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## 2020 Third Annual National Conference

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# Updates in Ulcerative Colitis

Gabriella McCarty, RN, MSN, NP-C

North Shore Gastroenterology

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# Disclosures

**Gabriella McCarty, RN, MSN, NP-C**

Speakers Bureau: AbbVie, Clinical Area- IBD

Speakers Bureau: Allergan/Abbvie, Clinical Area- IBS-D, IBS-C, CIC

Speakers Bureau: Pfizer, Clinical Area- IBD

Speakers Bureau: Salix, Clinical Area- IBS, HE

Speakers Bureau: Janssen, Clinical Area- IBD

# Objectives

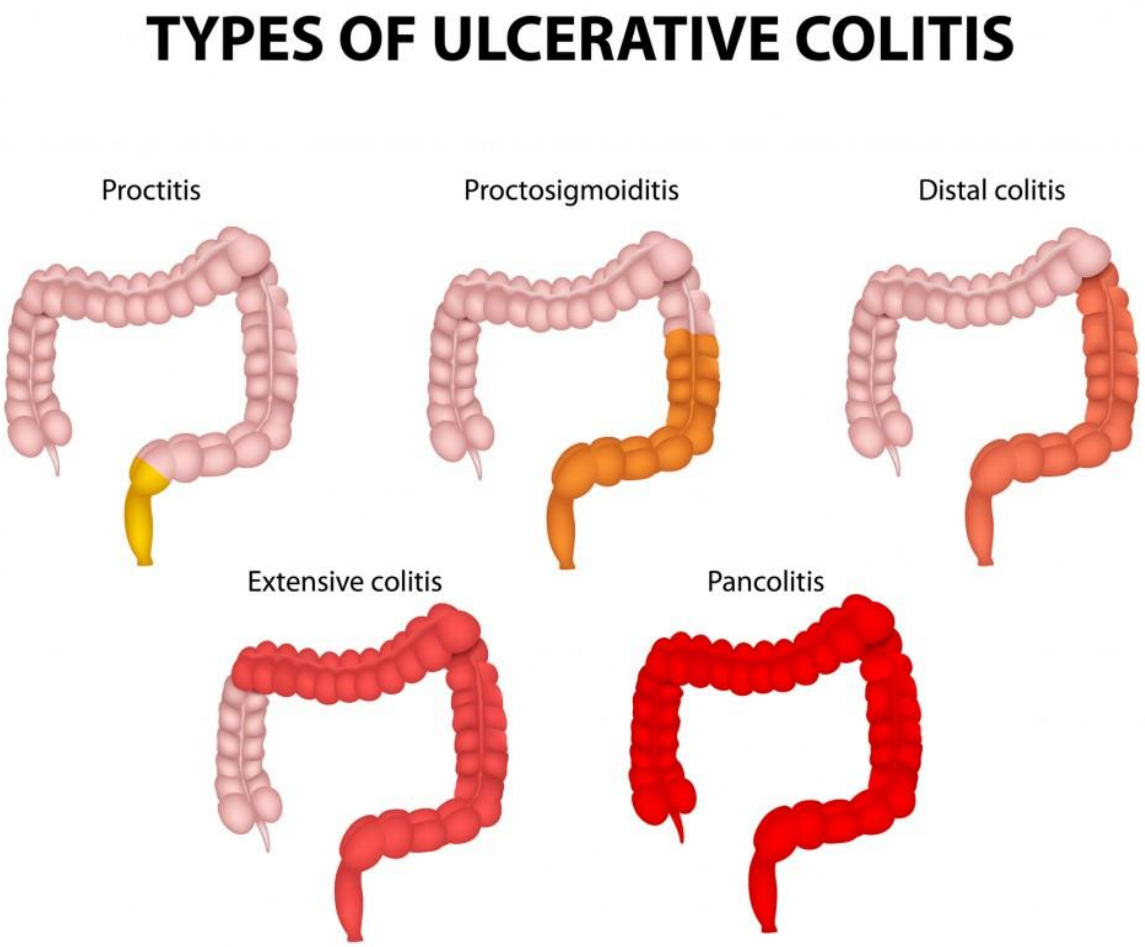
- Overview of ulcerative colitis (UC)
- Review current clinical treatment guidelines for UC
- Discuss upcoming diagnostics and treatment
- What is the role of APPs in UC patients

# Diagnosing UC

- Most common symptoms are rectal bleeding, urgency, tenesmus
- Rule out infectious causes of diarrhea (stool cultures, parasite screen, *C diff,* lactoferrin)
- Fecal calprotectin- noninvasive stool test that is a specific marker of inflammation indicative of disease activity and used to assess response and relapse of therapy
- Colonoscopy to ileum (*with biopsies of* affected and unaffected areas)
- Disease severity assessed by patient reported improvement of symptoms, endoscopic assessment of inflammation, disease course/treatment and disease impact of quality of life

Rubin DT et al. *Am J Gastroenterology*. 2019;114(3):384-413.

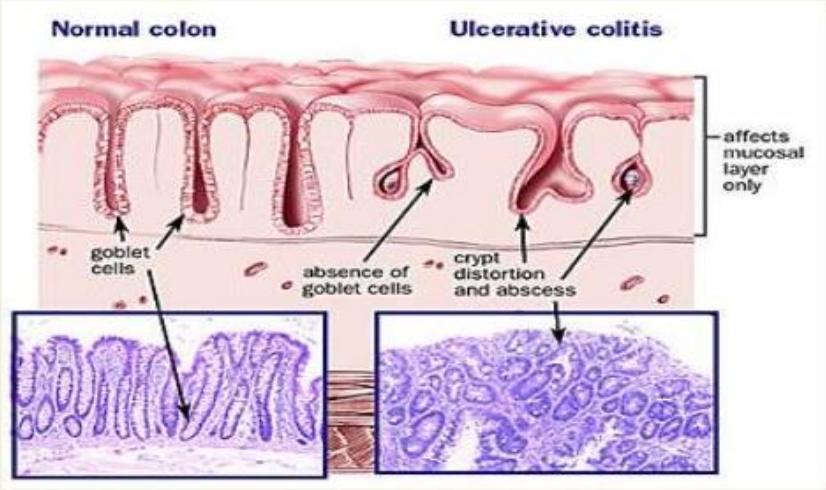
# Types of Ulcerative Colitis



# Symptoms Depend on Location

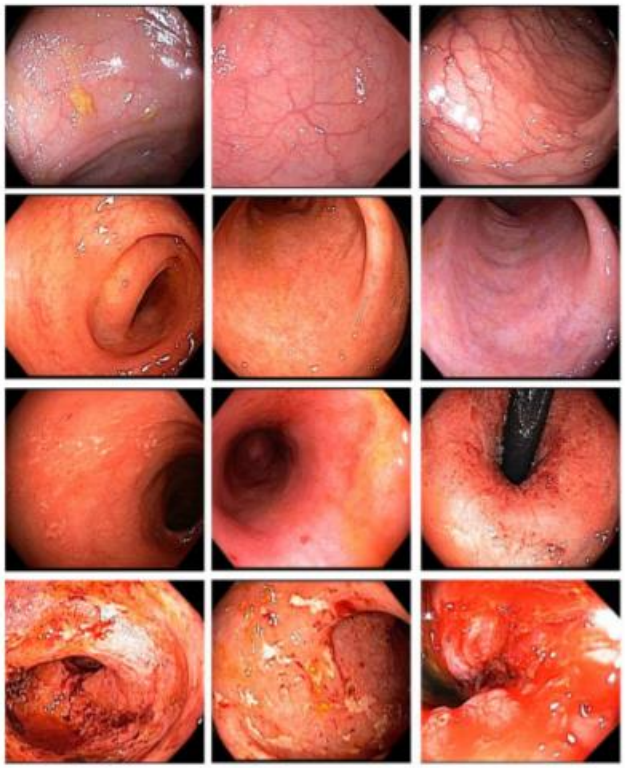
- Proctitis – constipation, tenesmus, rectal bleeding
- Proctosigmoiditis/left sided colitis – blood, mucous, frequency, urgency
- Pancolitis – passing only blood, abdominal pain, frequency, urgency, anemia, fatigue, anorexia, weight loss

# Pathology




- Limited to mucosa and submucosa of rectum and colon
- Distal, continuous involvement of colon
- Numerous ulcers with regenerating mucosa “pseudopolyps”, fissures, loss of vascular pattern, friable
- Neutrophil granulocyte formation
- Cryptitis

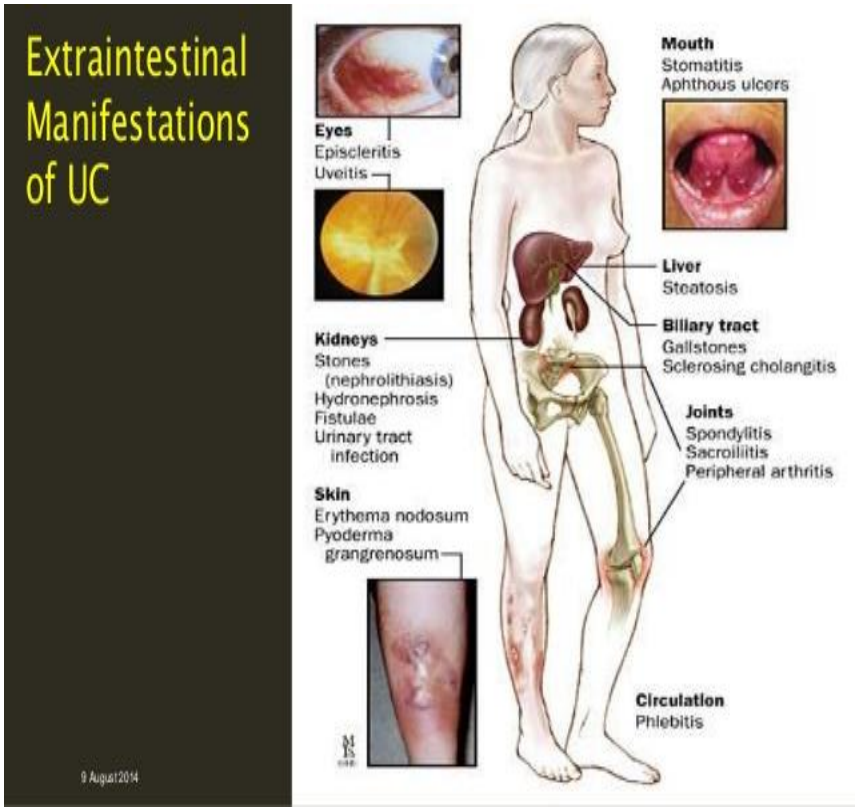
# Mayo Score in UC Endoscopy



| Endoscopic Assessment of Disease Activity | UCEIS Score | Mayo Score | Endoscopic Features |
|---|---|---|---|
| | 0 | 0 | Normal |
| | 1-3 | 1 | Erythema, decreased vascular pattern, mild friability |
| | 4-6 | 2 | Marked erythema, absent vascular pattern, friability, erosions |
| | 7-8 | 3 | Spontaneous bleeding, ulceration |

**Figure 1.** Sample endoscopic images of ulcerative colitis using the Mayo endoscopic subscore (49) and the Ulcerative Colitis Endoscopic Index of Severity (41). (Images courtesy of David T. Rubin, MD.)

# Extraintestinal Manifestations




- Arthritis (20%)
- Ankylosing spondylitis (3-5%)
- Erythema nodosum (10-15%)
- Pyoderma gandrenosum (rare)
- Primary Sclerosing Cholangitis (10%)

# What if UC Is Not Controlled?

- Significant morbidity and low incidence of mortality
- More likely to have psychological conditions of anxiety and depression and impaired social interactions or career progression
- Increased risk of dysplasia and colorectal cancer

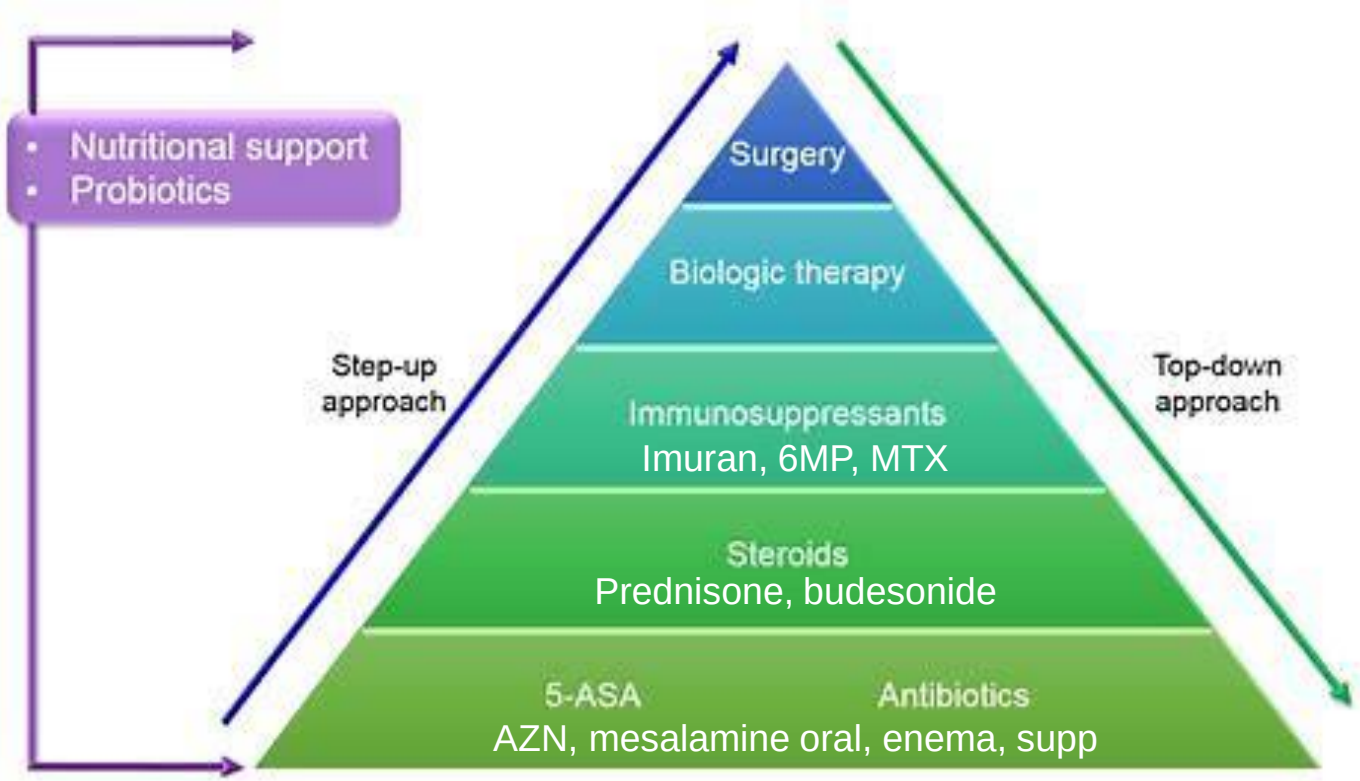
Rubin DT et al. *Am J Gastroenterology*. 2019;114(3):384-413.

# What Is the Goal?

- Inducing and maintaining both clinical and endoscopic remission
- Steroid-free remission
- Therapy is chosen based on activity, severity, extent of inflammation, prognostic factors

Rubin DT et al. *Am J Gastroenterology*. 2019;114(3):384-413.

# UC Treatment Pyramid




IBD Clinic 2020.
Ko et al. *Gastroenterology*. 2019; 156:748-764.

# Moderate-Severe UC Biologic Treatment

| | |
|---|---|
| **Anti-TNF** | Infliximab, adalimumab, golimumab<br>(biosimilars available for infliximab, adalimumab) |
| **Anti-integrins** | Vedolizumab |
| **JAK inhibitor** | Tofacitinib |
| **Interleukin-12/23 antagonist** | Ustekinumab |
| **Immunomodulators** | Thiopurines, methotrexate |

Feuerstein et al. *Gastroenterology*. 2020;158 :1450-1461).

# Emerging UC Treatment

- **Anti-integrins** Etrolizumab, abrilumab, AJM300, E6007
- **Anti-interleukins** Mirikizumab, brazikumab
- **JAK inhibitors** Upadacitinib, filgotinib, itacitinib, SHR0302
- **Jak 3 inhibitor/TYK2/Jak 1** PF-06651600/06700841
- **Pan-Jak** TD-1473/3504
- **S1P receptor modulators** Ozanimod, etrasimod
- **PSGL-1 agonist** Neihulizumab
- **DHODH inhibitor** IMU-83
- **DNA based synthetic immunomodulatory agent** Cobitolimod
- **Microbial therapies** FMT, SER-287
- **Stem cell therapy**
- **Anti-MadCAM-1** SHP647
- **REV inhibitor** ABX464
- **Adenisine A3 inhibitor** PBF-677
- **IL-6 inhibitor** Olamkicept
- **IL-22fc** UTTR1147A
- **Anti-IL 36** BI 655130
- **Anti-CD40** ABBV-323
- **LANCL2** BT-11
- **RIP1 kinase inhibitor** GSK2982772
- **Anti-OX40** KHK4083
- **TNFSF15 blocker** PF06480605

Clinicaltrials.gov

# Guidelines in UC

## ACG Clinical Guideline: Ulcerative Colitis in Adults

David T. Rubin, MD, FACG[1], Ashwin N. Ananthakrishnan, MD, MPH[2], Corey A. Siegel, MD, MS[3], Bryan G. Sauer, MD, MSc (Clin Res), FACG (GRADE Methodologist)[4] and Millie D. Long, MD, MPH, FACG[5]

**Ulcerative colitis (UC) is an idiopathic inflammatory disorder. These guidelines indicate the preferred approach to the management of adults with UC and represent the official practice recommendations of the American College of Gastroenterology. The scientific evidence for these guidelines was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process. In instances where the evidence was not appropriate for GRADE, but there was consensus of significant clinical merit, "key concept" statements were developed using expert consensus. These guidelines are meant to be broadly applicable and should be viewed as the preferred, but not only, approach to clinical scenarios.**

*Am J Gastroenterol 2019;114:384–413. https://doi.org/10.14309/ajg.0000000000000152; published online February 22, 2019*

INTRODUCTION

Ulcerative colitis (UC) is a chronic disease affecting the large intestine, with an increasing incidence worldwide. Nearly 1 million individuals each in the United States and Europe are affected by this condition and many more globally. Over the past decade, since the publication of the last guideline from the American College of Gastroenterology (ACG) on this topic, the management of disease has grown increasingly complex with availability of additional therapeutic classes. In addition, algorithms for initiating, optimizing, and monitoring response to existing therapies have undergone considerable evolution.

UC is a chronic immune-mediated inflammatory condition of the large intestine that is frequently associated with inflammation of the rectum but often extends proximally to involve additional areas of the colon. The absence of rectal involvement has been noted in fewer than 5% of adult patients with UC at diagnosis but may be seen in up to one-third of pediatric-onset colitis (1). The initial presentation of new UC is characterized by symptoms of an inflamed rectum, namely, bleeding, urgency, and tenesmus (a sense of pressure). The condition may present at any time and at all ages, but there is a predominant age distribution of onset that peaks between ages 15 and 30 years. The pattern of disease activity is most often described as relapsing and remitting, with symptoms of active disease alternating with periods of clinical quiescence, which is called remission. Some patients with UC have persistent disease activity despite diagnosis and medical therapy, and a small number of patients present with the rapid-onset progressive type of colitis known as fulminant disease (2,3).

UC causes significant morbidity and a described low incidence of mortality (4,5). Patients with active disease are more likely to have comorbid psychological conditions of anxiety and depression and are more likely to have impaired social interactions or career progression (6). Long-standing UC is also associated with a defined risk of dysplasia and colorectal cancer, which is believed to be related to long-standing unchecked inflammation (7–10).

Management of UC must involve a prompt and accurate diagnosis, assessment of the patient's risk of poor outcomes, and initiation of effective, safe, and tolerable medical therapies. The optimal goal of management is a sustained and durable period of steroid-free remission, accompanied by appropriate psychosocial support, normal health-related quality of life (QoL), prevention of morbidity including hospitalization and surgery, and prevention of cancer. An emerging goal in UC management is that of mucosal healing. To achieve these goals, understanding of the most effective diagnostic, treatment, and preventive strategies is necessary (11). As with any medical decision making, involvement of the patients' preferences forms an important component of care.

This clinical guideline addresses the diagnosis, treatment, and overall management of adult patients with UC, including an approach to the evaluation of the hospitalized patient and a separate section on colorectal cancer prevention. Additional recommendations regarding preventive care in inflammatory bowel disease (IBD) have been published by the ACG previously (12).

The guideline is structured in sections, each with recommendations, key concept statements, and summaries of the evidence. Each recommendation statement has an associated assessment of the quality of evidence and strength of recommendation based on the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process. The GRADE system was used to evaluate the quality of supporting evidence (Table 1) (13). A "strong" recommendation is made when the benefits clearly outweigh the negatives and/or the result of no action. "Conditional" is used when some uncertainty remains about the balance of benefits and potential harms. The quality of the evidence is graded from high to low. "High"-quality evidence indicates that further research is unlikely to change the authors' confidence in the estimate of effect and that we are very confident that the true effect

[1]Inflammatory Bowel Disease Center, University of Chicago Medicine, Chicago, IL, USA; [2]Division of Gastroenterology, Crohn's and Colitis Center, Massachusetts General Hospital, Boston, MA, USA; [3]Section of Gastroenterology and Hepatology, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; [4]Department of Medicine, University

Gastroenterology 2020;158:1400–1481

## CLINICAL PRACTICE GUIDELINES

### AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

Joseph D. Feuerstein,[1] Kim L. Isaacs,[2] Yecheskel Schneider,[3] Shazia Mehmood Siddique,[3] Yngve Falck-Ytter,[4,5] and Siddharth Singh,[6] on behalf of the AGA Institute Clinical Guidelines Committee

[1]Division of Gastroenterology and Center for Inflammatory Bowel Diseases, Beth Israel Deaconess Medical Center, Boston, Massachusetts; [2]Division of Gastroenterology and Hepatology, University of North Carolina School of Medicine, Chapel Hill, North Carolina; [3]Division of Gastroenterology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; [4]Division of Gastroenterology, Case Western Reserve University, Cleveland, Ohio; [5]Department of Veterans Affairs Northeast Ohio Healthcare System, Cleveland, Ohio; and [6]Division of Gastroenterology, University of California, San Diego, La Jolla, California

This document presents the official recommendations of the American Gastroenterological Association (AGA) on the management of moderate to severe ulcerative colitis (UC). The guideline was developed by the AGA Institute's Clinical Guidelines Committee and approved by the AGA Governing Board. It is accompanied by a technical review that provides a detailed synthesis of the evidence from which these recommendations were formulated.[1] Development of this guideline and the accompanying technical review was fully funded by the AGA Institute without additional outside funding. Members of the guideline panel and technical review panel were selected by the AGA Governing Board in consultation with the Clinical Guidelines Committee with careful consideration of all Institute of Medicine recommendations for clinical guideline development. Joseph Feuerstein was the guideline panel chair and Siddharth Singh was the methodologist and co-chair of the guideline panel. A patient representative was also included in the development and review process and had no recommended changes. The guideline and accompanying technical review underwent independent peer review, and a 30-day open public comment period; all comments were collated by the AGA staff, and were reviewed and carefully considered by the guideline panel and technical review teams, respectively. Changes were incorporated in revised documents, and where changes were not accepted, a thoughtful response document was created. After the public comment period, 2 pivotal clinical trials (VARSITY, UNIFI) were published and a critical safety update on tofacitinib was issued by the US Food and Drug Administration (FDA). At the recommendation of the Clinical Guidelines Committee, the technical review and clinical guidelines were updated to incorporate this new evidence as presented here. In accordance with the Clinical Guidelines Committee policies, all clinical guidelines are reviewed annually at the AGA Clinical Guideline Committee meeting for new information. The next update for these guidelines is anticipated in 3 years from publication.

UC is a chronic inflammatory bowel disease with peak onset in early adulthood.[2] Untreated, the natural history of the disease is one of relapsing and remitting mucosal inflammation. Based on population-based cohort studies, the majority of patients with UC have a mild to moderate course, generally most active at diagnosis and then in varying periods of remission or mild activity. Approximately 15% patients may experience an aggressive course, and 20% of these patients may require hospitalization for severe disease activity.[3,4] The 5- and 10-year cumulative risk of colectomy is 10%–15%, primarily limited to patients with moderate to severe disease activity; a subset of hospitalized patients with acute severe ulcerative colitis (ASUC) have short-term colectomy rates of 25%–30%.[5] Predictors of an aggressive disease course and colectomy are the following: young age at diagnosis (< 40 years old), extensive disease, severe endoscopic activity (presence of large and/or deep ulcers), presence of extra-intestinal manifestations, early need for corticosteroids, and elevated inflammatory markers.[6] For this guideline and the accompanying technical review, moderate to severe UC is defined based on the Truelove and Witts criteria and Mayo Clinic score (Table 1).[7–9] After excluding concomitant infections (such as *Clostridium difficile*), patients with moderate to severe disease are those who are dependent on or refractory to corticosteroids, have severe endoscopic disease activity (presence of ulcers), or are at high risk of colectomy. When reported, Mayo Clinic scores of 6–12 with an endoscopic subscore of 2 or 3 were considered moderate to severe disease. ASUC in this guideline is defined as hospitalized patients with the following Truelove and Witts criteria: ≥6 bloody bowel movements/day with at least 1 marker of systemic toxicity, including heart rate >90 beats/min, temperature >37.8°C, hemoglobin <10.5 g/dL, and/or erythrocyte sedimentation rate >30 mm/h.[9]

There are a number of different drug classes for long-term management of moderate to severe UC, including



IDENTIFICATION, ASSESSMENT AND INITIAL MEDICAL TREATMENT OF

## Ulcerative Colitis CLINICAL CARE PATHWAY


Review online at www.gastro.org/ucdecisiontool

# A Practical Approach for Biologic Therapy

| | |
|---|---|
| **Timing** | Early biologic therapy in moderate-severe disease, especially in the setting of high-risk features |
| **Selection** | Infliximab and vedolizumab favored (based on most studies) |
| **Safety considerations** | Anti-TNF therapy ~ very low absolute rate of risks; immunogenicity likely under recognized; Newer biologic therapies (ustekinumab, vedolizumab) ~ excellent safety profile, which may favor selection; Tofacitinib ~ multiple risks demonstrated, esp risk of PE, not recommended first line |
| **Special circumstances** | Acute severe UC- infliximab favored if response to salvage therapy with infliximab; Associated systemic condition- systemic therapy favored, anti-TNF, ustekinumab, tofacitinib) |
| **Other considerations** | Favorable safety profile, cost and insurance barriers, patient preference, optimization with proactive TDM |

Frasca J, Cheifetz, A. *Pract Gastroenterol*. 2020;Aug (XLIV-8):32-43.

# Comparative Effectiveness Studies in UC

| Study | Study Type | Outcomes | Findings |
|---|---|---|---|
| Singh et al. | Network meta-analysis | Induction of remission<br>Mucosal healing | Infliximag and vedolizumab superior to adalimumab and golibumab |
| Singh et al. | Network meta-analysis | Induction of remission<br>Endoscopic improvement | Infliximab superior to vedolizumab, tofacitinib and ustekinumab |
| Bonovas et al. | Network meta-analysis | Clinical response, clinical remission, mucosal healing | Infliximab superior to adalimumab, golibumab |
| Singh et al. | Propensity score-matched retrospective analysis of administrative claims data | Corticosterioid use | Infliximab superior to adalimumab |
| Singh et al. | Propensity score-matched retrospective analysis of nationwide cohort | All-cause hospitalization | Infliximab superior to adalimumab |
| Cholapranee et al. | Meta-analysis | Induction of mucosal healing | Infliximab superior to adalimumab |
| Faleck et al. | Propensity score-matched analysis of VICTORY Consortium | Clinical remission | Vedolizumab superior to anti-TNF agents |
| Sands et al. | Prospective RCT (VARSITY) | Clinical remission, endoscopic improvement, steroid-free remission | Vedolizumab superior to adalimumab-endoscopic improvements;<br>no difference in steroid-free remission |

Frasca J, Cheifetz, A. *Pract Gastroenterol*. 2020;Aug (XLIV-8):32-43.

# Emerging Diagnostics

- Need for identifying biomarkers predictive of response to individual therapies, facilitate optimal positioning of therapies
- Limited evidence regarding combination therapy of biologics and immunomodulators, especially with newer agents with lower immunogenicity and with better optimization of biologic agents through therapeutic drug monitoring
- Proposed treatment targets have moved beyond symptomatic improvement towards more objective end points, such as healing of the intestinal mucosa
  - This treat-to-target approach has been associated with improved disease outcomes such as diminished bowel damage, surgery and hospitalizations
  - Many patients with IBD require biologic therapy to achieve and maintain clinical and endoscopic remission, and antitumor necrosis factor antibodies remain the first-line biologic therapy in most areas of the world
  - Unfortunately, up to 1/3 of patients receiving this treatment are primary non-responders, and some patients that show an initial response can also lose response over time
  - TDM has been suggested as a useful tool to manage treatment, including monitoring for dose escalation, de-escalation or to switch treatment

Argollo et al. *Nat RevGastroenterol Hepatol.* Sept 2020.

# What Is This “Immunogenicity”

- Immunogenicity is recognized as a leading contributor to the loss of response to biologic therapies; as biologic agents are large, complex proteins, they trigger the formation of anti-drug antibodies (ADAs) specific to the agent administered
- It is recommended that patients who develop ADAs to a biologic therapy, with a consequent loss of response, should switch to a different agent with either the same or a different mechanism of action
- Giving biologic therapies in combination with concomitant immunosuppressive agents has been shown in several studies to reduce the development of ADAs

Severine et al. *Ther Adv Gastroenterology*. 2018;11:1-13.

# Therapeutic Drug Monitoring

- Used to check the drug trough concentration and assess for the presence of anti-drug antibodies
- Can be performed at any point of therapy in induction or maintenance
- Can be routine proactive when patient in remission or reactive during symptoms
- Available for all biologics (commonly anti-TNFs) and thioprines
- Drug failure can be 1) mechanistic, 2) non-immune-mediated pharmacokinetic or 3) immune-mediated pharmacokinetic
- ? Future – pharmacogenomics – drug-gene testing

Feuerstein J et al. *Gastroenterology*. 2017 (153); 827-834.

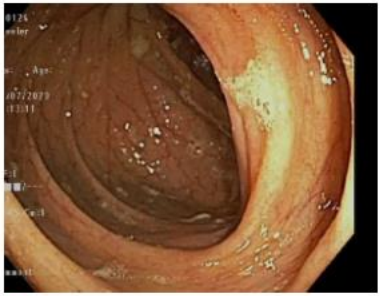
# Case Study

- M.W. is a 24 y/o WM first seen in February of 2020 with intermittent bright red blood in his stools x 1 year with occasional diarrhea/constipation
- No past medical or surgical hx, no prior colon
- No FHX of CRC, IBD
- Social: Works as a police office for the City of Cleveland, single
- Saw PCP and DRE was neg
- Med list: MVI, fish oil, biotin, flax seed
- No NSAIDs

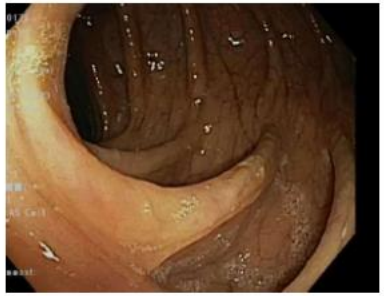
# Case Study

- Plan – Colonoscopy, CBC/CMP/ESR/CRP
- Findings – Labs wnl; colon done 3 days after OV showed severe proctitis
- Plan – mesalamine 1000mg supp qhs x 1 week then qohs; repeat FS in 6 months

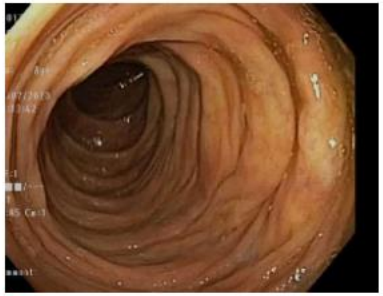
1 Terminal ileum



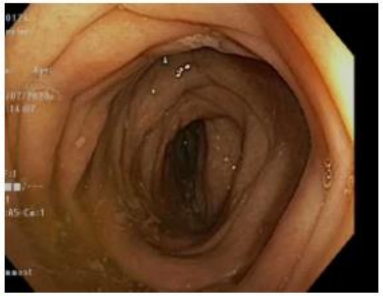
2 Cecum



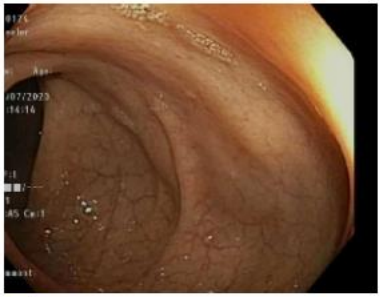
3 Cecum



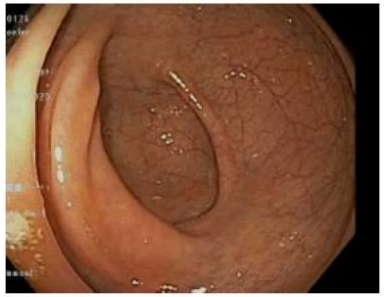
4 Ascending Colon



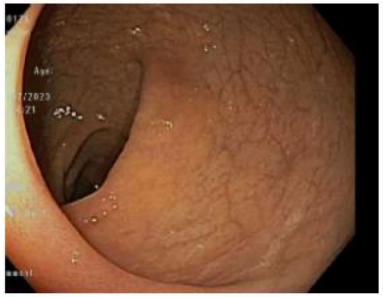
5 Hepatic Flexure



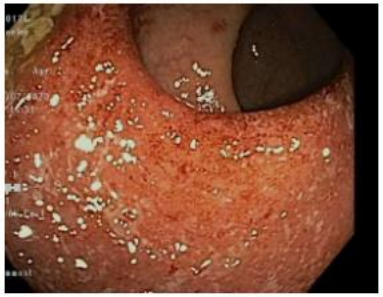
6 Hepatic Flexure



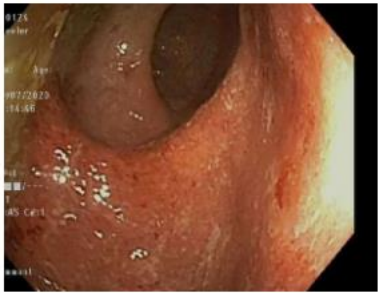
7 Transverse Colon



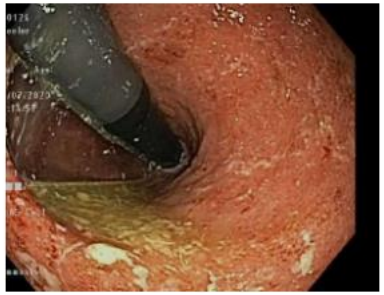
8 Transverse Colon



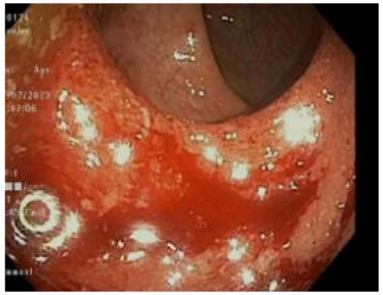
9 Descending Colon



10 Sigmoid Colon



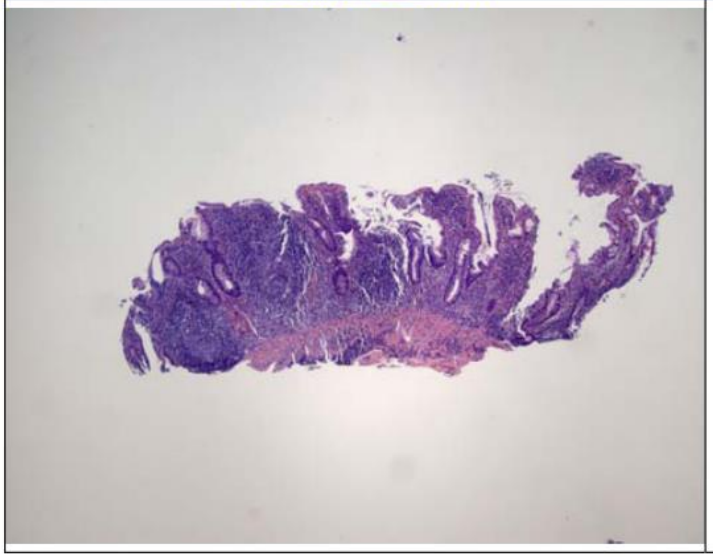
11 Sigmoid Colon



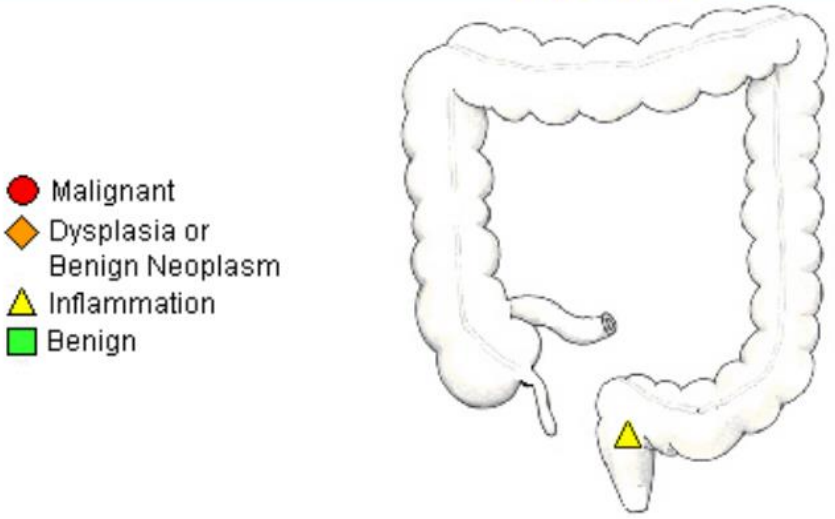
12 Rectum

# Case Study – Pathology Findings

**PHOTOMICROGRAPH**



**ORGAN DIAGRAM**




**DIAGNOSIS**

**RECTUM, BIOPSIES:**

**CHRONIC ACTIVE COLITIS WITH ULCER AND REGENERATIVE EPITHELIAL CHANGES.**

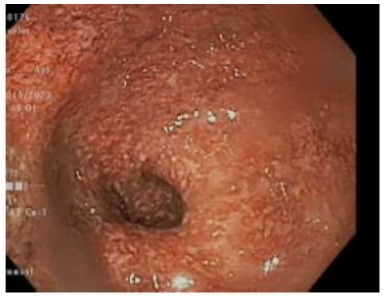
**COMMENT: The biopsy consists of several fragments of rectal mucosa with a marked basal lymphoplasmacytosis, crypt architectural disarray and diffuse cryptitis. The findings are highly suspicious for primary inflammatory bowel disease, although clinical and endoscopic correlation is recommended for a definitive diagnosis. There is no evidence of granulomas, dysplasia or malignancy.**

# Case Study – Fast Forward

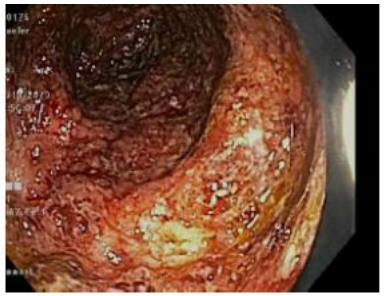
- June 2020 – Patient seen in the office for worsening S/S. Turns out he only took the mesalamine supp x 9 days (too expensive), but had felt better with them immediately. Got new insurance and resumed 2 weeks prior to this visit.
- Symptoms: Severe cramps, bloating, bloody diarrhea every hour, nocturnal as well, lost 15#. Mucous in stool.
- Increased stress at work (Cleveland Police Officer, worked 12 straight hours downtown riots on Saturday). Sat fever 102. No temp now. Hardly eating. Past week also using ibuprofen 600mg, 2 daily.

# Case Study

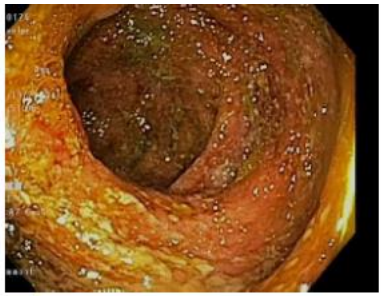
- Plan – FS planned for the following day, check CBC/CMP/ESR/CRP and fecal calprotectin. Continue mesalamine 1000mg supp qhs but add Prednisone 40mg PO daily with a taper dose of 10mg weekly. Stop NSAIDs. Fluid/electrolyte replacement.
- Findings – Labs WBC 11.74, H&H 35.6/11.5, PLT 479, Alb 3.3, ESR 54, CRP 11.1, Fecal Cal 1,103.9; Colon showed severe pancolitis UC (Mayo score 3).
- Plan – Increase Prednisone to 60mg, start Remicade 10mg/kg ASAP, Imuran 100mg PO daily, repeat colon in 6 months.



1



2 Sigmoid Colon



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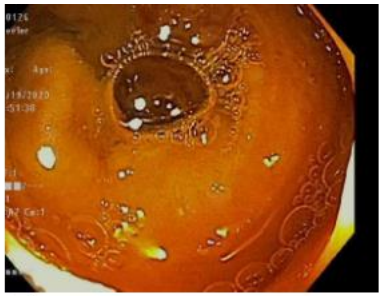
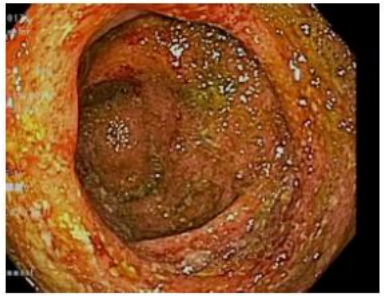
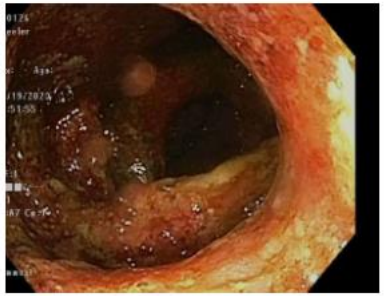


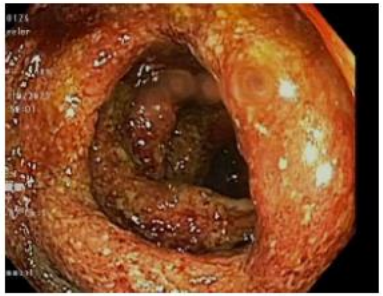
4 Terminal ileum



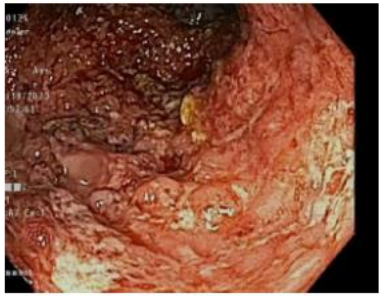
5 Ascending Colon



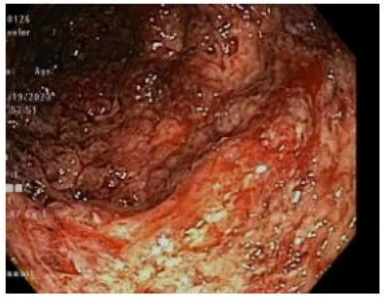
6 Hepatic Flexure



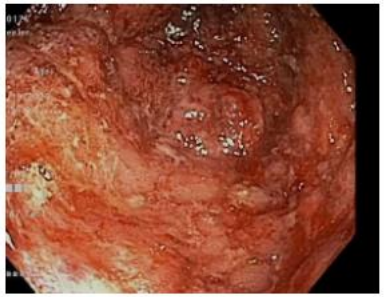
7 Transverse Colon



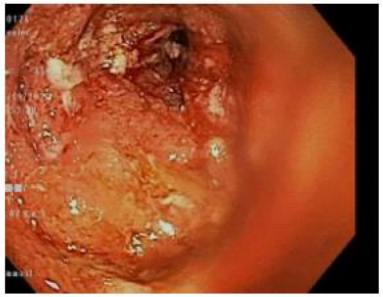
8 Splenic Flexure



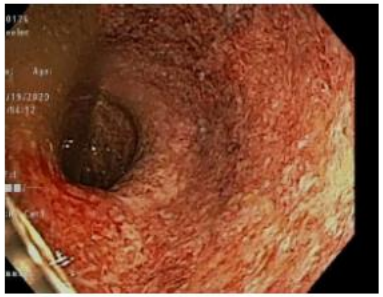
9 Descending Colon



10 Descending Colon

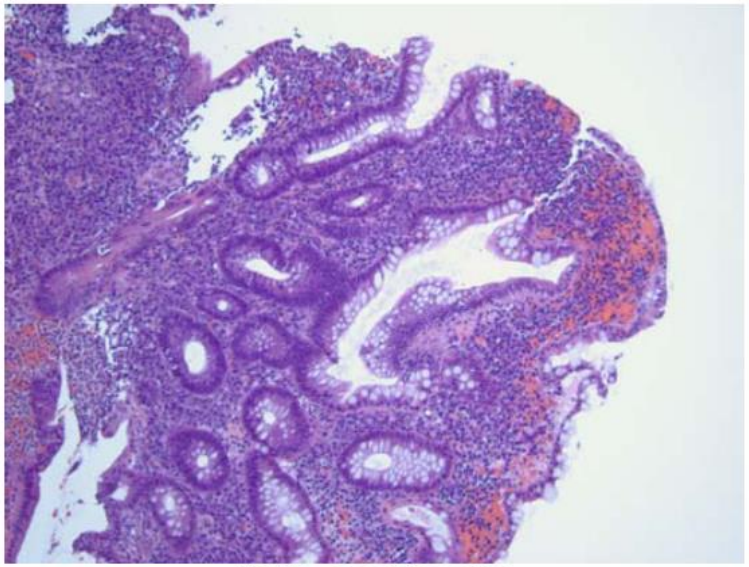


11 Rectosigmoid Junction



12 Rectum

# Case Study – Pathology Findings



Part A - ascending colon

**DIAGNOSIS**

**A. ASCENDING COLON, BIOPSY:**
**MARKED CHRONIC ACTIVE COLITIS WITH ULCER, NEGATIVE FOR DYSPLASIA.**

**B. SIGMOID COLON, BIOPSY:**
**CHRONIC ACTIVE COLITIS WITH EROSION, NEGATIVE FOR DYSPLASIA.**

# Case Study

- Remicade started 3 days after colonoscopy at 10mg/kg (1000mg), plan for 0, 2, 6 weeks then q8 weeks
- OV 2 days after first Remicade infusion, already improvement in sx. Mesalamine supp DC’d. Prednisone kept at 60mg x 1 week, then decreased to 40mg with 10mg weekly taper dose
- OV 2 weeks later, after 2$^{nd}$ Remicade infusion, feels significantly better, feels like a "whole new person". Denies abdominal discomfort. He has 3-4 formed stools daily
- We gave him a work excuse x 3 weeks
- Currently doing very well…

# Poor Prognostic Factors in UC Disease Severity

- Age <40 at diagnosis
- Extensive colitis, deep ulcers, severe endoscopic disease (Mayo subscore 3)
- Hospitalization for colitis
- Cdiff and CMV infection
- Elevated CRP/ESR
- Low serum albumin
- Steroid dependent disease
- The greater the number of poor prognostic factors, the worse the prognosis as measured by likelihood of colectomy
- Early initiation of biologics in UC may help prevent complications, such as colon cancer, hospitalizations and surgery

Rubin DT et al. *Am J Gastroenterology*. 2019;114(3):384-413; Frasca J, Cheifetz A. *Pract Gastroenterol.* 2020 Aug;XLIV-8:32-43.

# Predicting Severity?

- The ACE (Albumin, CRP and Endoscopy) Index in Acute Colitis
- More than three quarters of patients scoring 3 (albumin ≤30 g/L, CRP ≥50 mg/L, and increased endoscopic severity) did not respond to IV steroids
- This combination of parameters (ACE) identifies on admission a high-risk population who may benefit from earlier second-line medical treatment or surgical intervention

Grant et al. *Inflamm Bowel Dis.* June 23, 2020.

# Dietary Guidelines

- The International Organization for the Study of Inflammatory Bowel Disease (IOIBD) recently published consensus guidance that includes consuming a diet composed of carbohydrates, fats, and protein and limiting intake of processed foods and artificial sweeteners, while avoiding trans fats. We encourage patients with inactive IBD to eat a balanced diet.
- Malnutrition in patients with IBD can lead to weight loss, growth failure in children, bone disease, and/or micronutrient deficiencies.

DeLegge M. *Up To Date*. April 17, 2020.

# Monitoring

**Suggested laboratory tests for monitoring nutrition in patients with inflammatory bowel disease**

| | Ulcerative colitis | Crohn disease or indeterminate colitis | Conditional testing* |
|---|---|---|---|
| **Complete blood count** | X | X | |
| **CRP, ESR¶** | X | X | |
| **Albumin¶** | X | X | |
| **25-hydroxyvitamin D** | X | X | |
| **Iron, ferritin, TIBCΔ** | | | X |
| **Vitamin B12** | | | X |
| **Calcium** | | | X |
| **Phosphorus** | | | X |
| **Magnesium** | | | X |
| **Vitamin A** | | | X |
| **Vitamin E** | | | X |
| **PT or INR** | | | X |
| **Zinc** | | | X |
| **Folate** | | | X |
| **DXA scanning◇** | | | X |

The above tests and frequencies reflect the author's practice and may vary among providers. We perform these tests approximately every 6 to 12 months in patients with quiescent disease and may test more frequently in patients with active disease or known deficiency or in growing children.

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; TIBC: total iron-binding capacity; PT: prothrombin time; INR: international normalized ratio; DXA: dual-energy x-ray absorptiometry.
* These tests are performed in the case of malnutrition, malabsorption, symptoms of deficiency, or specific risk factors (eg, anemia, ileal resection, total parenteral or enteral nutrition, profuse diarrhea, or a high-output ostomy).
¶ CRP, ESR, and albumin primarily reflect the inflammatory state rather than nutritional status. This information is important for the interpretation of the other results, especially ferritin, which is increased in the setting of inflammation.
Δ Iron studies should be checked at diagnosis and then as needed for patients with unexplained anemia.
◇ DXA scanning is recommended in adults with risk factors for bone disease, including prolonged corticosteroid use or low-trauma fracture (refer to UpToDate content on metabolic bone disease in inflammatory bowel disease). There are no generally accepted standards for frequency of DXA scanning in children with inflammatory bowel disease.

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## Health Maintenance Summary

### Vaccines and Infections

**Influenza:** All patients >6 months of age should receive annual inactivated influenza vaccine, irrespective of immunosuppression status.

**MMR:** IBD Patients not immune to MMR should receive a 2-dose series, at least 4 weeks apart. If immune status is uncertain, IgG antibody titer should be checked. MMR should not be given to patients currently on systemic immunosuppressive* therapy.

**Pneumococcus:** All patients >19 years age receiving systemic immunosuppression* should receive PCV13, followed by PPSV23 at least 8 weeks later, and a booster of PPSV23 5 years later.

**Varicella:** Seroprotection status should be checked with varicella zoster virus IgG antibodies in all patients without documented vaccination record or exposure. All patients who are not immune should receive a 2-dose series, 4–8 weeks apart, ≥4 weeks before immunosuppression, if therapy can be postponed.

**Zoster:** All patients receiving JAK inhibitor therapy should receive the recombinant adjuvanted zoster vaccine. Risk of zoster should be considered with combinations of other immunosuppressive* therapies.

**TB:** Screen for latent TB in all patients with IBD, at baseline. Perform clinical risk assessment for TB exposure annually in all patients with IBD.

### Cancer Screening

**Colorectal Cancer:** All IBD patients with extensive colitis (>1/3 of the colon) for ≥ 8 years should undergo surveillance colonoscopy every 1–3 years, depending on cancer risk;

- IBD patients with a diagnosis of PSC should undergo colonoscopy, starting at the time of PSC diagnosis, and annually thereafter.
- IBD patients with features that are high-risk for developing colon cancer (i.e. prior history of adenomatous polyps, dysplasia, family history of colon cancer and extensive colitis) should have colonoscopies more frequently than every 3 years.

**Cervical Cancer:** All women with IBD who are being treated with systemic immunosuppression* should undergo cervical cancer by cytology annually (if cytology alone) or every 2 years (if HPV negative).

**Skin Cancer:** All IBD patients being treated with systemic immunosuppression* should have annual total body skin exams to screen for skin cancer.

### Other Protection

**Osteoporosis:** Screen for osteoporosis by central (hip and spine) DXA scan in all patients with IBD if ANY risk factors for osteoporosis; low BMI, >3 months cumulative steroid exposure, smoker, post-menopausal, hypogonadism. Repeat in 5 years if initial screen is normal.

**Depression/Anxiety:** Screen all patients with IBD for depression (PHQ9) and anxiety (GAD7) at baseline, and annually. Refer for counseling/therapy when identified.

**Smoking:** Screen all patients with IBD for smoking status at baseline, and refer current smokers for smoking cessation therapy.

* Systemic immunosuppression refers to current treatment with prednisone (>20mg/day for more than 14 days), azathioprine (>2.5 mg/kg/day) mercaptopurine (>1.5 mg/kg/day), methotrexate (>0.4 mg/kg/week), cyclosporine, tacrolimus, infliximab, adalimumab, golimumab, certolizumab, ustekinumab, or tofacitinib.

Crohn's & Colitis Foundation Professional Education Sub-Committee; Jill Gaidos MD, Alan Moss MD, Mariastella Serrano MD, Gaurav Syal MD • 6/10/2020

# CRC Prevention in UC

- Screening and surveillance colonoscopy to assess for dysplasia in patients with UC extent greater than rectum to start 8 years after initial diagnosis
- If UC and PSC, then colon annually
- Surveillance every 1-3 years based on combined CRC risk factors in UC and findings on previous colonoscopy
- During colon, identify raised lesions and abnormal pit patterns and perform targeted biopsies (unclear whether segmental random biopsies or still required)
- Fecal DNA testing and CT colonography are not recommended

Rubin DT et al. *Am J Gastroenterology.* 2019;114(3):384-413.

# COVID 19 and IBD

- IBD itself does not increase the risk of COVID-19.
- Being on immune therapies for IBD may increase the risk for some infections, but the currently available information does not show an increased risk of infection with SARS-CoV-2 or development of COVID-19 in individuals with IBD or who are on the standard therapies. However, it is helpful to clarify which medications affect the immune system and which ones do not (immunosuppressive agents include steroids, 6MP, MTX, anti-TNFs, Anti-IL 12/23, Anti-integrin, JAK inhibitors).
- Treatments that do NOT suppress your immune system (5ASAs, antibiotics, diet).
- Keeping your IBD in remission is believed to be protective against COVID-19, but also healthier for you. Needing steroids or hospitalization for a relapse is never an ideal situation, but especially now when medical resources may be strained.
- Stay on your IBD medications. Flares or needing to take steroids may put you at greater risk than taking your other IBD medications.

ACG. March 2020.

# Guidance in managing IBD therapy in setting of Covid-19

- **No symptoms, no testing**
  Do not withhold IBD therapies, try to dose reduce steroids
- **No symptoms, positive test**
  Withhold IBD therapy for a minimum of 10 days. If no symptoms of Covid-19, resume IBD therapy
- **Positive test for SARS-CoV-2 and symptoms of Covid-19**
  When to restart- Symptom based strategy:

  1. ≥10 days have passed since Covid-19 symptoms onset and
  2. ≥ 3 days (72 hours) have passed since recovery- defined as resolution of fever without use of fever-reducing medications and improvement in respiratory symptoms (eg, cough, SOB)
  3. In severe Covid-19, a greater time frame from recovery may be appropriate depending on severity of IBD and need to re-start medication

- If test-based strategy is required, the above clinical parameters must be met
  PLUS 2 consecutive negative Covid tests taken 24 hours apart

Adapted from OIBD Recommendations: Best practice guidance for when to re-start IBD therapy in patients who have had confirmed or suspected Covid-19

# Role of APPs

- More frequent office visits
- Monitoring/managing medications
- Monitoring nutritional status
- Smoking cessation
- Depression
- Contraception/pregnancy
- Vaccinations
- Lab monitoring
- Dexa scans

# Keep in Mind!

- Evaluating UC during relapses should include assessment of severity of symptoms and potential triggers
  - Enteric infections (particularly *C diff*)
  - NSAID use
  - Recent smoking cessation
  - Non-adherence to therapy

Rubin DT et al. *Am J Gastroenterology.* 2019;114(3):384-413.

# Don’t Forget the Crohn’s Colitis Foundation!

- Crohnscolitisfoundation.org
  - Professionals
  - For your patients
  - Appeal letters
- Plethera of information including school/employment accommodations, disability, financial resources, medication dose escalations, prior authorization letters, other testing including fecal calprotectin, etc…(references professional journal articles)

# Thank You!


Our usual colonoscopy equipment is down today, so we're going to be using a tapeworm with a GoPro strapped to its head.
Blazek
5-27
Get signed Loose Parts books at LoosePartsComic.com!
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# Q&A