18.

ENDODERMAL DERIVATIVES, FORMATION OF THE GUT AND ITS SUBSEQUENT ROTATION

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READING ASSIGNMENT: Larsen 3rd edition: Review Chapter 6: pp. 134—149; Chapter 9, pp. 235-259.

SUMMARY: The gut is formed as a critical byproduct of the folding of the germ disc. The primitive bowel extends from the buccopharyngeal membrane to the cloacal membrane. It is portioned into a foregut, a midgut, and a hindgut. The foregut, which gives rise to the largest number of structures forms the pharynx and its derivatives, the lower respiratory tract, the esophagus, the stomach, the duodenum, proximal to the ampulla of Vater, the liver, the pancreas, and the biliary apparatus. From the stomach on, these structures are supplied by the celiac artery. The midgut is supplied by the superior mesenteric artery, and the hindgut is supplied by the inferior mesenteric artery. These vessels define the segmentation of the bowel. The stomach rotates 90° clockwise as it grows, which has major consequences for the positioning of the mesenteries, the duodenum, bile duct, and pancreas. The liver and biliary system arise from the hepatic diverticulum, which grows into the ventral mesentery and septum transversum. The hepatic diverticulum divides into a cranial and a caudal division: the cranial forms the liver and the smaller, caudal forms the extrahepatic biliary system. The pancreas arises from dorsal and ventral pancreatic buds. The rotation of the stomach brings the buds together so that they can fuse into a definitive pancreas. The midgut grows rapidly and herniates into the umbilical cord, where it rotates 90° counterclockwise. Upon its return to the abdomen the gut rotates another 180°. The cecum then grows down to the iliac fossa. The hindgut gives rise to the cloaca, which becomes portioned into an anterior urogenital sinus and a posterior rectum by the growth of Tourneux's and Rathke's folds, which form the urorectal septum. The mouth perforates at about the 4th week and the anus at about the 8th week of development.

LEARNING OBJECTIVES: The basic objective can be summed up easily: know your gut! This includes how it forms, its divisions and how they are distinguished, its derivatives and how they form. Concentrate on the stomach and understand its rotation and the consequences of that rotation. Try to imagine what would happen if something fails, because anything you can correctly imagine probably actually occurs and causes disease. Think of the mesenteries, the liver, the pancreas, and the gall bladder in the context of the rotating stomach. Go on to the midgut and learn the consequences of its prodigious growth and grotesque total of 270° of rotation. Think of where the midgut goes to develop and what it must do to come home. Imagine again the failure of the midgut to do what is expected of it, and try to construct in your mind the hideous defects that arise when the midgut misbehaves. Again, think of what has to happen to the mesenteries as the ascending and descending colon become retroperitoneal. Finally learn about the formation of the hindgut and the partitioning of the cloaca. One last time, give your imagination free rein to envision the consequences of errors. Be sure you know the role, not only of growth in the process of development, but also of death and what happens when death is inadequate.

GLOSSARY:

Volvulus: intestinal obstruction due to a knotting and twisting of the bowel.
Polyhydramnios: an excess of amniotic fluid, occurs when fetus cannot swallow amniotic fluid.
Recanalize: reopening of an occluded lumen
Cuddling: asymmetric growth and rotation
Mesogastrium: gut associated mesentary

TEXT:

<u>The primitive gut forms during the 4th week (Figs. 18-1, 18-2, 18-3)</u>

The gut is formed during the 4th week of embryonic life as the beneficent consequence of the folding of the body. During this brief period, the embryo undergoes a spectacular transformation; a flat trilaminar pancake, the germ disc becomes a recognizable, vertebrate. The rapid growth of the disc in length combines with the stagnation of the yolk sac to cause the disc to bend so that its dorsal surface becomes convex. The notochord, however, makes the dorsal-most region of the embryo stiff. As a result, the ventral region, which is evidently more flexible, outdoes the dorsal region in folding and does the bulk of the job. Folding then accelerates in the cephalic and lateral regions on day 22 and in the caudal region on day 23. The result of all this flamboyant bending is that the edges of the cephalic, lateral and caudal folds are brought together in the ventral midline. The fusion of the endodermal, mesodermal, and ectodermal layers of the disc with their corresponding abutting

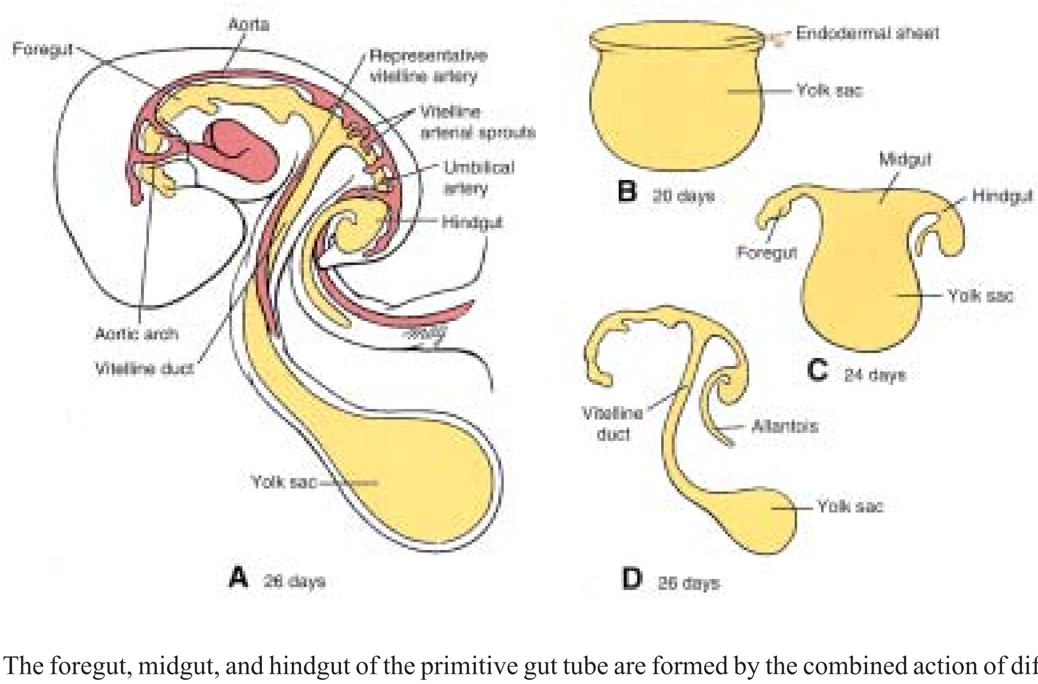

Fig. 18-1. *A,* The foregut, midgut, and hindgut of the primitive gut tube are formed by the combined action of differential growth and lateral and cephalocaudal folding. The foregut and hindgut are blindended tubes that terminate at the buccopharyngeal and cloacal membranes, respectively. The midgut at first is completely open to the cavity of the yolk sac *B, C,* As folding proceeds, however, this connection is constricted to form the narrow vitelline duct (D).

opposites gives rise to a 3-dimensional body form, famously likened (in the fevered imaginings of embryologists searching for a homey figure of speech) to that of a fish. Out of these elaborate processes of folding comes the primordial bowel. In essence the head, tail and lateral folds incorporate the dorsal part of the yolk sac into the embryo to form a bowel.

The meeting and resulting fusion of the cranial, lateral and caudal edges of the embryo creates, at the rostral (superior) end, the primordial foregut, and at the caudal (inferior) end the primordial hindgut, both of which are, at this stage, blind endoderm-lined tubes. The central midgut fuses far more slowly than the foregut and hindgut because it is impeded from doing so by the presence of the yolk sac, which is only slowly encroached upon, as the embryo folds upon it. The midgut thus remains broadly open to the yolk sac by a connection that constricts only gradually as development proceeds. The process of gut formation continues and by the end of the 6^{th} week a complete tube is finally recognizable with fore, mid, and hind components. The formerly ostentatious yolk sac, at this time has lost its relative

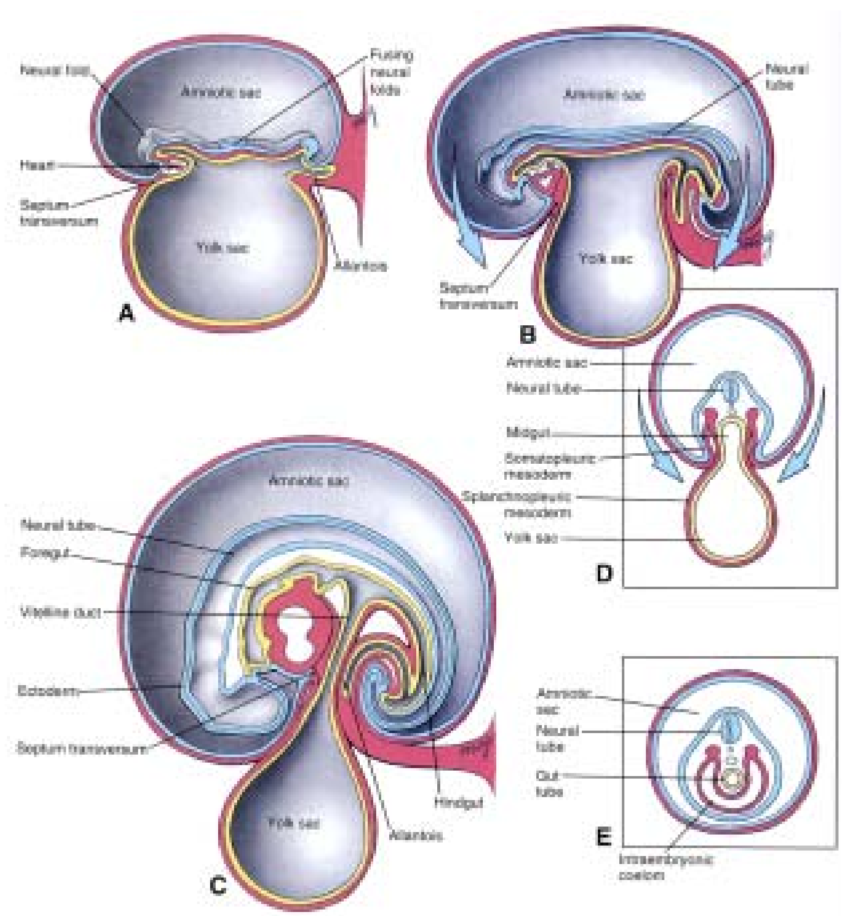

Fig. 18-2. The process of cephalocaudal and lateral folding that transforms the embryo from a flat disc to a three-dimensional vertebrate body form. As folding occurs, the embryo grows more rapidly than the yolk sac, the cavity of which remains continuous with the developing gut tube through the narrowing vitelline duct. The septum transversum forms cranial to the cardiogenic area in the germ disc, *A,* and is translocated to the future lower thoracic region through the folding of the cranial end of the embryo, B, C. The allantois and connecting stalk combine with the yolk sac and vitelline duct through the folding of the caudal end of the embryo, *A-C.* Fusion of the ectoderm, mesoderm, future coelomic cavities, and endoderm from opposite sides is prevented in the immediate vicinity of the vitelline duct, *D,* but not in the more cranial and caudal regions, *E.*

prominence and has been reduced to a slim stalk called the ***vitelline duct***. The cephalic end of the foregut is initially obliterated by the ***buccopharyngeal membrane***, which is driven into history by a relentless apoptosis of its component cells, and opens to give rise to a mouth by the end of the 4^{th} week. The caudal end of the hindgut is initially closed by the cloacal membrane, which opens, again as a result of apoptosis in all of the right places, during the 7^{th} week to form 2 orifices, those of the anus and the urogenital system.

The lateral plate mesoderm has split earlier into ***somatopleuric*** (adherent to ectoderm) and

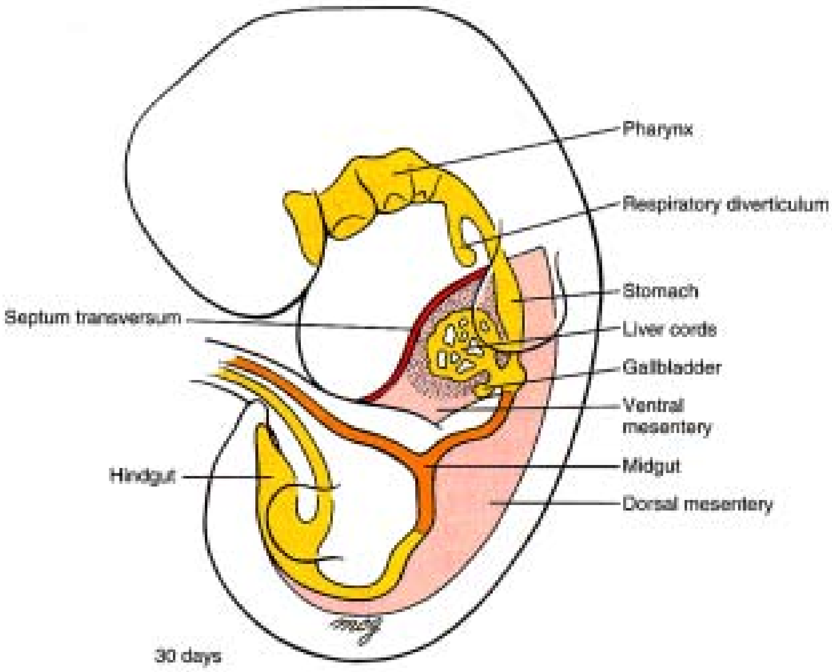

Fig. 18-3. Structure of the gut tube. The foregut consists of the pharynx, located superior to the respiratory diverticulum, the thoracic esophagus, and the abdominal foregut. The abdominal foregut forms the abdominal esophagus, stomach, and about half of the duodenum and gives rise to the liver, the 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.

splanchnopleuric (adherent to endoderm) layers. The space between these layers is originally open to the chorionic cavity but the folding of the embryo and its fusion along the ventral midline incorporates this space into the embryo as the ***intraembryonic coelom***. The splanchnopleuric membrane forms an overcoat around the gut tube and gives rise to the muscle and fibrous connective tissue of the bowel. The epithelial lining of the definitive gut arises from the endoderm, and the nerves and glia of the enteric nervous system come from the émigrés, which migrate to the bowel from the neural crest (but that is another story to be told and a different time, HD Lecture 19).

The intra-abdominal bowel hangs by a thread (*the dorsal mesentery*) in the coelomic cavity (Fig. 18-4)

At the time when the coelom can first be recognized, the gut, from the future esophagus to the proximal rectum, is attached to the dorsal body wall by the dorsal mesentery and to the ventral body wall by the ventral mesentery. The ventral mesentery, however, is marked for programmed cell death for most of its length, and all but a bit of it "dissolves" by the end of the 4^{th} week. Except for the persistent ventral bits, all that is left of the mesentery, is a thin bilayered cord, the ***dorsal mesentery***, from which the bowel is suspended in the coelomic cavity, which later becomes the peritoneal cavity. This method of suspension allows the intraperitoneal gut to wriggle around and move, which it must do, but also creates some danger because the mesentery does not prevent the gut from literally moving around so much that it ties itself into a knot (volvulus). To keep this from occurring, parts of the dorsal mesentery flatten into the body wall and the bowel becomes retroperitoneal.

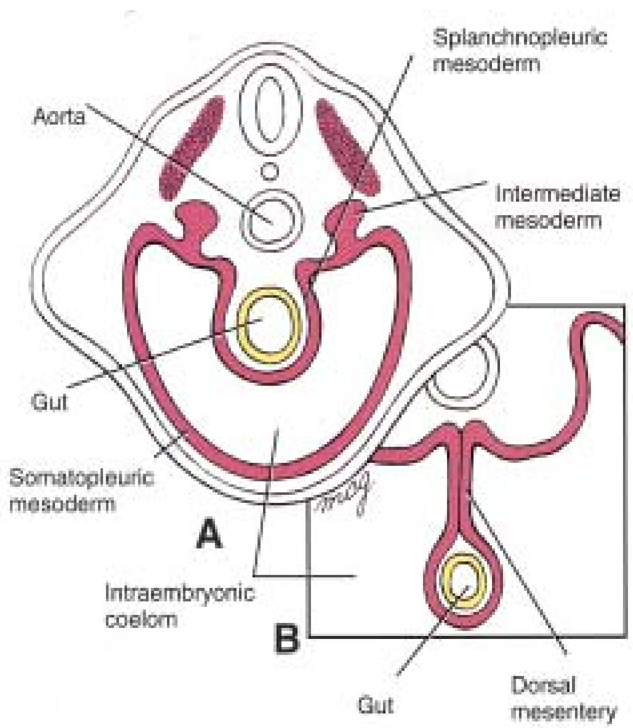

Fig. 18-4. Formation of the dorsal mesentery. *A,* The primitive gut tube initially hangs from the posterior body wall by a broad bar of mesenchyme but, B, in regions inferior to the septum transversum this connection thins out to form a membranous dorsal mesentery composed of reflected peritoneum.

The foregut is not just a primordial bowel but gives rise to many derivatives only some of which are part of the gut. Derivatives include (Fig. 18-3):

1. The pharynx and its derivatives
2. The lower respiratory tract
3. The esophagus
4. The stomach
5. The duodenum, proximal to the ampulla of Vater
6. The liver
7. The pancreas
8. The biliary apparatus

From the stomach to the biliary apparatus, these derivatives are all supplied by branches of the celiac artery, which can thus be thought of by those who are gut-centric as "the artery of the foregut".

The esophagus arises within the thoracic foregut rostral to the developing septum transversum (Figs. 18-3, 18-5)

The esophagus elongates rapidly and grows in a counterintuitive fashion, from the top up, that is, it appears to get longer at its cranial end faster than at its caudal end. As a result, the stomach does not descend below the esophagus but arises from a section of the foregut that lies just below the septum transversum, and which has previously been fate-mapped to develop as stomach. The epithelium of the esophagus also grows in a counter-intuitive manner. Its proliferation is initially exuberant, sufficiently so that it obliterates the cavity of the foregut. This requires the strategic intervention of apoptosis. The

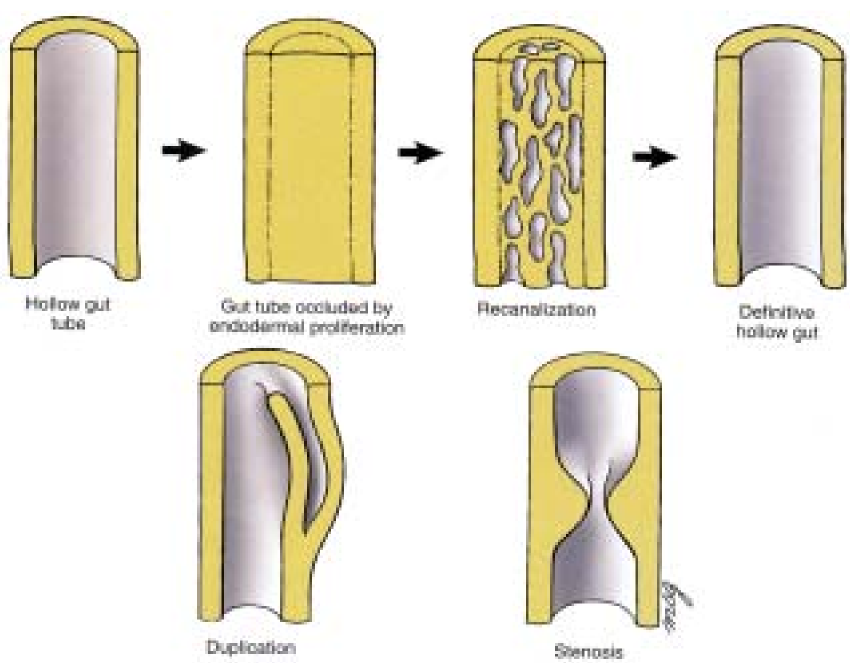

Fig. 18-5. Formation of the definitive gut lumen. Proliferation of the endodermal lining completely occludes the gut tube during the sixth week. Recanalization is completed by week 9. Incomplete or abnormal recanalization may result in duplication of the lumen or stenosis of the gut tube.

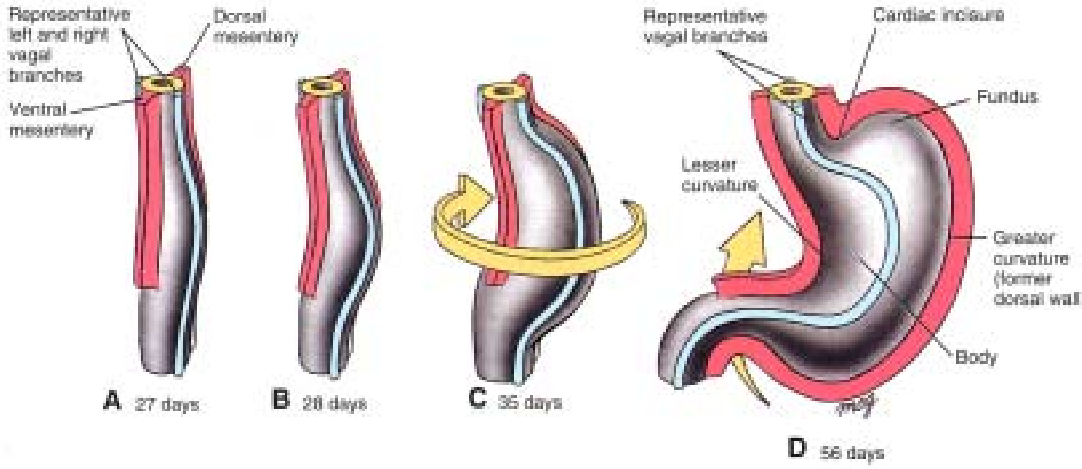

Fig. 18-6. Rotations of the stomach. *A-C,* Oblique frontal views; *D,* direct frontal view. The posterior wall of the stomach expands during the fourth and fifth weeks to form the greater curvature. During the seventh week, the stomach rotates clockwise on its longitudinal axis (when viewed from above).

effect of the embryonic grim reaper is to recanalize the esophagus, which is completed at the end of the embryonic period at the 8th week. If recanalization fails, the absorption of amniotic fluid by the fetal gut fails too. The result of this failure is polyhydramnios, literally too much amniotic fluid. That is a medical tip off to dire trouble in the newborn (esophageal atresia and/or tracheo-esophageal fistula), which can be thwarted only by the rapid intervention of a pediatric surgeon to recanalize artificially what nature forgot to do naturally. The striated muscle of the upper and middle esophagus develops from the caudal branchial arches, while the smooth muscle arises from the splanchnopleuric mesenchyme.

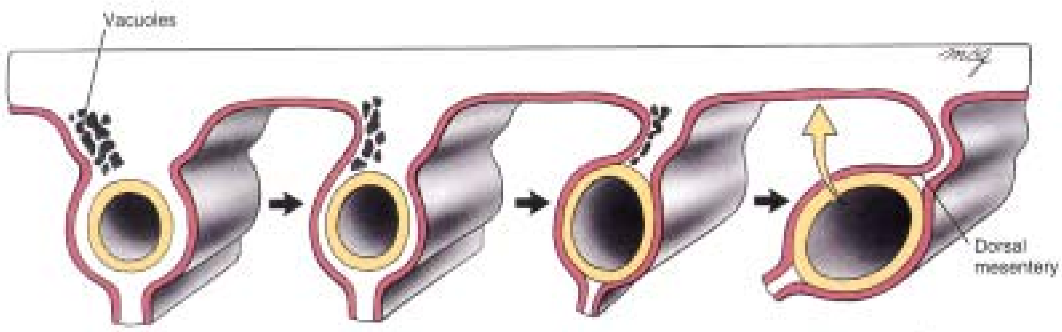

Fig. 18-7. The rotation of the stomach around its longitudinal axis commences with vacuolization of the right side of the thick mesenchymal bar that initially suspends the stomach from the posterior body wall.

The development of the stomach involves an elaborate process of cuddling (asymmetric growth and rotation)(Figs. 18-6, 18-7, 18-8)

The stomach makes its entrance to the stage of development as a fusiform enlargement of the caudal foregut (Fig. 18-3). Its growth is oddly asymmetrical in that the dorsal surface of the stomach grows far faster than the ventral. This peculiarity in growth gives rise to the greater and lesser curvatures that characterize the adult organ. The stomach also rotates as it grows, so that it eventually completes a neat 90° clockwise quarter turn around its longitudinal axis. This spin that the stomach puts onto development converts the original left vagus nerve to the anterior vagal trunk and the right vagus nerve to the posterior vagal trunk. The lesser curvature moves to the right and the greater curvature moves to the left. The cranial end of the primordial stomach moves to the left and slightly inferiorly while the caudal end of the organ moves to the right and superiorly. The net effect of these movements is that the stomach acquires a nearly transverse position across the abdomen.

The rotation of the stomach has profound consequences for the mesentery, the duodenum, and the pancreas. Before the stomach rotates, it is suspended from the posterior wall of the abdominal cavity by the *dorsal mesentery* (called the **dorsal mesogastrium** in the trade in honor of its gastric attachment), which therefore has to adjust its growth to allow the stomach to execute its movements. The dorsal mesogastrium is originally located in the midline. As the stomach spins, the dorsal mesogastrium is

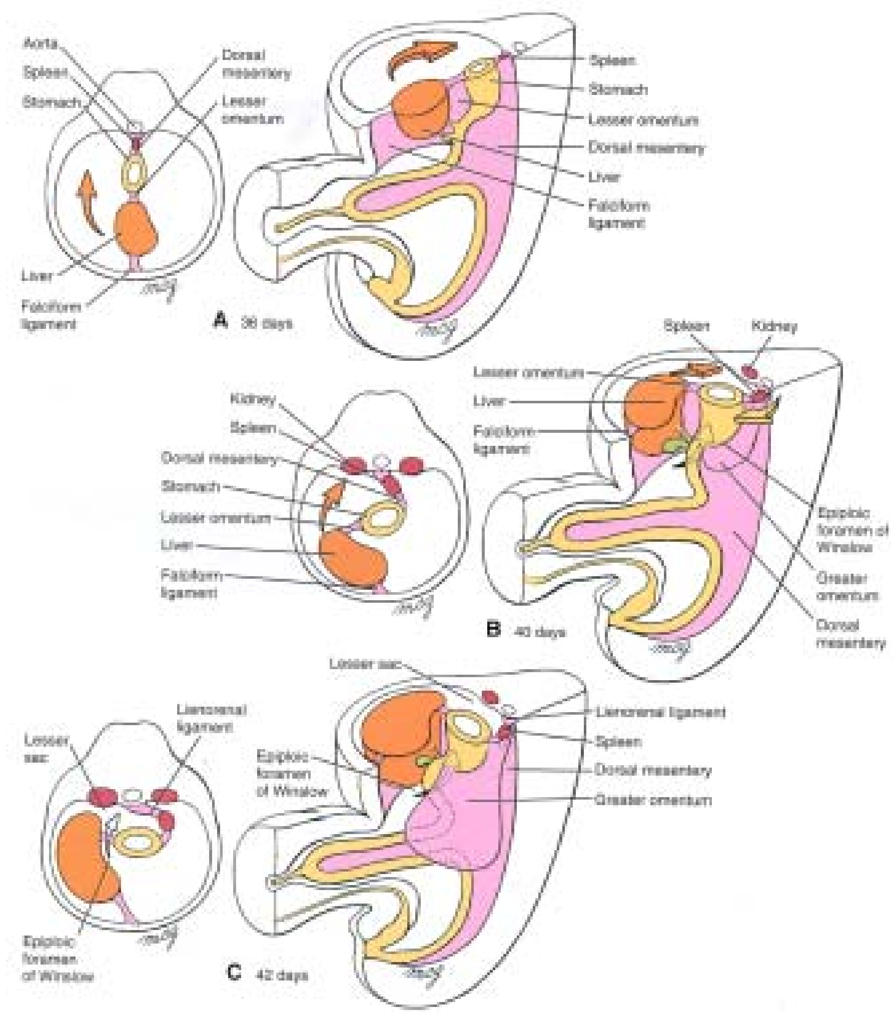

Fig. 18-**8.** Development of the greater omentum and lesser sac. *A, B,* The rotation of the stomach and growth of the dorsal mesogastrium create a sac (the greater omentum) that dangles from the greater curvature of the stomach. B, C. When the duodenum swings to the right, it becomes secondarily fused 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.

carried to the left. This translocation creates the ***lesser sac*** (a.k.a the ***omental bursa***). The ventral mesogastrium is one of the bits of ventral mesentery that does not become totally obliterated. It is retained and attaches the caudal esophagus, stomach, and the superior duodenum to the liver and the developing abdominal wall. To allow the omental bursa to form, the ever-present process of apoptosis hollows out clefts within the dorsal mesogastrium. These clefts allow the dorsal mesogastrium to expand as the stomach rotates. The superior margin of the ***lesser sac*** is the diaphragm (***infracardiac bursa***). The inferior recess of the dorsal mesogastrium forms an originally hollow 4-layered ***greater omentum***, the layers of which ultimately fuse to almost obliterate the inferior recess of the lesser sac. The massive growth of the greater omentum leaves it draped like an apron dangling from the stomach over the inferior organs of the abdomen. The lesser sac communicates with the peritoneal cavity (the greater sac in this terminology) through the epiploic foramen.

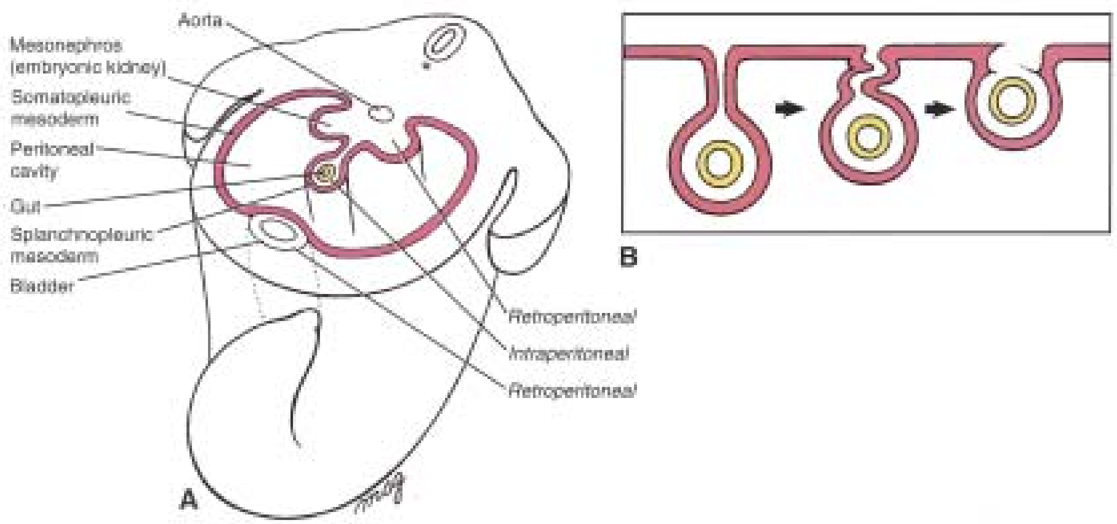

Fig. 18-9. The distinction between intraperitoneal, retroperitoneal, and secondarily retroperitoneal positions of the viscera. *A,* Viscera suspended within the peritoneal cavity by a mesentery are called intraperitoneal, whereas organs embedded in the body wall and covered by peritoneum are called retroperitoneal. *B,* The mesentery suspending some intraperitoneal organs disappears as both mesentery and organ fuse with the body wall. These organs are then called secondarily retroperitoneal.

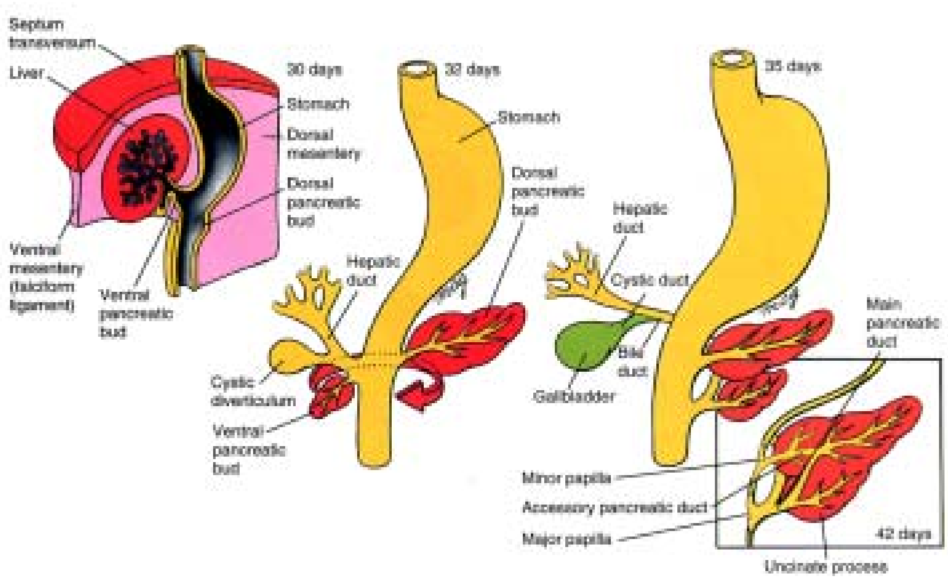

Fig. 18-10. Development of the liver, gallbladder, pancreas, and their duct systems from endodermal diverticula of the duodenum. The liver bud sprouts during the fourth week and expands in the ventral mesentery. The cystic diverticulum and ventral pancreatic bud also grow into the ventral mesentery, 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.

<u>The duodenum is positioned by the stomach but its development is a foregut-midgut partnership (Figs. 18-9, 18-10, also see Fig. 18-16)</u>

The duodenum develops from the most caudal region of the foregut in cooperation with the most cranial region of the midgut. The rotation and growth of the stomach bend the aspiring duodenum into the shape of a C and drive it to the right against the dorsal body wall. The duodenum evidently likes this position because it sticks to the body wall and loses its mesentery, becoming secondarily retroperitoneal. The junction of the bile duct at the approximate apex of the duodenal "C" marks the foregut-midgut junction. The duodenum, as a reflection of its dual origin, receives blood both from branches of the celiac (the artery of the foregut) and the superior mesenteric arteries (the artery of the midgut). As is commonplace in the developing bowel, the lumen of the primordial duodenum becomes occluded by the

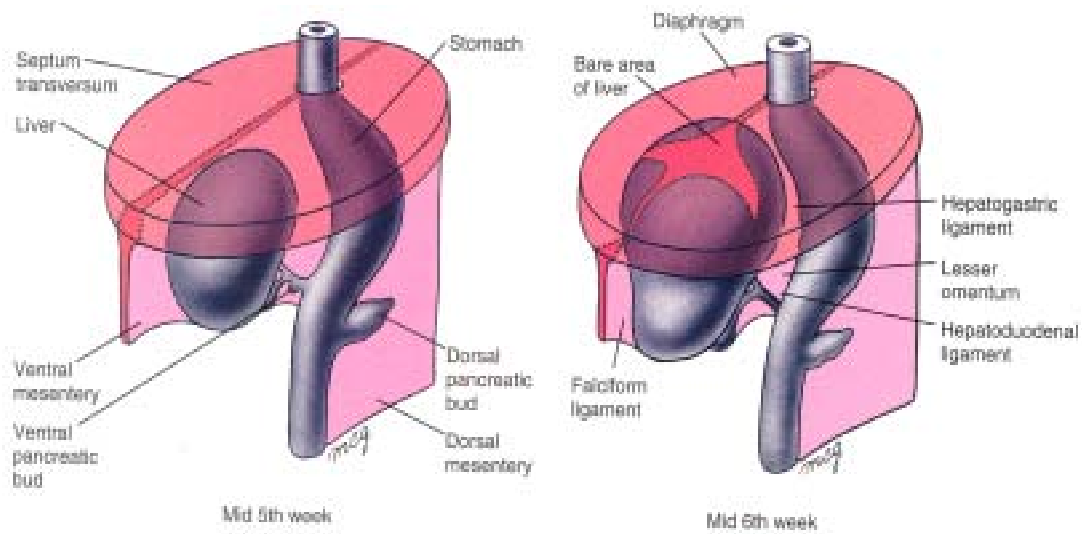

Fig. 18-11. Formation of the liver and associated membranes. As the liver bud grows into the ventral mesentery, its expanding crown makes direct contact with the developing diaphragm. The ventral mesentery that encloses the growing liver bud differentiates into the visceral peritoneum of the liver, which 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.

exuberant growth of its epithelium about the 5th or 6th week of development and the duodenum is recanalized, a process that ends at about the 8th week. The complexity of the development of the duodenum means that it is not infrequently involved in a congenital defect. These include an obstructing annular pancreas and atresia or stenosis due to the failure of recanalization. Symptoms, predictably (see above), include polyhydramnios and bile stained vomiting.

The liver and biliary apparatus develop from the caudal foregut (Figs. 18-10, 18-11)

The liver and biliary tracts arise from a ventral bud (the hepatic diverticulum) that develops on the ventral surface of the foregut early in the 4th week. The hepatic diverticulum grows into the ventral mesogastrium and septum transversum. As it grows, distinctive strands of proliferating cells can be recognized within it. The hepatic diverticulum divides into 2 unequal parts. The cranial part grows faster and becomes bigger, developing into cords of liver cells and the intrahepatic biliary apparatus. This is the liver parenchyma. The stroma and Kupfer cells of the liver develop from the splanchnopleuric mesenchyme in the vicinity. The early liver is a hospitable tissue with a lenient immigration policy, which allows it to be colonized by hematological immigrants. These cells kick in and function at about the 6th week. The right and left lobes of the primordial liver are initially equal in size; however, as it ages the leaning of the liver shifts to right, the lobe of which becomes larger and divides to form the caudate and quadrate lobes of liver. At the end of the 9th week, the liver is one big organ and accounts for > 10% of the body weight. This proportion shrinks at term, but is still large at ~5% of body weight.

The caudal part of the hepatic diverticulum is smaller than its cranial counterpart and forms the gallbladder and extrahepatic biliary ducts. Its duct becomes the cystic duct. Like the bowel, the cystic duct is occluded by the exuberant growth of its epithelium and it too must be recanalized. The stalk that connects the hepatic and cystic ducts forms the common bile duct. The bile duct first attaches to the duodenum ventrally but as the duodenum and stomach rotate the bile duct attachment is carried dorsally. Bile begins to form and flow at about the 12th week.

The ventral mesentery is useful to the stomach, duodenum, and liver (Fig. 18-11)

The ventral mesentery continues to develop and give rise to an abundance of derivatives as it is invaded by the developing liver. Its thin 2-layered membrane, which is the caudal part of the septum transversum, forms the lesser omentum. This structure is the thin portion of the ventral mesentery between the liver and the stomach/duodenum. The portion between the liver and stomach is the hepatogastric ligament; the portion between the liver and the duodenum is the hepatoduodenal ligament. The ventral mesentery-derived membrane surrounds the liver and becomes its visceral peritoneum (except for the bare area where the liver comes into contact with the diaphragm) and then unites

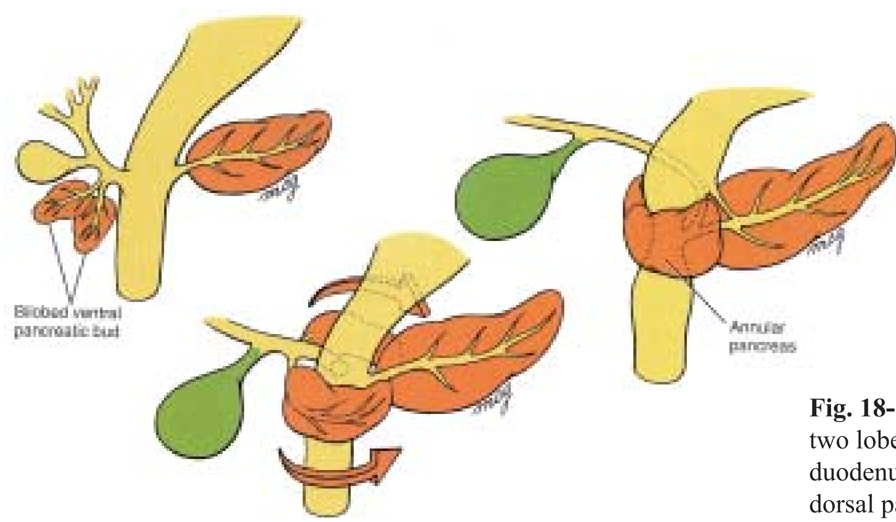

Fig. 18-12. The ventral pancreas may consist of two lobes. If the lobes migrate around the duodenum in opposite directions to fuse with the dorsal pancreatic bud, an annular pancreas is formed.

ventrally over the liver as the falciform ligament, which attaches to the anterior abdominal wall. The umbilical vein runs in the free border of the falciform ligament.

The pancreas has a dual origin (Figs. 18-10, 18-11, 18-12)

The pancreas develops from dorsal and ventral pancreatic buds that arise in the caudal foregut (proximal duodenum). The dorsal pancreatic bud in the larger of the two and it makes its appearance first. It grows out of the primordial duodenum, heading into the dorsal mesentery, which its cells invade. The ventral pancreatic bud develops from the duodenal wall close to the bile duct. As the duodenum and stomach rotate, the ventral pancreatic bud is carried dorsally with the common bile duct. As a result of this motion, the ventral pancreatic bud moves to the dorsal mesentery posterior and inferior to the dorsal pancreatic bud, which is waiting for its ventral counterpart within the mesentery. The two buds then fuse. The ventral pancreatic bud is responsible for the formation of the uncinate process and the inferior part of the head of the pancreas. The dorsal pancreatic bud is responsible for the formation of the bulk of the pancreas. Despite its lesser role in the formation of the organ, the ventral pancreatic bud forms the main pancreatic duct (of Wirsung). The duct of the dorsal pancreatic bud connects to it, but may persist in a frequent anomaly as a persistent dorsal or accessory duct (of Santorini).

The rotation of the stomach brings the dorsal mesogastrium to the left where it fuses with the posterior abdominal wall behind the spleen, giving rise to the lienorenal ligament.

<u>The midgut is the last to form, but is the fastest growing region of the bowel and even out rotates the stomach (Fig. 18-13)</u>

Derivatives of the midgut include:
1. the small intestine (except for the proximal duodenum)
2. the cecum
3. the appendix
4. the ascending colon
5. the right 1/2 to 2/3 of the proximal part of the transverse colon.

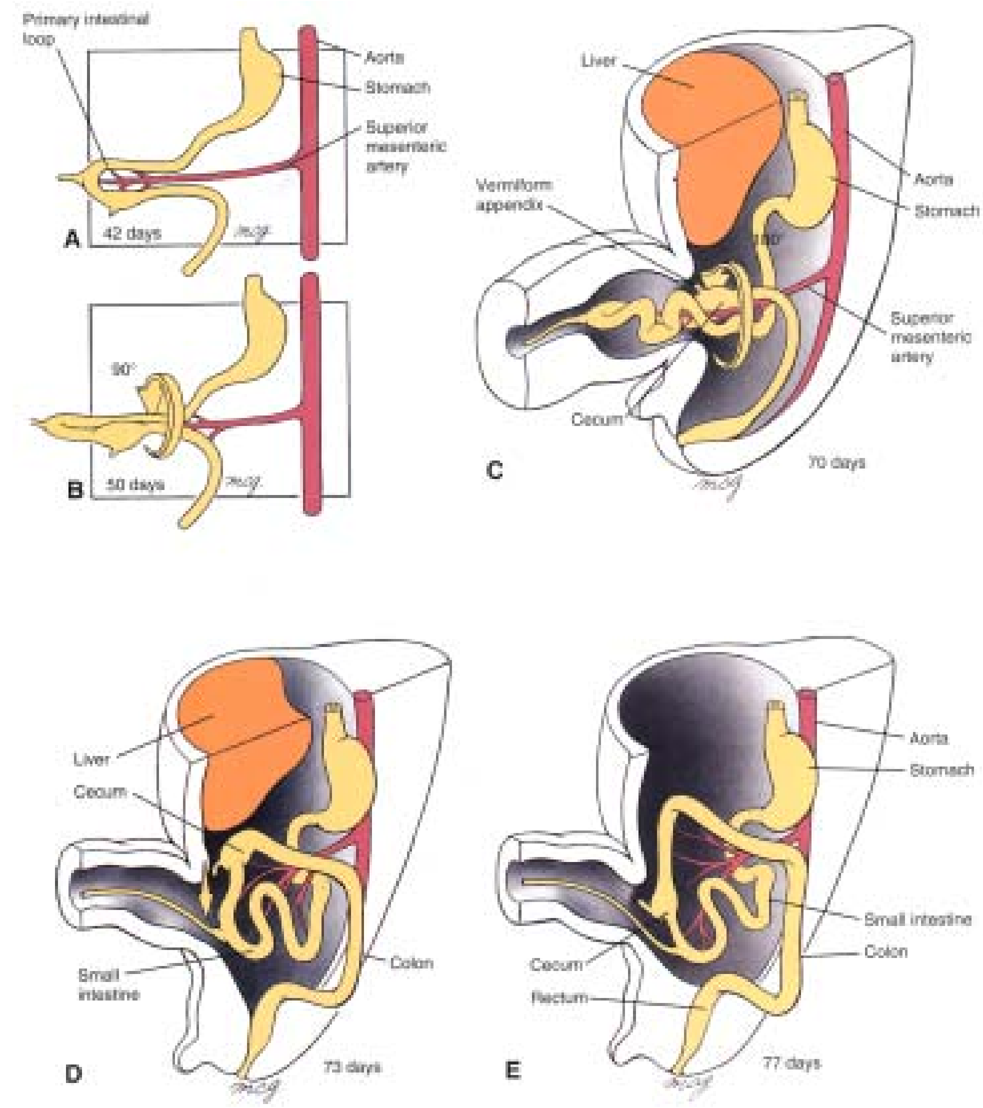

Fig. 18-13. Herniation and rotations of the intestine. *A, B,* At the end of the sixth week, the primary intestinal loop herniates into the umbilicus, rotating through 90 degrees counterclockwise (in frontal view). C, The small intestine elongates to form jejunal-ileal loops, the cecum and appendix grow, 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.

All are supplied by the branches of the superior mesenteric artery.

The major characteristic of the growth of the midgut is massivity. The rate of growth is so great that the bowel herniates right out of the abdomen, a process made possible by the late closure of the ventral body wall. Initially, the gut communicates with the yolk sac via the yolk stalk or vitelline duct. The vitelline duct is at the leading edge of a U-shaped loop of gut formed by the rapidly growing bowel. The loop projects into the umbilical cord. This projection begins during the 6th week and represents a migration of the bowel into the extraembryonic coelom. At this point in time, the intra and extraembryonic coeloms communicate at the umbilicus. The midgut loop has a cranial and a caudal limb with the vitelline duct at the apex. The cranial loop grows faster than its caudal colleague and it forms loops as it grows. Meanwhile. the caudal loop grows fat in a spot, which gives rise to the cecal diverticulum. The gut loops within the umbilical cord, the gut loop rotates 90° counterclockwise (as viewed from a vantage point that looks at the ventral surface of the embryo) around the axis of the superior mesenteric artery. This rotation brings the cranial limb of the midgut loop to the right and the caudal limb to the left. During the 10th week, the intestines now return to the abdomen, a process known to its aficionados as the reduction of the midgut hernia. The small intestine returns to the abdomen first. As the intestines return, they do it politically, putting spin on the reduction; in fact they rotate 180°, for a total of 270° of rotation (90° in the umbilical cord + 180° on the return = 270°).

When the gut returns to the abdomen, the cecum and appendix now lie on the caudal surface of the liver. The cecum does not belong there, so it grows on down to the iliac fossa, where it presumably is comfortable and stays. The engine for the descent of the cecum is the growing colon, a process of growth that creates the ascending colon. The dorsal mesenteries press against the posterior abdominal wall. The colon then becomes secondarily retroperitoneal.

Problems that arise with the tricky development of the midgut include omphalocele (blessedly rare, 1/6000 births), which occurs when the midgut fails to return to the abdomen. The bowel is covered ventrally only by amnion or peritoneum. More common is an umbilical hernia, in which a defect remains in the incompletely fused abdominal wall, with a resulting defect in the linea alba. The protruding mass of gut is covered by skin. A Meckel's diverticulum arises from a persistent vitelline duct, which can form a through and through channel from the inside of the bowel to the exterior (omphalomesenteric fistula) or remain as a cyst (omphalomesenteric cyst) or a fibrous band, depending on the vigor and timing of apoptosis. Meckel's diverticulum, which is twice as common in males than in females, can make a great deal of trouble. It often contains a gastric epithelium, which makes acid and ulcerates the small intestine. The persistent fibrous band can cause an obstruction, which is hard to diagnose, mimicking appendicitis, and carrying a 2.5-15% mortality. A big cause of this trouble is that one cannot make a diagnosis unless one thinks of it. Meckel's is just not on the tip of enough tongues; awareness can save lives.

The hindgut gives rise to a sewer, which forms the terminal bowel and the urogenital sinus (Figs. 18-3, 18-14, 18-15, 18-16)

The portion of the hindgut under the cloacal membrane dilates into the sewer (the translation of the Latin word **cloaca**, which is used by most people in medicine who are, in this case, unfailingly polite). A slim diverticulum, the **allantois** leads out of it and projects into the umbilical stalk. The allantois is slated for death and becomes a source of major clinical trouble when it survives.

The cloaca is partitioned into a posterior rectum and an anterior urogenital sinus, by a partition

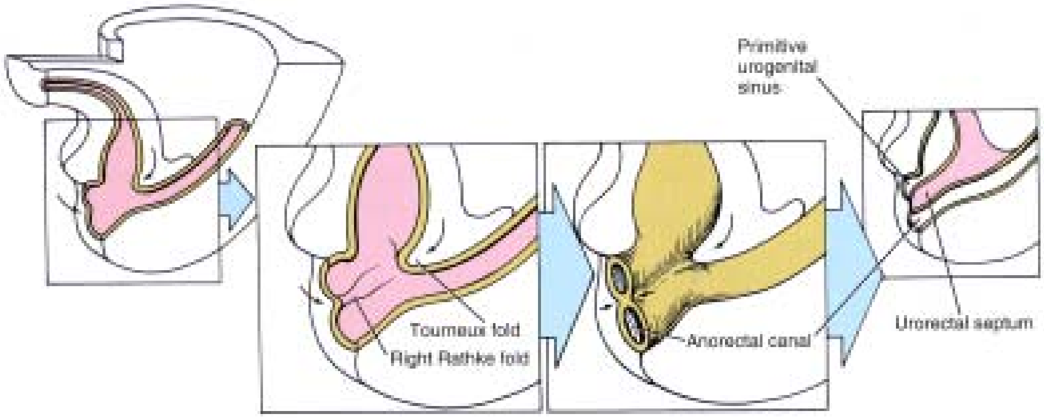

Fig. 18-14. Subdivision of the cloaca into an anterior primitive urogenital sinus and a posterior rectum between 4 and 6 weeks. The urorectal septum that divides the cloaca is composed of three distinct septa. Initially, a superior Tourneaux fold grows inferiorly to the level of the future pelvic urethra. Separation is then completed by left and right Rathke folds that grow in a coronal plane.

called the **urorectal** septum. The urogenital sinus gives rise to the bladder, the pelvic urethra, and the definitive urogenital sinus (the precursor in males of the penile urethra and in females of the vestibule of the vagina). The distal edge of the urorectal septum fuses with the cloacal membrane dividing the membrane into an anterior urogenital membrane and a posterior anal membrane. The zone where the membranes meet becomes the perineum. The urorectal septum is formed by 3 folds, a superior fold of Tourneux, and 2 lateral folds of Rathke. The Tourneux fold appears in the 4th week and grows inferiorly between the allantois and the cloaca.

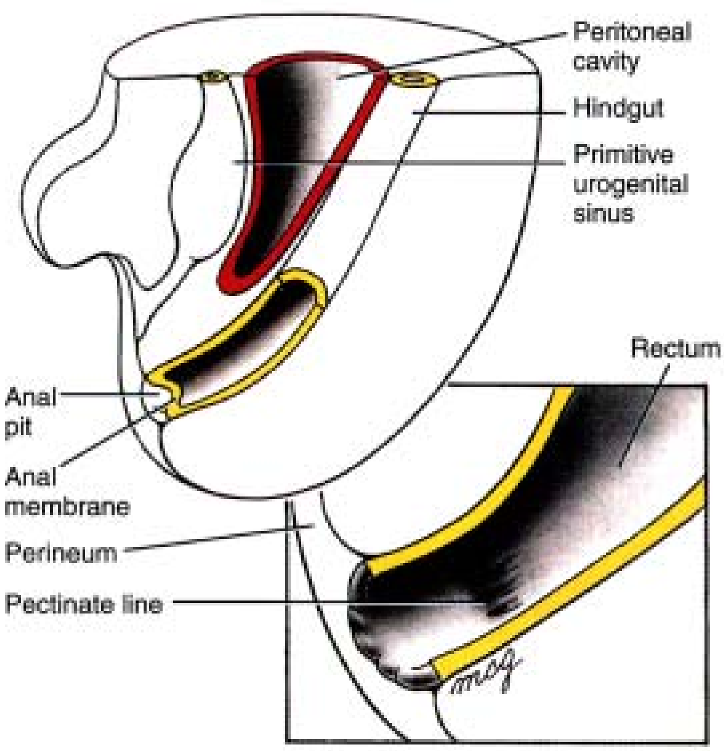

Fig. 18-15. The lower third of the anorectal canal is formed by an ectodermal invagination called the anal pit. The border between the superior end of the anal pit and the inferior end of the rectum is demarcated by mucosal folds called the pectinate line in the adult.

After the cloaca is portioned and a rectum can be recognized the anal membrane has to open and the anorectal canal has to be completed. The superior 2/3 of the anorectal canal forms from the distal part of the hindgut. The inferior 1/3 is formed from the ectoderm of a structure called the anal pit, just outside of the original cloacal membrane. The pit is created by proliferating mesenchyme under a raised border that is created when the anal membrane perforates. The membrane should perforate (if all goes well) on the 8th week. The location of

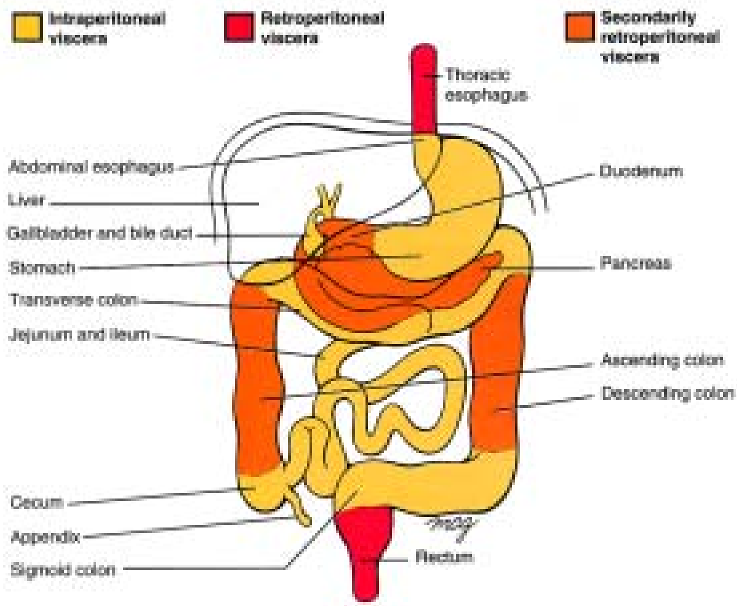

Fig. 18-16. Intraperitoneal, retroperitoneal, and secondarily retroperitoneal organs of the abdominal gastrointestinal tract.

the anal membrane is marked by the **pectinate lin**e. Above this line, the blood supply is from branches of the inferior mesenteric artery, the artery of the hindgut. Below the pectinate line, the blood supply is from branches of the internal iliac arteries. Anastomoses between branches of the superior rectal vein and the inferior rectal vein in the rectal mucosa and submucosa may swell into hemorrhoids if portal