Gastrointestinal Tract Development

Endoderm $\rightarrow$ cell sheet $\rightarrow$ tubular gut
  Lateral folding
  Ventral bending cranially $\rightarrow$ Head fold
  Ventral bending caudally $\rightarrow$ Tail fold

Yolk sac is connected to the gut in the middle
  Yolk stalk, omphalomesenteric duct, or vitelline duct
Yolk stalk is progressively delineated.
Embryonic Gut

Regions:
- Foregut → Lateral fold and head fold
- Hindgut → Lateral fold and tail fold
- Midgut → Yolk Stalk Region

Anterior intestinal portal – foregut / midgut transition

Posterior intestinal portal - midgut / hindgut transition


Cloacal plate or Proctodeal membrane = ectoderm-endoderm bilayer, separates the ectoderm lined proctodeum from the gut endoderm.
Embryonic Gut

Straight tube suspended by the dorsal mesentery

Only ventral connection is the transverse septum level of stomach and cranial duodenum.

Transverse septum - mesoderm initially between developing heart and the cranial margin of the embryonic disc

Cranial flexure displaces the transverse septum between the heart and the yolk sac – Forming the initial partition separating the thoracic and abdominal cavities → part of the diaphragm

Hindgut – evagination is the allantois
Foregut Derivatives

Oropharyngeal membrane (cranial end)
Pharynx (derivatives of the pharyngeal pouches, tongue, thyroid gland)
Thoracic esophagus (lung buds)
Abdominal esophagus
Stomach
Cranial half of duodenum (liver, gallbladder, pancreas)
Caudal end = Ampulla of Vater (common bile and pancreatic ducts drain into gut)
Pharynx

Pharyngeal:

Pouches (endoderm); Grooves (ectoderm); Arches (mesoderm)
Pharyngeal Pouches

Pharyngeal Pouch #1 – Caudal to Arch #1
   Auditory tube (Eustachian tube), tympanic cavity

Pharyngeal Pouch #2 – Caudal to Arch #2
   Supratonsillar fossae associated with Palatine tonsils

Pharyngeal Pouch #3 – Caudal to Arch #3
   Inferior parathyroid, Thymus

Pharyngeal Pouch #4 – Caudal to Arch #4
   Superior parathyroids, Postbranchial body
Tongue

Lateral Lingual Swellings – paired lateral swellings from the 1st pharyngeal arch (ventral)

2 unpaired medial swellings from the ventral midline of the pharynx
   Tuberculum impar
   Copula

Contribution from the 3rd and 4th pharyngeal arches

Oral Tongue (anterior 2/3) forms from the expansion of lateral swellings and the tuberculum impar - median sulcus of the tongue is the site of midline fusion

Base of the tongue is formed from the copula with contribution from the 3rd and 4th pharyngeal arches

The epiglottis forms from a swelling caudal to the copula
Thyroid Diverticulum
Midventral thickening, between Pharyngeal Pouch 1 and 2 (base of the tongue)
Single outgrowth elongates in a caudal direction
Bifurcates to form the bi-lobed Thyroid gland

The connection – thyroglossal duct regresses about week 7

The site of the thyroid diverticulum persist as the foramen cecum – between the tuberculum impar and the copula
Esophagus

Thoracic Esophagus buds off the lung buds → Respiratory Tract
Abdominal Esophagus – abruptly narrows – extends to the Stomach

Differentiation of Epithelium:
- 7th – 8th Week – epithelium is stratified columnar, Lumen becomes partially occluded
- Appearance of large vacuoles
- Vacuoles coalesce – recanalization
- 12th Week - Epithelium is multilayered and ciliated
- 16th Week – Stratified squamous epithelium
Stomach

Stomach - initially symmetrical and fusiform (spindle)

Differential growth - dorsal > ventral - creates the Greater curvature of the stomach (dorsal side) and Lesser curvature (ventral side)

90° rotation of the stomach around craniocaudal axis
greater curvature is to the left and caudal
lesser curvature is to the right and cranial

Dorsal mesogastrium (dorsal mesentery) – differential growth is responsible for the rotation. Dorsal mesogastrium becomes the greater omentum
Dorsal mesogastrium becomes the greater omentum
Stomach rotation moves the duodenum to the left and cranially.
Liver is Derived from the Duodenum

Endodermal thickening – ventral side of Duodenum

Hepatic diverticulum - grows ventrally into the transverse septum

Hepatic diverticulum branches into many Hepatic cords that form hepatocytes and the drainage ducts (bile canaliculi, hepatic ducts).

Gastrohepatic omentum – connection to the stomach – becomes the lesser omentum

Falciform ligament – ventral mesentery connection to the body wall
Gallbladder / Cystic Duct

Cystic diverticulum arises from a ventral endodermal thickening just posterior to the hepatic diverticulum.

The cystic diverticulum gives rise to the gallbladder and cystic duct.

Hepatic duct and cystic duct merge to form the common bile duct.
Pancreas

Pancreas forms from two distinct outgrowths from the duodenum

Dorsal pancreatic bud grows into the dorsal mesentery

Ventral pancreatic bud sprouts from the hepatic diverticulum into the ventral mesentery caudal to the forming gallblader

The main duct of the ventral pancreas bud merges at the proximal end of the common bile duct

The mouth of the common bile duct is displaced to the dorsal mesentery
Pancreas

The dorsal and ventral pancreatic rudiments fuse.

The dorsal duct degenerates and the dorsal and ventral parts merge their duct systems. The ventral duct becomes the main pancreatic duct (Duct of Wirsung).

Where the common bile duct and pancreatic ducts empty into the duodenum is called the Ampulla of Vater.

Exocrine function - acinar cells - production of digestive enzymes.

Endocrine function - islets of Langerhans - production of insulin and glucagon (β cells and α cells).
Spleen

The Spleen is an intra-abdominal organ that is not an endodermal derivative.

The Spleen is mesodermal and develops in the dorsal mesogastrium.

The Spleen is a vascular lymphatic organ.

The Spleen moves to the left side of the abdominal cavity with the rotation of the stomach.

Initially a hematopoietic organ, later gets colonized by T-lymphocyte precursor cells.
Dorsal mesogastrium becomes the greater omentum
Formation of the Intestine

Midgut derivatives:
- Caudal half of duodenum
- Jejunum
- Ileum
- Cecum
- Appendix
- Ascending colon
- Right 2/3 of transverse colon

Hindgut derivatives:
- Left 1/3 of transverse colon
- Descending colon
- Sigmoid colon
- Rectum
- Cloacal membrane at caudal end
Primary Intestinal Loop

The intestine is essentially a long straight tube, but it’s development is complicated by its length.

Two important points of reference:
- Yolk Stalk – near border of small and large intestine
- Superior Mesenteric Artery – branch of Dorsal Aorta

Ileum – elongates too rapidly for the size of the abdominal cavity causing a herniation into the umbilicus

Dorsal-ventral hairpin - called the primary intestinal loop.
Intestine Development

Cranial part of loop gives rise to most of the ileum

Caudal loop becomes part of ileum, the ascending colon and 2/3 of the transverse colon

Initially - the loop does a 90° counterclockwise rotation (viewed from the front) - cranial loop ➔ right, caudal loop ➔ left

Jejunum and Ileum lengthens resulting in a series of folds called the jejunal-ileal loops
Retraction

Cecum defines junction between small and large intestines – producing the appendix

Retraction of the loop into the abdomen

Associated with a $180^\circ$ rotation - total rotation is $270^\circ$

Cecum lies just inferior to the liver

The cecum moves in a cranial to caudal direction to lie in the lower left abdomen
Primary intestinal loop

Aorta
Stomach
Superior mesenteric artery

A
42 days

B
90°
50 days

C
Liver
Aorta
Stomach
Superior mesenteric artery
Cecum
70 days
Ascending and Descending Colon

Dorsal mesentery associated with the ascending and descending colon shortens and disappears

These regions adhere directly to the dorsal body wall

Transverse colon does not become fixed
Cloaca

Cloaca (latin = sewer) - where allantois and gastrointestinal tract merge

Cloaca is partitioned into the rectum (posterior) and the primitive urogenital sinus (anterior) - by the growth of the urorectal septum

Urorectal septum is the composite of two septal system - Tourneux fold (central) and Rathke folds (lateral)

Urorectal septum fuses with cloacal membrane - forming the urogenital membrane and the anal membrane
Anorectal Canal

Anorectal canal - between rectum and anus
Superior 2/3 is endodermal from hindgut
Inferior 1/3 is derived from the proctodeum - ectodermal

The Ectodermal-Endodermal boundary in adult is marked by an irregular folding of mucosa in the anorectal canal called the Pectinate line
Canalization and Histogenesis

The developing digestive tract lumen becomes occluded and secondary lumina form and coalesce during recanalization.

Stomach – Gastric mucosa – folds called rugae, pits called gastric pits, HCl secretion begins postnatal.

Intestine - Intestinal Villi form by mesodermal growth during recanalization.

Intestinal Crypts form at the base of the intestinal villi.

Each crypts contains a clone of Epithelial Stem Cells that produce intestinal cells throughout adult life.

Intestinal epithelial cells have a 4 day life span.
1400 cells/villus shed into lumen/day

- 4 days
- 3 days
- 2 days
- 1 day
- 0 days

Enterocyte

Goblet cell

Villus

Enteroendocrine cell

Stem cell

Crypt

Paneth cell

Stem cell

Crypt
Anomalies - Foregut

Esophagus:
- Esophageal stenosis (narrowing) – abnormal recanalization – impaired swallowing
- Esophageal atresia (abnormal opening) – abnormal branching of the respiratory tract – impaired swallowing

Stomach:
- Pyloric stenosis – hypertrophy of smooth muscle, projectile vomiting
- Heterotopic gastric mucosa – Misplaced gastric mucosa cells
Anomalies - Foregut

Liver:
  Biliary atresia – abnormal hepatic duct formation – varying severity postnatal jaundice

Pancreas:
  Annular pancreas – Pancreatic tissue encircling the duodenum sometimes causing obstruction
  Heterotopic pancreatic tissue
  Misplaced pancreatic cells
Anomalies - Midgut

Duodenal stenosis and atresia – abnormal recanalization

Persistent vitelline duct –
  Meckel’s diverticulum - (2-4% of population) – blind pouch

Fibrous cord – connection to umbilicus

Volvulus – intestinal rotation → bowel strangulation

Umbilicoil fistula – direct opening
Anomalies – Midgut Omphalocele

Failure of the umbilicus to close - newborn with organs protruding from the abdominal walll

Organs protruding into a thin sac of amniotic tissue from normal herniation - incomplete retraction

Organs in a sac of peritoneum and amniotic tissue - indicates normal herniation and retraction, but a secondary herniation resulting from the failure of the ventral abdominal wall to close
Anomalies - Midgut
Abnormal Rotation and Fixation

Spectrum of abnormalities

Non-rotation

Reverse rotation

Mixed rotation

Subhepatic cecum
Non-Rotation

Called left-sided colon

1\textsuperscript{st} rotation is Normal

2\textsuperscript{nd} rotation is Absent

Cranial loop ends up on the right side

Caudal loop on the left side

Some organs may or may not get fixed to the body wall
Reverse Rotation

Normal 1\textsuperscript{st} rotation

2\textsuperscript{nd} rotation is clockwise instead of counter clockwise

Net rotation is 90° clockwise

This is equivalent to a 270° counter clockwise rotation except the duodenum is ventral to the transverse colon and does not get fixed to dorsal wall, transverse colon does get fixed
Mixed Rotation

Cranial and caudal loops behave independently

Cranial loop rotates only the 1\textsuperscript{st} 90°

Caudal loop only rotates the 2\textsuperscript{nd} 180°

Results in misplaced organs - abnormal fixation

Typical outcome from abnormal rotations -
obstructions of the gastrointestinal tract,
compression of intestinal vasculature - resulting in
intestinal ischemia; compression of lymphatic
vessels - resulting in gastrointestinal bleeding
Cephalic limb (limb a) of intestinal loop undergoes normal 90° counterclockwise rotation; caudal limb (limb b) does not rotate.

Caudal Limb (b) undergoes normal 180° counterclockwise rotation; cephalic limb (a) does not rotate.

Resulting gut anomaly:
- Aorta
- Stomach
- Cecum
- Transverse colon
- Descending colon
- Small intestine

91 days
Anomalies – Midgut
Subhepatic Cecum
Intestinal Duplication, Diverticula, and Atresia

Unknown Causes
Anomalies - Hindgut

Hirschsprung’s Disease – Dilation of the colon – defective neural crest migration \( \rightarrow \) absence of parasympathetic ganglia in the colon wall

Imperforate anus – absence of anal opening
Hindgut Fistula

Often connecting the hindgut to the urogenital system