Overview of Inflammatory Bowel Diseases (IBD) for Healthcare Professionals

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REVIEWED BY THE CROHN'S & COLITIS FOUNDATION'S

PROFESSIONAL EDUCATION COMMITTEE

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Objectives

1. Recognize the impact of IBD
2. Recognize the causes of IBD
3. Describe the clinical features and symptoms of IBD
4. Identify the techniques used to diagnose IBD
5. Develop a treatment plan based on disease activity and severity
6. List treatment options for mild, moderate, and severe IBD
7. Discuss special populations in IBD

Overview of IBD

- Definition
- Incidence
- Pathogenesis
- Cost

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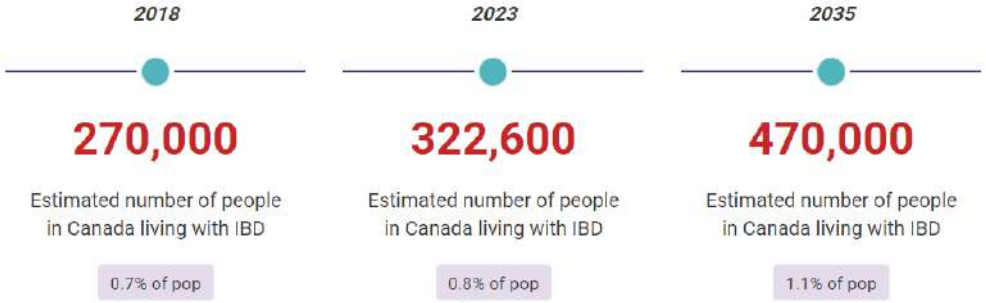
What Is Inflammatory Bowel Diseases?

- IBD is characterized by:
  - Chronic, immune-mediated inflammation in the gastrointestinal (GI) tract
  - Often has a progressive, destructive course
- The two major forms of IBD are Crohn's disease (CD) and ulcerative colitis (UC)
- **IBD is *not* IBS (irritable bowel syndrome)**
- Incidence of IBD has significantly increased over time in the U.S.
- An estimated 1.6-3.1 million are living with Crohn's or ulcerative colitis in the U.S.



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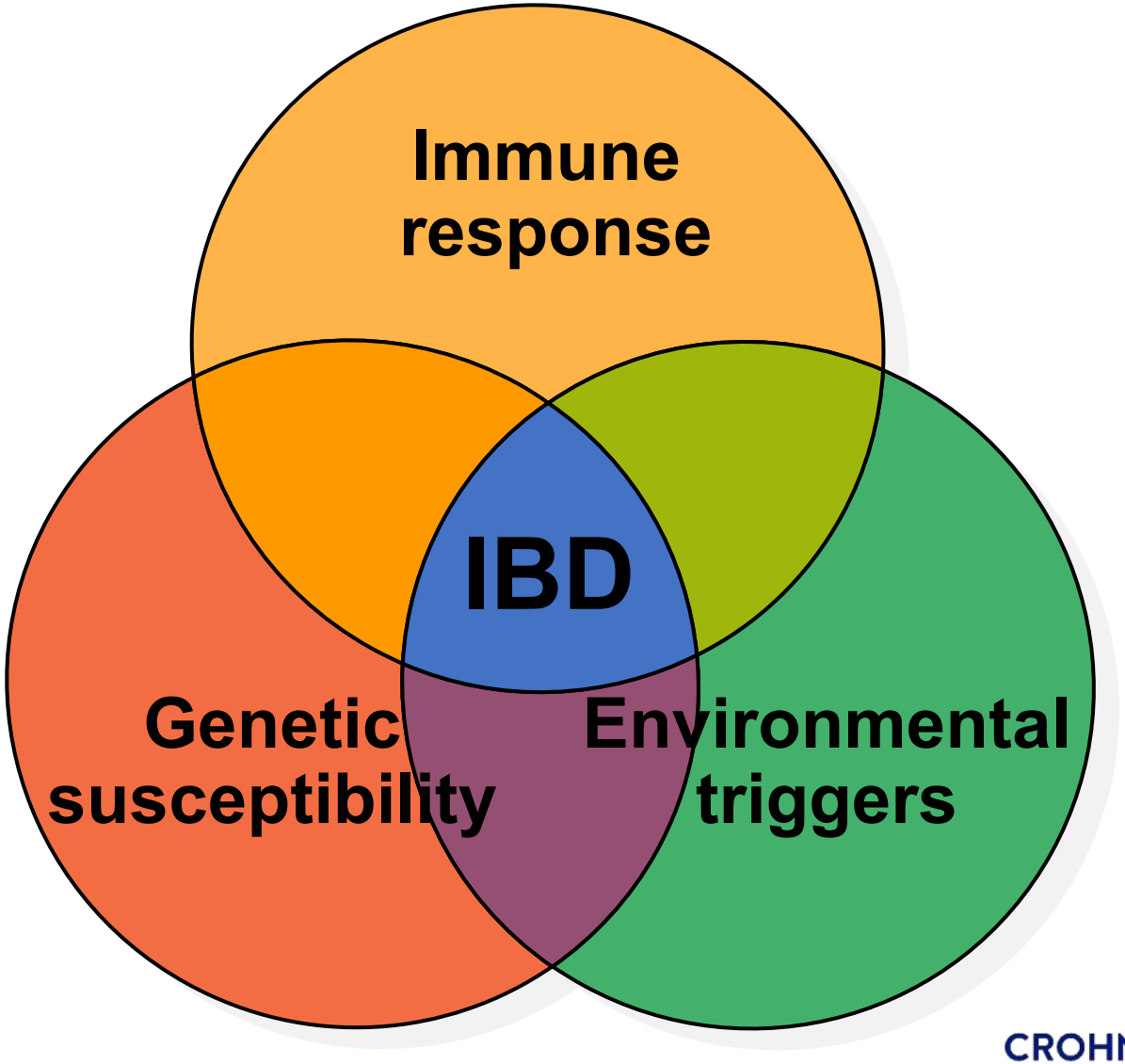
Pathogenesis of IBD



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Diagnosis of IBD

- Goals
- Differential Diagnosis
- Algorithm
- Clinical Features
- Symptoms
- Colonoscopy & Endoscopy
- Pathology
- Extraintestinal Manifestations

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Diagnosis of IBD

- Diagnostic goals should include:
  - Determining if CD vs. UC
    - Up to 10% are diagnosed as indeterminate colitis
  - Mapping the extent of disease burden
  - Identifying disease behavior (specifically for CD)
  - Recognizing severity
- There is no “gold standard” test for diagnosing IBD
- Must utilize history, exam findings, family history and diagnostic testing

Differential Diagnosis When Considering IBD

- Infectious colitis (including *Clostridiodes difficile*)
- Ischemic colitis
- Drug-induced (NSAID) enterocolitis
- Solitary rectal ulcer syndrome
- Radiation enterocolitis
- Sexually transmited infections
- Diversion colitis
- Endometriosis
- Malignancy
- Functional disorder (especially irritable bowel syndrome)
- Diverticular disease

Learn more about the most common conditions misdiagnosed as IBD at: www.crohnscolitisfoundation.org/clinical-pearls

Adapted from: Forcione DG, Sands BE. In: Sartor RB, Sandborn WJ. *Kirsner's Inflammatory Bowel Diseases.* 6th ed. New York, NY: Saunders; 2004:359-379.

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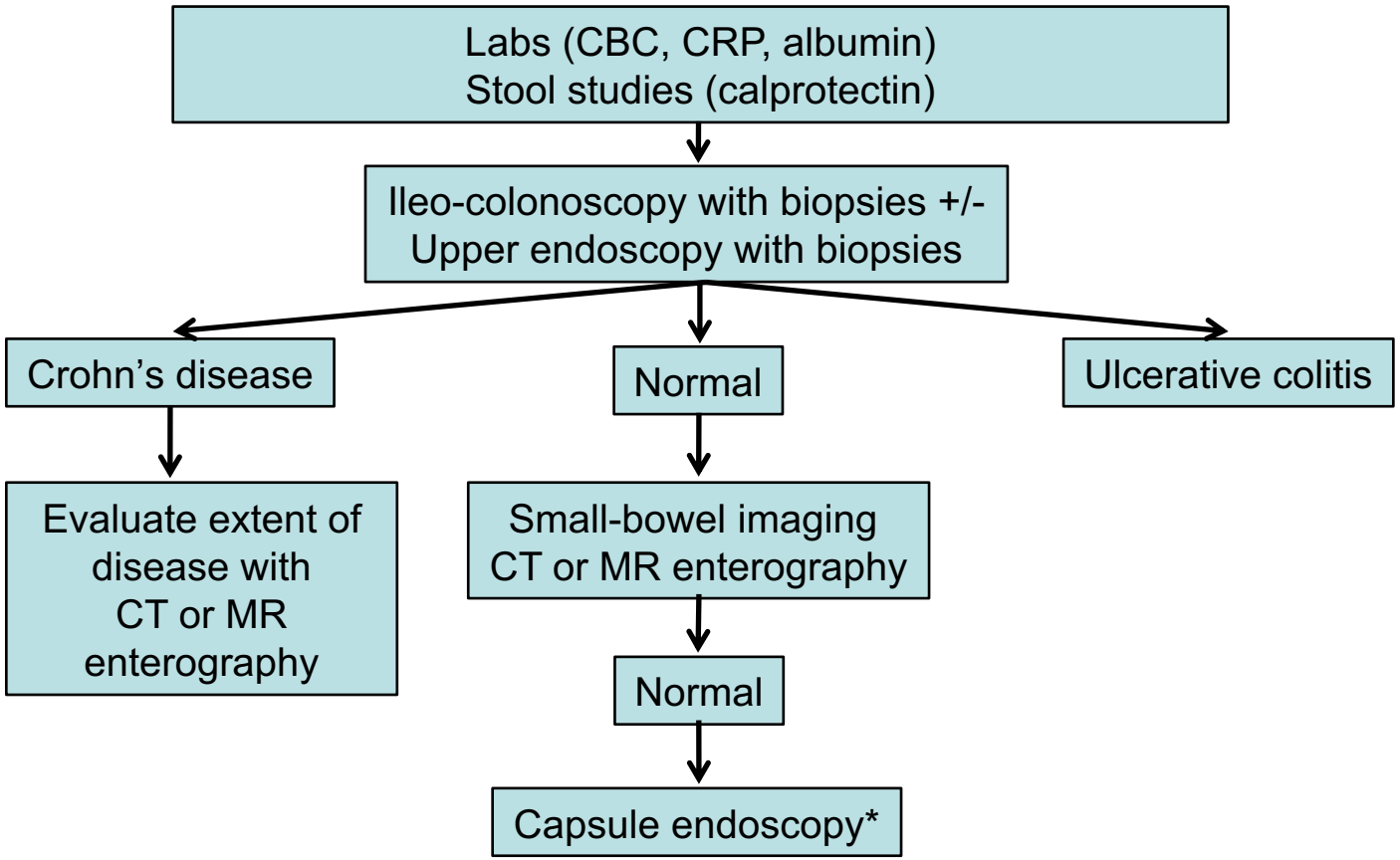
Proposed IBD Diagnostic Algorithm for First Presentation



*Consider if inflammatory markers are elevated, if iron deficiency is present or if there is elevated fecal calprotectin with negative prior diagnostic workup. Use with caution in patients with potential strictures.

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Clinical Features of UC and CD

Ulcerative Colitis	Crohn's Disease
Colon and rectum	Any part of the GI tract
Rectum universally involved	Rectum involved in 10% of cases
Mucosal and submucosal injury	Transmural injury that may lead to strictures or fistulae including perianal involvement
Continuous pattern of inflammation	Skip lesions
Acute onset	Insidious onset

~10% do not fit into either group and are deemed indeterminate colitis

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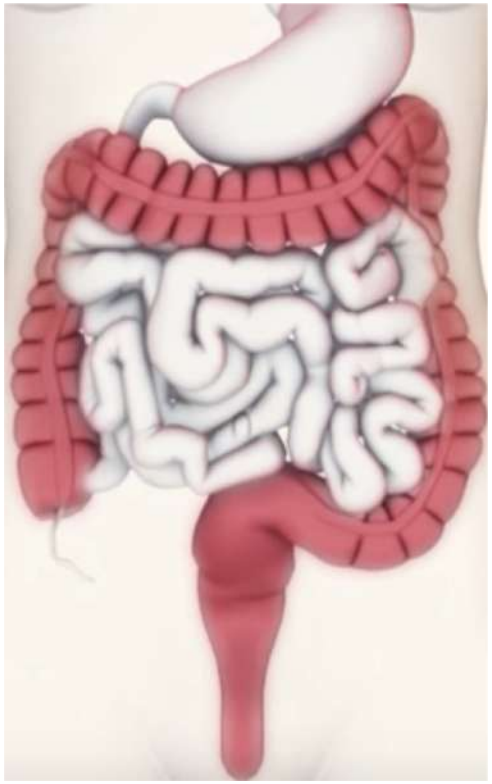
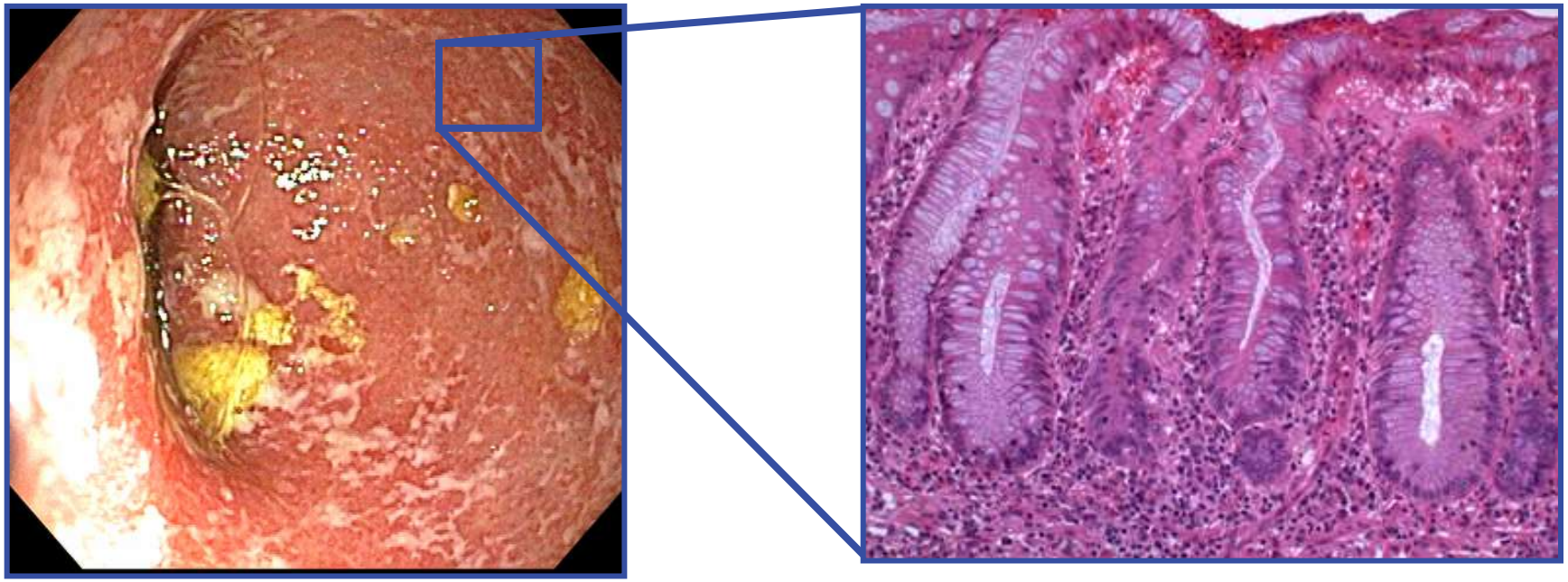
Predominant Symptoms of UC

- Rectal bleeding
- Frequent, small volume, loose stools
- Mucous discharge from the rectum
- Tenesmus, urgency, rectal pain
- Abdominal pain



Basson MD. Ulcerative colitis. http://emedicine.medscape.com/article/183084-overview. Updated February 14, 2017.

Ulcerative Colitis: Colonoscopy and Biopsy



Diffuse, prominent crypt architectural distortion and mucosal atrophy, with foci of crypt dropout. No granulomas.

Images courtesy of David T. Rubin, MD

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Endoscopic Severity of UC Using Mayo Score

Mayo Endoscopic Subscore	
Mucosal appearance at endoscopy	
Normal or inactive disease	0
Mild disease (erythema, decrease vascular pattern, mild friability)	1
Moderate disease (marked erythema, absent vascular pattern, friability, erosions)	2
Severe disease (spontaneous bleeding, ulceration)	3

Adapted from Lemmens et al. *Inflamm Bowel Dis.* 2013; 19(6): 1194-1201.

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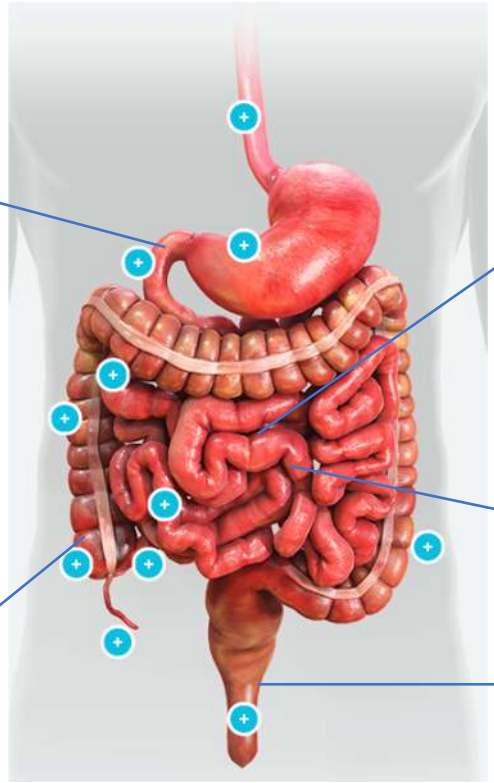
Clinical Features of CD: Depend on Location & Phenotype

1. **Inflammatory**
Small bowel:
abdominal pain, diarrhea, fever
Colonic:
diarrhea +/- hematochezia, weight loss, fever

2. **Stricturing**
Bowel obstructions

3. **Penetrating**
Abscesses, fistulae



Farmer RG, et.al. *Dig Dis Sci*. 1993;38(6):1137-1146.

Feuerstein D et. al. Mayo Clin Proc. 2017; 92(7):1088-1103

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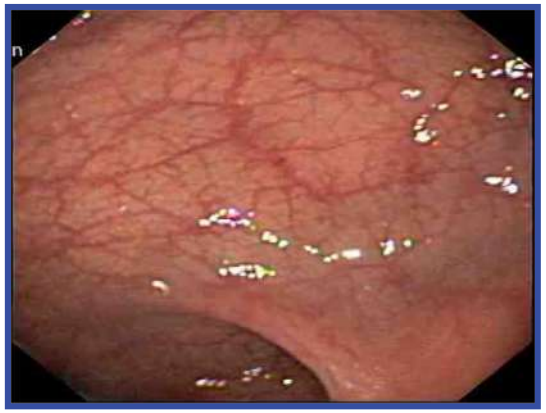
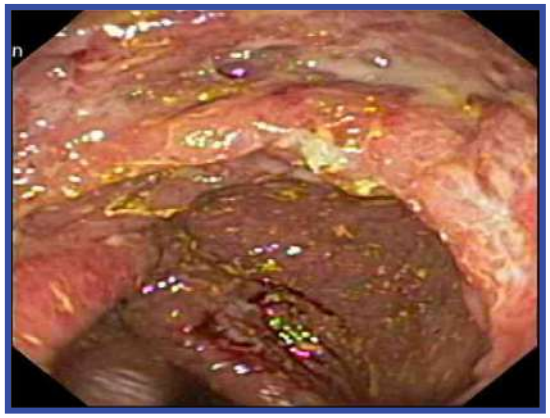
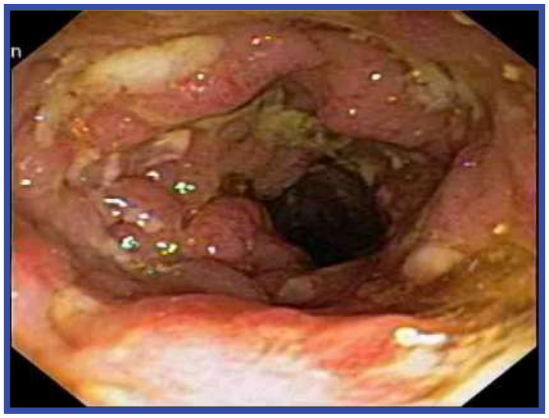
Endoscopy in CD



Normal Colon



Deep Ulceration



Ulcerations in the Ileum

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Endoscopic Severity of CD: Simple Endoscopic Score (SES-CD)

Variables	0	1	2	3
Size of ulcers, cm	None	0.1-0.5	0.5-2	>2
Ulcerated surface, %	None	<10	10-30	>30
Affected surface, %	Unaffected segment	<50	50-75	>75
Presence of stenosis	None	Single, can be passed	Multiple, can be passed	Cannot be passed

Adapted from Takenaka et al. *Inflamm Bowel Dis.* 2015; 21(8): 1832–1838.

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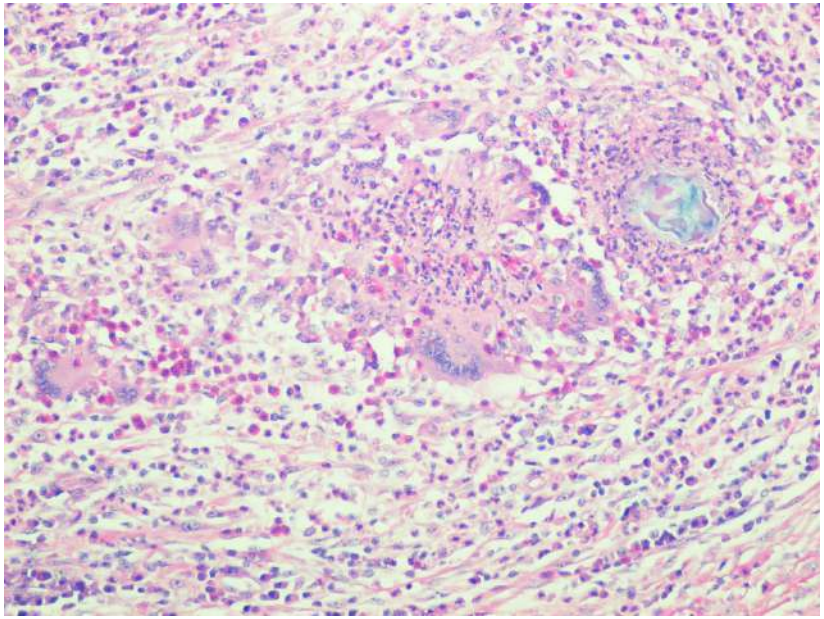
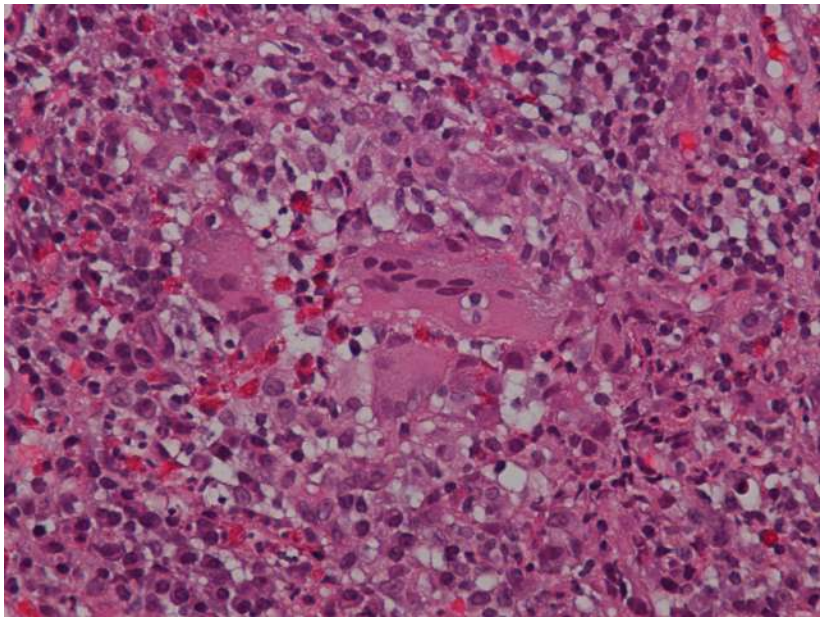
Pathology of CD: Transmural Inflammation & Granulomata





Images courtesy of Dr. Robert Lippman, McGuire VA Medical Center, Richmond, Virginia

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Extraintestinal Manifestations of IBD

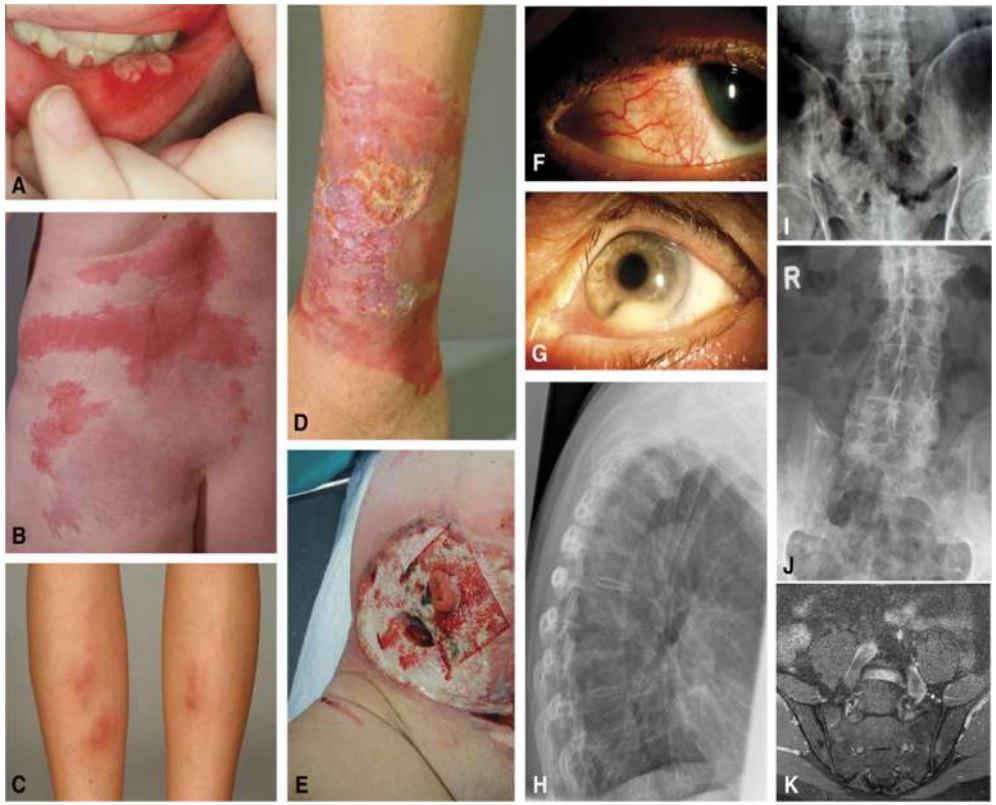

Figure 1. A, Oral aphthous ulcers, (B) Sweet's syndrome, (C) erythema nodosum, (D) pyoderma gangrenosum, (E) peristomal pyoderma gangrenosum, (F) episcleritis, (G) uveitis with hypopyon and dilated iris vessels, (H) conventional x-ray of the lateral spine demonstrating syndesmophytes (bamboo spine), (I) plane radiograph of the ileosacral joints with bilateral sacroiliitis, (J) plane radiography of the sacrum with bilateral ankylosis, (K) coronal magnetic resonance image of the sacroiliac joints with active inflammation mainly on the left side and chronic inflammatory changes on both sides.

Adapted from: Vavricka R. et al *Inflamm Bowel Dis.* 2015; 21(8): 1982-1992

Treatment of IBD

- Approach & Goals
- Medication Options for Mild, Moderate, & Severe IBD
- Adverse Effects

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Treatment of IBD

- Need to determine appropriate treatment based on:
  - IBD-related characteristics:
    - Disease activity
    - Disease severity
    - Complications of IBD
    - Response to prior IBD treatment(s)
  - Non-IBD characteristics:
    - Current infection
    - Comorbidities

Modified from AGA Institute Guidelines for the Identification, Assessment and Initial Medical Treatment in Crohn's Disease Clinical Decision Support Tool available at: https://s3.amazonaws.com/agaassets/pdf/guidelines/IBDCarePathway.pdf

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Determining Disease Activity and Severity

- Disease ***activity*** is based on:
  - Patient-reported outcomes (PROs)
    - Using disease activity scores, i.e. Harvey-Bradshaw Activity Index (CD), Modified Mayo Score or the Simple Clinical Colitis Activity Score for UC
  - Inflammatory burden
    - Based on extent of disease and severity of endoscopic findings and/or other non-invasive markers of inflammation, such as fecal calprotectin, ESR or CRP
- Disease ***severity*** is based on:
  - Risk factors for more severe disease prognosis

Siegel CA, Whitman CB, Spiegel BMR, *et al* Development of an index to define overall disease severity in IBD. Gut 2018;67:244-254.

Disease Activity for UC Using Simple Clinical Colitis Activity Index

SCCAI Remission < 2.5
Bowel frequency (day)
0 = 1–3
1 = 4–6
2 = 7–9
3 = >9
Bowel frequency (night)
1 = 1–3
2 = 4–6
Urgency of defecation
1 = hurry
2 = immediately
3 = incontinence
Blood in stool
1 = trace
2 = occasionally frank
3 = usually frank
General well-being
0 = very well
1 = slightly below par
2 = poor
3 = very poor
4 = terrible
Arthritis, pyoderma gangrenosum, erythema nodosum, uveitis
1 per manifestation

Extracolonic features include arthralgia, uveitis, rash, oral ulcers.

Score of < 4 is inactive disease.

Adapted from: Bewtra et al *Inflamm Bowel Dis.* 2015; 20(6): 1070-1078.

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Disease Activity for CD Using Harvey Bradshaw Activity Index

- Score* based on parameters of:
  - 1)Well-being of the patient (Score 0-4)
  - 2)Abdominal pain (Score 0-3)
  - 3)Number of liquid or soft stools (Score of 1 for each liquid bowel movement)
  - 4)Abdominal mass (Score 0-3)
  - 5) Complications (Score 1 per complication)

*Total score determines inactive disease (<5), mild disease (5-7), moderate disease (8-16), or severe disease (>16)

Can be found at: https://www.igibdscores.it/en/info-hbi.html

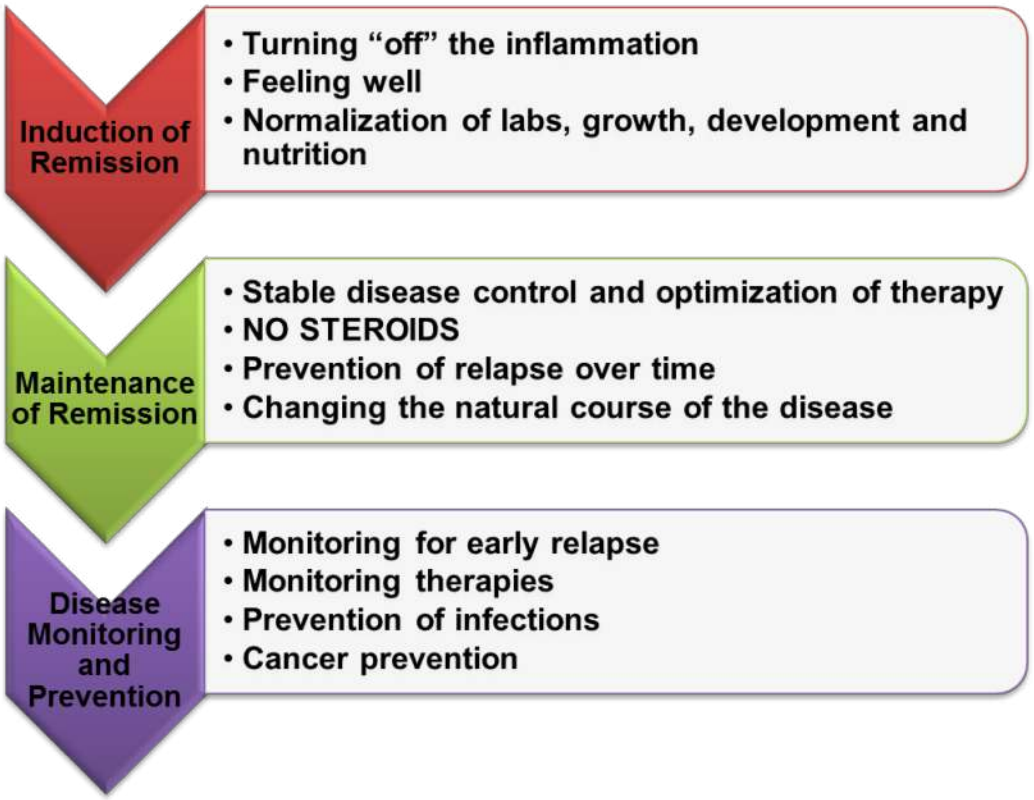
Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet 1980; 315 (8167): 514; IGIBD Scores https://www.igibdscores.it/en/info-hbi.html

Risk Factors for Having Severe or Complicated IBD

Ulcerative Colitis	Crohn's Disease
Age < 40 at diagnosis	Age < 30 at diagnosis
Extensive colonic involvement	Extensive anatomic involvement
Severe endoscopic disease activity (i.e. Mayo score ≥3, UCEIS ≥7)	Perianal and/or severe rectal disease
Requiring hospitalization for colitis	Deep ulcers
Elevated C-reactive protein	Prior surgical resection
Low serum albumin	Stricturing and/or penetrating behavior

1. Modified from Rubin DT et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastro 2019;114:384-419
2. Modified from AGA Institute Guidelines for the Identification, Assessment and Initial Medical Treatment in Crohn's Disease Clinical Decision Support Tool available at: https://s3.amazonaws.com/agaassets/pdf/guidelines/IBDCarePathway.pdf; *Gastroenterology* 2014 147702-705DOI: (10.1053/j.gastro.2014.07.022) Copyright © 2014

Goals of Treatment for IBD Patients



- Clinical remission (i.e. IBD symptoms have resolved)
- Mucosal improvement (i.e. overall decrease in mucosal inflammation)
- On a steroid-free treatment regimen

The medication that works best is the one your patient will take consistently.

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Why Is Mucosal Healing Important?

- In clinical practice, mucosal healing should guide medical therapy
  - Symptoms do not always correlate with mucosal inflammation
  - Need to assess disease activity prior to making medication changes
  - Growing evidence that mucosal healing is an important goal because it appears to be associated with improved long-term outcomes including:
    - Decreased likelihood of a flare
    - Decreased progression to disease complications
    - Decreased need for surgery and hospitalization

Pineton de Chambrun G, et al. *Nat Rev Gastroenterol Hepatol.* 2010;7(1):15-29.

Treatment Options for Mild IBD

Medication	CD/UC	Induction	Maintenance	Administration
Corticosteroids	CD, UC	+	-	Oral, IV, Rectal
Budesonide	CD, UC	+	-	Oral
Aminosalicylates	UC	+	+	Oral, Rectal

Potential Adverse Effects of Treatments for Mild IBD

Medication	Possible Adverse Effects
Corticosteroids	Sleep and mood disturbances, hypertension, glucose intolerance, cataracts, osteoporosis, myopathy, glaucoma, acne, edema, increased risk of infections
Budesonide	Headache, acne, nausea
Aminosalicylates	Nephrotoxicity, interstitial nephritis, nausea, GI disturbance, paradoxical diarrhea

1. Rubin DT et al. *Am J Gastroenterol*. 2019;114(3):384-413.
2. Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113(4):481-517.

Treatment Options for Moderate – Severe IBD

Medication	CD/UC	Induction	Maintenance	Administration
Thiopurines	CD, UC	-	+	Oral
Methotrexate	CD	-	+	Oral, IM
Anti-TNF Agents	CD, UC	+	+	IV, SC
Vedolizumab	CD, UC	+	+	IV, SC coming soon
Natalizumab	CD	+	+	IV
Ustekinumab	CD, UC	+	+	IV induction, SC maintenance
Tofacitinib	UC	+	+	Oral

Abbreviations: IM=intramuscular; anti-TNF= anti-tumor necrosis factor; IV=intravenous; SC=subcutaneous

1. Rubin DT et al. *Am J Gastroenterol*. 2019;114(3):384-413.
2. Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113(4):481-517.

Adverse Effects: Treatments for Moderate-Severe IBD

Medication	Possible Adverse Effects
Thiopurines	Bone marrow suppression, hepatotoxicity, pancreatitis, pneumonitis, GI upset, rash, alopecia, fever, arthralgia, lymphoproliferative disorders, myeloid neoplasias, hepatosplenic T-cell lymphoma (young males), non-melanoma skin cancer, hemophagocytic lymphohistiocytosis (after EBV or CMV infection)
Methotrexate	Bone marrow suppression, alopecia, hepatic fibrosis, hypersensitivity pneumonitis, increased risk of infection
Anti-Tumor Necrosis Factor Agents	Increased risk of infection, infusion or injection site reactions, dermatologic and neurologic manifestations, melanoma, lymphoma
Vedolizumab	Upper respiratory tract infections, infusion related reaction
Natalizumab	Headache, rash, nausea, increased risk of infection, infusion related reaction, arthralgia, progressive multifocal leukoencephalopathy (in those with +JC virus antibody)
Ustekinumab	Injection site reaction, cold symptoms, headache, fatigue, increased risk of infection
Tofacitinib	Herpes Zoster, lipid abnormalities, venothromboembolism (specifically pulmonary embolism)

1. Rubin DT et al. *Am J Gastroenterol*. 2019;114(3):384-413.
2. Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113(4):481-517.

Prior to Starting Medications

Medication	Testing Prior to Starting	Recommended Monitoring
Mesalamines	Consider baseline renal function test	Annual renal function monitoring
Corticosteroids		Document plan for long-term therapy, consider ophthalmology exam, DEXA.
Thiopurines	TPMT enzyme activity, CBC and liver function	Routine CBC and liver function while on therapy
Methotrexate	CBC, liver and renal function	Routine CBC, liver and renal function monitoring while on therapy
Anti-Tumor Necrosis Factor Agents	TB screening prior to start, check Hepatitis B panel, CBC and liver function	Assess for TB exposure annually while on therapy; CBC and liver function routinely while on therapy
Vedolizumab	CBC and liver function	CBC and liver function periodically while on therapy
Natalizumab	Enrollment in CD Touch® Prescribing Program	Assess for signs/symptoms suggestive of PML, routine CBC and liver function testing, JC virus antibody testing every 6 months, per CD Touch® Prescribing Program
Ustekinumab	TB screening prior to start, check Hepatitis B panel, CBC and liver function	Assess for TB exposure annually while on therapy; CBC and liver function routinely while on therapy
Tofacitinab	CBC, liver, fasting lipid panel and TB	Assess for TB exposure annually while on therapy, routine CBC and liver function monitoring while on therapy; repeat fasting lipid panel 4-8 weeks after start of therapy.

1. Adapted from: Crohn's & Colitis Foundation; Diagnosing and Monitoring IBD Brochure. 2. Farray FA et al. Am J Gastro 2017;112(2):241-258. 3. Tysabri [Medication Guide/Package Insert]. Cambridge, MA: Biogen Inc. Revised August 2019.
4. Vedolizumab [Medication Guide/Package Insert]. Deerfield, IL: Takeda Pharmaceuticals, Inc; May 2014
5. Ustekinumab [Medication Guide/Package Insert]. Janssen Biotech, Inc. September 2016. 6. Tofacitinib [Medication Guide/Package Insert]. NY, NY: Pfizer. Revised December 2019.

Surgery as Treatment in IBD

- When to Consider

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When to Consider Surgery in IBD

- Prevalence
  - 10%–20% of patients with UC have surgery
  - Approximately 2/3 of Crohn's patients will need surgery
- Indications for surgery:
  - Dysplasia or cancer
  - Disease unresponsive to medications
    - Due to ongoing active symptoms, persistent fistulas or abscess
  - Intolerable medical side effects
  - Complication of disease
    - Stricture
    - Abscess
    - Fistulae
    - Toxic megacolon
    - Colonic perforation

Maggiori L. et al. Nat Rev Gastroetenterol Hepatol 2013;10:297-306.

Additional Considerations in IBD

- Special Populations

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Treating Special Populations with IBD

- During Pregnancy
  - Important for patients to be in remission prior to conception on a treatment regimen that can be safely continued throughout pregnancy
  - Ensure health maintenance is up-to-date prior to conception
  - Pregnancy educational video: https://www.crohnscolitisfoundation.org/science-and-professionals/education-resources/educational-videos-professionals
- Elderly Patients
  - Important to minimize polypharmacy
  - Long-term use of steroids is not appropriate maintenance treatment
- Patients with Prior Malignancy
  - No evidence that any IBD medications increases the risk for solid tumors
  - Discuss risks vs. benefits of treatment

1. Mahadevan U et al. Gastroenterology 2019;156:1508-1424.
2. Ha C et al. Clin Geriatr Med 2014;30:67-78.
3. Loo SY et al. J Crohns Colitis 2019;13:1302-1310.

Comprehensive Care for IBD

- Health Maintenance

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Health Maintenance Checklist for Adults with IBD

Vaccine-Preventable Illnesses	Which Patients	Check Titer	How Often
Influenza (non-live)	All	No	Annually
PCV13 (Prevnar) and PPSV23 (Pneumovax)	All ≥ 65 years All on/planning immunosuppression[1]	No	• If ≥ 65 years: PCV13 then PPSV23, separated by ≥ 1 year • If ≥ 19 years AND immunosuppressed[1]: PCV13 then PPSV23 at least 8 weeks later; 2nd dose of PPSV23 after 5 years
Tdap	All	No	• 1[st] dose ≥ 19 years if not previously given • Tetanus and diphtheria toxoid (Td) booster every 10 years
HPV	All ≤ 26 years	No	3-dose series at 0, 1–2, and 6 months
Group B Meningococcal meningitis	Ages 16–23 at high risk	No	• MenB-4C, 2 doses, ≥ 1 month apart • MenB-FHbp, 2 doses, ≥ 6 months apart
Hepatitis A	All	Yes (HAV IgG)	• 2-dose series: Havrix at 0 and 6 months or Vaqta at 0 and 6–18 months apart • 3-dose series: Twinrix (HepA-HepB) 0, 1 and 6 months
Hepatitis B	All	Yes (HBsAg, HBsAb, HBc IgG)	• 2-dose series: Heplisav-B at least 4 weeks apart • 3-dose series: Engerix-B, Recombivax HB or Twinrix (HepA-HepB) given at 0, 1 and 6 months
MMR (live vaccine)*	If non-immune	Yes (IgG titers)	2-dose series, at least 4 weeks apart (≥ 4 weeks before immunosuppression[1])
Varicella/Chicken Pox (live vaccine)*	If non-immune	Yes (IgG titers)	• 2-dose series, 4–8 weeks apart (≥ 4 weeks before immunosuppression[1])
Zoster (recombinant vaccine preferred)	All patients > 50 Any starting tofacitinib	No	• 2-dose series, 2–6 months apart (minimum 4 weeks apart)

Cancer Prevention	Which Patients	How Often
Cervical PAP Smear	All women on systemic immunosuppression[1]	Annual
Full Skin Screen	All on systemic immunosuppression[1]	Annual
Colonoscopy	All with extensive disease for > 8 years	Every 1–3 years

Other Screenings	Which Patients	How Often
DEXA Scan	Women ≥ 65, and all at high risk[2]	Once identified, and no sooner than 2 years later based on DEXA findings
PPD or IGRA	Prior to anti-TNF or anti-IL-12/23	Once (annual repeat if potential TB exposure or in a high-risk region)
Smoking status	All	Annual
Depression check	All	Annual

https://www.crohnscolitisfoundation.org/science-and-professionals/education-resources/health-maintenance-checklists

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Summary

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Key Points

- The incidence and prevalence of IBD in the U.S. And Canada are increasing
- The diagnosis of IBD is based on suggestive clinical symptoms, radiographic and/or endoscopic + pathologic findings consistent with Crohn's disease or ulcerative colitis
- The choice of treatment should be based on the disease activity (i.e. patient reported symptoms) and disease severity (i.e. risk factors suggestive of more complicated IBD)
- The goals of treatment are clinical remission (i.e. absence of symptoms) and mucosal improvement (i.e. decreased intestinal inflammation) on a steroid-free treatment regimen
- It is important to discuss the risks and benefits of treatment options with your patient prior to starting therapy to improve compliance
- Lab monitoring prior to starting and throughout treatment as well as ensuring preventive health measures are up-to-date can lower the risk of adverse effects from medication use

Crohn's & Colitis Foundation Resources

- For Healthcare Providers
- For Patients & Caregivers

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Crohn's & Colitis Foundation Resources

For Healthcare Providers:

- Online modules on diagnosis, treatment, and surgery
- Fact sheets on nutrition & anemia
- GI Tract Guide
- Educational videos on pregnancy, TDM, biosimilars
- Live training opportunities
- Clinical Pearls
- Online community
- Research Journals
- Dedicated webpage for PAs, NPs, RNs

www.crohnscolitisfoundation.org/prescribereducation

To Share With Your Patients:

- Brochures and fact sheets
- IBD stories
- Treatment options in UC and Crohn's disease
- Mental and emotional well-being
- Diet and nutrition
- Complementary medicine
- Youth and parent resources
- IBD help center
- Camp Oasis
- Financial and insurance information

www.crohnscolitisfoundation.org/

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Thank You

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