Pathology of GI tract

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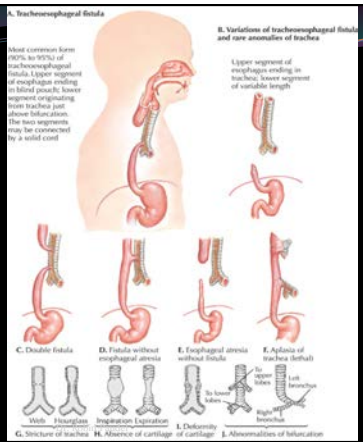
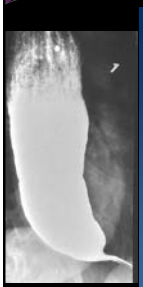
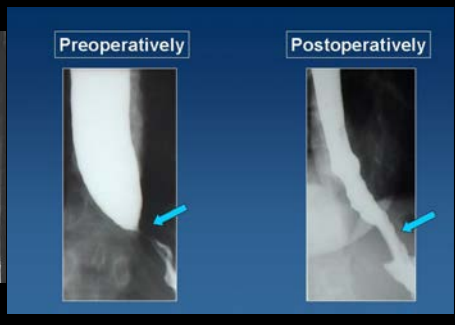
Esophagus

- 1. Congenital and mechanical disorders
  - a. Tracheoesophageal fistula
    - i. Definition: congenital connection between the esophagus and trachea
    - ii. Often associated with esophageal atresia
    - iii. Often discovered soon after birth because of aspiration
  - b. Esophageal webs
    - i. Definition: web like protrusions of the esophageal mucosa into the lumen
    - ii. Presentation: dysphagia
    - iii. ***Plummer-Vinson syndrome*** .
      - ***Middle aged women***
      - **Esophageal webs**
      - **Iron deficiency anemia**
      - **Increased risk of carcinoma**
    - iv. Schatzki ring: weblike narrowing at gastroesophageal junction



- c. Achalasia
  - i. Definition: failure of the lower esophageal sphincter (LES)to relax with swallowing
  - ii. Etiology
    - Unknown in most cases
    - South America → Chagas disease
  - iii. Presentation: progressive dysphagia
  - iv. Gross: esophageal dilation proximal to the LES
  - v. Barium swallow: "bird-beak" sign
  - vi. Micro: loss of ganglion cells in the myenteric plexus
  - vii. Treatment: LES balloon dilation or myotomy
  - viii. Increased risk of esophageal carcinoma





Hematemesis and esophageal bleeding

- a. Mallory-Weiss syndrome
  - i. Definition: laceration at the gastroesophageal junction produced by severe prolonged vomiting
  - ii. Most common cause: alcoholism
  - iii. Presentation: hematemesis
  - iv. Gross: linear lacerations at the gastroesophageal junction
  - v. Complications: Boerhaave syndrome: esophageal rupture (rare)
- Mallory-Weiss tears versus esophageal varices

- b. Esophageal varices
  - i. Definition: dilated submucosal veins in the lower third of the esophagus, usually secondary to portal hypertension
  - ii. Most common cause: cirrhosis
  - iii. Presentation
    - Asymptomatic
    - Massive hematemesis when ruptured
  - iv. Complication: potentially fatal hemorrhage
  - v. Treatment: band ligation, sclerotherapy, or balloon tamponade

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Esophagitis

- a. Gastroesophageal reflux disease (reflux esophagitis)
  - i. Definition: esophageal irritation and inflammation due to reflux of gastric secretions into the esophagus
  - ii. Presentation: heartburn and regurgitation
  - iii. Complications
    - . Bleeding
    - . Stricture
    - . Bronchospasm and asthma
    - . Barrett esophagus
- b. Barrett esophagus
  - i. Definition: metaplasia of the squamous esophageal mucosa to a more protective columnar type because of chronic exposure to gastric secretions
  - ii. Incidence is increasing
  - iii. Cause: gastroesophageal reflux disease (GERD)
  - iv. Gross: irregular gastroesophageal (GE) junction with tongues of red granular mucosa extending up into the esophagus
  - v. Increased risk of dysplasia and esophageal adenocarcinoma

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Esophageal carcinoma

- a. Squamous cell carcinoma (SCC) of the esophagus
  - i. Epidemiology
    - . SCC is the most common type of esophageal cancer in the world, but not in the United States.
    - . Males> females; age usually >50 . African Americans> Caucasians
  - ii. Risk factors
    - . Heavy smoking and alcohol use
    - . Achalasia
    - . Plummer-Vinson syndrome
    - . Tylosis
    - . Prior lye ingestion

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- iii. Presentation
  - . Often asymptomatic until late in the course
  - . Progressive dysphagia
  - . Weight loss and anorexia
  - . Bleeding
  - . Hoarseness or cough (advanced cancers)
- iv. Diagnosis: endoscopy and biopsy
- v. Treatment: surgery
- vi. Prognosis: poor
- b. Adenocarcinoma of the esophagus
  - i. More common than SCC in the United States
  - ii. Caucasians> African Americans
  - iii. Arises in the distal esophagus
  - iv. Associated with *Barrett esophagus and dysplasia*
  - v. Prognosis: poor

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Stomach

- 1. Congenital disorders
  - a. Pyloric stenosis
    - i. Definition: congenital stenosis of the pylorus due to marked muscular hypertrophy of the pyloric sphincter, resulting in gastric outlet obstruction
    - ii. Males> females
    - iii. Associated with Turner and Edwards syndromes
    - iv. Presentation
      - . Onset of regurgitation and vomiting in the second week of life
      - . Waves of peristalsis are visible on the abdomen
      - . Palpable oval abdominal mass
    - v. Treatment: surgery

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- b. Congenital diaphragmatic hernia
  - i. Definition: congenital defect in the diaphragm, resulting in herniation of the abdominal organs into the thoracic cavity
  - ii. The stomach is the most commonly herniated organ
  - iii. Often associated with intestinal malrotation
  - iv. Complications: respiratory compromise

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- 2. Hypertrophic gastropathy
  - a. Menetrier disease
    - i. Middle-aged men
    - ii. Gross: enlarged rugal folds in the body and fundus
    - iii. Micro: massive hyperplasia with replacement of the parietal and chief cells
    - iv. Decreased acid production
    - v. Protein losing enteropathy
    - vi. Increased risk of gastric cancer
  - b. Zollinger-Ellison syndrome
    - i. Pancreatic gastrinoma producing gastrin
    - ii. Gross: enlarged rugal folds
    - iii. Increased acid secretion
    - iv. Presentation: multiple intractable peptic ulcers

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Acute inflammation and stress ulcers

- a. Acute hemorrhagic gastritis
  - i. Definition: acute inflammation, erosion, and hemorrhage of the gastric mucosa due to a breakdown of the mucosal barrier and acid-induced injury
  - ii. Etiology
    - . (Chronic) aspirin or NSAID use
    - . Alcohol use
    - . Smoking
    - . Post surgery
    - . Burns
    - . Ischemia
    - . Stress
    - . Uremia
    - . Chemotherapy
  - iii. Presentation
    - . Epigastric abdominal pain
    - . Gastric hemorrhage, hematemesis, and melena

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- b. Gastric stress ulcers
  - i. Gross: multiple, small, round, superficial ulcers of the stomach and duodenum
  - ii. Etiology
    - . NSAID use
    - . Severe stress
    - . Sepsis
    - . Shock
    - . Severe burns or trauma (Curling ulcers)
    - . Elevated intracranial pressure (Cushing ulcers)
  - iii. High incidence in intensive care unit (ICU) patients
  - iv. Complication: bleeding

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Chronic gastritis

- a. Definition: chronic inflammation of the gastric mucosa eventually leading to atrophy (chronic atrophic gastritis)
- b. Fundic type (type A)
  - . Autoimmune atrophic gastritis
  - . Involves the body and the fundus
  - . *Autoantibodies to parietal cells and/or intrinsic factor*
  - . Loss of parietal cells
  - . Decreased acid secretion
  - . Increased serum gastrin (G-cell hyperplasia)
  - . *Pernicious anemia: megaloblastic anemia due to lack of intrinsic factor and* B12 malabsorption

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- i. Gross: loss of rugal folds in the body and fundus
- ii. Micro:
  - . Mucosal atrophy with loss of glands and parietal cells
  - . Chronic lymphoplasmacytic inflammation
  - . Intestinal metaplasia
- iii. Increased risk of gastric carcinoma

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- Antral type (type B)
  - i. *Helicobacter pylori gastritis*
  - ii. Most common form of chronic gastritis in the United States
  - iii. *Helicobacter pylori*
    - . Curved, gram-negative rods
    - . Urease producing
    - . Risk of infection increases with age
    - . Associated with chronic gastritis (type B)
    - . Associated with duodenal and gastric peptic ulcers
    - . Associated with gastric carcinoma
  - iv. Micro
    - . *H. pylori organisms are visible in the mucous layer of the surface epithelium . Foci of acute inflammation*
    - . Chronic inflammation with lymphoid follicles . Intestinal metaplasia
  - v. Increased risk of gastric carcinoma

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- Chronic peptic ulcer
- Malignancies

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Small and Large Intestine

1. Mechanical obstruction

- a. Volvulus
  - i. Definition: twisting *of a segment of bowel on its vascular mesentery, resulting* in intestinal obstruction and infarction
  - ii. *Often associated with congenital abnormalities such as intestinal malrotation*
  - iii. Locations: sigmoid colon, cecum, and small bowel
  - iv. Complication: infarction and peritonitis

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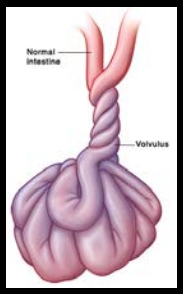

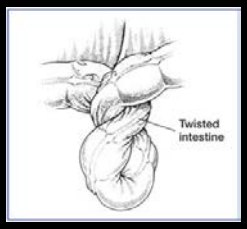

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- b. Intussusception
  - i. Definition: telescoping *of a proximal segment of the bowel into the distal segment*
  - ii. Most common in infants and children
  - iii. In adults it may be associated with a mass *or tumor*
  - iv. Presentation: intestinal obstruction, abdominal pain, and "currant -jelly" stools
  - v. Complication: infarction *of the intussuscepted segment*
- c. Incarcerated hernia
  - i. Definition: segment *of bowel becomes imprisoned within a hernia*
  - ii. Complications: intestinal obstruction and infarction

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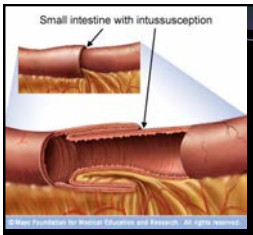

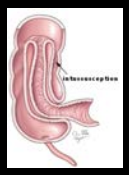

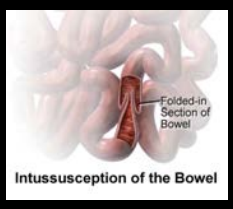

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- d. Hirschsprung disease
  - i. Synonym: congenital aganglionic megacolon
  - ii. Definition: *congenital absence of ganglion cells in the rectum and sigmoid* colon resulting in intestinal obstruction
  - iii. Presentation
    - . Males> females
    - . Delayed passage *of meconium*
    - . Constipation, abdominal distention, and vomiting
    - . Associated with Down syndrome
  - iv. Gross
    - . Affected segment is narrowed
    - . Proximal dilatation (megacolon)
  - v. Micro: absence of ganglion cells in Auerbach and Meissner plexuses
  - vi. Diagnosis: rectal biopsy
  - vii. Treatment: resection of affected segment

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Malabsorption syndromes

- a. Celiac sprue
  - i. Synonyms: gluten-sensitive enteropathy, nontropical sprue
  - ii. Definition: *hypersensitivity to gluten (and gliadin), resulting in loss of small* bowel villi and malabsorption
  - iii. Genetic predisposition: HLA-B8,DR3, and DQ
  - iv. Micro
    - . Loss of villi
    - . Increased intraepithelial lymphocytes
    - . Increased plasma cells in the lamina propria
  - v. Presentation
    - . Usually presents in childhood with malabsorption . Abdominal distention, bloating, and flatulence
    - . Diarrhea, steatorrhea, and weight loss
  - vi. Associated with dermatitis herpetiformis
  - vii. Treatment: dietary restriction of gluten

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- b. Tropical sprue
  - i. Definition: mal absorptive disease of unknown etiology (infection and/or nutritional deficiency) affecting travelers to tropical regions, such as the Caribbean and South America
  - ii. Micro: similar to celiac sprue
  - iii. Treatment: antibiotics, vitamin B12, and folate

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- c. Whipple disease
  - i. Definition: rare infectious disease involving many organs, including small intestines, joints, lung, heart, liver, spleen, and CNS
  - ii. Caucasian males; age 30-50 years
  - iii. Organism: *Trophermyma whippleii*
  - iv. Presentation: malabsorption, weight loss, and diarrhea
  - v. Micro: small bowel lamina propria is filled with macrophages stuffed with PAS-positive, rod-shaped bacilli
  - vi. Treatment: antibiotics

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Inflammatory bowel disease

- a. Three major categories
  - i. Crohn disease (CD) (synonym: regional enteritis)
  - ii. Ulcerative colitis (UC)
  - iii. Colitis of indeterminate type
- b. Epidemiology
  - i. Females> males
  - ii. Caucasians> non-Caucasians
  - iii. Age distribution
    - . CD: bimodal with peaks at ages 10-30 and 50-70 years
    - . UC: peaks at age 20-30 years

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  - iv. Increasing incidence
  - v. Ulcerative colitis is more common than Crohn disease
- c. Presentation
  - i. Episodes of bloody diarrhea or stools with mucus
  - ii. Crampy lower abdominal pain
  - iii. Fever
  - iv. Perianal fistulas (CD)
  - v. Extraintestinal manifestations (UC > CD)
  - vi. CD of the small bowel may present with malabsorption
  - vii. CD may mimic appendicitis
- d. Diagnosis
  - i. Diagnosis of exclusion
  - ii. Endoscopy and biopsy

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	Crohn Disease	Ulcerative Colitis
Most common site	Terminal ileum	Rectum
Distribution	Mouth to anus	Rectum → colon "back-wash" ileitis
Spread	Discontinuous/"skip"	Continuous
Gross features	• Focal aphthous ulcers with intervening normal mucosa • Linear fissures • Cobblestone • 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 studies • Obstruction • Abscesses • Fistulas • Sinus tracts	Toxic megacolon
Genetic association		HLA-B27
Extraintestinal manifestations	Uncommon	Common (e.g., arthritis, spondylitis, primary sclerosing cholangitis, erythema nodosum, pyoderma gangrenosum)
Cancer risk	Slight 1–3%	5–25%

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Ischemic bowel disease

- i. Definition: decreased blood flow and ischemia of the bowel secondary to atherosclerosis with thrombosis, thromboembolism, or reduced cardiac output from shock
- ii. Most common in older individuals
- iii. Presentation: abdominal pain and bloody diarrhea
- iv. Distribution: tends to affect watershed areas (e.g., splenic flexure)
- v. Gross: hemorrhagic infarction
- vi. Treatment: surgical resection
- vii. Prognosis: poor; over 50% mortality

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Hemorrhoids

- i. Definition: tortuous dilated submucosal veins caused by increased venous pressure
- ii. Risk factors
  - . Constipation and prolonged straining during bowel movements
  - . Pregnancy
  - . Cirrhosis
- iii. Complications
  - . Thrombosis (painful)
  - . Infection

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Angiodysplasia

- i. Definition: arteriovenous malformations of the intestines
- ii. Common in individuals over age 55
- iii. Occur in the cecum and right colon
- iv. Presentation: multiple episodes of rectal bleeding
- v. Associated with Osler-Weber-Rendu syndrome and the CREST(cyanosis,raynaud phenomenon,eophageal dysmobility,sclerodactaly,telangiectasis)syndrome
- vi. Treatment: surgical resection

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Melanosis coli

- i. Common with laxative abuse
- ii. Gross: black pigmentation of the colon
- iii. Can mimic colitis or malignancy

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Pseudomembranous colitis (antibiotic-associated colitis)

- i. Definition: acute colitis characterized by the formation of inflammatory pseudomembranes in the intestines
- ii. Organism: *Clostridium difficile*
- iii. Often brought on by a course of broad-spectrum antibiotics (especially clindamycin and ampicillin)
- iv. Presentation: diarrhea, fever, and abdominal cramps
- v. Gross: yellow-tan mucosal membranes
- vi. Micro:
  - . Superficial colonic necrosis with an overlying pseudomembrane
  - . Pseudomembranes are mushroom-shaped inflammatory exudates composed of neutrophils, mucin, fibrin, and necrotic cellular debris
- vii. Diagnosis: detection of C. *difficile toxin in the stool*
- viii. Treatment: vancomycin or *metronidazole*

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Diverticula

- a. Meckel diverticulum
  - i. Definition: congenital small bowel diverticulum
  - ii. Remnant of the vitelline (omphalomesenteric) duct
  - iii. "Rule of 2s"
    - 2% of the normal population
    - 2 feet from the ileocecal valve
    - 2 cm in length
    - 2 years old or younger at the time of diagnosis
    - 2% of carcinoid tumors occur in a Meckel diverticulum
  - iv. Presentation
    - . Most are asymptomatic
    - . May contain rests of ectopic gastric mucosa and present with intestinal bleeding

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Colonic diverticulosis

- i. Definition: acquired outpouching of the bowel wall, characterized by herniation of the mucosa and submucosa through the muscularis propria
- ii. Epidemiology
  - . Extremely common in the United States
  - . Incidence increases with age
- iii. Risk factor: *low-fiber diet leads to increased intraluminal pressure*
- iv. Location: most common in the sigmoid colon
- v. Presentation
  - . Often asymptomatic
  - . Constipation alternating with diarrhea
  - . Left lower quadrant abdominal cramping and discomfort
  - . Occult bleeding and an iron deficiency anemia
  - . Lower GI hemorrhage
- vi. Complications
  - . Diverticulitis
  - . Fistulas
  - . Perforation and peritonitis

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. Neoplasia

- a. Adenomatous colonic polyps
  - i. Definition: benign neoplasm of the colonic mucosa that has the potential to progress to colonic adenocarcinoma
  - ii. Presentation
    - . Commonly asymptomatic
    - . Occult bleeding and iron deficiency anemia
- iii. Prognostic features
  - . Tubular versus villous histology
  - . Size of polyps
  - . Degree of dysplasia

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- iv. Diagnosis
  - . Hemoccult positive stools
  - . Endoscopy

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Familial adenomatous polyposis (FAP)

- i. Synonym: adenomatous polyposis coli (APC)
- ii. Genetics
  - . Autosomal dominant
  - . *APC gene on chromosome 5q*
- iii. Develop thousands of colonic *adenomatous polyps*
- iv. Diagnosis: discovery of more than 100 adenomatous polyps on endoscopy
- v. Complication: by age 40, virtually 100% will develop an invasive adenocarcinoma

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Gardner syndrome

- i. Autosomal dominant
- ii. Variant of FAP characterized by
  - . Numerous colonic *adenomatous polyps*
  - . Multiple osteomas
  - . Fibromatosis
  - . Epidermal inclusion cysts

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Turcot syndrome

- i. Rare variant of FAP characterized by
  - . Numerous colonic *adenomatous polyps*
  - . CNS tumors (gliomas)

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Hereditary nonpolyposis colorectal cancer (HNPCC)

- i. Synonym: Lynch syndrome
- ii. Genetics
  - . Autosomal dominant
  - . Mutation of DNA nucleotide mismatch repair gene
- iii. Colon cancer
- iv. Increased risk of endometrial and ovarian carcinoma

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Peutz-Jeghers syndrome

- i. Autosomal dominant
- ii. Multiple *hamartomatous polyps (primarily in the small intestine)*
- iii. Melanin pigmentation of the oral mucosa
- iv. Increased risk of cancer of the lung, pancreas, breast, and uterus

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Colonic adenocarcinoma

- i. Third most common tumor in terms of incidence and mortality in the United States
- ii. Risk factors
  - . Low-fiber diet
  - . Diet low in fruits and vegetable
  - . High red meat and animal fat consumption
  - . Adenomatous polyps
  - . Hereditary polyposis syndromes
  - . Lynch syndrome
  - . Ulcerative colitis
- iii. Genetics
  - . Multiple mutations are involved
  - APC gene
  - . K-ras oncogene
  - .DCC gene
  - . p53 gene

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- iv . Diagnosis
  - . Hemoccult positive stool
  - . Endoscopy with biopsy
- v. Pattern of spread
  - . Lymphatic spread to mesenteric lymph nodes
  - . Distant spread to liver, lungs, and bone
- vi. Staging: modified Dukes' (Astler-Coller) staging system
- vii. Treatment
  - . Surgical resection
  - . Chemotherapy for metastatic disease
  - . Monitor CEA levels

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Carcinoid tumors

- i. Neuroendocrine tumor often producing *serotonin*
- ii. Locations: appendix *(most common) and terminal ileum*
- iii. Metastasis to the liver may result in carcinoid heart disease
- iv. Carcinoid syndrome
  - . Diarrhea
  - . Cutaneous flushing
  - . Bronchospasm and wheezing
  - . Fibrosis
- v. Diagnosis: urinary 5-HIAA (5-hydroxyindoleacetic acid)

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