



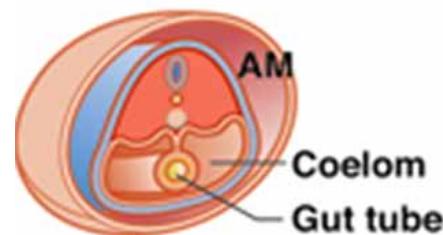
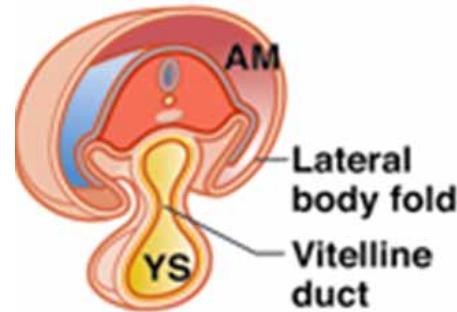
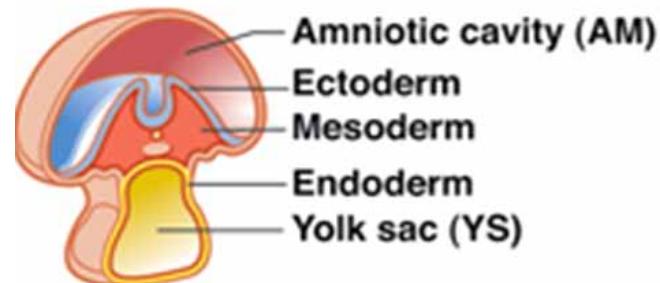
# Gastroenterology: Embryology and Associated Disorders

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# Primitive Gut Tube

## Primitive gut tube

- Incorporates yolk sac during development
- Endoderm
  - Epithelial lining of the mucosa
- Mesoderm
  - Lamina propria
  - Muscularis mucosa
  - Submucosa
  - Muscularis externa
  - Serosa
- Primitive gut tube divisions
  - Foregut
  - Midgut
  - Hindgut



- FA 2013: 308.1 • FA 2012: 138.3 • FA 2011: 130.3
  - ME 3e: 334.1 • ME 4e: 334.1

# Primitive Gut Tube Divisions

	Foregut	Midgut	Hindgut
<b>Artery</b>	Celiac artery	Superior mesenteric artery	Inferior mesenteric artery
<b>Parasympathetic</b>	Vagus nerves	Vagus nerves	Pelvic splanchnic nerves
<b>Sympathetic</b>	Preganglionics: thoracic splanchnic nerves T5–T9  Postganglionics: celiac ganglion	Preganglionics: thoracic splanchnic nerves T9–T12  Postganglionics: superior mesenteric ganglion	Preganglionics: lumbar splanchnic nerves L1–L2  Postganglionics: inferior mesenteric ganglion
<b>Referred pain</b>	Epigastrium	Umbilical	Hypogastrium
<b>Organs</b>	Esophagus Stomach Duodenum (1st, 2nd parts) Liver Pancreas Biliary apparatus Gallbladder	Duodenum (2nd, 3rd, 4th parts) Jejunum Ileum Cecum Appendix Ascending colon Transverse colon (proximal)	Transverse colon (distal third-splenic flexure) Descending colon Sigmoid colon Rectum Anal canal (above pectinate line)

- FA 2010: 312.2 • FA 2012: 339.2 • FA 2011: 311.3
- ME 3e: 335.1 • ME 4e: 335.1

# Early Mesenteric and Visceral Development

## Early development

- Dorsal embryonic mesentery

Suspends foregut, midgut, and hindgut from dorsal body wall

- Ventral embryonic mesentery

Suspends foregut from ventral body wall

- Visceral development

Spleen, pancreas, liver, and biliary structures develop within mesentery

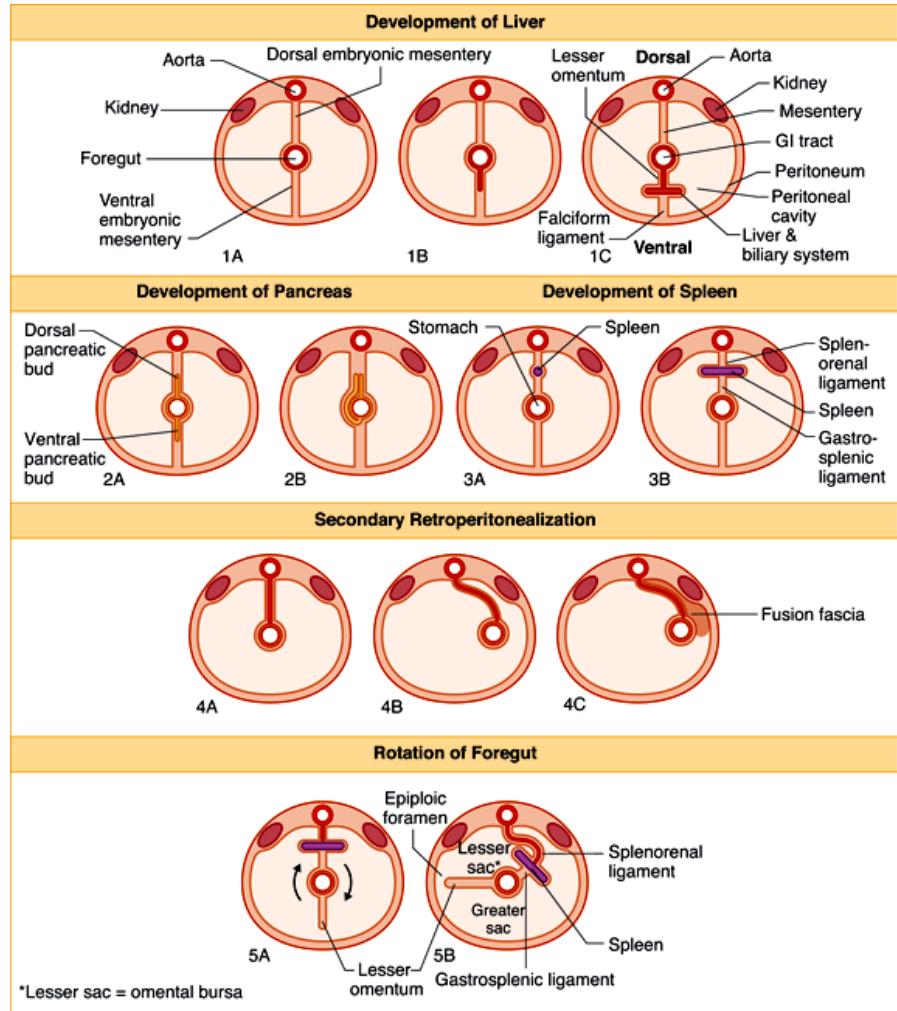
Abdominal foregut rotates 90° clockwise

Right upper quadrant

Liver, pylorus (stomach), proximal duodenum

Left upper quadrant

Spleen



- FA 2013: 308.1 • FA 2012: 138.3 • FA 2011: 311.3
  - ME 3e: 334.1 • ME 4e: 334.1

# Midgut Rotation

## Midgut rotation (weeks 6–10)

- Herniates through umbilical ring
- Rotates 270° counterclockwise, around axis of superior mesenteric artery
- Returns to abdomen
- Final position of midgut structures in abdominal cavity

Jejunum: left

Ileum: right

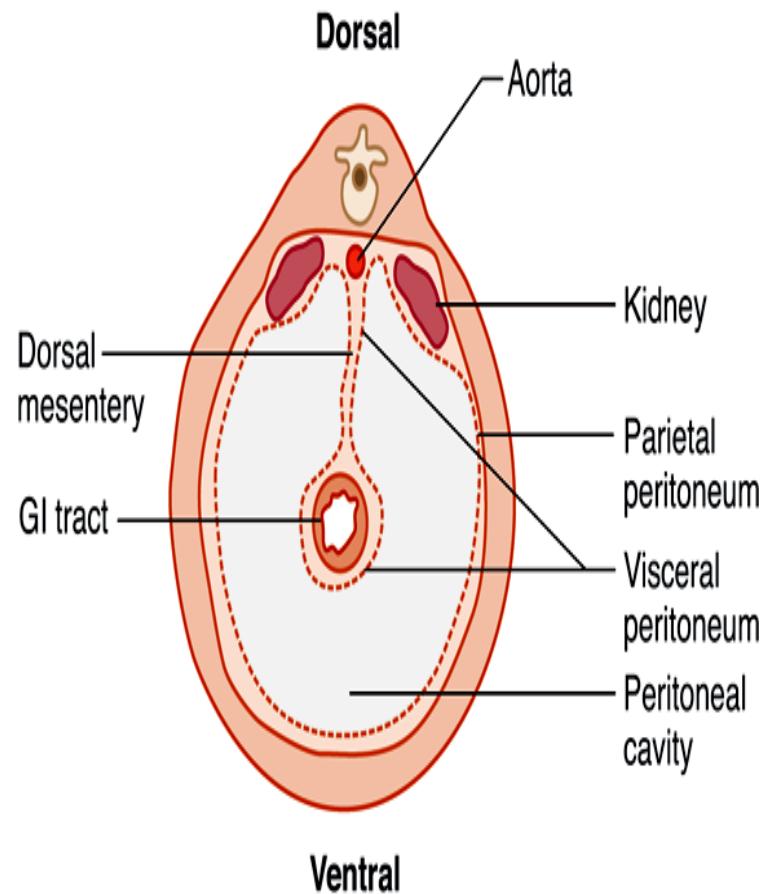
Colon assumes inverted U-shape

# Peritoneum

- Serous membrane lining surface of intra-abdominal structures
- Two layers: parietal and visceral

## Parietal peritoneum

- Lines body wall
- Covers retroperitoneal organs along anterior surfaces
- Innervated by
  - Intercostal nerves
  - Ilioinguinal nerve
  - Iliohypogastric nerves
- Sensitive to somatic pain



# Peritoneum

## Visceral peritoneum

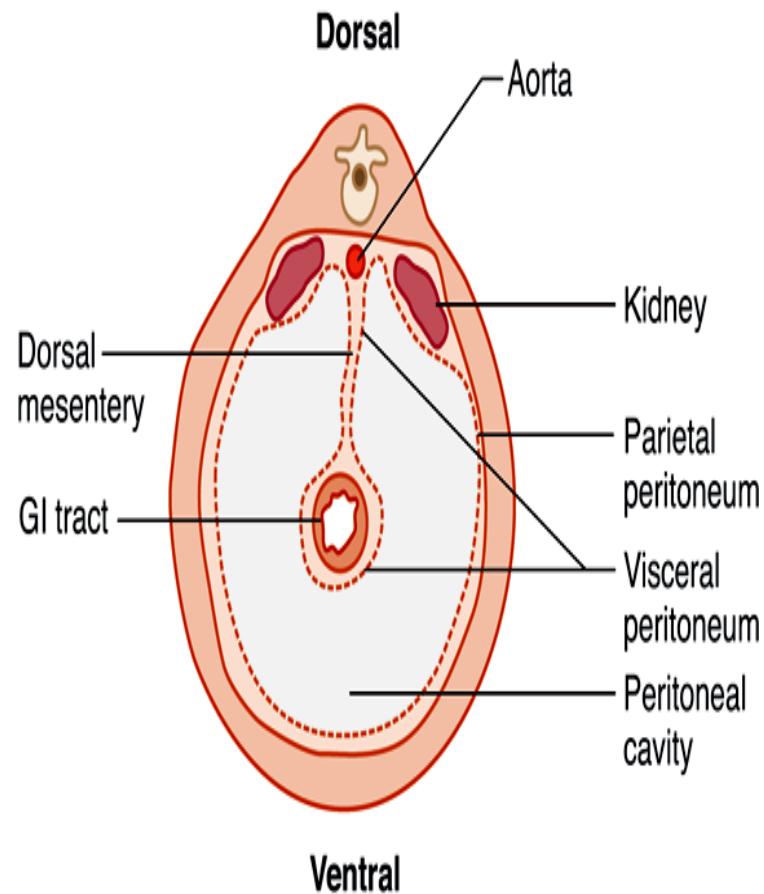
- Encloses intraperitoneal organs
- Reflects onto itself, forming mesenteries

Suspend organs from body wall

Provide passageway for blood vessels, nerves, and lymphatics

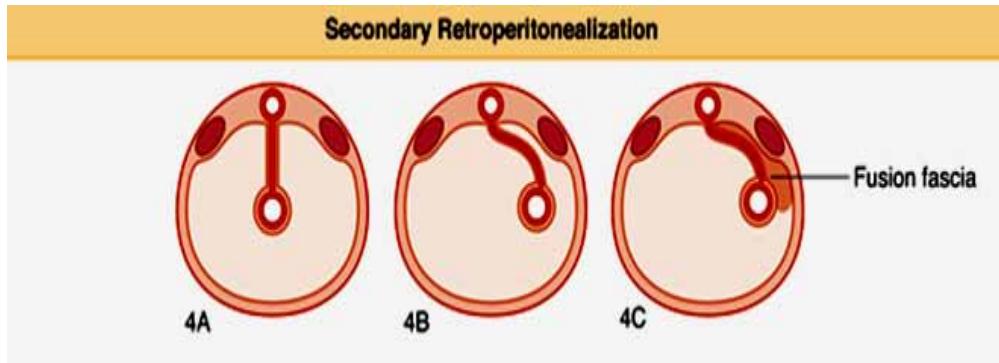
## Examples of mesentery remnants:

- Greater and lesser omentum
- Transverse and sigmoid mesocolon
- Intra-abdominal ligaments, e.g., gastrohepatic ligament



# Visceral Organ Classification

Major Secondarily  
Retroperitoneal Organs  
(lost a mesentery during  
development)



Duodenum (2nd, 3rd parts)

Head, neck, and body of  
pancreas

Ascending colon

Descending colon

Upper rectum

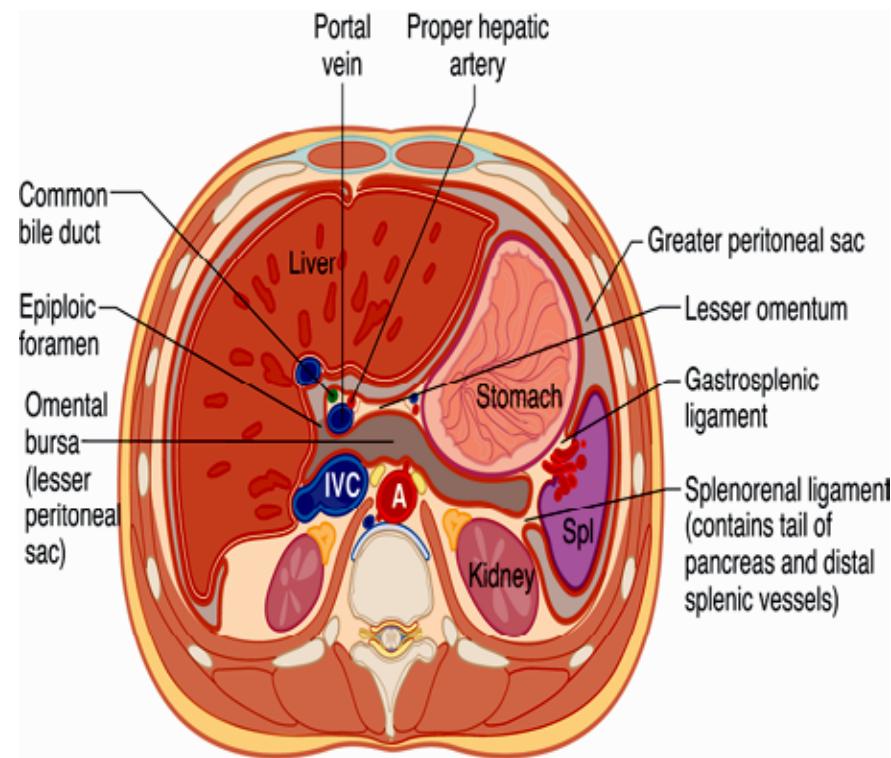
- FA 2013: 309.2 • FA 2012: 336.1 • FA 2011: 308.1
- ME 3e: 337.1 • ME 4e: 337.1

# Peritoneal Cavity

- Potential space between parietal and visceral peritoneum

## Epiploic foramen

- Also known as foramen of Winslow
- Communication between lesser and greater sacs
- Clinical significance: temporary control of bleeding from the liver
- Contains portal triad



# Tracheoesophageal Fistula

## Embryology

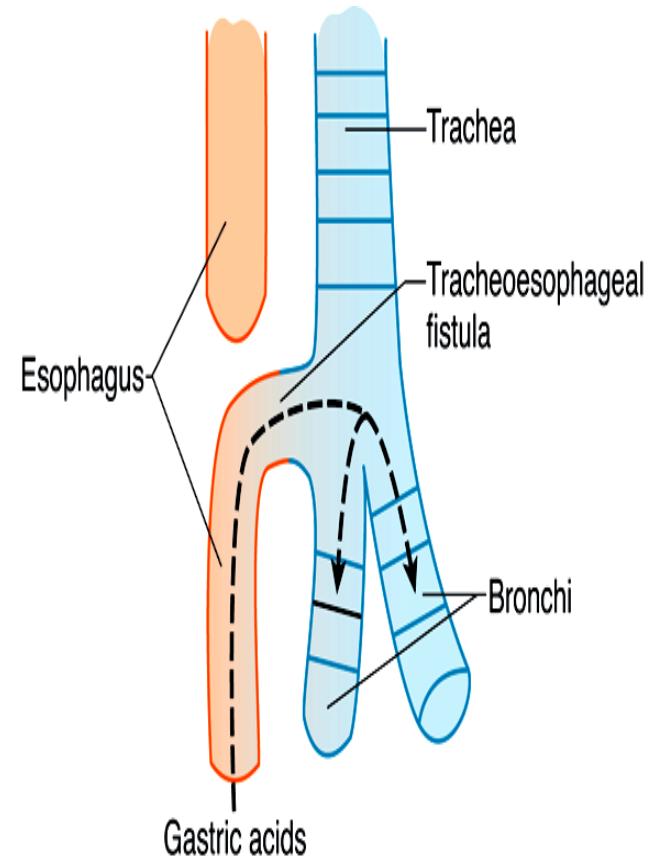
- Lower respiratory system develops from diverticulum of ventral foregut

## Definition

- Abnormal communication between trachea and esophagus
- Malformation of tracheoesophageal septum

## Signs and symptoms

- Polyhydramnios (prenatal)
- Pneumonitis
- Regurgitation
- Cyanosis and gagging
- Inability to pass nasogastric tube



# Hypertrophic Pyloric Stenosis

- Hypertrophy of pyloric muscularis externa  
→ luminal narrowing

## Characteristics

- Within 2 weeks of birth
- Typically seen in firstborn males

## Signs and symptoms

- Polyhydramnios
- Difficulty feeding
- Projectile, ***non-bilious*** vomiting
- Palpable knot (right costal margin)

## Treatment

- Surgery: pyloromyotomy



# Congenital Diaphragmatic Hernia

- Incompletely developed or defective diaphragm

## Characteristics

- Associated with intestinal malrotation
- Complicated by lung hypoplasia

## Signs and symptoms

- Respiratory distress

## Treatment

- Endotracheal intubation
- Mechanical ventilation until lung maturity
- Surgical repair



# Duodenal Atresia

- Duodenal occlusion due to failure of gut tube recanalization

## Characteristics

- Associated with trisomy 21

## Signs and symptoms

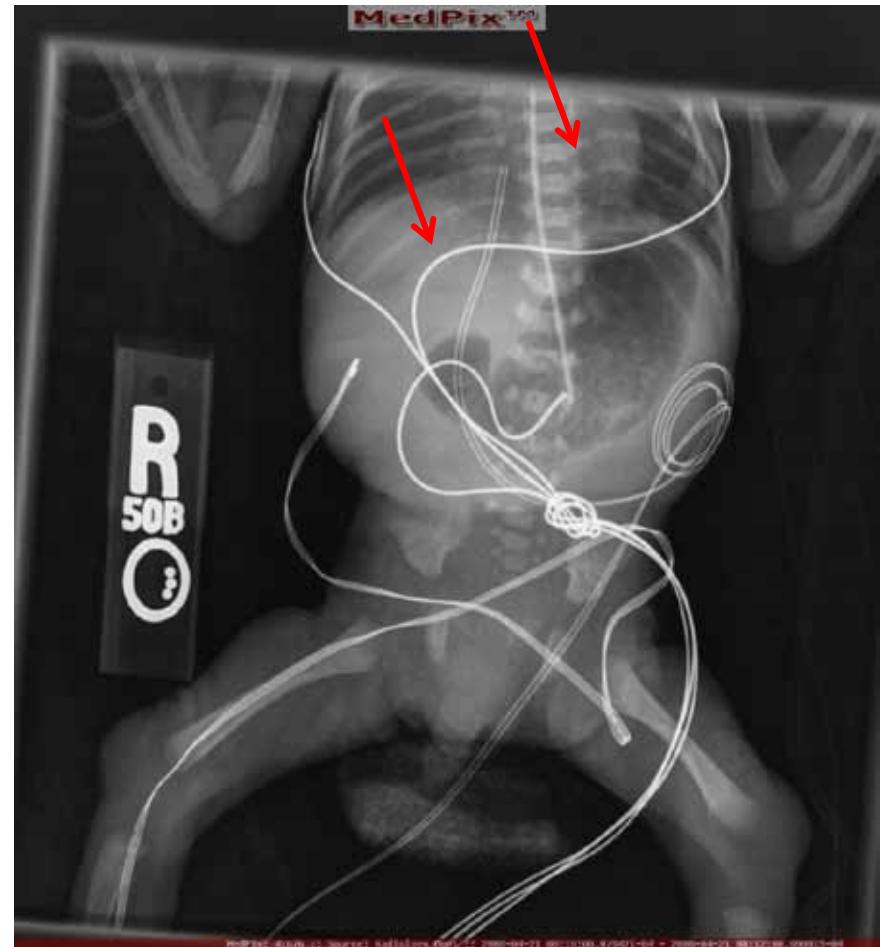
- Polyhydramnios
- **Bilious** vomiting on first day of life

## Diagnosis

- X-ray: “double-bubble” sign

## Treatment

- Surgical repair



- FA 2013: 308.1 • FA 2012: 138.3 • FA 2011: 130.3
  - ME 3e: 357.1 • ME 4e: 357.1

# Small Bowel Atresias

- Vascular accidents in utero, causing incomplete lumen formation
- Single or multiple

## Signs and symptoms

- **Bilious** vomiting on first day of life

## Diagnosis

- X-ray:
  - Distended bowel proximal to atresia
  - Decreased or absent air distal to atresia

## Treatment

- Surgical repair

# Gut Malrotation and Volvulus

## Malrotation

- Incomplete midgut rotation between weeks 6–10
- Associated with volvulus
  - Acute intestinal occlusion
  - First year of life
  - Bilious** vomiting
  - Decreased or absent stool output
  - Abdominal pain and distension

## Diagnosis

- Ultrasound
- Contrast radiographic studies

## Treatment

- Surgical repair

# Gastroschisis

- Defective closure of lateral body folds during embryogenesis

Abdominal wall weakness at site of right umbilical vein

Predisposes to herniation of abdominal viscera

## Characteristics

- Site of herniation is right to umbilicus (not through)
- Not enclosed within amniotic sac

## Treatment

- Surgical reduction and abdominal wall closure

# Omphalocele

- Failure of midgut to return to abdominal cavity during embryogenesis

## Characteristics

- Midgut loop remains herniated into umbilical stalk
- Enclosed by amnion
- Associated with other congenital abnormalities (70% of cases)

Beckwith-Wiedemann syndrome

Chromosomal abnormalities

Congenital heart disease

- Severity of associated abnormalities determines prognosis

## Treatment

- Surgical reduction and abdominal wall closure

# Meckel's Diverticulum

- Failure of vitelline duct to obliterate

## Characteristics

- 2% of the population is affected
- 2 feet from the ileocecal valve
- 2 cm long
- Age  $\leq$  2 years
- 2% of carcinoid tumors occur within Meckel's diverticulum



- FA 2013: 330.1 • FA 2012: 357.1 • FA 2011: 327.4
  - ME 3e: 357.1 • ME 4e: 357.1

# Meckel's Diverticulum

## Signs and symptoms

- Asymptomatic in most cases
- Intermittent painless rectal bleeding (if gastric epithelium is present)
- Lead point for bowel obstruction/intussusception and diverticulitis

## Diagnosis

- Meckel's radionuclide scan: technetium-99m

## Treatment

- Surgical excision



Meckel's diverticulum. commons.wikimedia.org

# Vitelline Fistula

- Failure of vitelline duct to obliterate during weeks 5–6 of embryogenesis
- Persistent connection between intestinal lumen and umbilicus

## Signs and symptoms

- Meconium drainage from umbilicus

## Treatment

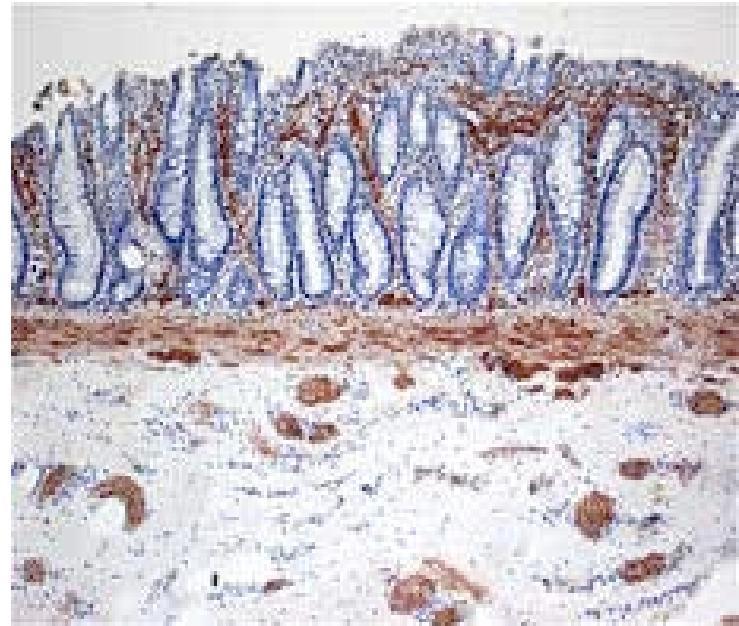
- Surgical excision

# Hirschsprung's Disease

- Failure of neural crest cells to form myenteric plexus in sigmoid colon and rectum
- Loss of peristalsis of affected regions

## Signs and symptoms

- Fecal retention
- Abdominal distension
- Bowel perforation with sepsis
- Fluid and electrolyte imbalances



Histopathology of Hirschsprung's disease:  
enzyme histochemistry showing aberrant AChE-positive fibers  
(brown) in the lamina propria mucosae. commons.wikimedia.org

# Hirschsprung's Disease

## Diagnosis

- Barium enema
- Rectal biopsy

## Treatment

- Correction of fluid and electrolyte abnormalities
- Surgical repair



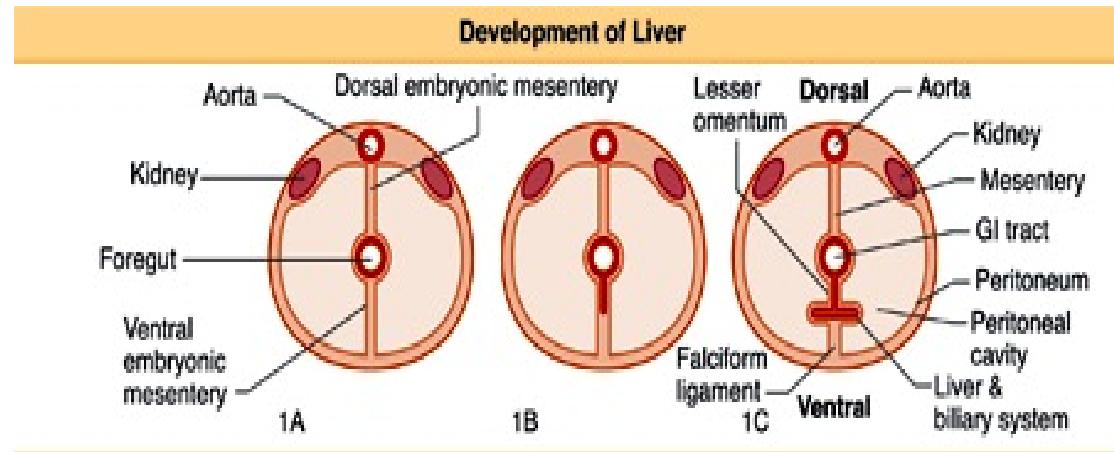
Source: Nicholas Lange. Used with permission.

- FA 2013: 330.2 • FA 2012: 357.3 • FA 2011: 328.2
  - ME 3e: 358.2 • ME 4e: 358.2

# Liver Development

## Characteristics

- Outgrowth of foregut endoderm (hepatic diverticulum)
- Hepatic diverticulum enters ventral mesentery
- Differentiates distally into liver and gallbladder
- Differentiates proximally into biliary ductal system
- Ventral embryonic mesentery between liver and foregut: lesser omentum
- Ventral embryonic mesentery between liver and ventral body wall: falciform ligament



- FA 2013: 312.2 • FA 2012: 339.2 • FA 2011: 311.2
  - ME 3e: 335.1 • ME 4e: 335.1

# **Extrahepatic Biliary Atresia**

- Incomplete canalization of lumen of biliary ducts

## **Signs and symptoms**

- Icterus
- Hyperbilirubinemia (mostly direct)
- Clay-colored stool
- Dark-colored urine

## **Treatment**

- Surgical exploration and repair
- Liver transplant for uncorrectable disease

# Pancreas Development

## Characteristics

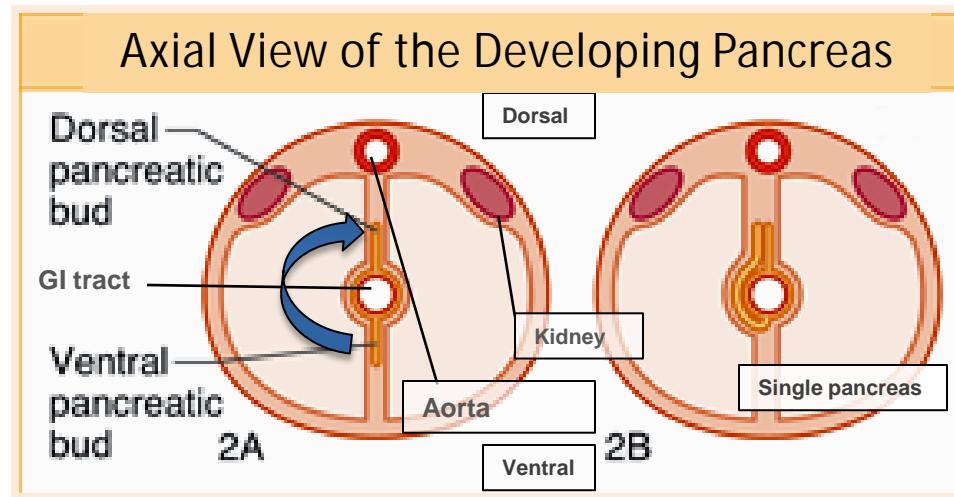
- Pancreatic buds evaginate from foregut endoderm
- Ventral bud rotates around gut tube
- Fuses with dorsal bud

### Dorsal pancreatic bud

Neck, body, and tail

### Ventral pancreatic bud

Head and uncinate process



### Pancreatic ducts

Proximal 1/3 of dorsal pancreatic duct regresses upon bud fusion

Ventral and dorsal ducts fuse to form main pancreatic duct

Main pancreatic duct joins common bile duct, emptying into duodenum via major papillae

# Congenital Anomalies of the Pancreas

## Pancreas divisum

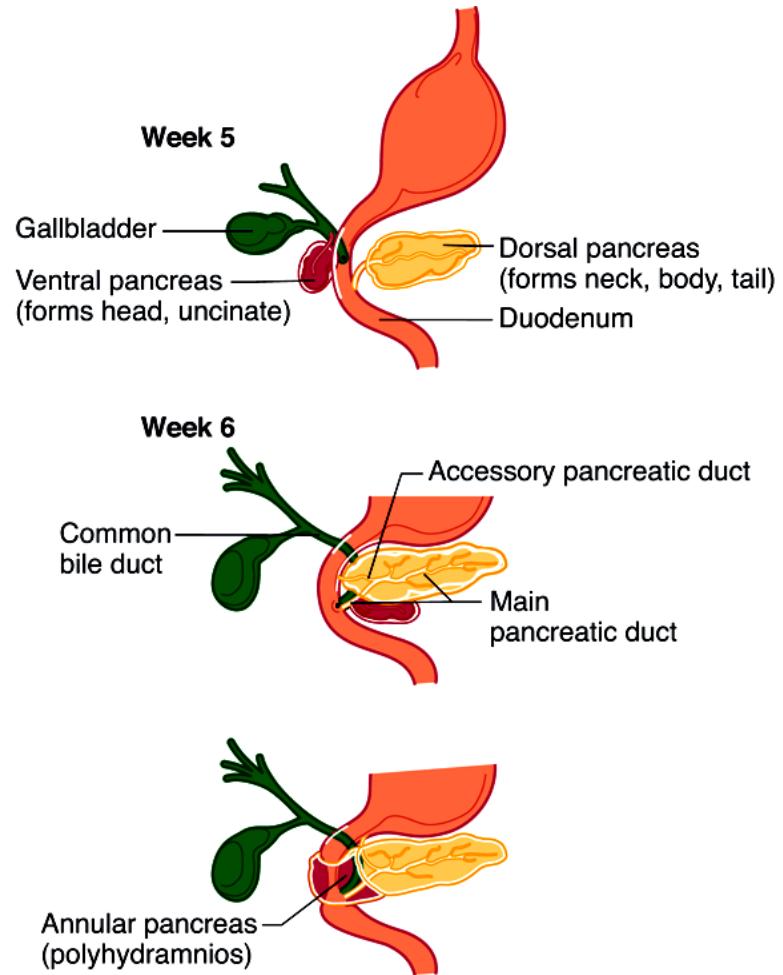
- Failure of ducts to fuse
- Most common congenital anomaly of the pancreas
- Usually asymptomatic
- Drainage is preserved via major and minor papillae

## Signs and symptoms

- Symptoms occur when orifice of minor papilla inadequately drains the accessory ducts
- Recurrent pancreatitis

## Treatment

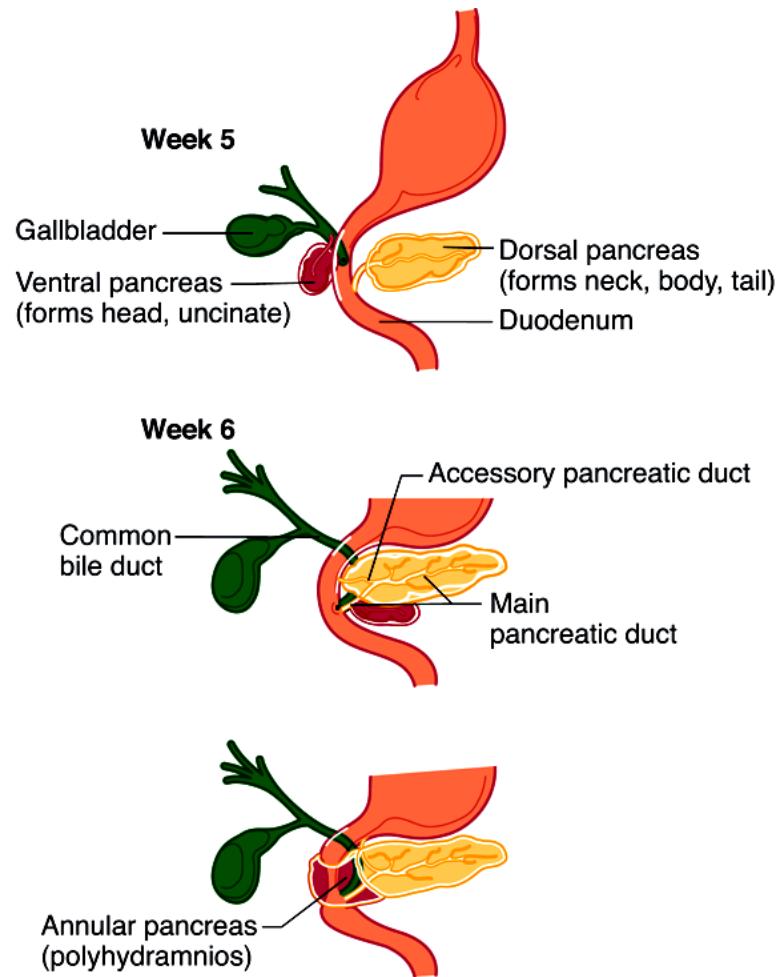
- Endoscopic or surgical repair



# Congenital Anomalies of the Pancreas

## Annular pancreas

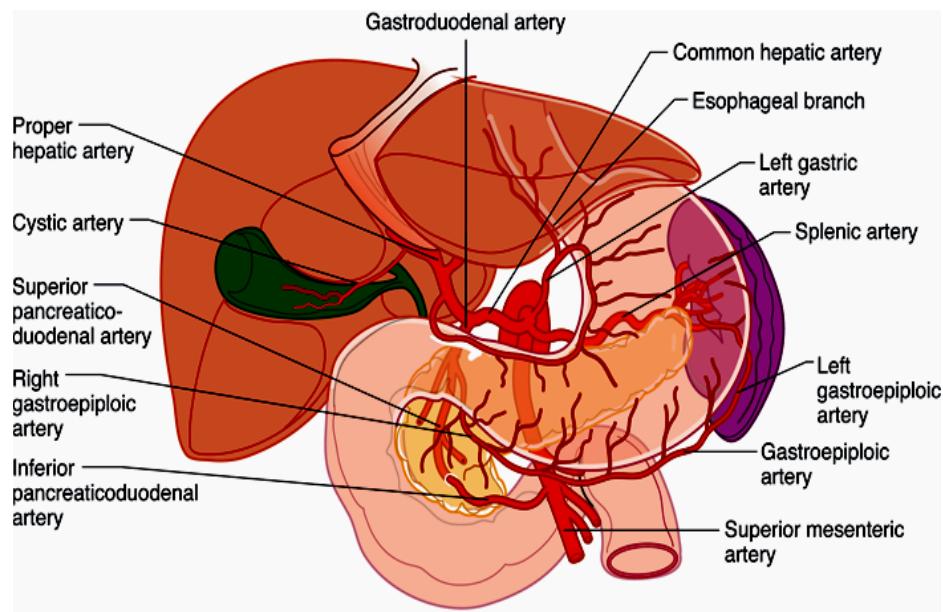
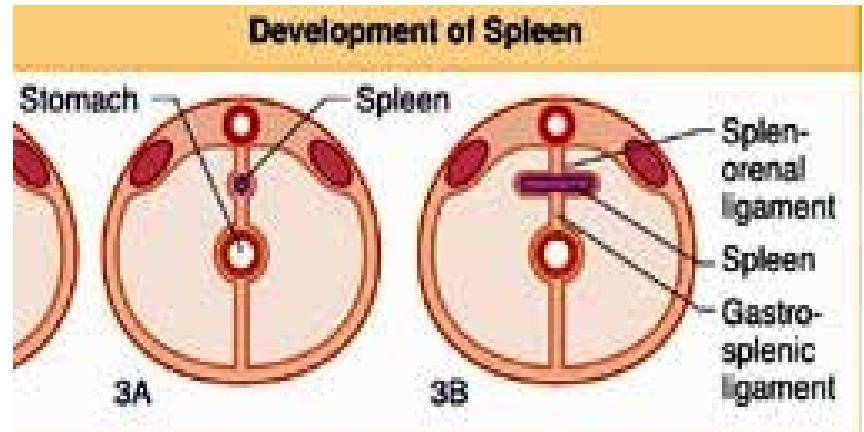
- Due to incomplete rotation and fusion of buds
- Pancreas encircles duodenum, leading to constriction and obstruction of duodenum
- Causes *polyhydramnios*
- If obstructive symptoms are severe, surgical correction is required



# Spleen Development

## Characteristics

- Develops from mesoderm within dorsal embryonic mesentery
- Mesentery between spleen and foregut: gastrosplenic ligament
- Mesentery between spleen and dorsal body wall: splenorenal ligament
- Spleen is supplied by splenic artery, arising from the celiac trunk





# Gastroenterology: Anatomy, Histology, and Physiology

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# Gastrointestinal Anatomy

## Layers of gut wall

- Mucosa

- Epithelium, varies by regional function

- Lamina propria, loose connective tissue

- Muscularis mucosae, smooth muscle involved in gut motility

- Submucosa

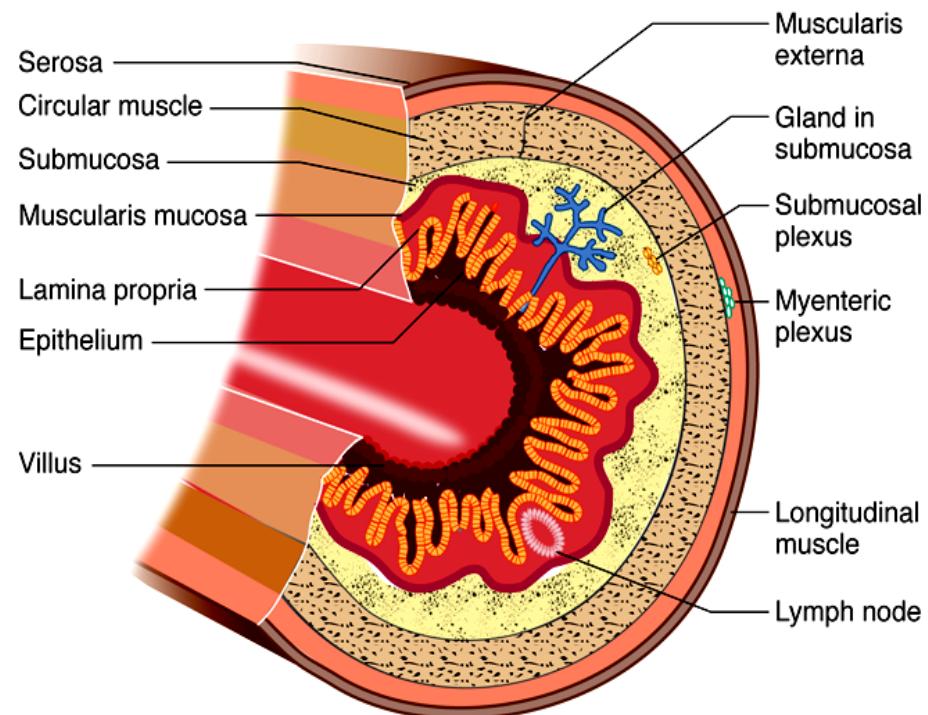
- Contains mucus-secreting glands

- Muscularis externa

- Inner circular and outer longitudinal

- Controls luminal size and produces peristalsis

- Serosa



# Gastrointestinal Innervation

## Intrinsic innervation (enteric)

- Located in gastrointestinal wall
- Autonomous generation of peristalsis and glandular secretion
- Meissner's plexus
  - Located in submucosa
  - Parasympathetic input
  - Secretory motor innervation
- Auerbach's plexus
  - Located between muscle layers of muscularis externa
  - Parasympathetic and sympathetic input
  - Intrinsic motility and peristalsis

## Extrinsic innervation

- Modulates intrinsic innervation (peristalsis, glandular secretions)
- Parasympathetic → stimulation
- Sympathetic → inhibition

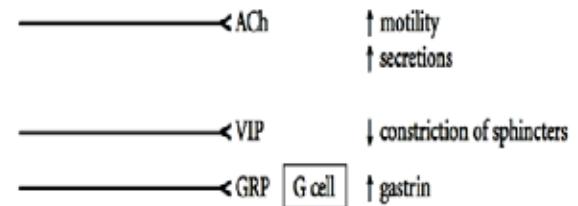
### Sympathetic

The diagram below illustrates how the synaptic junction at the end of a nerve fiber releases norepinephrine (NE), which then induces responses in the gastrointestinal (GI) system:



An increase in sympathetic activity slows processes.

### Parasympathetic



An increase in parasympathetic activity promotes digestive and absorptive processes.

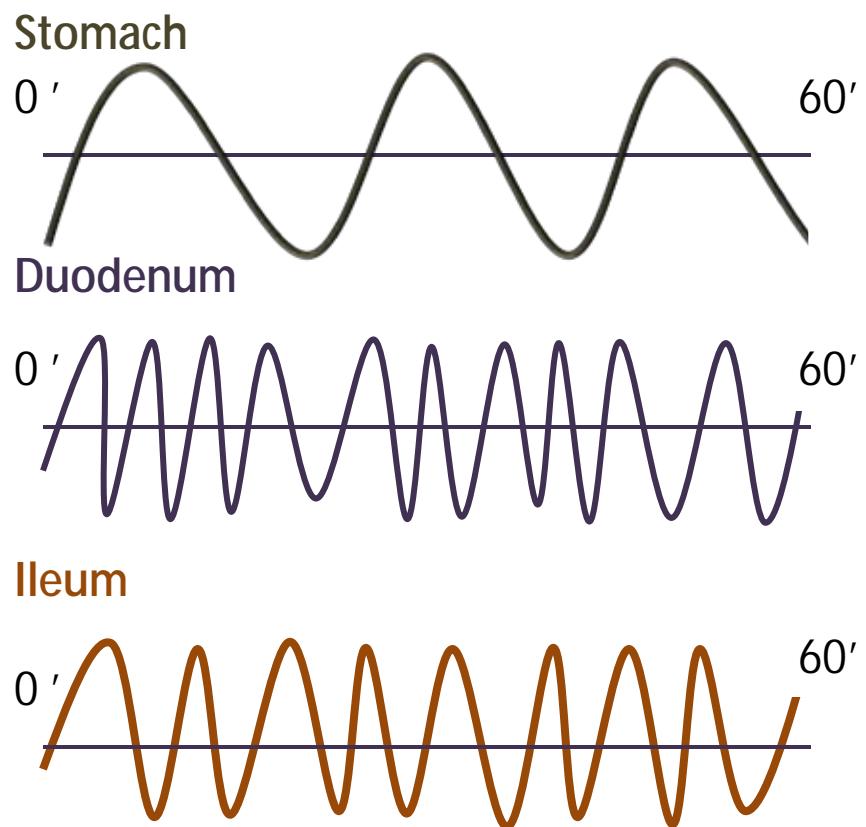
VIP = vasoactive intestinal peptide, an inhibitory parasympathetic transmitter

GRP = gastrin-releasing peptide; stimulates the release of gastrin from G cells

# Gastrointestinal Motility

## Basal electric rhythm

- Stomach: 3 waves/min
- Duodenum: 12 waves/min
- Ileum: 8–9 waves/min



# Gastrointestinal Immune Function

## General characteristics

- Lumen is colonized by 500 species of bacteria
- Function
  - Produces vitamin K
  - Assists digestion
  - Protects against overgrowth of pathogenic bacteria
- Immunosurveillance and defense maintained by specialized cells and lymphoid follicles

# Regional Histologic Characteristics

Different Characteristics	
Esophagus	Non-keratinized stratified squamous epithelium
Stomach	Mucous, chief, parietal, and enteroendocrine (EE) cells, gastric pits and glands
Duodenum	Goblet, Paneth, and EE cells, Brunner's glands, villi, and crypts of Lieberkuhn
Jejunum	Villi and microvilli, plica and crypts and same cells as duodenum
Ileum	Peyer's patches, M cells, crypts of Lieberkuhn
Colon	Crypts but no villi, mucous secreting and absorptive cells

# Salivary Glands

	Location	Composition	
Parotid	Surface of masseter muscle Anterior to external auditory meatus Drains at level of 2nd upper molar	25% of volume of saliva Serous	Low $\text{Na}^+$ & $\text{Cl}^-$ High in $\text{K}^+$ & $\text{HCO}_3^-$ Alkaline pH Hypotonic to isotonic Lipase Amylase Lysozyme Defensins Lactoferrin IgA Mucins Growth factors
Sub-mandibular	Inside lower edge of mandible Drains at floor of mouth	70% of volume of saliva Mixed (mucinous + serous)	
Sub-lingual	Base of tongue Drains at sublingual caruncle	5% of volume of saliva Mixed (mucinous + serous)	

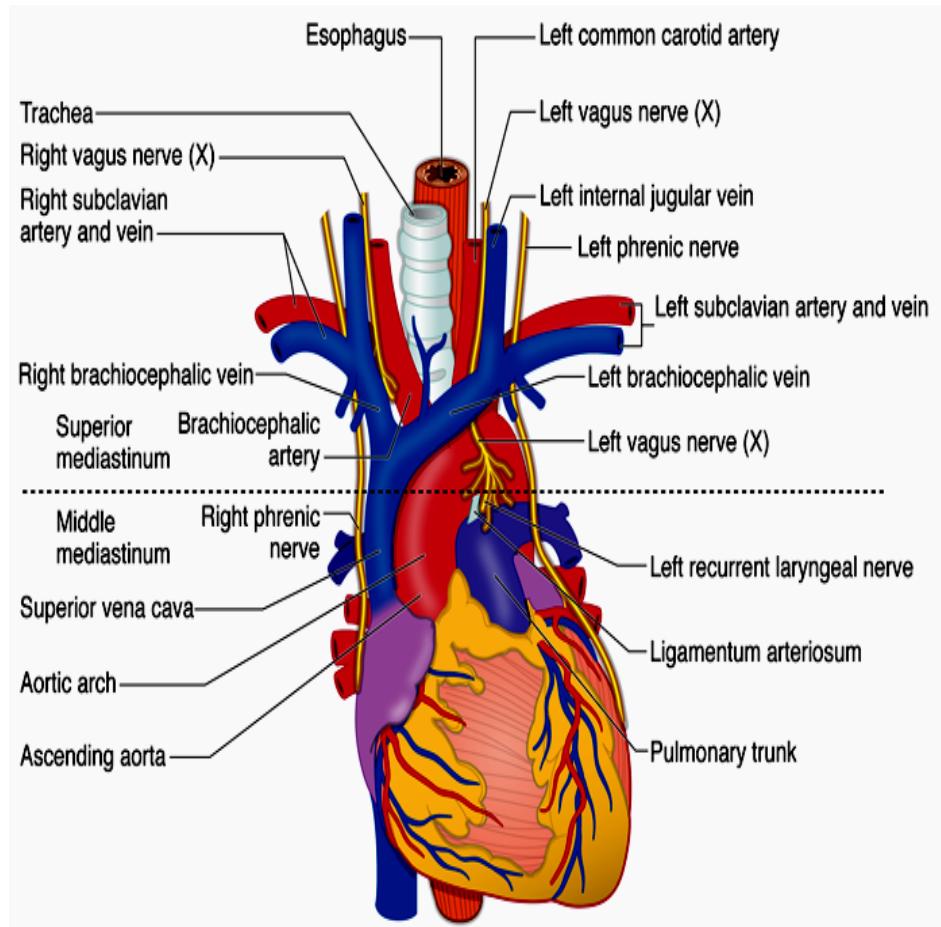
- FA 2013: 320.2 • FA 2012: 347.2 • FA 2011: 318.2
- ME 3e: 342.2 • ME 4e: 342.2

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# Esophagus

## Characteristics

- Mediastinum, behind trachea and **left atrium**
- Enters abdominal cavity through esophageal hiatus of diaphragm at level of T10
- Four narrow points:
  - At origin (pharynx)
  - Arch of aorta
  - Left primary bronchus
  - Esophageal hiatus



# Esophagus

	Anatomical Characteristics	Histology	Blood Supply	Venous Drainage	Innervation
Upper 1/3	Skeletal muscle		Inferior thyroid artery branches	Inferior thyroid veins	
Middle 1/3	Both skeletal and smooth muscle	Nonkeratinized stratified squamous epithelium	Bronchial arteries and aorta	Bronchial, azygos, and hemiazygos veins	Cervical and thoracic sympathetic chain (spinal segments T1–T10)
Lower 1/3	Smooth muscle	Mucous glands	Inferior phrenic artery Left gastric artery branches	Portal venous system	Vagus nerve

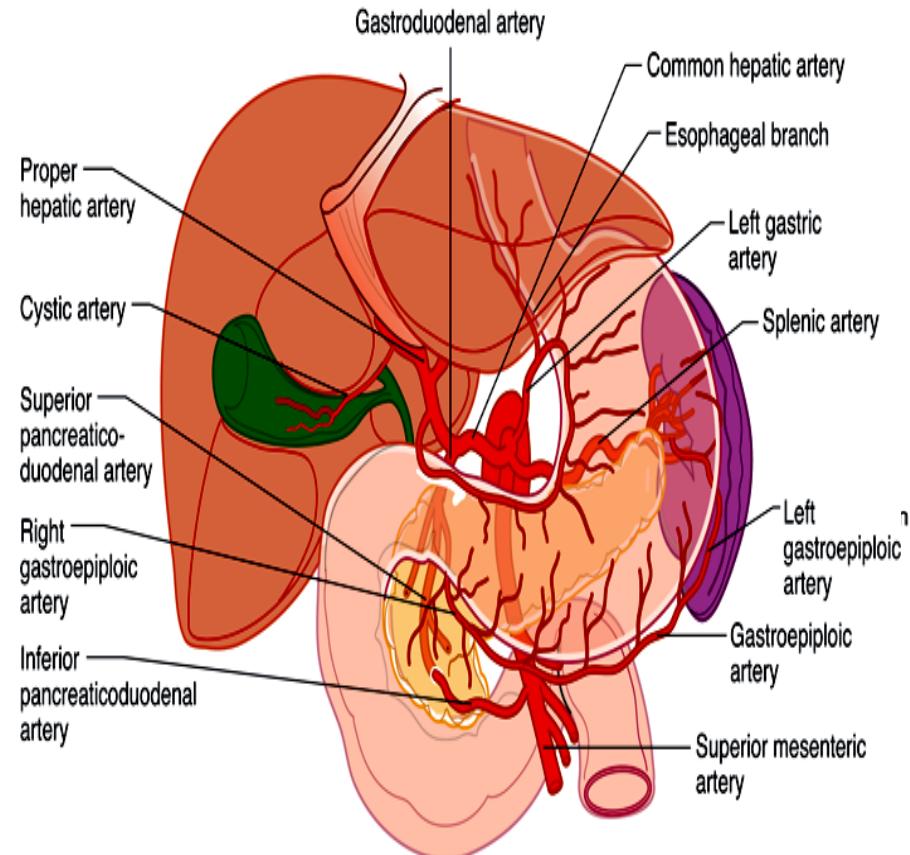
- FA 2013: 304.4 • FA 2012: 338.2 • FA 2011: 310.3
- ME 3e: 336.1 • ME 4e: 336.1

GI2\_3 2

# Stomach

## General characteristics

- Intraperitoneal organ
- Suspended by
  - Hepatogastric ligament
  - Gastrocolic ligament
  - Gastrosplenic ligament
- Blood supply
  - Left gastric artery (celiac trunk)
  - Right gastric artery (common hepatic)
  - Right gastroepiploic (gastroduodenal)
  - Left gastroepiploic (splenic)
  - Short gastric arteries (splenic)
- Innervation
  - Parasympathetic: vagus nerves
  - Sympathetic: celiac plexus



# Stomach

## General characteristics

- Macroscopically

- Mucosal folds (rugae)

- Cardia, body, and pyloric antrum

- Histology

- Simple columnar epithelium

- Gastric pits extending into glands

- Function

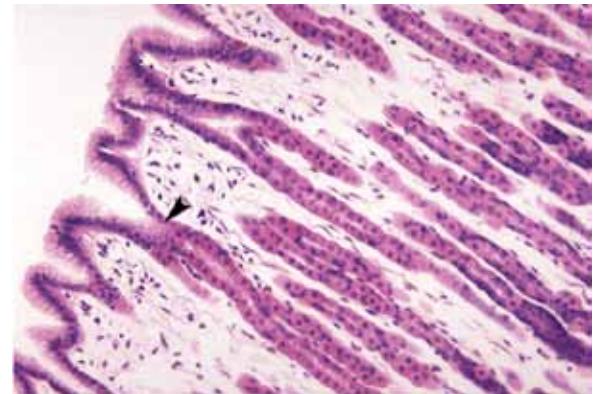
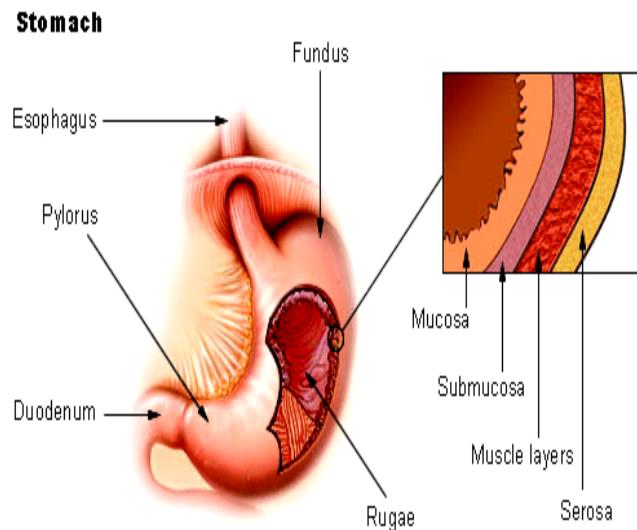
- Initial chemical and enzymatic breakdown of food

- Transformation of food into chyme

- Ionic composition of gastric secretions

- High in  $H^+$ ,  $K^+$ ,  $Cl^-$

- Low in  $Na^+$



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# Gastric Cell Types and Function

	Secretory Product	Function	Regulation
<b>Mucous cells</b>	Mucus	Protection against acid	Increased by vagal stimulation, pancreatic, biliary secretion
<b>Chief cells (not present in pylorus)</b>	Pepsinogen	Initial digestion of proteins	Increased by vagal stimulation, HCl and gastrin
<b>Parietal cells</b>	HCl  Intrinsic factor	Protects against bacteria and activates pepsinogen  Absorbs vitamin B <sub>12</sub>	Increased by histamine, Ach and gastrin  Decreased by low pH (somatostatin), prostaglandin, GIP, secretin
<b>G-cells (type of EE cell)</b>	Gastrin	Stimulate chief, parietal and enterochromaffin cells	Increased by stomach distention, high pH, AA's, peptides, vagal stimulation  Decreased by low pH , somatostatin

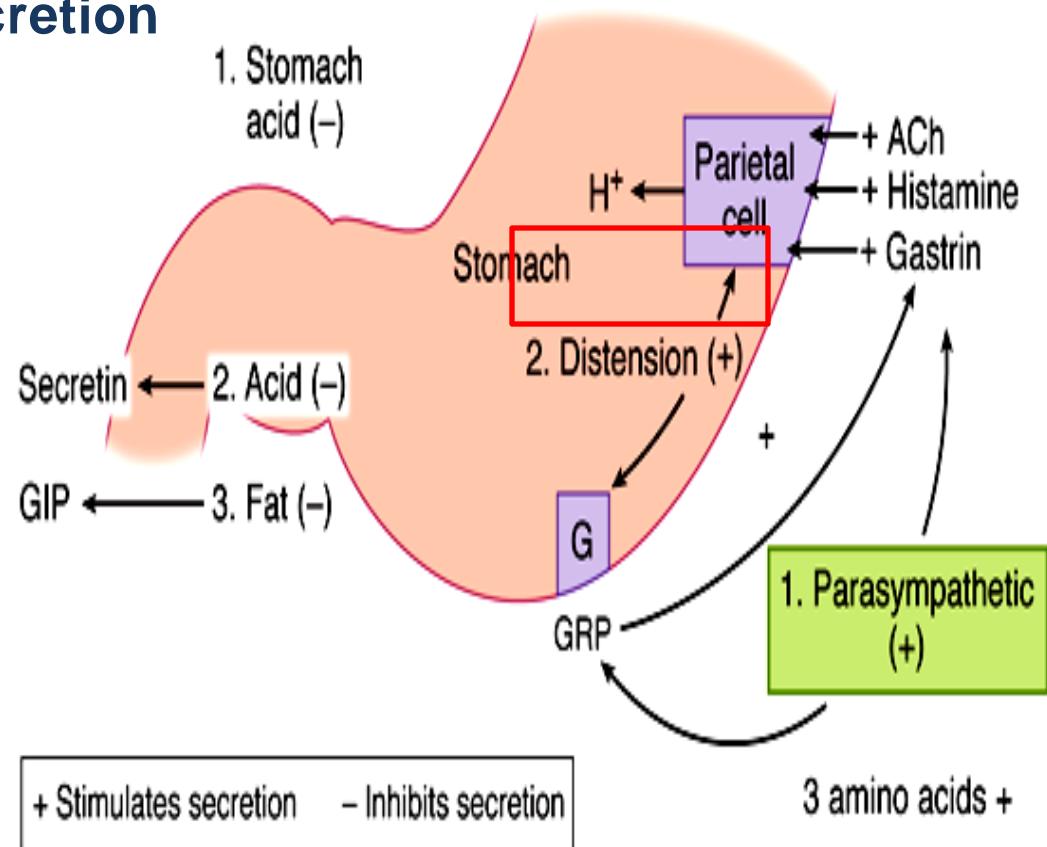
- FA 2013: 320.1 • FA 2012: 347.1 • FA 2011: 318.1
  - ME 3e: 348.1 • ME 4e: 348.1

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# Gastric Acid Secretion Control

## Factors stimulating HCl secretion

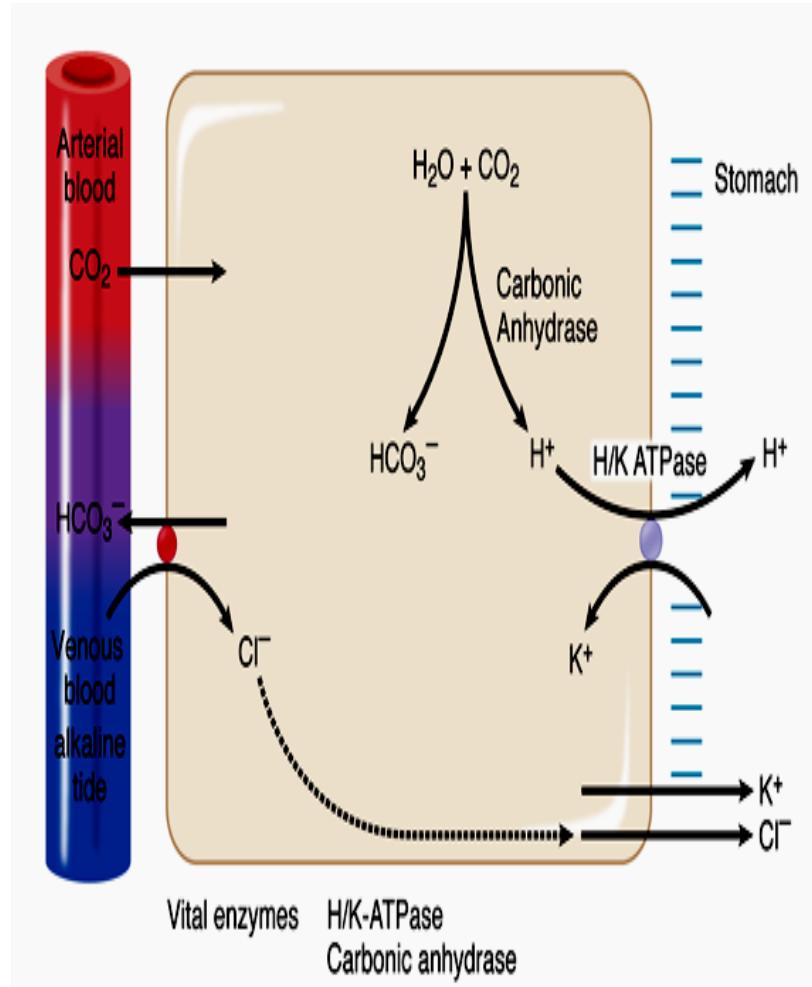
- Stomach distension
- Acetylcholine
- Histamine
- Gastrin



# Cellular Mechanisms of Acid Secretion

## Acid secretion steps

- Carbonic anhydrase facilitates conversion of  $\text{CO}_2 \longrightarrow \text{H}^+$  and  $\text{HCO}_3^-$
- $\text{H}^+$  secreted by  $\text{H}^+/\text{K}^+$ - ATPase
- $\text{H}^+$  pumping raises intracellular  $\text{HCO}_3^-$  and its gradient across basal membrane, providing net force for pumping  $\text{Cl}^-$  into cell
- $\text{Cl}^-$  diffuses through channels into lumen



# Small Intestines

## General characteristics

- Intraperitoneal (except 2nd, 3rd and 4th portions of duodenum)
- Blood supply

Gastroduodenal artery (common hepatic)

Superior pancreaticoduodenal artery (gastroduodenal)

Inferior pancreaticoduodenal artery (superior mesenteric)

Superior mesenteric artery – small intestines

- Venous drainage

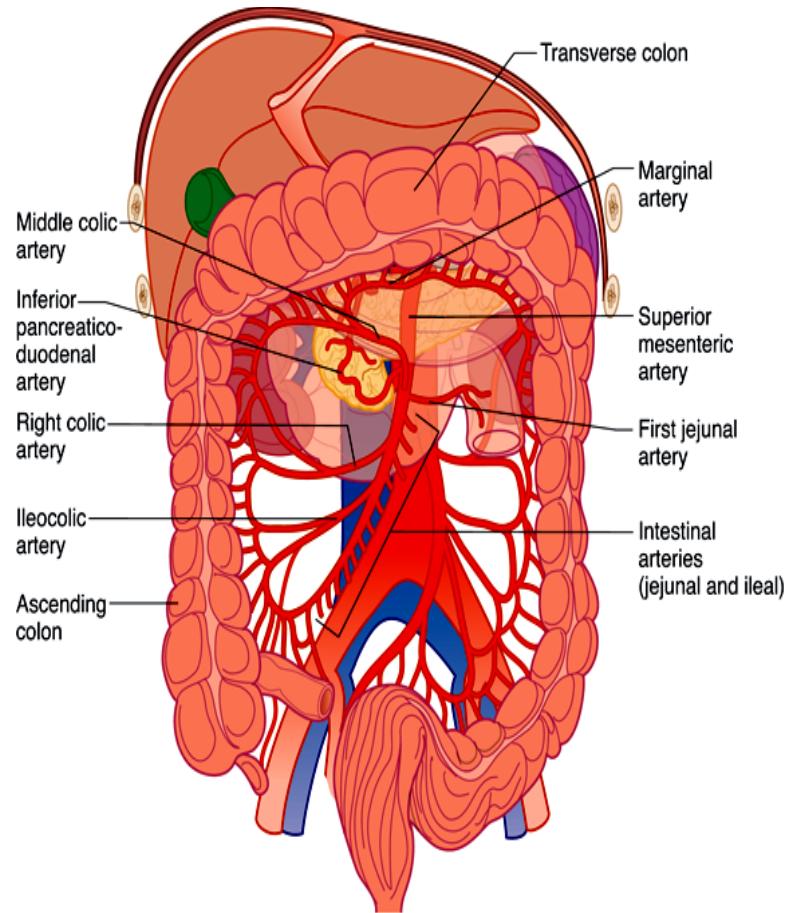
Hepatic portal system

- Innervation

Sympathetic: inhibitory by thoracic splanchnic nerves (T5-T12)

Parasympathetic: stimulatory by vagus nerves

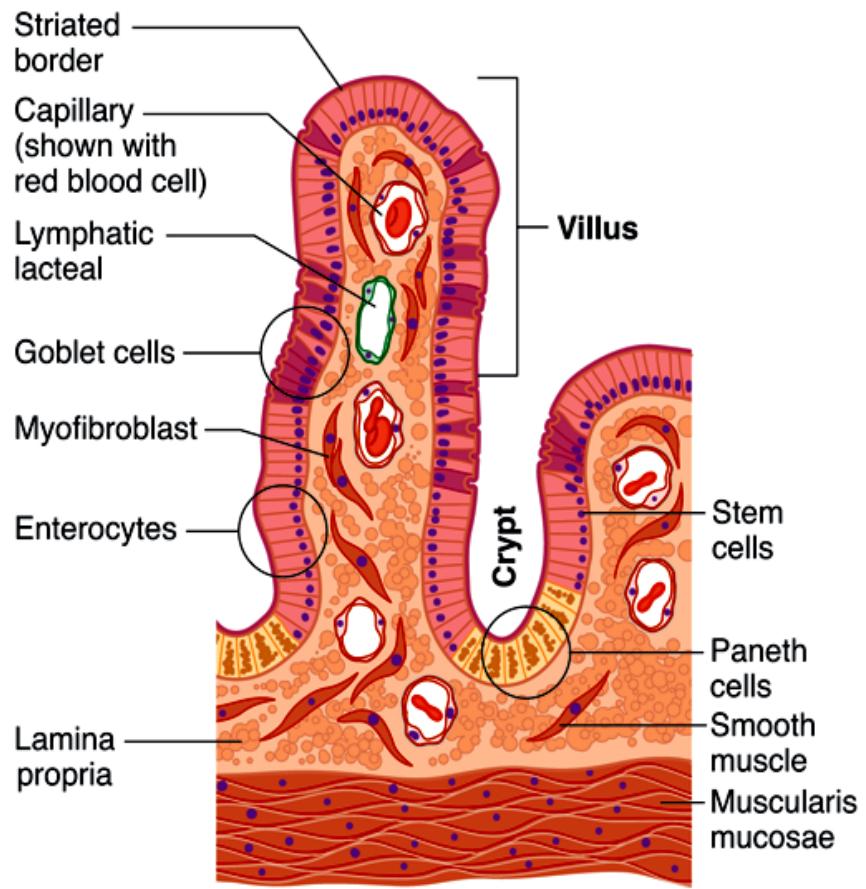
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# Small Intestines

## Histology

- Multi-layered wall
- Mucosal layer
  - Simple columnar epithelium
  - Villi and crypts
- Lamina propria
  - Network of vessels
  - GALT
- Muscularis mucosae
- Serosa



- FA 2013: 311.2 • FA 2012: 338.2 • FA 2011: 310.1
  - ME 3e: 344.1 • ME 4e: 344.1

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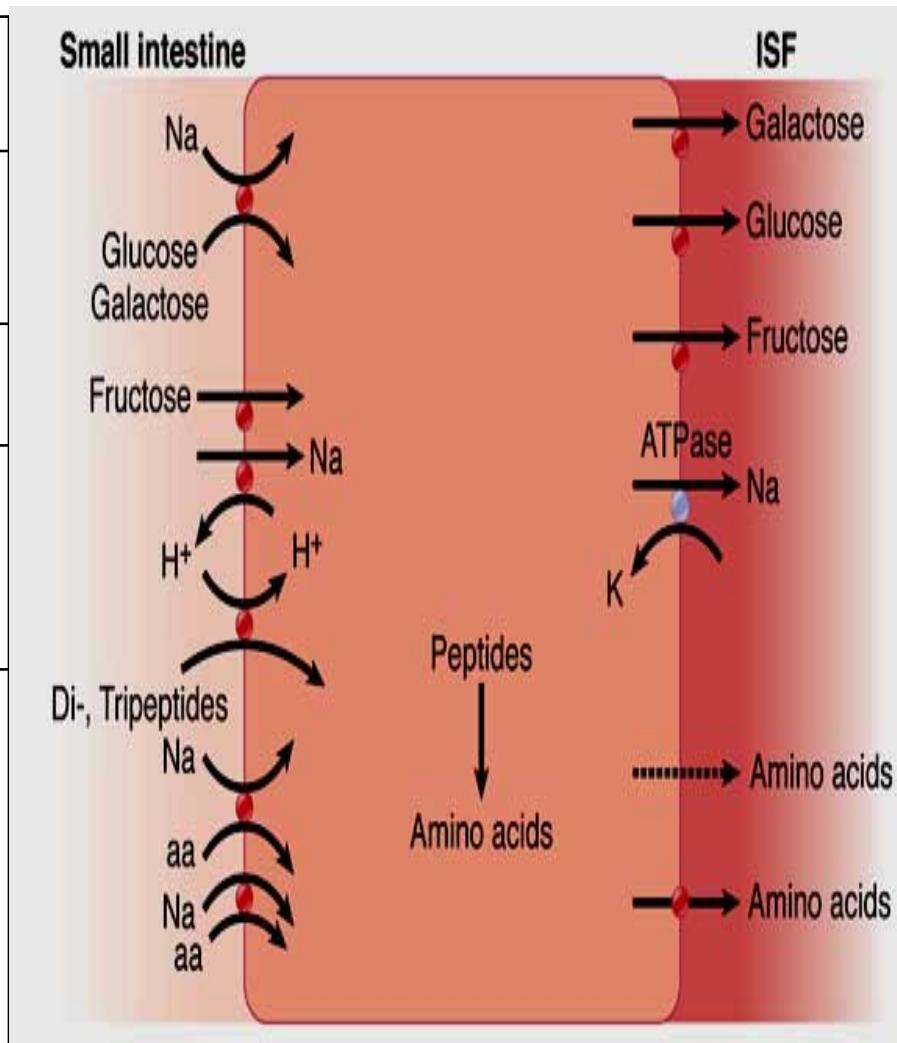
# Small Intestine Cell Types and Function

	Product	Function
<b>Goblet cells Brunner's gland (duodenum)</b>	Mucous	Protection of the surface from acid
<b>Enterocytes</b>	Digestive enzymes	Digestion and absorption
<b>Paneth cells</b>	Lysozymes Defensins	Protection from pathogenic microorganisms
<b>Enteroendocrine (EE) cells</b>	Various hormones	Various functions
<b>Stem cells</b>	All other cell types	Epithelial generation

- FA 2013: 319
- FA 2012: 346
- FA 2011: 317
- ME 3e: 336
- ME 4e: 336

# Absorption and Digestion

	Site of Absorption
<b>Electrolytes</b>	Small intestines Iron and $\text{Ca}^{2+}$ mostly in duodenum
<b>Triglycerides</b>	Small intestines
<b>Carbohydrates (glucose, galactose, and fructose)</b>	Small intestines
<b>Protein (AAs, di-peptides, and tri-peptides)</b>	Small intestines



- FA 2013: 321 • FA 2012: 349 • FA 2011: 320
- ME 3e: 352-354 • ME 4e: 352-354

# Ileum Facts

## Important characteristics

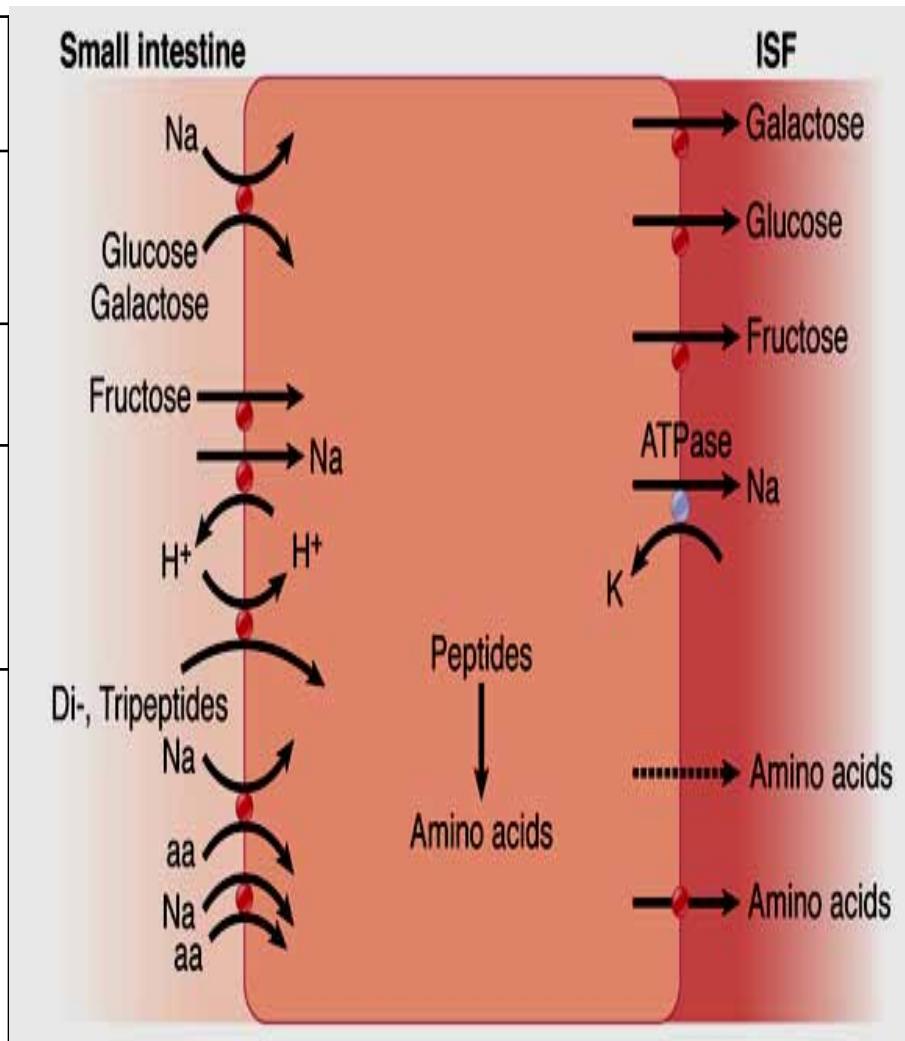
- Immune surveillance role
  - Mucosa more densely infiltrated with lymphocytes, antigen-presenting cells, and M cells
  - High density of Payer's patches
- Only GI site for B12 and bile salt absorption
- Bicarbonate secretion



Cross section of ILEUM, with Peyer's patch in red.  
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# Absorption and Digestion

	Site of Absorption
<b>Electrolytes</b>	Small intestines Iron and $\text{Ca}^{2+}$ mostly in duodenum
<b>Triglycerides</b>	Small intestines
<b>Carbohydrates (glucose, galactose, and fructose)</b>	Small intestines
<b>Protein (AAs, di-peptides, and tri-peptides)</b>	Small intestines



- FA 2013: 323 • FA 2012: 349 • FA 2011: 320
- ME 3e: 352 • ME 4e: 352

# Gastrointestinal Hormones

	<b>Source</b>	<b>Stimulus</b>	<b>Action</b>
<b>Gastrin</b>	G cells (antrum, duodenum, and pancreas)	Stomach distension, vagal stimulation, peptides, and AAs	↑ gastric H <sup>+</sup> secretion ↑ pepsinogen secretion
<b>CCK</b>	I cells (duodenum)	Fat and AAs entering duodenum	↓ gastric-emptying ↑ pancreatic secretion
<b>GIP</b>	K cells (duodenum)	Fat, CHO, AAs	↓ gastric secretion ↑ insulin release
<b>Secretin</b>	S cells (duodenum)	Acid entering duodenum	↓ gastric secretion and motility ↑ HCO <sub>3</sub> <sup>-</sup> secretion
<b>Somatostatin</b>	D cells (pancreatic islets)	Low pH chyme entering duodenum	Great inhibitor
<b>VIP</b>	Parasympathetic ganglia	Distension and vagal stimuli	↑ water and electrolyte secretion
<b>Motilin</b>	Enterochromaffin cells	>2 hours fasting	Initiates myenteric motor complexes

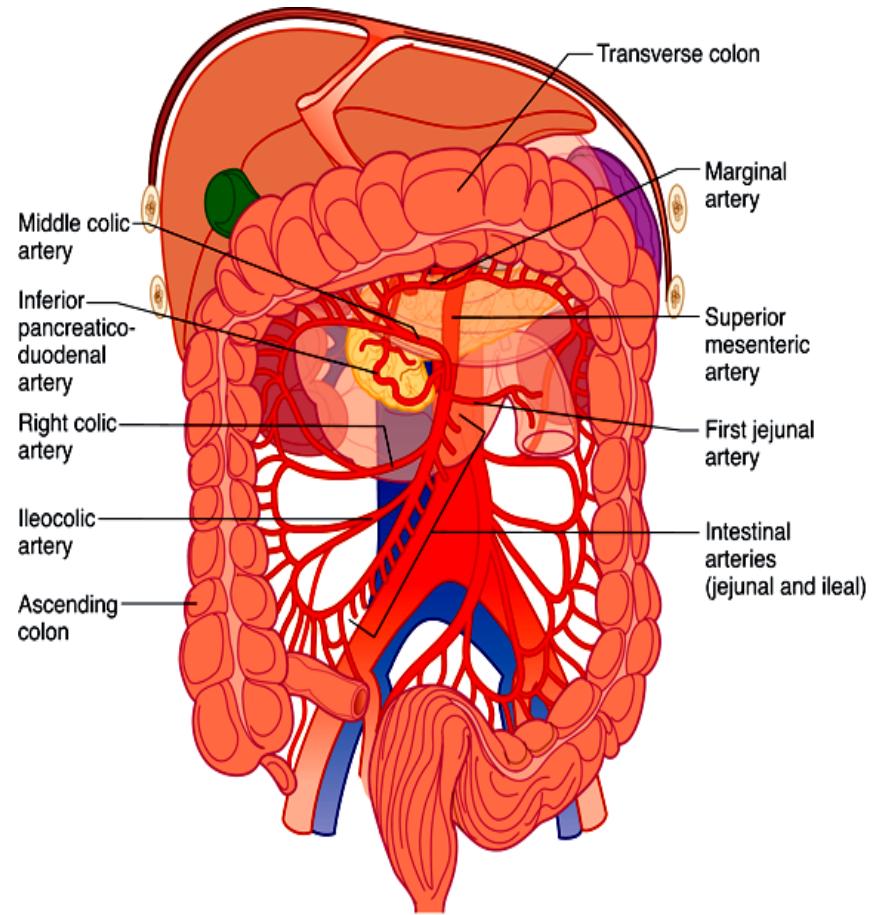
- FA 2013: 319 • FA 2012: 346 • FA 2011: 317
- ME 3e: 346 • ME 4e: 336

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# Large Intestine

## General characteristics

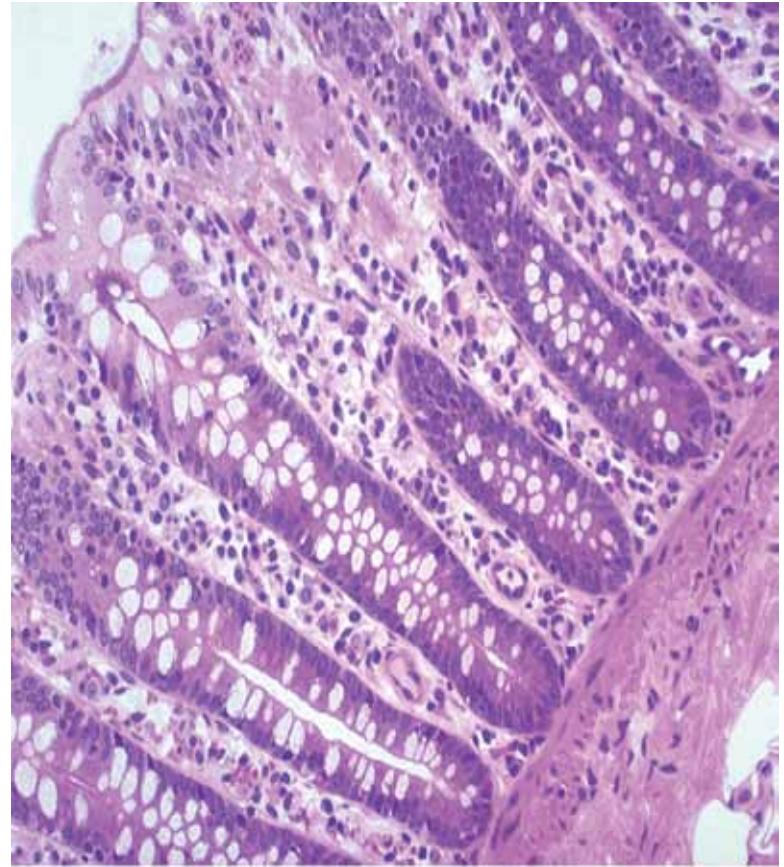
- Intraperitoneal: cecum, appendix, transverse colon, sigmoid, and upper 1/3 of rectum
- Secondarily retroperitoneal: ascending and descending colon
- Blood supply
  - SMA (cecum, appendix, ascending colon, and proximal transverse colon)
  - IMA (distal colon up to proximal rectum)
  - Internal iliac artery (remaining rectum and anus)
- Innervation
  - Sympathetic: splanchnic nerves (L1–L2)
  - Parasympathetic: splanchnic nerves (S2–S4)



# Large Intestine

## Histology

- Lack of plicae and villi
- Short crypts of Lieberkuhn
- Goblet cells
- Absorptive enterocytes
- Enteroendocrine cells
- Lymphoid follicles



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## Function

- $\text{Na}^+$  and  $\text{H}_2\text{O}$  reabsorption
- $\text{K}^+$  and  $\text{HCO}_3^-$  secretion

# Anus

## Characteristics

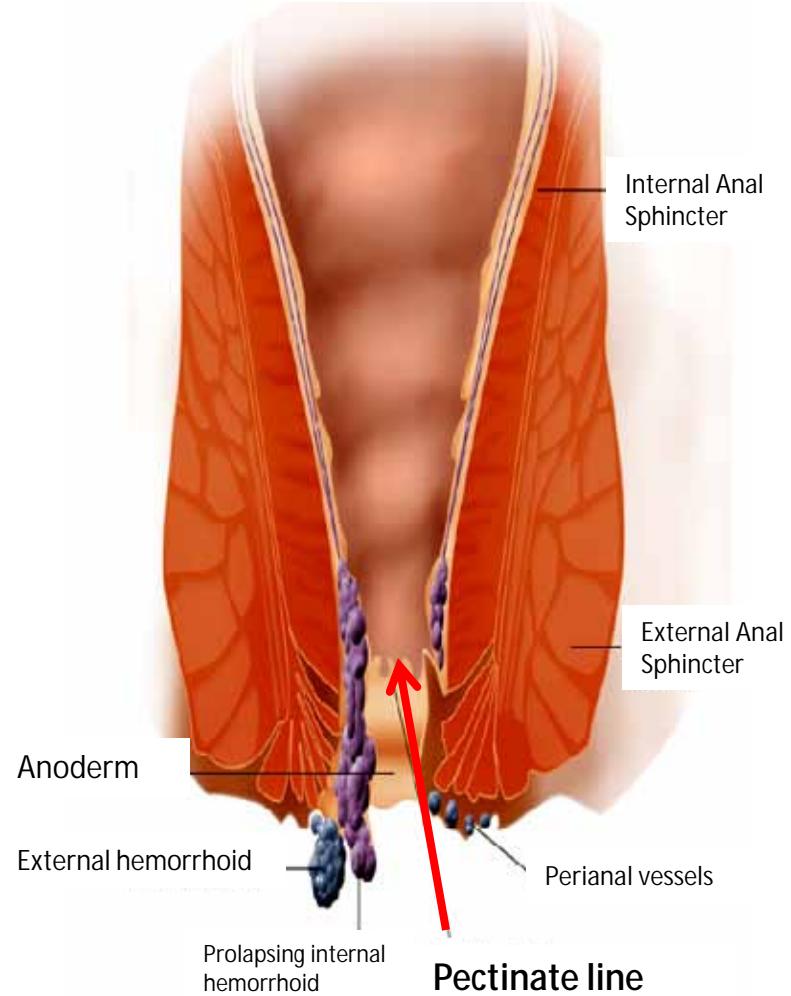
- Pectinate line: boundary between epithelial cells (endoderm) and stratified squamous cells (ectoderm)

### Above pectinate line

- Blood supply: inferior mesenteric artery
- Venous drainage: portal system
- No somatic innervation
- Carcinomas = adenocarcinomas

### Below pectinate line

- Blood supply: internal iliac artery
- Venous drainage: IVC
- Somatic innervation (pain felt locally)
- Carcinomas = squamous cell carcinomas



# Liver

## General characteristics

- Intraperitoneal organ
- Divided into 2 lobes by falciform ligament
- Blood supply

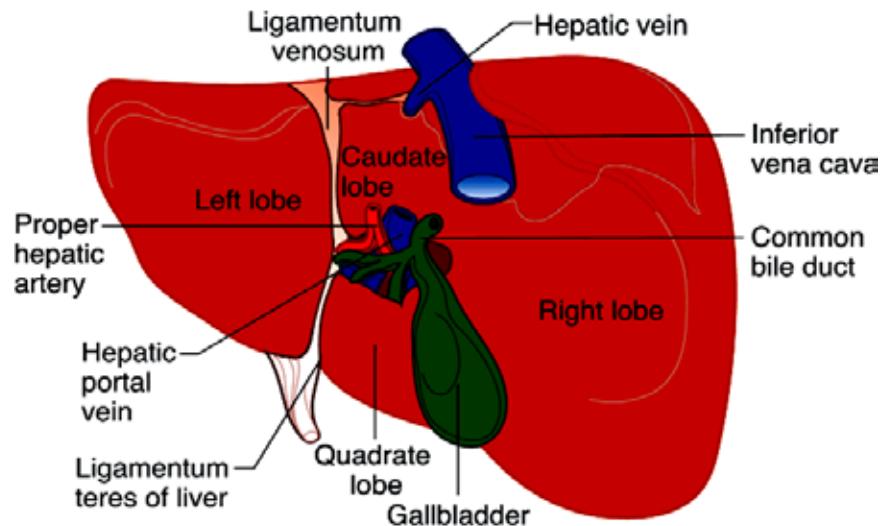
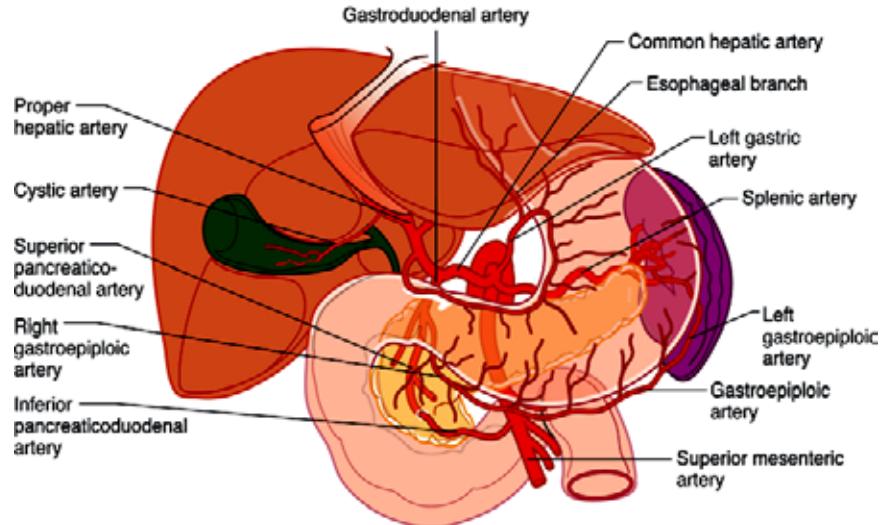
Dual supply

75% portal vein

25% hepatic artery

- Venous drainage

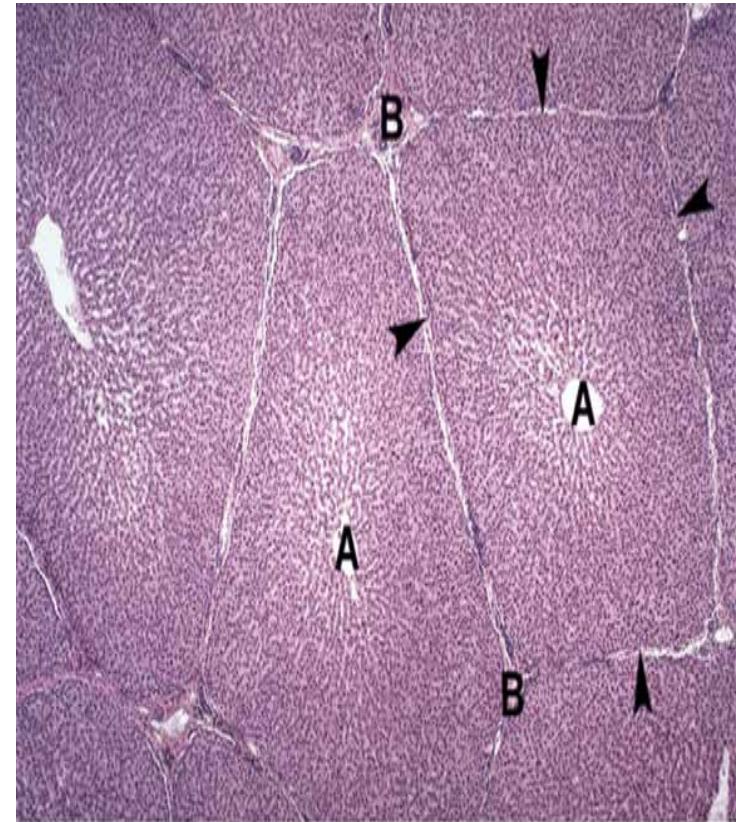
Inferior vena cava



# Liver: Hepatic Lobule

## Histology

- Divided into **hepatic** lobules
- Apices contain portal triads
- Center contains central vein
- Formed by hepatocytes (surround sinusoids)
- Blood and bile flow:
  - Blood from portal triad to central vein
  - Bile from central vein to portal triad



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A= Central vein  
B= Portal triad  
Arrow heads= Connective tissue

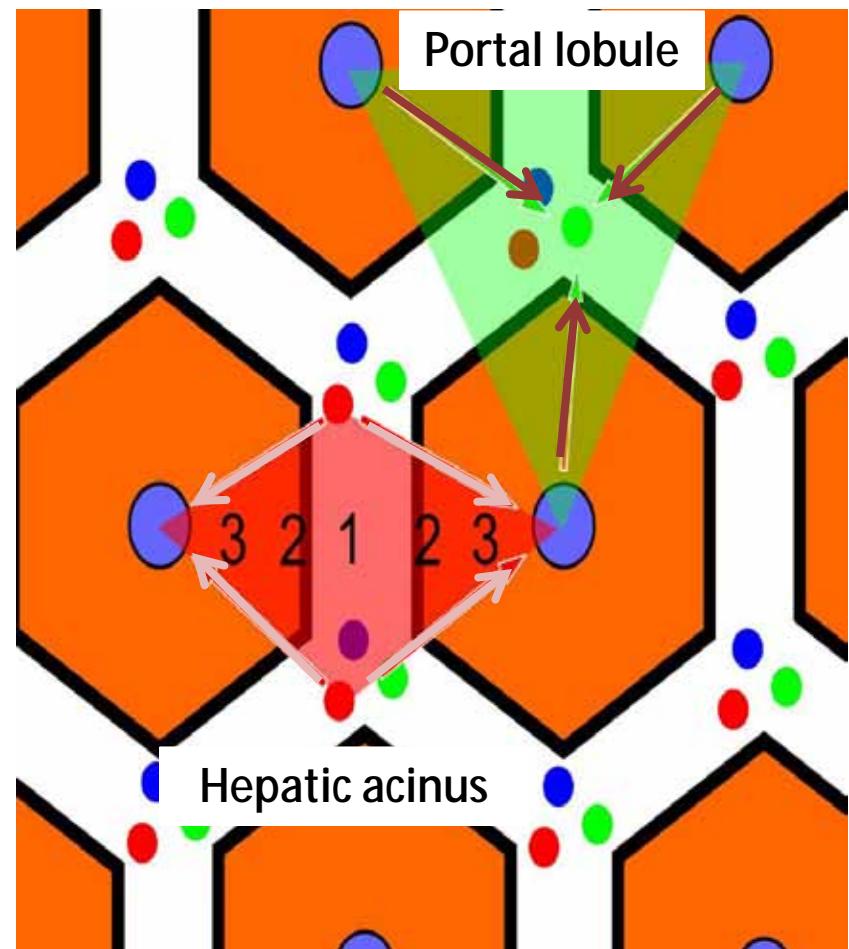
# Liver: Portal Lobule & Hepatic Acinus

## Portal lobule

- Triangular structure
- Central vein at each corner
- Portal tract in the center
- Bile flow from periphery to center

## Hepatic acinus

- Metabolic functional unit
- Diamond shape
- Connects 2 adjacent hepatic arteries and 2 central veins
- Divided into 3 zones:
  - Zone 1: most oxygenated blood
  - Zone 2: mix of 1 and 3
  - Zone 3: least oxygenated blood



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# Liver Cells

## Hepatocytes

- Functionally polarized
- Multiple apical and basal surfaces
  - Apical surfaces: 2 hepatocytes connect to each other
  - Basal surfaces: hepatocytes adjacent to a sinusoid
- Space of Disse: between capillary endothelial cell and hepatocytes

## Kupffer cells

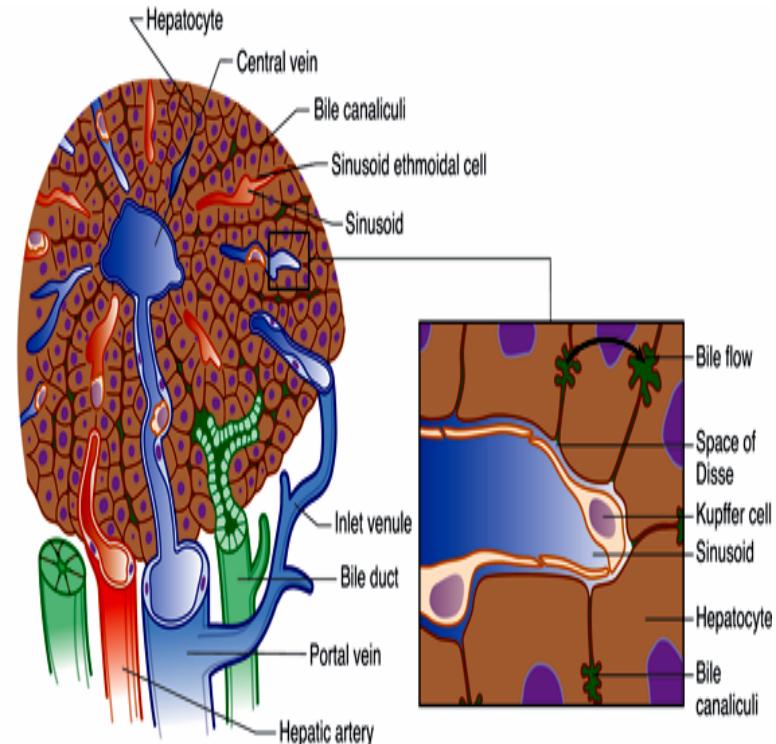
- Specialized monocytes (space of Disse)

## Ito cells (stellate cells)

- Mesenchymal cells: storage of fat soluble vitamins

## Bile duct epithelial cells

- Modulate transport of bile



# Bile

## General characteristics

- Mixture of bile salts (conjugated bile acids):

Conjugated bilirubin

Cholesterol

Phospholipids

Electrolytes

Water

## Function

- Fat emulsification and absorption
- Medium for hepatic excretion of endogenous metabolites
- Conduit for IgA secretion

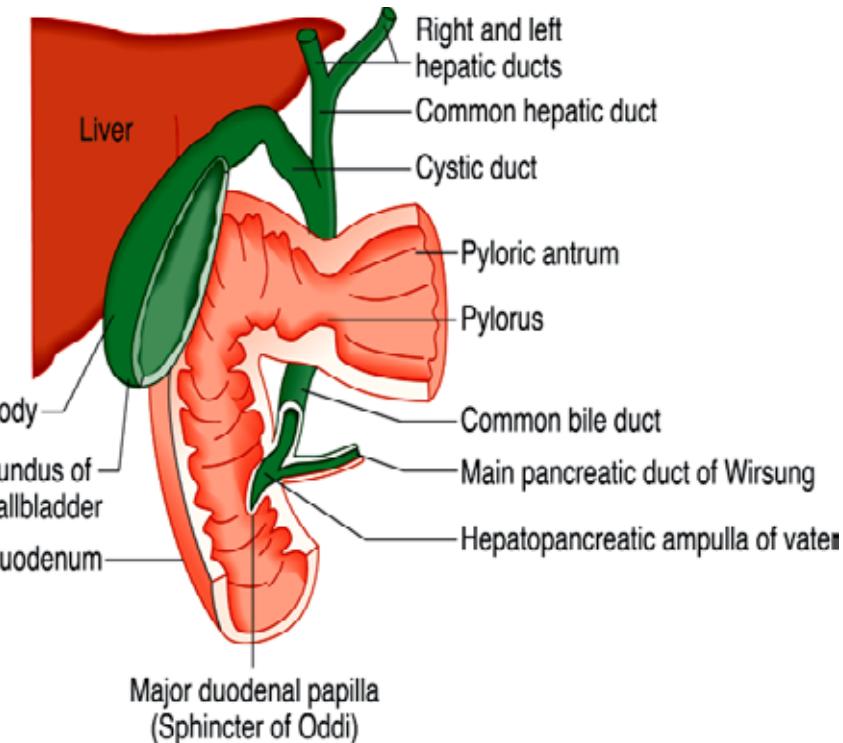


ERCP image showing the biliary tree and main pancreatic duct  
Commons.wikimedia.org. Used with permission

# Gallbladder

## General characteristics

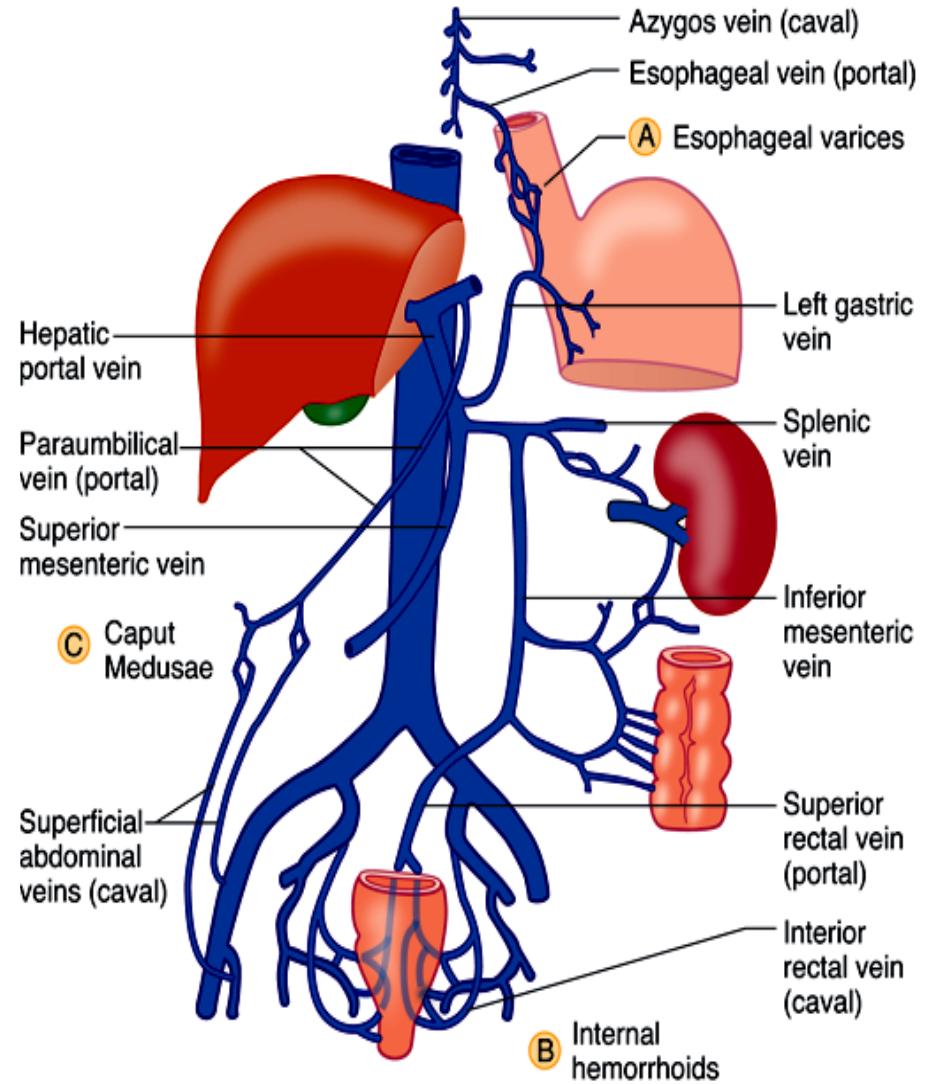
- Intraperitoneal organ
- Stores and concentrates bile
- Bile flow: gall bladder → cystic duct → common bile duct → duodenum
- Blood supply: cystic artery (right hepatic artery)
- Venous drainage: cystic vein (portal vein)
- Stimulated by CCK



# Hepatic Portal System

## General characteristics

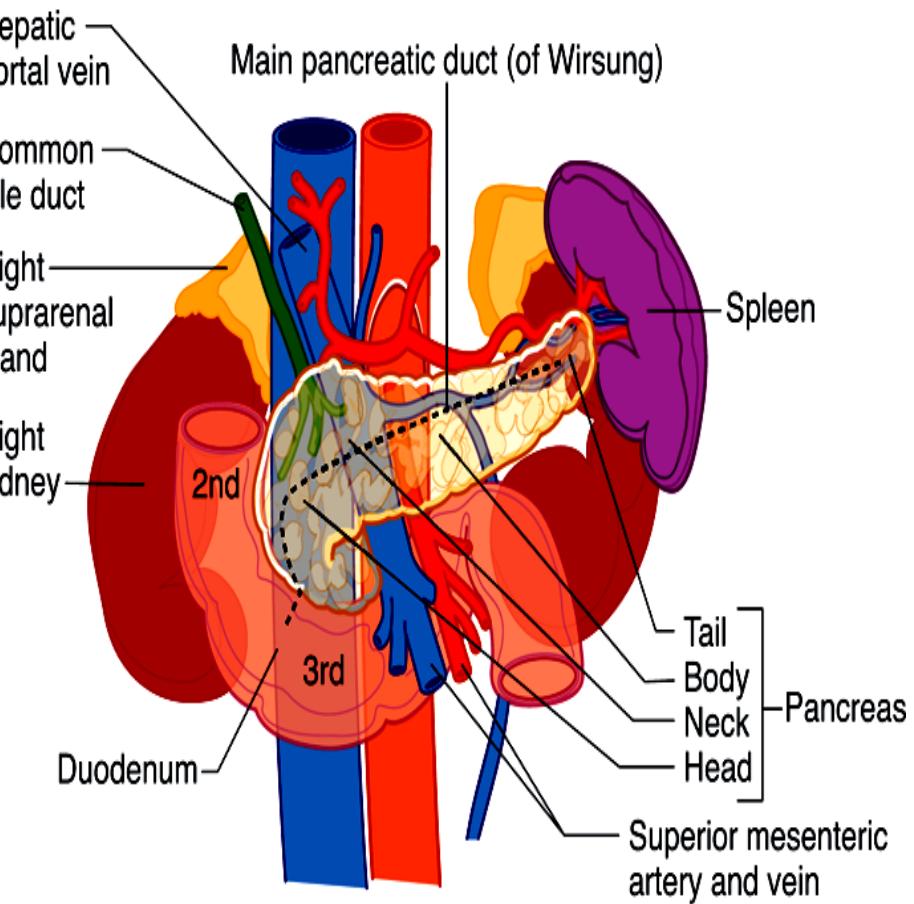
- Network of veins receiving blood from GI tract to liver
- Formed by:
  - Superior mesenteric vein
  - Inferior mesenteric vein
  - Splenic vein
- Sites of anastomoses with caval system:
  - Esophageal veins
  - Rectal veins
  - Thoracoepigastric veins
- Clinical correlate:
  - Esophageal varices
  - Hemorrhoids
  - Caput medusae



# Pancreas

## General characteristics

- Retroperitoneal organ
- Four anatomical parts
  - Head, neck, body, and tail
- Blood supply
  - Superior pancreaticoduodenal artery (gastroduodenal)
  - Inferior pancreaticoduodenal artery (SMA)
  - Splenic artery
- Venous drainage
  - Portal vein



# Exocrine Pancreas

## General characteristics

- Branched tubulo-acinar gland

## Acinus

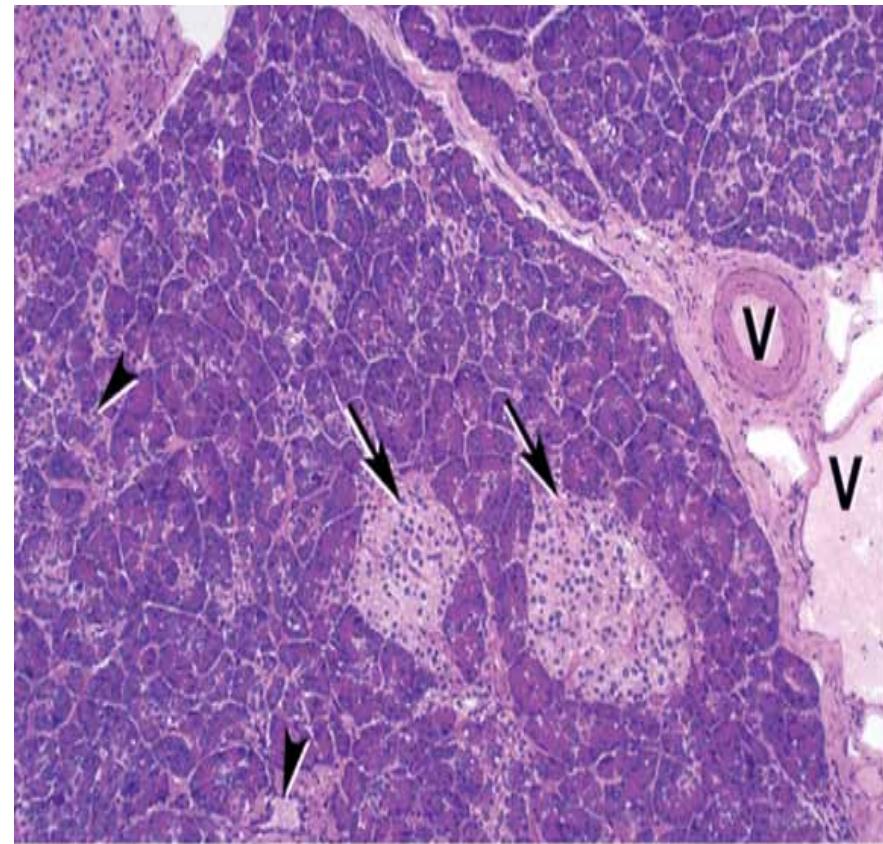
- Functional unit
- Secretory cells

Produce 15 digestive enzymes stored in granules

Drain via duct of Wirsung and duct of Santorini into duodenum

Ducts lined by epithelial cells secreting  $\text{HCO}_3^-$

- Secretion stimulated by  
Secretin  
CCK  
ACh



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# Inguinal Region

## Inguinal canal

- Oblique passageway parallel and superior to inguinal ligament

Entrance: deep inguinal ring

Exit: superficial inguinal ring

- Contents

Ilioinguinal nerve

Round ligament of the uterus (women)

Spermatic cord and contents (men)

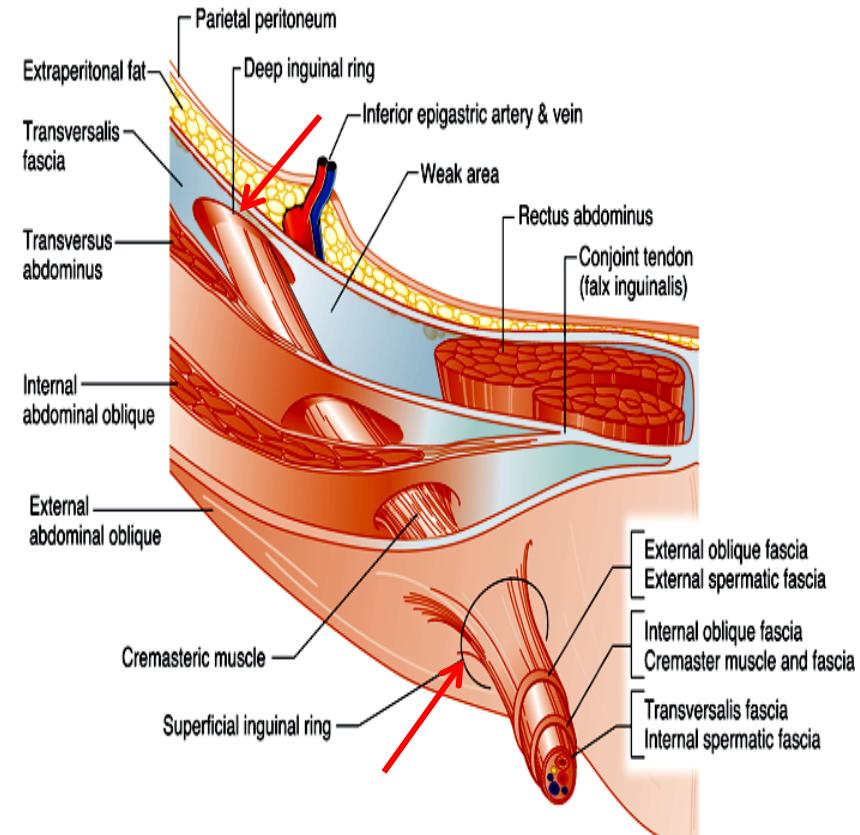
- Boundaries

Roof: internal abdominal oblique and transverse abdominis

Anterior wall: aponeurosis of external abdominal oblique

Floor: inguinal ligament

Posterior wall: transversalis fascia



# Hernias

## Definition

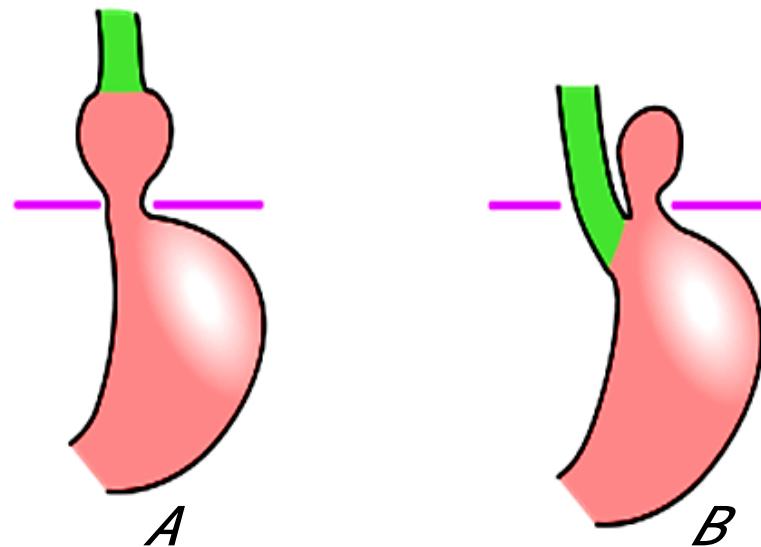
- Protrusion of an organ or part of an organ through a point of weakness or cavity wall defect

## Types of hernia

- Diaphragmatic, indirect inguinal, direct inguinal, femoral

## Diaphragmatic hernia

- Congenital
- Adult
- Sliding hiatal (A)
- Paraesophageal (B)



# Hernias

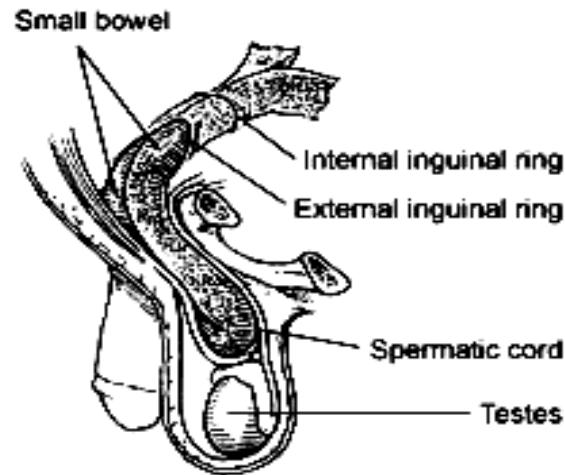
## Indirect inguinal hernia

- Outside of Hesselbach's triangle
- **Lateral** to inferior epigastric vessels
- Men > women
- Associated with hydrocele in infants
- Within spermatic cord
- Internal ring

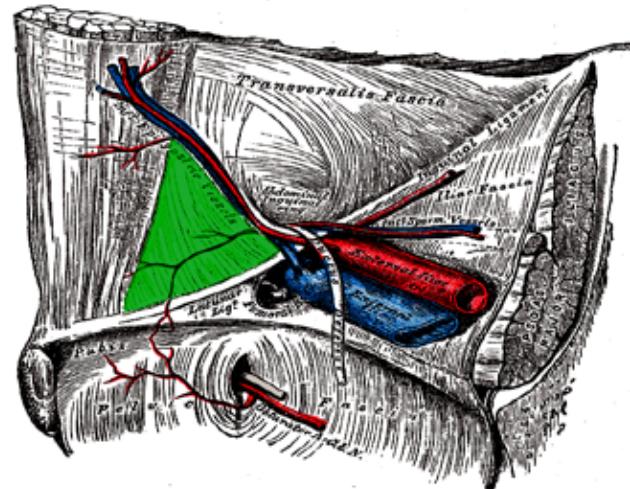
## Direct inguinal hernia

- Through Hesselbach's triangle
- **Medial** to inferior epigastric vessels
- Outside spermatic cord
- External ring

### Inguinal Hernia



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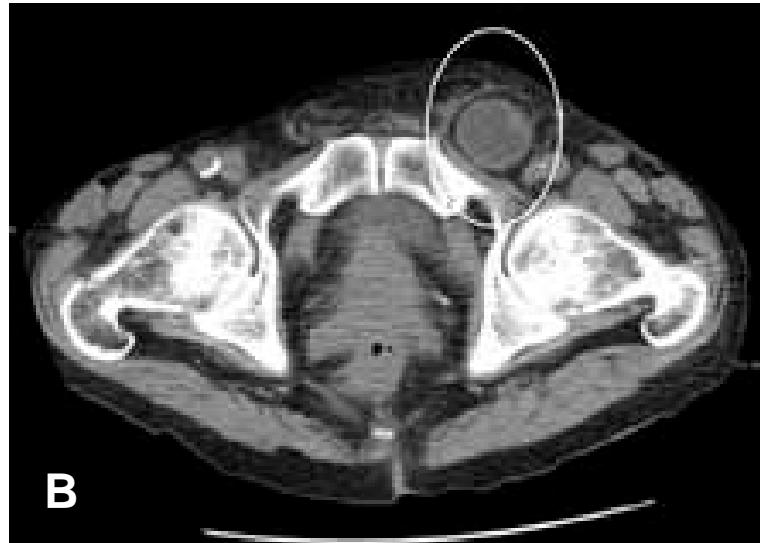


# Inguinal Hernias



**A**

An incarcerated inguinal hernia on the left with dilated loops of bowel above. Commons.wikimedia.org. Used with permission



**B**

An incarcerated inguinal hernia as seen on cross sectional CT scan. Commons.wikimedia.org. Used with permission



**C**

Frontal view of an inguinal hernia (right). Commons.wikimedia.org. Used with permission

- FA 2013: 318 • FA 2012: 345 • FA 2011: 316
- ME 3e: 357.3 • ME 4e: 357.3

# Femoral Region

## General characteristics

- Anatomical landmarks – femoral triangle

Inguinal ligament superiorly

Adductor longus muscle medially

Sartorius muscle laterally

- Important structures (lateral to medial):

Femoral Nerve

Femoral Artery

Femoral Vein

Femoral Lymphatics

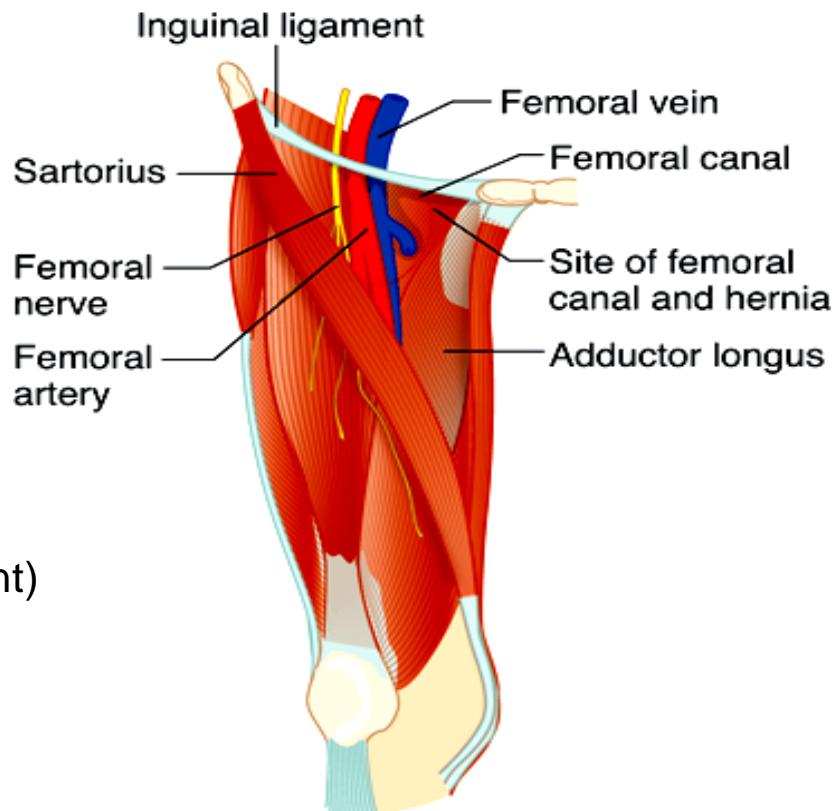
- Site of femoral hernia (below inguinal ligament)

Women > men

Leading cause of bowel incarceration

- Site for emergency vascular access

Femoral sheath contains femoral artery, vein, and canal





# Gastrointestinal Pathology

Megan Murray, M.D., Ph.D. Candidate  
University of Buffalo

# Salivary Gland Tumors

## Characteristics

- Relatively rare
- Most occur in parotid glands and are benign

Malignant tumors are most common after age 60

Benign tumors typically present after age 40

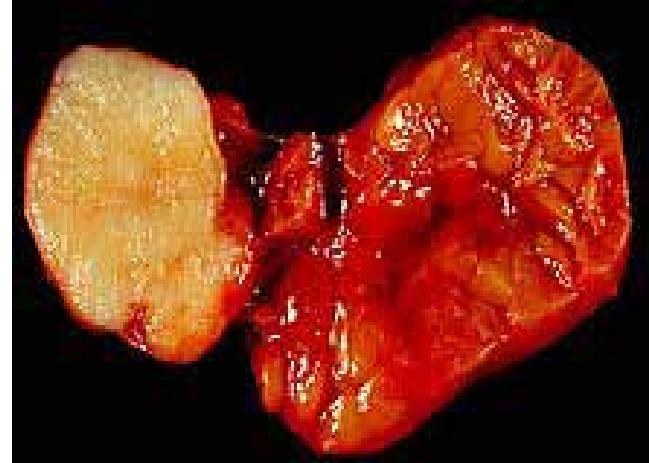
## Risk factors

- Radiation therapy
- Tobacco and alcohol not significant (except Warthin's tumors)

# Salivary Gland Tumor Types

## Pleomorphic adenoma

- Most common tumor type
- Benign with high rate of recurrence
- Painless, movable mass
- Up to 10% will transform into carcinomas



Pleomorphic adenoma. Commons.Wikimedia.org.  
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## Warthin's tumor

- Also known as papillary cystadenoma lymphomatosum
- Multiple papillae
- Surrounded by stromal tissue with lymphoid germinal centers



Warthin's tumor. Commons.Wikimedia.org.  
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## Mucoepidermoid carcinoma

- Most common malignant salivary tumor

# Zenker's Diverticulum

- Outpocketing of mucosa of posterior pharynx, just above cricopharyngeus muscle

## Signs and symptoms

- Halitosis
- Difficulty initiating swallowing
- Regurgitation of undigested food

## Diagnosis

- Barium swallow

## Treatment

- Surgery: cricopharyngeal myotomy and diverticulectomy



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# Achalasia

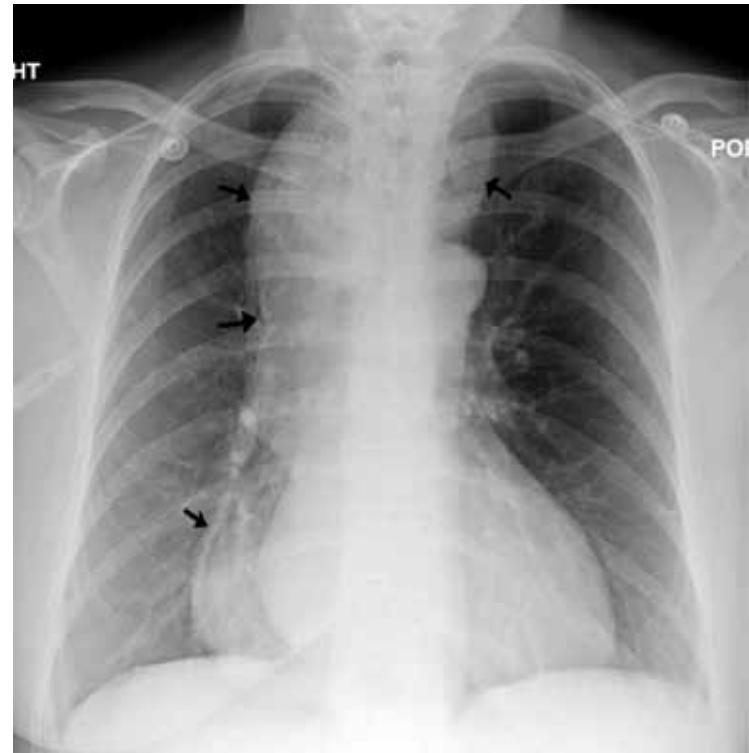
- Failure of lower esophageal sphincter (LES) to relax with swallowing due to loss of ganglion cells
- Increased LES tone
- Aperistalsis

## Etiology

- Most cases: unknown

## Risk factors

- Chagas disease
- CREST syndrome



CXR showing achalasia. Arrows point to outline of the massively dilated esophagus. Commons.wikimedia.org. Used with permission

# Achalasia

## Signs and symptoms

- Progressive dysphagia to both solids and liquids

## Diagnosis

- Contrast, barium swallow study  
“Bird-beak” sign
- Esophageal manometry
- Increased risk for esophageal carcinoma

## Treatment

- Balloon dilation of LES or surgical myotomy
- Calcium channel blockers, nitrates, botulinum toxin



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# Schatzki Ring

- Thin circumferential “ledge” made of mucosa, submucosa
- Upper surface covered with squamous epithelium
- Lower surface may be columnar epithelium
- Usually located at squamocolumnar junction proximal to the LES

## Sign and symptoms

- Intermittent dysphagia to solids

## Diagnosis

- Barium swallow

## Treatment

- Dilation procedures



Endoscopic image of Schatzki ring, seen in the esophagus with gastroesophageal junction in the background.  
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# Plummer-Vinson Syndrome

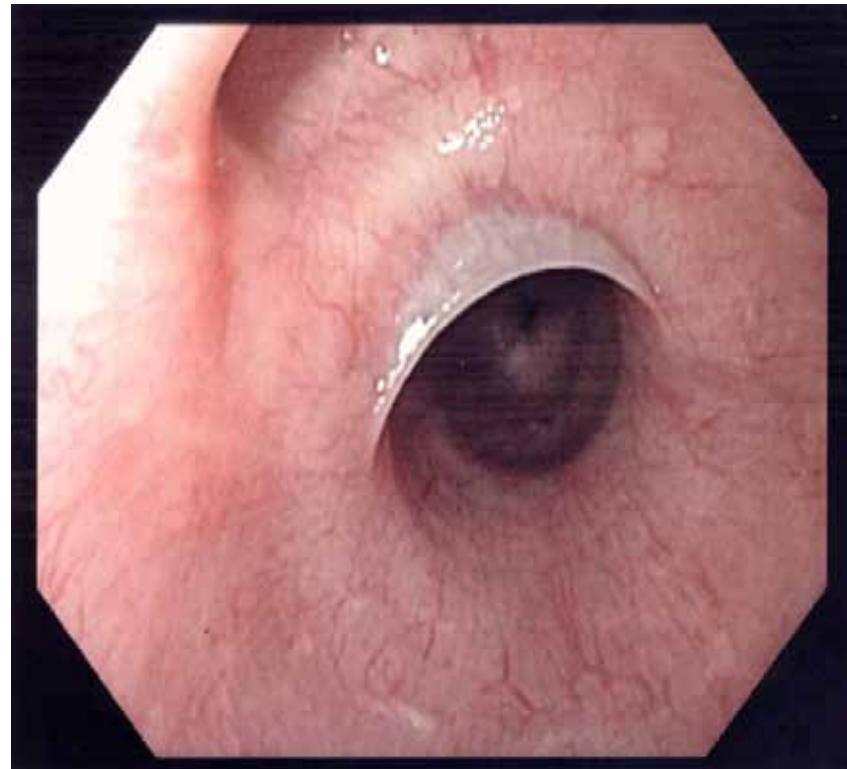
- Presents as a triad:
  - Dysphagia due to esophageal webs
  - Glossitis
  - Iron deficiency anemia

## Characteristics

- Disease of middle-aged women
- Increased risk of esophageal carcinoma

## Treatment

- Correction of iron deficiency
- Dilation procedure



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# Esophageal Rupture

## Mallory-Weiss Syndrome

- Linear lacerations of mucosa at gastroesophageal junction
- Severe, prolonged vomiting
- Hematemesis (usually self-limited)

## Boerhaave's Syndrome

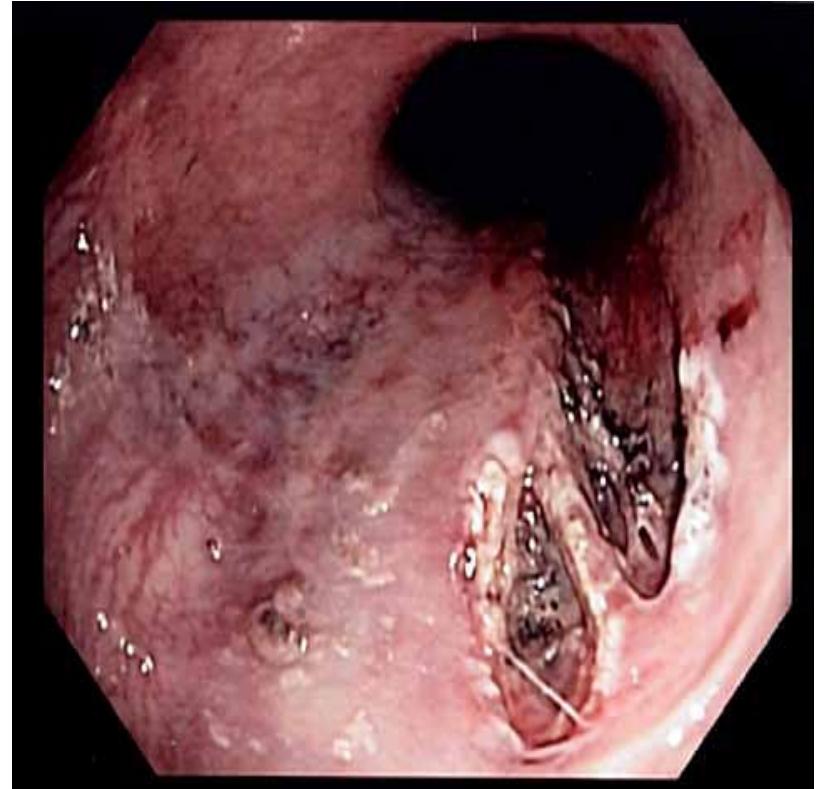
- Transmural esophageal rupture
- Can lead to sepsis and death

## Diagnosis

- Chest x-ray and esophagram
- Endoscopy for Mallory-Weiss tears

## Treatment

- Supportive care (Mallory-Weiss)
- Antibiotics/surgery (Boerhaave's)



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# Esophageal Varices

- Dilated submucosal veins in lower third of esophagus

## Etiology

- Secondary to portal hypertension

## Signs and symptoms

- Asymptomatic unless rupture occurs
- Hematemesis

## Diagnosis

- Endoscopy

## Treatment

- $\beta$ -blockers (propranolol) for non-bleeding varices
- Band ligation + octreotide
  - Sclerotherapy if banding unsuccessful
- Balloon tamponade + TIPS



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# Gastroesophageal Reflux Disease (GERD)

- Abnormal reflux of gastric secretions

## Risk factors

- Nicotine, alcohol, caffeine
- Anticholinergics
- Hiatal hernia
- Increased intra-abdominal pressure
- Associated with obesity

## Signs and symptoms

- Substernal or epigastric pain
- Sore throat, metallic taste, hoarseness
- Cough, wheezing

## Diagnosis

- Clinical
- 24-hour pH monitor

## Treatment

- Proton pump inhibitors (PPIs)
  - Surgery if PPIs fail



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# Barrett's Esophagus

- Lower esophageal epithelial lining changes from normal nonkeratinized stratified squamous epithelium to intestinal columnar epithelium = metaplasia
- Complication of chronic reflux disease
- Metaplasia can progress to esophageal adenocarcinoma

## Diagnosis

- Endoscopic biopsy

## Treatment

- Endoscopic surveillance every 2–3 years
- Surgical resection for high-grade dysplasia and neoplasia



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# Esophageal Carcinoma Types

## Squamous cell carcinoma

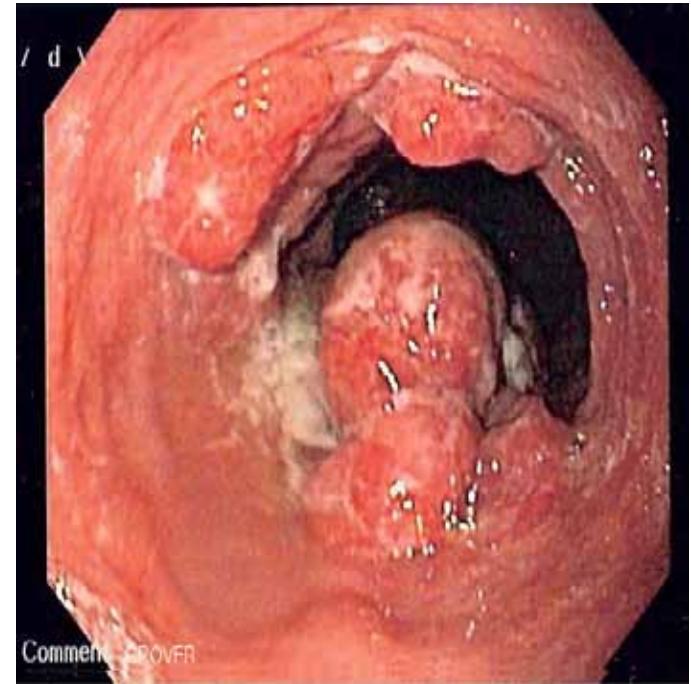
- Most common type of esophageal cancer worldwide
- Squamous cell: upper 2/3 of esophagus
- More common in males and African-Americans

## Adenocarcinoma

- Most common type of esophageal cancer in U.S.
- Typically age 50
- Adenocarcinoma: lower 1/3 of esophagus

## Risk factors

- Smoking and alcohol (especially squamous cell)
- Achalasia
- Plummer-Vinson syndrome
- Lye ingestion history
- Barrett esophagus (adenocarcinoma but not squamous)



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# Esophageal Carcinoma

## Signs and symptoms

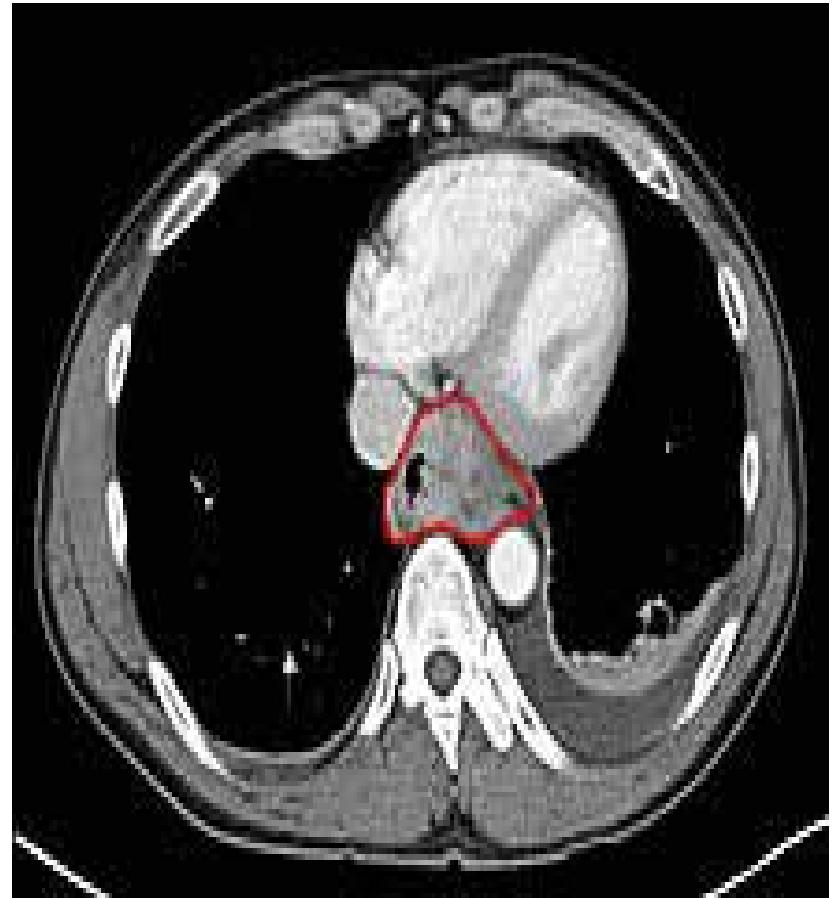
- Asymptomatic until late in disease
- Symptoms due to mass effect
- Progressive dysphagia
- Weight loss and anorexia
- Bleeding
- Hoarseness
- Cough

## Diagnosis

- Endoscopy and biopsy

## Treatment

- Surgical resection
- Poor prognosis



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# Ménétrier Disease

- Diffuse hyperplasia of surface mucous-secreting cells and decrease of parietal cells

## Epidemiology

- Middle-aged males
- Associated with protein-losing gastropathy and hypochlorhydria

## Pathophysiology

- Grossly: enlargement of gastric rugal folds in proximal stomach
- Local overexpression of transforming growth factor-alpha (TGF- $\alpha$ )



Ménétrier's disease with so much pit hyperplasia that giant folds appear to be covered by myriad polyps resembling hyperplastic polyps. The muscularis propria is the folded structure at the bottom center.

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# Ménétrier Disease

## Signs and symptoms

- Epigastric pain
- Weight loss
- Diarrhea
- Hypoproteinemia
- Increased risk of gastric cancer
- May regress spontaneously

## Treatment

- Epidermal growth factor receptor blockade (if no regression)
- Surgical gastric resection (severe cases/cancer)



Ménétrier disease seen at CT, coronal reconstruction. There is also a liver cyst.

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# Zollinger-Ellison Syndrome

- Acid hypersecretion and intractable peptic ulceration due to cancer of gastrin-producing cells
- May be associated with MEN type I

## Signs and symptoms

- Enlargement of gastric rugal folds
- Multiple, distal, large, recurrent ulcers
- Diarrhea

## Diagnosis

- ↑ gastric acid **and** ↑ gastrin
- Secretin stimulation test

## Treatment

- Surgery
- PPIs if not resectable



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# Acute Gastritis

- Acute inflammatory process causing erosion and hemorrhage of gastric mucosa

## Etiology

- Chronic aspirin or other NSAID use
- Alcohol use and smoking
- Uremia
- Chemotherapeutic drugs
- Surgery or burns

## Signs and symptoms

- Epigastric pain
- Hematemesis or melena

# Gastric Stress Ulcers

- Acute multiple, superficial, small, stomach and duodenal ulcers

## Predisposing factors

- Elevated intracranial pressure
- Severe sepsis
- Shock
- Burns or trauma
- High incidence in ICU patients

## Treatment

- Control of predisposing factors
- Adequate patient hydration
- Hemorrhage control, if present

# Chronic Gastritis

- Chronic inflammatory process of gastric mucosa, leading to atrophy
- Types A (fundic) and B (antral)

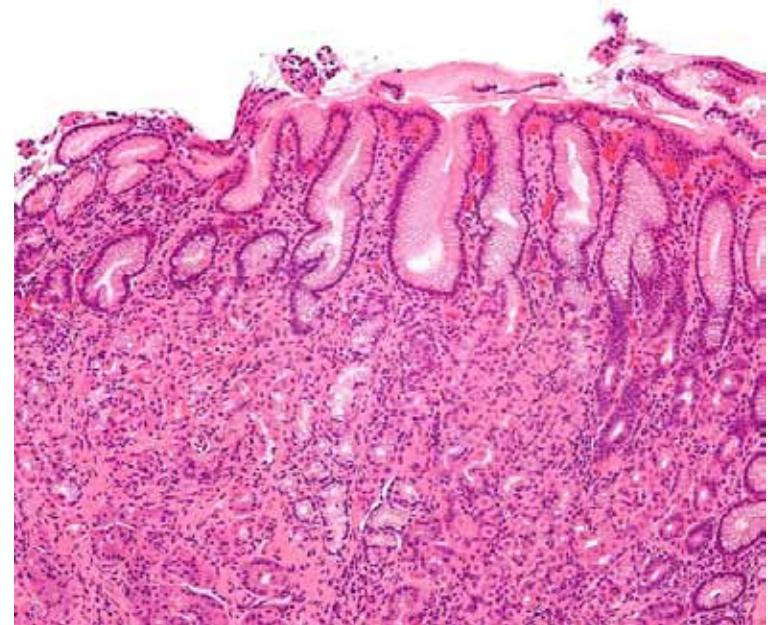
## Type A

- Autoimmune condition involving body and fundus
- Autoantibodies against parietal cells and/or intrinsic factor are present
- CD4 cells thought to mediate parietal cell destruction

Decreased acid secretion

Increased serum gastrin levels

Pernicious anemia



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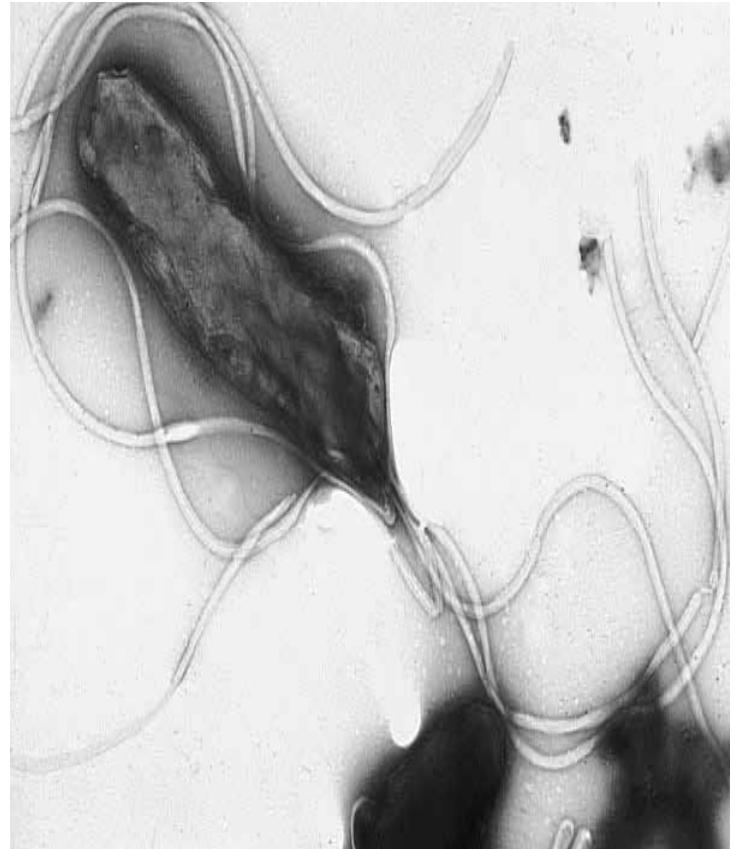
- FA 2013: 327.1 • FA 2012: 354.1 • FA 2011: 324.2  
• ME 3e: 356.2 • ME 4e: 356.2

# Chronic Gastritis

## Type B

- Also known as *Helicobacter pylori* gastritis
- Most common form in U.S.
- Associated with gastric colonization by *H. pylori*

*H. pylori* attaches to gastric epithelial cells but does not invade mucosal surface
- Continuous gastric inflammation



Electron micrograph of *H. pylori* possessing multiple flagella.  
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- FA 2013: 327.1 • FA 2012: 354.1 • FA 2011: 324.2  
• ME 3e: 356.2 • ME 4e: 356.2

# Peptic Ulcers

- Ulcers of distal stomach and proximal duodenum caused by gastric secretions
- Localized in stomach, duodenum, or both

## Risk factors

- *H. pylori* infection
- Chronic NSAID and aspirin use



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- FA 2012: 354.4
- FA 2011: 325.1
- ME 3e: 356.2
- ME 4e: 356.2

# Peptic Ulcers

## Duodenal ulcers

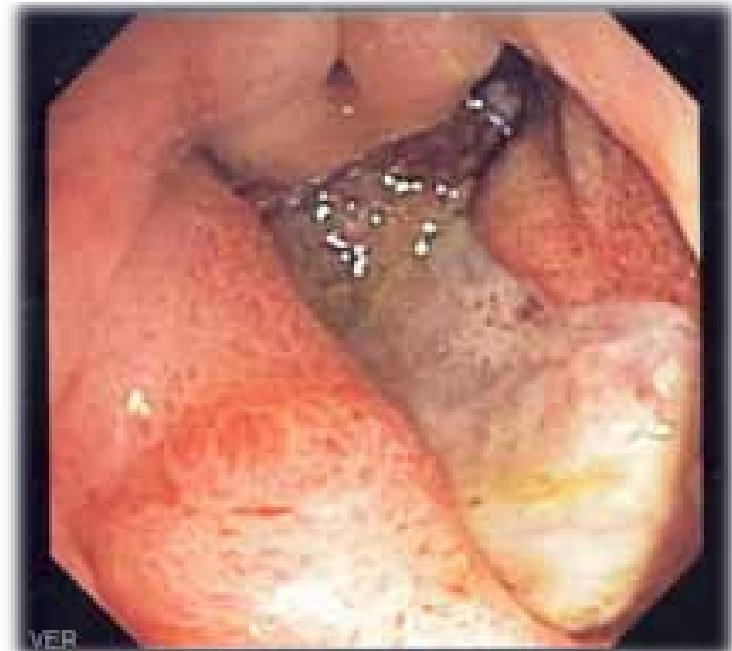
- More common than gastric ulcers
- Due to *H. pylori* infection
- Located in anterior wall of proximal duodenum

## Associations

- MEN type 1
- Cirrhosis
- COPD
- Abnormal ↑ in gastric acid secretion and rate of gastric emptying

## Signs and symptoms

- Burning epigastric pain
- Relieved by food intake for duodenal ulcers, not usually for gastric ulcers



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- FA 2013: 327.4
- FA 2012: 354.4
- FA 2011: 325.1
- ME 3e: 356.2
- ME 4e: 356.2

# Peptic Ulcers

## Gastric ulcers

- 75% association with *H. pylori*
- Located in lesser curvature of antrum
- Endoscopy

Small, demarcated, or “punched out” solitary ulcers

Round or oval-shaped

Overhanging margins

Radiating mucosal folds

- Burning epigastric pain that worsens with eating
- Treatment: amoxicillin, clarithromycin, PPIs



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# Gastric Carcinoma

## Epidemiology

- Decreased incidence in U.S.

## Risk factors

- Long-term exposure to smoked fish, meat, nitrosamines, and pickled vegetables
- Decreased fruit and vegetable intake
- Benzo[a]pyrene exposure
- Chronic *H. pylori* infection
- Chronic atrophic gastritis
- Smoking
- Blood type A
- Prior subtotal gastrectomy
- Ménétrier disease



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- FA 2013: 327.3
- FA 2012: 354.3
- FA 2011: 324.4
- ME 3e: 356.2
- ME 4e: 356.2

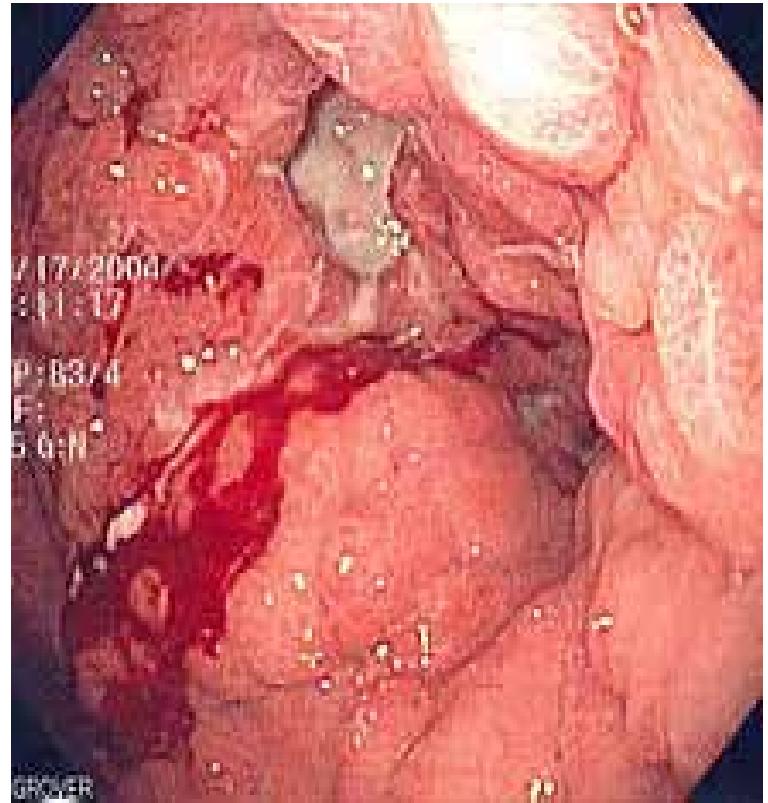
# Gastric Carcinoma

## Endoscopy

- Most commonly located in lesser curvature of antrum
- Large, irregular ulcers with heaped-up margins

## Histological types

- Intestinal type
  - Gland-forming adenocarcinoma of the intestines
- Diffuse type
  - Diffuse infiltration of stomach by poorly differentiated tumor cells (signet-ring cells)
  - Grossly appears as linitis plastica



Linitis plastica

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# Gastric Carcinoma

## Signs and symptoms

- Asymptomatic until late in disease
- Weight loss and anorexia
- Epigastric pain
- Early satiety
- Occult bleeding

## Diagnosis

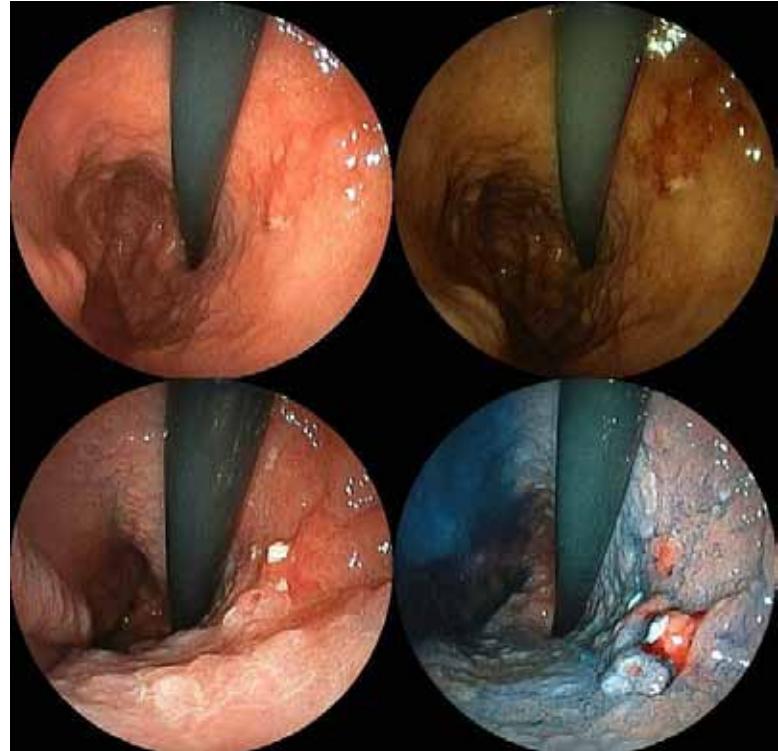
- Endoscopic biopsy

## Treatment

- Surgical resection
- Poor prognosis (5-year survival rate 20%)
- Distant metastases may occur in:

Left supraclavicular lymph nodes (Virchow's sentinel nodes)

Ovaries (Krukenberg tumors)



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# Volvulus

- Twisting of a segment of bowel on its vascular mesentery

## Risk factors

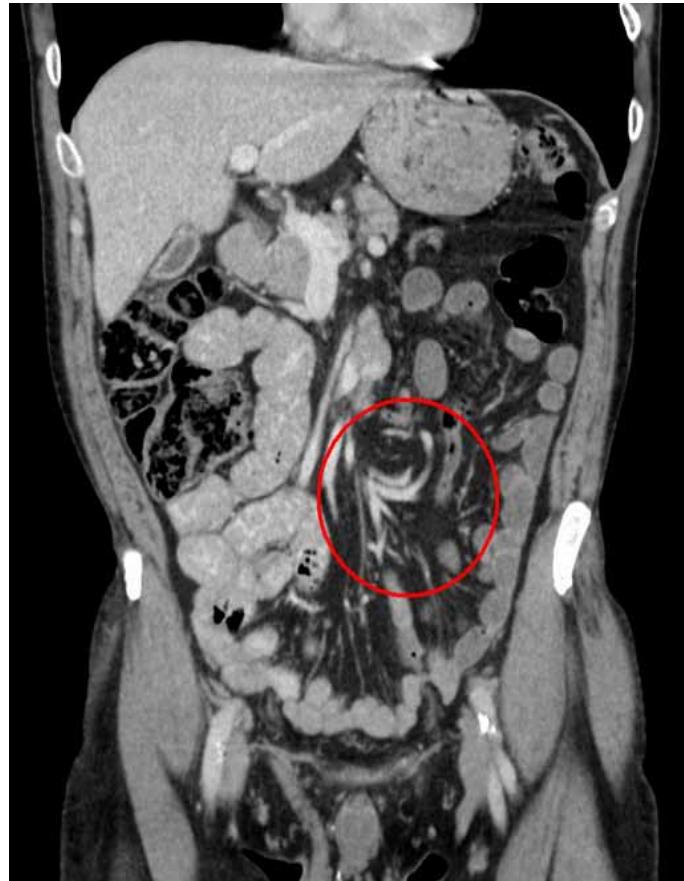
- Congenital gut malrotation
- Redundant mesentery (cecum and sigmoid colon)

## Signs and symptoms

- Acute obstruction: nausea, vomiting, abdominal pain and tenderness
  - Can progress to bowel ischemia, necrosis, and perforation
- Chronic or intermittent obstructive symptoms and abdominal distension

## Treatment

- Endoscopic detorsion or surgical correction



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# Intussusception

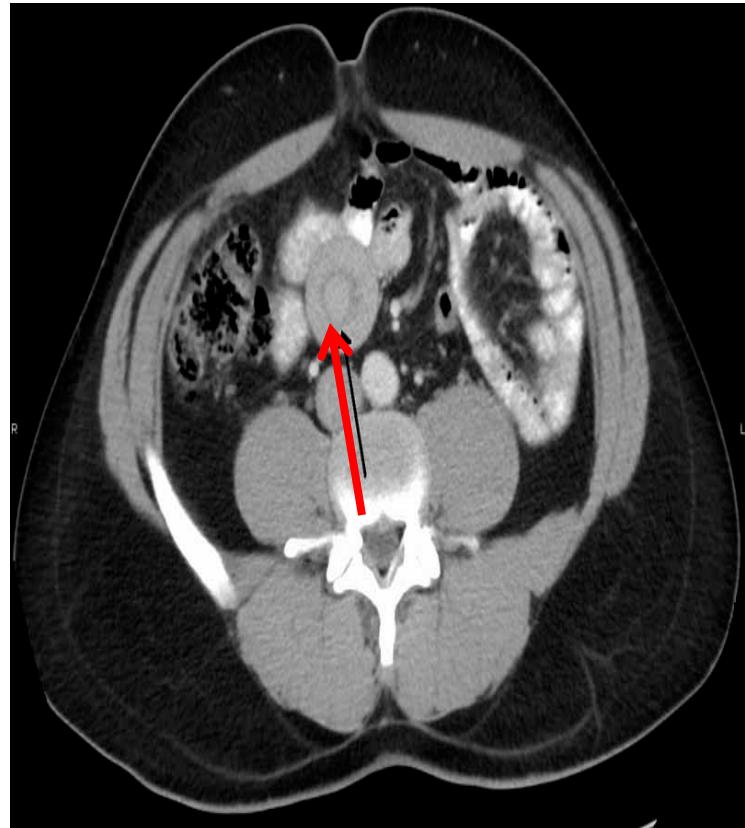
- Segment of intestine becomes drawn into the lumen and propelled distally
- Most common in infants and children
  - Often follows a viral enteritis in children
- Concern for malignancy in adults

## Signs and symptoms

- Nausea, vomiting, and abdominal pain
- CT scan: “target sign”

## Treatment

- Non-surgical: radiologic reduction (children only)
- Surgery



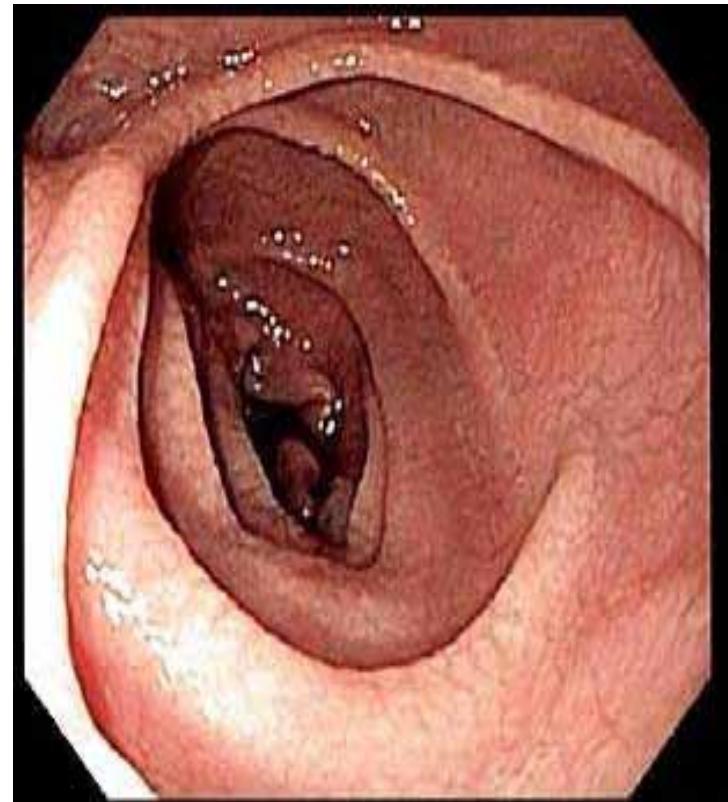
Commons.wikimedia.org. Used with permission

# Celiac Sprue

- Also known as gluten-sensitive enteropathy or nontropical sprue
- Hypersensitivity reaction to gluten and gliadin in diet

## Pathophysiology

- Over time, exposure leads to:
  - Increased plasma cell density within lamina propria
  - Increased intra-epithelial lymphocytes
  - Destruction and loss of small bowel enterocytes and villi
  - Malabsorption
- Associated with HLA-DQ2, DQ8



Endoscopy: duodenum of patient with celiac disease showing scalloping of folds and "cracked-mud" appearance to mucosa.  
Commons.wikimedia.org. Used with permission

# Celiac Sprue

## Signs and symptoms

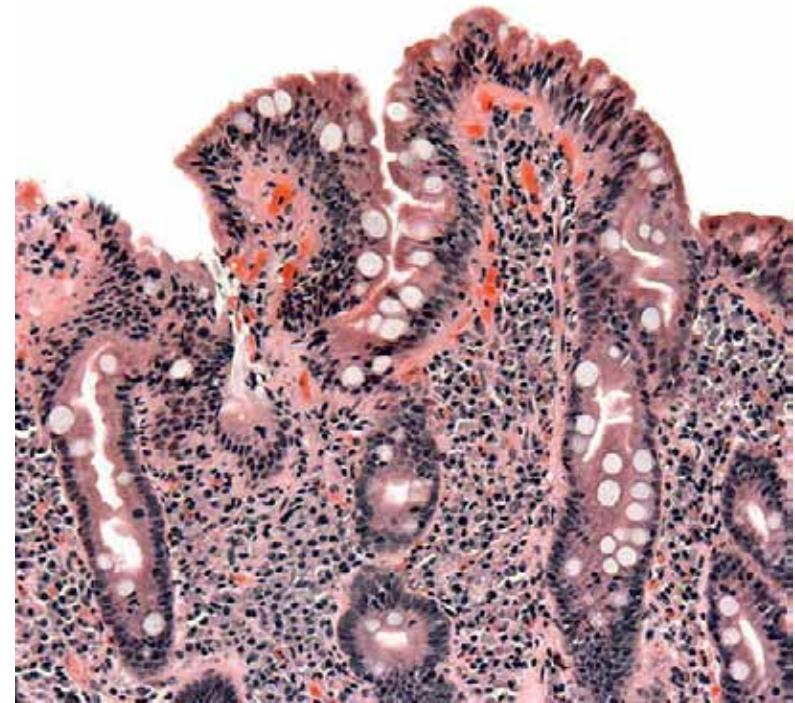
- Malabsorption in childhood
- Flatulence, bloating, and distention
- Diarrhea, steatorrhea
- Weight loss
- Associated with dermatitis herpetiformis
- Associated with small bowel lymphoma

## Diagnosis

- Antigliadin, antiendomysial, and anti-transglutaminase antibodies
- Small bowel biopsy
- Skin biopsy

## Treatment

- Dietary restriction of gluten



Biopsy of small bowel showing celiac disease: blunting of villi, crypt hyperplasia, and lymphocyte infiltration of crypts  
Commons.wikimedia.org. Used with permission

# Tropical Sprue

## Etiology

- Unknown
- Associated with tropical regions (Caribbean and South America)
- Intestinal microbial infection
  - Enterocyte injury
  - Intestinal stasis
  - Bacterial overgrowth
  - Inflammatory response causing villous destruction

## Signs and symptoms

- Steatorrhea and malabsorption
- Volume depletion and electrolyte imbalance
- Symptomatic anemia

## Diagnosis

- Biopsy

## Treatment

- Doxycycline/tetracycline + folic acid

# Whipple Disease

- Infectious disease caused by *Tropheryma whipplei* involving many organs

## Signs and symptoms

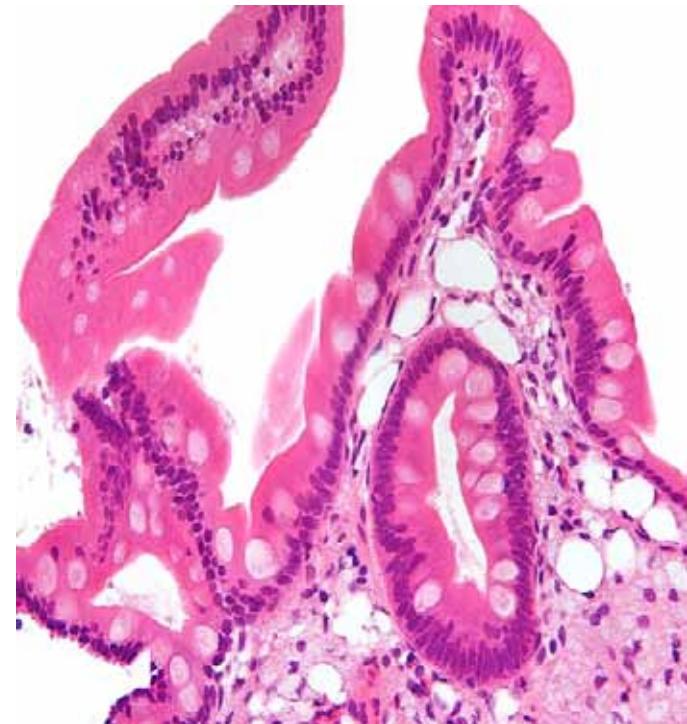
- Diarrhea, malabsorption, weight loss, abdominal pain, and arthralgia
- Can present with CNS involvement

## Diagnosis

- Biopsy
  - Small bowel lamina propria infiltrated with macrophages
  - PAS-positive, Gram-positive, rod-shaped bacilli
- PCR of stool

## Treatment

- Ceftriaxone, followed by TMP/SMX for 1 year
- Sulfa allergy: penicillin or streptomycin



High magnification micrograph showing characteristic foamy macrophages in lamina propria. H&E stain.  
Commons.wikimedia.org. Used with permission

# Inflammatory Bowel Disease

## Classification

- Crohn's disease, also called regional enteritis
- Ulcerative colitis (UC)
- Colitis of indeterminate type

## Common characteristics

- Women > men
- Caucasians > non-Caucasians
- Age distribution
  - Crohn's: bimodal distribution
  - UC: peaks at age 20–30
- UC > Crohn's
- Bloody diarrhea, or mucous stools
- Colicky lower abdominal pain and/or fever
- Crohn's: perianal fistulas, malabsorption
- Extraintestinal manifestations (Crohn's > UC)
- Diagnosis: endoscopic biopsy



Erythema nodosum on the back of a Crohn's patient.  
Commons.wikimedia.org. Used with permission

- FA 2013: 328.2
- FA 2012: 355.2
- FA 2011: 326.1
- ME 3e: 359.1
- ME 4e: 359.1

# Inflammatory Bowel Disease

	Crohn's Disease	Ulcerative Colitis
Most common site	Terminal ileum	Rectum
Distribution	Mouth to anus	Rectum → colon “backwash” ileitis
Spread	Discontinuous/“skip”	Continuous
Gross features	Focal aphthous ulcers Linear fissures Cobblestone appearance Thickened bowel wall “Creeping fat”	Extensive ulceration Pseudopolyps
Micro	Noncaseating granulomas	Crypt abscesses
Inflammation	Transmural	Limited to mucosa and submucosa
Complications	Strictures “String sign” on barium study Obstruction Abscesses Fistulas Sinus tracts	Toxic megacolon
Genetic association		HLA-B27
Extraintestinal manifestations	Common (arthritis, spondylitis, primary sclerosing cholangitis, erythema nodosum, pyoderma gangrenosum, uveitis)	Common (arthritis, spondylitis, primary sclerosing cholangitis, erythema nodosum, pyoderma gangrenosum, uveitis)
Cancer risk	Slight 1–3%	5–25%

- FA 2013: 328.2
- FA 2012: 355.2
- FA 2011: 326.1
- ME 3e: 359.1
- ME 4e: 359.1

# Inflammatory Bowel Disease

## Treatment

- Aminosalicylates (mesalamine, sulfasalazine)

5-ASA derivatives

Used in maintenance of chronic Crohn's and UC

Sulfasalazine associated with many adverse effects

- Steroids for acute exacerbations, unresponsive to 5-ASA derivatives

- Azathioprine/6-mercaptopurine for maintenance of steroid-free remission

- Infliximab

Monoclonal antibody to TNF

Used in severe and fistulizing Crohn's

Adverse effects

Fever and hypotension

Increased risk of infection (reactivation of latent TB); do PPD screening prior to use



UC affecting left side of the colon. Image shows confluent superficial ulceration and loss of mucosal architecture. Crohn's may be similar in appearance, which can make diagnosing UC a challenge. Commons.wikimedia.org. Used with permission

# Ischemic Bowel Disease

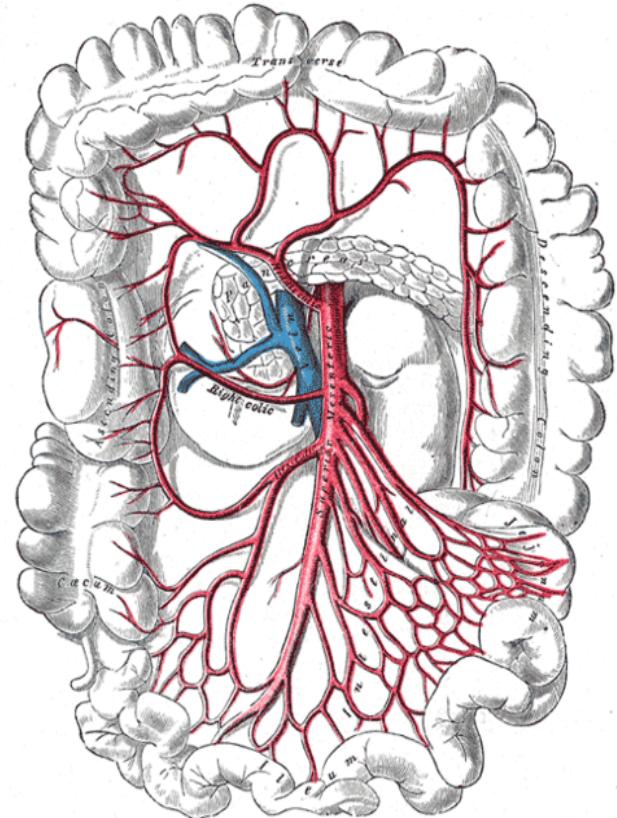
- Decreased blood flow and ischemia of bowel
- Associated with
  - Atherosclerosis, thrombus and thromboembolic disease
  - Blood flow disruption: CHD or shock
- More common in older people

## Signs and symptoms

- Acute abdominal pain and bloody diarrhea
- Intermittent abdominal pain
  - Associated with food intake
- Areas at risk
  - Watershed areas
  - Splenic flexure of the colon

## Treatment

- Surgical resection



Frontal view of superior mesenteric artery and branches.  
Large vessel (blue) beside the SMA is the superior mesenteric vein.  
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# Hemorrhoids

- Tortuous dilatation of submucosal veins in the anus and lower rectum, caused by increased venous pressure

## Risk factors

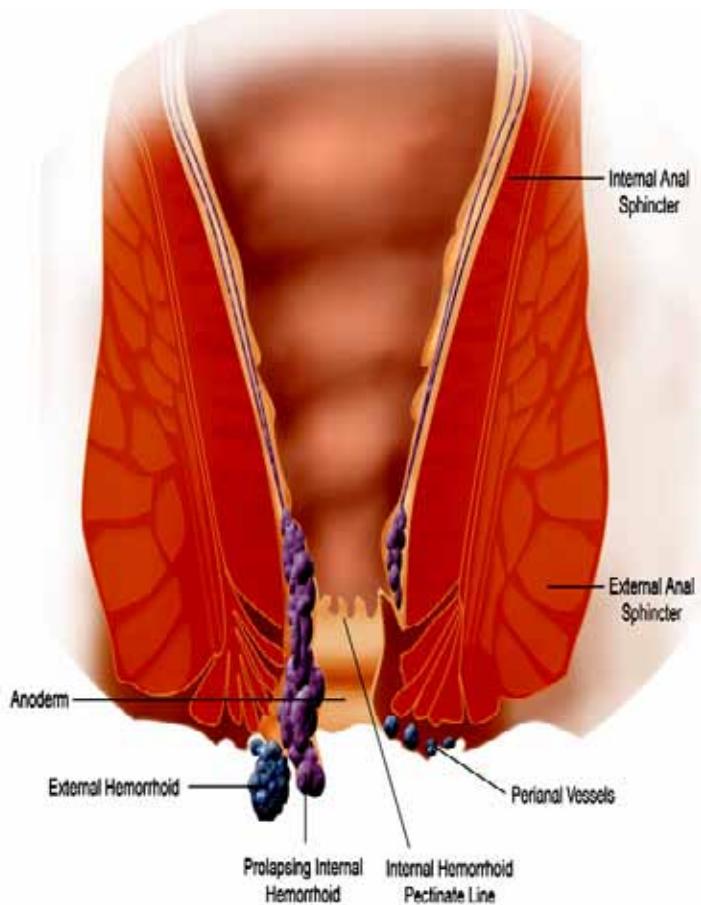
- Constipation and prolonged straining
- Pregnancy
- Cirrhosis

## Signs and symptoms

- Pain (dependent on location)
- Itching

## Complications

- Thrombosis
- Bleeding



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# Angiodysplasia

- Arteriovenous malformations within intestines

## Epidemiology

- Age >55

## Risk factors

- Osler-Weber-Rendu syndrome
- CREST syndrome

## Signs and symptoms

- Lower GI bleeding, common in cecum and right colon

## Treatment

- Surgical resection



inent: GROVER

Angiodysplasia in the colon being treated with argon plasma coagulation via probe through colonoscope.  
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# Melanosis Coli

## Characteristics

- Black pigmentation of colon due to laxative abuse
- Mucosal and submucosal macrophages ingest laxative pigment
- Mimics more serious pathologies such as colitis and malignancy



Melanosis coli identified on colonoscopy as a brownish moiré pattern on colon wall.

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# Pseudomembranous Colitis

- Also known as antibiotic-associated colitis
- Acute colitis due to selective overgrowth of *Clostridium difficile*, in the setting of broad-spectrum antibiotic use

## Associations

- Clindamycin and ampicillin use, but can occur with any antibiotic
- Ischemic bowel disease

## Endoscopic findings

- Mucosal membranes

Yellow-tan

Mushroom-shaped inflammatory exudates



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# Pseudomembranous Colitis

## Pseudomembrane histology

- Composed of neutrophils, mucin, fibrin, and necrotic cellular debris
- Underlying pseudomembranes are necrotic luminal epithelial cells

## Signs and symptoms

- Diarrhea, fever, and abdominal cramps

## Diagnosis

- Stool assessment for *C. difficile* toxin

## Treatment

- Metronidazole
- Vancomycin/fidaxomicin if persistent



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# Appendicitis

- Obstruction of appendiceal orifice by a fecolith

## Pathophysiology



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Obstruction



↑ pressure



Vascular  
occlusion



Mucosal breakdown



Peritonitis

# Appendicitis

## Signs and symptoms

- Visceral pain (periumbilical region)
- Localized later to right iliac region
- Nausea, vomiting, and fever
- Leukocytosis

## Complications

- Peritonitis
- Sepsis and death if untreated

## Treatment

- Appendectomy
- Antibiotics



Arrow shows fecalith.

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# Colonic Diverticulosis

- Acquired outpouchings of mucosa and submucosa through bowel wall

## Epidemiology

- Common in United States
- Major risk factor: low-fiber diet
- Most common location: sigmoid colon

## Signs and symptoms

- May be asymptomatic
- Lower GI bleeding
- Constipation alternating with diarrhea
- Left lower quadrant abdominal cramping

## Complications

- Diverticulitis
  - Fever and abdominal pain
  - Bleeding typically absent
- Can progress to perforation, peritonitis, and sepsis
- Fistula development



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# Adenomatous Colonic Polyps

- Benign neoplasms of colonic mucosa

## Signs and symptoms

- Usually asymptomatic
- Occult bleeding
- Iron deficiency anemia
- May progress to colonic adenocarcinoma  
10 years progression

## Diagnosis

- Colonoscopy

## Histology

- Tubular versus villous
- Pedunculated versus sessile appearance
- Size
- Degree of dysplasia



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# Familial Adenomatous Polyposis

## Characteristics

- Autosomal dominant mutation of APC gene (5q21)
- 100% risk of developing colorectal carcinoma, often age <30
- Increased risk for duodenal adenocarcinoma and adenocarcinoma of papilla of Vater
- Flexible sigmoidoscopy every 1-2 years starting age 12
- Diagnosis: >100 adenomatous polyps on endoscopy
- Recommendation: total colectomy



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# Gardner Syndrome

## Characteristics

- Autosomal dominant variant of familial adenomatous polyposis
- Numerous colonic adenomatous polyps
- Increased risk for development of colon cancer
- Associated with development of multiple, soft-tissue tumors

Osteomas

Lipomas

Fibromatosis

Epidermal inclusion cysts

# Turcot Syndrome

## Characteristics

- Rare variant of familial adenomatous polyposis
- Numerous colonic adenomatous polyps
- Central nervous system tumors (particularly gliomas)

# Heredity Nonpolyposis Colorectal Cancer

## Characteristics

- Also known as Lynch syndrome
- Autosomal dominant mutation of a DNA nucleotide mismatch repair gene
- Increased risk for colon cancer, endometrial, and ovarian carcinoma

## Syndrome characteristics

- 3 family members (in 2 generations) with colon cancer
- 1 case should be diagnosed age <50
- Non-affected family members:

Start screening for colon cancer at age 25

Colonoscopy every 1–2 years

# Peutz-Jeghers Syndrome

## Characteristics

- Autosomal dominant condition
- Multiple hamartomatous polyps
- Melanotic spots on lips, buccal mucosa, and skin
- Increased risk for development of cancers in:
  - Lungs
  - Pancreas
  - Breast
  - Uterus
- Most common presentation: intussusception



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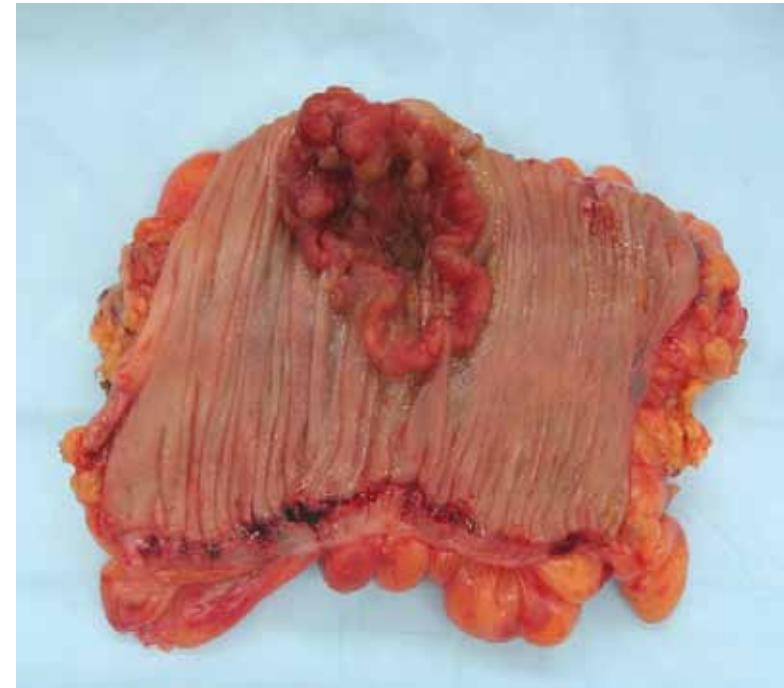
# Adenocarcinoma of the Colon

## Epidemiology

- Third most common tumor (incidence and mortality) in United States
- Lifetime risk of colon cancer (general population): <6%

## Risk factors

- Diet:
  - Low in fiber, few fruits and vegetables
  - High in red meat and animal fat
- Smoking
- Presence of colonic polyps
- Mutations affecting:
  - APC gene
  - K-ras oncogene
  - DCC gene (tumor suppressor gene)
  - p53 gene



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- FA 2013: 332.1 • FA 2012: 359.1 • FA 2011: 329.2
  - ME 3e: 358.4 • ME 4e: 358.4

# Adenocarcinoma of the Colon

	Right-sided Cancer	Left-sided Cancer
Gross	Polypoid mass	Circumferential growth: "napkin-ring" configuration
Barium studies	Polypoid mass	"Apple-core" lesion
Presentation	<ul style="list-style-type: none"><li>• Bleeding</li><li>• Occult blood in stool</li><li>• Iron deficiency anemia</li></ul>	<ul style="list-style-type: none"><li>• Change in bowel habits</li><li>• Constipation or diarrhea</li><li>• Reduced caliber stools</li><li>• Obstruction</li></ul>

# Adenocarcinoma of the Colon

## Diagnosis

- Direct endoscopy and biopsy
- Histology: reveals stage of disease

Stage	TNM Stage	Characteristics
Stage 0	Tis N0 M0	Tis: Tumor confined to mucosa; cancer- <i>in-situ</i>
Stage I	T1 N0 M0	T1: Tumor invades submucosa
Stage I	T2 N0 M0	T2: Tumor invades muscularis propria
Stage II-A	T3 N0 M0	T3: Tumor invades subserosa or beyond (without other organs involved)
Stage II-B	T4 N0 M0	T4: Tumor invades adjacent organs or perforates the visceral peritoneum
Stage III-A	T1-2 N1 M0	N1: Metastasis to 1–3 regional lymph nodes. T1 or T2
Stage III-B	T3-4 N1 M0	N1: Metastasis to 1–3 regional lymph nodes. T3 or T4
Stage III-C	any T, N2 M0	N2: Metastasis to 4 or more regional lymph nodes. Any T
Stage IV	any T, any N, M1	M1: Distant metastases present. Any T, any N

- FA 2013: 332.1
- FA 2012: 359.1
- FA 2011: 329.2
- ME 3e: 358.4
- ME 4e: 358.4

# Adenocarcinoma of the Colon

## Metastasis

- Occurs via spread to mesenteric lymph nodes
- Distant spread to liver, lungs, and bone

## Treatment

- Surgical resection if localized to mucosa, submucosa, and muscularis layers
- Chemotherapy for distant metastasis
  - 5-fluorouracil (5-FU)

# Carcinoid Tumors

## Characteristics

- Neuroendocrine tumors producing serotonin
- Most common location: appendix and terminal ileum
- Characterized by:
  - Diarrhea
  - Cutaneous flushing
  - Bronchospasm and wheezing
  - Fibrosis
- Diagnosis: elevated urinary 5-HIAA
- Treatment: surgery, octreotide



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# Osmotic Laxatives

## Generic names

- Magnesium hydroxide, magnesium citrate, polyethylene glycol, lactulose

## Mechanism of action

- Provide intraluminal osmotic load

## Uses

- Constipation
- Hepatic encephalopathy (lactulose):

Degraded by gut flora into lactic and acetic acids; promote excretion of  $\text{NH}_4^+$

## Adverse effects

- Diarrhea and dehydration

# Ondansetron and Metoclopramide

## Ondansetron/Granisetron/Dolasetron

- 5-HT<sub>3</sub> antagonist
- Used to treat and control vomiting (chemotherapy/post-op patients)
- Adverse effects: headache and constipation

## Metoclopramide

- D2 receptor antagonist
- Increases resting tone, contractility, lower esophageal sphincter tone, and gastric motility
- Used in diabetic and post-surgical gastroparesis
- Adverse effects: Parkinsonian-like effects, restlessness, drowsiness, fatigue, depression, nausea, and diarrhea
- Can interact with and affect efficacy of digoxin and diabetic drugs
- Contraindicated in small bowel obstruction and Parkinson's disease



# Liver and Pancreas Pathology

Megan Murray, M.D., Ph.D. Candidate  
University of Buffalo

# Acute Pancreatitis

- Acute inflammation of the pancreas

## Etiology

- Biliary obstruction (gallstones), alcohol, hypercalcemia, severe hypertriglyceridemia
- Shock, infection, trauma, scorpion stings
- Drugs (pentamidine, didanosine, azathioprine, sulfa drugs)
- ERCP-induced

## Pathophysiology

- Premature activation of trypsinogen into trypsin (within pancreas)
- Activation of pancreatic zymogens
- Autodigestion of the pancreas

## Gross characteristics

- Focal hemorrhage and liquefaction
- Chalky, white-yellow fat necrosis of adjacent adipose tissue

# Acute Pancreatitis

## Histology

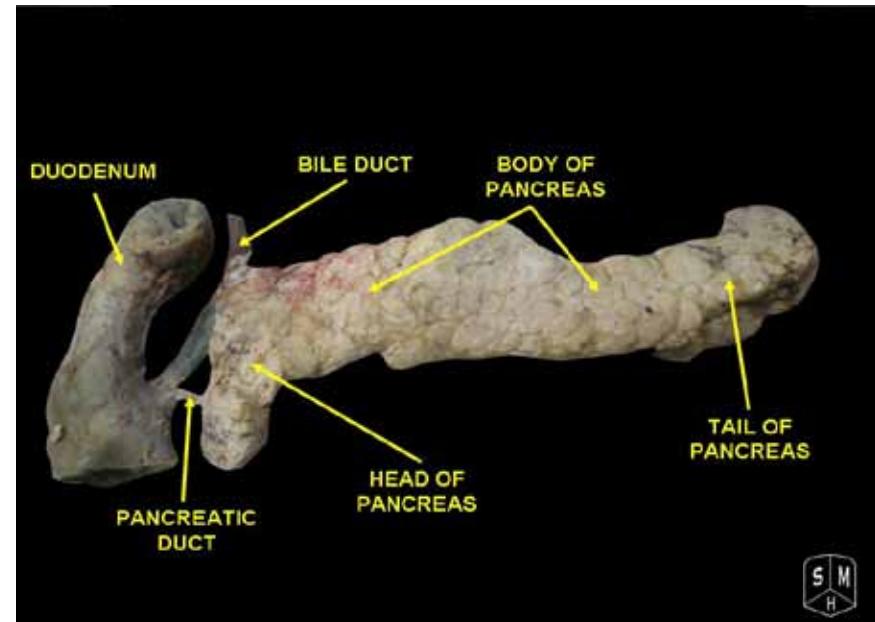
- Liquefactive necrosis of pancreatic parenchyma
- Acute inflammation and enzymatic fat necrosis

## Laboratory studies

- ↑ amylase and lipase; leukocytosis, hyperglycemia, ↑ LDH and AST, hypocalcemia, ↑ BUN

## Signs and symptoms

- Epigastric pain radiating to the back
- Cullen's sign, Grey-Turner's sign (rare)
- Shock, fever
- DIC
- Pseudocyst and its infection
- ARDS



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- FA 2013: 339.3
- FA 2012: 366.3
- FA 2011: 335.3
- ME 3e: 359.2
- ME 4e: 359.2

# Acute Pancreatitis

## Diagnosis

- CT scan (most accurate test)

## Treatment

- Supportive management
  - IV fluids
  - Bowel rest
  - Pain medication
- ERCP (if needed)
- Antibiotics (if severe)
- Surgical debridement (if indicated)

## Prognosis

- Mortality rate of severe pancreatitis can be 30%



Fluoroscopic image of common bile duct stone seen at the time of ERCP.  
The stone is impacted in the distal common bile duct.  
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# Chronic Pancreatitis

- Chronic inflammation, atrophy, and fibrosis secondary to repeated episodes of pancreatitis

## Risk factors

- Long-standing alcohol abuse
- Bile stones

## Pathology

- Grossly firm, white, and fibrotic
- Histology: extensive fibrosis, parenchymal atrophy, and chronic inflammation

# Chronic Pancreatitis

## Signs and symptoms

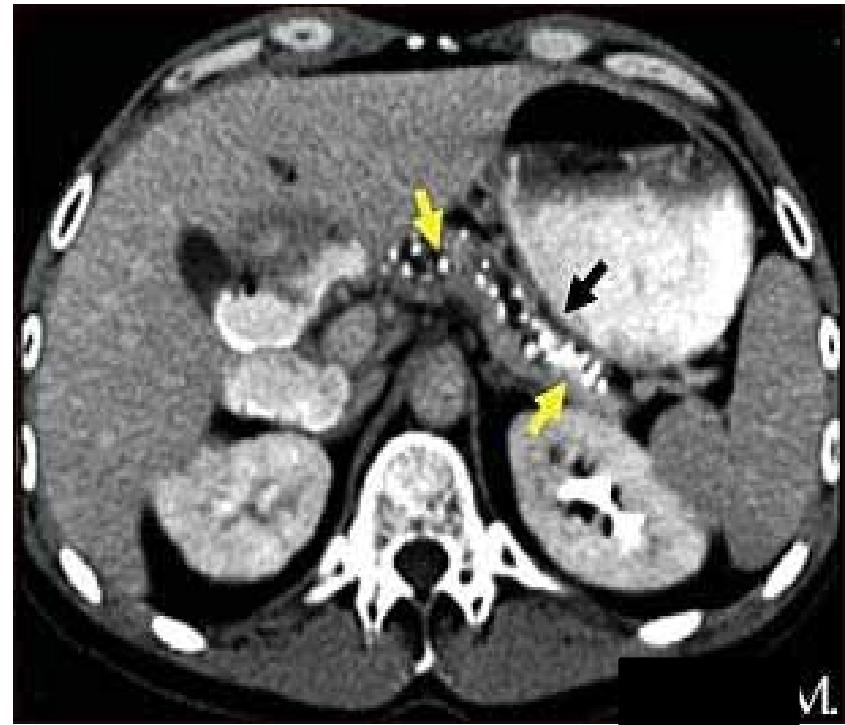
- Chronic abdominal pain
- Exocrine pancreatic insufficiency
- Malabsorption
- Calcifications, pseudocyst formation, and secondary diabetes mellitus

## Diagnosis

- History of repeated pancreatitis
- X-ray and CT scan: calcification of the pancreas
- Secretin test: most accurate test

## Treatment

- Replacement of deficient enzymes



CT scan of the upper abdomen showing multiple white-colored calcifications.  
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# Pancreatic Tumors

Insulinoma	Gastrinoma	Glucagonoma	Somatostatinoma	VIPoma
β-cells (pancreas)	G-cells (pancreas and duodenum)	α- cells (pancreas)	δ- cells (pancreas)	Neuroendocrine tumors (90% from the pancreas)
Most common 90% single and benign	20% associated with MEN 1	25% benign and confined to pancreas	50% malignant	Mostly single 60-80% malignant
Signs of hypoglycemia	Zollinger- Ellison syndrome	Migratory necrolytic dermatitis + diabetes	Diabetes, steatorrhea and gallstones	Diarrhea, hypokalemia, and achlorhydria
↑ c-peptide Insulin >8 mg/dL + hypoglycemia	↑ gastrin + ↑ acid	↑ glucagon + CT findings of localized tumor or metastasis	↑ somatostatin + triad + lesion on CT scan	CT scan
Surgery when resectable				
Glucose	PPIs	Octreotide Interferon α	Octreotide Interferon α	Octreotide

- FA 2013: 319
- FA 2012: 346
- FA 2011: 317
- ME 3e: 381.2
- ME 4e: 381.2

GI4\_2 1

# Pancreatic Carcinoma

## Epidemiology

- Fourth cause of cancer death in the United States
- Age >50
- Smoking is significant risk factor

## Histology

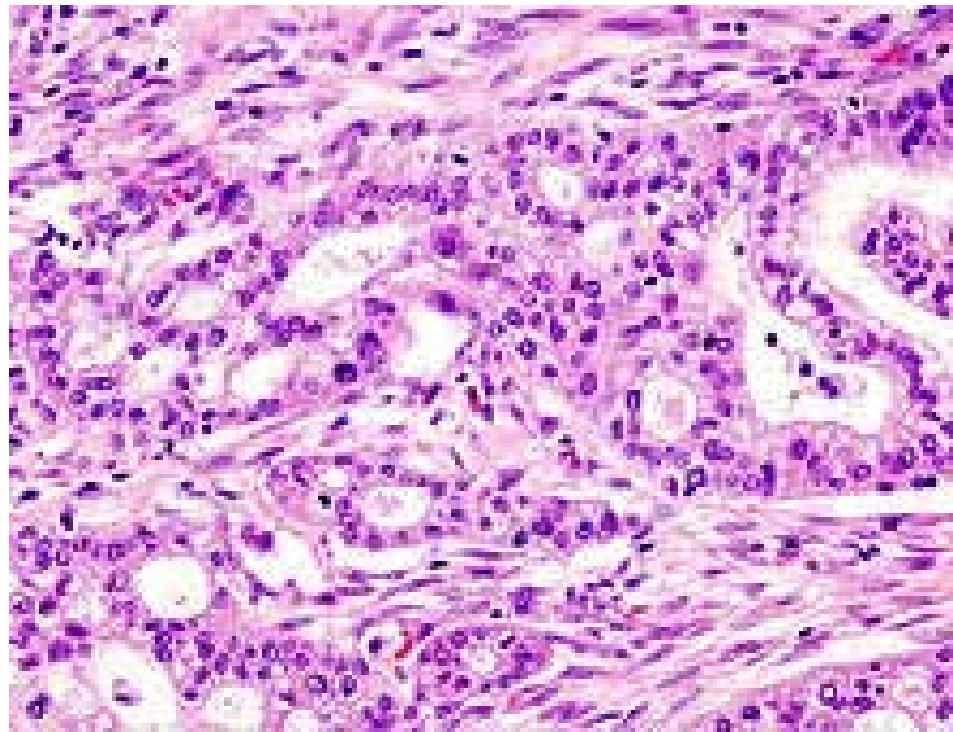
- Arises from duct epithelium

## Signs and symptoms

- Vague until late in the disease
- Abdominal pain
- Obstructive jaundice
- Migratory thrombophlebitis

## Lab studies

- ↑ alkaline phosphatase and bilirubin
- ↑ CA 19-9 and CEA (less specific)



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- FA 2013: 340.2
- FA 2012: 367.2
- FA 2011: 336.1
- ME 3e: 359.2
- ME 4e: 359.2

# Pancreatic Carcinoma

## Diagnosis

- CT scan
  - Dilation of bile and pancreatic ducts
- Endoscopic biopsy

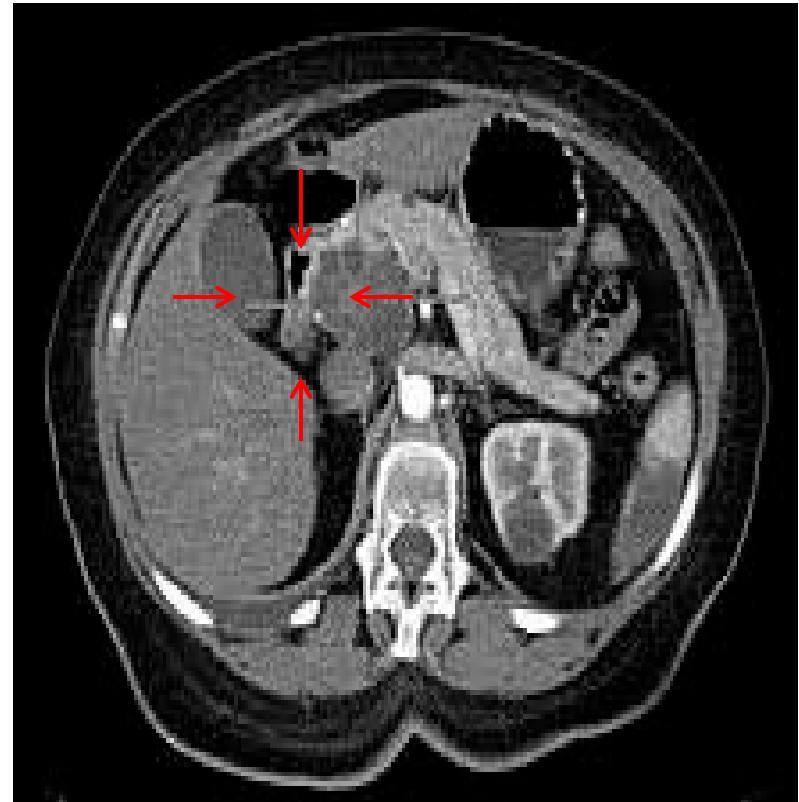
## Treatment

- Whipple procedure (when resectable)
- Prognosis is poor

7 months (palliative)

18 months (Whipple procedure)

Overall 5-year survival rate is 5%;  
15-20% if successfully resected



Axial CT image with IV contrast. Macrocytic adenocarcinoma of the pancreatic head.

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# Jaundice

- Bilirubin levels >2-3 mg/dL, presenting with yellow skin and sclera

## Classification

- Hepatocellular ( $\uparrow$  direct/  $\uparrow\uparrow$  indirect,  $\uparrow$  urine bilirubin, normal/ $\downarrow$  urobilinogen)
- Obstructive ( $\uparrow\uparrow$  direct/  $\uparrow$  indirect,  $\uparrow$  urine bilirubin,  $\downarrow$  urobilinogen)
- Hemolytic ( $\uparrow$  indirect, absent urine bilirubin,  $\uparrow$  urobilinogen)

Unconjugated (Indirect)	Conjugated (Direct)
Increased RBC turnover (hemolytic anemia)	Biliary tract obstruction
Physiologic (newborn babies)	Biliary tract disease (primary sclerosis cholangitis and primary biliary cirrhosis)
Hereditary (Gilbert and Crigler-Najjar syndromes)	Hereditary (Dubin-Johnson and Rotor syndromes)
	Liver disease (cirrhosis and hepatitis)

# Neonatal Jaundice

## Characteristics

- Increased RBC breakdown
- Immature liver
  - UDP-glucuronyltransferase unable to conjugate bilirubin
- High levels of bilirubin may lead to kernicterus



MRI of the head. Hyperintense basal ganglia lesions on T2-weighted images.  
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# Hereditary Hyperbilirubinemias

## Unconjugated

- Gilbert syndrome
  - Mildly defective UGT
  - Asymptomatic hyperbilirubinemia (symptoms triggered by fasting and stress)
- Crigler-Najjar syndrome
  - Absence or deficiency of UGT
  - Type 1 (absence of UGT) is fatal; type 2 (deficiency of UGT) causes jaundice

## Conjugated

- Dubin-Johnson
  - Defective excretion of bilirubin due to defective canalicular cationic transport protein
  - Causes black pigmentation of liver
  - No clinical consequences
- Rotor syndrome
  - Same as Dubin Johnson but milder and without black liver

# Cirrhosis

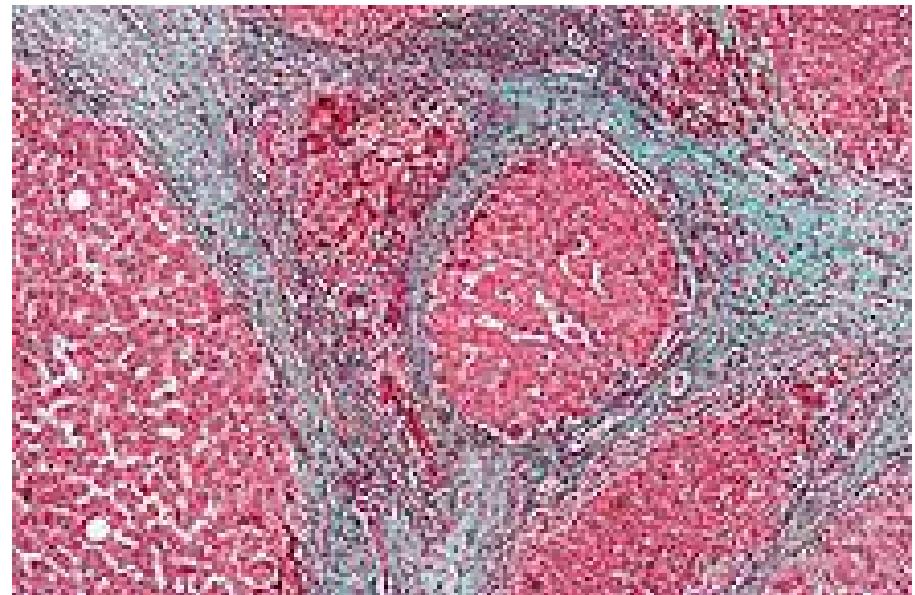
- End-stage liver disease
- Disruption of liver architecture by bands of fibrosis

## Etiology

- Chronic alcohol abuse
- Viral hepatitis
- Biliary tract disease
- Hemochromatosis
- Wilson disease
- $\alpha$ -1 antitrypsin deficiency
- Idiopathic

## Pathophysiology

- Fibrosis is mediated by hepatic Ito cells
- Micronodular (<3 mm), macronodular (>3 mm), or mixed



Micrograph showing cirrhosis. Trichrome stain.  
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# Cirrhosis

## Signs and symptoms

- **Portal hypertension**

- Ascites
- Stomach and esophageal varices
- Hemorrhoids
- Caput medusae
- Splenomegaly

- **Liver failure**

- Hepatic encephalopathy
- Spider angioma
- Palmar erythema
- Gynecomastia
- Hypoalbuminemia
- Decreased clotting

- **Hepatorenal syndrome**



Massive ascites and caput medusae.  
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# Alcoholic Liver Disease

## Steatosis

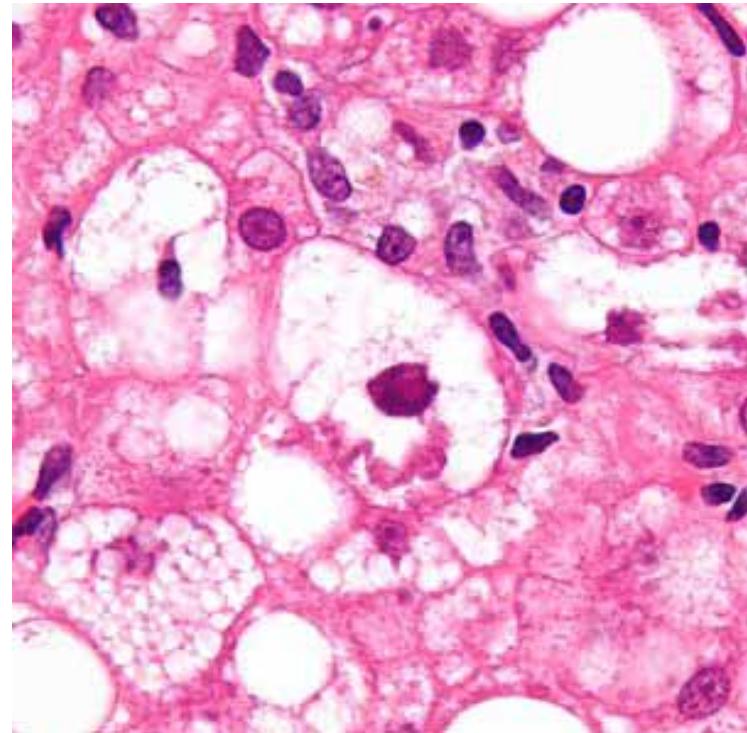
- Liver enlargement
- Centrilobular macrovesicular steatosis (reversible)
- May progress to central vein fibrosis (irreversible)

## Hepatitis

- Acute illness following heavy drinking/binging
- May be asymptomatic
- Upper quadrant pain, hepatomegaly, and jaundice
- Fulminant liver failure may occur
- Hepatocyte swelling and necrosis, Mallory bodies

## Cirrhosis

- Develops in 15% of alcoholics
- Requires liver transplantation
- Associated with micronodular cirrhosis



Micrograph showing a **Mallory body** with characteristic *twisted-rope* appearance (center of image, within a ballooning hepatocyte). H&E stain.

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# Wilson's Disease

- Autosomal recessive disorder
- Mutation of *ATP7B* gene (13q)
- Canalicular copper-transporting ATPase dysfunction

## Signs and symptoms

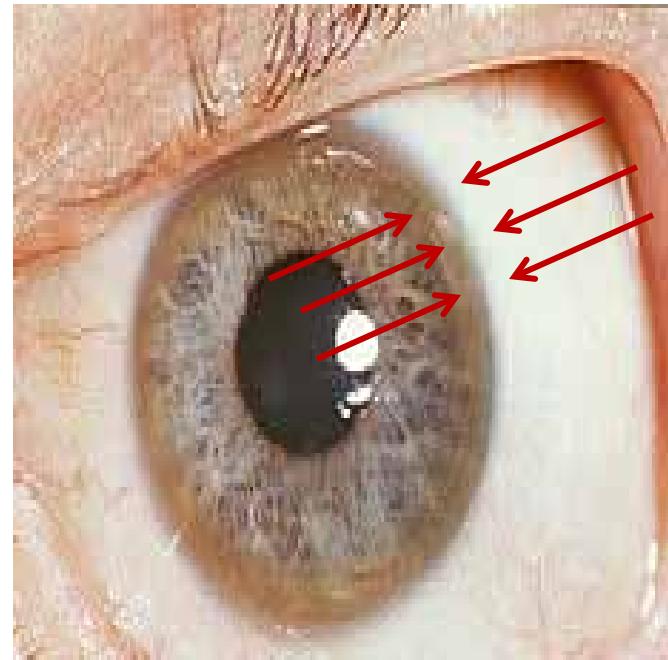
- Liver: fatty change, chronic hepatitis, and micronodular cirrhosis
- Eyes: Kayser-Fleischer rings
- Brain: neurologic, psychiatric, and movement disorders

## Diagnosis

- ↓ serum ceruloplasmin levels
- ↑ tissue copper levels (liver biopsy)
- ↑ urinary copper excretion

## Treatment

- Copper chelators: D-penicillamine or trientine, administered with zinc
- Liver transplantation (curative)



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# Hemochromatosis

- Autosomal recessive disorder of the HFE gene on q6p (C282Y most common mutation)
- Increased small-intestinal absorption of iron
- Secondary hemochromatosis: multiple transfusions for chronic anemia

## Epidemiology

- Men > women (2-3x)
- Northern European descent (increased risk)

## Pathophysiology

- Increased serum iron levels, leading to deposition and injury

# Hemochromatosis

## Signs and symptoms

- Micronodular cirrhosis
- 200x increased risk of hepatocellular carcinoma
- Secondary diabetes mellitus
- “Bronze” skin
- Cardiomegaly, congestive heart failure, and arrhythmia
- Osteopenia and osteoporosis
- Hair loss, hypogonadism

## Diagnosis

- ↑ serum iron and ferritin levels
- Biopsy: increased tissue iron levels (Prussian blue stain)

## Treatment

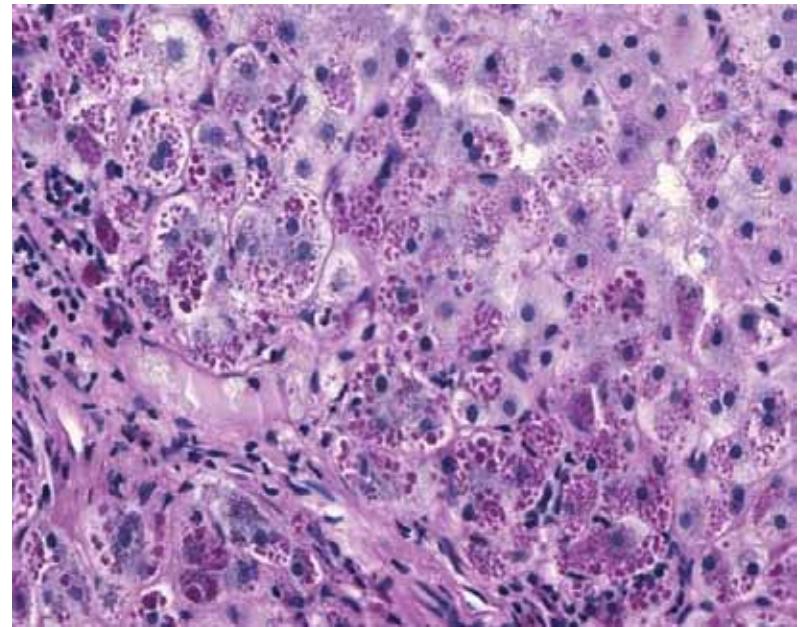
- Phlebotomy, chelation therapy: deferoxamine and deferasirox

# Alpha-1 Antitrypsin Deficiency

- Autosomal recessive disorder
- Alteration of alpha-1 antitrypsin molecule configuration

## Alpha-1 antitrypsin

- Protease inhibitor
- Inhibits neutrophil elastase, trypsin, chymotrypsin, and bacterial proteases
- Produced by Pi gene on chromosome 14 (> 75 gene variants described)
- Homozygous PiZZ deficiency variant:  
Severely reduced enzyme levels



PAS with diastase stain shows characteristic diastase-resistant pink globules

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# Alpha 1-Antitrypsin Deficiency

## Signs and symptoms

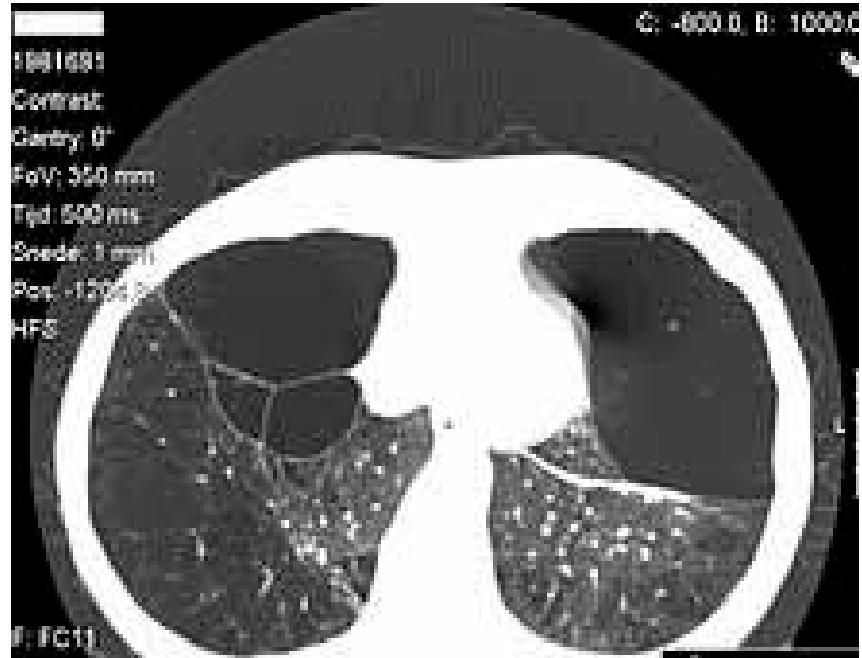
- Lungs
  - Panacinar emphysema
- Liver
  - Micronodular cirrhosis
  - ↑ risk for hepatocellular carcinoma

## Diagnosis

- Biopsy
- PAS positive, eosinophilic cytoplasmic globules within hepatocytes

## Treatment

- Smoking cessation to slow progression of emphysema
- Alpha-1 antitrypsin replacement
- Lung transplant



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# Reye's Syndrome

- Rare and potentially fatal metabolic liver disease
- Occurs in young children treated with aspirin following viral illness
- Etiology and mechanism are unknown
- Associated with varicella or influenza infection

## Pathophysiology (theory)

- Toxins induce mitochondrial dysfunction
- Inhibition of oxidative phosphorylation and fatty acid beta-oxidation

## Histology

- Liver: cytoplasmic fatty vacuolization within hepatocytes
- Brain: astrocyte edema and neuron loss
- Kidneys: edema and fatty degeneration of proximal tubules
- All tissues: pleomorphic and swollen mitochondria

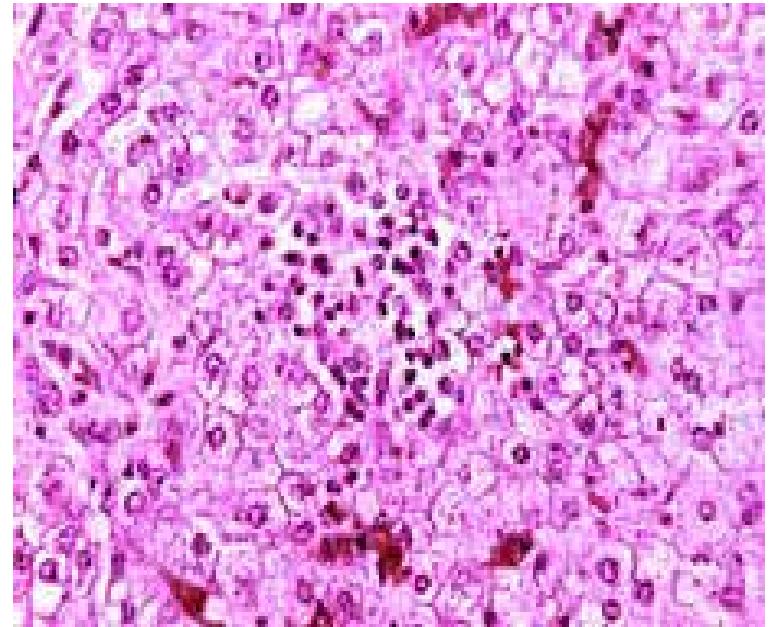
# Reye Syndrome

## Signs and symptoms

- Hyperammonemia
- Cerebral edema
- Increased intracranial pressure
- Encephalopathy
- Hepatic fatty change

## Treatment

- 75% completely recover
- 25% can develop coma, permanent neurologic deficits, or death
- Supportive care



Histopathology of autopsy liver from child who died of Reye syndrome. Hepatocytes are pale-staining due to intracellular fat droplets. Commons.wikimedia.org. Used with permission

# Non-Alcoholic Steatohepatitis (NASH)

- Disease of lipid accumulation in hepatocytes
- Most common liver disease in the United States
- Men = women
- Associated with obesity, hyperinsulinemia, insulin resistance, and type 2 diabetes mellitus

## Pathophysiology

- Imbalance of fatty acid metabolism leading to steatosis
- Mediated by insulin resistance
- Oxidative stress due to dysregulated cytokine production, lysosomal cathepsin release, mitochondrial dysfunction, and cellular apoptosis
- Chronic state of hepatic inflammation and fibrosis

# Non-Alcoholic Steatohepatitis (NASH)

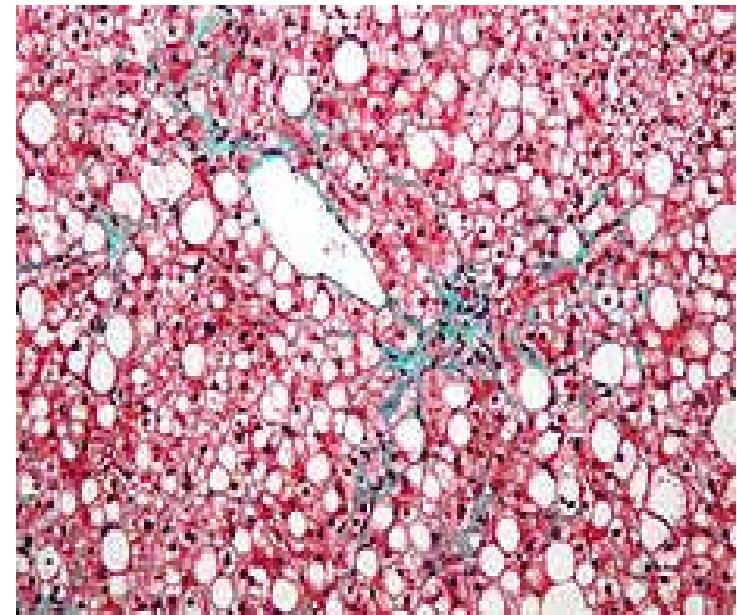
## Signs and symptoms

- Generally asymptomatic
- ↑ transaminase levels
- ↑ alkaline phosphatase
- Hepatomegally
- Disease course varies

Steatosis without specific injury

Cirrhosis

Increased risk for hepatocellular carcinoma



Marked macrovesicular steatosis. Trichrome stain.  
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## Diagnosis

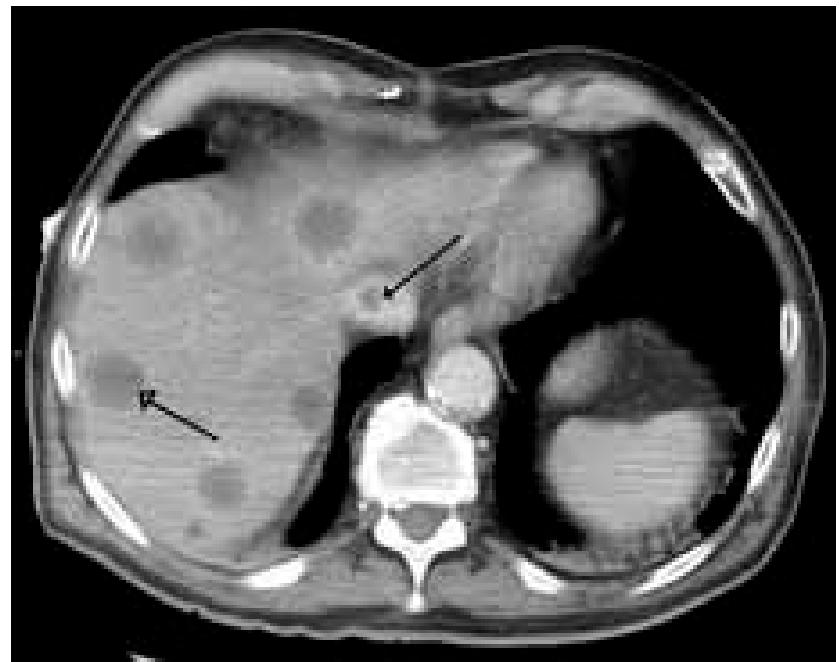
- Diagnosis of exclusion

# Budd-Chiari Syndrome

- Occlusion of hepatic veins by a thrombus
- Few cases are idiopathic
- Underlying predisposition to vascular thrombosis

## Risk factors

- Polycythemia vera
- Pregnancy
- Oral contraceptives
- Paroxysmal nocturnal hemoglobinuria
- Hepatocellular carcinoma



Budd-Chiari syndrome secondary to cancer, note clot in the inferior vena cava and the metastasis in the liver.  
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# Budd-Chiari Syndrome

## Signs and symptoms

- Hepatomegaly
- Ascites

## Histology

- Centrilobular congestion and necrosis

## Treatment

- General management of ascites
- Anticoagulation and antithrombolytic therapy
- Angioplasty
- 2-year mortality rate of 80-85% (medical therapy alone)
- Surgical decompression or shunting
- Liver transplantation

# Chronic Passive Congestion of the Liver

- Due to right-sided heart failure

## Histology

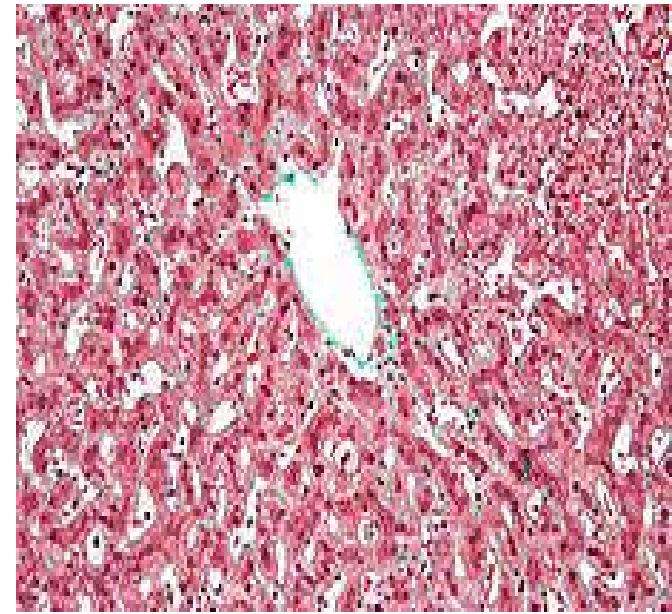
- Liver parenchyma: nutmeg pattern
- Dark areas: congested central vein regions
- Light areas: portal tracts
- Centrilobular congestion

## Signs and symptoms

- Cirrhosis
- Peripheral edema
- Ascites

## Treatment

- Management of underlying condition
- Management of cirrhosis



Perisinusoidal fibrosis and centrilobular (zone III) sinusoidal dilation.

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# Hemangioma

- Benign vascular tumor
- Subcapsular, red, spongy mass
- Most common primary liver tumor

## Signs and symptoms

- Asymptomatic (incidental finding)
- Clinically insignificant

## Treatment

- Surgical resection, enucleation, or endovascular embolization for symptomatic patients



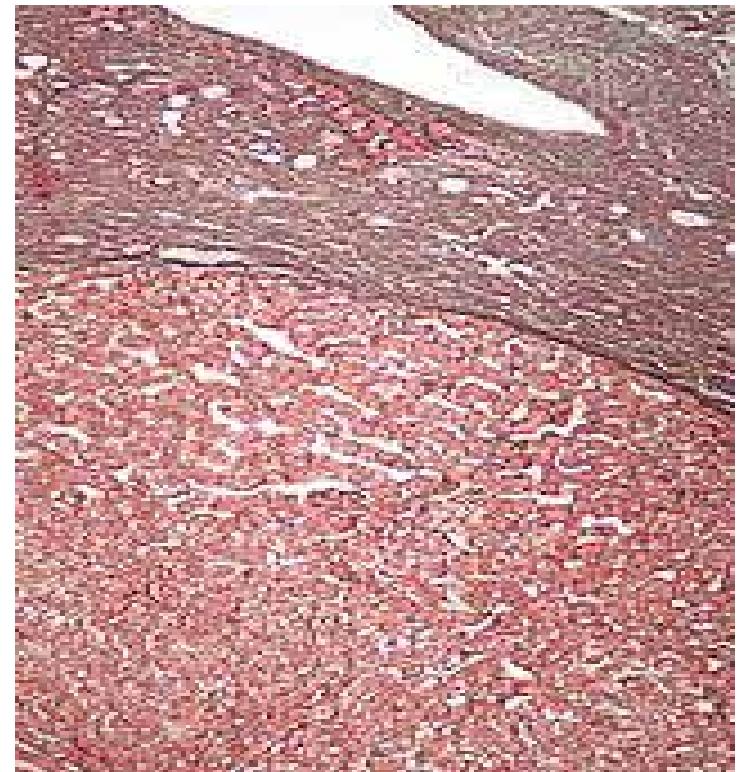
CT showing liver hemangioma.  
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# Hepatocellular Adenoma

- Benign, rare tumor
- Associated with oral contraceptive use

## Pathogenesis

- Exposure of hepatic vasculature to hormones, causing vascular ectasia
- Also associated with diabetes mellitus and glycogen storage diseases



Hepatic adenoma demonstrating a regular reticulin scaffold.  
Reticulin stain.

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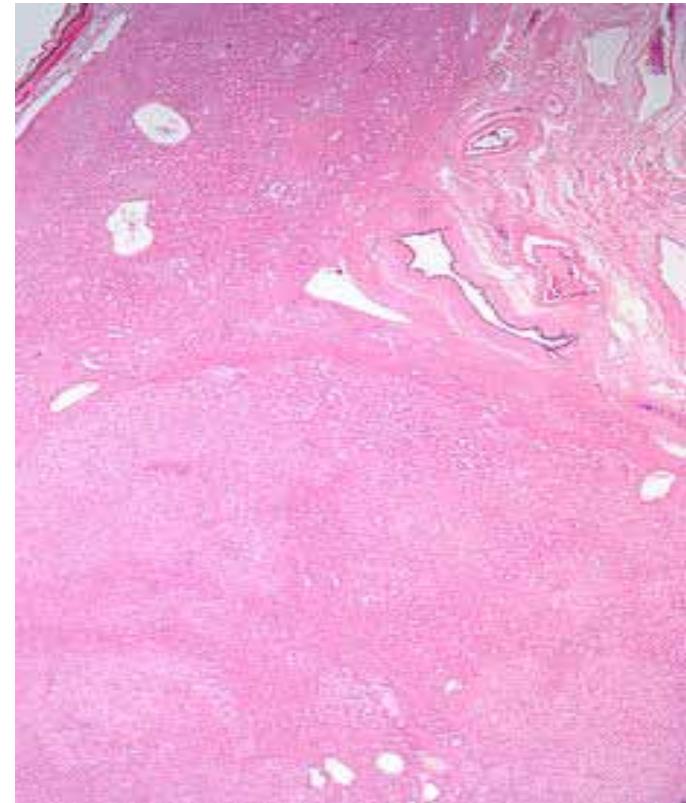
# Hepatocellular Adenoma

## Tumor characteristics

- Sheets of hepatocytes without bile ducts or portal areas
- Kupffer cells
- Grossly: tan, smooth, well-circumscribed
- Large blood vessels
- Necrosis within the lesion
- Risk of rupture and hemorrhage

## Treatment

- May regress after oral contraceptives are discontinued
- Pregnancy should be avoided
- Surgical resection if symptomatic
- Endovascular embolization



Hepatic adenoma.  
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# Hepatocellular Carcinoma

## Characteristics

- Most common primary malignant liver tumor in adults
- Incidence higher in Asia and Japan
- Cell of origin: hepatic stem cell

## Risk factors

- Cirrhosis
- Hepatitis B and C
- Alcohol
- Exposure to aflatoxin B1



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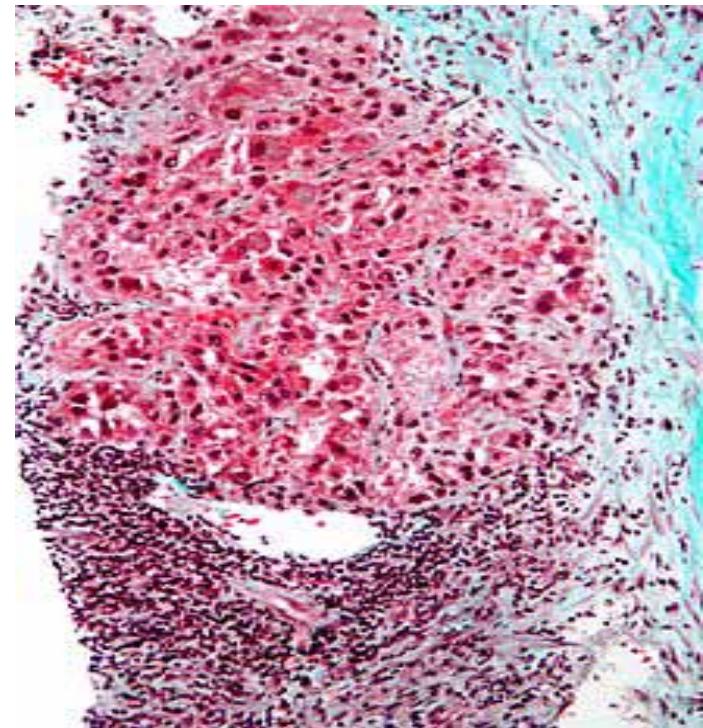
# Hepatocellular Carcinoma

## Signs and symptoms

- Single mass or diffuse growth
- Mass effect symptoms (biliary obstruction)
- Serum tumor marker: alpha fetoprotein
- Tendency for hematogenous spread

## Treatment

- Aggressive surgical resection
- Ablative therapy
- Liver transplantation
- Untreated: liver failure and death



Micrograph of hepatocellular carcinoma. Liver biopsy Trichrome stain.  
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# Metastatic Liver Tumors

## Generalities

- Common primary sites include
  - Colon
  - Breast
  - Lung
- Multiple well-circumscribed masses
- Poor prognosis

## Treatment

- Management according to clinical guidelines governing primary tumor



Cut surface of a liver showing multiple metastatic nodules originating from pancreatic cancer.

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# Viral Hepatitis

- Viral-mediated hepatic diseases
- Can be asymptomatic
- Generalized symptoms (malaise, weakness, nausea, and anorexia)
- Hepatobiliary specific symptoms (jaundice or dark urine)

## Labs

- ↑ ALT
- ↑ AST

## Diagnosis

- Serologic confirmation of a specific virus
- Non-hepatitis viruses which can infect the liver:  
Epstein-Barr virus, cytomegalovirus, herpes, and yellow fever

# Viral Hepatitis

## Acute hepatitis

- Hepatitis for <6 months
- Histology

Lobular disarray

Hepatocyte swelling (balloon cells)

Apoptotic hepatocytes (Councilman bodies)

Lymphocyte infiltration within portal tracts and lobules

Hepatocyte regeneration

Cholestasis

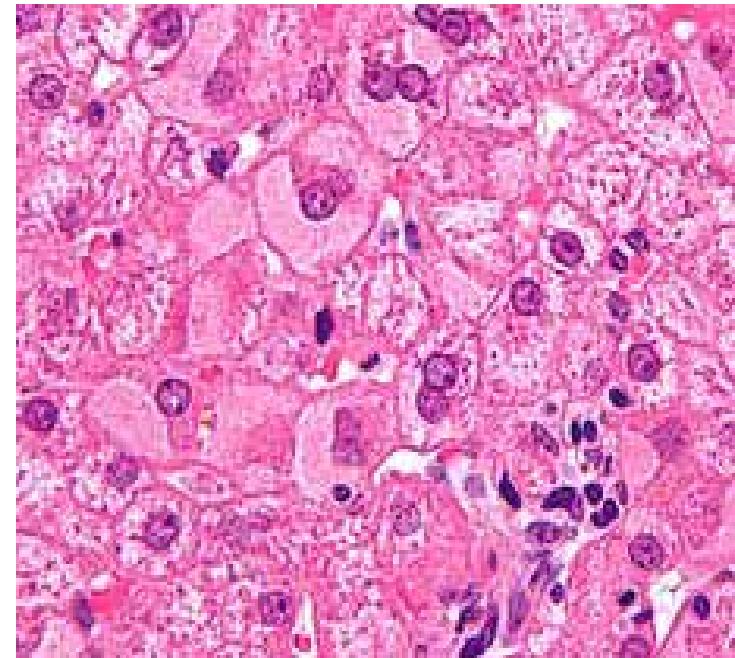
## Chronic viral hepatitis

- Hepatitis for >6 months
- Histology

Inflammation confined to portal tracts

Reactivation: inflammation spills into parenchyma

Hepatitis B has characteristic “ground glass” appearance



Micrograph showing ground glass hepatocytes and accumulations of viral antigen in the endoplasmic reticulum.  
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# Hepatitis A

## General characteristics

- Hepatitis A virus is a picornavirus
- Transmission: fecal-oral
- Manifests as acute mild hepatitis
- Diagnosis: anti-HAV IgM
- Treatment: supportive
- No chronicity

# Hepatitis B

## General characteristics

- Caused by hepadnavirus (enveloped DNA)
- Transmission: sexual, parenteral
- Clinical manifestations:
  - Acute infection
  - Chronic hepatitis, with progression to cirrhosis and HCC
- Diagnosis: symptoms and serum levels of HBsAg, HBeAg, anti-HBc IgM, HBV DNA
- Treatment
  - No effective therapy for acute hep B
  - Lamivudine, telbivudine, adefovir, entecavir, tenofovir, interferon  $\alpha$  for chronic hep B
- Vaccination: recombinant HBsAg
- Population at risk: IV drug users, men who have sex with men, close contact with carriers of hep B, health workers, exposure to blood and blood products

# Hepatitis B Markers

Abbreviation	Name and description
HBV	Hepatitis B virus, a hepadnavirus (enveloped, partially double-stranded DNA virus): Dane particle = infectious HBV
HBsAg	Antigen found on surface of HBV, also found on spheres and filaments in patient's blood: positive during acute disease; continued presence indicates carrier state
HBsAb	Antibody to HBsAg; provides immunity to hepatitis B (vaccination)
HBcAg	Antigen associated with core of HBV
HBcAb	Antibody to HBcAg, positive during window phase; IgM HBcAb is an indicator of recent disease, IgG is an indicator of chronic disease
HBeAg	A second, different antigenic determinant on the HBV core; important indicator of transmissibility
HBeAb	Antibody to e antigen, indicates low transmissibility
Delta agent	Small RNA virus with HBsAg envelope, defective virus that replicates only in HBV-infected cells and can cause fulminant hepatitis

- FA 2013: 163
- FA 2012: 191
- FA 2011: 172
- ME 3e: 363
- ME 4e: 363

# Hepatitis B Serology

	HBsAg HBeAg HBV-DNA	HBcAb IgM	HBcAb IgG	HBsAb IgG
Acute infection	+	+	-	-
Window period	-	+	-	-
Prior infection	-	-	+	+
Immunization	-	-	-	+
Chronic infection	+	+	+	-

- FA 2013: 163
- FA 2012: 191
- FA 2011: 172
- ME 3e: 363
- ME 4e: 363

# Hepatitis C

## General characteristics

- Caused by a flavivirus
- Transmission: sexual, parenteral
- Insidious and subclinical onset
- 80% progress to chronic disease
- Serologic findings
  - PCR-RNA viral load level
  - IgM antibodies
- Treatment:
  - Acute hep C: interferon
  - Chronic hep C: interferon + ribavirin + boceprevir/telaprevir
  - Cirrhosis: liver transplantation

# Hepatitis D

## General characteristics

- Caused by defective enveloped circular RNA virus
- Replicates only in HBV infected cells
- Transmission: sexual, parenteral
- 1-5% present with fulminant liver failure
- 80-90% progress to chronic infection
- Increased risk for hepatocellular carcinoma
- Diagnosis: IgM antibody
- Treatment: supportive
- Hep B vaccination is effective against hep D

# Hepatitis E

## General characteristics

- Caused by a hepevirus
- Transmission: fecal-oral
- Fatality in pregnancy up to 20%
- No chronicity
- Diagnosis: IgM antibody
- Treatment: supportive



Pregnant woman.  
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- FA 2013: 163
- FA 2012: 191
- FA 2011: 172
- ME 3e: 363
- ME 4e: 363

# Hepatitis Viruses

Virus Name	Hepatitis A (HAV)	Hepatitis B (HBV)	Hepatitis C (HCV)	Hepatitis D (HDV)	Hepatitis E (HEV)
Virus	Picornavirus naked capsid RNA	Hepadnavirus enveloped DNA	Flavivirus enveloped RNA	Defective enveloped circular RNA	Hepevirus naked capsid RNA
Transmission	Fecal-oral	Parenteral, sexual	Parenteral, sexual	Parenteral, sexual	Fecal-oral
Severity	Mild	Occasionally severe	Usually subclinical	Co-infection with HBV occasionally severe; superinfection with HBV often severe	Normal patients: mild; Pregnant patients: severe
Chronicity or carrier state	No	Yes	Yes (high)	Yes	No
Clinical diseases	Acute hepatitis	Acute hepatitis Chronic hepatitis Cirrhosis HCC	Acute hepatitis Chronic hepatitis Cirrhosis HCC	Acute hepatitis Chronic hepatitis Cirrhosis HCC	Acute hepatitis
Laboratory diagnosis	Symptoms and anti-HAV IgM	Symptoms and serum levels of HBsAg, HBeAg, and anti-HBc IgM	Symptoms and anti-HCV ELISA	Anti-HDV ELISA	

- FA 2013: 163
- FA 2012: 191
- FA 2011: 172
- ME 3e: 363
- ME 4e: 363

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