

Lecture - Gastrointestinal Development

Endoderm Development

Introduction

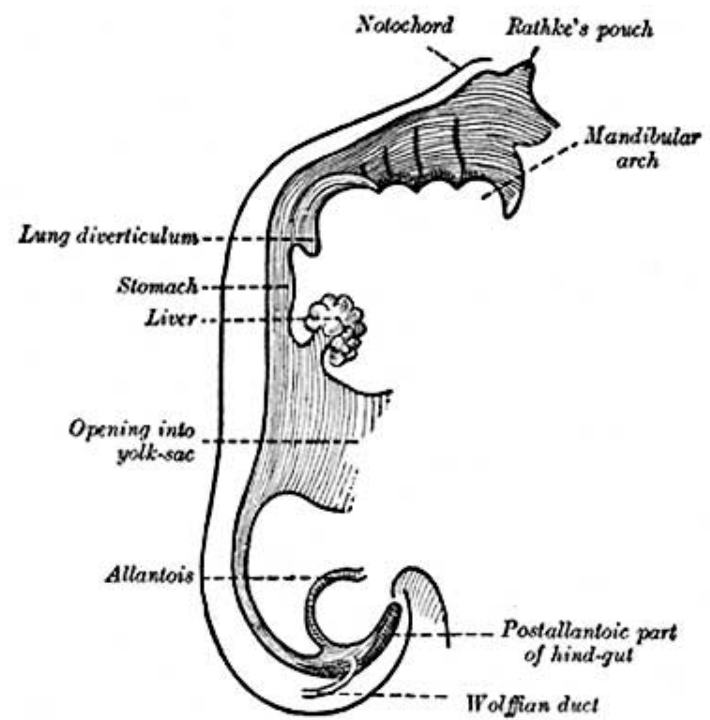
This lecture will cover the early development of the endoderm layer of the trilaminar embryo as it contributes to the lining, glands and organs of the gastrointestinal tract (GIT). The endoderm contribution to the respiratory system will be covered in a [separate lecture](#).

Gastrulation, or gut formation, was historically the easiest observable feature of frog development. In human development, during the 4th week the 3 distinct portions (fore-, mid- and hind-gut) extend the length of the embryo and will contribute different structures.

The oral cavity (mouth) is formed following breakdown of the [buccopharyngeal membrane](#) (= oropharyngeal or oral) and the opening means that it contains amniotic fluid, which is also swallowed later in development.

The large mid-gut is generated by lateral embryonic folding which "pinches off" a pocket of the yolk sac, the 2 compartments continue to communicate through the vitelline duct.

The hindgut (cloaca) will later be divided into separate urogenital and rectal regions that end at the cloacal membrane.



The early developing gastrointestinal tract

Note that we will be returning in the laboratory and later (head, endocrine, neural crest) to discuss the gastrointestinal tract, associated organs and physical growth changes.

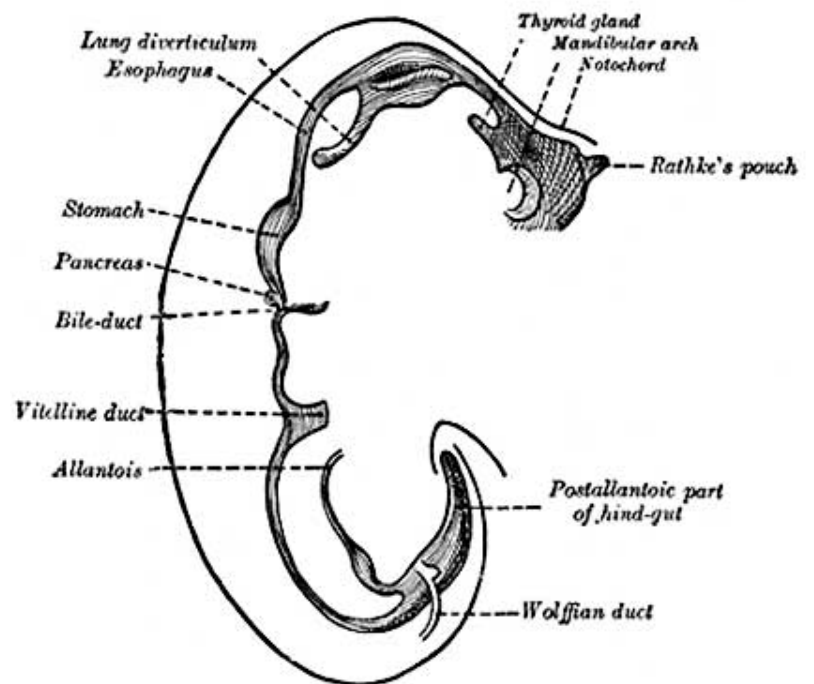
Lecture - Video and Audio (to be watched on or before Monday)

[Expand]

Midgut Rotation - Recent Article [Expand]

Lecture Objectives

- Understanding of germ layer contributions to the early gastrointestinal tract (GIT)
- Understanding of the folding of the GIT
- Understanding of three main GIT embryonic divisions
- Understanding of associated organ development (liver, pancreas, spleen)
- Brief understanding of mechanical changes (rotations) during GIT development
- Brief understanding of gastrointestinal abnormalities



The later developing gastrointestinal tract

Lecture Resources

Movies [Expand]

References [Expand]

Germ Layer Contributions

- **Endoderm** - epithelium and associated glands.
- **Mesoderm** (splanchnic) - mesentry, connective tissues, smooth muscle, blood vessels.

- **Ectoderm** (neural crest) - enteric nervous system.

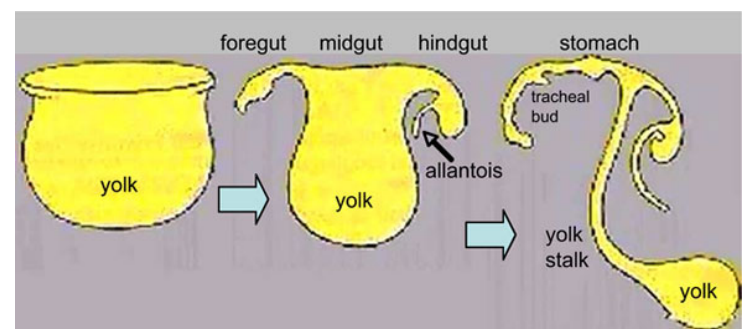
Both endoderm and mesoderm will contribute to associated organs.

Folding of the embryonic disc occurs ventrally around the notochord, which forms a rod-like region running rostro-caudally in the midline.

In relation to the notochord:

- **Laterally** (either side of the notochord) lies mesoderm.
- **Rostrally** (above the notochord end) lies the buccopharyngeal membrane, above this again is the mesoderm region forming the heart.
- **Caudally** (below the notochord end) lies the primitive streak (where gastrulation occurred), below this again is the cloacal membrane.
- **Dorsally** (above the notochord) lies the neural tube then ectoderm.
- **Ventrally** (beneath the notochord) lies the mesoderm then endoderm.

The ventral endoderm (shown yellow) has grown to line a space called the yolk sac. Folding of the embryonic disc "pinches off" part of this yolk sac forming the first primitive GIT.



Coelomic Cavity

- The mesoderm initially undergoes segmentation to form paraxial, intermediate mesoderm and **lateral plate mesoderm**.
- Paraxial mesoderm segments into somites and lateral plate mesoderm divides into somatic and **splanchnic mesoderm**.
- The space forming between them is the **coelomic cavity**, that will form the 3 major body cavities (pericardial, pleural, **peritoneal**)
- Most of the gastrointestinal tract will eventually lie within the peritoneal cavity.

- **Mesoderm and Ectoderm Cartoons**

-

- Paraxial and Lateral Plate

-

- Somatic and Splanchnic

(Note only the righthand side is shown, lefthand side would be identical.)

Week 4

(Gestational age **GA** 6 weeks) Carnegie stage 11

-

- Stage 11 25 days, Low power ventral view of the Buccopharyngeal Membrane

- Higher power ventrolateral view of the Buccopharyngeal Membrane

- Close up view of the degenerating Buccopharyngeal Membrane

- Stage 12 Week 4, 26 days

- Stage 12 Cloacal membrane

Liver Development

Endoderm and splanchnic mesoderm at the level of the transverse septum (week 4)

- Stage 11 - hepatic diverticulum development
- Stage 12 - cell differentiation, septum transversum forming liver stroma, hepatic diverticulum forming hepatic trabeculae
- Stage 13 - epithelial cord proliferation enmeshing stromal capillaries

The liver initially occupies the entire anterior body. All blood vessels enter the liver (placental, vitelline) and leave to enter the heart.

Stomach

- During week 4 at the level where the stomach will form the tube begins to dilate, forming an **enlarged lumen**.
- The dorsal border grows more rapidly than ventral first rotation (of 90 degrees), which establishes the greater curvature of the stomach.
- A second rotation (of 90 degrees) occurs on the longitudinal axis establishing the adult orientation of the stomach.

Week 5

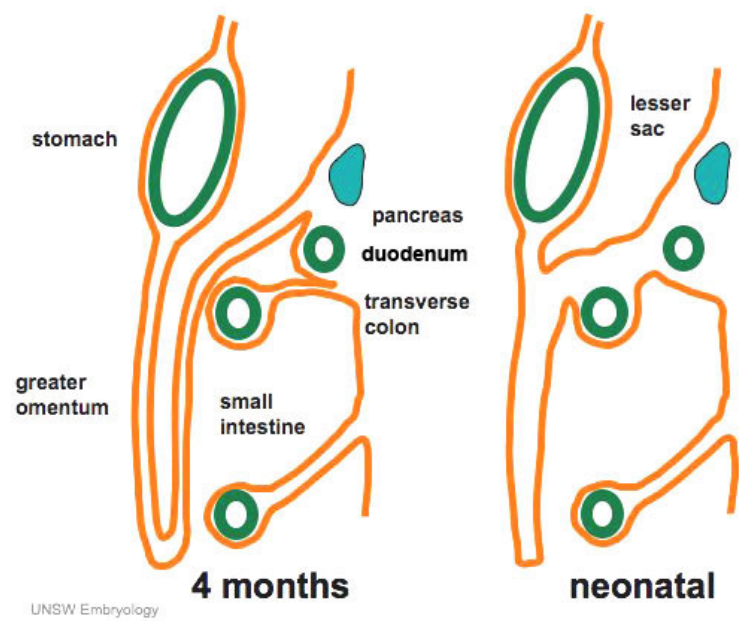
(GA 7 weeks)

Canalization

- Beginning at week 5 endoderm in the GIT wall proliferates
- By week 6 totally blocking (occluding)
- over the next two weeks this tissue degenerates reforming a hollow gut tube.
- By the end of week 8 the GIT endoderm tube is a tube once more.
- The process is called recanalization (hollow, then solid, then hollow again)
- Abnormalities in this process can lead to abnormalities such as atresia, stenosis or duplications.

Mesentery Development

- Ventral mesentery lost except at level of stomach and liver.
 - contributing the lesser omentum and falciform ligament.
- Dorsal mesentery forms the adult structure along the length of the tract and allows blood vessel, lymph and neural connection.
- At the level of the stomach the dorsal mesogastrium extends as a fold forming the greater omentum
 - continues to grow and extend down into the peritoneal cavity and eventually lies anterior to the small intestines.
 - This fold of mesentery will also fuse to form a single sheet.



Spleen

- Mesoderm within the dorsal mesogastrium (week 5) form a long strip of cells adjacent to the forming stomach above the developing pancreas.
- Vascular and immune organ, no direct GIT function.

Week 8 - 10

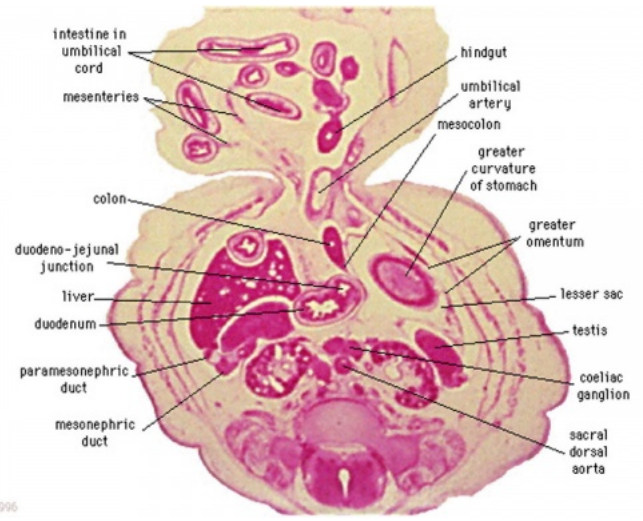
(GA 10-12 weeks)

Intestine Herniation

- **neural crest** migration into the wall forms enteric nervous system (peristalsis, secretion)
- midgut grows in length as a loop extending ventrally, returning as hindgut
- connected by dorsal

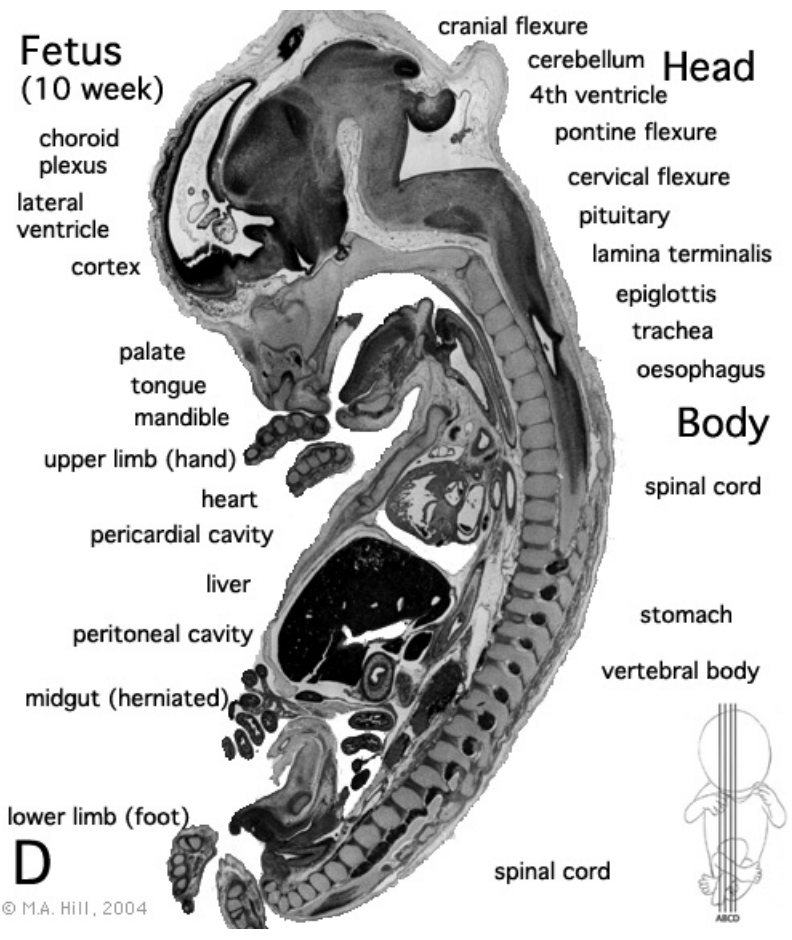
mesentery

- rotates to form adult anatomical position (abnormalities of rotation)
- continued body growth "engulfs" the intestine by about week 11.

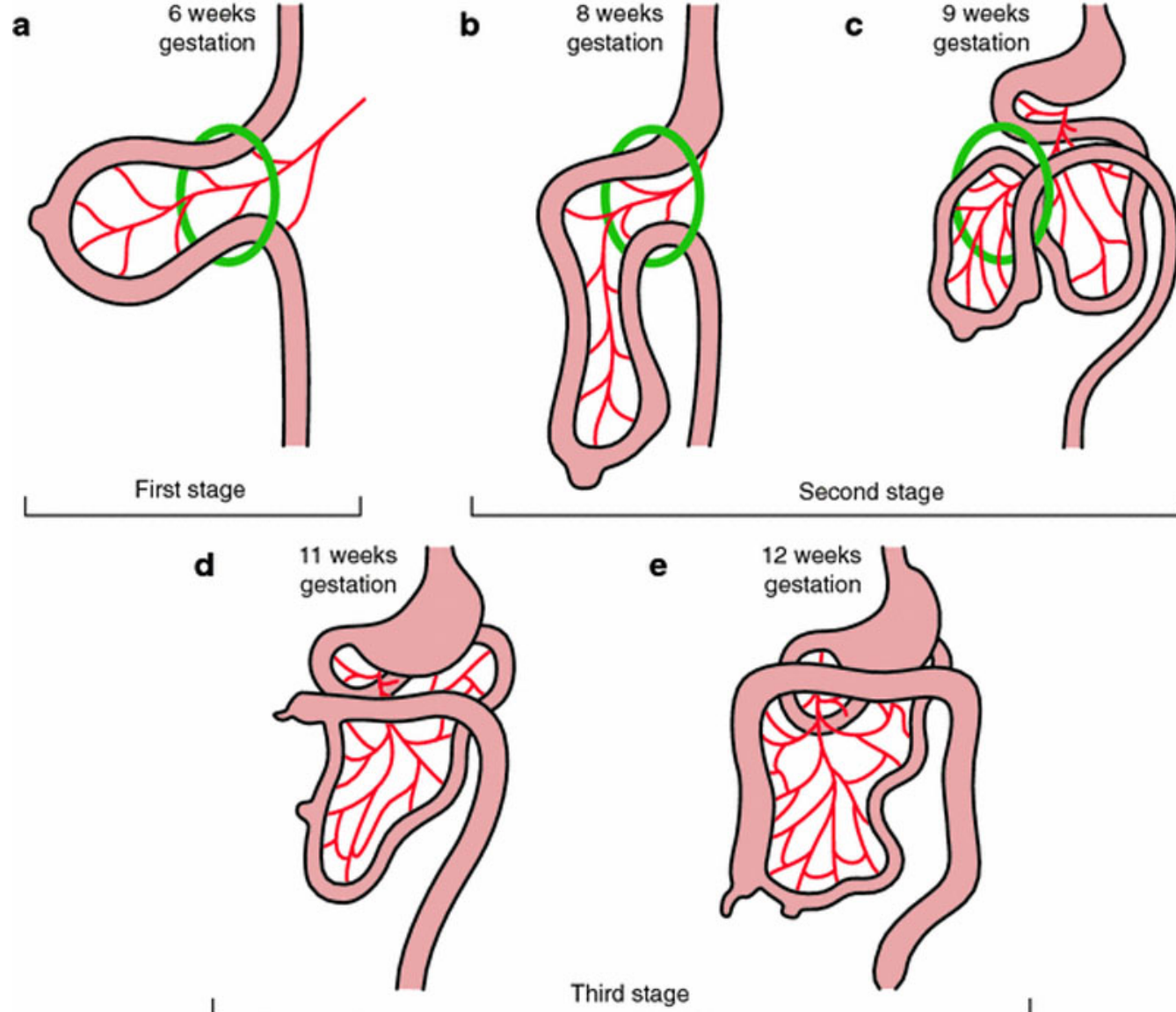


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Intestine Rotation



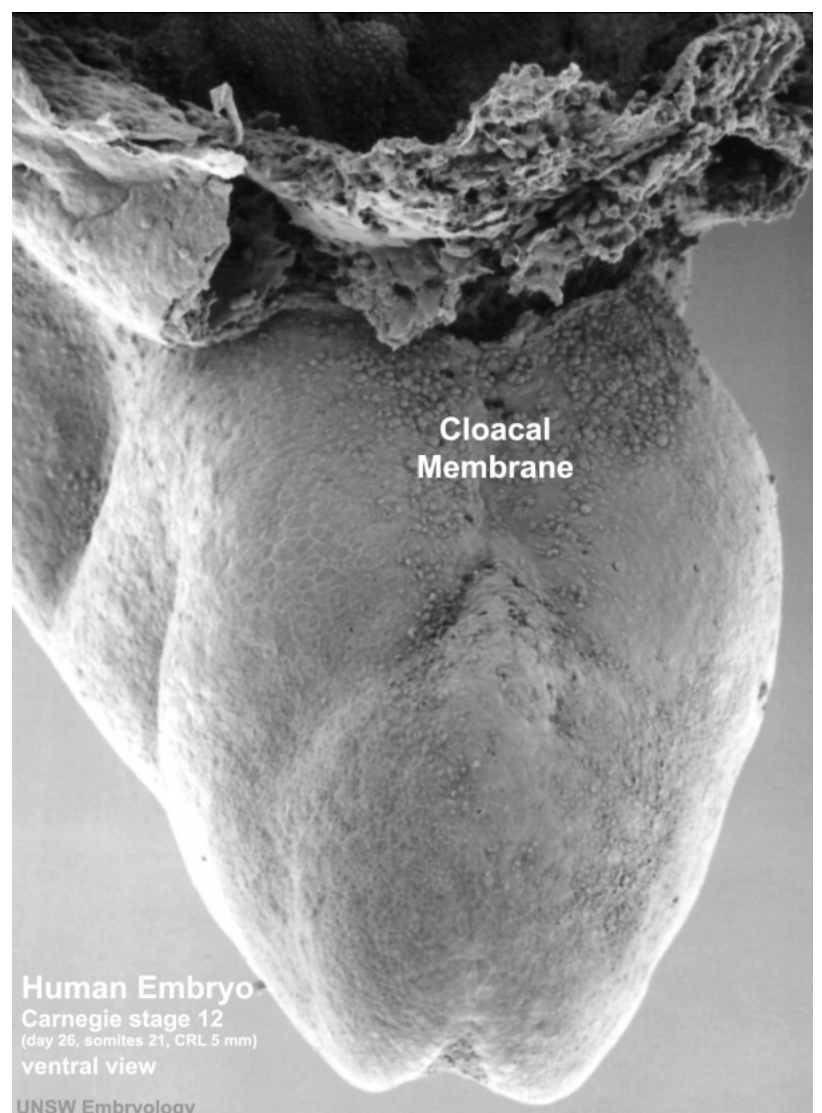
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Normal intestinal rotation (note these are gestational age **GA** weeks)^[1]

Hindgut

- Initially the **cloaca** forms a common urinary, genital, GIT space
- This is divided by formation of a **septum** into anterior urinary and dorsal rectal (superior Tourneux fold; lateral Rathke folds)
- hindgut - distal third transverse colon, descending and sigmoid colon, rectum.
- anal pit - distal third of anorectal canal (ectodermal)

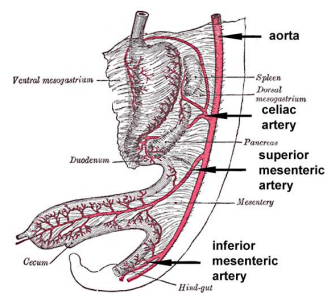


Gastrointestinal Tract Divisions

During the 4th week the 3 distinct

portions (fore-, mid- and hind-gut) extend the length of the embryo and will contribute different components of the GIT. These 3 divisions are also later defined by the vascular (artery) supply to each of these divisions.

1. **Foregut** - celiac artery (Adult: pharynx, esophagus, stomach, upper duodenum, respiratory tract, liver, gallbladder pancreas)
2. **Midgut** - superior mesenteric artery (Adult: lower duodenum, jejunum, ileum, cecum, appendix, ascending colon, half transverse colon)
3. **Hindgut** - inferior mesenteric artery (Adult: half transverse colon, descending colon, rectum, superior part



Gastrointestinal Tract Blood Supply

Fetal

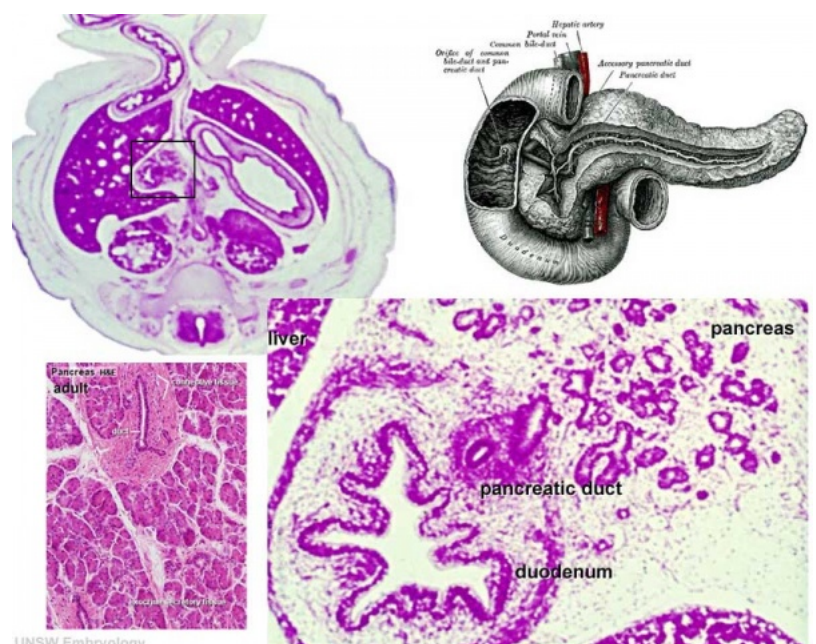
Liver

- Differentiates to form the hepatic diverticulum and hepatic primordium, generates the gall bladder then divides into right and left hepatic (liver) buds.
- Hepatic Buds - form hepatocytes, produce bile from week 13 (forms meconium of newborn)
 - Left Hepatic Bud - left lobe, quadrate, caudate (both q and c anatomically Left) caudate lobe of human liver consists of 3 anatomical parts: Spiegel's lobe, caudate process, and paracaval portion.
 - Right Hepatic Bud - right lobe
- Bile duct - 3 connecting stalks (cystic duct, hepatic ducts) which fuse.
- Early liver also involved in blood formation, after the yolk sac and blood islands acting as a primary site.

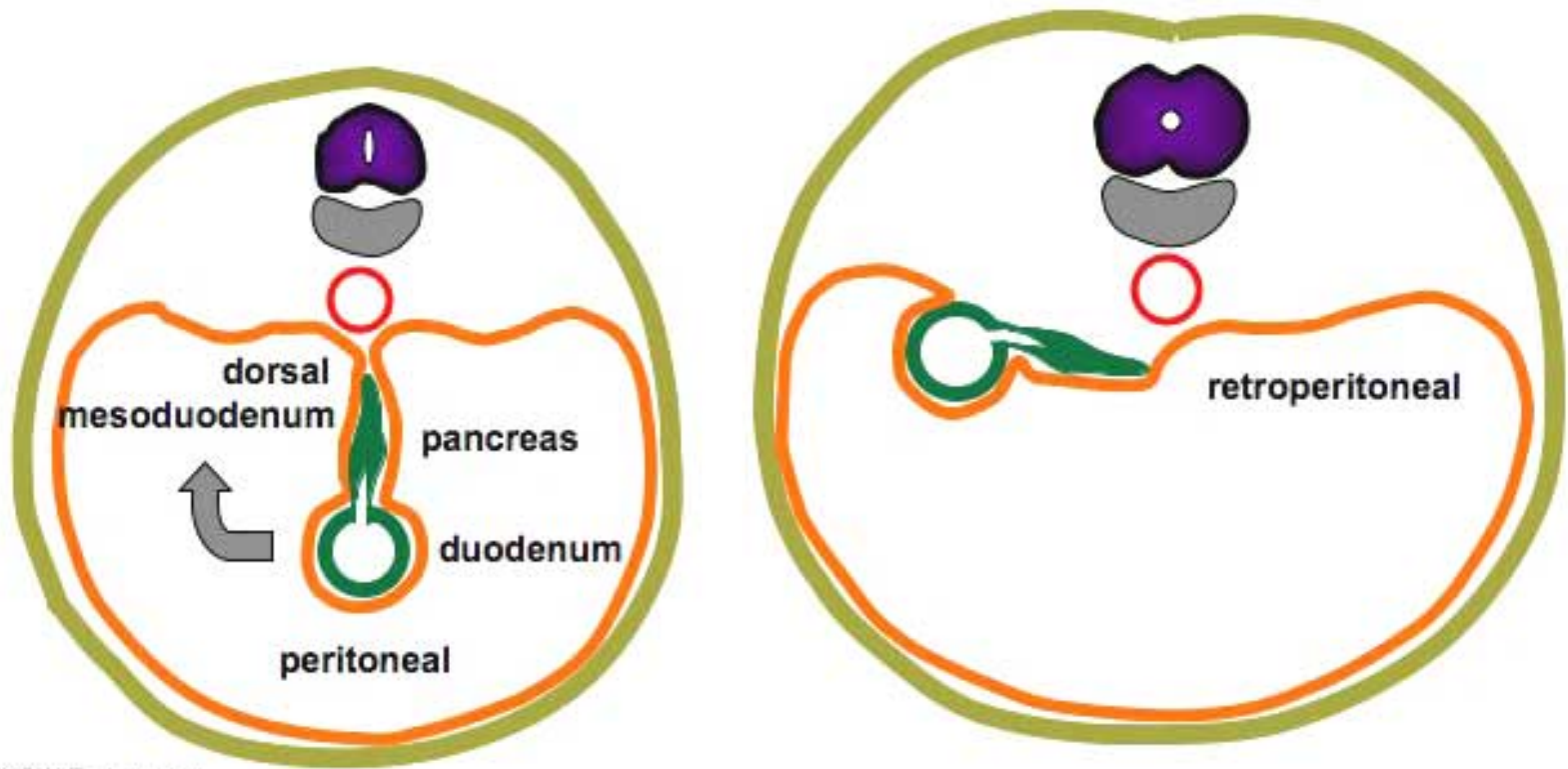
Liver Development

Pancreas

- Pancreatic buds - endoderm, covered in splanchnic mesoderm
- Pancreatic bud formation – duodenal level endoderm, splanchnic mesoderm forms dorsal and ventral mesentery, **dorsal bud** (larger, first), **ventral bud** (smaller, later)
- Duodenum growth/rotation – brings ventral and dorsal buds together, fusion of buds, exocrine function (postnatal function)



- Pancreatic duct – ventral bud duct and distal part of dorsal bud
- Pancreatic islets - endocrine function (**week 10** onwards)

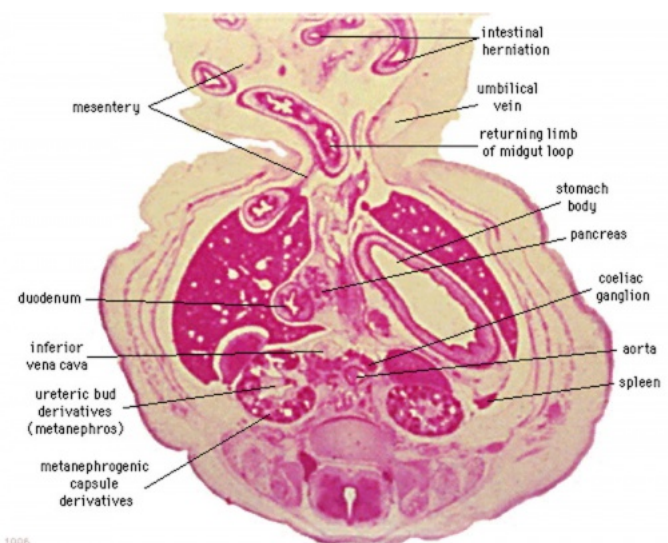


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Pancreas Development

Spleen

- Mesoderm within the dorsal mesogastrum form a long strip of cells adjacent to the forming stomach above the developing pancreas.
- The spleen is located on the left side of the abdomen and has a role initially in blood and then immune system development.
- The spleen's haematopoietic function (blood cell formation) is lost with embryo development and lymphoid precursor cells migrate into the developing organ.
- Vascularization of the spleen arises initially by branches from the dorsal aorta.



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Spleen week 8 stage 22 embryo

Gastrointestinal Tract Abnormalities

Lumen Abnormalities

There are several types of abnormalities that impact upon the continuity of the gastrointestinal tract lumen.

Atresia

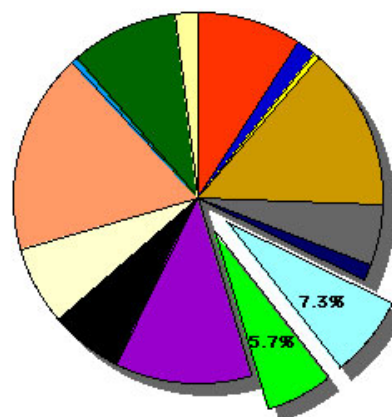
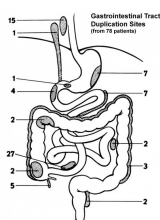
- Interruption of the lumen (esophageal atresia, duodenal atresia, extrahepatic biliary atresia, anorectal atresia)

Stenosis

- Narrowing of the lumen (duodenal stenosis, pyloric stenosis)

Duplication

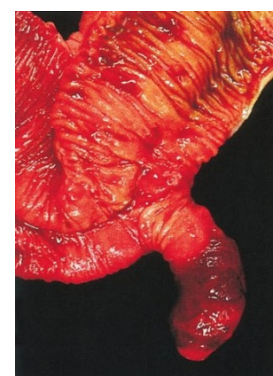
- Incomplete recanalization resulting in parallel lumens, this is really a specialized form of stenosis.



Data source : Congenital Malformations Australia 1981-92

Meckel's Diverticulum

- This abnormality is a very common (incidence of 1-2% in the general population) and results from improper closure and absorption of the vitelline duct during early development.
 - vitelline duct (omphalomesenteric duct, yolk stalk) is a transient developmental duct that connects the yolk to the primitive GIT.



Meckel's

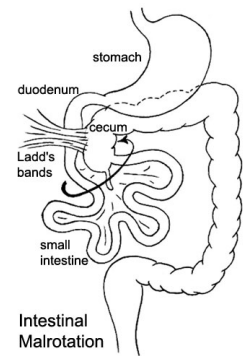
Intestinal Malrotation

Presents clinically in symptomatic malrotation as:

- Neonates - bilious vomiting and bloody stools.
- Newborn - bilious vomiting and failure to thrive.
- Infants - recurrent abdominal pain, intestinal obstruction, malabsorption/diarrhea, peritonitis/septic shock, solid food intolerance, common bile duct obstruction, abdominal distention, and failure to thrive.

Ladd's Bands - are a series of bands crossing the duodenum which can cause duodenal obstruction.

Links: [Intestinal Malrotation](#)

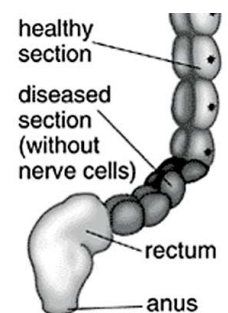


Intestinal malrotation

Intestinal Aganglionosis

(intestinal aganglionosis, Hirschsprung's disease, aganglionic colon, megacolon, congenital aganglionic megacolon, congenital megacolon)

- A condition caused by the lack of enteric nervous system (neural ganglia) in the intestinal tract responsible for gastric motility (peristalsis).
- Neural crest cells
 - migrate initially into the cranial end of the GIT.
 - migrate during embryonic development caudally down the GIT.
- Aganglionosis typically at the anal end of GIT.
 - increased severity as it extends cranially.



Gastroschisis

Gastroschisis (omphalocele, paraomphalocele, laparoschisis, abdominoschisis, abdominal hernia) is a congenital abdominal wall defect which results in herniation of fetal abdominal viscera (intestines and/or organs) into the amniotic cavity.

Incidence of gastroschisis has been reported at 1.66/10,000, occurring more frequently in young mothers (less than 20 years old).

By definition, it is a body wall defect, not a gastrointestinal tract defect, which in turn impacts upon GIT development.

This indirect developmental effect (one system impacting upon another) occurs in several other systems.



- **Omphalocele** - appears similar to gastrochisis, herniation of the bowel, liver and other organs into the intact umbilical cord, the tissues being **covered by membranes** unless the latter are ruptured.

[Gastrochisis](#)

Final Thoughts- After Birth

Remember that the GIT does not function until after birth consider:

- [metabolic disorders](#) discovered by [neonatal diagnosis](#)
- Neonatal feeding difficulties due to cleft lip and cleft palate.

Links: [Gastrointestinal Tract - Abnormalities](#)

1. ↑ Vicki Martin, Charles Shaw-Smith **Review of genetic factors in intestinal malrotation.** *Pediatr. Surg. Int.*: 2010, 26(8);769-81
[PubMed 20549505](#) | [PMC2908440](#)
2. ↑ R J Bower, W K Sieber, W B Kiesewetter **Alimentary tract duplications in children.** *Ann. Surg.*: 1978, 188(5);669-74
[PubMed 718292](#)

Terms

[Gastrointestinal Tract Terms](#) [Expand]

Glossary Links

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