

## DEVELOPMENT OF THE GASTROINTESTINAL SYSTEM - HIGHLIGHTS

### Objectives

Students are expected to be able to:

1. describe the role of folding of the embryo in the formation of the primitive gut tube;
2. list the derivatives of the foregut, midgut and hindgut and name the artery supplying each;
3. define the term “mesentery” and state its functions;
4. briefly describe the formation of the structures derived from the caudal foregut, midgut and hindgut, and state the fate of the mesenteries associated with them;
5. state the relationship of the developing spleen to the dorsal mesogastrum;
6. explain the following in terms of abnormal development of the gut : intestinal stenosis or atresia; annular pancreas; “Meckel’s diverticulum”; omphalocele; imperforate anus

### Introduction

As a result of the folding of the embryo, *endoderm* lining the yolk sac is incorporated into the embryo as the *primitive gut tube* which can be divided into the *foregut*, *midgut* and *hindgut*. Initially, the *midgut* maintains a connection with the yolk sac via the *yolk stalk (vitelline duct)* but, later, both the yolk sac and the vitelline duct usually disappear. The endodermal cells will form the epithelial lining of the gut, as well as epithelial components of accessory structures (e.g., liver), while surrounding (splanchnic) mesoderm will form the muscle, connective tissue and membranous coverings.

At first, the primitive gut tube is a midline structure, much of which is suspended in the *intraembryonic coelom* (later the *peritoneal or abdominal cavity*) by mesentery which contains the blood vessels, nerves and lymphatics of the gut. Mesentery is a thin, double-layered membrane which reflects from the lining (*parietal peritoneum*) of the coelom, then splits to surround the gut tube as *visceral peritoneum*. A *dorsal mesentery* is found in association with all three parts of the gut tube, whereas a *ventral mesentery* is associated only with the foregut and its derivatives.

### *Fate of Mesenteries*

Differential growth and rotation of different parts of the primitive gut leads to changes in the length and orientation of the mesenteries. This may lead to partial or complete fusion of mesenteries to the parietal peritoneum, a process known as (*zygosis*). As a result, some parts of the intestine become fixed to the posterior abdominal wall and are said to be *retroperitoneal*, i.e., they no longer have a “free” mesentery. More correctly, they are *secondarily retroperitoneal*, to distinguish them from structures which develop behind the peritoneum (e.g., the kidney) and never have a mesentery. During surgery, fixed parts of the gut can be mobilized by separating the mesentery along the lines of fusion, thus preserving the blood vessels within the mesentery.

The *foregut*, *midgut* and *hindgut* each forms a specific part of the definitive gut, with its own artery. The following table summarizes the derivatives of the foregut, midgut and hindgut and their arterial supply.

PART	DERIVATIVES	ARTERY
Foregut	<b>Proximal:</b> oral cavity, pharynx, upper oesophagus, respiratory tract	various
	<b>Distal:</b> lower oesophagus, stomach, small intestine (prox. ½ duodenum) liver, gall bladder, pancreas	coeliac
Midgut	small intestine (distal ½ duodenum, jejunum, ileum), large intestine (caecum, appendix, ascending colon, prox. ⅔ transverse colon)	superior mesenteric
Hindgut	large intestine (distal ⅓ transverse colon, descending colon, sigmoid colon, rectum, anal canal)	inferior mesenteric

During development, proliferating endoderm cells completely occlude the lumen of the gut tube which then has to become recanalized, as a result of apoptosis of cells and subsequent necrosis.

### Caudal Foregut

**Oesophagus** - its terminal part passes through the diaphragm into the peritoneal cavity.

**Stomach** - appears as a spindle-shaped dilation of the foregut, just distal to the oesophagus. Growth is faster along its dorsal surface, causing a pronounced curve along both the dorsal surface (**greater curvature**) and ventral surface (**lesser curvature**). In addition, the stomach rotates around its longitudinal axis, so that the original left side becomes the definitive ventral (anterior) surface and the right side becomes the dorsal (posterior) surface. There is also rotation around the antero-posterior axis, so that the proximal end of the stomach (**cardia**) moves to the left and the distal end (**pylorus**) to the right.

The rotation around the longitudinal axis also involves the oesophagus, explaining why the left vagus is located on the anterior surface of the oesophagus and the right vagus on the posterior surface.

**Duodenum** - the first half is derived from the foregut (hence supplied by the coeliac artery) and the second half from the midgut (hence supplied by the superior mesenteric artery). Rotation of the developing stomach swings the pyloric end to the right, carrying the first part of the duodenum with it. Consequently, the duodenum becomes a C-shaped loop.

**Liver, Gall Bladder and Bile Duct** - all develop from an outgrowth of the most caudal part of the foregut. The outgrowth, or **hepatic diverticulum (liver bud)**, grows into the mesoderm of the ventral mesentery. The endoderm forms the lining of the **bile duct** system, as well as the epithelial **parenchymal cells** of the liver, while the mesoderm of the ventral mesentery and **septum transversum** will form the other components of the liver. The **gall bladder** and **cystic duct** arise as outgrowths from the main hepatic diverticulum, as does part of the pancreas (described below). The duct system maintains its connection to the foregut (duodenum) via the **common bile duct**.

**Pancreas** - arises as a **ventral pancreatic bud** from the hepatic diverticulum, and a **dorsal pancreatic bud** which grows into the dorsal mesentery from the foregut. As the stomach and duodenum rotate, the dorsal pancreatic bud moves to the left and the ventral bud to the right. The ventral bud, together with the bile duct, continues to migrate, passing posterior to the duodenum. Eventually, the two pancreatic buds meet and fuse. The dorsal bud forms the **body** and **tail** of the pancreas, while the ventral bud forms the **head** and the **uncinate process**. The ducts of the two buds also join, and it is the terminal part of the ventral duct that usually forms the main duct, thus retaining its connection with the bile duct. Although the terminal part of the dorsal duct usually disappears, it may persist as an accessory duct, entering the duodenum independently.

During the migration of the ventral pancreatic bud, the superior mesenteric artery becomes trapped between it and the dorsal bud, a position it maintains in the adult, where it can be seen emerging between the uncinata process and body of the pancreas.

**Spleen** - although not part of the gastrointestinal system, the spleen develops from mesoderm in the part of the dorsal mesentery that suspends the stomach and receives its blood supply from the coeliac artery.

### **Mesenteries of the Foregut**

#### **i. Dorsal Mesentery**

Rotation of the stomach around its longitudinal axis causes the dorsal mesentery attached to it (**dorsal mesogastrium**) to be stretched and pulled to the left. As a result, a recess, the **lesser sac (omental bursa)** is formed posterior to the stomach. The part of the dorsal mesogastrium containing the spleen partially fuses with the parietal peritoneum anterior to the developing left kidney. Hence the spleen comes to lie on the left side of the body and its mesentery is known as the **lienorenal ligament** (lien = spleen). The part of the dorsal mesogastrium between the spleen and stomach is the **gastrosplenic ligament**. Growth of the dorsal mesogastrium in an inferior direction results in an extensive fold of mesentery (**greater omentum**) hanging down from the greater curvature of the stomach, and containing an extension (**inferior recess**) of the lesser sac. Fusion of the two layers of the greater omentum later obliterates most of the inferior recess.

#### **ii. Ventral Mesentery**

As the liver grows into the ventral mesentery, the latter is converted into a thin envelope of **visceral peritoneum**. When the growing liver reaches the **septum transversum** (part of the diaphragm), the visceral peritoneum is reflected directly from the liver (**bare area**) on to the diaphragm, as parietal peritoneum. A persisting, inferior part of the ventral mesentery between the liver and the anterior body wall becomes the **falciform ligament**, and the **umbilical vein** runs in its lower free border. (After birth the umbilical vein becomes fibrosed, to form the **ligamentum teres**.)

The part of the ventral mesentery extending between the liver and stomach is the **lesser omentum (gastrohepatic ligament)**. The lesser omentum also has a free border (lower border of ventral mesentery) which contains the **bile duct, hepatic artery and portal vein**. It is here that the lesser sac communicates with the rest of the peritoneal cavity (**greater sac**), through a narrow opening, the **epiploic foramen**.

### **Midgut**

During the 5<sup>th</sup> week of development, the midgut undergoes rapid elongation, resulting in a **primary midgut loop**, with the vitelline duct at its apex. The vitelline duct acts as a landmark, dividing the loop into a **proximal (cranial)** and a **distal (caudal) limb**. As a consequence of its rapid growth, the midgut loop can no longer be accommodated in the peritoneal cavity so it “herniates” into the body stalk (umbilical cord). At this stage, growth of the proximal limb outpaces that of the distal limb.

During herniation, the midgut loop rotates 90° counter-clockwise (viewed from the ventral [anterior] aspect), so that the proximal limb lies to the right of the distal limb. The midgut continues to grow and the future caecum appears as a sacculum in the distal limb. At about the 10<sup>th</sup> week, the midgut begins to return to the peritoneal cavity. By this time, the vitelline duct has usually disappeared, so that the apex of the loop is no longer connected to the body stalk. The proximal limb, consisting of coils of jejunum and ileum, is the first to return, followed by the distal limb, with the caecum entering last. As it re-enters the peritoneal cavity, the midgut rotates a further 180° counter-clockwise (270° in total). As a result, the transverse colon lies anterior to the proximal part of the small intestine, and the caecum lies to the right, under the liver. With further growth, the caecum migrates inferiorly to its final destination in the lower right quadrant of the peritoneal cavity, while the ascending colon occupies the right side of the cavity. At this stage, the appendix has developed as a small blind-ending diverticulum of the caecum.

### **Hindgut**

As the midgut is returning to the peritoneal cavity, the proximal part of the hindgut (distal transverse colon), together with its dorsal mesentery, falls to the left, resulting in the distal transverse colon lying horizontally and the descending colon occupying the left side of the peritoneal cavity. The descending colon gives way, in the lower, left quadrant, to the sigmoid colon which pursues an S-shaped course that returns it to the midline. The rectum and anal canal, representing the terminal parts of the hindgut, remain in the midline.

Initially, the distal hindgut opens into the **cloaca**, a sac which also has the allantois entering it. During the

5<sup>th</sup> week, a mesodermal septum (*urorectal septum*) begins to grow between the allantois and the hindgut, dividing the cloaca into an anterior *urogenital sinus* and a posterior *anorectal canal*. The latter forms the distal part of the rectum and part of the anal canal. The cloacal membrane also divides, forming a *urogenital membrane* and an *anal membrane*. The ectoderm immediately adjacent to the anal membrane sinks inwards to form the *anal pit*, so that, following breakdown of the anal membrane (about 8 weeks), the distal part of the anal canal, lined by ectoderm (somatic origin) has a different nerve and blood supply from the proximal part, lined by endoderm (visceral origin - supplied by the inferior mesenteric artery).

***Fate of the Dorsal Mesentery of the Midgut & Hindgut***

<b>Part of Intestine</b>	<b>Mesentery - lost (retroperitoneal)/retained (name)</b>
Duodenum (2 <sup>nd</sup> half)	retroperitoneal
Jejunum, ileum	retained (the mesentery)
Appendix	retained (mesoappendix)
Caecum, ascending colon	retroperitoneal
Transverse colon	retained (transverse mesocolon)
Descending colon	retroperitoneal
Sigmoid (pelvic) colon	retained (sigmoid mesocolon)
Rectum	retroperitoneal

**Clinical considerations:**

**Failure of gut tube to re-canalize - atresia or stenosis**

**Annular pancreas - constriction of duodenum**

**Malrotation of the midgut - twisting of intestine & gangrene**

**Persistent vitelline duct - Meckel's diverticulum**

**Failure of herniated midgut to return to abdominal cavity - omphalocele**

**Improper partitioning of cloaca - abnormal connections between rectum/anal canal and urogenital system**