

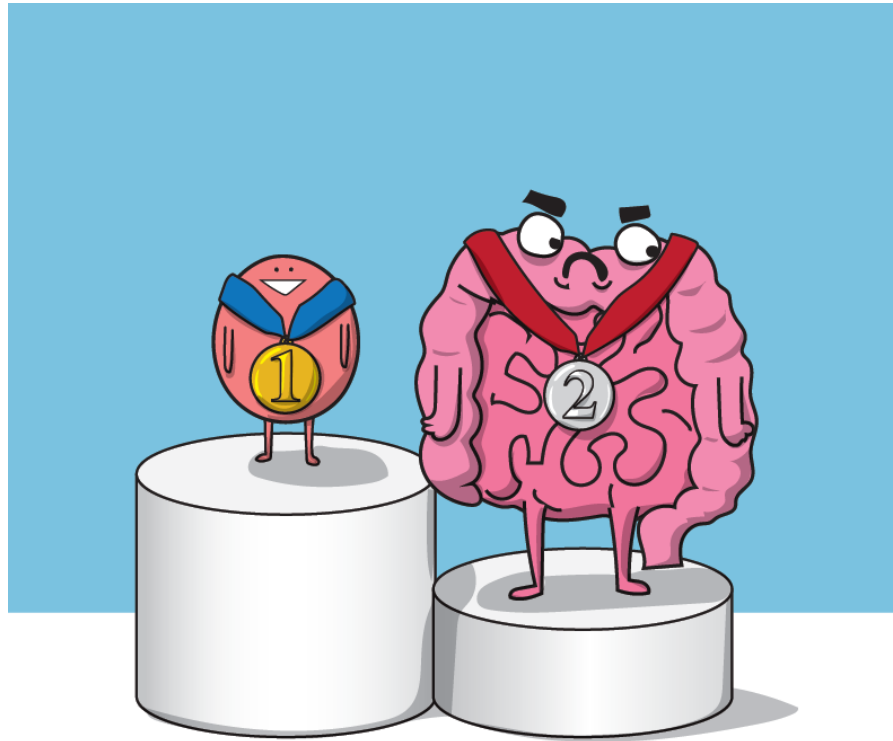
IBD AND DIFFERENTIAL DIAGNOSIS

2019 HOMECOMING WITH KCU-CME

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theAwkwardYeti.com

Disclosures

- None

Learning objectives

1. Describe common considerations for differential diagnosis for patients presenting with
 - *Abdominal pain*
 - *Diarrhea*
 - *Nausea/Vomiting*
 - *Hematochezia*
 - *Tenesmus*
2. Explain which GI infectious can mimic IBD
3. Review epidemiology, pathophysiology, and extraintestinal manifestations of IBD
4. Compare and Contrast Ulcerative Colitis and Crohn Disease
5. Explain diagnostic considerations in the work-up for IBD and Differential Diagnosis

Recall

- Best place to start is with thorough history and physical
- Develop DDx from most likely to least likely
- Prioritize diagnostic work up

A 21-year-old female presents with concerns of intermittent RLQ abdominal pain, weight loss, and fatigue for the last four weeks.

- **IBD**
 - *Crohn Disease (CD) > Ulcerative Colitis (UC)*
- ***Yersinia enterocolitica* infection**
- **Appendicitis**
- **Ovarian**
 - *Cyst vs ectopic*
- **Anorexia/Bulimia**
- Diverticulitis

Pre-Op and Pre-Consult CT with IV or Oral Contrast

- Note that historically—when not done—Crohn disease is frequently diagnosed at the time of laparotomy for presumed appendicitis.

GI Infections that can mimic CD or UC

- Bacterial, fungal, viral, or protozoal in origin
- *Campylobacter colitis*
 - can mimic the endoscopic appearance of severe UC and can cause a relapse of established UC.
- *Salmonella*
 - can cause watery or bloody diarrhea, nausea, and vomiting.
- Shigellosis
 - causes watery diarrhea, abdominal pain, and fever followed by rectal tenesmus and by the passage of blood and mucus per rectum.
- All three are usually self-limited, but 1% of patients infected with *Salmonella* become asymptomatic carriers.
- *Yersinia enterocolitica* infection
 - occurs mainly in the terminal ileum and causes mucosal ulceration, neutrophil invasion, and thickening of the ileal wall.
- Other bacterial infections that may mimic IBD include
 - *C. difficile*
 - which presents with watery diarrhea, tenesmus, nausea, and vomiting
 - *E. coli*
 - three categories of which can cause colitis.
 - These are enterohemorrhagic, enteroinvasive, and enteroadherent *E. coli*, all of which can cause bloody diarrhea and abdominal tenderness.
- Gonorrhea, *Chlamydia*, and syphilis can also cause proctitis.

Diagnosis of bacterial colitis is made by sending stool specimens for bacterial culture and *C. difficile* toxin analysis.

Differential Considerations

- Abdominal pain, weight loss, and vomiting
 - *Late-teen and young-adult patients*
 - IBD is frequently diagnosed in this age group
 - Also the peak years for anorexia and bulimia
 - *Consider anorexia and bulimia*
 - *Consider inflammatory bowel disease (IBD)*
 - *Consider irritable bowel syndrome (IBS)*
- Recall hematochezia would help differentiate IBD (UC > CD) from IBS or Anorexia/Bulimia

Diverticulitis

- Confused with CD clinically and radiographically
 - *Both diseases cause*
 - fever, abdominal pain, tender abdominal mass, leukocytosis, elevated ESR, partial obstruction, and fistulas.
- CD more likely if
 - *Perianal disease or ileitis on small-bowel series*
 - *Significant endoscopic mucosal abnormalities*
 - *Endoscopic or clinical recurrence following segmental resection favors CD.*
- Diverticular-associated colitis is similar to CD, but mucosal abnormalities are limited to the sigmoid and descending colon

A 14-year-old female presents with crampy abdominal pain, low-grade fever, tenesmus, and diarrhea, with some passage of blood and mucus.

- **IBD**
 - *Ulcerative Colitis (UC) > Crohn Disease (CD)*
- **GI Infection**
 - *Shigellosis*
 - *E. Coli*
 - *Entamoeba histolytica or related species infection*
 - about 10% of the world's population
 - Colonoscopy reveals focal punctate ulcers with normal intervening mucosa; diagnosis is made by biopsy or serum amebic antibodies
- Ischemic colitis
- Radiation colitis

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Ischemic colitis

- Commonly confused with IBD
- Present with sudden onset of left lower quadrant pain, urgency to defecate, and the passage of bright red blood per rectum
- Similar to UC
 - *The ischemic process can be chronic and diffuse, as in UC*
- Similar to CD
 - *The ischemic process can be segmental, as in CD*
 - *Colonic inflammation due to ischemia might persist and result in transmural scarring and stricture formation*
- Consider in:
 - *Elderly*
 - *Following abdominal aortic aneurysm repair*
 - *When a patient has a hypercoagulable state*
 - *Severe cardiac or peripheral vascular disorder*
 - *Cocaine use*
- Endoscopic examination often demonstrates a normal-appearing rectum and a sharp transition to an area of inflammation in the descending colon and splenic flexure.

Radiation colitis

- The effects of radiotherapy on the GI tract can be difficult to distinguish from IBD.
- Acute symptoms can occur within 1–2 weeks of starting therapy
- Patients develop bloody, mucoid diarrhea and tenesmus
 - *When the rectum and sigmoid are irradiated similar to distal UC*
- Late symptoms include can be similar to CD
 - *malabsorption and weight loss*
 - *stricturing with obstruction and bacterial overgrowth may occur*
 - *Fistulas can penetrate the bladder, vagina, or abdominal wall*
- Flexible sigmoidoscopy reveals mucosal granularity, friability, numerous telangiectasias, and occasionally discrete ulcerations. **Biopsy can be diagnostic.**

Differential Considerations

- Several other diagnoses must be considered before establishing a diagnosis IBD
 - *particularly in the absence of typical endoscopic findings*
 - *in populations at higher risk for other diagnoses*

IBD

- Similar features to many other diseases
- Variety of presentations and progressions (specifically CD)
- 15% of IBD is Indeterminate colitis
 - *unable to be distinguished CD vs UC*

Diarrhea

- In additions to IBD, consider the following conditions in patients with diarrhea as a dominant symptom:
 - *Celiac disease*
 - *Microscopic colitis*
 - *Irritable bowel syndrome*
 - *Lactose intolerance*
 - *Functional diarrhea*
 - *Gastrointestinal infections*
 - *AIDS*
 - *Colorectal malignancy (eg, adenocarcinoma, lymphoma)*

NSAID colitis

- Several types of colitis are associated with nonsteroidal anti-inflammatory drugs (NSAIDs)
 - *including de novo colitis*
 - *reactivation of IBD*
 - *proctitis caused by use of suppositories*
- Most patients present with
 - *diarrhea and abdominal pain*
- Complications include
 - *stricture, bleeding, obstruction, perforation, and fistulization*
- Withdrawal of these agents is crucial, and in cases of reactivated IBD, standard therapies are indicated.

Collagenous colitis and Lymphocytic colitis

- Completely normal endoscopic appearances
- Collagenous colitis
 - *Histology*
 - increased subepithelial collagen deposition and colitis with increased intraepithelial lymphocytes
 - *F>M*
 - *Sixth or seventh decades of life*
 - *The main symptom is chronic watery diarrhea.*
 - *Risk factors include*
 - smoking, use of NSAIDs, proton pump inhibitors, or beta blockers; and a history of autoimmune disease.
- Lymphocytic colitis
 - *Histology*
 - No subepithelial collagen deposition on pathologic section, but intraepithelial lymphocytes are increased
 - *has features similar to collagenous colitis including age at onset and clinical presentation*
 - *almost equal incidence in men and women*
 - *Risk factors include*
 - Use of **sertraline**, smoking, use of NSAIDs, proton pump inhibitors, ~~or beta blockers~~; and a history of autoimmune disease.
 - *Up to 27% frequency of celiac disease, so should be excluded in all patients with lymphocytic colitis, particularly if diarrhea does not respond to conventional therapy.*

Abdominal pain with GIB/intestinal ulceration

- *Ischemic colitis*
- *Radiation-induced colitis*
- *Arteriovenous malformations*
- *Nonsteroidal anti-inflammatory drug (NSAID) enteropathy*
- *Behcet disease*
 - *Vasculitis*
 - *Ulceration (oral, genital, ocular, GI)*
- *Colorectal malignancy*
- *Gastrointestinal infections*

The World Gastroenterology Organization indicates the following symptoms may be associated with inflammatory damage of the digestive tract:

- *Diarrhea:*
 - Presence of mucus/blood in stool; occurs at night; incontinence
- *Constipation:*
 - May be the primary symptom in UC limited to the rectum; obstipation may occur; may proceed to bowel obstruction
- *Bowel movement abnormalities:*
 - Presence of pain or rectal bleeding, severe urgency, tenesmus
- *Abdominal cramping and pain:*
 - Commonly present in the right lower quadrant in CD; occur in the periumbilical or in the left lower quadrant in moderate to severe UC
- *Nausea and vomiting:*
 - More often in CD than in UC
- *Sometimes IBD has nonspecific gastrointestinal symptoms:*
 - *Gastric or duodenal Crohn disease manifests as seemingly refractory peptic ulcer disease*

J. Larry Jameson, Anthony S. Fauci, Dennis L. Kasper, Stephen L. Hauser, Dan L. Longo, Joseph Loscalzo

TABLE 319-6

Diseases That Mimic IBD

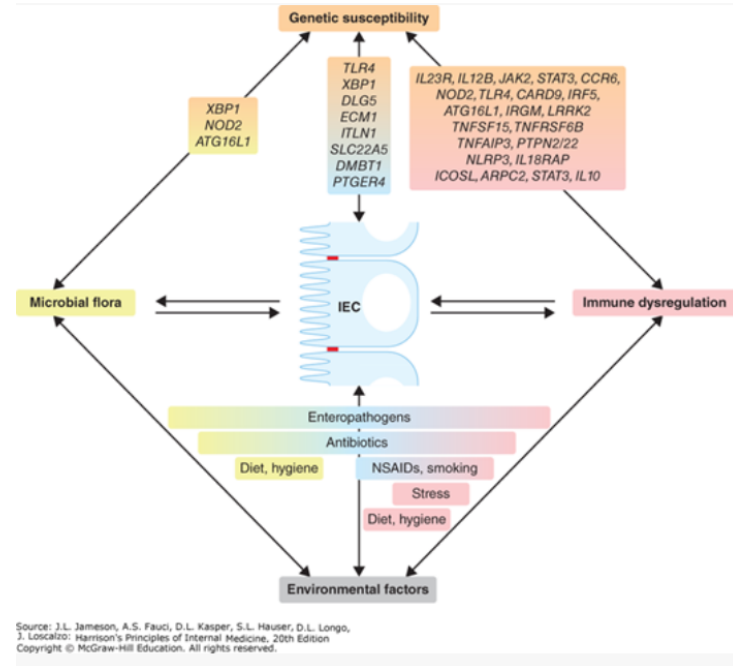
Infectious Etiologies		
Bacterial	Mycobacterial	Viral
<i>Salmonella</i>	Tuberculosis	Cytomegalovirus
<i>Shigella</i>	<i>Mycobacterium avium</i>	Herpes simplex
Toxigenic		HIV
<i>Escherichia coli</i>	Parasitic	Fungal
<i>Campylobacter</i>	Amebiasis	Histoplasmosis
<i>Yersinia</i>	<i>Isospora</i>	<i>Candida</i>
<i>Clostridium difficile</i>	<i>Trichuris trichiura</i>	<i>Aspergillus</i>
Gonorrhea	Hookworm	
<i>Chlamydia trachomatis</i>	<i>Strongyloides</i>	
Noninfectious Etiologies		
Inflammatory	Neoplastic	Drugs and Chemicals
Appendicitis	Lymphoma	NSAIDs
Diverticulitis	Metastatic	Phosphosoda
Diversion colitis	Carcinoma	Cathartic colon
Collagenous/lymphocytic colitis	Carcinoma of the ileum	Gold
		Oral contraceptives
Ischemic colitis	Carcinoid	Cocaine
Radiation colitis/enteritis	Familial polyposis	Ipilimumab
		Mycophenolate mofetil
Solitary rectal ulcer syndrome		
Eosinophilic gastroenteritis		
Neutropenic colitis		
Behçet's syndrome		
Graft-versus-host disease		

Abbreviation: IBD, inflammatory bowel disease; NSAIDs, nonsteroidal anti-inflammatory drugs.

IBD Review

IBD = Chronic state of dysregulated inflammation

- The normal homeostasis between
 - *Microbiota*
 - *Epithelial cells that line interior of intestines (Intestinal Epithelial Cells- IECs)*
 - *Immune cells within tissues*
- Disrupted by
 - *Environment*
 - Antibiotics, smoking, enteropathogens, diet, NSAIDs
 - *Genetic factors*
 - Polygenic



Our Gut Microbiota

- Play crucial roles in:
 - *regulating our primary metabolism*
 - *protecting us from pathogens*
 - *developing our immune system*
- IBD = Imbalances in the intestinal bacterial community have been implicated in many diseases
 - *Extensive microbiome sequencing studies*
 - *Higher pro-inflammatory bacteria (*Ruminococcus gnavus*) present in IBD (CD specifically) than in rest of population*

EPIDEMIOLOGY

- Westernized nations
- Environmental factors + similar genetic backgrounds
- Bimodal distribution
 - *Second through Fourth decades (20-29)*
 - *Seventh through Ninth decades*
- Not gender specific
- Jewish > Non-Jewish Caucasian > African Americans > Hispanic > Asian
- Urban > Rural
- Higher socioeconomic status > lower socioeconomic status

EPIDEMIOLOGY

- Smoking
 - *May prevent UC*
 - *May cause CD*
- OCP use may increase incidence of CD
- Appendectomy for confirmed appendicitis (before age 20) may protect against developing UC
- Antibiotic use within first year of life → 2.9 x increased risk of IBD in childhood
- Breastfeeding may be protective

EPIDEMIOLOGY

- Infection with
 - *Salmonella, Shigella, Campylobacter or C. Diff increases risk of IBD 2-3 x*
- Diet
 - *High in animal protein, sugars, sweets, oils, fish and shellfish, high omega 6 and low omega 3 dietary fat → increased risk of IBD*
- Appendectomy for confirmed appendicitis (before age 20) may protect against developing UC
- 5-10% familial association
 - *The rest are sporadic IBD*
 - *1 parent with IBD 10% chance in children*
 - *2 parents with IBD 36% chance in children*

EPIDEMIOLOGY

- African American > Non-Hispanic white
 - *Develop esophagoduodenal CD, colorectal and perianal disease*
 - *Less likely to have ileal involvement*
 - *More likely to have uveitis and sacroiliitis*
- Hispanic
 - *Increased incidence of perianal CD, erythema nodosum, and proximal extent of dz*
- Fistulizing CD
 - *1/3 Hispanic*
 - *1/4 African American*
 - *1/2 Asian*

INFLAMMATORY BOWEL DISEASE

ULCERATIVE COLITIS

- Continuous
- Mucosal
- Rectum → Proximal
- Backwash ileitis
- Increased risk of Colon CA
 - *Surveillance colonoscopy with multiple biopsies*
 - *Risk factors include long-duration disease, extensive disease, family history of colon cancer, PSC, a colon stricture, and the presence of post inflammatory pseudopolyps on colonoscopy*

CROHN DISEASE

- Skip lesions
- Transmural
- Anywhere in GI tract
- Rectum typically spared
- TI involvement in 90%
- Cobblestoning
- Non-caseating granulomas
- Fistulas, Fissures, Abscess, Stenosis
- Increased risk of Colon CA (Crohn colitis)
 - *Surveillance colonoscopy with multiple biopsies*
 - *Risk factors include are long-duration and extensive disease, bypassed colon segments, colon strictures, PSC, and family history of colon cancer*

TABLE 319-5

Different Clinical, Endoscopic, and Radiographic Features

	Ulcerative Colitis	Crohn's Disease
Clinical		
Gross blood in stool	Yes	Occasionally
Mucus	Yes	Occasionally
Systemic symptoms	Occasionally	Frequently
Pain	Occasionally	Frequently
Abdominal mass	Rarely	Yes
Significant perineal disease	No	Frequently
Fistulas	No	Yes
Small intestinal obstruction	No	Frequently
Colonic obstruction	Rarely	Frequently
Response to antibiotics	No	Yes
Recurrence after surgery	No	Yes
Endoscopic		
Rectal sparing	Rarely	Frequently
Continuous disease	Yes	Occasionally
"Cobblestoning"	No	Yes
Granuloma on biopsy	No	Occasionally
Radiographic		
Small bowel significantly abnormal	No	Yes
Abnormal terminal ileum	No	Yes
Segmental colitis	No	Yes
Asymmetric colitis	No	Yes
Stricture	Occasionally	Frequently

Associated symptoms

- Anorexia
 - *Fear of eating*
- Nausea +/- Vomiting
- Weight loss
- Malaise
- Fever
 - *Typical low grade, high grade think complication like abscess*

Extraintestinal manifestations

DERMATOLOGIC

- Erythema nodosum (EN)
- Pyoderma gangrenosum (PG)
- Psoriasis
- Perianal skin tags
- Oral mucosal lesions
 - include aphthous stomatitis and “cobblestone” lesions of the buccal mucosa

RHEUMATOLOGIC

- Peripheral arthritis
- Ankylosing spondylitis (AS)
- Sacroiliitis
- Hypertrophic osteoarthropathy, pelvic/femoral osteomyelitis, and relapsing polychondritis.

OCULAR

- Conjunctivitis
- Anterior uveitis/iritis
- Episcleritis

Extraintestinal manifestations

HEPATOBIILIARY

- Hepatic steatosis
- Cholelithiasis (occurs in 10–35% of CD patients with ileitis or ileal resection)
 - *caused by malabsorption of bile acids, resulting in depletion of the bile salt pool and the secretion of lithogenic bile.*
- Primary sclerosing cholangitis (PSC)- characterized by both intrahepatic and extrahepatic bile duct inflammation and fibrosis, frequently leading to biliary cirrhosis and hepatic failure;
 - *~5% of patients with UC have PSC, but 50–75% of patients with PSC have IBD*
 - *Gallbladder polyps in patients with PSC have a high incidence of malignancy and cholecystectomy is recommended*

UROLOGIC

- Renal calculi, ureteral obstruction, and ileal bladder fistulas

METABOLIC BONE DISORDERS

- Low bone mass
 - *absolute risk of an osteoporotic fracture is about 1% per person per year*
- Osteonecrosis developed within 6 months of starting glucocorticoids.

THROMBOEMBOLIC DISORDERS

- Patients with IBD have an increased risk of both venous and arterial thrombosis even if the disease is not active.

Work-Up

Should be done

- *CRP > ESR*
- *CBC*

Anemia, Leukocytosis, Thrombocytopenia

- *Iron studies*
- *Chemistry*

Electrolytes, Renal/Liver, Albumin

- *Stool Studies*

Stool culture (bacterial), C. Diff toxin, Ova and Parasite

Fecal lactoferrin

Indicates intestinal inflammation

Fecal calprotectin

Correlates with histologic inflammation- predict relapses and detect pouchitis



Work-Up prior to GI Consult

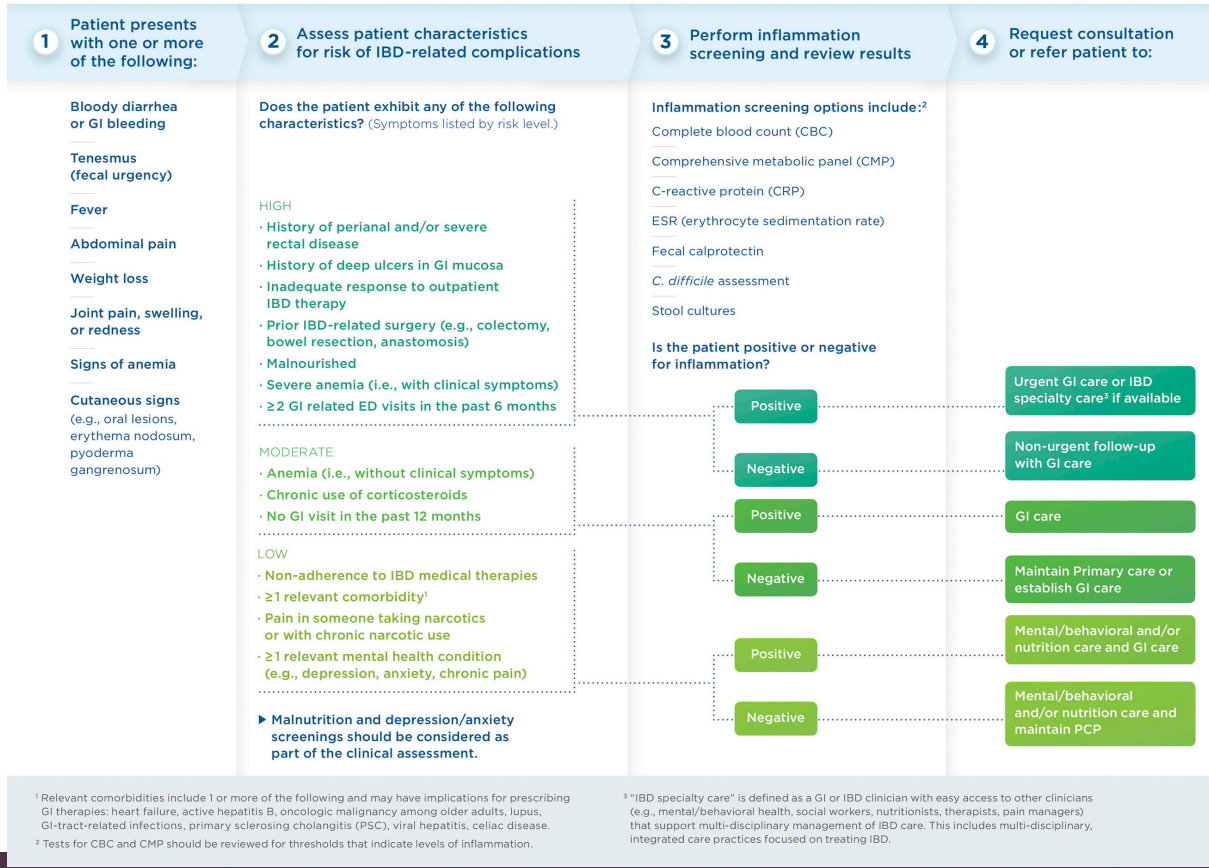
Could be considered

- *HIV*
 - Acid fast smear and culture (Mycobacterium avium intracellulare complex)
- *Gonorrhea, Chlamydia, Syphilis, CMV, HSV (proctitis)*
- *Magnesium and Calcium – low in CD with malabsorption*
- *B12*
- *Vitamin D*
- *IBD expanded profile*
 - Marginally helpful but depends on prevalence in certain population
 - pANCA (perinuclear antineutrophil cytoplasmic antibody)
 - *Typically more common in UC [60-70% compared to 5-10% in CD]*
 - ASCA (anti-saccharomyces cerevisiae antibody)
 - *Typically more common in CD [60-70% compared to 10-15% UC]*

Work-Up

- Diagnostic imaging
 - *Single contrast barium enema*
 - “String sign” – narrowing from inflammation or stricture in CD
 - “Lead pipe” colon = Loss of haustra in UC
 - *CT with IV and oral contrast*
 - *CT or MR Enterography (small bowel disease) Oral and IV contrast*
 - Small bowel follow through (SBFT)
 - *MR > CT for CD pelvic lesion concerns*
 - *Sigmoidoscopy*
 - *Colonoscopy*
 - *Esophagoduodenoscopy*

IBD CARE REFERRAL PATHWAY PRIMARY CARE PROVIDER SETTING



¹ Relevant comorbidities include 1 or more of the following and may have implications for prescribing GI therapies: heart failure, active hepatitis B, oncologic malignancy among older adults, lupus, GI-tract-related infections, primary sclerosing cholangitis (PSC), viral hepatitis, celiac disease.

² Tests for CBC and CMP should be reviewed for thresholds that indicate levels of inflammation.

³ "IBD specialty care" is defined as a GI or IBD clinician with easy access to other clinicians (e.g., mental/behavioral health, social workers, nutritionists, therapists, pain managers) that support multi-disciplinary management of IBD care. This includes multi-disciplinary, integrated care practices focused on treating IBD.

Questions?

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Resources

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