Development of the Gastrointestinal Tract

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Folding of the embryo results in the formation of the gut consisting of 3 parts:

**Foregut** - extends from the buccopharyngeal membrane to the septum transversum

**Midgut** - communicates with vitelline tube and yolk sac

**Hindgut** - communicates with the allantoic diverticulum and extends to the cloacal membrane
The foregut is divided into 3 parts

1st part - Pharynx
- associated with paired branchial arches

2nd (Thoracic) part -
gives rise to the respiratory bud and oesophagus

3rd (abdominal) part
- passes through septum transversum
- gives rise to abdominal part of oesophagus, stomach and half of the duodenum
The dorsal aorta supplies arteries to the gut

Aortic arches
- supply the pharynx

Set of 5 arteries
- supply thoracic part of oesophagus

Vitelline arteries
- initially supply the yolk sac and form a plexus around the gut. This develops into the arterial supply of the abdominal part of the gut.
Three main arteries formed from the vitelline plexus supply the foregut, midgut and hindgut.

- **Coeliac axis** supplies foregut in the septum transversum.
- **Superior mesenteric artery** supplies midgut.
- **Inferior mesenteric artery** supplies hindgut.

The boundaries of the foregut, midgut and hindgut are determined by their respective blood supply.
Stages in the Development of the Oesophagus

- **Elongation** occurs during the 2\(^{nd}\) month; by the 8th week the proliferating epithelium has partly occluded the lumen.

- **Recanalization** occurs during the 3\(^{rd}\) month by vacuolation in the multilayered columnar epithelium.

- **Differentiation** of stratified squamous epithelium occurs during the 4\(^{th}\) month.

- **Induction** of muscle formation in the splanchnic mesoderm occurs during the 2\(^{nd}\) month in response to signals from the endoderm. Initially only smooth muscle forms.

- **Transdifferentiation** of smooth to skeletal muscle occurs in the upper two-thirds of the oesophagus.

Transdifferentiation is the direct transformation of one differentiated cell type to another.
Development of the Stomach

This will be considered under 3 aspects:

• Growth
• Histological differentiation
• Position adjustment
Growth of the stomach

- **4th - 8th week** the developing stomach grows in all directions to become a sac-like structure.
- **5th week** - the dorsal border grows faster than the ventral border giving rise to the greater and lesser curvatures, respectively.
- **8th week** the stomach acquires its characteristic shape.

28 days (4 weeks)
35 days (5 weeks)
56 days (8 weeks)

Differential growth gives shapes to the stomach.
Differentiation of the Stomach

- **Foregut endoderm**
  - epithelium
  - gastric pits
  - gastric glands

- **Splanchnic mesoderm**
  - connective tissue
  - smooth muscle
  - blood vessels

- **Neural crest**
  - autonomic nerve plexuses
  - submucosal and myenteric
Histological Differentiation of the Stomach

Differentiation occurs during the 2nd-3rd months

Time frame

- **8 weeks**
  - rughae
  - pits
  - smooth muscle

- **10 - 20 weeks**
  - chief (zymogen)
  - parietal (oxyntic) cells

- **8-9 months**
  - glands become functional
  - secrete HCl and enzymes
Position adjustment of the stomach

a. Descent - Due to rapid elongation of the oesophagus, the cardiac end of the stomach descends from C2 at 4 weeks to T11 at 12 weeks.

b. Tilting - from a vertical position at 4 weeks to an oblique position by 8 weeks. This is due to more rapid growth along the greater curvature.

c. Rotation - 90° around a vertical axis, so that the original dorsal border (greater curvature) becomes left and the original left surface becomes ventral (anterior).

d. Shift to the left - of both the dorsal mesentery and the stomach.
The stomach develops in the septum transversum and has dorsal and ventral mesenteries.

28 day embryo: TS at the level of septum transversum.

**Lateral structures**
- Paraxial mesoderm
- Intermediate cell mass
- Pleuro-peritoneal canal

**Midline structures**
- Neural tube
- Notochord
- Dorsal aorta
- Dorsal mesentery
- Developing Stomach
- Ventral mesentery
The liver and spleen develop within the mesenteries of the stomach.

The spleen develops in the dorsal mesentery.

The liver develops in the ventral mesentery.
The stomach undergoes 90° rotation around cranio-caudal axis during the 5th week.

It hinges on the dorsal mesentery and folds 90° to the right.

The dorsal mesentery shifts to the left.

The vagus nerves serve as markers:

Left ➔ ventral
Right ➔ dorsal.
The omental bursa forms as a result of rotation of the stomach.

It communicates with the peritoneal cavity on the right.

Note peritoneal ligaments related to the stomach:

- Lieno-renal lig.
- Lieno-gastric lig.
- Lesser omentum
- Falciform lig.

- Dorsal mesentery
- Ventral mesentery
As rotation occurs, the dorsal mesentery of the stomach shifts to the left.

- **vacuolation**
- **proliferation**

This occurs by differential proliferation and vacuolation at the broad base of the dorsal mesentery.

The stomach is also shifted bodily to the left due to growth of the liver on the right side.
The Duodenum

- is derived from the terminal end of the foregut and the proximal end of the midgut;
- receives a dual blood supply from foregut and midgut arteries (coeliac and superior mesenteric)
- the origins of the liver and pancreatic buds are just proximal to the junction of the two parts
- becomes $C$-shaped through differential growth
- rotates $90^\circ$ to the right, the same rotation as occurs in the stomach
- becomes secondarily retroperitoneal, and loses its mesentery. Consequently the pancreas, developing in its mesentery also becomes retroperitoneal.
- its lumen is obliterated by rapid cell proliferation during the 2nd month (5-8 weeks) and is re-canalized by apoptosis soon after.
The Duodenum

Derived from the:
- distal end of foregut
- proximal end of midgut

becomes C-shaped by differential growth

Receives a dual blood supply from foregut and midgut arteries (coeliac and superior mesenteric arteries)

Gives rise to the liver and pancreatic buds from the distal foregut.

Originally in the midline, it rotates 90° to the right (the same rotation as occurs in the stomach)

It loses its mesentery and becomes secondarily retroperitoneal
The lumen of the duodenum is obliterated by rapid cell proliferation during the 2nd month ......

...... and is re-canalized by apoptosis soon after.

4 weeks

8 weeks

9 weeks

10 weeks
Duodenal Atresia and Stenosis

Most cases of duodenal atresia result from incomplete recanalization of the lumen distal to the duodenal papilla.

Clinical Features:
- repeated bile-stained vomiting on first day postnatal
- double bubble - bubble in stomach and bubble in dilated part of the duodenum separated by the air-free pyloric canal.
- no intestinal gas shadows
- relieved by resection of obstructed segment

About 25% of cases are associated with Down syndrome
The Midgut at 5 weeks consists of a simple loop suspended by a dorsal mesentery. It communicates with the yolk sac through the vitelline duct. Swelling in the caudal limb marks the future caecum and is supplied by the superior mesenteric artery.
Midgut Derivatives

The cranial limb elongates greatly to form the jejunum and two-thirds of the ileum.

The proximal part of the vitelline duct persists in 2% of individuals as Meckel’s diverticulum.

The caudal limb forms:
- Distal end of ileum
- Caecum & appendix
- Ascending colon
- Transverse colon
Midgut Herniation
At 6 weeks the midgut loop elongates rapidly and the liver enlarges. The abdominal cavity becomes relatively small and part of the intestine herniates into the extra-embryonic coelom, through the coelomic opening next to the umbilical cord.

Midgut Retraction
During the 10th week the abdomen enlarges and the intestine returns into the abdominal cavity. As this occurs, the midgut loop rotates so that the different parts of the intestine acquire their definitive positions in the abdominal cavity.
The caecum in the caudal limb of the midgut loop is taken as a landmark for rotation. It 'rotates' through a total of $270^\circ$ anticlockwise to acquire its definitive position.

Rotation occurs in two stages:

a. At 6 weeks: $90^\circ$ anti-clockwise
   - the caecum is shifted to the left

b. At 10 weeks: $180^\circ$ anticlockwise
   - the caecum acquires its definitive position
Three positions of the caecum during midgut development:

- **Caecum situated caudally**
  - 6 weeks

- **Caecum below right lobe of liver**
  - 10 weeks

- **Caecum in right iliac fossa**
  - 11 weeks
Retraction and Rotation of the Midgut Derivatives

During the return of the gut, the loops of small intestine (cranial limb) return first, and are situated to the right of the dorsal mesentery.

The descending colon (hindgut) is shifted to the left.

The caecum is the last to return, and has to be located to the right.
Atresia of the Jejunum, Ileum and Colon

- Atresias of the small intestine and colon are rare.
- Most cases are segmental rather than localized, i.e., they involve a long segment of the jejunum or ileum.
- Some cases involve a large segment of the midgut loop derivatives—termed “apple peel” atresia because a short segment of intestine distal to the atresia is coiled around the superior mesenteric artery remnant.

Atresias of the jejunum, ileum or colon, unlike duodenal atresia, result from arterial occlusion rather than failure of recanalization.

Most cases present as intestinal obstruction a few days after birth.
Malrotation of the gut

- Clockwise rotation results in intestinal situs inversus
- Failure of rotation may result in left-sided caecum, appendix and ascending colon
- Incomplete rotation - subhepatic caecum and appendix
  Some cases of malrotation are asymptomatic but may cause diagnostic problems in cases of appendicitis in later life

Volvulus is a rotation of an intestinal loop around a branch of the superior mesenteric artery
- it may cause intestinal obstruction or even gangrene
  -some cases correct spontaneously but surgical intervention is usually performed

Intussusception is the invagination of a segment of intestine in itself, causing obstruction
Persistent Vitello-intestinal Duct and Meckel’s Diverticulum

There are various degrees of persistence of vitelline duct:

- Vitelline fistula - meconium oozes out of umbilicus
- Vitelline cyst - part of duct is not obliterated
- Vitelline cord - attaches ileum to umbilicus
- Meckel’s diverticulum - persistent proximal part of vitelline duct occurs in 2% of normal individuals

Combinations of the above may also occur

Persistent vitelline duct of any degree may contain ectopic gastric mucosa and pancreatic acini causing intestinal ulceration and bleeding
Any type of persistent vitelline duct may contain **ectopic gastric mucosa and pancreatic acini** causing intestinal ulceration and bleeding.
Omphalocoele

- Herniation of abdominal viscera through a large umbilical ring
- Defect of lateral plate mesoderm
- Viscera covered by peritoneal and amniotic membrane
- 50% have other serious congenital or chromosome abnormalities

Gastroschisis

- Herniation of viscera through ruptured abdominal wall defect into the amniotic cavity
- To the right of the umbilicus
- No covering membranes; viscera bathed directly in amniotic fluid.
- Less commonly associated with other anomalies
The Hindgut

26 days: After formation of the tail fold, the allantois and hind gut open into a common chamber the cloaca. The cloacal membrane separates cloaca from the proctodaeum.

The allantois appears at about 16 days as a small diverticulum projecting from the caudal end of the yolk sac into the connecting stalk.

The urorectal septum separates the hindgut from the allantois. It grows towards the cloacal membrane. It is derived from mesoderm at the junction between the connecting stalk and yolk sac.
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The Hindgut

- Allantois
- Proctodaeum lined by ectoderm
- Cloacal membrane
- Cloaca lined by endoderm
- Hindgut
- Urorectal septum
During the 7th week the cloacal membrane disappears, exposing a ventral urogenital sinus opening and a dorsal anal opening.

The tip of the urorectal septum, separating the two openings forms the perineal body.

The urorectal septum grows towards the cloacal membrane but does not fuse with it. It is derived from mesoderm at the junction between the connecting stalk and yolk sac.
The urorectal septum is composed of two folds:
1. A superior, midline fold of Tourneux
2. Paired (right and left) lateral Rathke folds

Transverse sections of hindgut

Tourneux fold

Rathke fold

Tourneux and Rathke folds fused to form urorectal septum

Urogenital opening

Perineal body

Anal opening
Defects in the Fusion of the Tourneux Fold and the Rathke fold Result in Various Forms of Uro-rectal Fistula

Depending on the level of the defect and the sex of the embryo the fistulas may be:

- Recto - vesical
- Recto - urethral
- Recto - vaginal
- Recto - vestibular
- Ano - perineal
The Anal Canal

• At the end of the 8th week, after rupture of the cloacal membrane, proliferation of ectoderm occludes the anal opening.

• During the 9th week the opening is recanalized.

• Thus the terminal part of the anal canal is ectodermal in origin and supplied by the inferior rectal artery.

• The junction between ectoderm and endoderm is the pectinate line.
Pattern of Histodifferentiation in the Gastrointestinal Tract

4 weeks: formation of primordia
- stomach dilatation;
- duodenal loop;
- midgut loop;
- caecal dilatation

5 - 6 weeks - development of circular muscle - splanchnopleure

6-7 weeks - proliferation with occlusion of lumen in oesophagus and SI

8-9 weeks - recanalization - oesophagus and duodenum
Differentiation of epithelial derivatives
- pits and gland rudiments in stomach
- Villi and crypts in intestines + glands in duodenum
Differentiation of longitudinal muscle

9 - 10 weeks - differentiation of cell types - oxyntic cells, chief cells, mucus neck cells, surface epithelial cells
Aganglionic Megacolon - Hirschsprung Disease

Due to congenital absence of parasympathetic ganglia in the colon. This is a neural crest migration defect. It may be due to a genetic mutation of the RET gene, a tyrosine kinase receptor involved in neural crest cell migration.

It varies in extent - 80% involve sigmoid colon and rectum; 3% involve the whole colon.
The End

Go to Liver and Pancreas.ppt