

## Digestive System

### DIVISIONS OF THE GUT TUBE

As a result of cephalocaudal and lateral folding of the embryo, a portion of the endoderm-lined yolk sac cavity is incorporated into the embryo to form the **primitive gut**. Two other portions of the endoderm-lined cavity, the **yolk sac** and the **allantois**, remain outside the embryo. In the cephalic and caudal parts of the embryo, the primitive gut forms a blind-ending tube, the **foregut** and **hindgut**, respectively. The middle part, the **midgut**, remains temporally connected to the yolk sac by means of the **vitelline duct**, or **yolk stalk**.

Development of the primitive gut and its derivatives is usually discussed in four sections:

- (a) The **pharyngeal gut**, or **pharynx**, extends from the oropharyngeal membrane to the respiratory diverticulum and is part of the foregut; this section is particularly important for development of the head and neck.
- (b) The remainder of the **foregut** lies caudal to the pharyngeal tube and extends as far caudally as the liver outgrowth.
- (c) The **midgut** begins caudal to the liver bud and extends to the junction of the right two-thirds and left third of the transverse colon in the adult.
- (d) The **hindgut** extends from the left third of the transverse colon to the cloacal membrane.

**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. The **stroma** (connective tissue) for the glands is derived from visceral mesoderm. Muscle, connective tissue, and peritoneal components of the wall of the gut also are derived from visceral mesoderm.

### MESENTERIES

Portions of the gut tube and its derivatives are suspended from the dorsal and ventral body wall by **mesenteries**, double layers of peritoneum that enclose an organ and connect it to the body wall. Such organs are called **intraperitoneal**, whereas organs that lie against the posterior body wall and are covered by peritoneum on their anterior surface only (e.g., the kidneys) are considered **retroperitoneal**. **Peritoneal ligaments** are double layers of peritoneum (mesenteries) that pass from one organ to another or from an organ to the body wall. Mesenteries and ligaments provide pathways for vessels, nerves, and lymphatics to and from abdominal viscera.

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**, which 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**. Dorsal mesentery of the jejunal and ileal loops forms the **mesentery proper**.

**Ventral mesentery**, which exists only in the region of the terminal part of the esophagus, the stomach, and the upper part of the duodenum, is derived from the **septum transversum**. Growth of the liver into the mesenchyme of the septum transversum divides the ventral mesentery into

- (a) the **lesser omentum**, extending from the lower portion of the esophagus, the stomach, and the upper portion of the duodenum to the liver and
- (b) the **falciform ligament**, extending from the liver to the ventral body wall.

## **FOREGUT**

### **Esophagus**

When the embryo is approximately 4 weeks old, the **respiratory diverticulum (lung bud)** appears at the ventral wall of the foregut at the border with the pharyngeal gut. The **tracheoesophageal septum** gradually partitions this **diverticulum** from the dorsal part of the foregut. In this manner the foregut divides into a ventral portion, the **respiratory primordium**, and a dorsal portion, the **esophagus**. At first the esophagus is short, but with descent of the heart and lungs it lengthens rapidly. The muscular coat, which is formed by surrounding splanchnic mesenchyme, is striated in its upper two-thirds and innervated by the vagus; the muscle coat is smooth in the lower third and is innervated by the splanchnic plexus.

### **Esophageal Abnormalities**

**Esophageal atresia** and/or **tracheoesophageal fistula** results either from spontaneous posterior deviation of the **tracheoesophageal septum** or from some mechanical factor pushing the dorsal wall of the foregut anteriorly. In its most common form the proximal part of the esophagus ends as a blind sac, and the distal part is connected to the trachea by a narrow canal just above the bifurcation. Other types of defects in this region occur much less frequently.

Atresia of the esophagus prevents normal passage of amniotic fluid into the intestinal tract, resulting in accumulation of excess fluid in the amniotic sac (**polyhydramnios**). In addition to atresias, the lumen of the esophagus may narrow, producing **esophageal stenosis**, usually in the lower third.

## STOMACH

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

The stomach rotates 90° clockwise around its longitudinal axis, causing its left side to face anteriorly and its right side to face posteriorly.

Hence the left vagus nerve, initially innervating the left side of the stomach, now innervates the anterior wall; similarly, the right vagus nerve innervates the posterior wall. During this rotation the original posterior wall of the stomach grows faster than the anterior portion, forming the **greater** and **lesser curvatures**.

The cephalic and caudal ends of the stomach originally lie in the midline, but during further growth the stomach rotates around an anteroposterior axis, such that the caudal or **pyloric part** moves to the right and upward and the cephalic or **cardiac portion** moves to the left and slightly downward. The stomach thus assumes its final position, its axis running from above left to below right.

Since the stomach is attached to the dorsal body wall by the **dorsal mesogastrium** and to the ventral body wall by the **ventral mesogastrium**, its rotation and disproportionate growth alter the position of these mesenteries. Rotation about the longitudinal axis pulls the dorsal mesogastrium to the left, creating a space behind the stomach called the **omental bursa (lesser peritoneal sac)**. This rotation also pulls the ventral mesogastrium to the right. As this process continues in the fifth week of development, the spleen primordium appears as a mesodermal proliferation between the two leaves of the dorsal mesogastrium.

With continued rotation of the stomach, the dorsal mesogastrium lengthens, and the portion between the spleen and dorsal midline swings to the left and fuses with the peritoneum of the posterior abdominal wall. The posterior leaf of the dorsal mesogastrium and the peritoneum along this line of fusion degenerate. The spleen, which remains intraperitoneal, is then connected to the body wall in the region of the left kidney by the **lienorenal ligament** and to the stomach by the **gastrolenal ligament**. Lengthening and fusion of the dorsal mesogastrium to the posterior body wall also determine the final position of the pancreas. Initially the organ grows into the dorsal mesoduodenum, but eventually its tail extends into the dorsal mesogastrium. Since this portion of the dorsal mesogastrium fuses with the dorsal body wall, the tail of the pancreas lies against this region. Once the posterior leaf of the dorsal mesogastrium and the peritoneum of the posterior body wall degenerate along the line of fusion, the tail of the pancreas is covered by peritoneum on its anterior surface only and therefore lies in a **retroperitoneal** position. (Organs, such as the pancreas, that are originally covered by

peritoneum, but later fuse with the posterior body wall to become retroperitoneal, are said to be **secondarily retroperitoneal**.)

As a result of rotation of the stomach about its anteroposterior axis, the dorsal mesogastrium bulges down. It continues to grow down and forms a double-layered sac extending over the transverse colon and small intestinal loops like an apron. This double-leaved apron is the **greater omentum**; later its layers fuse to form a single sheet hanging from the greater curvature of the stomach. The posterior layer of the greater omentum also fuses with the mesentery of the transverse colon.

The **lesser omentum** and **falciform ligament** form from the ventral mesogastrium, which itself is derived from mesoderm of the septum transversum.

When liver cords grow into the septum, it thins to form

- (a) the peritoneum of the liver,
  - (b) the **falciform ligament**, extending from the liver to the ventral body wall, and
  - (c) the **lesser omentum**, extending from the stomach and upper duodenum to the liver.
- The free margin of the falciform ligament contains the umbilical vein, which is obliterated after birth to form the **round ligament of the liver (ligamentum teres hepatis)**. The free margin of the lesser omentum connecting the duodenum and liver (**hepatoduodenal ligament**) contains the bile duct, portal vein, and hepatic artery (**portal triad**). This free margin also forms the roof of the **epiploic foramen of Winslow**, which is the opening connecting the omental bursa (lesser sac) with the rest of the peritoneal cavity (greater sac).

## **DUODENUM**

The terminal part of the foregut and the cephalic part of the midgut form the duodenum. The junction of the two parts is directly distal to the origin of the liver bud. As the stomach rotates, the duodenum takes on the form of a C shaped loop and rotates to the right. This rotation, together with rapid growth of the head of the pancreas, swings the duodenum from its initial midline position to the left side of the abdominal cavity. The duodenum and head of the pancreas press against the dorsal body wall, and the right surface of the dorsal mesoduodenum fuses with the adjacent peritoneum. Both layers subsequently disappear, and the duodenum and head of the pancreas become fixed in a **retroperitoneal position**. The entire pancreas thus obtains a retroperitoneal position. The dorsal mesoduodenum disappears entirely except in the region of the pylorus of the stomach, where a small portion of the duodenum (**duodenal cap**) retains its mesentery and remains intraperitoneal.

During the second month, the lumen of the duodenum is obliterated by proliferation of cells in its walls. However, the lumen is recanalized shortly thereafter. Since the **foregut** is supplied by the **celiac artery** and the midgut is supplied by the **superior mesenteric artery**, the duodenum is supplied by branches of both arteries.

**LIVER AND GALLBLADDER**

The liver primordium appears in the middle of the third week as an outgrowth of the endodermal epithelium at the distal end of the foregut. This outgrowth, the **hepatic diverticulum**, or **liver bud**, consists of rapidly proliferating cells that penetrate the **septum transversum**, that is, the mesodermal plate between the pericardial cavity and the stalk of the yolk sac. While hepatic cells continue to penetrate the septum, the connection between the hepatic diverticulum and the foregut (duodenum) narrows, forming the **bile duct**. A small ventral outgrowth is formed by the bile duct, and this outgrowth gives rise to the **gallbladder** and the **cystic duct**. During further development, epithelial liver cords intermingle with the vitelline and umbilical veins, which form hepatic sinusoids. Liver cords differentiate into the **parenchyma (liver cells)** and form the lining of the biliary ducts. **Hematopoietic cells, Kupffer cells, and connective tissue cells** are derived from mesoderm of the septum transversum. When liver cells have invaded the entire septum transversum, so that the organ bulges caudally into the abdominal cavity, mesoderm of the septum transversum lying between the liver and the foregut and the liver and ventral abdominal wall becomes membranous, forming the **lesser omentum** and **falciform ligament**, respectively. Together, having formed the peritoneal connection between the foregut and the ventral abdominal wall, they are known as the **ventral mesogastrium**.

Mesoderm on the surface of the liver differentiates into visceral peritoneum except on its cranial surface. In this region, the liver remains in contact with the rest of the original septum transversum. This portion of the septum, which consists of densely packed mesoderm, will form the central tendon of the **diaphragm**. The surface of the liver that is in contact with the future diaphragm is never covered by peritoneum; it is the **bare area of the liver**.

In the 10th week of development the weight of the liver is approximately 10% of the total body weight. Although this may be attributed partly to the large numbers of sinusoids, another important factor is its **hematopoietic function**. Large nests of proliferating cells, which produce red and white blood cells, lie between hepatic cells and walls of the vessels. This activity gradually subsides during the last 2 months of intrauterine life, and only small hematopoietic islands remain at birth. The weight of the liver is then only 5% of the total body weight.

Another important function of the liver begins at approximately the 12<sup>th</sup> week, when bile is formed by hepatic cells. Meanwhile, since the **gallbladder** and **cystic duct** have developed and the cystic duct has joined the hepatic duct to form the **bile duct**, bile can enter the gastrointestinal tract. As a result, its contents take on a dark green color. Because of positional changes of the duodenum, the entrance of the bile duct gradually shifts from its initial anterior position to a posterior one, and consequently, the bile duct passes behind the duodenum.



## PANCREAS

The pancreas is formed by two buds originating from the endodermal lining of the duodenum. Whereas the **dorsal pancreatic bud** is in the dorsal mesentery, the **ventral pancreatic bud** is close to the bile duct. When the duodenum rotates to the right and becomes C-shaped, the ventral pancreatic bud moves dorsally in a manner similar to the shifting of the entrance of the bile duct. Finally the ventral bud comes to lie immediately below and behind the dorsal bud. Later the parenchyma and the duct systems of the dorsal and ventral pancreatic buds fuse.

The ventral bud forms the **uncinate process** and inferior part of the head of the pancreas. The remaining part of the gland is derived from the dorsal bud. The **main pancreatic duct** (of **Wirsung**) is formed by the distal part of the dorsal pancreatic duct and the entire ventral pancreatic duct.

The proximal part of the dorsal pancreatic duct either is obliterated or persists as a small channel, the **accessory pancreatic duct** (of **Santorini**). The main pancreatic duct, together with the bile duct, enters the duodenum at the site of the **major papilla**; the entrance of the accessory duct (when present) is at the site of the **minor papilla**. In about 10% of cases the duct system fails to fuse, and the original double system persists. In the third month of fetal life, **pancreatic islets** (of **Langerhans**) develop from the parenchymatous pancreatic tissue and scatter throughout the pancreas. **Insulin secretion** begins at approximately the fifth month. Glucagon- and somatostatin-secreting cells also develop from parenchymal cells. Splanchnic mesoderm surrounding the pancreatic buds forms the pancreatic connective tissue.

## Midgut

In the 5-week-old embryo, the midgut is suspended from the dorsal abdominal wall by a short mesentery and communicates with the yolk sac by way of the **vitelline duct** or **yolk stalk**. In the adult the midgut begins immediately distal to the entrance of the bile duct into the duodenum and terminates at the junction of the proximal two-thirds of the transverse colon with the distal third. Over its entire length the midgut is supplied by the **superior mesenteric artery**. Development of the midgut is characterized by rapid elongation of the gut and its mesentery, resulting in formation of the **primary intestinal loop**. At its apex, the loop remains in open connection with the yolk sac by way of the narrow **vitelline duct**. The cephalic limb of the loop develops into the distal part of the duodenum, the jejunum, and part of the ileum. The caudal limb becomes the lower portion of the ileum, the cecum, the appendix, the ascending colon, and the proximal two-thirds of the transverse colon.

## PHYSIOLOGICAL HERNIATION

Development of the primary intestinal loop is characterized by rapid elongation, particularly of the cephalic limb. As a result of the rapid growth and expansion of the

liver, the abdominal cavity temporarily becomes too small to contain all the intestinal loops, and they enter the extraembryonic cavity in the umbilical cord during the sixth week of development (**physiological umbilical herniation**).

### **RETRACTION OF HERNIATED LOOPS**

During the 10th week, herniated intestinal loops begin to return to the abdominal cavity. Although the factors responsible for this return are not precisely known, it is thought that regression of the mesonephric kidney, reduced growth of the liver, and expansion of the abdominal cavity play important roles. The proximal portion of the jejunum, the first part to reenter the abdominal cavity, comes to lie on the left side. The later returning loops gradually settle more and more to the right. The **cecal bud**, which appears at about the sixth week as a small conical dilation of the caudal limb of the primary intestinal loop, is the last part of the gut to reenter the abdominal cavity. Temporarily it lies in the right upper quadrant directly below the right lobe of the liver. From here it descends into the right iliac fossa, placing the **ascending colon** and **hepatic flexure** on the right side of the abdominal cavity. During this process the distal end of the cecal bud forms a narrow diverticulum, the **appendix**. Since the appendix develops during descent of the colon, its final position frequently is posterior to the cecum or colon. These positions of the appendix are called **retrocecal** or **retrocolic**, respectively.

### **MESENTERIES OF THE INTESTINAL LOOPS**

The mesentery of the primary intestinal loop, the **mesentery proper**, undergoes profound changes with rotation and coiling of the bowel. When the caudal limb of the loop moves to the right side of the abdominal cavity, the dorsal mesentery twists around the origin of the **superior mesenteric artery**. Later, when the ascending and descending portions of the colon obtain their definitive positions, their mesenteries press against the peritoneum of the posterior abdominal wall. After fusion of these layers, the ascending and descending colons are permanently anchored in a retroperitoneal position. The appendix, lower end of the cecum, and sigmoid colon, however, retain their free mesenteries.

The fate of the transverse mesocolon is different. It fuses with the posterior wall of the greater omentum but maintains its mobility. Its line of attachment finally extends from the hepatic flexure of the ascending colon to the splenic flexure of the descending colon.

The mesentery of the jejunoileal loops is at first continuous with that of the ascending colon. When the mesentery of the ascending mesocolon fuses with the posterior abdominal wall, the mesentery of the jejunoileal loops obtains a new line of attachment that extends from the area where the duodenum becomes intraperitoneal to the ileocecal junction.

## **Hindgut**

The hindgut gives rise to the distal third of the transverse colon, the descending colon, the sigmoid, the rectum, and the upper part of the anal canal. The endoderm of the hindgut also forms the internal lining of the bladder and urethra. The terminal portion of the hindgut enters into the posterior region of the cloaca, the primitive **anorectal canal**; the allantois enters into the anterior portion, the primitive **urogenital sinus**. The cloaca itself is an endoderm-lined cavity covered at its ventral boundary by surface ectoderm. This boundary between the endoderm and the ectoderm forms the **cloacal membrane**. A layer of mesoderm, the **urorectal septum**, separates the region between the allantois and hindgut. This septum is derived from the merging of mesoderm covering the yolk sac and surrounding the allantois. As the embryo grows and caudal folding continues, the tip of the urorectal septum comes to lie close to the cloacal membrane, although the two structures never make contact. At the end of the seventh week, the cloacal membrane ruptures, creating the anal opening for the hindgut and a ventral opening for the urogenital sinus. Between the two, the tip of the urorectal septum forms the perineal body. At this time, proliferation of ectoderm closes the caudalmost region of the anal canal. During the ninth week, this region recanalizes. Thus, the caudal part of the anal canal originates in the ectoderm, and it is supplied by the **inferior rectal arteries**, branches of the **internal pudendal arteries**. The cranial part of the anal canal originates in the endoderm and is supplied by the **superior rectal artery**, a continuation of the **inferior mesenteric artery**, the artery of the hindgut. The junction between the endodermal and ectodermal regions of the anal canal is delineated by the **pectinate line**, just below the anal columns. At this line, the epithelium changes from columnar to stratified squamous epithelium.