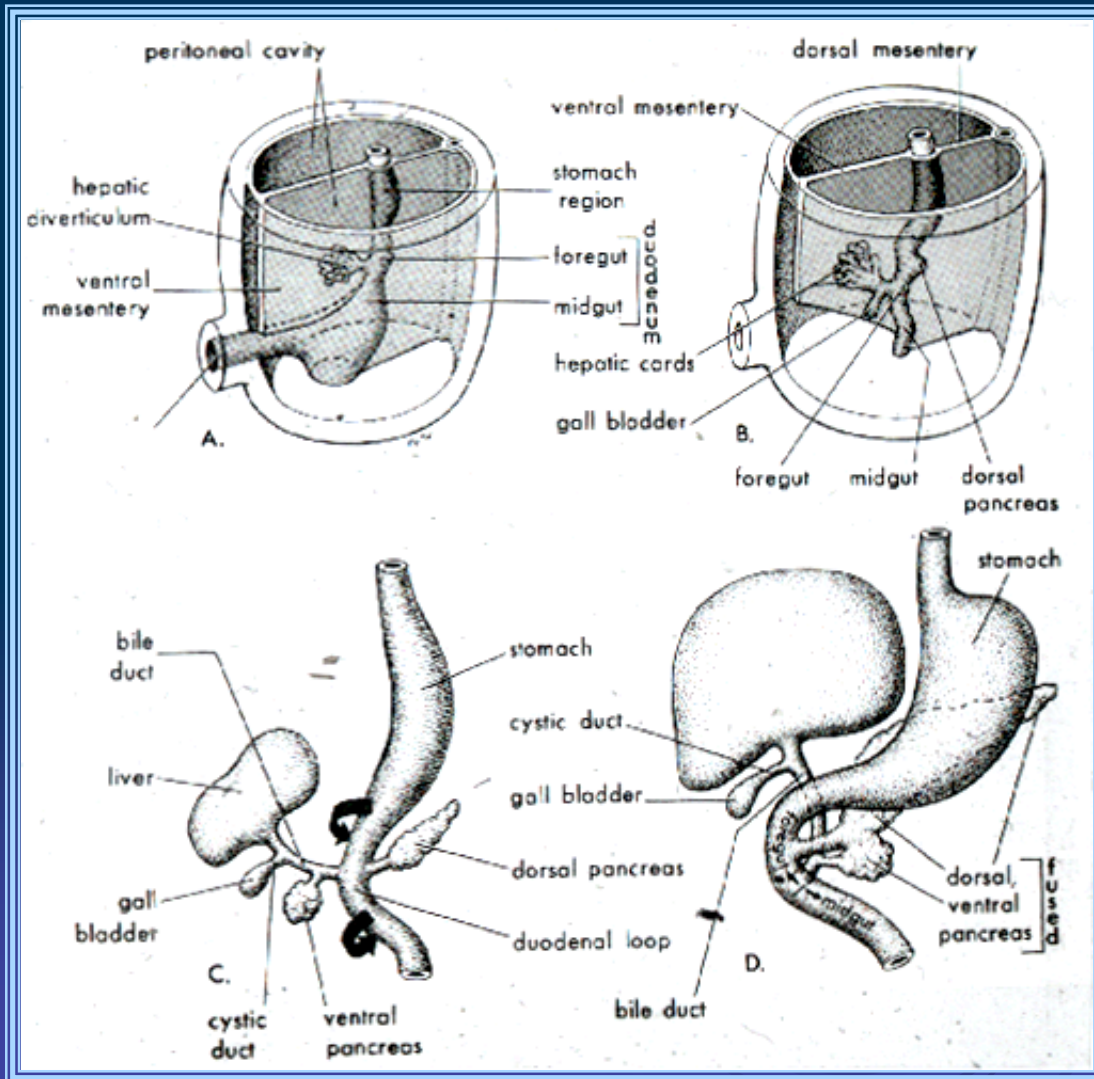


Figure 9-6. Development of the liver, gallbladder, pancreas, and their duct systems from endodermal diverticula of the duodenum. The liver bud sprouts during the fourth week and expands in the ventral mesentery. The cystic diverticulum and ventral pancreatic bud also grow into the ventral mesentery, whereas the dorsal pancreatic bud grows into the dorsal mesentery. During the fifth week, the ventral pancreatic bud migrates around the posterior side (former right side) of the duodenum to fuse with the dorsal pancreatic bud. The main duct of the ventral bud ultimately becomes the major pancreatic duct, which drains the entire pancreas.

Hepatic diverticulum grows from the duodenum into the ventral mesentery



- Begins ~ week 4
- Divides into cranial and caudal buds.
- **Cranial bud grows faster and becomes the hepatic parenchyma;**
 - Hematopoietic colonists arrive ~ week 6
- **Caudal bud gives rise to the biliary system.**

Ventral mesentery forms falciform ligament, hepatic peritoneum, and lesser omentum

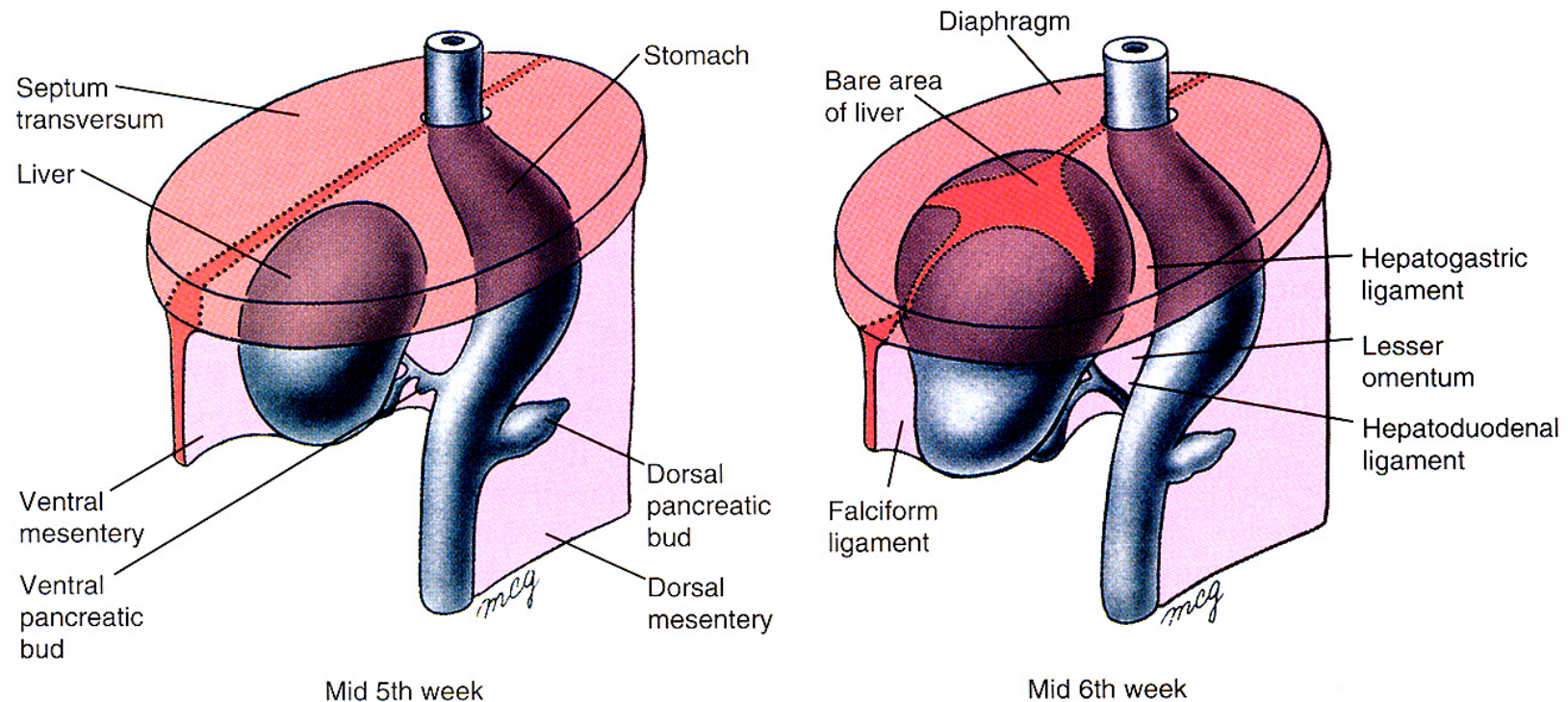
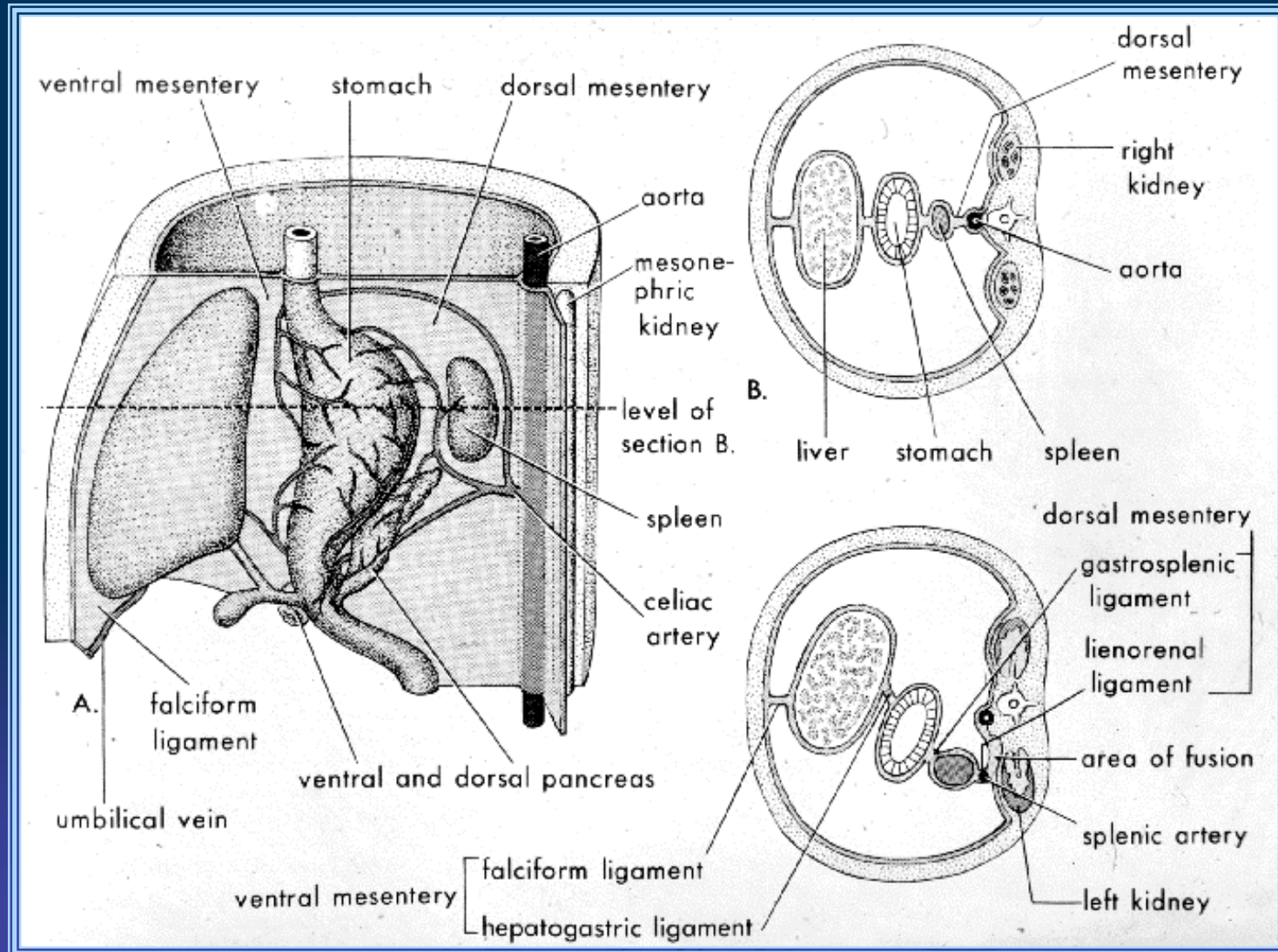
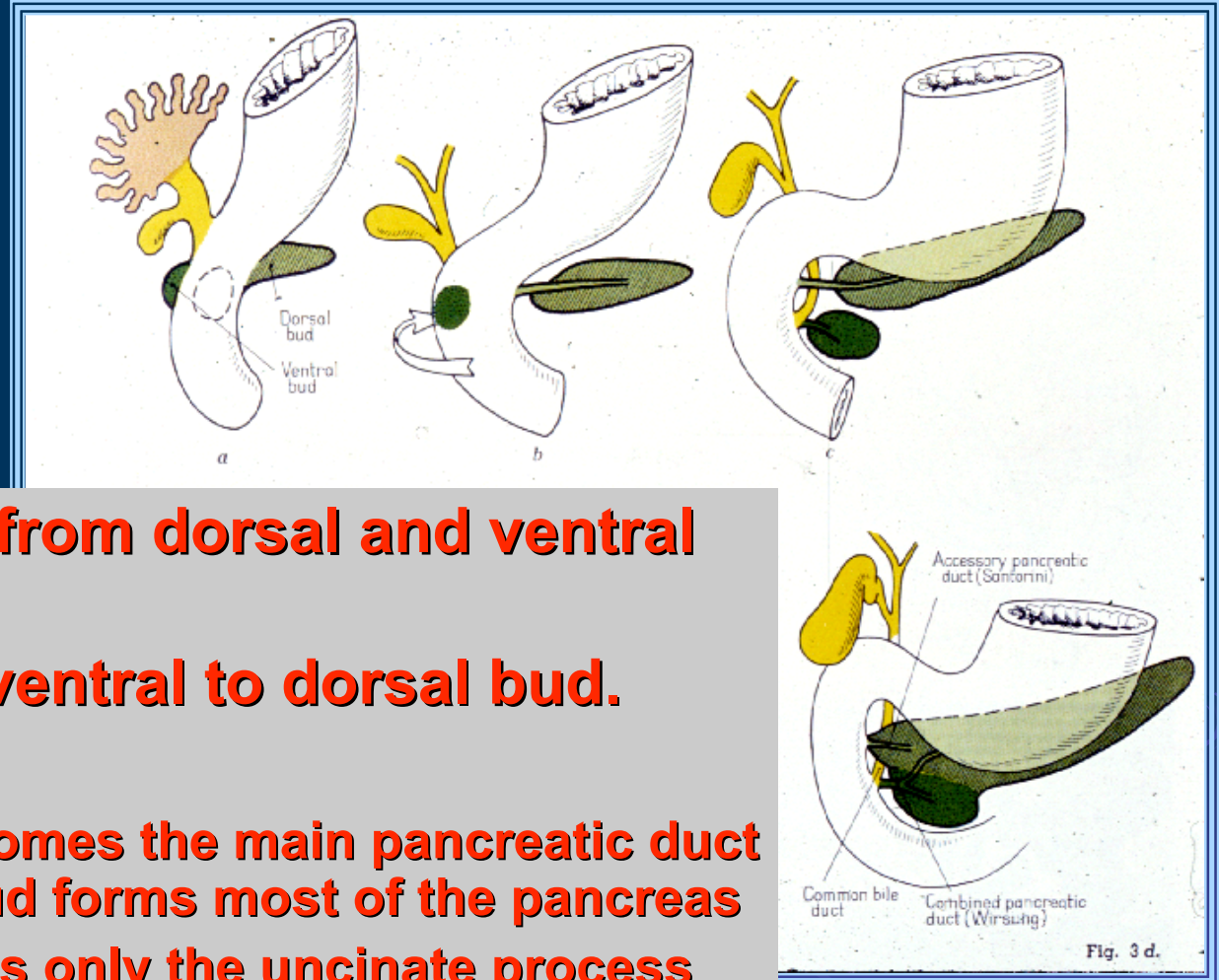


Figure 9–8. Formation of the liver and associated membranes. As the liver bud grows into the ventral mesentery, its expanding crown makes direct contact with the developing diaphragm. The ventral mesentery that encloses the growing liver bud differentiates into the visceral peritoneum of the liver, which is reflected onto the diaphragm. This zone of reflection, which encircles the area where the liver directly contacts the diaphragm (the bare area), becomes the coronary ligament. The remnant of ventral mesentery connecting the liver with the anterior body wall becomes the falciform ligament, whereas the ventral mesentery between the liver and lesser curvature of the stomach forms the lesser omentum.

Ventral mesogastrium supports liver and stomach



Rotation of the stomach shapes the pancreas



- **Pancreas arises from dorsal and ventral buds.**
- **Rotation brings ventral to dorsal bud.**
- **Buds fuse.**
 - **Ventral duct becomes the main pancreatic duct but the dorsal bud forms most of the pancreas**
 - **Ventral bud forms only the uncinete process and inferior part of the head of the pancreas.**

Aberrant rotation causes an annular pancreas

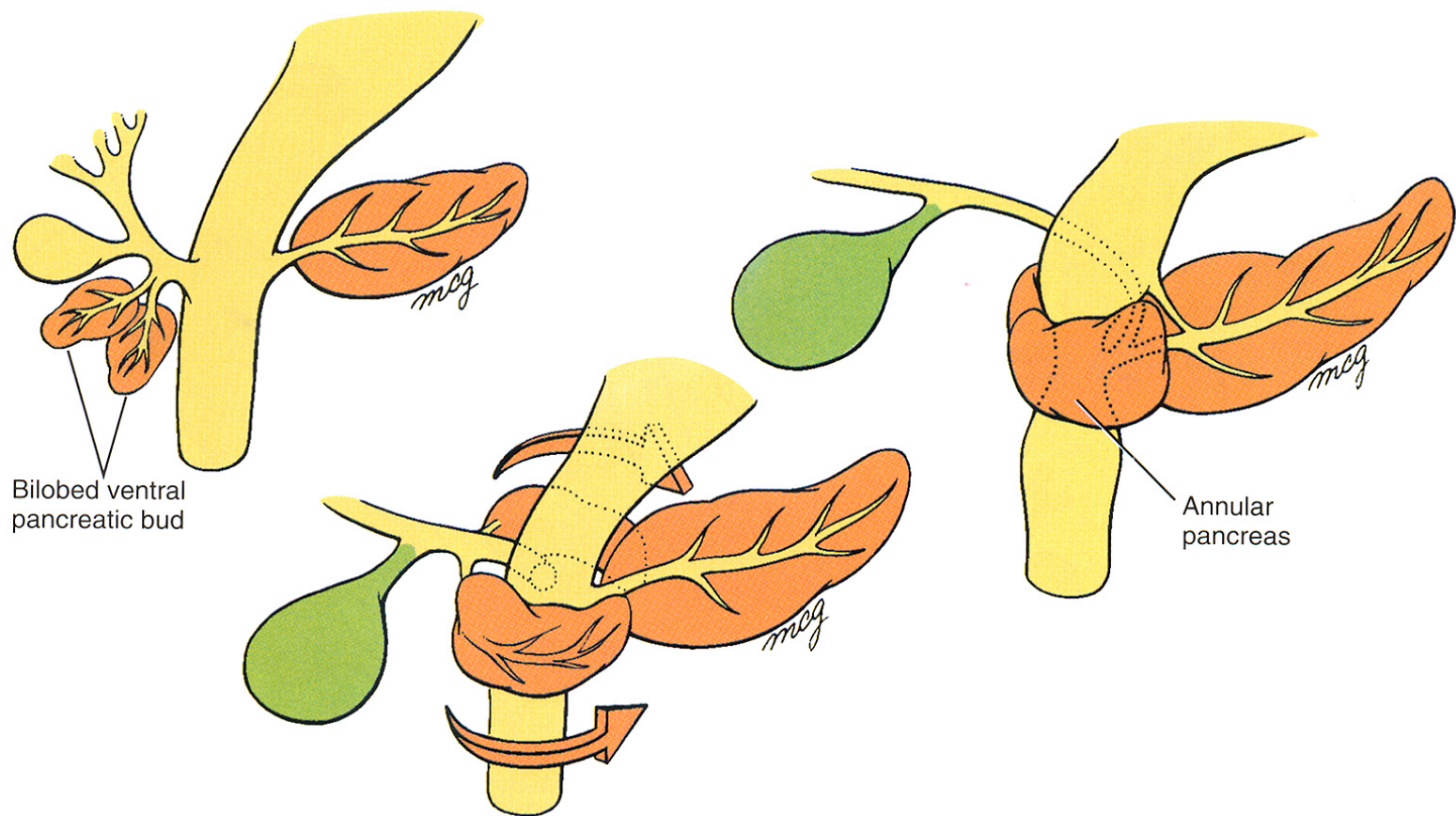


Figure 9-7. The ventral pancreas may consist of two lobes. If the lobes migrate around the duodenum in opposite directions to fuse with the dorsal pancreatic bud, an annular pancreas is formed.

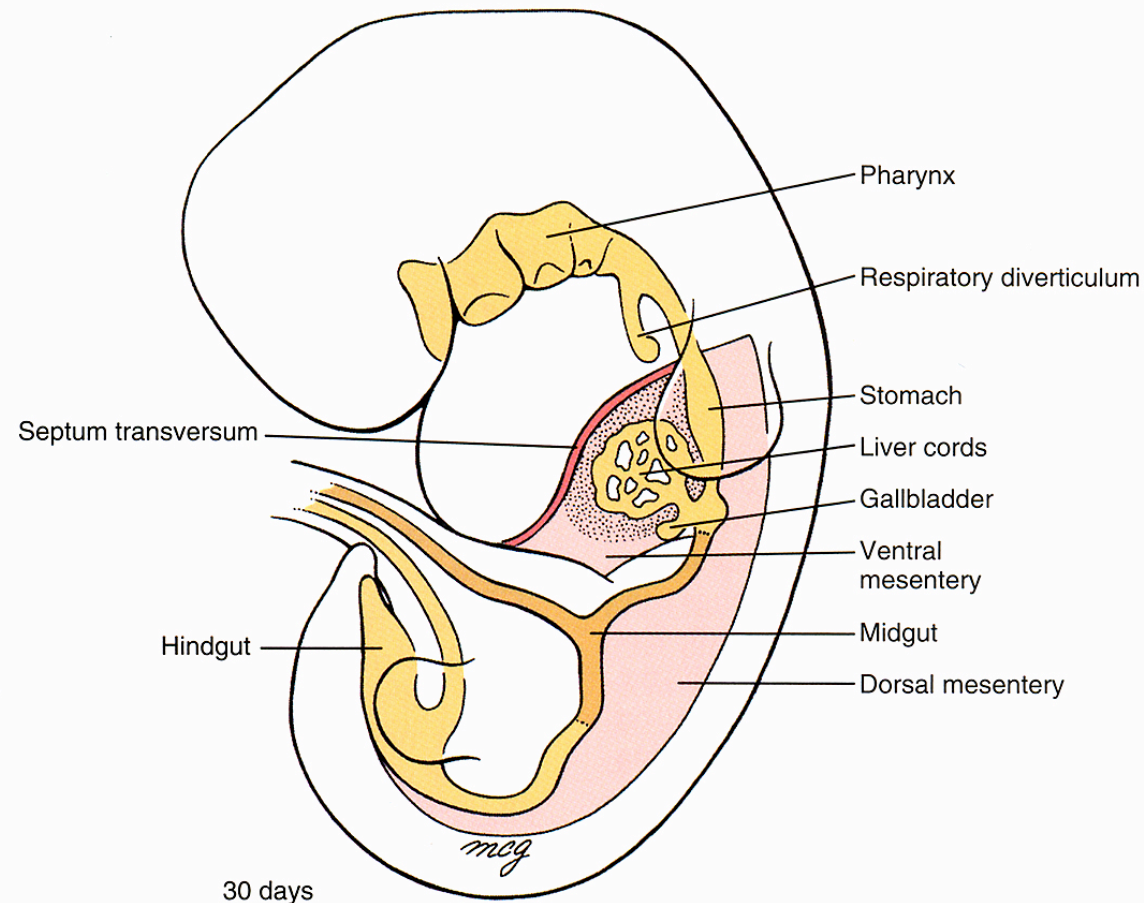


Figure 9–2. Structure of the gut tube. The foregut consists of the pharynx, located superior to the respiratory diverticulum, the thoracic esophagus, and the abdominal foregut. The abdominal foregut forms the abdominal esophagus, stomach, and about half of the duodenum and gives rise to the liver, the gallbladder, the pancreas, and their associated ducts. The midgut forms half of the duodenum, the jejunum and ileum, the ascending colon, and about two thirds of the transverse colon. The hindgut forms one third of the transverse colon, the descending colon and sigmoid colon, and the upper two thirds of the anorectal canal. The abdominal esophagus, stomach, and superior part of the duodenum are suspended by dorsal and ventral mesenteries; the abdominal gut tube excluding the rectum is suspended in the abdominal cavity by a dorsal mesentery only.

Derivatives of the midgut

- Small intestine (except for the proximal duodenum).
 - Cecum
 - Appendix
 - Ascending colon
 - Right 1/2 to 2/3 of the proximal transverse colon
- All are supplied by the superior mesenteric artery (“the artery of the midgut”)

The midgut grows rapidly and herniates into the umbilical cord

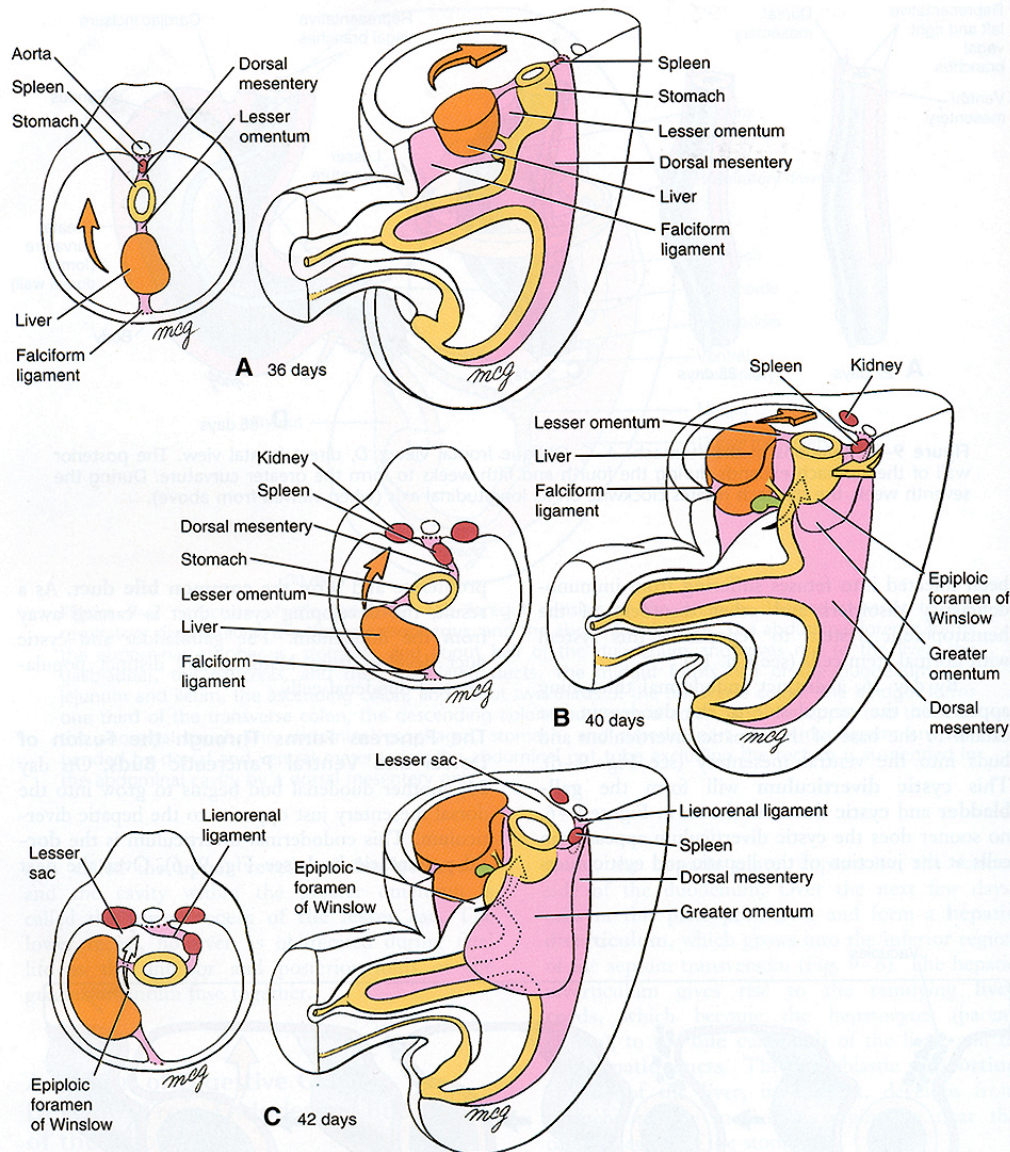
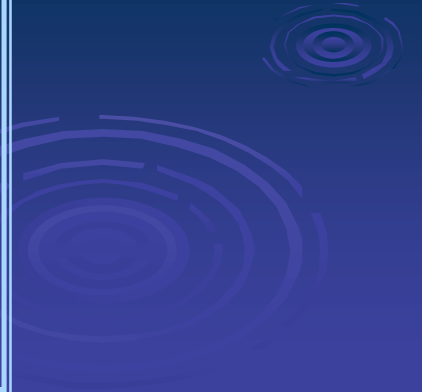
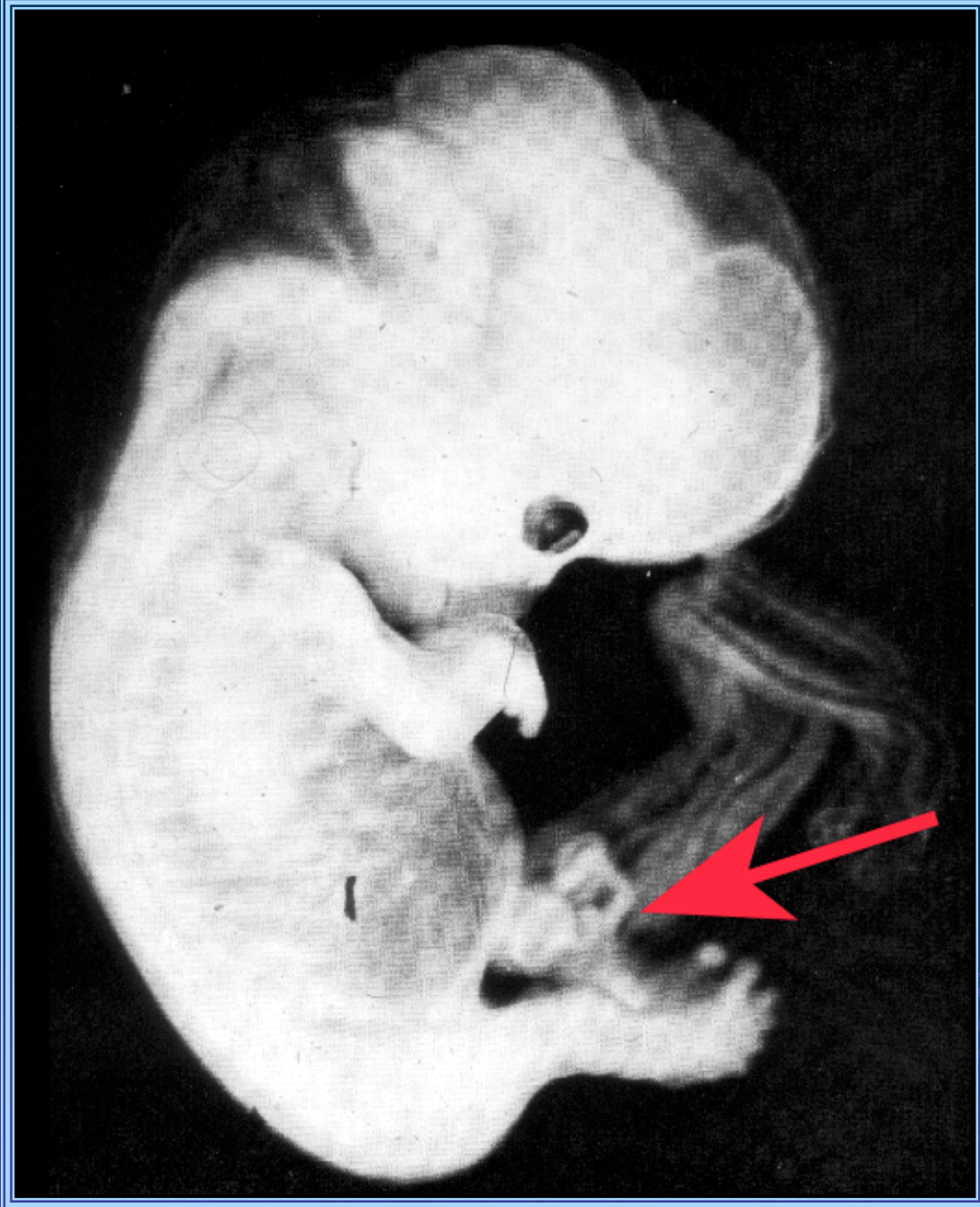


Figure 9-5. Development of the greater omentum and lesser sac. *A, B*, The rotation of the stomach and growth of the dorsal mesogastrum create a sac (the greater omentum) that dangles from the greater curvature of the stomach. *B, C*, When the duodenum swings to the right, it becomes secondarily fused to the body wall, enclosing the space posterior to the stomach and within the expanding cavity of the greater omentum. This space is the lesser sac of the peritoneal cavity. The remainder of the peritoneal cavity is now called the greater sac. The principal passageway between the greater and lesser sacs is the epiploic foramen of Winslow.

Week 6



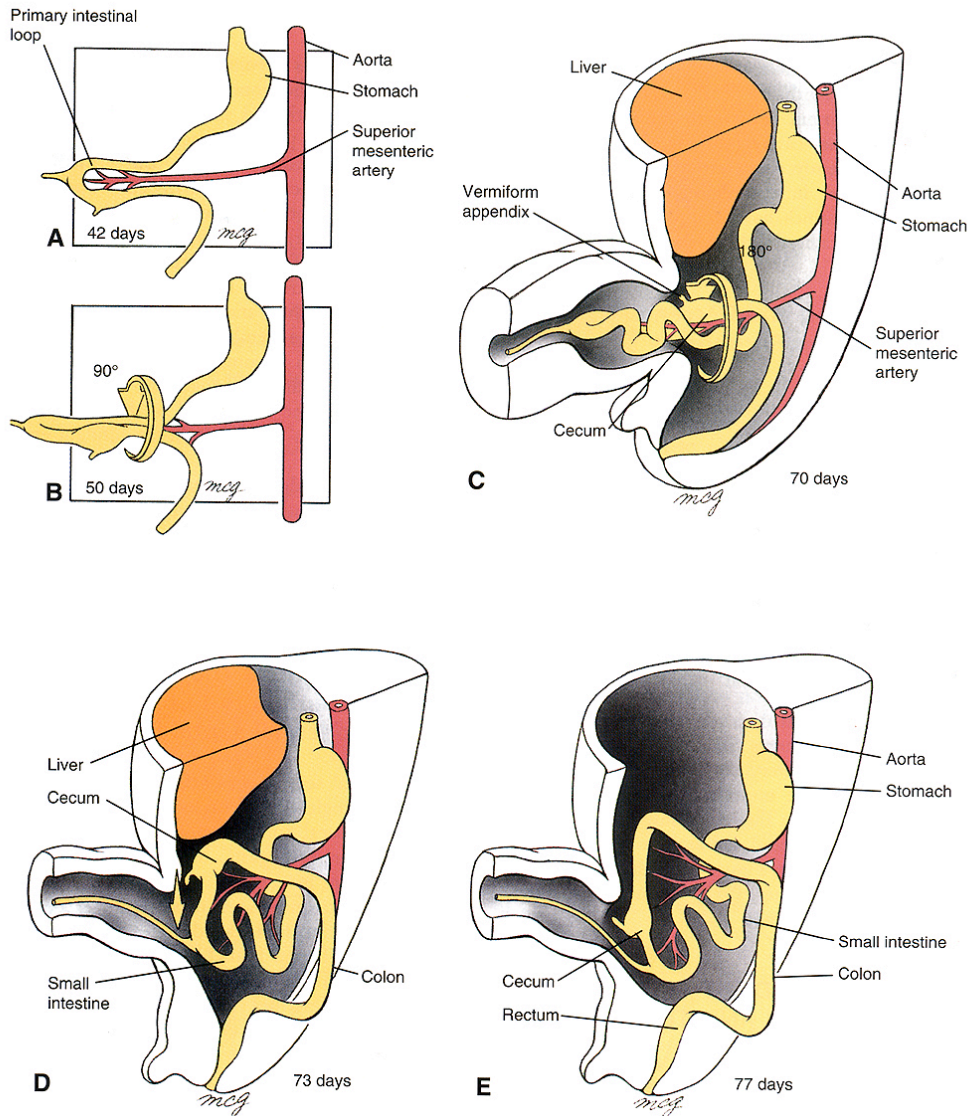


Figure 9-9. Herniation and rotations of the intestine. *A, B,* At the end of the sixth week, the primary intestinal loop herniates into the umbilicus, rotating through 90 degrees counterclockwise (in frontal view). *C,* The small intestine elongates to form jejunal-ileal loops, the cecum and appendix grow, and, at the end of the 10th week, the primary intestinal loop retracts into the abdominal cavity, rotating an additional 180 degrees counterclockwise. *D, E,* During the 11th week, the retracting midgut completes this rotation as the cecum is positioned just inferior to the liver. The cecum is then displaced inferiorly, pulling down the proximal hindgut to form the ascending colon. The descending colon is simultaneously fixed on the left side of the posterior abdominal wall. The jejunum, ileum, and transverse colon and sigmoid colon remain suspended by mesentery.

The midgut rotates around an axis of the superior mesenteric artery:

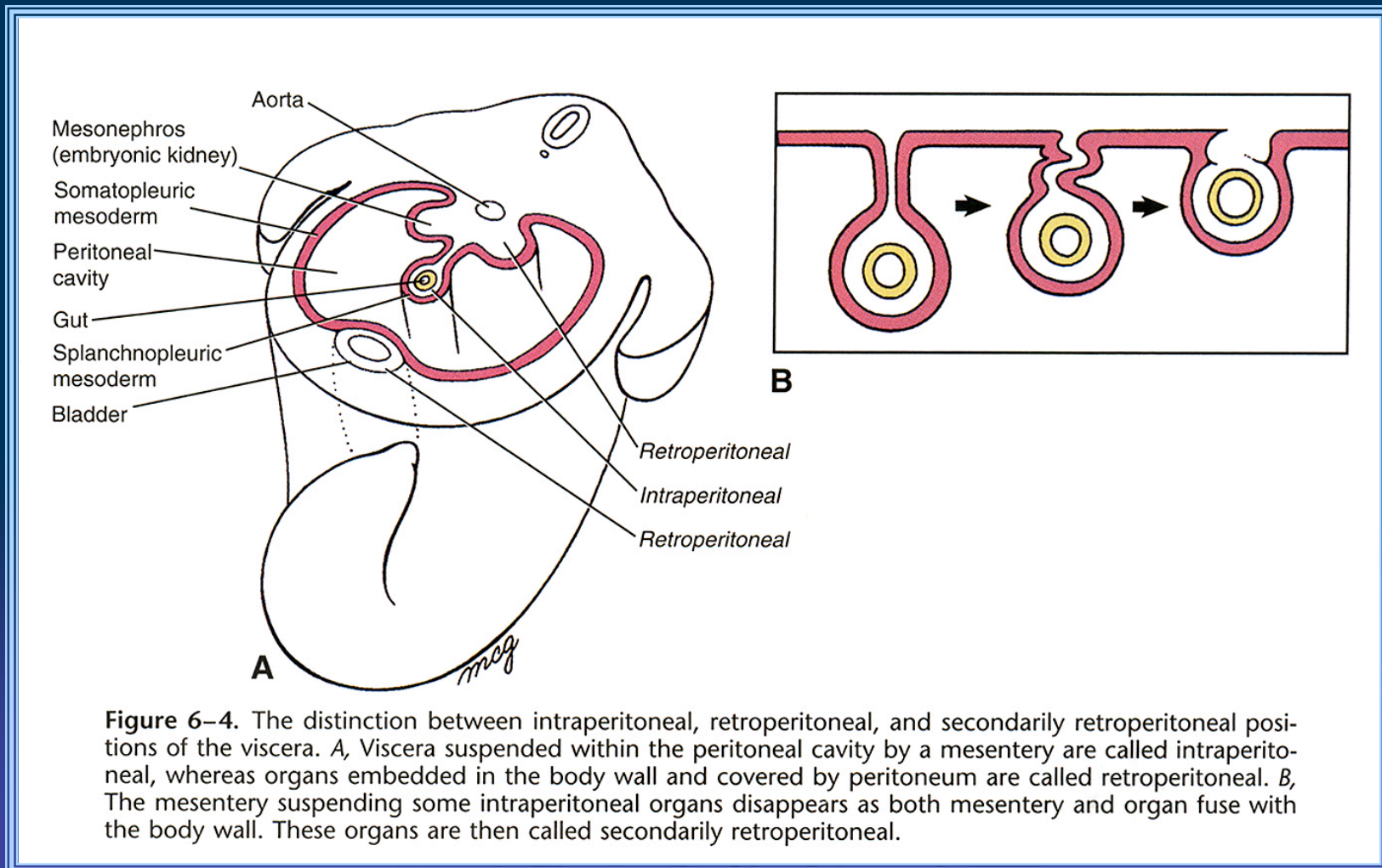
1. 90°
2. 180°

Midgut hernia reduced at week 10.

Rotation of the midgut

- 1. Cranial and caudal loop form.
- 2. Cranial growth >>> caudal growth.
- 3. Apex of loop is vitelline duct.
- 4. Cranial loop moves to right and caudal loop to left (90° counterclockwise).
- 4. Reduction of midgut hernia with rotation a further 180°.
 - Brings cecum to right
 - Moves down
 - Becomes secondarily retroperitoneal.

Loops of bowel fuse with the body wall and become secondarily retroperitoneal



**Intraperitoneal
viscera**

**Retroperitoneal
viscera**

**Secondarily
retroperitoneal
viscera**

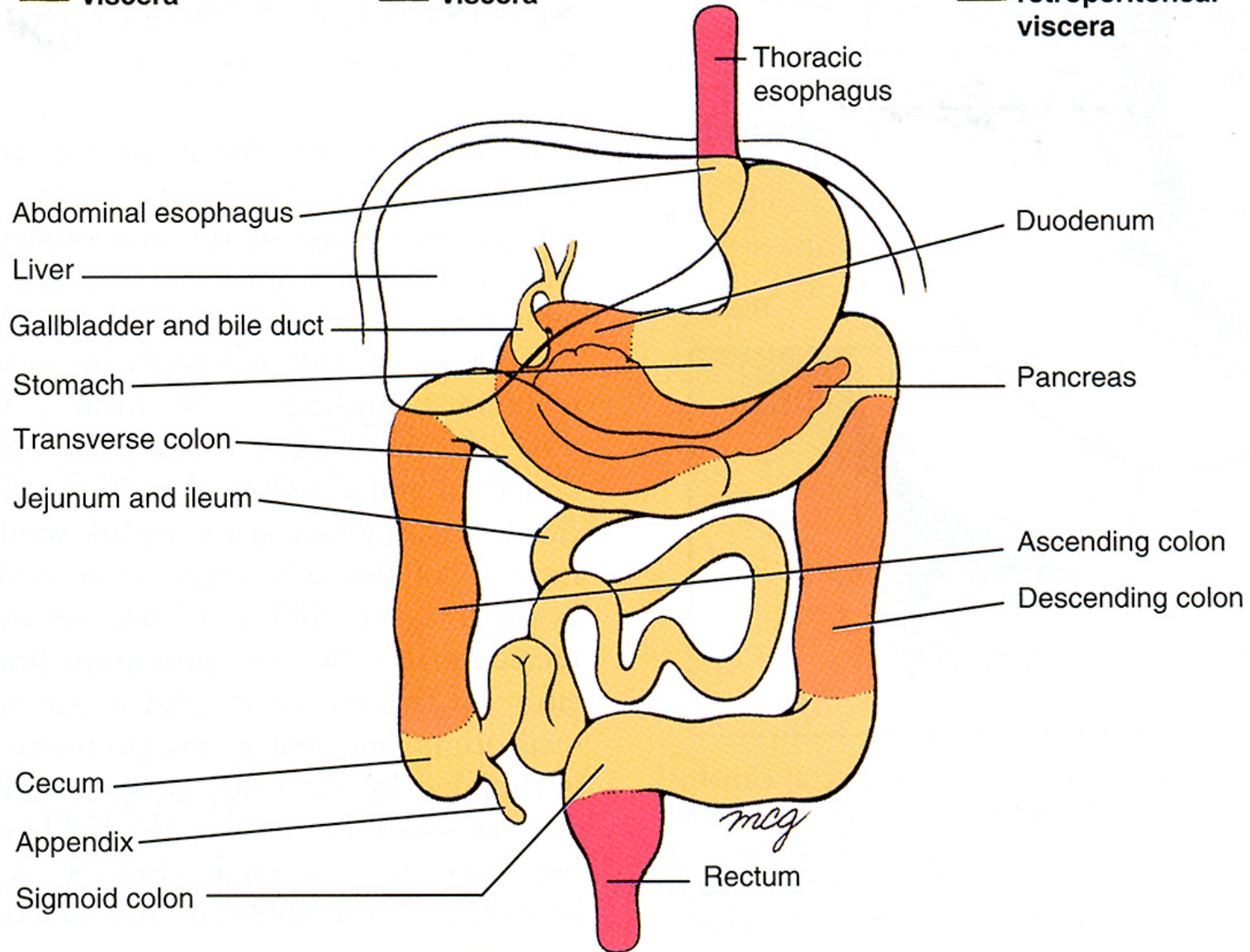


Figure 9–10. Intraperitoneal, retroperitoneal, and secondarily retroperitoneal organs of the abdominal gastrointestinal tract.

Volvulus is a serious complication of excessive flexibility

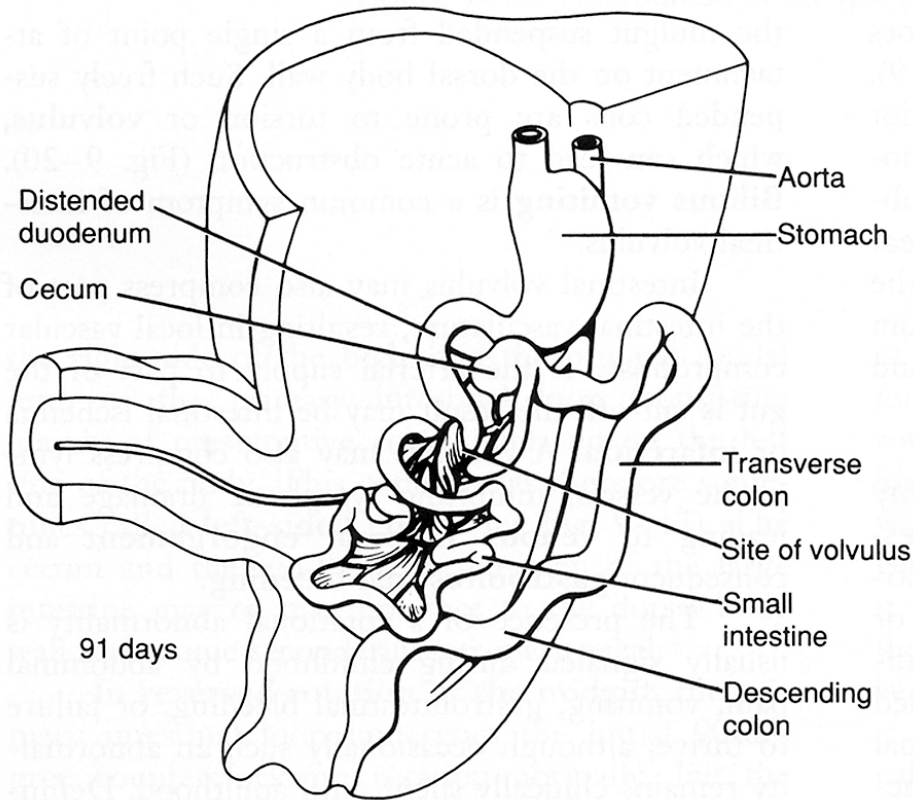
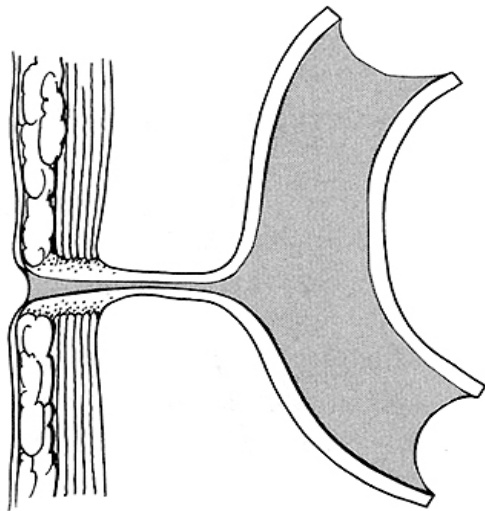


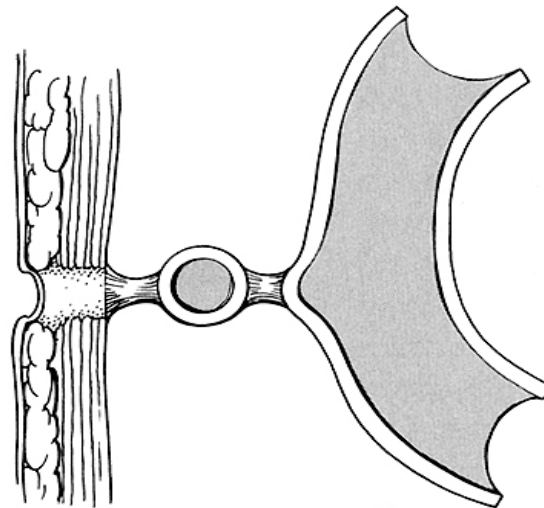
Figure 9-20. Volvulus. Volvulus may occur as suspended regions of the gut twist around themselves, constricting the intestine and/or compromising its blood supply.



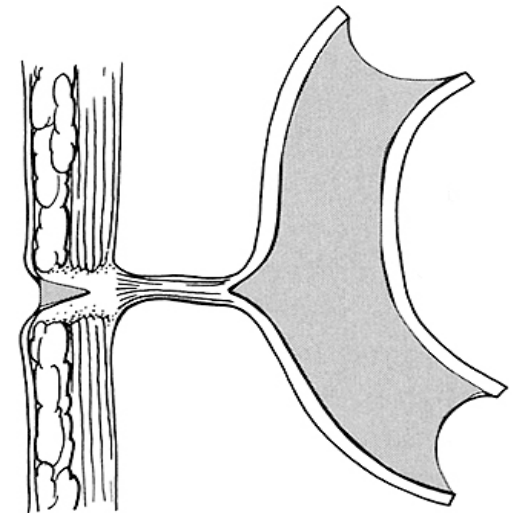
A Persistent attachment to umbilicus Meckel's diverticulum



B Omphalomesenteric fistula



C Omphalomesenteric cyst



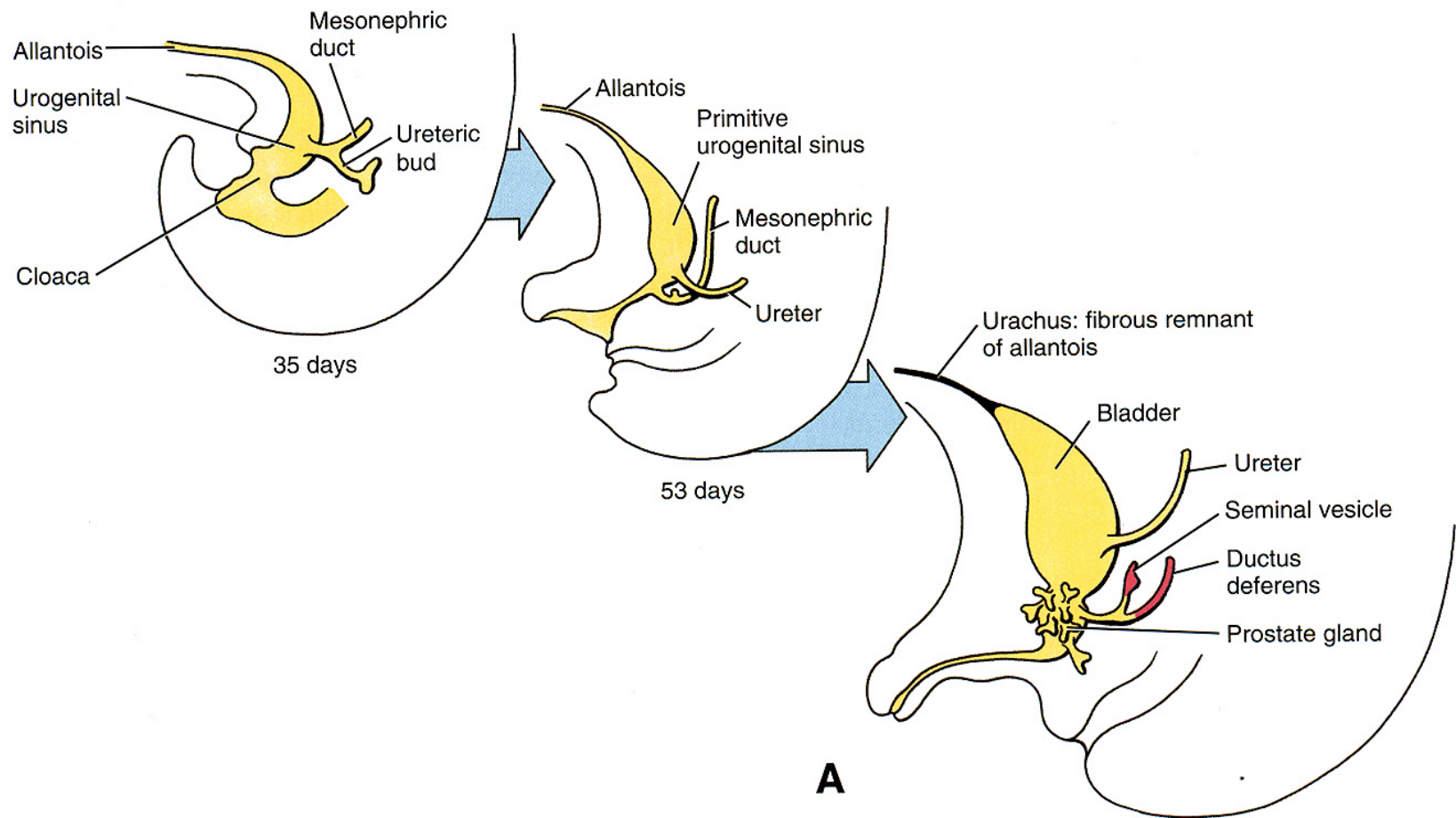
D Omphalomesenteric ligament (fibrous band)

Figure 9–21. Meckel's diverticulum. *A*, A typical Meckel's diverticulum is a finger-like projection of the ileum located about 100 cm proximal to the cecum. A Meckel's diverticulum may form (*B*) a patent fistula connecting the umbilicus with the ileum, (*C*) an isolated cyst suspended by ligaments, or (*D*) a fibrous band connecting the ileum and anterior body wall at the level of the umbilicus. (Drawings courtesy of Children's Hospital Medical Center, Cincinnati, OH.)

Derivatives of the hindgut

- Left 1/3 to 1/2 of the distal transverse colon
- Descending colon
- Sigmoid colon
- Rectum
- Superior part of anal canal
- Epithelium of urinary bladder and most of the urethra
- **All are supplied by the inferior mesenteric artery, “the artery of the”. hindgut**

The hindgut is originally a cloaca-partioned to form rectum and urogenital sinus



Urorectal septum divides the cloaca

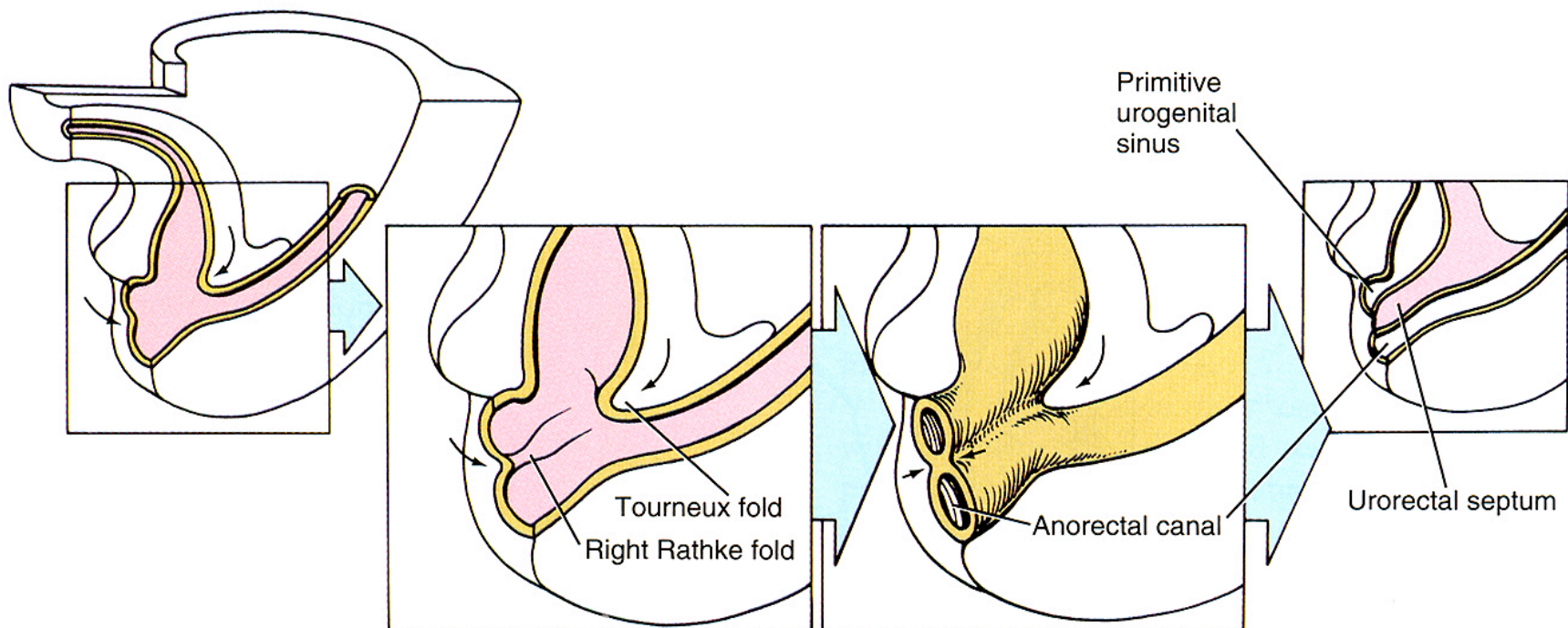


Figure 9–11. Subdivision of the cloaca into an anterior primitive urogenital sinus and a posterior rectum between 4 and 6 weeks. The urorectal septum that divides the cloaca is composed of three distinct septa. Initially, a superior Tourneux fold grows inferiorly to the level of the future pelvic urethra. Separation is then completed by left and right Rathke folds that grow in a coronal plane.

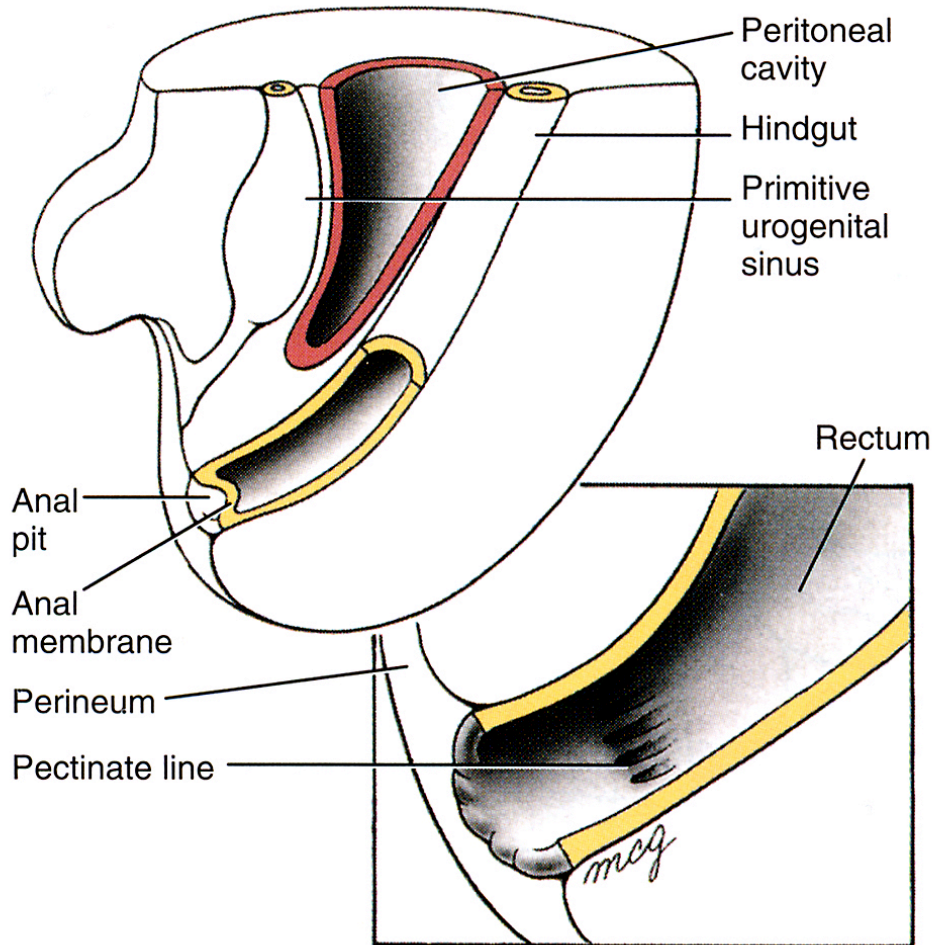
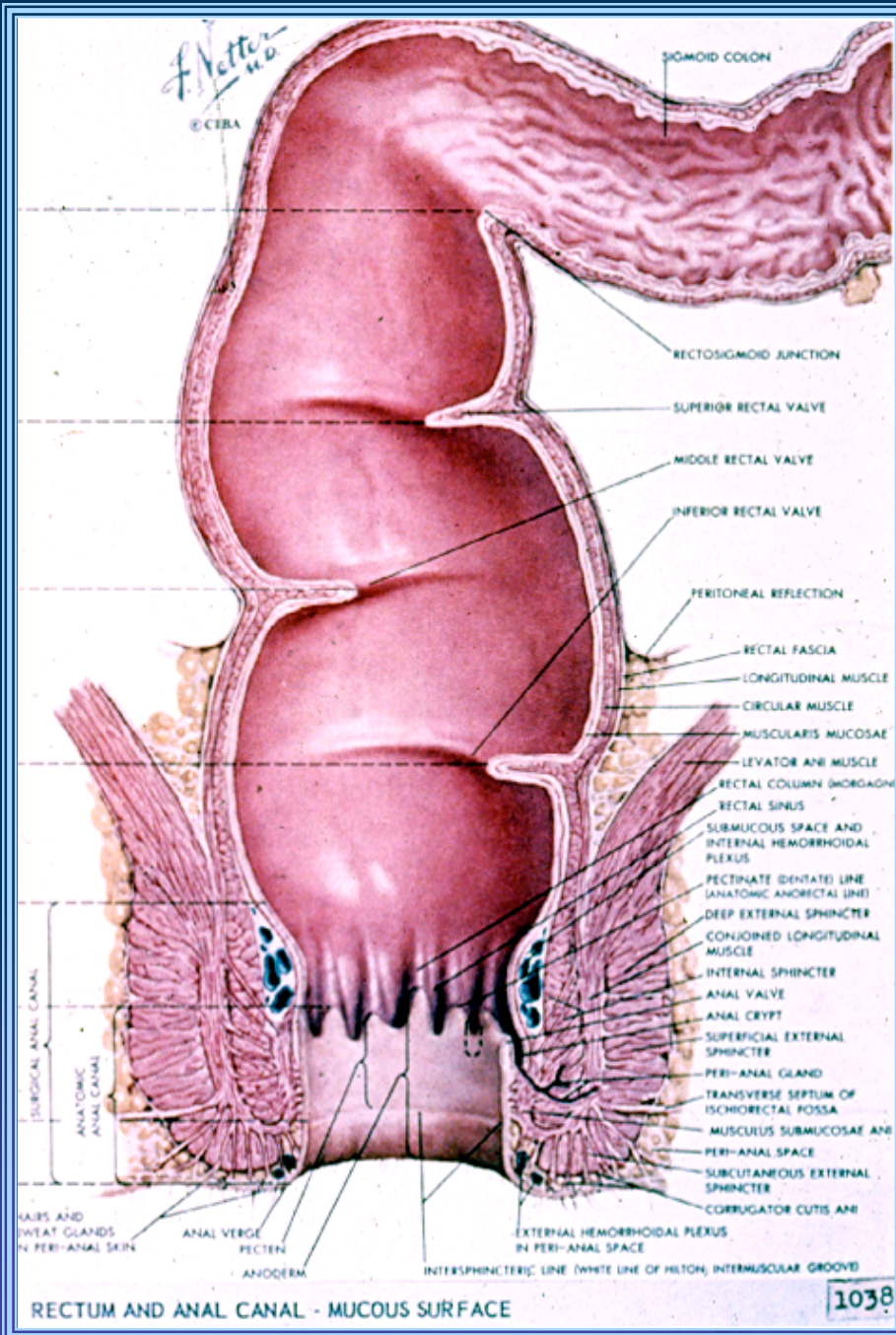


Figure 9–12. The lower third of the anorectal canal is formed by an ectodermal invagination called the anal pit. The border between the superior end of the anal pit and the inferior end of the rectum is demarcated by mucosal folds called the pectinate line in the adult.

**Hindgut
forms
superior 2/3
of rectal
canal;
proctodeum
forms lower
1/3; divided
at pectinate
line**

Never forget
the pectinate
line



If anything can go wrong it will; anorectal malformations

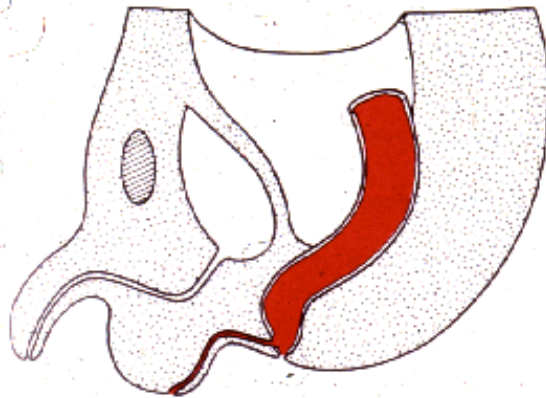


Fig. 2. — Imperforate anus with scrotal fistula.

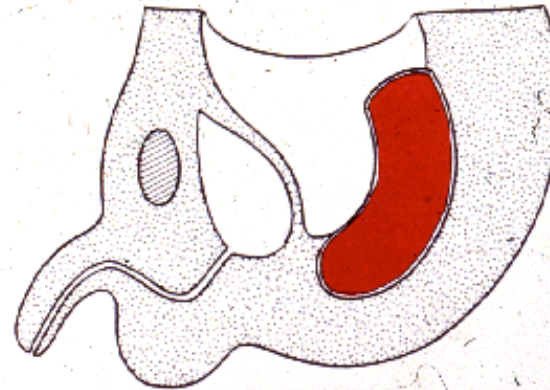


Fig. 3. — Rectal atresia.

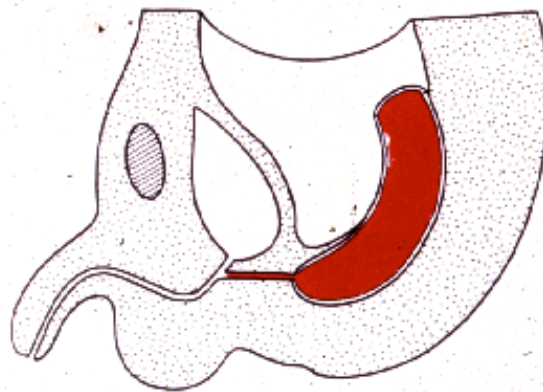


Fig. 4. — Rectal atresia with urinary fistula.

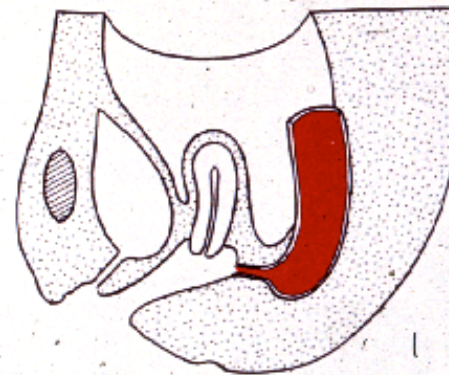


Fig. 5. — Rectal atresia with vaginal fistula.

The END

Have a nice day!

