

SMALL INTESTINE

Diagnostically the most hidden part of the GI tract.
Too far for endoscopy; much overlap by barium radiography.
Signs and symptoms are generally vague for localization.

- I. DEVELOPMENTAL ABNORMALITIES:** All more frequent than at other GI sites.
- A. Atresia:** (no lumen) and **stenosis** (narrow lumen): intestinal more common than in stomach, less than in esophagus. Anorectal atresias also common.
 - B. Duplication:** an extra segment of bowel; usually in the mesentery; may communicate with bowel lumen.
 - C. Diverticulum:** an outpouching of mucosa with or without other layers; ~~Congenital~~ diverticula usually have all layers of bowel wall ("true" diverticulum), generally in small bowel; ~~Acquired~~ diverticula typically have no muscle or a partial muscular coat ("false" diverticulum), usually in left colon.
 - D. Enterogenous Cyst:** a sac lined by GI type mucosa. Duplication, diverticula and enterogenous cysts may be related in pathogenesis, especially to the closing of the enteric canal; they may be associated with vertebral defects.
 - E. Other abdominal cysts:** lymphatic, mesothelial, inflammatory, and hemorrhagic; pseudocysts have no specific lining.
 - F. Meckel diverticulum:** the persistent proximal portion of the Omphalo-mesenteric (vitello-intestinal) duct--the link between the gut and the yolk sac. It is the most frequent congenital diverticulum, about 2% of the population. Located 2 ft. proximal to the ileocecal valve. May be attached to umbilicus. Frequently has heterotopic mucosa, especially gastric. **Complications:** in about 10% of cases.
 - 1. ~~Peptic Ulcer:~~ from heterotopic gastric glands.
 - ~~2. Volvulus:~~ twisting on an anchoring cord.
 - ~~2.~~
 - 3. **Intussusception:** invagination of diverticulum back into the ileum.

II. MECHANICAL LESIONS

Often produce sudden abdominal emergencies ("acute abdomen"). Rapid diagnosis and intervention needed to prevent permanent effects of ischemia.

- A. **Volvulus** - twisting of a loop of bowel, e.g. on its mesentery, on an adhesion, on a Meckel diverticulum. Compressed bowel lumen leads to obstruction: compressed blood supply leads to ischemia and infarction. Most in small bowel; remainder in sigmoid colon and cecum.
- B. **Intussusception** - invagination, telescoping of one segment of the bowel into the part distal to it. Ileocecal valve most common site. Needs leading edge, e.g. a tumor. Children affected more than adults. Enlarged lymphoid tissue (e.g. from adenovirus) may get drawn along; polyps; tumors. Compressed blood vessels and luminal obstruction are main complications.
- C. **Adhesion** - scar between peritoneal surfaces. Source of obstruction, ischemia and volvulus. Most common mechanical lesion. Usually a complication of prior surgery or inflammation; damage to peritoneal surface from handling, inflammation, ischemia, foreign bodies, radiation.
- D. **Hernia** - protrusion of bowel beyond its normal confines, e.g. through a mesenteric defect or into the inguinal canal. Incarcerated hernia: when bowel gets stuck; strangulated hernia: when blood supply is choked off. Obstruction and ischemia are complications. Inguinal canal is main site; femoral, umbilical and diaphragmatic less common.
- E. **Perforation** - communication of bowel lumen to peritoneal surface. Catastrophic due to sudden exposure of chemical and bacterial contents to large surface. Perforations may be walled off by omentum or other organs. Causes: peptic, inflammatory, foreign bodies, trauma. Shock is the result.
- F. **Obstruction** - blockage of intestinal flow; due to external kinking or compression from hernia, volvulus, intussusception, adhesions; internal blockage from tumor; and loss of muscular propulsion especially after surgery, "paralytic ileus".

III. GASTROINTESTINAL INFECTION

A. Defense mechanisms

1. Stomach: low pH kills many microbes
2. Small intestine: motility sweeps microbes along; (obstruction promotes overgrowth)
3. Colon: massive population of non-pathogenic bacteria resists colonization by pathogens; (antibiotics can disrupt balance)
4. Lymphoid tissue in gut mucosa

B. Types of infection

1. Intraluminal proliferation with cytotoxin production; e.g. Clostridium difficile
2. Mucosal adherence, enterotoxin production, secretory diarrhea, but no histopathologically recognizable lesion; e.g. cholera
3. Mucosal adherence, damage to the microvillus border; e.g. enteropathic E. coli
4. Mucosal invasion and intramucosal microbial proliferation; e.g. shigella
5. Mucosal invasion with spread to lymph nodes; e.g. salmonella
6. Mucosal invasion with systemic spread; e.g. typhoid

C. Small Intestinal Infection

Important site of infectious and noninfectious inflammation.

1. Cholera: vibrio-toxin alters flow of fluid across mucosa leading to severe watery diarrhea. Death can result from dehydration. No obvious lesion. Physiologic damage.
2. Typhoid fever: Salmonella typhi absorbed in small bowel through Peyer patches with no lesion; enter blood, from which they can be cultured during first week or two of illness. Multiply in blood; excreted by liver in bile; can continue to grow in gall bladder and gut; positive fecal cultures after second week. Bacilli reabsorbed in Peyer patches where an immune reaction leads to ulceration and necrosis of lymphoid tissue. Ulcers follow long axis of bowel. Microscopically, lymphoid tissue is filled with bacteria, large histiocytes, some lymphoid cells and few if any polymorphs. Leukopenia is characteristic. Perforation and hemorrhage can occur, usually after 3rd week. Ulcers heal without scars. Bacilli can affect many organs, e.g. heart, bone and kidneys, and can persist in gallbladder and kidney leading to a carrier state.
3. Yersinia: an infection in children and young adults simulating acute appendicitis but primarily affecting mesenteric lymph nodes and the lymphoid tissue of the terminal ileum and appendix. Granulomas with central purulent necrosis occur in the lymphoid tissue.
4. Tuberculosis: as in lung, lesions may be of primary [from milk], or secondary type. Usually secondary to swallowed bacilli from lung lesion. Produces ulcers which are annular or oval lying transverse to the long axis of the bowel (unlike typhoid). Scars form causing strictures. Perforation can occur.
5. Whipple disease: a chronic systemic disease with mainly GI lesions. Intestinal mucosa fills with foamy macrophages containing PAS positive granular bodies presumed to be bacilli; lymph nodes also contain these; characterized by molecular technics as *Tropheryma whippelli*, but never cultured. Responds to antibiotics. Can be fatal if untreated.
6. Infections in AIDS: Usually no inflammatory response due to immune deficiency. "Weak" organisms, e.g. Mycobacterium avium intracellulare, cryptosporidiosis, candida.
7. Parasitic: A number of parasites can affect the small intestine, such as hookworms, ascaris, giardia, and tapeworms. They generally cause few or mild lesions despite resulting in anemia, diarrhea, pain, malabsorption, weight loss, and chronic debilitation.

IV. CROHN DISEASE

A chronic, noninfectious, progressive, relapsing inflammatory disease of unknown cause, resulting in transmural inflammation and scars, discontinuously distributed in the GI tract, typically in the ileum and colon. Most common in young adults. Lesions start as small, punctate inflammatory mucosal foci and progress to deep serpiginous ulcers that can fissure through the wall. Mucosa can appear cobblestoned from long ulcers separating swollen unulcerated parts. Transmural inflammation is the hallmark, with lymphoid aggregates in the subserosa and submucosa often oriented to dilated lymphatics.

Submucosal edema or fibrosis; mucosa less affected. Non-necrotizing granulomas in 50%-70% of cases; in lymph nodes as well as bowel. Scars greatly thicken the wall, typically like a hose pipe. "Skip" areas are characteristic; diseased alternating with normal segments.

A pathogenetic theory suggests that inappropriate responses to bacterial components may lead to the development and persistence of intestinal inflammation.

Terminal ileum - most frequently involved.

Anorectal area - frequent

Colon - frequent

Stomach, duodenum and jejunum - uncommon

A. Complications

Anal fissures

Adhesions between loops of bowel

Fistulas (communications between two hollow organs) in 10%; ileoileal fistula most frequent;

Abscesses around bowel

Hemorrhage not severe

Obstruction due to fibrosis

Carcinoma complicates Crohn disease but not as much as with ulcerative colitis.

Systemic changes in joints, eyes, liver, and skin.

B. Prognosis

Crohn disease is characterized clinically by pain and diarrhea in episodic attacks with periods of quiescence. Surgery is needed for the complications; relapse is common. Mortality rate is not high but morbidity is.

C. Differential Diagnosis

-Ulcerative colitis: when colon disease is present (see below).

-Ischemic bowel disease: ischemic scars can simulate Crohn but microscopically different: no fissures, granulomas or transmural chronic inflammation. Age of patient usually higher in ischemia.

-Diverticulitis of colon: Crohn disease of left colon may resemble diverticulitis, (a more common lesion); age of patient usually higher in diverticulitis.

-Chronic appendicitis can simulate Crohn disease. Crohn isolated to appendix rarely occurs.

V. INTESTINAL MALABSORPTION

This covers a wide range of conditions that result in poor nutrition. Includes defects in secretions from the stomach, pancreas and liver, deficiencies in enzymes in the absorptive cells of the bowel, damage to mucosa by infection, food sensitivity, immunological factors and drugs and disturbances in the microbial ecology of the bowel.

This subject is more interactive with physiology and biochemistry than the other GI diseases. Many of these conditions show few morphologic changes. Here we cover intestinal diseases; not pancreatic, etc.

A. Celiac disease (sprue): a condition in the genetically predisposed in which reversible small intestinal mucosal damage is caused by permanent intolerance to dietary gluten, 'gluten-induced enteropathy' (or less commonly, other proteins).

Morphologic changes:

- a. Villous atrophy: shortened or flat villi;
- b. Crypt hyperplasia: thickened basal layer of mucosa
- c. Surface enterocytes lose their height, vertical orientation, and microvillous absorptive surface.
- d. T-lymphocytes increase in mucosa, both among the enterocytes and in the lamina propria.

Jejunum most severely damaged. Enterocytes injured and lost; crypt cells undergo hyperplasia to compensate but do not succeed. Mucosa can become completely flattened; malabsorption leads to diarrhea, weight loss, calcium loss, and anemia.

Elimination of gluten, a wheat protein, from diet results in recovery of mucosa; this is the diagnostic test as well as the therapy. Takes several weeks to obtain normal structure. A confirmatory test is to reintroduce gluten and demonstrate mucosal damage by biopsy.

Sensitivity to other proteins, e.g., soy beans, cow's milk, can produce similar changes.

Patients with celiac disease have an increased risk for small bowel malignant T-cell (enteropathy associated) lymphomas and carcinomas of bowel and esophagus.

Celiac disease was once thought to be rare and confined to childhood (where the most overt cases occur). More sensitive diagnostic methods show it to be common with varied clinical features, e.g., osteoporosis, growth retardation, infertility, pregnancy failure, anemia; prevalence among those of northern European origin is about 1%

Tropical sprue: a celiac syndrome probably of infectious origin occurring in the tropics. It responds to antibiotics but the causative agent(s) is unknown.

B. Other intestinal causes of malabsorption

Microbial and parasitic infestations.

Altered small bowel bacterial populations can distort the normal luminal metabolic processes carried out by gut flora. Can be caused by:

1. antibiotics
2. blind loops where stagnation prevents adequate emptying of bowel lead to bacterial overgrowth, e.g.,
 - a. proximal limb of gastroenterostomy;
 - b. short-circuited bowel after fistula formation;
 - c. diverticula - especially in jejunum
 - d. strictures - dilated proximal bowel may permit bacterial overgrowth.
3. any disease damaging mucosa or affecting propulsion e.g., Crohn, Whipple, scleroderma, amyloid, tuberculosis, diabetes, dumping syndrome (hyperosmolar dump).

C. Clinical features of malabsorption

1. Diarrhea, steatorrhea, weight loss, abdominal pain, fatigue anemia, edema, osteomalacia.

VI. VASCULAR DISORDERS OF THE GASTROINTESTINAL TRACT

Common in large and small intestines. Rare in esophagus and stomach. May be primary cardiovascular or secondary to mechanical lesions, e.g. volvulus. Sudden occlusion produces acute abdomen; needs rapid diagnosis and intervention to prevent infarct. Gradual occlusion produces chronic disorder.

A. Ischemia

The two main causes of bowel ischemia are vascular obstruction and hypotension. Most ischemic lesions are the result of ~~both~~ factors acting together.

Vascular obstruction:

-large arteries - usually atherosclerosis near aorta with or without thrombosis; emboli; complete obstruction is not necessary to produce ischemia
-veins - external pressure: volvulus, hernia;
internal blockage: thrombosis from infections.
-mural vessels - vasculitis, intravascular coagulation.

Hypotension: heart failure, shock, vasoconstriction. Shock from a myocardial infarct or surgery, plus a moderate degree of arteriosclerosis account for many cases of ischemic bowel lesions.

The pathogenesis of ischemic lesions of the bowel is basically that of other organs. Transient ischemia may cause pain or be silent. Persistent ischemia may cause reversible or irreversible damage. Infarction leads to coagulation necrosis, inflammation, granulation tissue and scarring; can perforate.

Bowel ischemia is characterized by several special features:

- a. mucosa is more sensitive to ischemia than is the muscularis; ulcers form; if superficial may heal without scars.
- b. intraluminal bacteria can become pathogenic when mucosal defense is damaged by ischemia.
- c. infarcts caused by venous occlusion are more frequent in the bowel than elsewhere.
- d. hemorrhage is more frequent in bowel infarcts than elsewhere, because of collaterals.

Gross features of ischemic bowel

Hemorrhage, submucosal edema, loss of muscle tone, and mucosal exudates or slough lead to a dilated, wet, swollen, reddish-blue, mottled, boggy, friable bowel.

Microscopic features

Mucosa dies first, often patchy with a surface membrane of mucus, polys, fibrin and necrotic tissue. Submucosa is swollen by edema and later by hemorrhage; granulation tissue and scars follow. Muscularis propria is most resistant to ischemia but when it dies it does not regenerate as mucosa can; it becomes scarred. Ischemia is the main cause of scarred bowel muscle; virtually pathognomonic of infarction. Scars can lead to strictures, usually concentric, and serosal adhesions.

Colon and small bowel ischemia

Ischemia produces the same lesions in the small and large bowel--the stomach and esophagus are rarely affected by infarction.

The colon has a relatively inferior blood supply than the small bowel. The splenic flexure and descending colon have the poorest perfusion.

B. Vascular abnormalities. These are less common than ischemic lesions.

1. **Angiodysplasia:** small ectatic thin-walled vessels in the mucosa and submucosa prone to hemorrhage, typically in the right colon of the elderly and believed to be due to outflow obstruction; can produce considerable blood loss; difficult to find clinically and pathologically.

2. **Vascular malformations and hemangiomas** can be source of

hemorrhage

3. **Varices:** large dilated veins; do not occur in the bowel but at the gastroesophageal, umbilical and anorectal regions--the sites of communication between the systemic and portal venous systems. These, especially in esophagus, enlarge when portal venous pressure is elevated, typically in liver cirrhosis.

esophageal bleeding - catastrophic

hemorrhoidal bleeding - minor

VII. TUMORS OF THE SMALL INTESTINE

The small bowel has the lowest incidence of epithelial tumors, i.e., adenomas and carcinomas, of the digestive tract. Small bowel carcinomas account for less than 1% of all intestinal carcinomas.

The periampullary area is the commonest site in the small bowel for adenomas and carcinomas. There is no gross or microscopic difference between small and large bowel carcinomas or adenomas. Celiac disease and Crohn disease are associated with some increase in small bowel carcinomas.

Carcinoid tumors, lymphoma, smooth muscle tumors and metastatic tumors are relatively common and are more frequent than primary carcinomas in the small bowel.

A. Carcinoid tumor:

A neoplasm of the diffuse endocrine system (neuroendocrine or APUD systems), typically the serotonin secreting cell; others produce gastrin, somatostatin, etc; argentaffin, argyrophil and immunohistochemical reactions help in diagnosis; dense core secretory granules by electron microscopy; usually of low grade malignancy; they arise below the surface: deep mucosa or submucosa

B. Carcinoid syndrome

Clinical state due to excessive production of serotonin (5-hydroxytryptamine [5-HT])

Occurs with liver metastases from a carcinoid 5-HT and kinins cause:

-episodic diarrhea-gut hypermotility

-flushing of face - vasomotor

-episodic bronchoconstriction

-5-hydroxyindole acetic acid (5-HIAA) can be measured in urine

C. Zollinger-Ellison syndrome

Hypersecretion of gastrin from a carcinoid (gastrinoma) causing severe peptic

ulceration
Serum gastrin levels elevated
Gastrinoma may be in pancreas, duodenum or stomach.

APPENDIX

I. ACUTE APPENDICITIS

Most common abdominal emergency up to age 30.

An important model for the diagnosis of the acute abdomen, pathogenesis of acute inflammation and complications of inflammation.

A. Pathogenesis

Obstruction, due to: lymphoid tissue hypertrophy (typically in children), edematous mucosa, fecolith or tumor. (When acute appendicitis occurs in a patient aged >50 years, rule out neoplasm in cecum or appendix). Obstruction leads to blockage of mucus drainage. Intraluminal pressure on mucosa leads to secondary bacterial infection, then inflammation.

B. Morphologic changes

Polyps in mucosa, surface erosion, exudate in lumen. Later spread to submucosa, muscle and serosa. Tissue necrosis more frequent and rapid than in other GI lesions due to obstruction, higher pressure and vascular thrombosis. Concentrated polyps cause liquefactive necrosis.

C. Complications

Perforation
Peritonitis
Periappendiceal abscess
Metastatic abscesses
Chronic appendicitis
Fibrosis
Diverticula
Mucocele

II. MUCOCELE: dilatation of a lumen due to accumulation of mucus; a macroscopic diagnosis.

Simple mucocele: appendiceal dilatation with mucus due to obstruction; usually postinflammatory with proximal scarring.
Epithelium is flat and atrophic.

III. TUMORS OF THE APPENDIX

A. Carcinoid tumor:

The most frequent tumor of the appendix
Starts in deep mucosa or submucosa
Appendiceal carcinoids: rarely metastasize; appendectomy usually sufficient if tumor is small (less than 1.5 cm)
(Small bowel carcinoids are more aggressive).

B. Mucinous cystadenoma: a mucocele lined by benign neoplastic epithelium (not a flattened atrophic lining as in a simple mucocele).

Usually more mucus than in simple mucocele; may rupture wall and spread to peritoneum.

- C. **Adenocarcinoma** and **mucinous cystadenocarcinoma** may arise from a cystadenoma or adenoma.
- D. **Pseudomyxoma peritonei**: widespread loculated mucinous deposits on the peritoneum; due to ruptured neoplastic mucocele; usually from a malignant mucinous neoplasm, e.g. of appendix.

TNM classification of small intestinal carcinoma

- T1 Lamina propria, submucosa
T2 Muscularis propria
T3 Subserosa, non-peritonealized perimuscular tissues (mesentery, retroperitoneum) ≤ 2 cm
T4 Visceral peritoneum, other organs/structures (including mesentery, retroperitoneum >2 cm)
N1 Regional

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