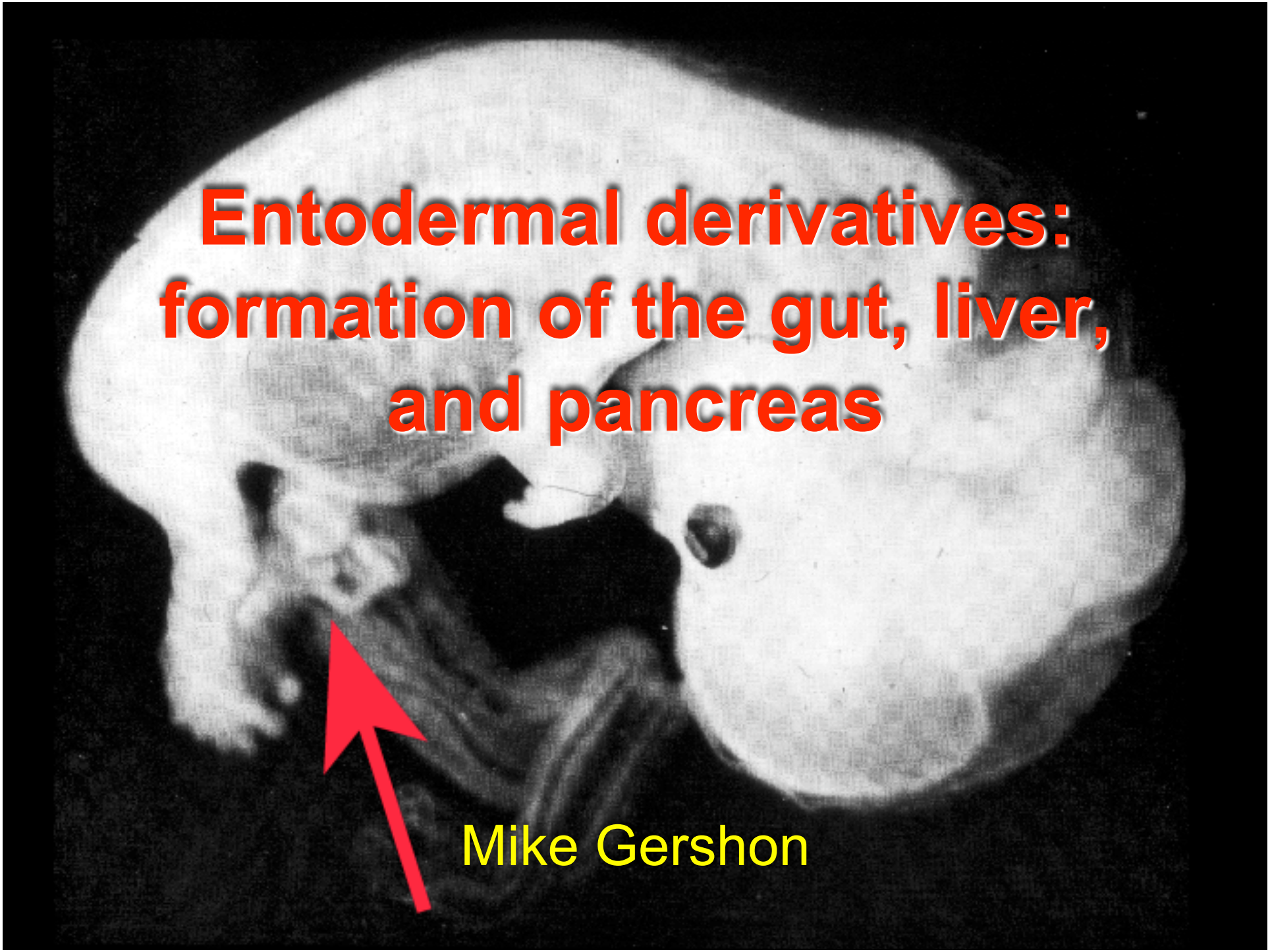
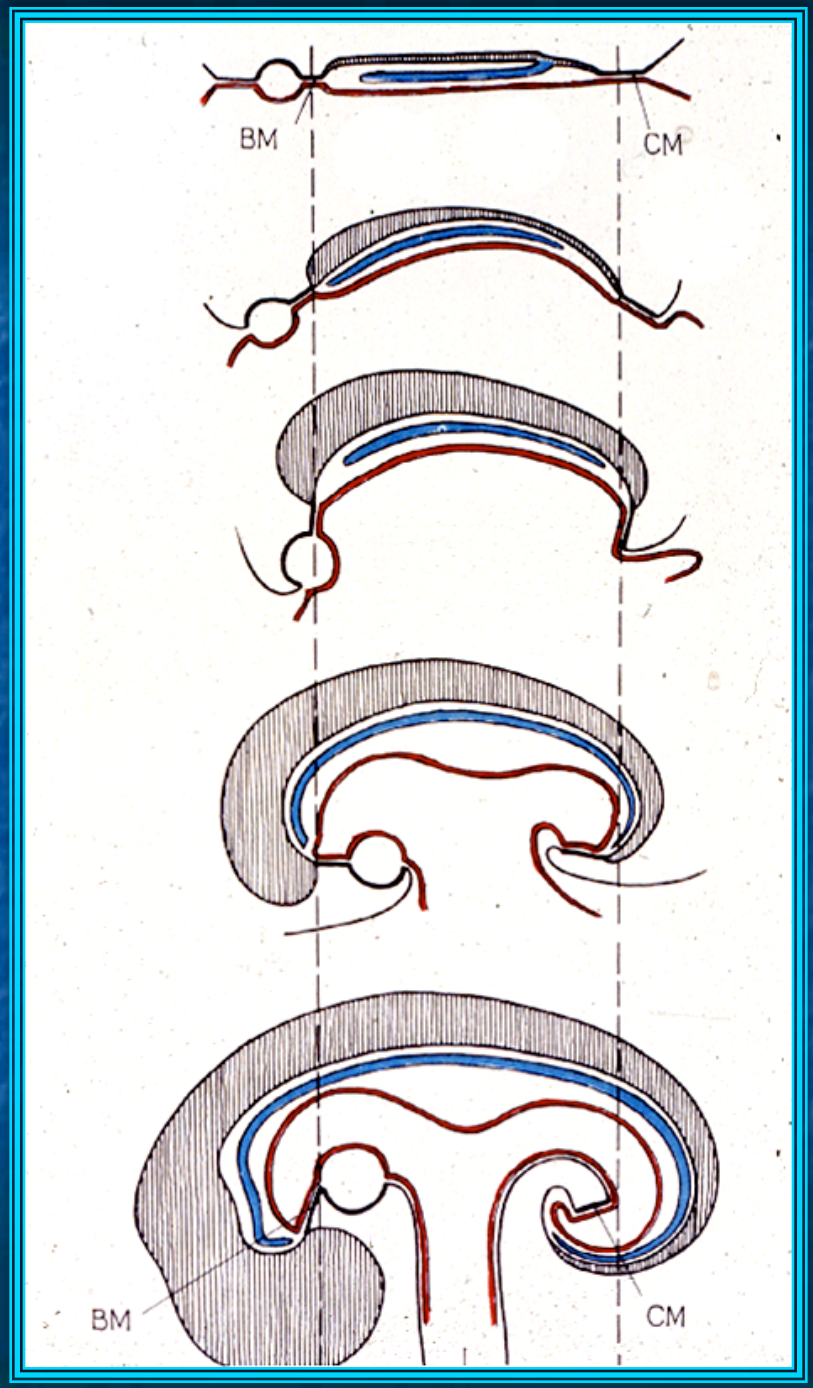
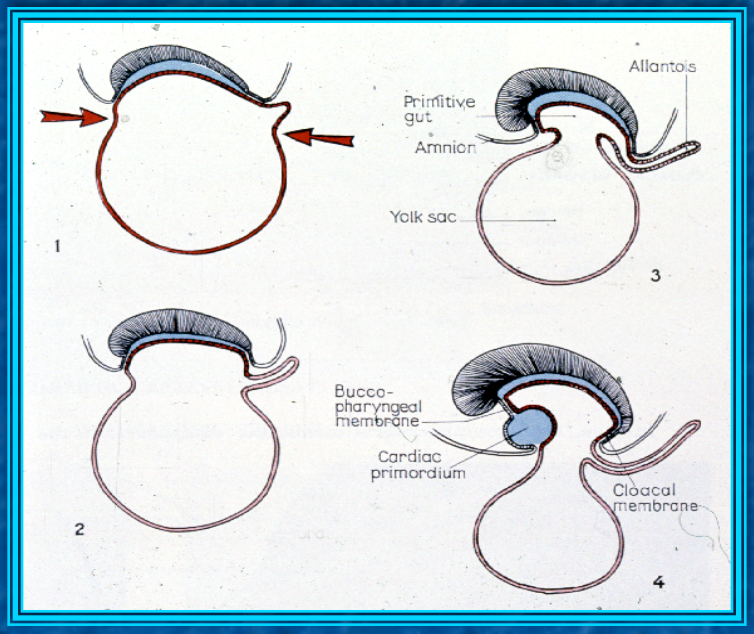

Entodermal derivatives:
formation of the gut, liver,
and pancreas
Mike Gershon

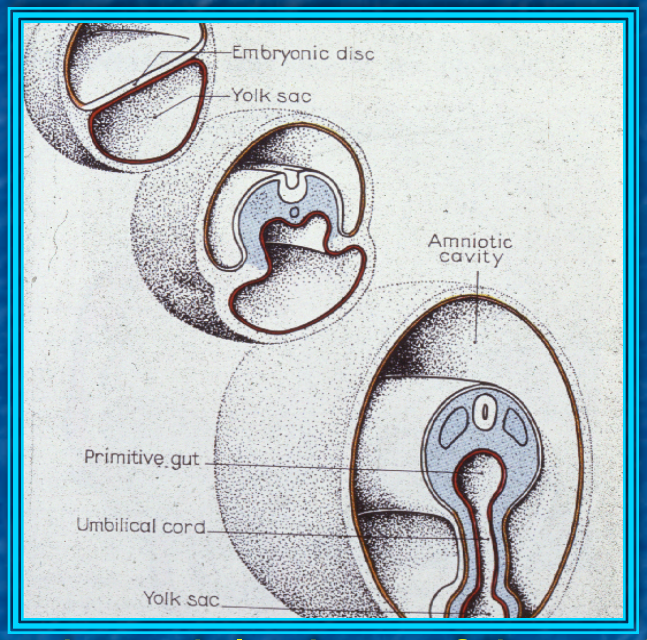


Folding forms the gut

- 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.

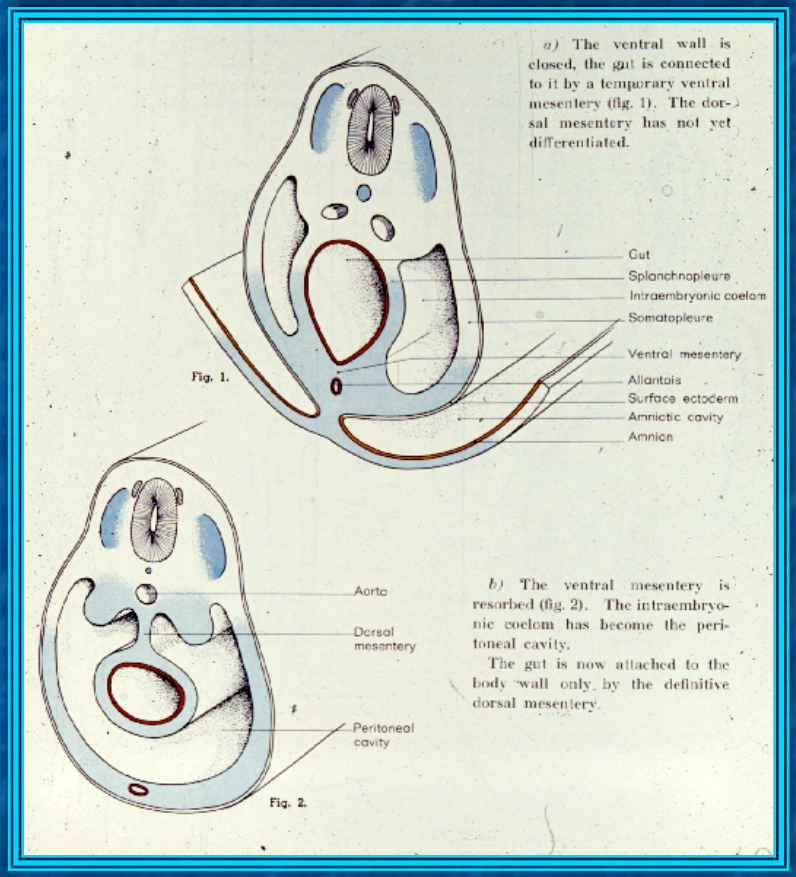
Cephalocaudal and lateral folding occur simultaneously

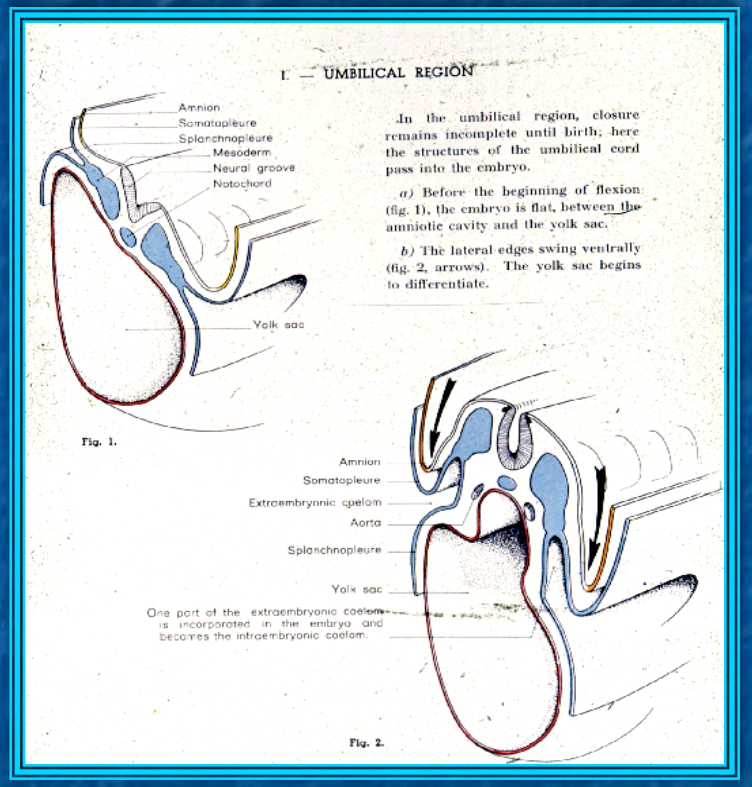




- Meeting and fusion of cranial, lateral, and caudal edges of the embryo create the primordial foregut and hindgut
  - Slow fusion of midgut-due to presence of yolk sac. Midgut remains open until week 6-connects to yolk sac via *vitelline duct*.
  - Buccopharyngeal membrane opens at 4 and cloacal membrane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

Flexion delimits the bowel





- After the gut forms, it is attached to the body wall by dorsal and ventral mesenteries; ventral is lost except in region of liver. Vitelline duct remains in umbilical cord.

IN CROSS SECTION

c) The ventral wall begins to form (fig. 3). The gut is delineated, surrounded by intra-embryonic coelom.

d) At the level of the umbilicus, the ventral wall does not close completely (fig. 4).

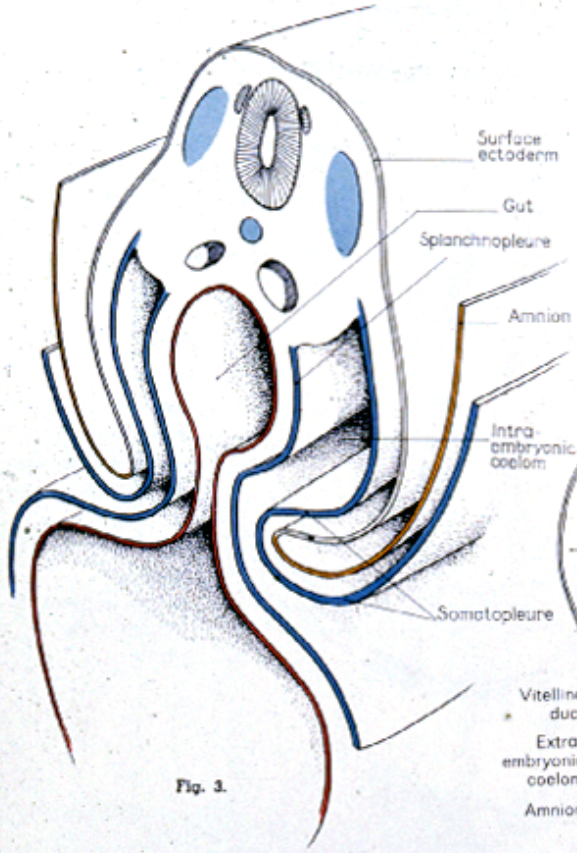


Fig. 3.

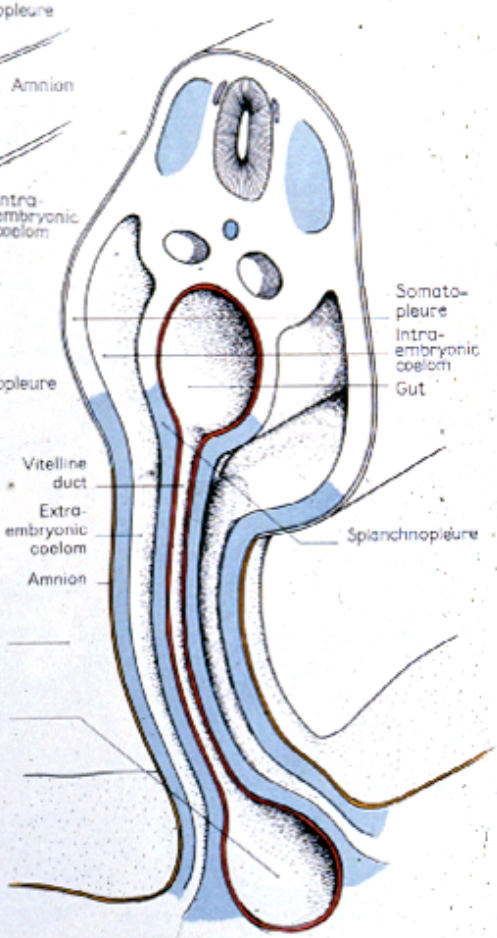
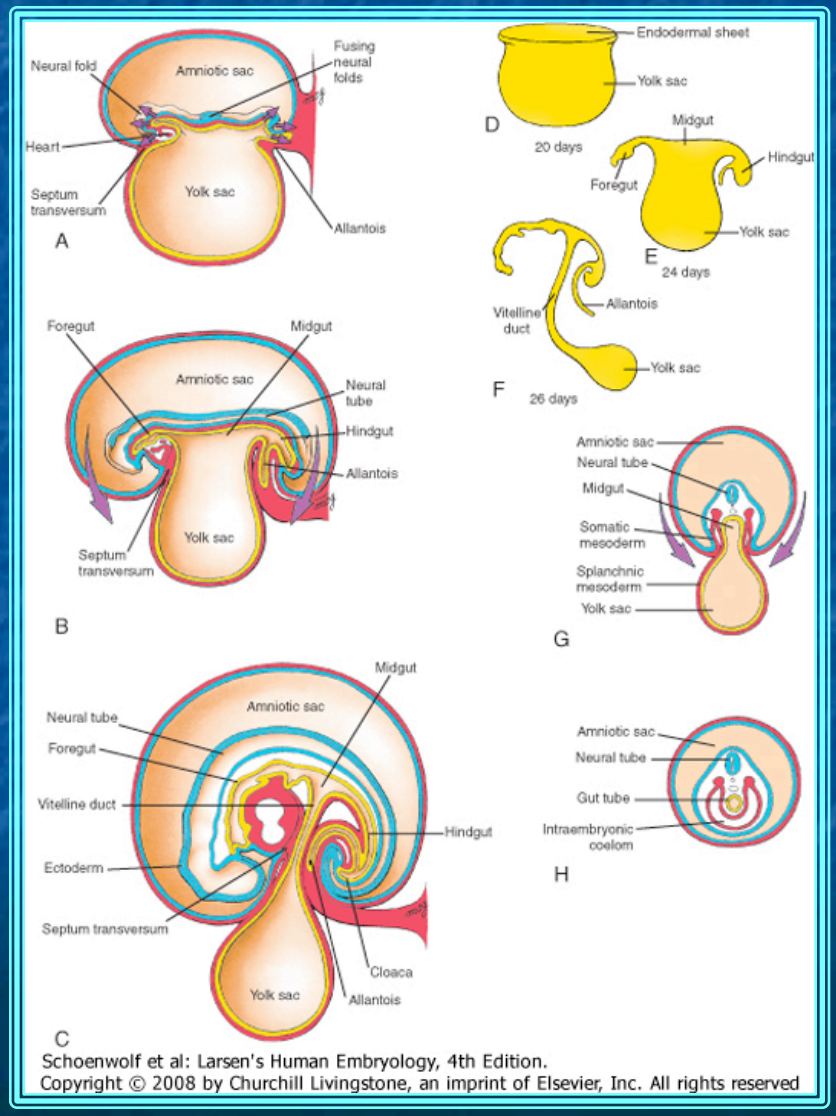


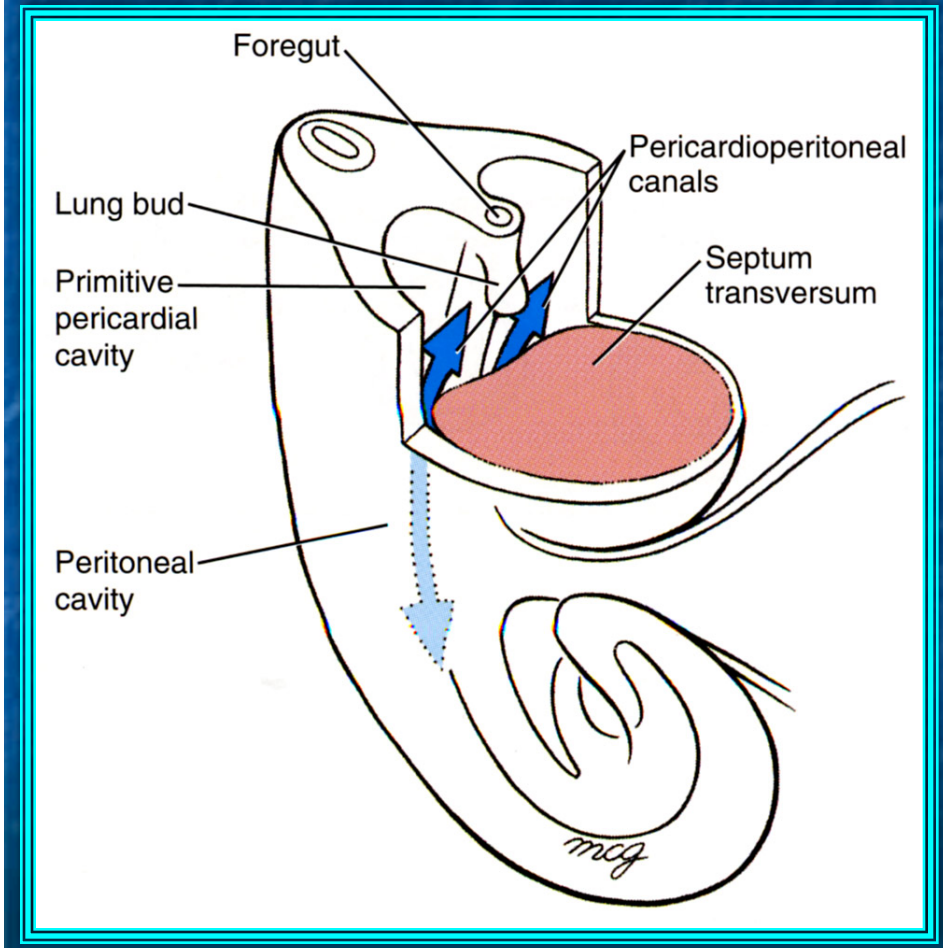
Fig. 4.

Anterior-posterior and lateral folding form the primitive gut



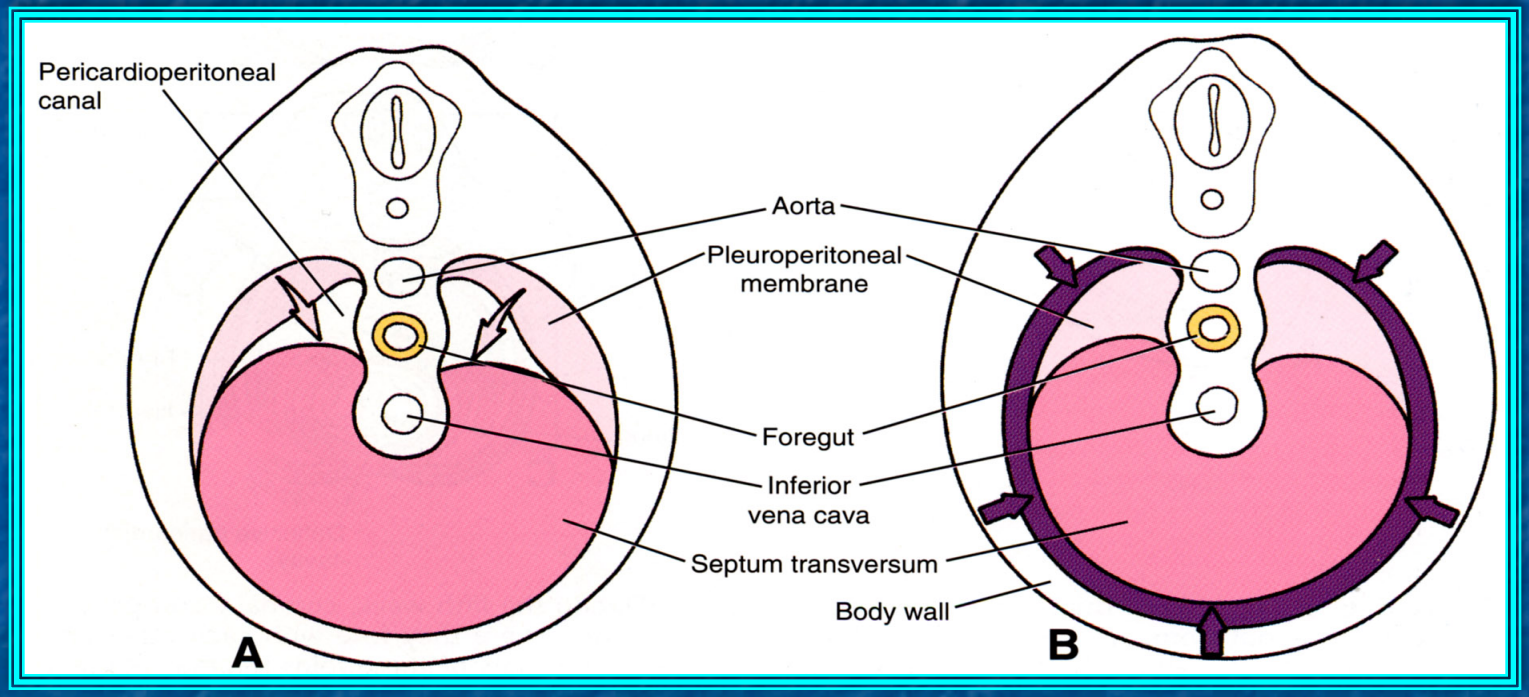
- Embryonic disc grows faster in length than the yolk sac causing the embryo to bend.
  - Dorsal surface grows more rapidly than the ventral
- Lateral folding
  - Fusion with apposing side except in the region of the yolk sac, and allantois
- Folding brings the heart and septum transversum caudal to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

The septum transversum partially separates the thoracic and abdominal cavities



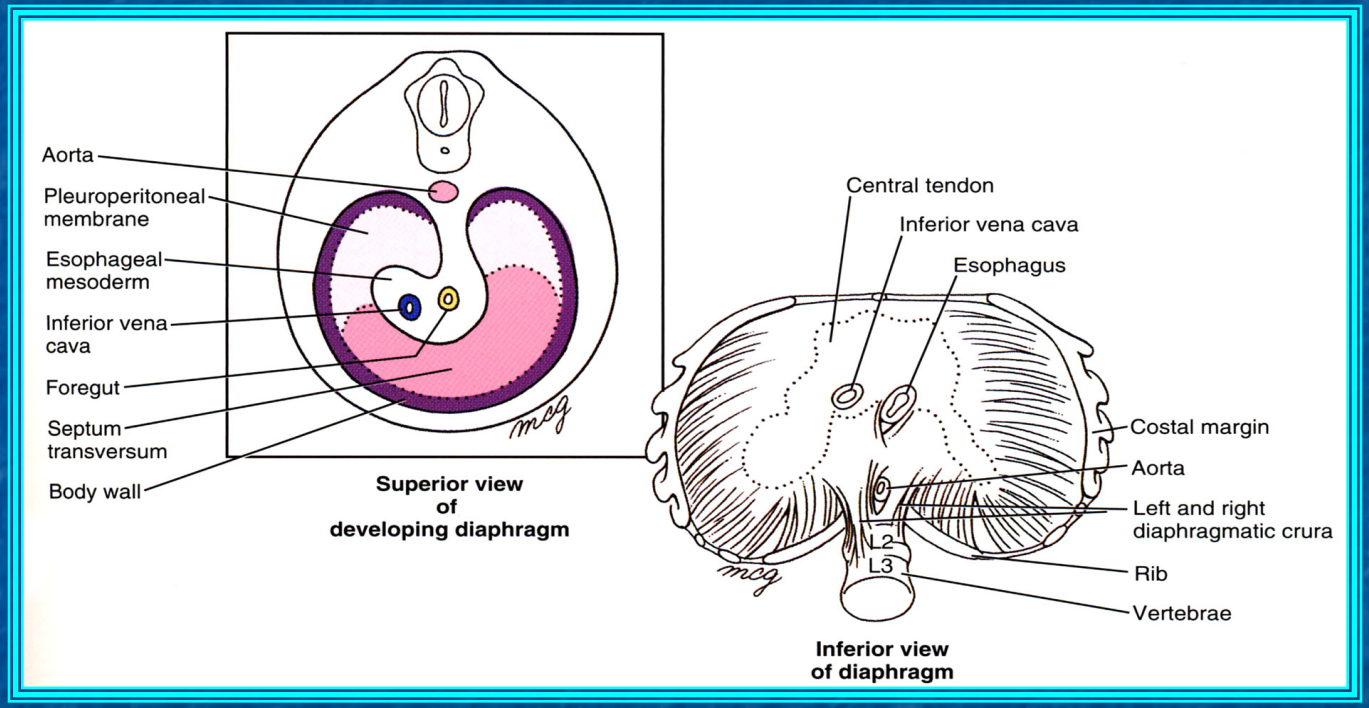
- The superior portion is the primitive pericardial cavity.
- The inferior portion is the future peritoneal cavity.
- The pericardial and peritoneal cavities communicate through the pericardioperitoneal canals

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

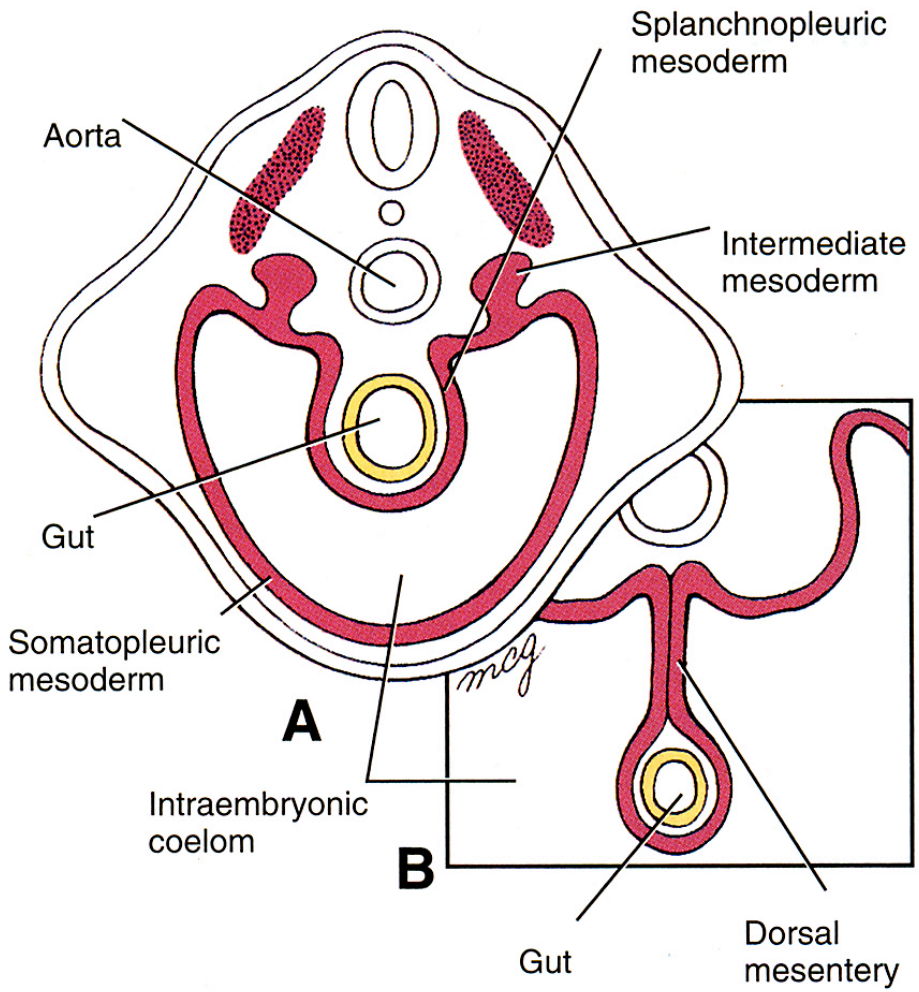
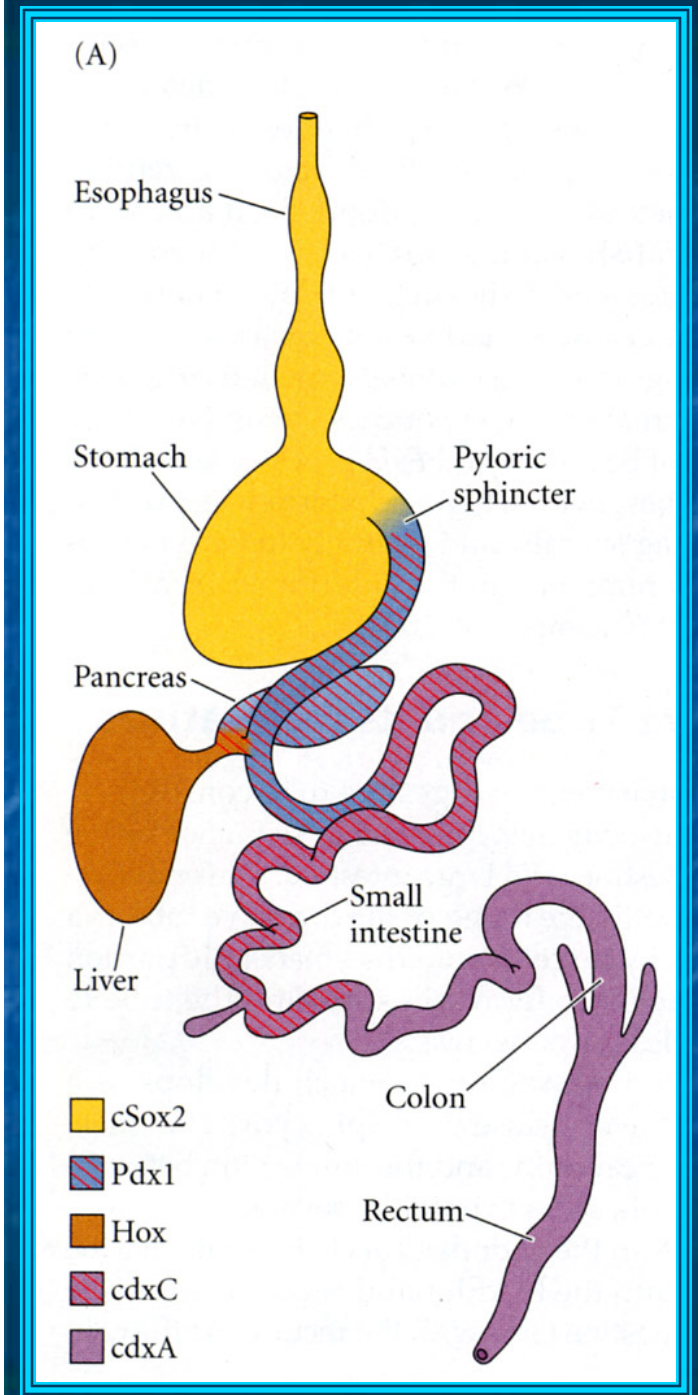


Figure 6–3. Formation of the dorsal mesentery. *A,* The primitive gut tube initially hangs from the posterior body wall by a broad bar of mesenchyme but, *B,* in regions inferior to the septum transversum this connection thins out to form a membranous dorsal mesentery composed of reflected peritoneum.

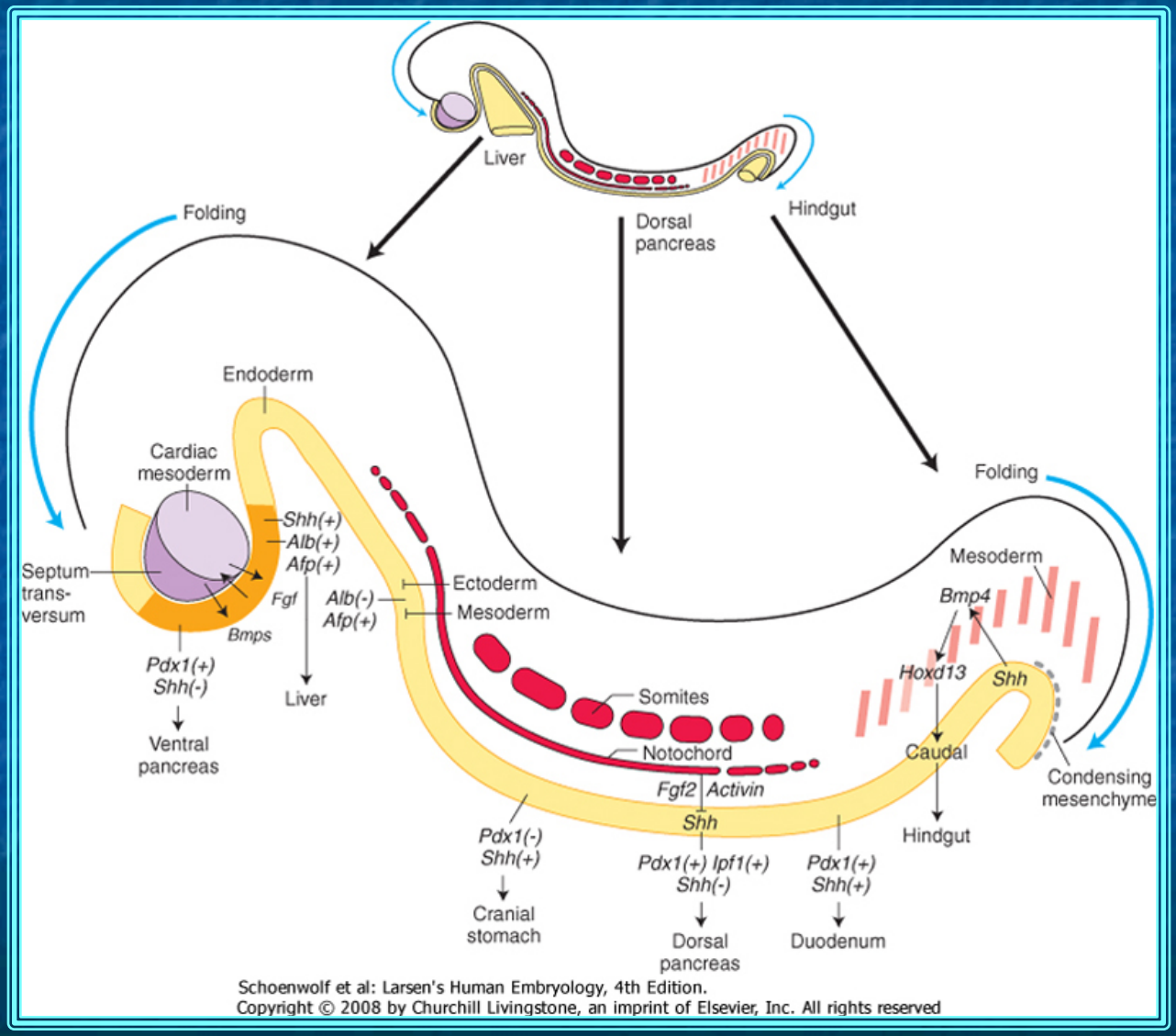
The dorsal mesentery thins to allow the gut to be flexibly suspended



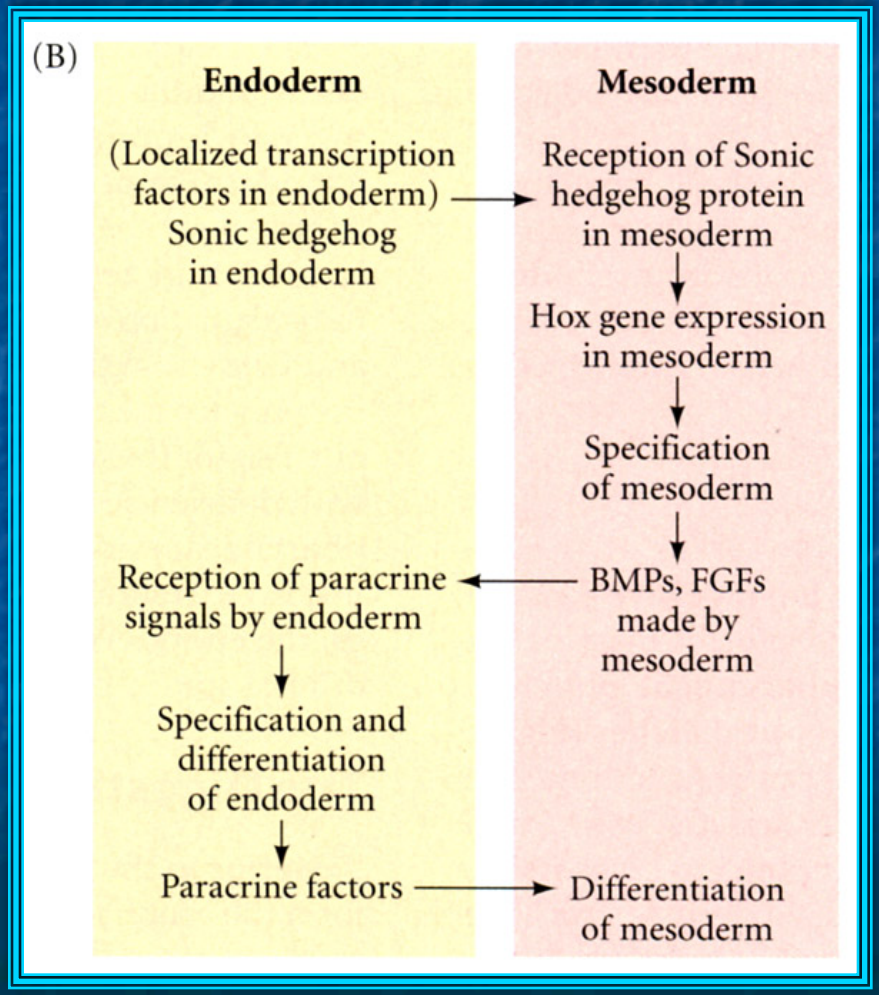
The gut is regionally specified early in development

- 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

Signals and transcription factors specify regionalization of the gut

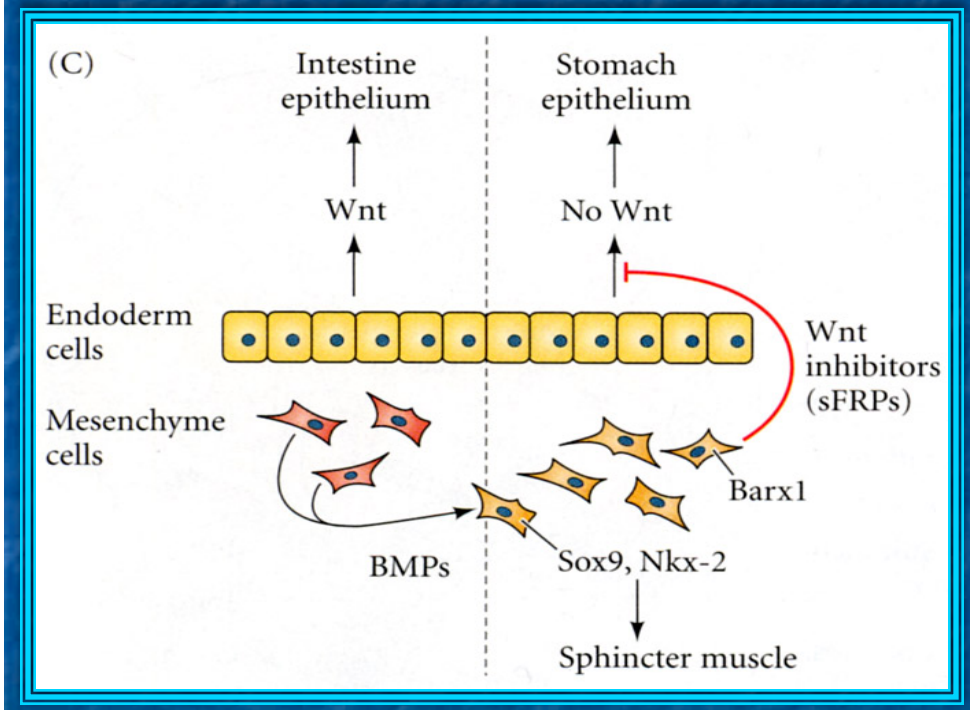


The boundaries of GI regions are set by endodermal mesodermal cross-talk



- 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

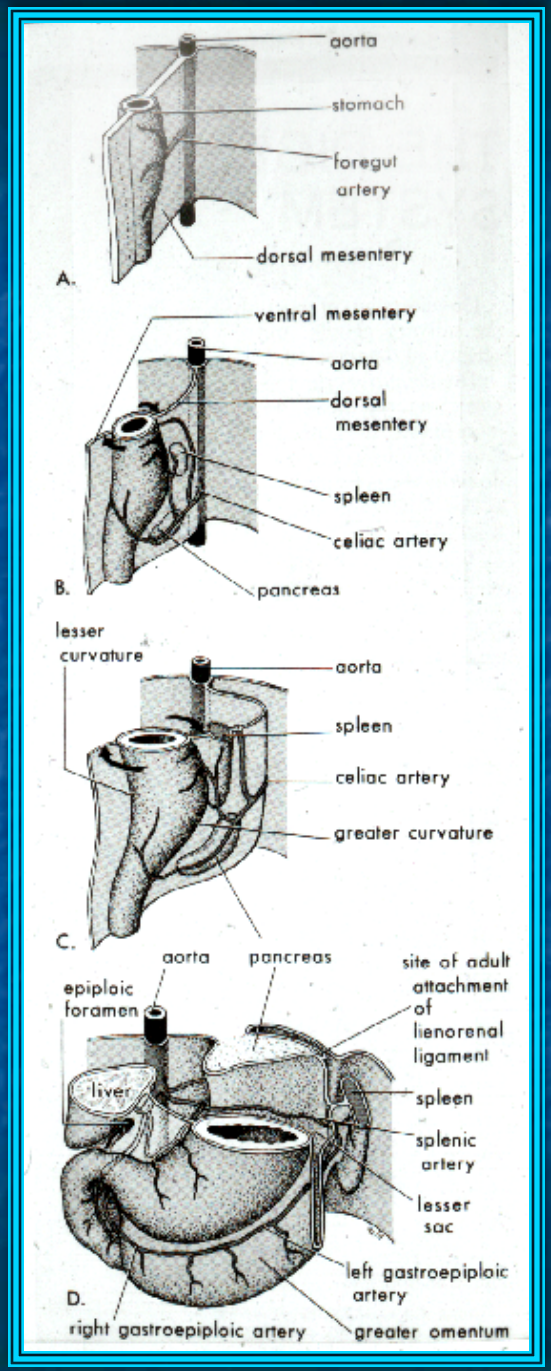


- Wnt signaling specifies intestinal epithelium.
  - Wnt = intestine
  - No Wnt = stomach
- Mesenchyme of stomach expresses Barx1 and secretes Wnt inhibitors (SFRP1, 2).
- Mesenchyme of intestine secretes BMP4
  - Induces mesenchyme anterior to it to express Sox9 + Nkx-2
  - Become pyloric sphincter

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

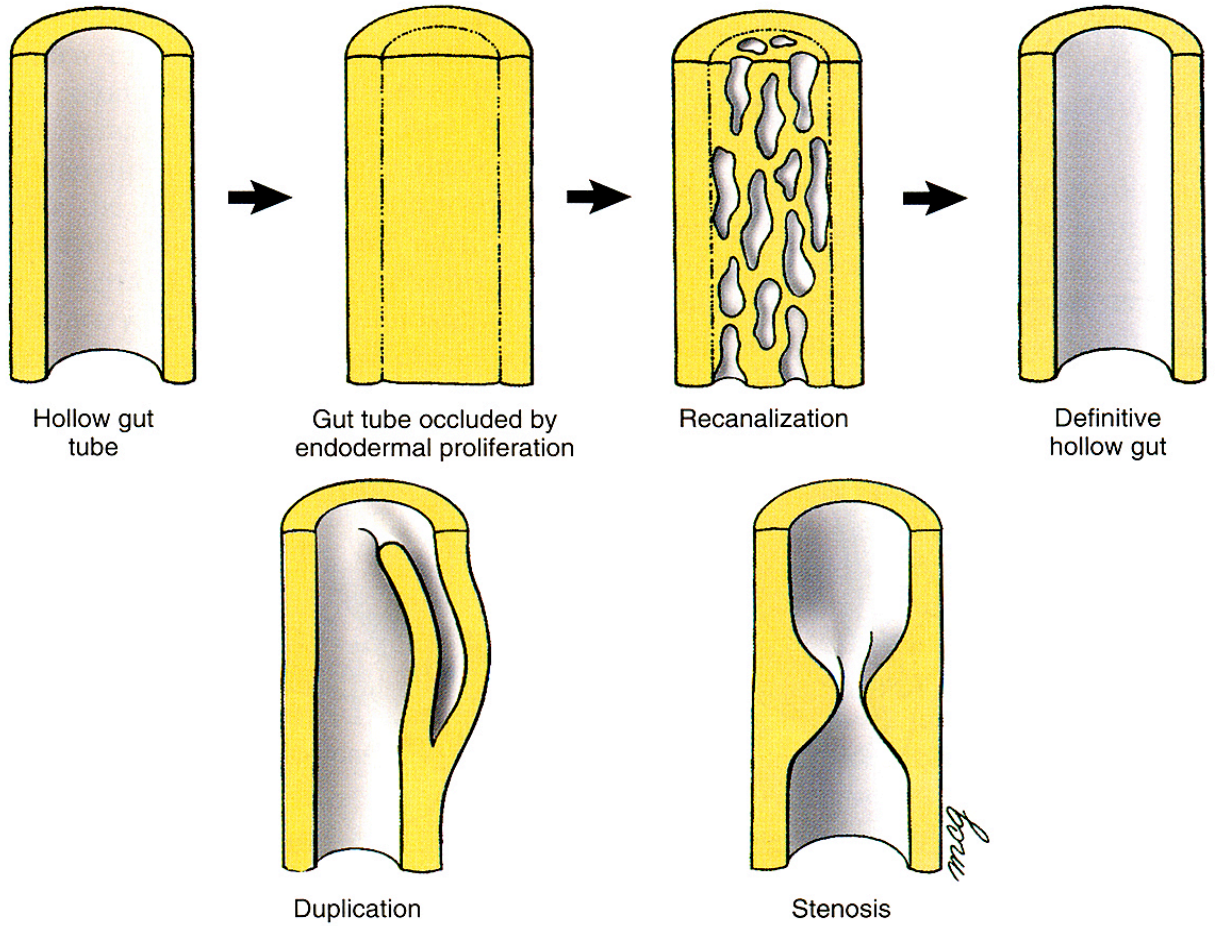


Figure 9–13. Formation of the definitive gut lumen. Proliferation of the endodermal lining completely occludes the gut tube during the sixth week. Recanalization is completed by week 9. Incomplete or abnormal recanalization may result in duplication of the lumen or stenosis of the gut tube.

The stomach rotates 90° in a clockwise direction

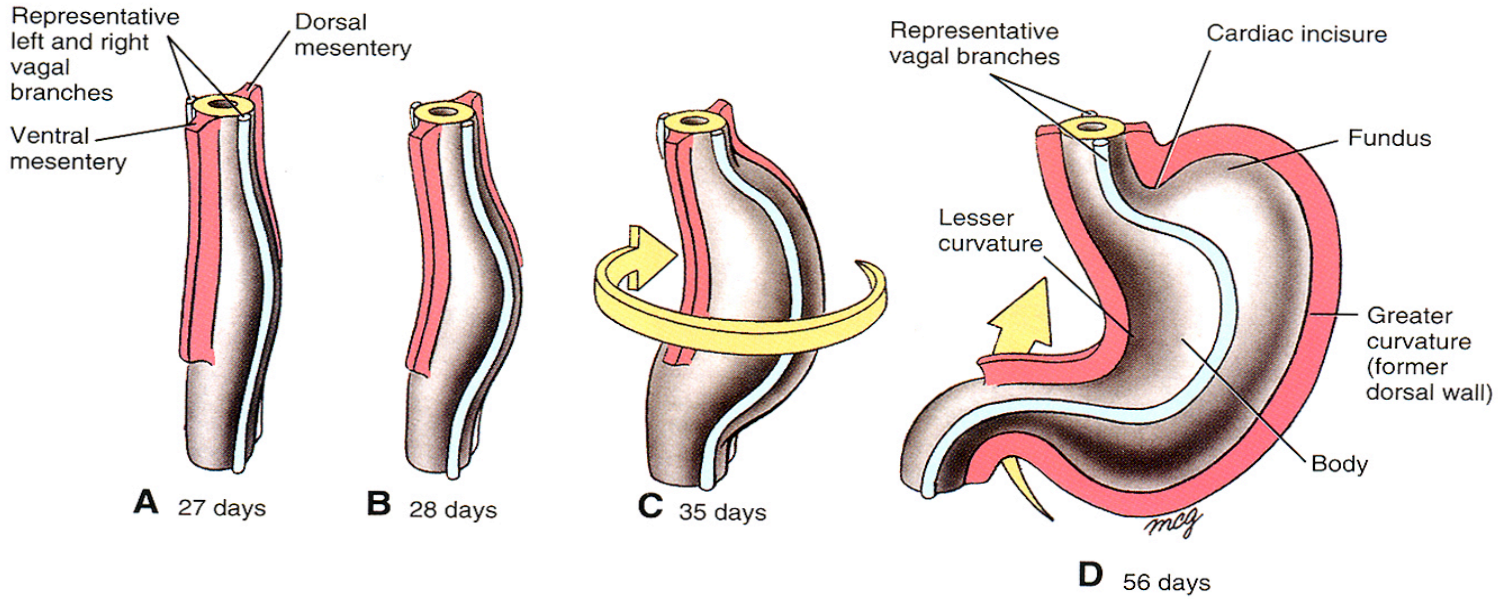
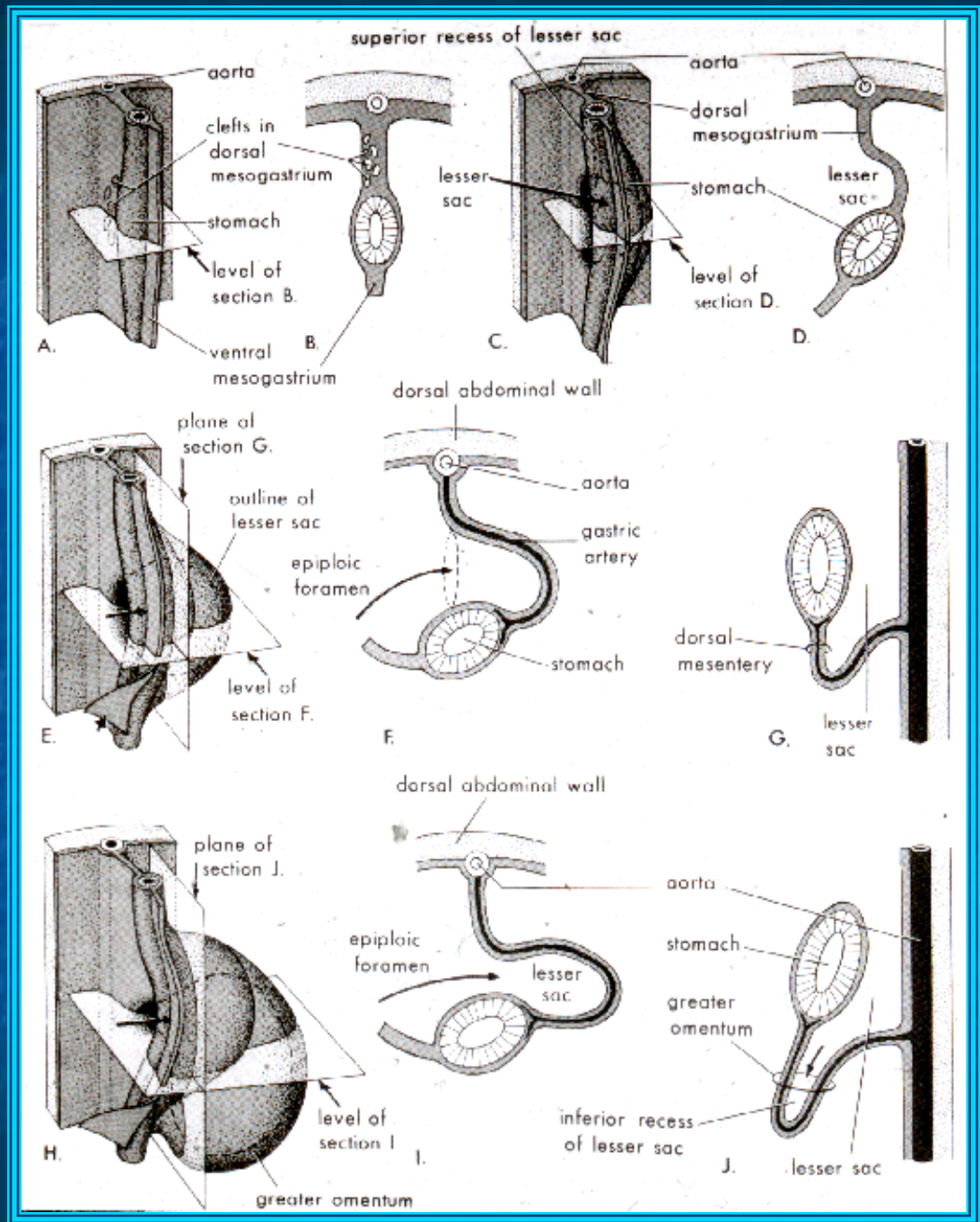


Figure 9–3. Rotations of the stomach. *A–C,* Oblique frontal views; *D,* direct frontal view. The posterior wall of the stomach expands during the fourth and fifth weeks to form the greater curvature. During the seventh week, the stomach rotates clockwise on its longitudinal axis (when viewed from above).

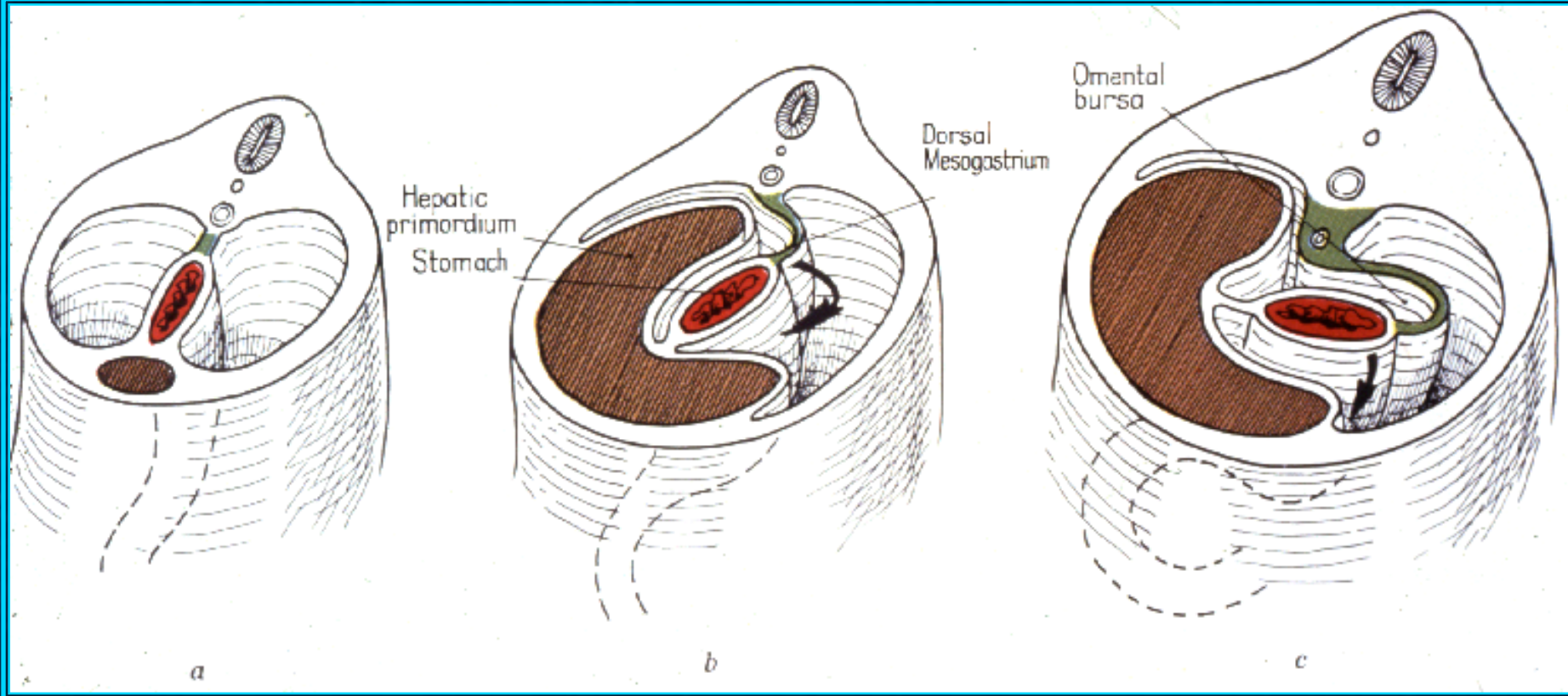
- Dorsal surface grows faster than the ventral to create the greater and lesser curvature. Acquires a transverse position



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

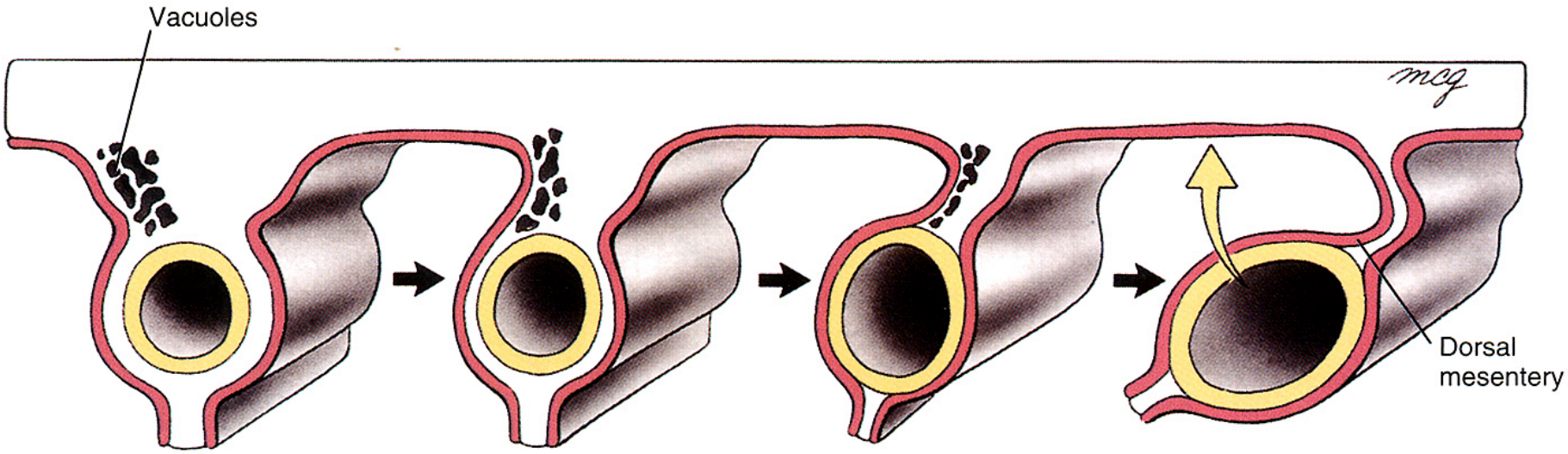


Figure 9–4. The rotation of the stomach around its longitudinal axis commences with vacuolization of the right side of the thick mesenchymal bar that initially suspends the stomach from the posterior body wall.

Liver, biliary system **and** pancreas arise from the duodenum

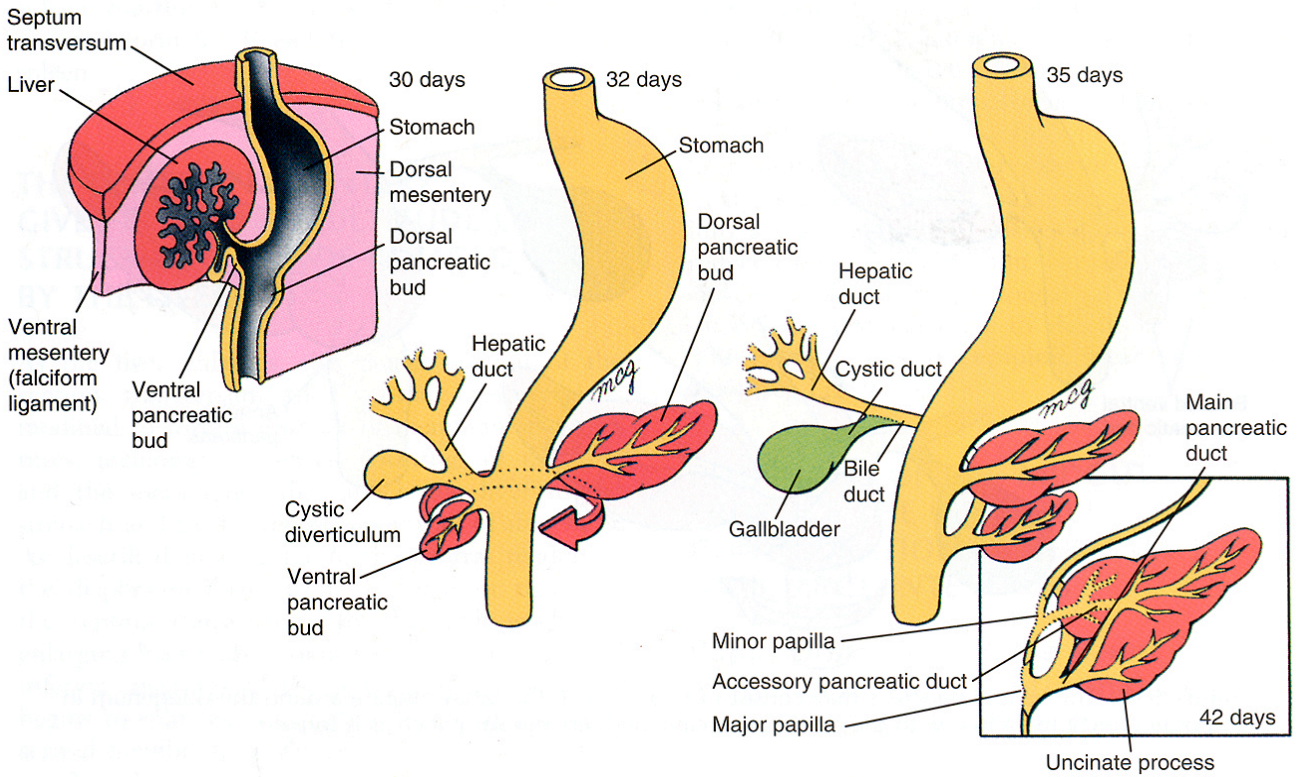
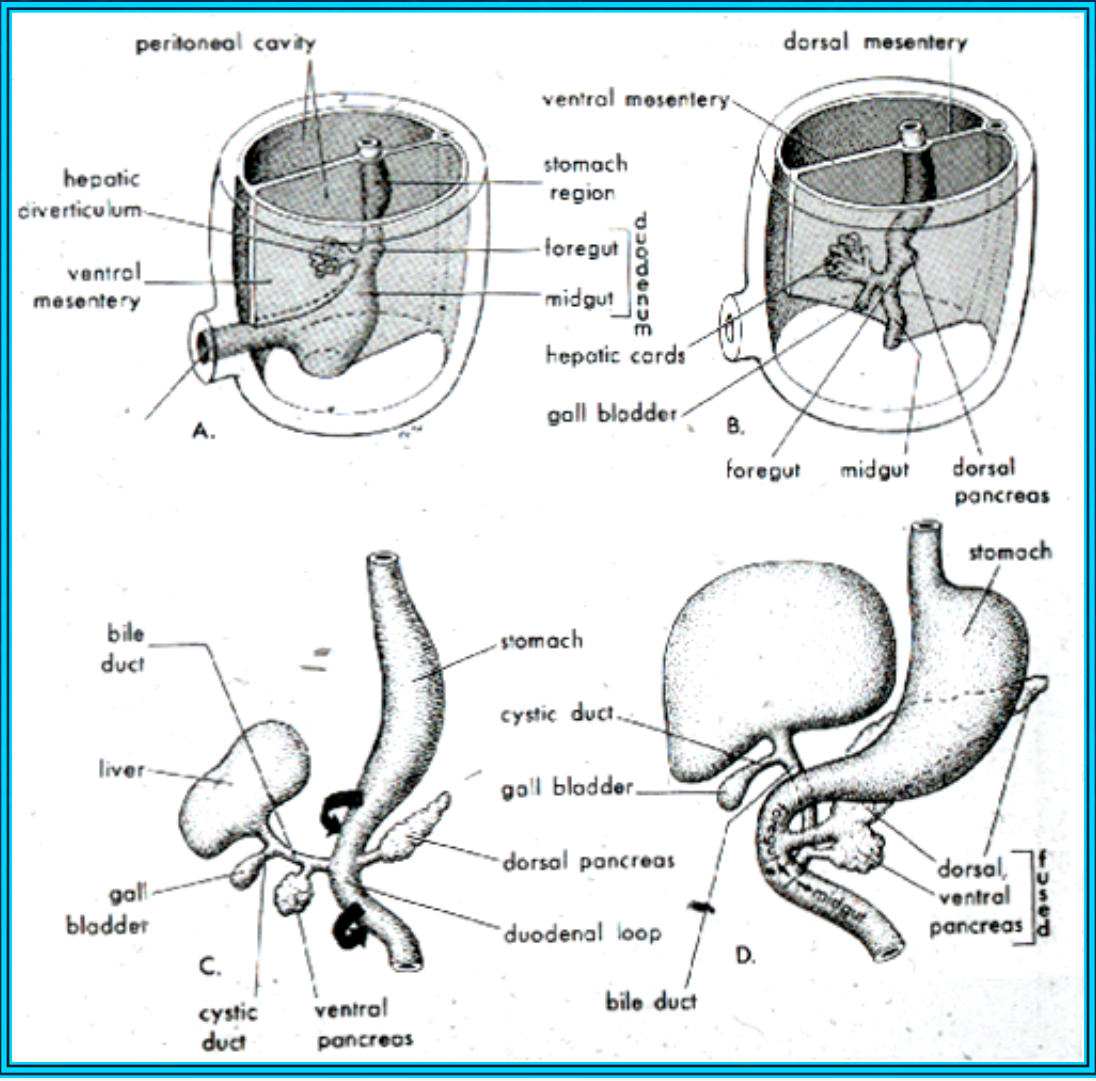


Figure 9–6. Development of the liver, gallbladder, pancreas, and their duct systems from endodermal diverticula of the duodenum. The liver bud sprouts during the fourth week and expands in the ventral mesentery. The cystic diverticulum and ventral pancreatic bud also grow into the ventral mesentery, 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

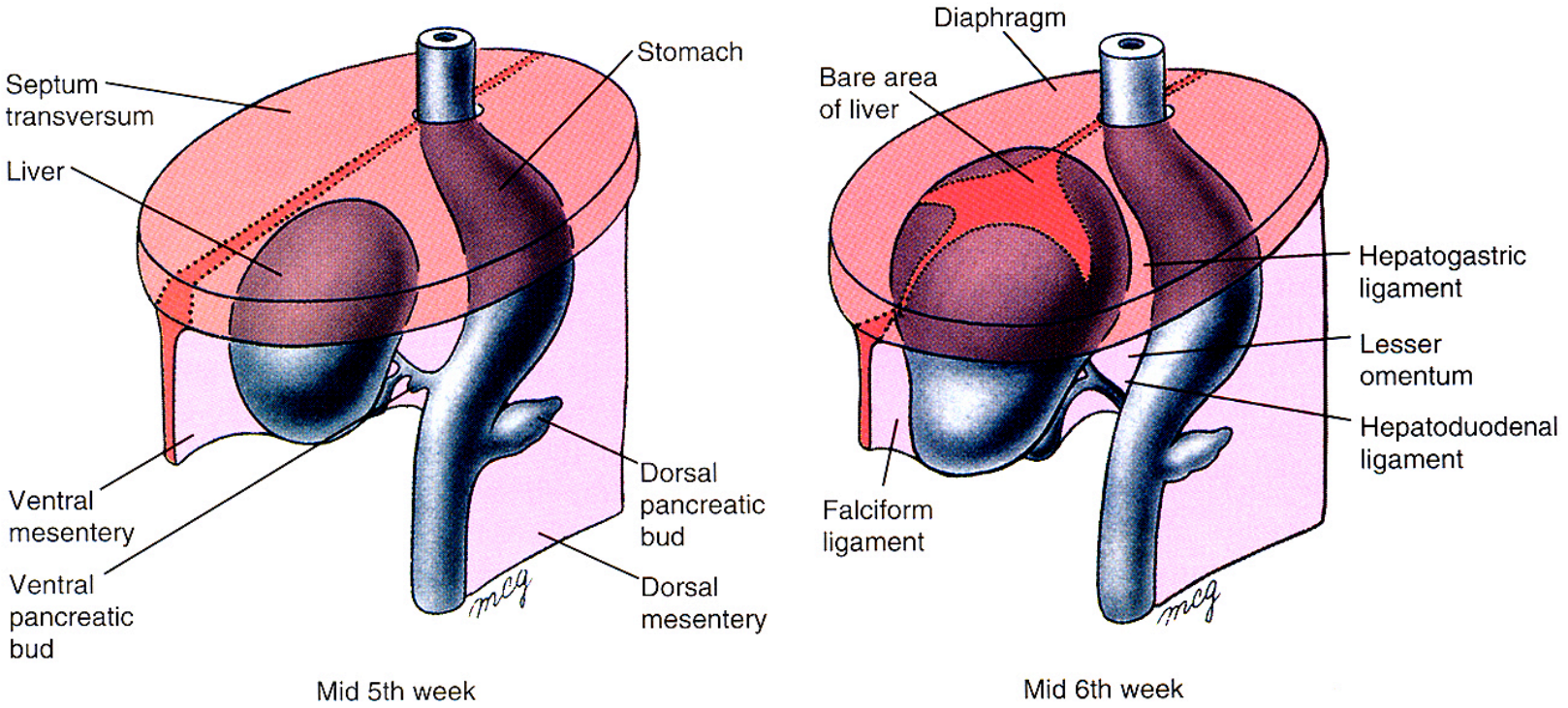
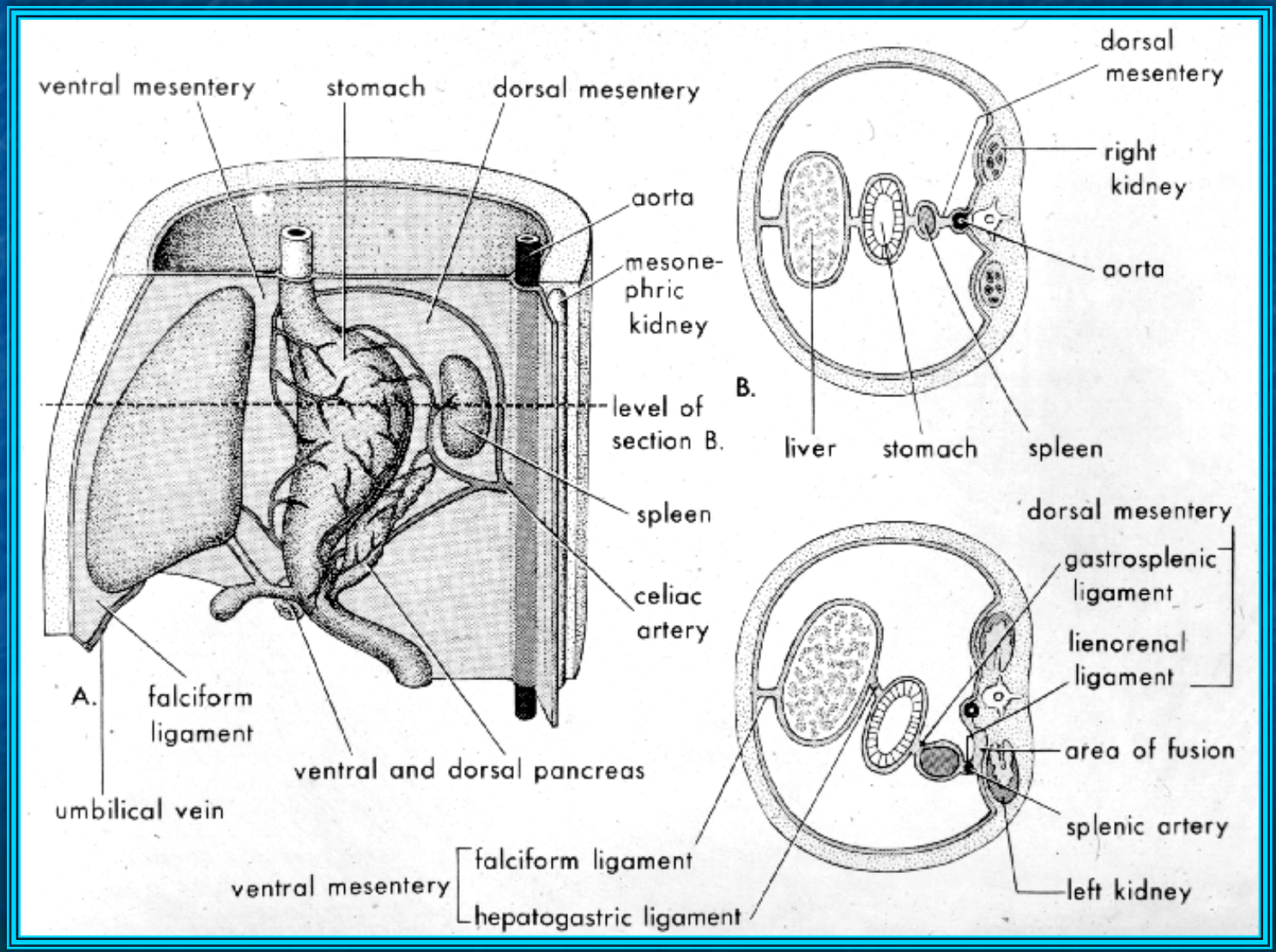
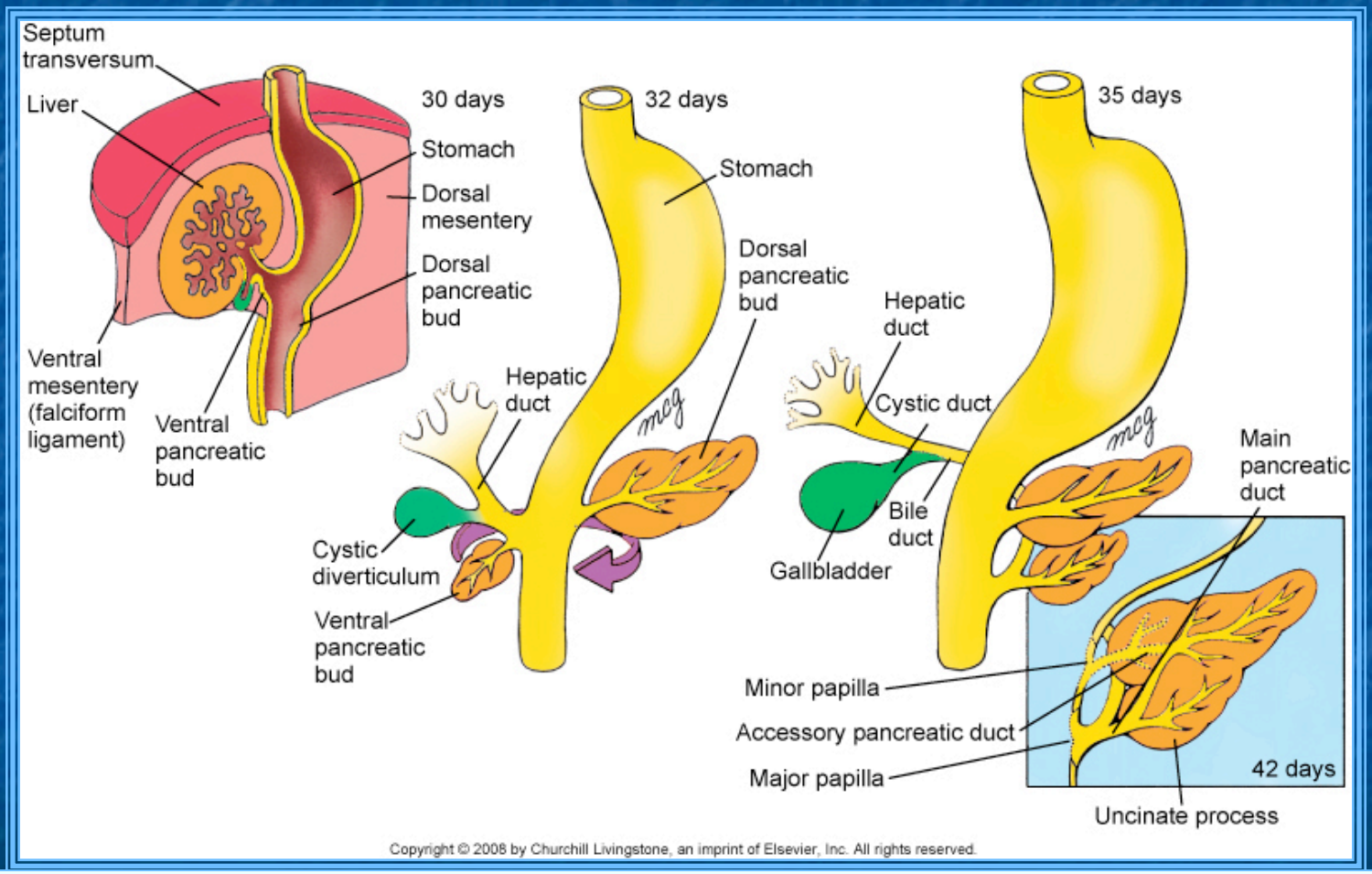


Figure 9–8. Formation of the liver and associated membranes. As the liver bud grows into the ventral mesentery, its expanding crown makes direct contact with the developing diaphragm. The ventral mesentery that encloses the growing liver bud differentiates into the visceral peritoneum of the liver, which 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 uncinate process and inferior part of the head of the pancreas

Aberrant rotation causes an annular pancreas

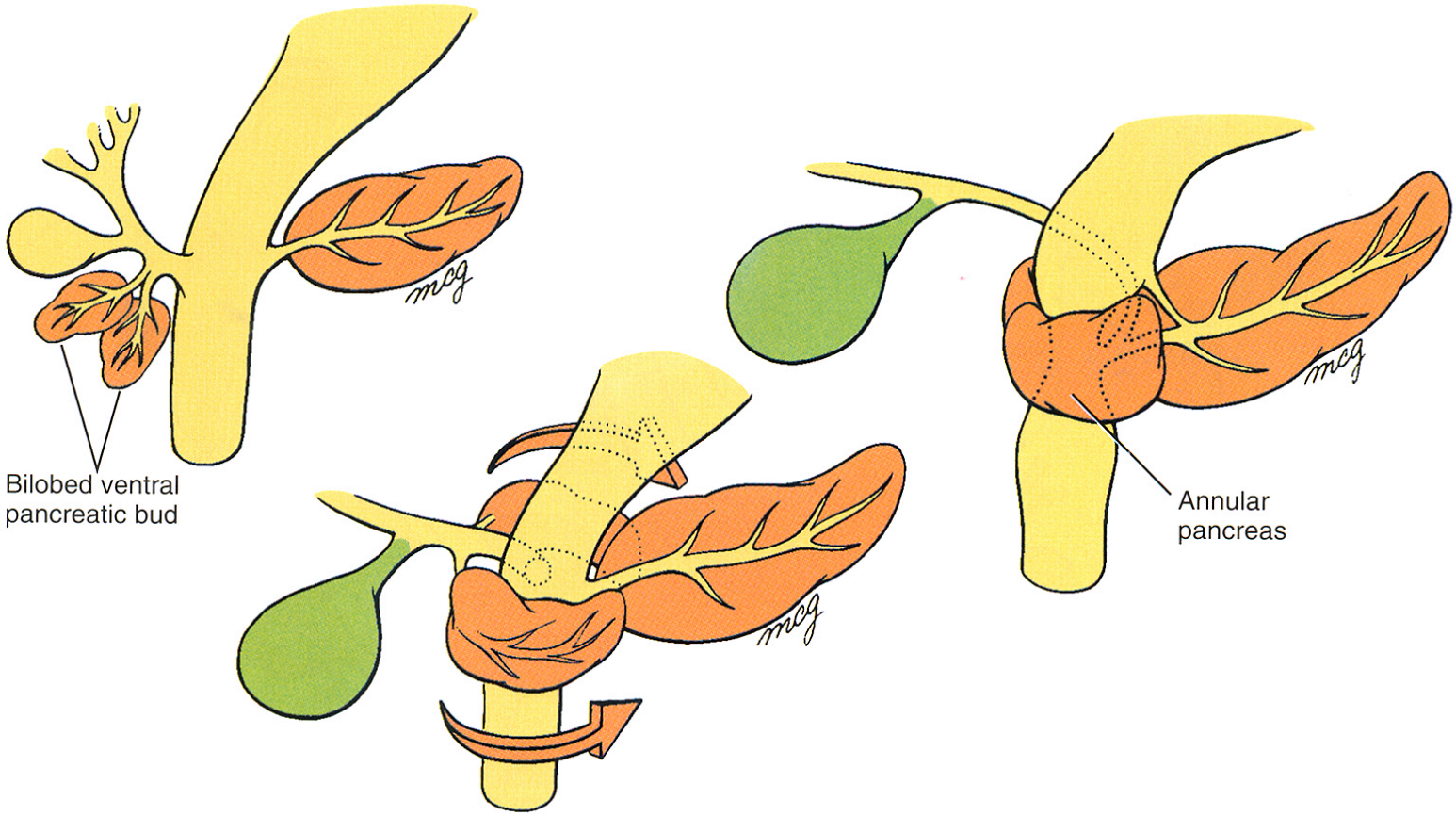
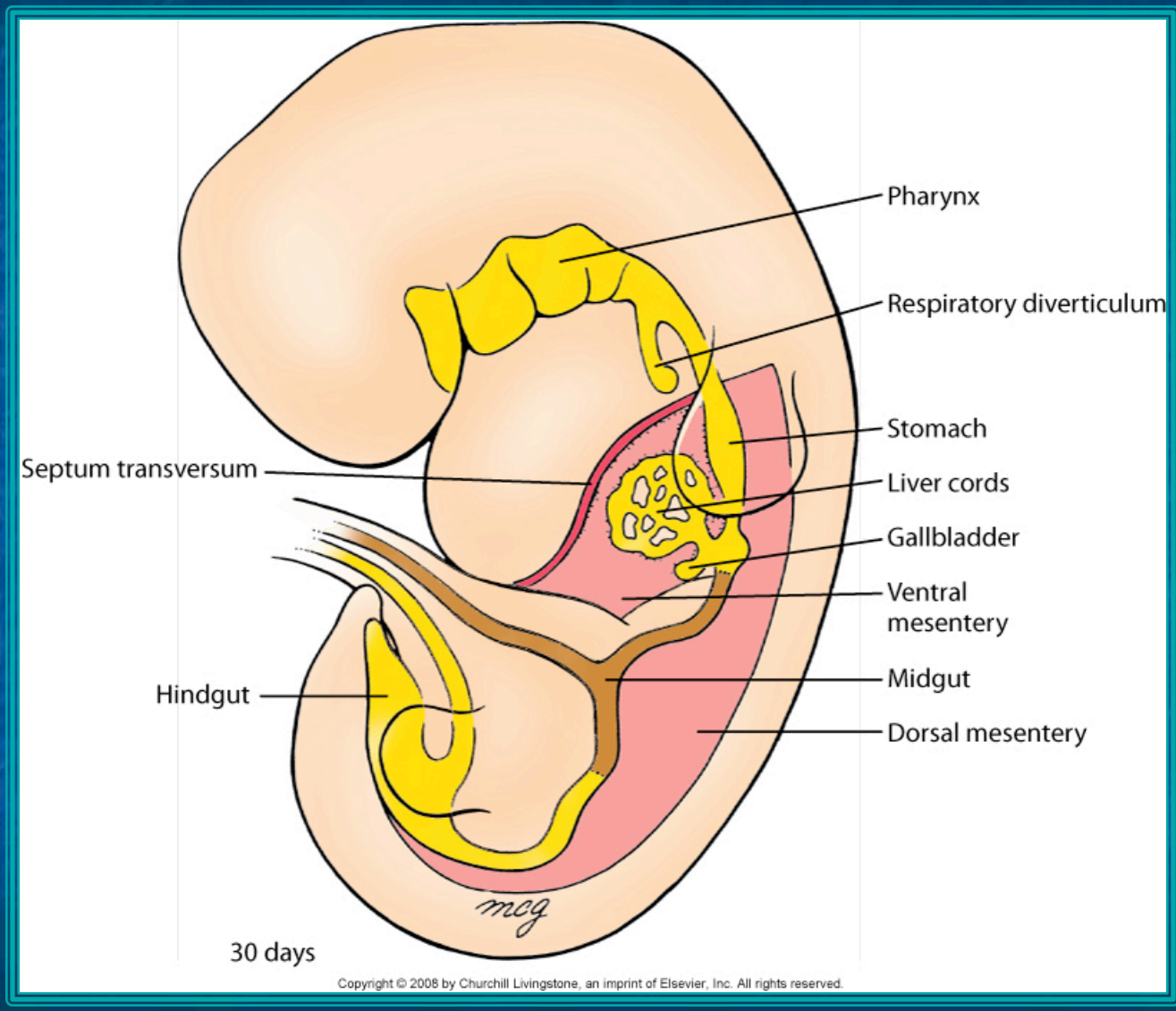


Figure 9–7. The ventral pancreas may consist of two lobes. If the lobes migrate around the duodenum in opposite directions to fuse with the dorsal pancreatic bud, an annular pancreas is formed.

Review of the Gut Tube



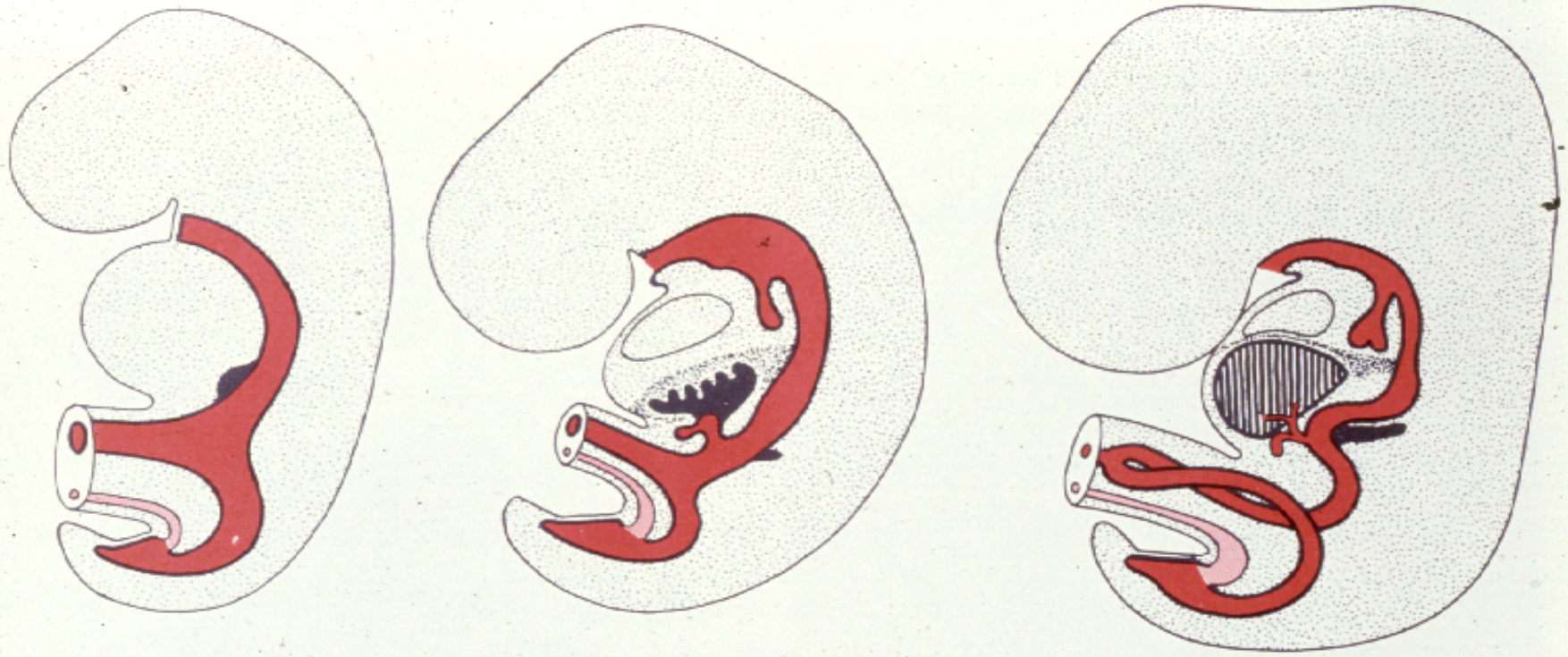
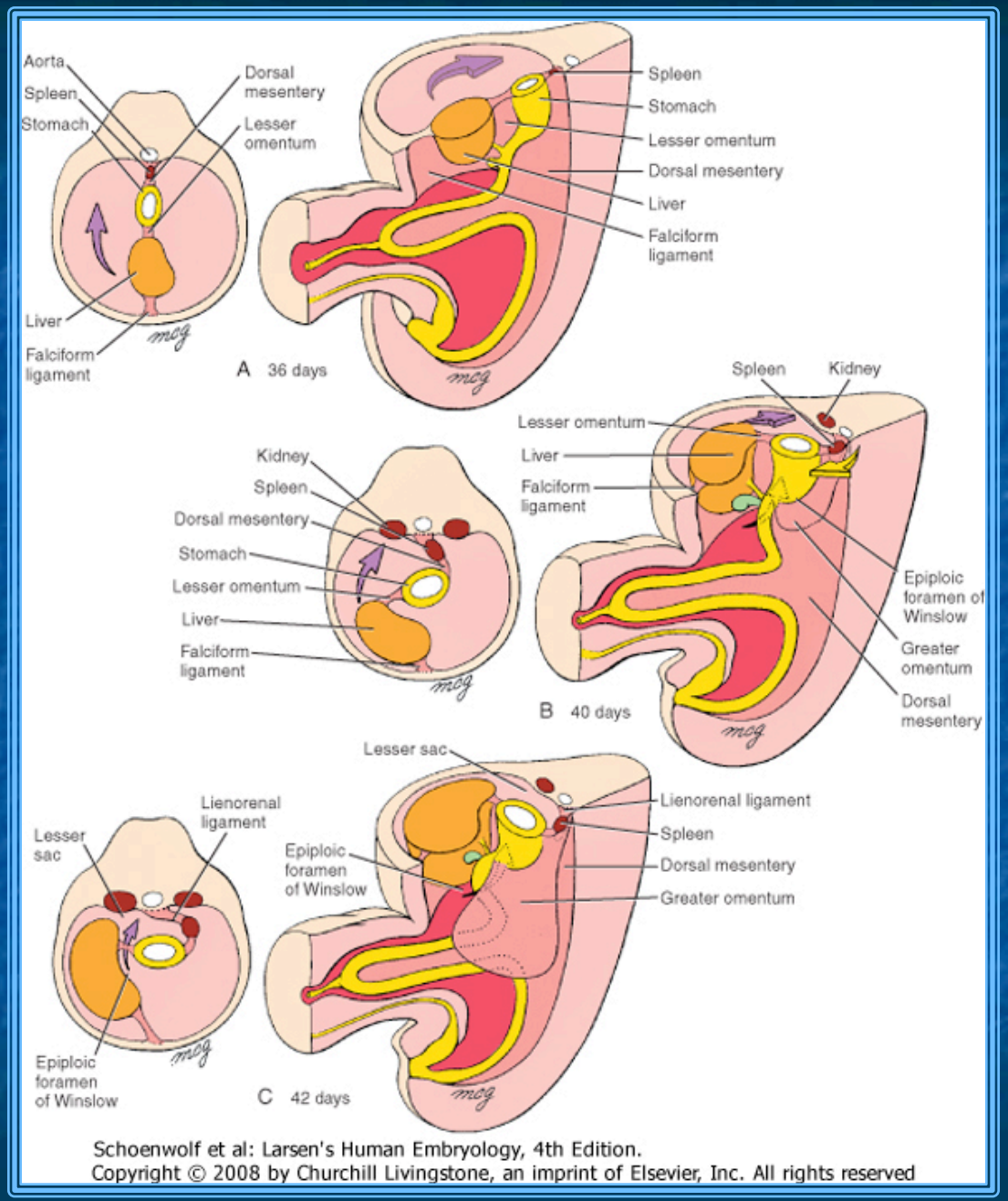


Fig. 1. — *Diagrammatic sagittal sections of human embryos.*

Derivatives of the midgut

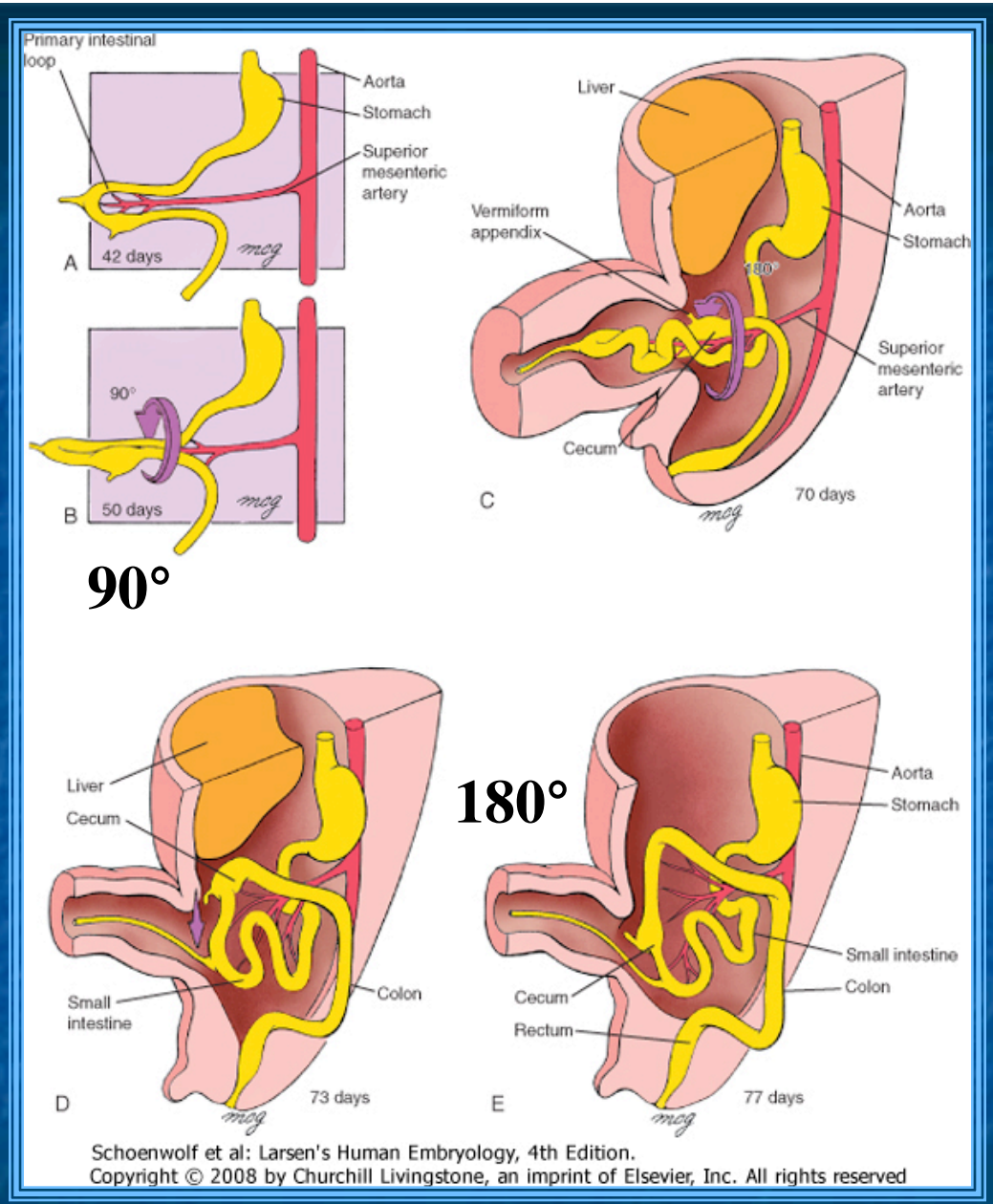
- Small intestine (except for the proximal duodenum.
- Cecum
- Appendix
- Ascending colon
- Right 1/2 to 2/3 of the proximal transverse colon
- All are supplied by the superior mesenteric artery (“the artery of the midgut”)



Schoenwolf et al: Larsen's Human Embryology, 4th Edition.

The midgut grows rapidly and herniates into the umbilical cord

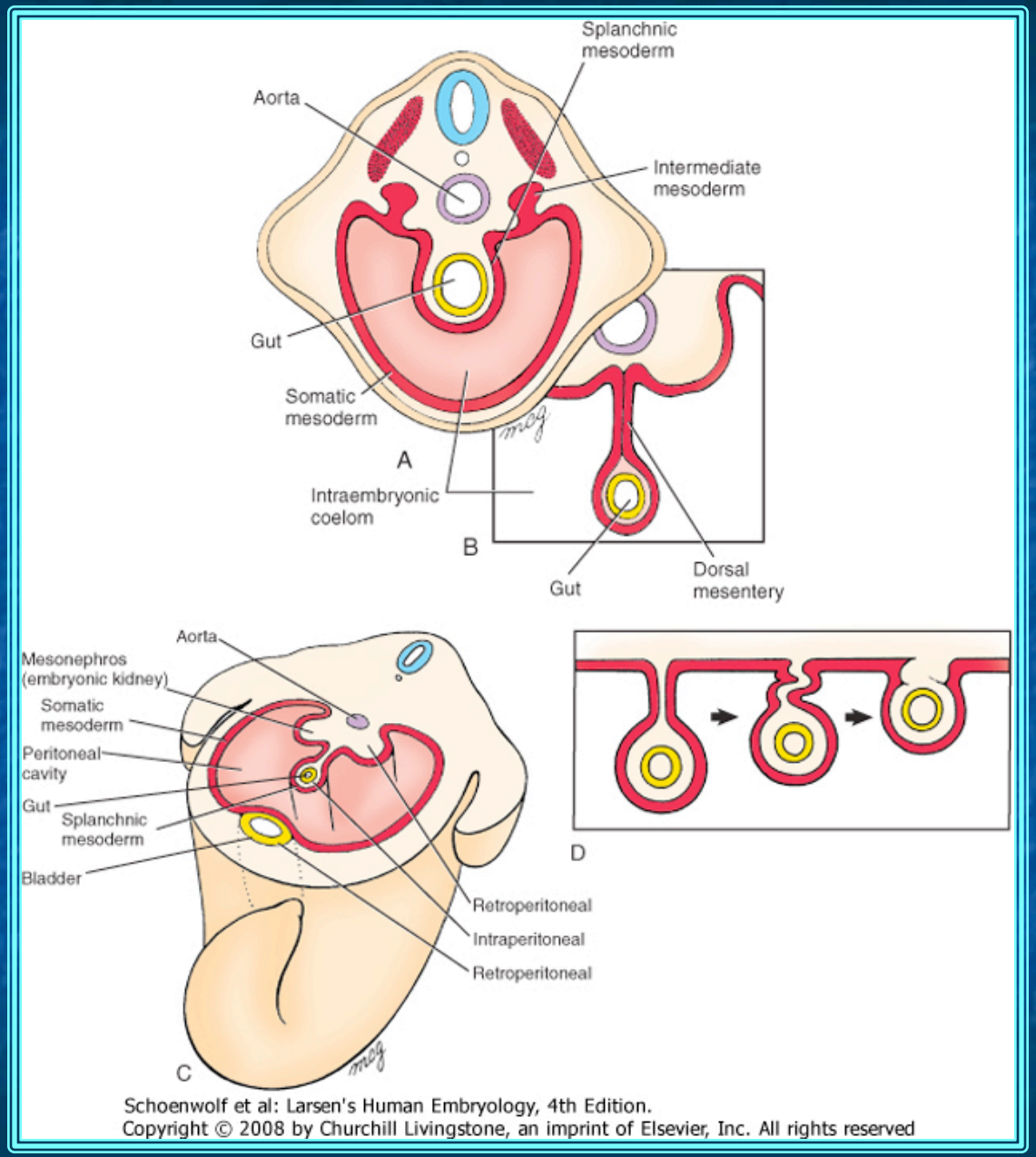
Week 6



The midgut rotates around an axis of the superior mesenteric artery

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 retro-peritoneal

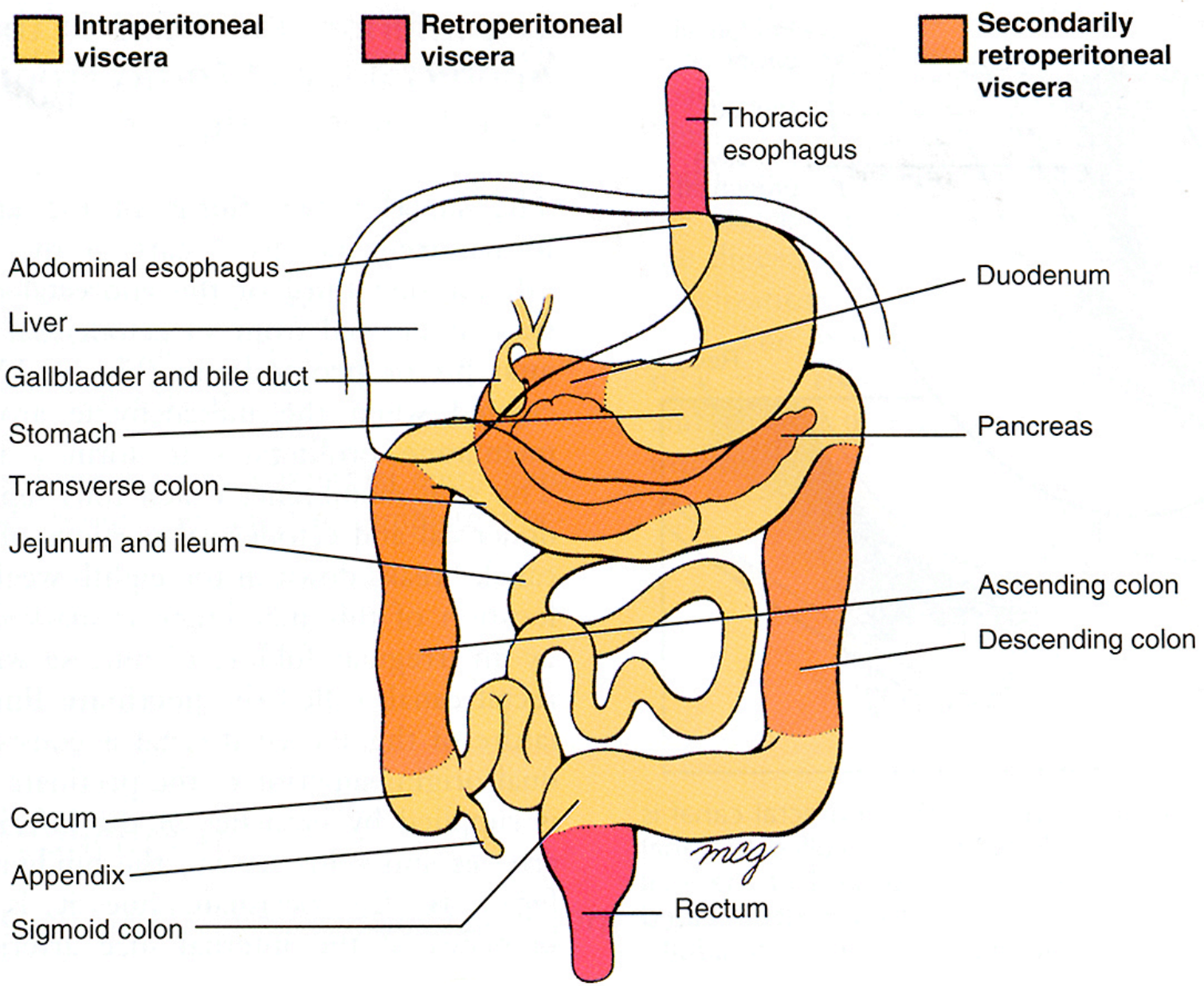


Figure 9–10. Intraperitoneal, retroperitoneal, and secondarily retroperitoneal organs of the abdominal gastrointestinal tract.

Volvulus is a serious complication of excessive flexibility

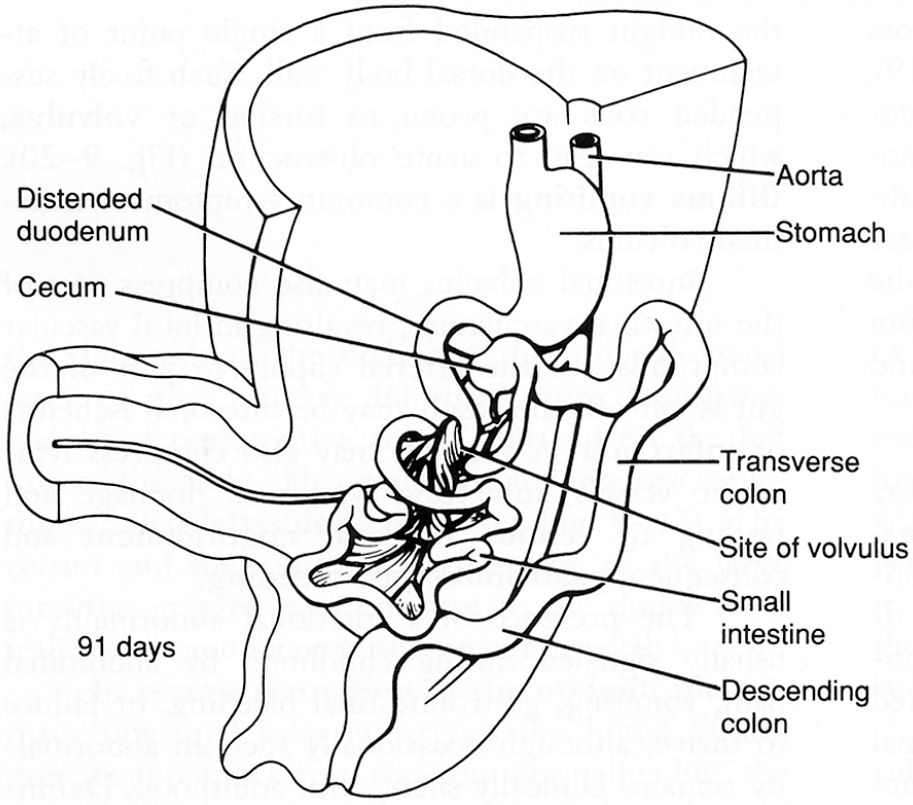
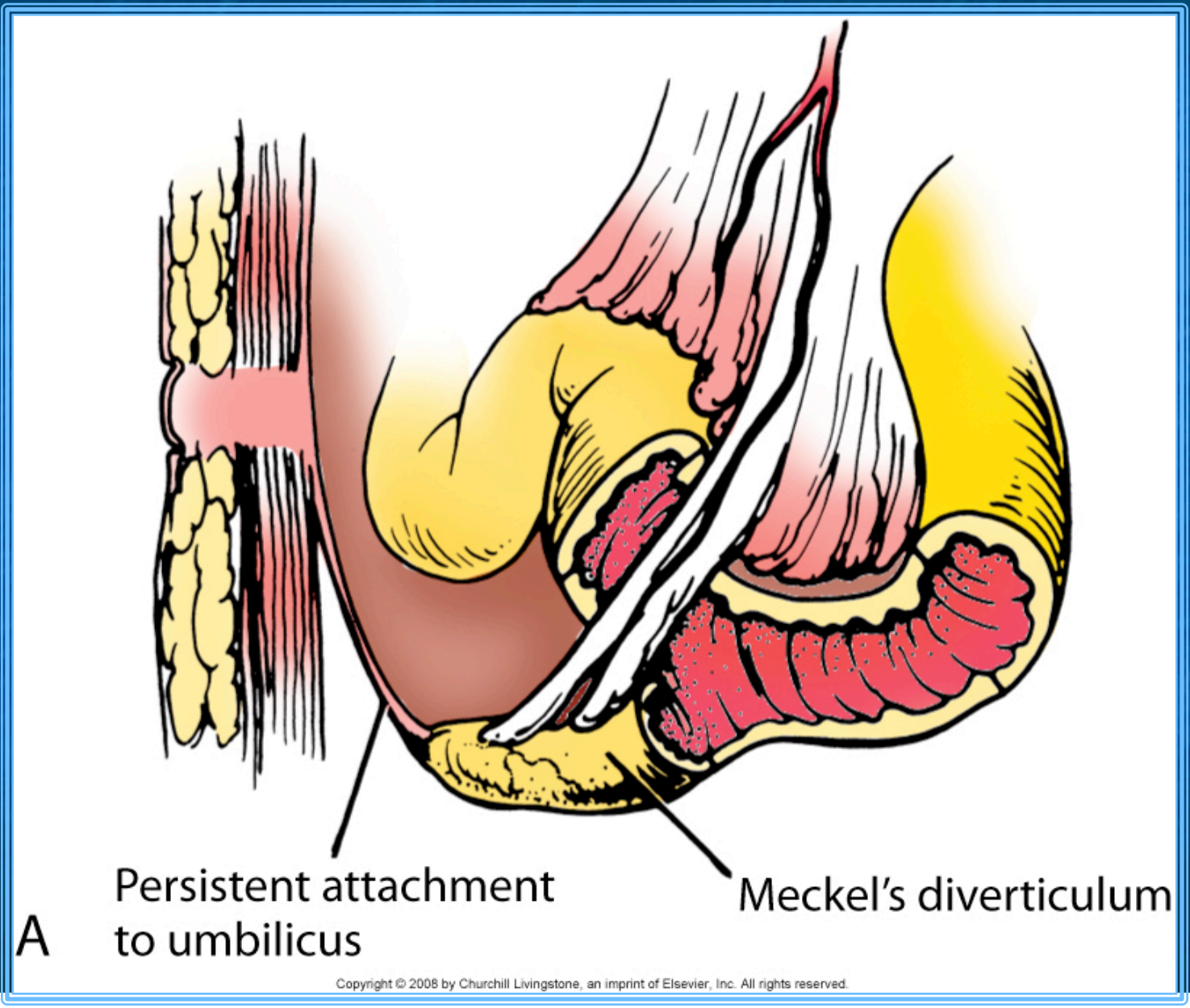
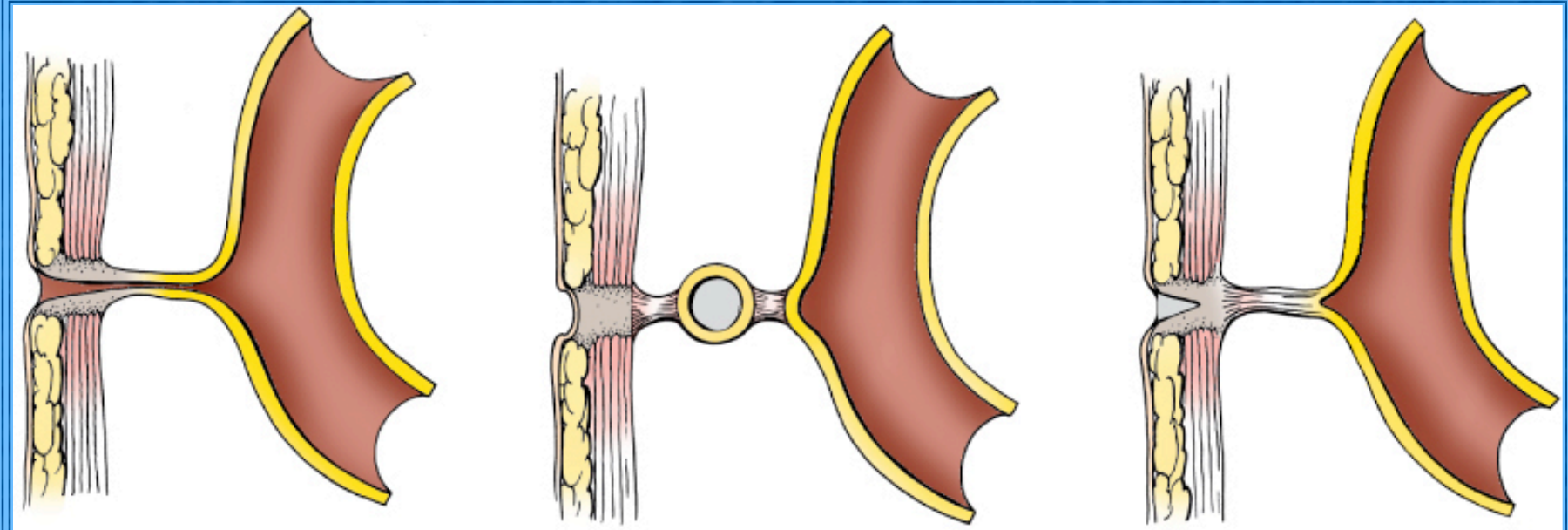


Figure 9–20. Volvulus. Volvulus may occur as suspended regions of the gut twist around themselves, constricting the intestine and/or compromising its blood supply.

Meckel's diverticulum is bad news





B Omphalomesenteric fistula

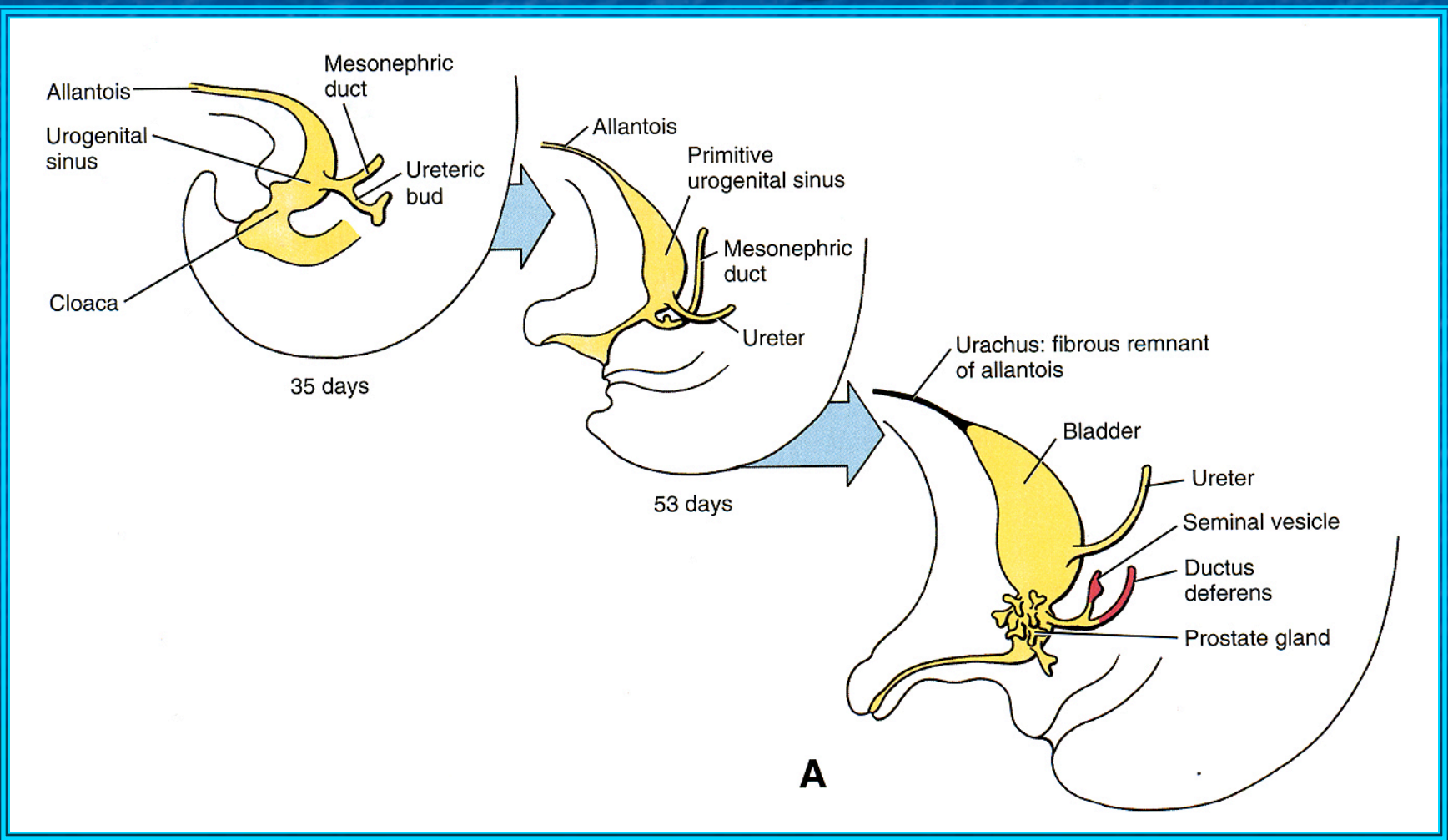
C Omphalomesenteric cyst

D Omphalomesenteric ligament (fibrous band)

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 unrinary bladder and most of 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

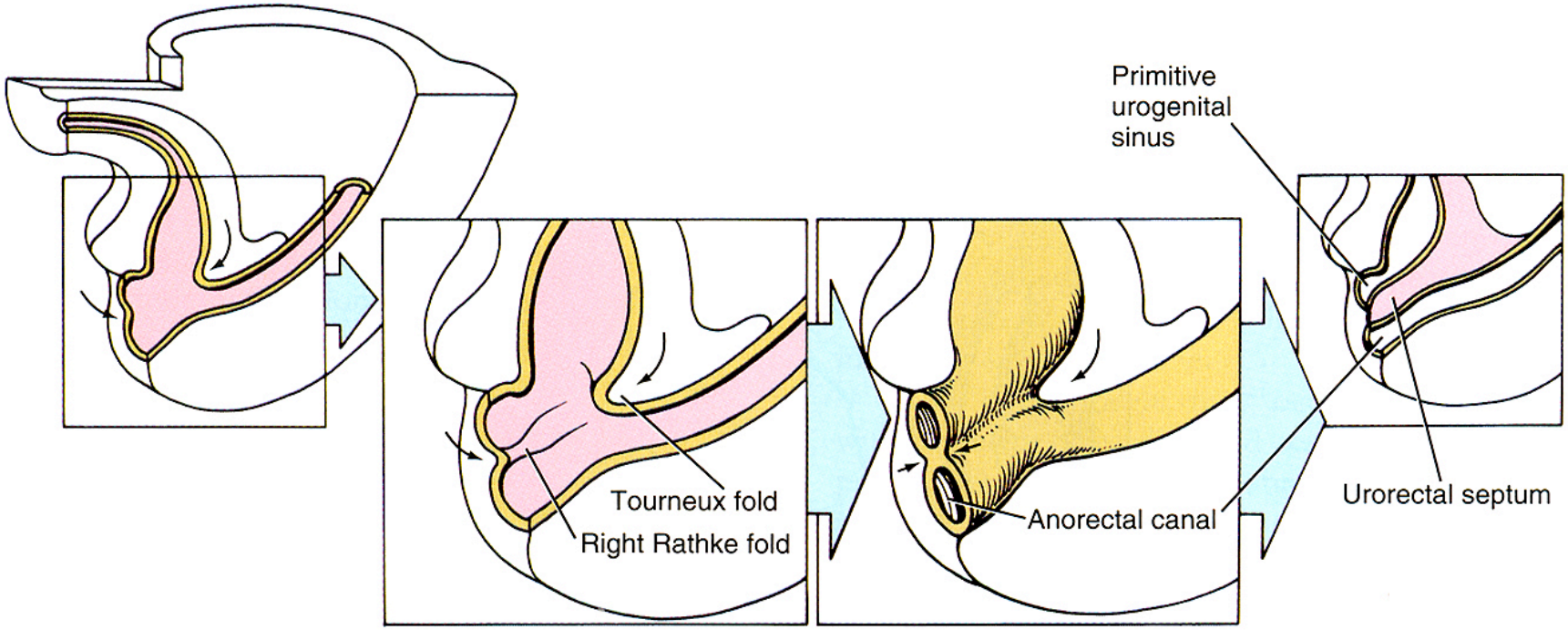


Figure 9–11. Subdivision of the cloaca into an anterior primitive urogenital sinus and a posterior rectum between 4 and 6 weeks. The urorectal septum that divides the cloaca is composed of three distinct septa. Initially, a superior Tourneaux fold grows inferiorly to the level of the future pelvic urethra.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

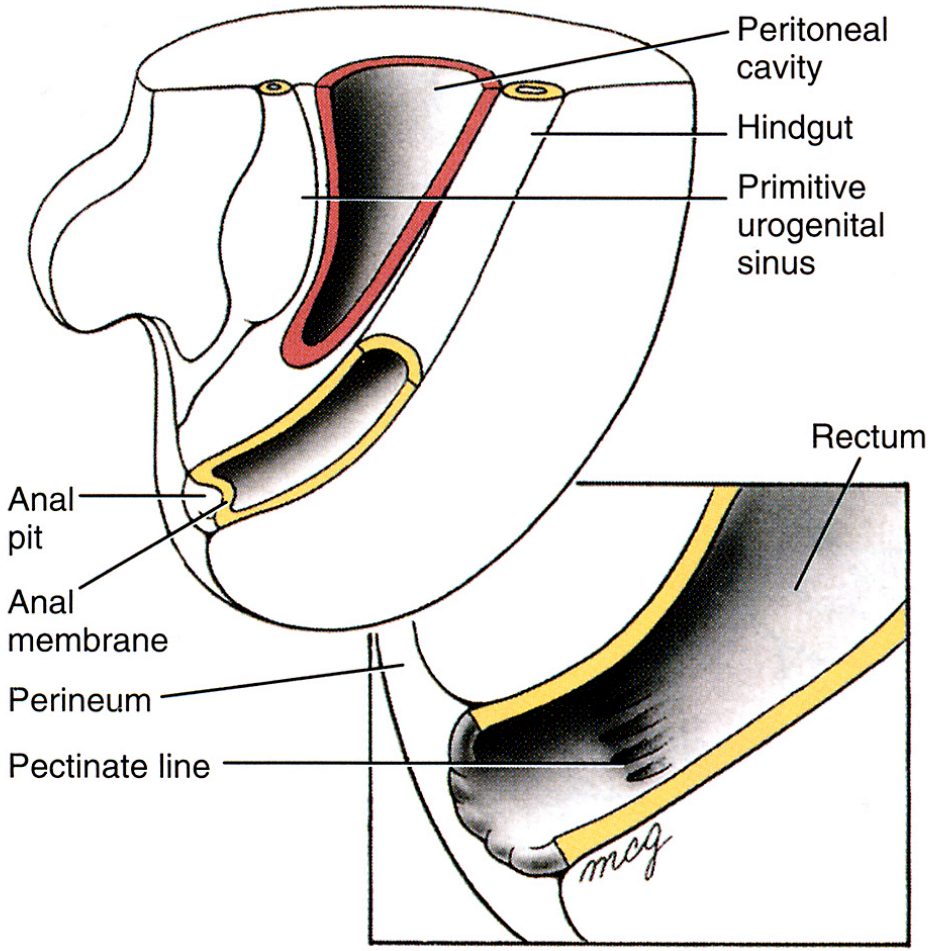
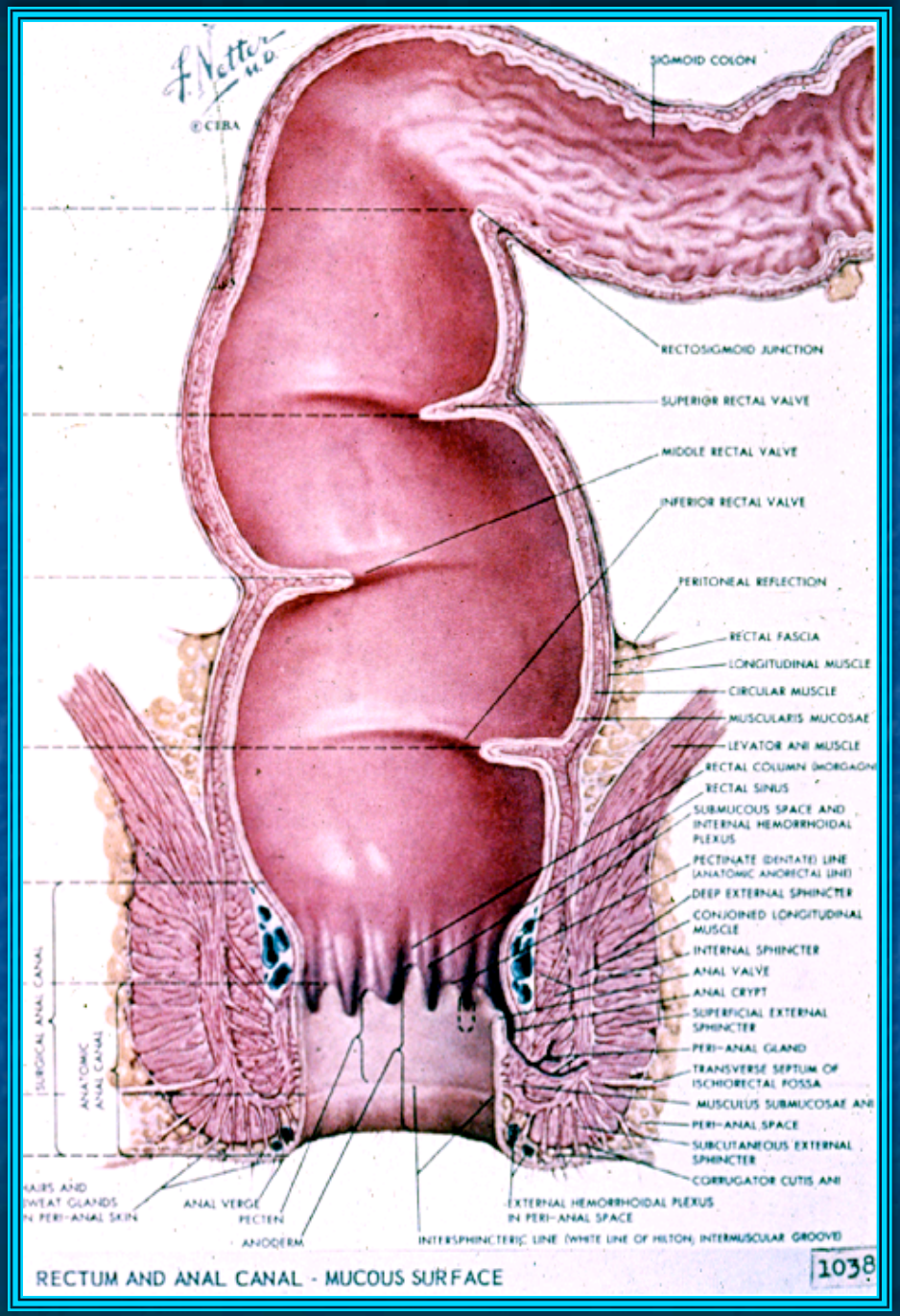


Figure 9–12. The lower third of the anorectal canal is formed by an ectodermal invagination called the anal pit. The border between the superior end of the anal pit and the inferior end of the rectum is demarcated by mucosal folds called the pectinate line in the adult.

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

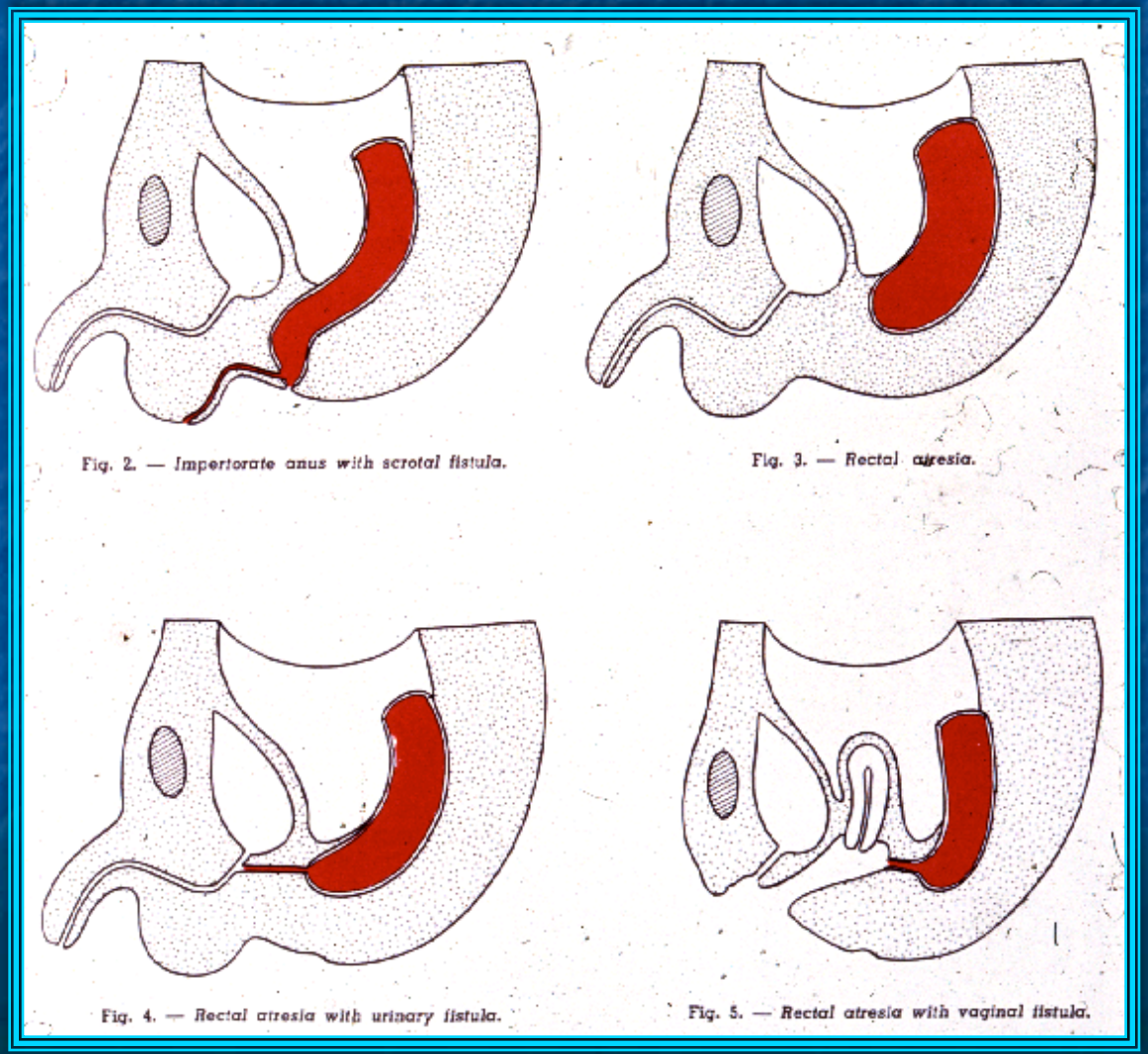


Fig. 2. — *Imperforate anus with scrotal fistula.*

Fig. 3. — *Rectal atresia.*

Fig. 4. — *Rectal atresia with urinary fistula.*

Fig. 5. — *Rectal atresia with vaginal fistula.*

The END

Have a nice day!