



Approach to Patients with Chronic Diarrhea For Internists



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Chronic Diarrhea

- **Definition: Diarrhea for a duration of >4 weeks**
 - Increased fluidity of stool
 - Stool frequency >2 times/day
 - Stool weight >200 grams/day

- **Onset of symptoms**



- Suggestive for infections esp. bacteria
- Less common: post-infectious IBS, IBD, lactose intolerance

Progressive



- Most causes of chronic diarrhea

Intermittent



- Functional diarrhea/IBS-D
- Some non-malignant causes of chronic diarrhea

Overview: Approach to Chronic Diarrhea

- Functional vs organic
 - Duration: <6 mo, 6 mo – 2 yr, >2 yr
 - Infectious vs non-infectious
 - Small bowel vs large bowel
 - Steatorrhea vs watery vs mucous/bloody
 - For watery diarrhea → secretory vs osmotic
 - Underlying disease/certain risks e.g. HIV, SLE, DM
-
- Any clinical clues (signs or symptoms)
 - Algorithm ?



Inflammatory Diarrhea

Inflammatory bowel disease (IBD)

- Ulcerative colitis (UC)
- Crohn's disease

Malignancy/neoplasm

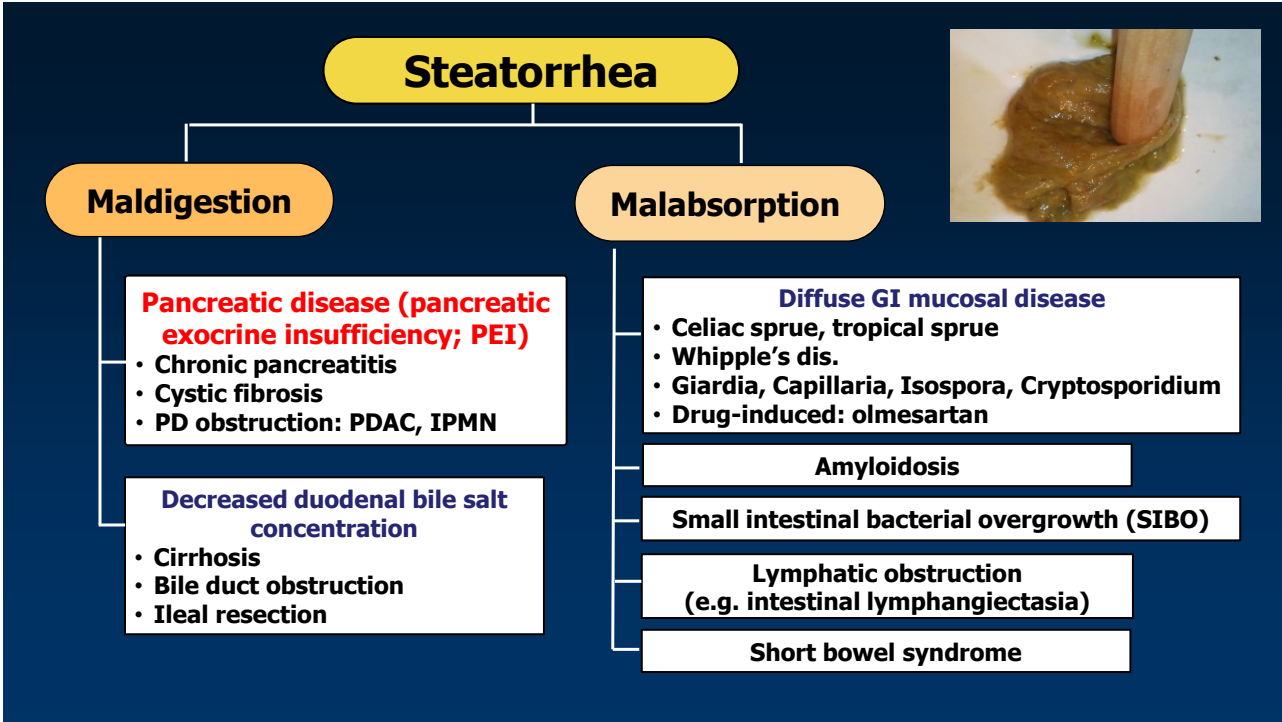
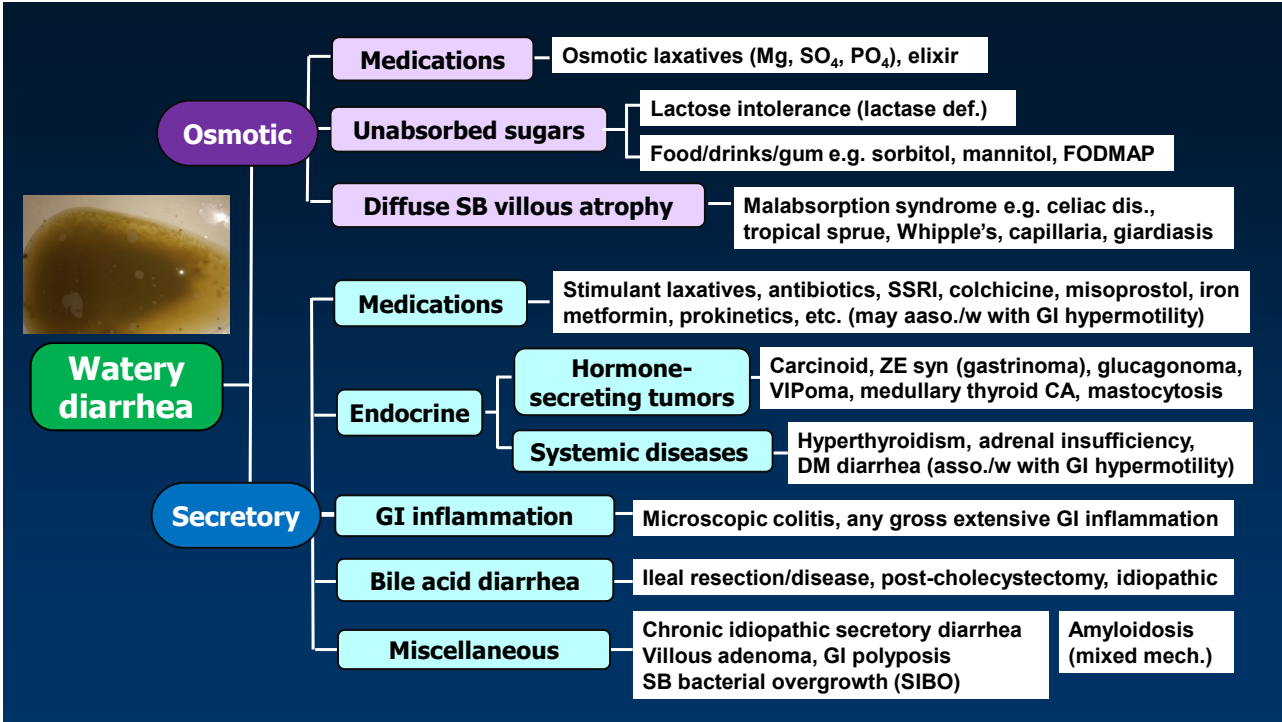
- Colon cancer
- GI polyposis
- GI lymphoma

Infections

- C. difficile, Yersinia, STD (chlamydia, SY)
- CMV, amebiasis,
- TB, MAC, fungus

Chronic inflammation and/or ischemia from miscellaneous causes

- Eosinophilic enterocolitis (EGID)
- Drug-induced: NSAIDs, MMF, immune checkpoint inhibitors (irAEs)
- Radiation enterocolitis
- Chronic ischemic enterocolitis
- GI vasculitis, PAN, Behcet's dis.
- GVHD
- Amyloidosis



Chronic Diarrhea: Risk/Underlying Conditions

	Disease or disease complications	Treatment-related complications	Associated conditions
HIV	<ul style="list-style-type: none"> • AIDS enteropathy • OIs e.g. TB, MAC, CMV cryptosporidium, isospora, microspora 	<ul style="list-style-type: none"> • ARV-induced diarrhea 	<ul style="list-style-type: none"> • STD proctitis (chlamydia, GC, SY) • Amoebic colitis • GI lymphoma
SLE	<ul style="list-style-type: none"> • Protein-losing enteropathy (PLE) • Mesenteric vasculitis • Mesenteric venous thrombosis (MVT) 	<ul style="list-style-type: none"> • Drug-induced: MMF • OIs from immunosuppression 	<ul style="list-style-type: none"> • Autoimmune GI diseases e.g. celiac dis., IBD, autoimmune enteropathy
DM	<ul style="list-style-type: none"> • Diabetic diarrhea • SIBO 	<ul style="list-style-type: none"> • Artificial sweeteners • Drug-induced: metformin, GLP1RA 	<ul style="list-style-type: none"> • Pancreatic exocrine insufficiency • Microscopic colitis

Chronic Diarrhea: Clues from History Taking

- **Related to certain diet** – food allergy, CHO intolerance, celiac
- **Drugs** – laxatives, Mg compounds, colchicine, misoprostol, MF
- **Chewing gums, artificial sweeteners** – osmotic diarrhea
- **Weight loss** – malabsorption, TB, HIV, hyperthyroid, malignancy
- **Fever** – infectious colitis, C. difficile, chronic infection (HIV, TB), IBD, lymphoma, SLE
- **Flushing** – carcinoid syndrome, mastocytosis, medullary thyroid cancer
- **Long Hx of DM + microvascular complications** – diabetic diarrhea/enteropathy
- **Hx of TB or contact TB** – TB enterocolitis
- **Previous GI surgery** – SIBO, recurrent disease, GI fistula
- **Post cholecystectomy** – bile salt diarrhea
- **Post radiation** – radiation enterocolitis, SIBO
- **Hx of pancreatitis, chronic alcohol use, steatorrhea** – chronic pancreatitis
- **SLE, connective tissue disease** – vasculitis, autoimmune enteritis
- **Recurrent PU, kidney stones** – ZE syndrome, MEN I/II
- **Response to previous treatment** – antibiotics, antiparasites, steroids, cholestyramine

Chronic Diarrhea: Clues from Physical Exam

- **Tachycardia, tremor, sweating** – thyrotoxicosis, carcinoid
- **Postural hypotension** – DM, Addison's disease
- **Localized abdominal pain** – Intra-abdominal infection, diverticulitis, tumor
- **Clubbing of fingers** – IBD, IPSID, Whipple, celiac, CA, Grave's disease
- **Mucosal hyperpigmentation** – Peutz-Jeghers syndrome
- **Nail dysplasia, hyperpigmentation** – Cronkhite-Canada syndrome
- **Oral ulcers** – IBD (Crohn > UC), Behcet's disease, SLE
- **Lymphadenopathy** – lymphoma, TB, CA, IPSID, HIV, Whipple disease
- **Cutaneous vasculitis** – CNT disease
- **Dermatitis herpetiformis** – Celiac
- **Erythema nodosum** – IBD (Crohn > UC), TB
- **Pyoderma gangrenosum** – IBD (UC > Crohn)
- **Genital ulcer** – Behcet's disease
- **Arthralgia/arthritis, sacroiliitis** – IBD
- **Uveitis** – IBD, CNT disease

Physical Findings - Hints in Chronic Diarrhea

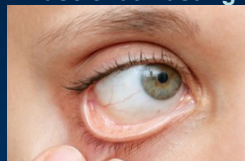
Signs of malnutrition



Muscle/fat wasting



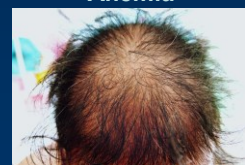
Edema



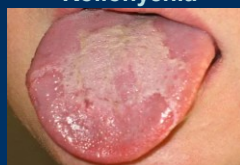
Anemia



Koilonychia



Alopecia



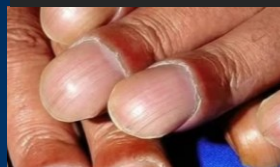
Glossitis

Lymphadenopathy



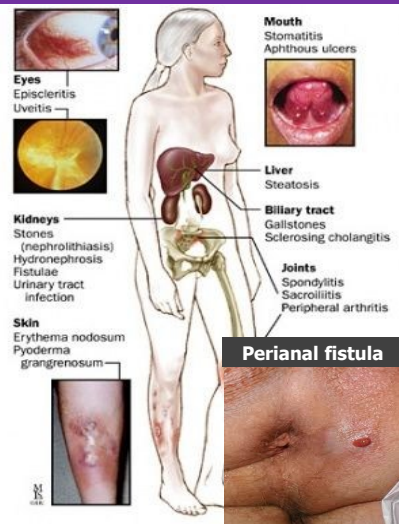
HIV, lymphoma, CA

Clubbing of finger



IBD, IPSID, Celiac dis.

Extraintestinal signs of IBD



Cederholm T, et al. Clin Nutr 2015
Rogler G, et al. Gastroenterology 2021

Physical Findings - Hints in Chronic Diarrhea

Carcinoid syndrome

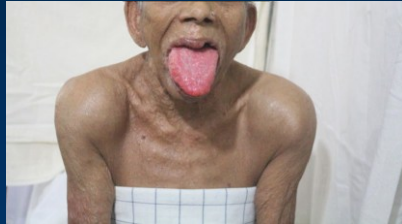


Flushing
Bronchospasm, wheezing
Heart murmur (Rt side)
Pellagra (3D: diarrhea, dementia, dermatitis)

Amyloidosis



Periorbital purpura



Macroglossia
Shoulder pad sign

Glucagonoma



Migratory necrolytic erythema

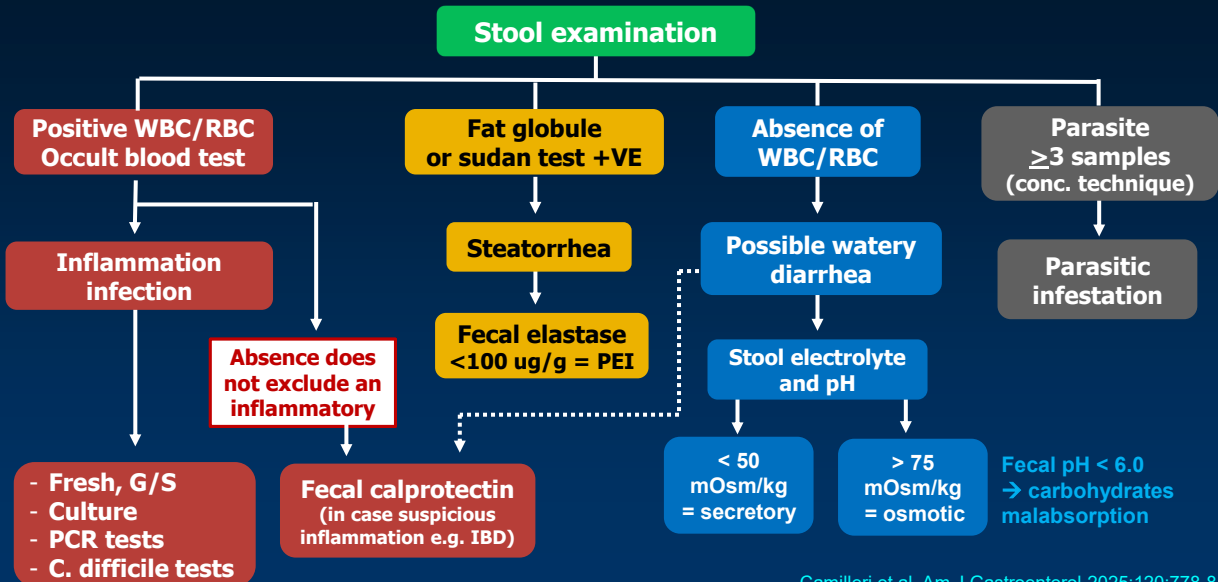
Celiac disease



Dermatitis herpetiformis

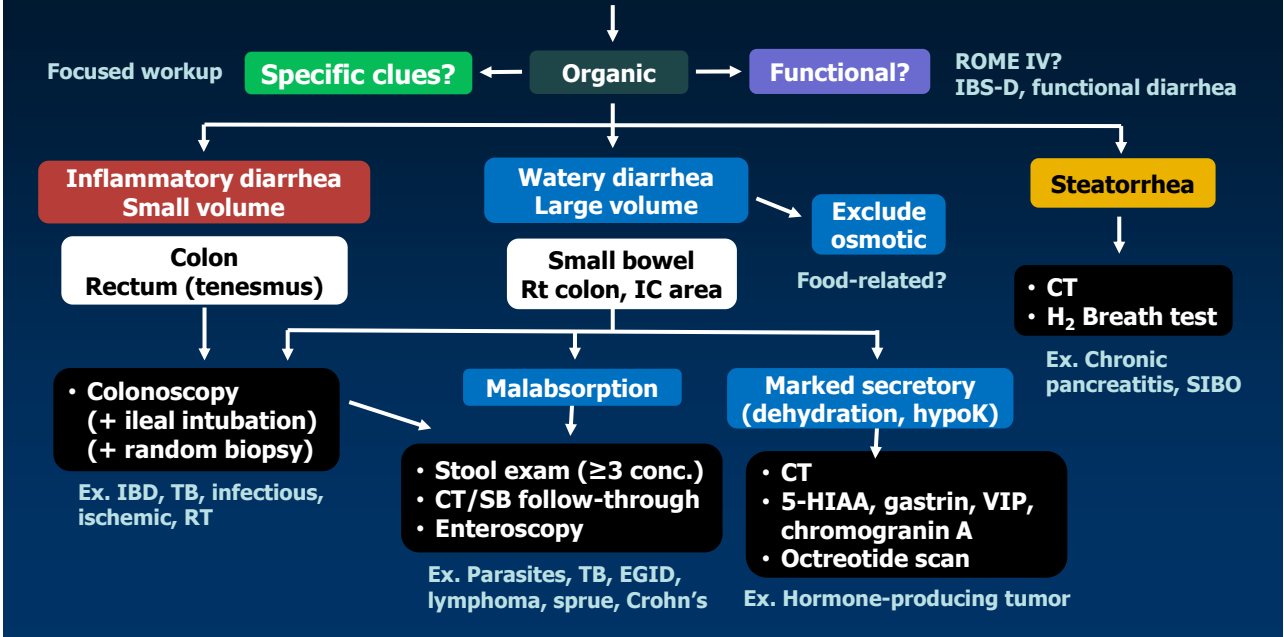
Suganthan et al. Clin Case Rep 2021;9:1801-02
Reunala T, et al. Nutrients 2018;10(5):602

Role of Stool Tests in Chronic Diarrhea

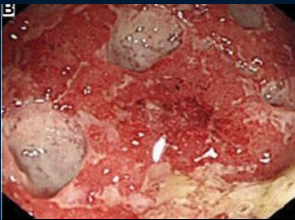


Camilleri et al. Am J Gastroenterol 2025;120:778-84
Smalley et al. Gastroenterology 2019;157:851-54

Approach to Chronic Diarrhea



Colonoscopy: Infectious Causes of Chronic Diarrhea



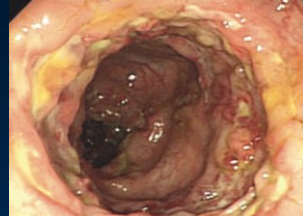
CMV colitis

- Ulcers (deep, punch-out, geographic), colitis
- Bx: viral inclusion, IHC



C. diff. colitis (CDAC)

- Colitis, yellowish exudate (pseudomembrane)
- From rectum/sigmoid



TB colitis

- Irregular/nodular circumferential ulcers, yellowish exudates, esp. ileocecal area, deformed IC valve
- Bx: caseating granulomas, AFB+, PCR for TB+



MAC

- Colitis with ulcerations
- Duodenum (most common) and colon
- Bx: foamy histiocytes, PAS+, mAFB+



Amoebic colitis

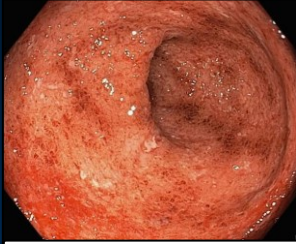
- Multiple punctate ulcers, normal intervening mucosa (or mild colitis)
- Cecum and left colon
- Bx: E. hist trophozoites



MAC

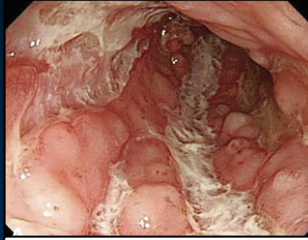
- Colitis with ulcerations
- Duodenum (most common) and colon
- Bx: foamy histiocytes, PAS+, mAFB+

Colonoscopy: Non-infectious Causes of Chronic Diarrhea



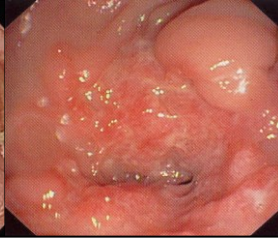
Ulcerative colitis (UC)

- Mucosal granularity, colitis, shallow ulcers
- From rectum → cecum



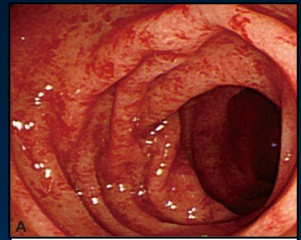
Crohn's disease

- Longitudinal, deep ulcers, cobble-stone appearance, skip lesions (normal intervening mucosa), fistula, stricture
- Esp. ileocecal and perianal area



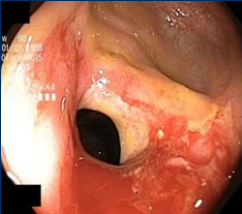
CA colon

- Polypoid or ulcerative mass



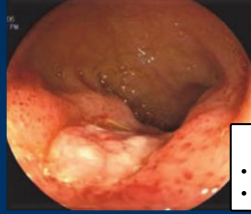
Eosinophilic colitis

- Colitis (or normal)
- Bx: ↑ EOS >50 /HPF



NSAID colopathy

- Ulcerations (single/multiple, shallow/deep)
- Esp. near IC valve
- diaphragm-like stricture



Behcet's

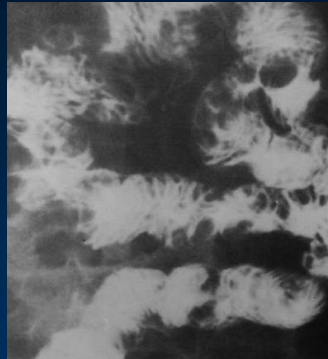
- Punch-out ulcers
- Ileocecal area



Malabsorption syndrome

- Dilated small bowel loops (enlarged, floppy)
- Segmentation and flocculation of barium
- Increased fluid, rapid transit
- Featureless bowel (loss of folds)

SB Follow-through: Typical Findings



GI polyposis (PJS)

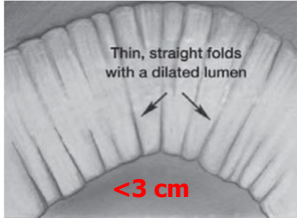
- Multiple SB polyps/masses
- D/Dx: Lymphoma, metastases



Systemic sclerosis

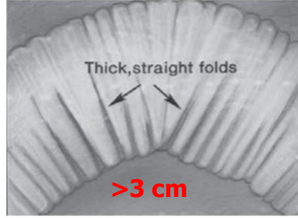
- Dilated SB with decreased distance between adjacent valvulae conniventes (hidebound bowel)
- Wide-mouthed sacculations
- Hypomotility, loosen LES with GERD

Small Bowel Disease from Long GI Study



Type I (thin, straight folds)

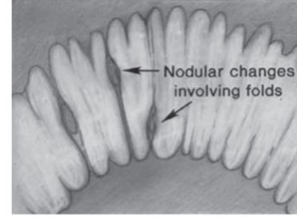
- Mechanical obstruction
- Paralytic ileus
- Scleroderma
- Sprue



Type II (thick, straight folds)
Segmental
Diffuse

- Segmental**
- Ischemia
 - Radiation enteritis
 - Intramural hemorrhage
 - Adjacent inflammatory process

- Diffuse**
- Venous congestion
 - Hypoalbumin
 - Cirrhosis



Type III (thick, nodular folds)
Segmental
Diffuse

- Segmental**
- Crohn's dis.
 - Infection
 - Lymphoma
 - Metastases

- Diffuse**
- Whipple dis.
 - Lymphangiectasia
 - Nodular lymphoid hyperplasia
 - Polyposis syn.
 - EGID
 - Amyloidosis
 - Mastocytosis
 - Lymphoma
 - Metastases

CT Scan Checklists: Bowel Findings

Bowel wall thickening

- Enhancement pattern



- Length of involvement

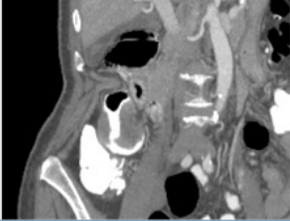
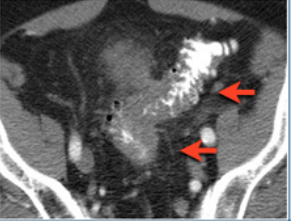

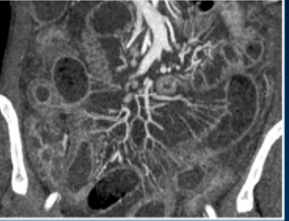
- Mural thickness

- Mesentery
- Patency of mesenteric vessels
 - Edema
 - Lymph nodes
 - Fistula






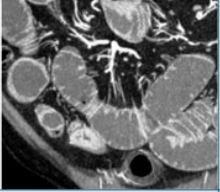
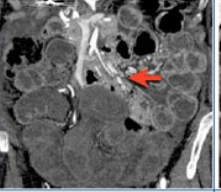

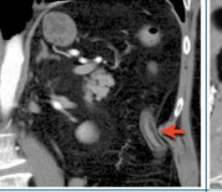
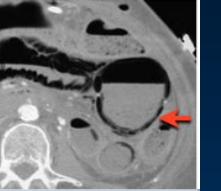
- Lumen contents
- Blood - Fat
 - Small bowel feces sign

- The bowel wall should be thin, usually $< 3\text{ mm}$ in thickness
- A diameter $> 3\text{ cm}$ is considered dilated

CT Scan: Length of Involvement

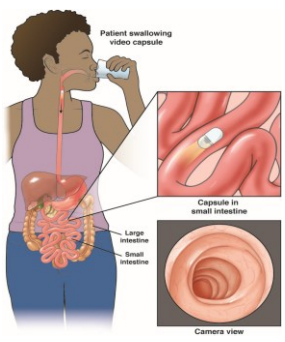
Focal < 5 cm	Focal 5 - 10 cm	Segmental 10-30 cm	Diffuse
			
1. Adenocarcinoma	1. Diverticulitis 2. Crohn's disease 3. Ischemia	1. Ischemia 2. Submucosal hemorrhh. 3. Radiation 4. Infection 5. Crohn's disease 6. Lymphoma	1. Infectious Enterocolitis 2. Ulcerative Colitis 3. Edema from low protein or cirrhosis 4. SLE

CT Scan: Bowel Wall Enhancement Pattern

White 	Gray 	Target - Water 	Target - Fat 	Gas 
				
1. Acute IBD due to vasodilatation with acute hyperemia 2. Shock Bowel injury to intramural vessels 3. Reperfusion after ischemia 4. Hemorrhage	1. Chronic Crohn's 2. Ischemia 3. Neoplasm	1. Portal hypertension 2. Infection - Shigella, Salmonella, E. Coli, CMV, Crypto - Pseudomemb. colitis - AIDS 3. Acute Ulc. Colitis 4. Acute Crohn's 5. Typhlitis 6. AIDS 7. Ischemia	1. Chronic Ulc. Colitis 2. Chronic Crohn's 3. Obesity 4. Chemotherapy 5. Celiac disease	1. Ischemia 2. Infection 3. Trauma 4. Benign causes - Connect tissue disease - IBD - COPD - Obstruction 5. Pseudo-pneumatosis

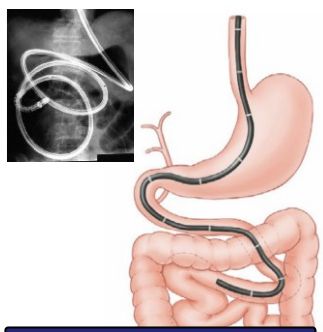
Small Bowel Endoscopy

Video Capsule Endoscopy (VCE)



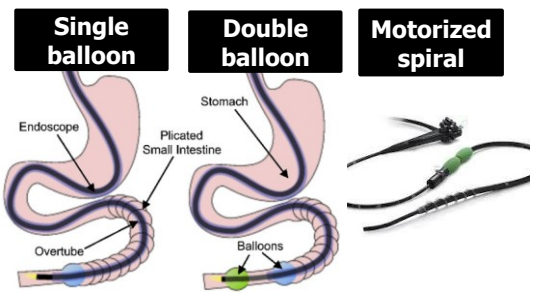
- Non-invasive
- Cannot biopsy
- Contraindicated when luminal stricture is suspected

Push Enteroscopy



- Minimal invasive
- Use a colonoscope
- Can reach only the proximal jejunum
- Allow mucosal biopsy

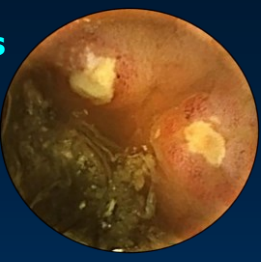
Device-assisted Endoscopy



- Invasive
- Time-consuming
- Can examine the entire small bowel
- Complications: bowel injury, pancreatitis
- Allow mucosal biopsy

VCE/Enteroscopy: Findings in Chronic Diarrhea

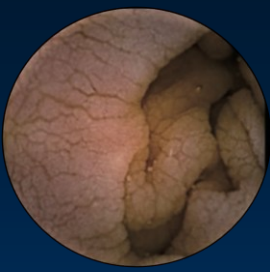
Ulcers



Mucosal ulceration /inflammation

- Crohn's disease
- NSAID-induced enteropathy
- Infectious, TB, CMV
- Vasculitis
- Lymphoma

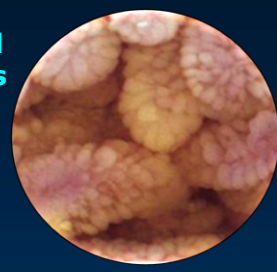
Blunt villi



Sprue-like enteropathy

- Celiac disease
- Tropical sprue
- Capillariasis
- HIV, Giardiasis, protozoa
- Drug-induced enteropathy e.g. Olmesartan

Dilated lacteals



Intestinal lymphangiectasia

- Protein losing enteropathy
- Steatorrhea
- Intestinal lymphatic drainage obstruction (lymphoma, TB, cancer)

Valero M et al. Clin Endosc 2018
 Shen B et al, ASGE Standards of Practice Committee; Gastrointest Endosc 2010

Pancreatic Disease and Chronic Diarrhea

- **Causes:**
 - Chronic pancreatitis (most common)
 - Pancreatic neoplasms e.g. IPMN, PDAC
- **Clinical clues:**
 - Risk factors: heavy alcohol, family Hx
 - Hx of recurrent pancreatitis or epigastric pain
 - Steatorrhea, wt. loss, fat-soluble vitamin def., DM
- **Imaging diagnosis of chronic pancreatitis:**

Pancreatic exocrine insufficiency (PEI)

**Fecal elastase
<100 ug/g stool**

Plain film	US	CT	MRCP	ERCP	EUS
S ~50% Sp 95%	S 48-96% Sp 75-90%	S 56-95% Sp 85-100%	Sens 88-91% Spec 92-98%	Sens 68-100% Spec 89-100%	Sens 85-100% Spec 85-100%



Thank You for Your Kind Attention

