

Overview

The COVID-19 pandemic is an unprecedented challenge for all healthcare systems worldwide. Gastroenterologists and clinicians who actively manage patients with inflammatory bowel disease (IBD), including ulcerative colitis (UC), need to ensure they are taking steps to minimize the risk of infection for their patients.

Russell D. Cohen, MD, shares his expert perspective as an author of the recently published *AGA Clinical Practice Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic*. Dr. Cohen highlights emerging evidence and the potential risk of IBD patients for COVID-19, as well as recommendations for the treatment and management of patients with IBD during the coronavirus pandemic. In addition, he reviews the publicly accessible SECURE-IBD international registry and its impact tracking COVID-19 in patients with IBD. Dr. Cohen further discusses how to identify, appropriately manage, and monitor patients with UC who test positive for COVID-19, through the use of an algorithm to guide complex clinical decisions for those who are symptomatic with or without suspicion of active UC inflammation.

Target Audience

This activity was developed for gastroenterologists, physician assistants, nurse practitioners, nurses and other healthcare providers who manage patients with inflammatory bowel disease and other healthcare professionals who have an interest in ulcerative colitis during the COVID-19 pandemic.

Learning Objectives

At the conclusion of this activity, participants should be better able to:

- Summarize the relative risk and signs of SARS-CoV-2 infection among patients with ulcerative colitis (UC)
- Modify management and education of UC patients not infected with SARS-CoV-2 in order to reduce the risk of such infection
- Safely modify UC treatments in patients testing positive for SARS-CoV-2 but asymptomatic
- Safely modify UC treatments in patients with symptomatic COVID-19, including those with active UC inflammation

Faculty

Russell D. Cohen, MD
Professor of Medicine, Pritzker School of Medicine
Director, Inflammatory Bowel Disease Center
Co-Director, Advanced IBD Fellowship Program
The University of Chicago Medicine
Chicago, Illinois

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All clinical areas: Inflammatory Bowel Disease

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Additional content planners

Victoria Anderson (Medical writer)

Individual stockholder Abbott – clinical area: N/A

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Editor's Note: This is a transcript of an audio webcast presented on July 1, 2020.


Abbreviations:

5-ASA, 5-aminosalicylates
 6-MP, 6-mercaptopurine
 ACE2, angiotensin-converting enzyme 2
 AGA, American Gastroenterological Association
 CFR, case fatality rates
 CMV, cytomegalovirus
 IOIBD, The International Organization for the Study of Inflammatory Bowel Diseases

Dr. Russel Cohen: Thank you. I really appreciate this opportunity to present on behalf of the Annenberg Center. I really want to welcome everyone. This is going to be an exciting time for us, and I'm going to go through things. I do want to encourage you to please download the slides, because I'm not going to read every word on the slide to you. I am going to reference some slides, and you can go back to them later.

Overview


- Module 1: Risks and signs of SARS-CoV-2 in IBD population
- Module 2: Management of UC patients not infected with SARS-CoV-2
- Module 3: Medication management of UC patients testing positive for SARS-CoV-2 but who are asymptomatic
- Module 4: Medication management of UC patients with symptomatic COVID-19 but without suspicion of active UC inflammation
- Module 5: Medication management of UC patients with symptomatic COVID-19 with symptoms of active inflammation




This is actually a really nice program, because we're going to go through, step-by-step the issues about the risk of SARS-CoV-2 in IBD. What do you do with patients with IBD or ulcerative colitis who are not infected with the SARS CoV-2? And then the next step is, what if they test positive, but they're asymptomatic? And then the next step is what if they test positive and are symptomatic, but their IBD is okay? And the final step is, what if they test positive *and* are symptomatic with CoV *and* with their IBD? So, this should be a soup to nuts for you all.

Module 1: Risks and signs of SARS-CoV-2 in IBD population

- COVID-19 is the disease caused by the SARS-CoV-2 virus.
- Management of IBD patients involves treating uncontrolled inflammation, with most patients requiring immune-based therapies.
- These therapies, however, *may* weaken the immune system and potentially place IBD patients at an increased risk of infections and complications, including those from COVID-19.




As you all know, COVID-19 is the disease caused by the SARS CoV-2 virus. That was the original SARS CoV virus. That was CoV-1. They didn't call it one, because there was only one at the time. I think they were hoping it would stop there, but it didn't. And we're concerned, because as you know, patients with IBD have uncontrolled inflammation, and the therapies can be immune suppressant. So, are we putting our patients at higher risk?



World Health Organization Coronavirus disease (COVID-19) Situation Report – 161

Data as received by WHO from national authorities by 10:00 CEST, 29 June 2020

Situation in numbers (by WHO Region)		
Total (new cases in last 24 hours)		
Globally	10,021,401 cases (178,328)	499,913 deaths (4153)
Africa	288,347 cases (9532)	5879 deaths (94)
Americas	5,042,486 cases (108,514)	244,791 deaths (2860)
Eastern Mediterranean	1,041,774 cases (17,552)	23,888 deaths (439)
Europe	2,673,131 cases (16,694)	196,835 deaths (294)
South-East Asia	760,816 cases (24,962)	21,078 deaths (457)
Western Pacific	214,106 cases (1074)	7429 deaths (9)



WHO.int. Coronavirus disease (COVID-19) Situation Report-161. Data received June 29, 2020.

Globally, the COVID-19 issue is...Of course, the numbers are going to go up over time. This is a nice slide. It shows globally there's 10 million cases, and half of them are in the Americas.¹ You can see the death rate across, on the far-right column, are the death rates or the death cases. You can calculate the rates to see, as well. So, certainly there is a problem in many parts of the world, particularly now in the Americas as we're, unfortunately, seeing.

Meeting the Medical Needs of Patients with **Ulcerative Colitis**

During the **COVID-19** Pandemic

Current Status: Interactive COVID Map in the United States

The *New York Times* Interactive COVID Map and Case Count

By The New York Times Updated June 29, 2020, 8:19 A.M. E.T.

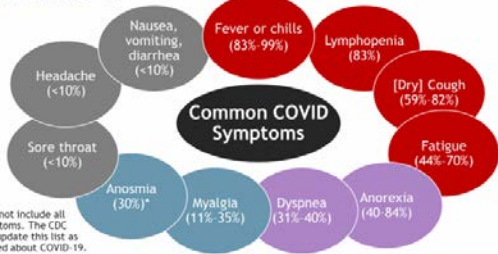


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Continued in the US: Latest Map and Case Count, <https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html>, Accessed June 29, 2020.

And that brings me to the next slide here. I actually did this presentation about a week ago, and we were a lot better off a week ago than we are now in the country. I recommend you get involved in this *New York Times* interactive COVID map.² It's amazing, very helpful. There is also some other great resources. You go to newyorktimes.com. As you can see here on the pink graph, March was wonderful. We heard about things, and it wasn't our problem, supposedly, and then you can see where April takes off. The red line, the dark red line is the seven-day average, and that gives you a better idea—so you don't get the peaks and troughs—of what's really going on. You can see, as we're heading out of May, into June, things are coming down nicely, even going about halfway through June. And then all of a sudden, things started increasing, which we presume is because the restrictions are opening up. I don't need to be the person to decipher that for you.

Symptoms Reported by the CDC for Patients With COVID-19



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CDC. (n.d.). Coronavirus Disease 2019 (COVID-19). Symptoms of Coronavirus. Updated June 2, 2020. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/symptoms.html>. Rubin DT, Cohen BC, et al. Gastroenterology. 2020;158(6):888-894.e3.

But it's important because your patients are going to call. You're going to get a million calls from people asking, "Well, maybe I have it. I think I have it." So, what are the **symptoms most common in patients who have COVID-19**. We colored them in red so it's easier to see.³⁻⁵

Virtually all patients who are positive have fevers or chills and or a dry cough, or a cough. If your patients do not have fevers, chills, or a cough, they are unlikely to have it. Now, of course they may be asymptomatic carriers, but that's a different issue, because patients calling you with symptoms... If they're calling you with some symptoms, "Well, I may be having this. I'm not sure." You're going to say they have lymphopenia. You're not going to know from the patient telephone call. Just checking from blood counts, you could see that in patients who have a virus that may be helpful. Fatigue, that's kind of a nonspecific.

I do want to point out that we heard early on that some studies showed over up to a third of patients had GI symptoms, but in most cases, those symptoms were, as you see on this slide in purple, anorexia. And being IBD centric, this presentation, that's not really an issue in IBD. Someone with IBD typically doesn't have anorexia, and if they do all of a sudden, it might be an indication of something else that's going on. It is not until you get to the gray boxes where you see diarrhea, nausea, vomiting. So, if you have patients who have isolated diarrhea calling you, as they probably will, or your nurse, which is even better than calling you, and say, "Well, I have diarrhea, and I may have COVID because I heard you have COVID, COVID can give you diarrhea." I would say, "Well, do you have fever, chills, or dry cough?" And if the answer is no, it is unlikely that they have COVID-19.

Common Gastro COVID Symptoms

- A significant proportion of patients with COVID-19 may have alterations in bowel habits or other digestive symptoms
 - 10.1% of hospitalized patients with COVID-19 in Wuhan presented with diarrhea and nausea 1 to 2 days prior to developing fever and dyspnea
 - Study (n=204) from Hubei, China reported 50.5% hospitalized patients presented with gastrointestinal-specific symptoms, including diarrhea (34%), vomiting (3.9%), or abdominal pain (1.9%)
- Symptoms may reflect inoculation of the GI tract from swallowing the virus and due to the ACE2 expression in the intestines
- Recent reports have focused on both GI-related manifestations of COVID-19, as well as the virus detected in the stool long after resolution of respiratory symptoms or even detection of virus in the oropharynx

ACE2, angiotensin-converting enzyme 2; GI, gastrointestinal.

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Rubin DT, Cohen BC, et al. Gastroenterology. 2020;158(6):888-894.e3. Wang D, et al. JAMA. 2020;323:1961-1968. Pan L, et al. Am J Gastroenterol. 2020;115:764-773.

This just basically says what I showed you. Most studies show about 10% with the diarrhea issues. There was one study in China where the patients who were hospitalized, about a third of them had diarrhea,⁶ but that's different than patients [who were] just outpatient, too. And then there were these theories. We don't know. The GI tract,

Meeting the Medical Needs of Patients with **Ulcerative Colitis**

During the **COVID-19** Pandemic

you could obviously swallow the virus; you're coughing up things. There's ACE2 expression. The intestines, and the acetylcholinesterase 2 receptor is where the virus binds, and there have been reports of finding the virus in the stool, even after patients have no further symptoms.⁷

Risk Factors of IBD Patients to Consider

- Patients with active UC and CD have a greater tissue concentration of ACE2, which allows SARS-CoV-2 spike protein to bind the host cell and infect humans
- Serine protease level is ~10 times higher in patients with IBD than in healthy subjects, suggesting an increased risk of infection in these patients
- Digestive system is vulnerable to COVID-19 infection

ACE2, angiotensin-converting enzyme 2.



Sánchez P, et al. *Gastroenterology*. 2020;158:2502-2504. Garg H, et al. *Gut*. 2020;69:841-851. Jabbari A, et al. *Front Cell Infect Microbiol*. 2020;10:274.

Apparently, and this was certainly not my research, patients with active Crohn's and colitis have a higher concentration of ACE2. So, the SARS CoV-2 virus has a spike protein, which is actually a very traumatic description.⁸⁻¹⁰ You picture this virus, *bam*, right into that ACE2 receptor, and pumping into it and all its viral particles to infect you. And there's higher searing protease levels in IBD patients. Maybe there's an increased risk of infection, but the numbers really haven't shown that to be true.

Virus Detected in Stool

- Studies reveal ACE2 was also highly expressed in esophagus upper and stratified epithelial cells and absorptive enterocytes from ileum and colon
- SARS-CoV-2 virus detected in the stool in >20% of patients nearly 5 weeks after respiratory samples tested negative
- Evidence also suggests potential for coronavirus transmission through fecal shedding
- Two independent laboratories from China isolated live COVID-19 from stool of patients

ACE2, angiotensin-converting enzyme 2.



Gu J, et al. *Gastroenterology*. 2020;158(11):8-13. Centers for Disease Control and Prevention. *Coronavirus Disease 2019 (COVID-19)*. *JAMA*. 2020;323(18):e2020075. *Gastroenterology*. Posted March 16, 2020. Research 02. *Gut*. 2020. Wu Y, et al. *Lancet Gastroenterol Hepatol*. 2020.

cells could, in a cell Petri dish, could be in fact, but I'm not aware of any proof of patient-to-patient transmission.¹¹⁻¹⁵ It was an interesting study a couple of months ago now from the Italian GI groups in Northern Italy, because they had unfortunately very low levels of personal protective equipment. And they showed that their rates of infection of their endoscopy staff was exceptionally low, even though they were treating COVID patients, because they had GI bleeds, whatever they may be, that they had to get a colonoscopy or upper endoscopy. And they had exceptionally low rates within their own staff.¹⁶ So, we don't believe that there's a high risk for transmitting through the stool to you or to other people through the stool. We're moving through months of this virus. We would think that there would be more data by now if that were the case. So, hopefully it's not, being a gastroenterologist.

IBD Patients Potentially at Risk for COVID-19

- Having IBD does not appear to increase the risk of SARS-CoV-2 infection or development of COVID-19
- Impact of immunosuppression on the severity of COVID-19 disease remains unclear
- Patients on immunosuppressive drugs for IBD should continue taking their medications
- Although no data indicate true risk of patient with IBD for COVID, there is data in relation to other immune diseases, such as diabetes

⊕ The risk of disease flare outweighs the chance of contracting coronavirus



2020 GI Society Message: COVID-19 clinical insights. *Gastro*. Posted March 16, 2020. Kennedy HA, et al. *Gut*. 2020;69:1048-1050.

It's hard for us to know whether IBD increases the risk of SARS-CoV-2 or COVID-19. Well, why? Well, because, even starting out right away in China, when things started getting crazy there, and they realized they had this virus, they reached out to their IBD patients and their rheumatoid arthritis patients and other patients on immunosuppressants, and they said, "Hey, if I were you, I would stay inside, wear a mask, social isolate." And many of you, if you do have patients with Crohn's and colitis know that they're not going out of their house. I mean, you have to like almost lure them out with a brick of gold on the end of a fishing line. They're not going out of the house for anything because they're petrified. It's hard to know, actually, if it increases the risk because our patients are very much taking the precautions that we're asking them to, which is nice, obviously.

They have found these ACE2 receptors in the esophagus and the small bowel ileum, the colon. And they [were] detected in the stool, as I mentioned. There is potential for shedding, but it hasn't been shown to happen in humans. The laboratories listed here that isolated the COVID-19 from the stool, they were able to show that

Meeting the Medical Needs of Patients with **Ulcerative Colitis**

During the **COVID-19** Pandemic

As a result, since we don't have higher rates that we're aware of, we do not recommend that our patients stop their medicines. I'm going to go through this repeatedly. So, patients who call and say, "Oh yeah, I heard there was SARS and CoV-2, and I'm afraid. Should I stop my medicines?" The answer is always going to be no. I'm going to go into more details in that briefly, too.

Immunocompromised Patient Groups

- Data show inflammatory and immune mechanisms are involved in every aspect of COVID-19 infection
- Risk factors in other immunocompromised patient groups include
 - Age >50 years
 - Individuals with type 2 diabetes, specifically those with obesity and hypertension
 - Prevalence of COVID-19 in patients with diabetes ranges from 10% to 20%
 - Patients using corticosteroids
 - Lymphopenia and neutropenia (liver and other solid-organ transplant recipients)

ALANI AH, et al. *Aliment Pharmacol Ther*. 2020;16(11):1491-1579. Goldenberg SL. *Practicingpatientmanagement.com*. April 2020. https://doi.org/10.1007/978-1-4939-9888-8_10

IBD Patients in China Diagnosed With COVID-19



- Chinese studies on patients using immunosuppressants
 - >72,000 cases of COVID-19 from China
 - Diabetes increased the mortality rate 3-fold, from 2.3% to 7.3% of cases
- Reported CFR of 10.5% and 7.3% in patients with CVD and diabetes, respectively, compared to 0.9% for people without any prior disease

CFR, case fatality rates; CVD, cardiovascular disease.

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Chinese Centre for Disease Control and Prevention, Goldenberg SL. *Practicingpatientmanagement.com*. April 2020. https://doi.org/10.1007/978-1-4939-9888-8_10
Y. https://doi.org/10.1007/978-1-4939-9888-8_10
Diabetes, CVD Tied to Worse Progress for COVID-19 Infection. *Posted February 25, 2020.*

This slide has a little picture, a Chinese flag. Showed that it's bad news if you're on immunosuppressants or if you're immunosuppressed. Diabetes increased the mortality rate 3-fold, and case fatality rates (CFR) of 10.5% if you had cardiovascular disease, and 7.3% with diabetes, while people without any prior disease was less than 1%.²⁰⁻²² Again, you're not going to really have much data on IBD there.

What do we know? Immunocompromised people who are at higher risk for... It says every aspect of the infection. So, for getting the infection and getting hospitalized for infection and ending up in the ICU and intubated, and unfortunately perhaps dying from it... It's older patients, people with comorbidities, such as diabetes, obesity, hypertension, corticosteroid use—and we're going to come back to that—and patients who already have lymphopenia neutropenia, with liver and other solid-organ transplant recipients.¹⁷⁻¹⁹ Now that does overlap with some of us, with our patients who are on the immunosuppressants azathioprine, 6-MP [6-mercaptopurine], perhaps methotrexate. So, while we are going to come back to this, we're kind of not starting those medicines right now unless we need to because we don't want patients to have very low blood counts because of the medicines. As you probably know, the biologic medicines do not plummet those blood counts.

AGA Clinical Practice Update



- Issues gastroenterologists should consider when managing IBD patients during current COVID-19 pandemic
- Patients' best protection against virus transmission:
 - Wash hands
 - Don't touch your face
 - Cough etiquette
 - Social distancing (2 meters or ≥6 feet)
 - Decrease time outside and avoid crowds
 - Wear mask when in public

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Rubin EF, Cohen TC, et al. *Gastroenterology*. 2020;158(4):585-602. *Gastroenterology Society of America. COVID-19 clinical insights. Gastrology. Posted March 16, 2020.*

It seems like eons ago, at the end of March, early April, Dave Rubin and I were approached by the AGA to do a clinical practice update and get it out as soon as possible, which we did.²³ The information I'm going to run through here. This slide shows what you should be telling everybody about washing your hands. Don't touch your face. I think that's one of the reasons why the masks also helped, too. Think about it. If you're wearing a mask, you're not touching your mouth. Cough etiquette, social distancing, avoiding crowds, and wearing a mask in public. Really reemphasize that with your patients and everybody in your social circles despite what you may hear from people who should be taking the responsibility of providing better information to us.

Meeting the Medical Needs of Patients with **Ulcerative Colitis**

During the **COVID-19** Pandemic

AGA Recommendations for Patients With IBD

- Continue IBD therapies and infusions
- Infusion centers should have protocols that include prescreening patients for exposure or symptoms of COVID-19:



The AGA does not endorse specific products. Current guidance may change as more information becomes available.



Rubin DT, Cohen BC, et al. *Gastroenterology*. 2020;S0016-5085(20)4612-0

We do recommend, as do all the other groups, staying on therapies. Do not tell your patients, "Don't go to your infusions." You should tell them to go their infusions. They should do the appropriate social distancing. As I explained to my patients, people at the infusion centers are more afraid of you than you are of them. And, remember the infusion centers have to deal with chemotherapy patients, too. So, they're very, very cautious there. They should be. You can verify if you use offsite centers that they're doing fever checks at the door, adequate spacing between the chairs, and adequate personal protective equipment, and deep cleaning.²³ I'd be shocked if they aren't already doing it. It seems that they're the ones teaching us on these, as well.

Joint Society Recommendations



- Patients on immunosuppressive drugs for IBD should continue taking their medications in the absence of COVID-19 symptoms
- The risk of disease flare outweighs the chance of contracting coronavirus
- Patients should follow CDC guidelines for at-risk groups avoiding crowds, exercise social distancing, and limiting travel
- Patients need to exercise social distancing and be up to date with influenza and pneumococcal vaccines

ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; ASGE, American Society for Gastrointestinal Endoscopy.



IOIBD Update on COVID-19 for Patients with Crohn's Disease and Ulcerative Colitis. IOIBD.org, Kennedy HA, et al. *ISG guidance*. *Gut*. 2020;69:164-190. Ali P, et al. *Lancet*. 2020; 5:525-527. Al-Ashri AH, et al. *Alliance Pharmaceutical*. 2020;10.1111/age.15176.

<<Slide 18: Joint Society Recommendations>>

You know that something's great when all the GI organizations hop on board, right? The joint society recommendations, you've got all those little insignias there of the different organizations. And if you want, you can join each of them and stick a patch on here and show them off to your kid. Pretty much across the board, we're recommending that if you just have patients who have

IBD, they're saying, "Oh, I'm scared. I heard about COVID. What should I do?" You keep them on their medicines. Although we are trying to get them off of steroids and onto non-steroid therapies, or at least off of systemic steroids and onto budesonide, if possible.^{24, 25} And you really want to emphasize the social issues that we talked about, too.

ACG, AGA, ASGE and IOIBD—Similar Key Points



- Encourage patients to stay on their IBD medications
- Reduce dose or stop steroids
- Offer remote office visits via telemedicine when possible
- Before initiating biologics, screen for opportunistic infections
- Reschedule elective nonurgent medical/surgical services (including endoscopic procedures)
- Classify procedures as nonurgent/postpone and nonurgent/perform
- High-priority procedures include cancer evaluations, prosthetic removals, and evaluation of significant symptoms
- For patients who need to be seen, minimize chance of exposure to COVID-19 before, during, and after each patient visit



Kennedy HA, et al. *Gut*. 2020;69:164-190. IOIBD Update on COVID-19 for Patients with Crohn's Disease and Ulcerative Colitis. IOIBD.org. Joint of Society Meeting: COVID-19 clinical insights. *Gastro*. Posted March 16, 2020.

Similar things, I want to point out on the left side of this, it mentions "reduce dose or stop steroids." We can mention there was recent data, as you may know, sick COVID patients who are in the hospital, who do better with dexamethasone, which isn't surprising because those patients are having this horrible immune response to the virus, but for people on the outside, we do not want them on steroids.^{24,25} I'm going to show you data in IBD clearly showing that steroids are bad. Get your patients off systemic steroids and onto budesonide, if possible, or onto a biologic. We're not really going on to azathioprine, 6-MP, or methotrexate right now.

On the right side, this information somewhat changes as your states go through various stages or your localities, because it shouldn't just be by state. Initially, we were only able to do urgent procedures and then semi-urgent procedures. Now, if you're getting up to probably a stage 4 in your state or phase 4, you can probably start doing your more elective procedures. You don't want patients to end up with colon cancers later on because they put things off worked better that are not treatable, just because they put things off because a COVID and you need to protect your staff and everyone involved from getting mandatory COVID testing. I live in Illinois. The state of Illinois requires 72 hours, within 72 hours of any procedure that the patients get tested by a reliable test. So again, as I mentioned, if they don't have a fever or

respiratory symptoms, it's unlikely that they have SARS-CoV-2. If you suspect, you can certainly send them for testing, and you actually want to monitor because some of the tests may be negative.



So, what do we do with patients who have ulcerative colitis who are not infected with SARS-CoV-2? We want to keep them in remission. And we also want to keep them out of the hospital, particularly if they... Unfortunately, as you know the rates are going up in certain states, and potentially in my state, too. I mean, in Chicago, we finally got ahold of things, and things were going great, but we'll have to see. The medical resources are limited. We don't want people coming into the hospital that don't need to be. So, you really want to emphasize to your patients, stay on therapy, because if you don't, you may end up in the hospital, and then you're really going to be sorry that you didn't do that. This slide actually is great because it has a little picture, and it shows the little thing. It's too bad we can't spin it around, but all this information is stuff that we covered already.

Additional Precautions

Check health in your state and community

- Be aware of indicators for COVID-19 in your community through online tools
- America's COVID warning system: <https://covidactnow.org/>
- Percentage of COVID-positive tests
- Overall case rates: goal is ≤5%-2% positive rates for 2 weeks

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Covid ActNow, America's COVID warning system. <https://covidactnow.org/>. Accessed June 11, 2020.

You should be aware of the rates in your community or where your patients live. I've got to tell you, this website, this covidactnow.org...²⁶ I don't want to tell you to go to right now because then you won't be paying attention to what I'm doing. But right after we're done, go to covidactnow.org. It's interactive. It shows your state. It even shows the states and the counties, where the rates are. It tells you what percent of the tests are positive that are done. So, in New York right now, only 1.1% of the tests that are done are positive. While in some states, it's 14% to 16% or 18% of the tests that are done, which is absurd. Then you can follow it over time, too. It's a great resource.

AGA & IOIBD Recommendations

- Reduction or withdrawal of corticosteroid
- Postpone elective medical procedures
- Remain in clinical trials
- Address patient anxiety
- Maintain infusion center visits
 - Ensure adequate safety and screening at center

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Rubin DT, Cohen BC, et al. Gastroenterology. 2020;158(16):2482-2485. Kennedy HA, et al. Gut. 2020;69:184-190. COVID Update for Patients with Crohn's Disease and Ulcerative Colitis. COVID-19. <https://www.ioibd.org/>. Accessed June 10, 2020. AGA, American Gastroenterological Association. IOIBD, The International Organization for the Study of Inflammatory Bowel Diseases.

For those who don't know, the IOIBD is the International Organization for the Study of Inflammatory Bowel Diseases, or something like that. Similar to the AGA, the same idea is getting patients off steroids. Don't do elective procedures. We do want to encourage patients to stay in clinical trials. The clinical trials are very regimented, and as long as the correct protective steps are taken, they should stay in the trials.²⁷ We don't want them to be kicked out of the trial and lose the opportunity to get valuable medicines for IBD at this point. Also, as you may know, some of the medicines we're studying in trials, they're also studying as a possible treatment for people who are sick with COVID, too. But we can talk about that in a bit.

And, certainly, address your patient's anxiety. You have to emphasize, especially if there are areas of the country or within their state where the rates are very low to at least get them outside, and the weather's probably nice somewhere. Explain to them that when they are near people, they have to be cautious, but also don't let them be hermits. They do need to go to get their infusions, and

they should get their appropriate blood tests for proper monitoring, as well too.

Patient Education Sources

- Crohn's & Colitis Foundation COVID-19 Resource
<https://www.crohnscolitisfoundation.org/coronavirus/what-ibd-patients-should-know>
- Stress and Anxiety related to COVID-19 Among IBD Patients
<https://www.crohnscolitisfoundation.org/coronavirus/mental-health>
- CDC—Coronavirus 2019 Homepage
<https://www.cdc.gov/coronavirus/2019-ncov/index.html>
- For patients COVID-free, adherence to UC treatment!!
- Prevent the need to start corticosteroid

Medication Management Positive for COVID-19 but Asymptomatic

Per AGA recommendations, patients with IBD who have known COVID-19 but have not developed COVID-19 symptoms, should

- Taper corticosteroids—lower doses of prednisone (<20 mg/d)
- Switch to budesonide when feasible
- Hold thiopurines, methotrexate, and tofacitinib temporarily
Restart after complete symptom resolution or when follow-up viral testing is negative or serologic tests demonstrate the convalescent stage of illness
- Delay dosing of biologic monoclonal antibodies by 2 weeks while monitoring symptoms of COVID-19
Re-start biologic therapies after 2 weeks if no symptoms or negative viral test

There are patient resources, and as I mentioned, you can download these slides, and take a picture of it if you want, and you can go to these websites as well too.

Module 3: Medication management of UC patients testing positive for SARS-CoV-2 but who are asymptomatic

- Management for asymptomatic UC patients
- Treatment adjustment for COVID-positive patients
- Testing
- Service considerations

The next scenario is you have a patient with IBD, ulcerative colitis, and they contact you, and they say, "I tested positive for SARS-CoV-2, but I'm not having symptoms." So, what do we do in that situation? In other words, they tested positive. Maybe someone in their workplace was tested, and everyone else had to get tested, and they turn up positive. But they're not having any COVID symptoms, and their IBD is okay.

What should you do? Number one, try to get them off their steroids or reduce their dose. If they're on prednisone, try to get them below 20 mg. Of course, we don't want them getting sick if they're doing that. Remember, with ulcerative colitis, many patients, most of their symptoms are from the distal disease. Put them on mesalamine enemas, budesonide foam, hydrocortisone, if you need to. That may help, although some of the hydrocortisone is systemically absorbed. Try to give you budesonide when feasible. Oral and rectal budesonide. The nameofthedrug.com often has patient assistance cards that are independent of the patient's income. (Unfortunately, I don't believe that they can be used by people with government insurance.) Also, we're suggesting if you get contacted by an IBD patient who is on azathioprine, 6-MP, methotrexate, or tofacitinib, hold off on the therapy at this point. You should restart after they're completely better, if they had symptoms, or if they had follow-up testing that was negative or serologic testing.²³

Right now, we're also suggesting that... hold off on the monoclonal antibodies for 2 weeks.²³ Again, these are patients who have IBD; they're on whatever therapy you have them on, and they tested positive for COVID, but they don't have COVID symptoms. Just to be on the safe side, probably within 2 weeks, you'll know within 2 weeks whether they develop COVID symptoms. If they do develop COVID symptoms, well, that's going to be our next module. But if they don't develop the COVID symptoms, then you can probably restart them after a couple of weeks.

Meeting the Medical Needs of Patients with **Ulcerative Colitis**

During the **COVID-19** Pandemic

Testing—Managing UC Treatment in Positive Asymptomatic Patients

- More testing is needed and could reveal more cases
- It is required to test patients before endoscopic procedures or surgery, even if they have no specific symptoms suggesting COVID-19
- Testing for SARS-CoV-2 infection is not required for IBD patients presenting diarrhea (unless they have fever and/or chills and/or cough)
- And more testing helps contain disease spread

Slide corrected based on more recent studies and clinical practice

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Talavera C, et al. *Aliment Pharmacol Ther*. 2020;34(11):1111-1124.

As you know, as you get more testing, you may reveal obviously more cases. Generally... this slide is a little outdated because it is required to test patients before undergoing any endoscopic procedures or surgeries, regardless of who they are. (Note, slide has been updated since the recording to reflect current practice). Generally, we do not—even though the slide says—we don't test IBD patients who have diarrhea for SARS-CoV-2. I'm sorry. There's a little error on this slide. That is not a recommendation because as I showed you earlier, if they don't have a fever and/or chills and/or cough, it's highly unlikely that they have the infection. We'll just skip over this to the next slide because that was an early slide that has been discounted by more studies, subsequently.

Considerations for Services—Infusion Service

- Patients should not attend if they are symptomatic for COVID-19
- Screen on arrival for symptoms and pyrexia.
- Parenteral electrolyte and iron replacement services should be reserved for urgent cases only.
- If capacity is reduced due to staff shortages, implement daily or weekly triage of infusions.

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Fennedy NA, et al. *Gut*. 2020;61:194-196.

So, what about the infusions? Like we said, patients should show up for their infusions, but not if they have active COVID-19. Remember, most of these patients in the infusion centers or chemo patients— patients receiving chemotherapy. So, if your patient has symptoms with COVID-19, they should be screened for symptoms and fever, and occasionally you might need other IBD therapies, if necessary.²⁴ And if you have your staff... you want to protect your staff, as well. You don't

want to lose your whole staff just because one turns positive. Consider having staff in maybe every other day, like a Monday, Wednesday, Friday staff, and a Tuesday, Thursday staff in your infusion area, that way... And even in your endoscopy area, maybe having rotating staff, so that way, if one of the group turns positive, you don't have to wipe out your entire staff for 2 weeks, but only those who were working those days with that group.

Considerations for Services—Endoscopy

- IBD surveillance procedures should be deferred.
- IBD disease assessment scopes need to be assessed for priority.
- Alternative methods of disease assessment, including the use of biomarkers, radiology, and capsule endoscopy should be considered.

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Fennedy NA, et al. *Gut*. 2020;61:194-196.

Right now, until very recently... So again, these slides change as you go to the next phase, and you're reopening. In Illinois, now we're in phase 4, so we are starting to do our surveillance procedures again, but we weren't before then. Certainly, depending on the prevalence of the virus in the community would determine when you can start doing those type of procedures. But also, as this slide points out, try to assess your patient's in non-endoscopic ways: biomarkers, so CRP, fecal calprotectin, fecal lactoferrin, radiology, when appropriate.²⁴ Capsule endoscopy is probably a little hard to argue doing that. I guess if you're maybe looking for a GI bleed or are trying to find a source, but just remember that if the capsule gets stuck, someone's got to go in and get it out, so probably think hard before you're do any capsule in these patients. I mean, at this time.

Considerations for Services—Imaging

- Capacity for outpatient imaging may be reduced.
- Access to different imaging modalities may vary during the pandemic, which may influence the choice of investigation for patients with IBD.

As far as the imaging, be respectful of that. The radiology areas until things are opening up, are also going to be limited, as well. Again, the slides says that as we go into better phases, now you're in a phase where if you're in a state where there's very low rates, and the radiology people want all the money back that they haven't been making, so, now they're opening up again, too. Just be aware of the availability.

Considerations for Services—Surgery

- Defer elective operations.
- Urgent management of perianal sepsis should be undertaken as a day-case procedure.
- Complex IBD surgery should be deferred where possible and its timing reviewed regularly.
- Emergency procedures (eg, subtotal colectomy in acute severe UC) will continue as part of routine care.
- Choice of postoperative therapy to prevent recurrence will need to be considered in the context of the COVID-19 pandemic.

Surgery, as you may have heard initially, patients who were sick with COVID or who are asymptomatic but had COVID and underwent surgery did very poorly. So, everyone drew back, and that was probably more in April. Now into May, now that we've had better testing and more testing, while we still do not want to do surgery on COVID patients, we are able to open up these surgical suites as the rates have gone down as well, too. And as I mentioned, you want to protect your staff and maybe having rotating groups that come in as well, too.

Sometimes if you want to avoid a very long surgery in a patient, let's say they do have COVID, but they have a bowel obstruction, they need it. Bringing up a loop ileostomy may be the way to go. Even if they have severe

colitis, because that'll at least defer things, and then subsequently a longer surgery can be done in a less risky time.²⁴

Considerations for Services—Clinical Trials

Participant screening, recruitment, and continuation (for those already recruited) should be reviewed at local level for appropriateness in the current clinical situation.

So, the clinical trials, I mentioned earlier, don't let your patients fall out of the clinical trials. But in reality, you have to protect the patient. They come first. As things open up, and as we get to better levels of reopening as where we are now, at least in Illinois, and some other states, we're allowing the clinical trials to move forward. When things were bad with the infection rates, we were not doing the scopes, the clinical trials. Companies allowed us to skip the endoscopy or colonoscopies because it really wasn't something that we could justify, but they let the patients stay on the on therapy. Hopefully, we'll be emerging from that too.

Module 4: Medication management of UC patients with symptomatic COVID-19 but without suspicion of active UC inflammation

- Treatment adjustment for symptomatic patients
- AGA decision tool
- UC patients with severe COVID symptoms
- Therapy considerations

Let us say you have a different scenario, and then moving along, the patient tests positive for COVID-19 *and* they have symptoms of COVID-19, but their IBD has been fine. So, they have the fevers and chills or whatever, the cough, and they said, "Hey, I had this fever and cough. They tested me for COVID. I'm positive. My ulcerative colitis is doing fine. What do I do?" Well, if the patients

are well... We already went through some of the guidelines, and I do recommend you download them. Right now, we try to avoid things that cause more inflammation. And we're going to talk a little bit about dosing of medicines. So, I'm going to show you some of the recommendations from Dave Ruben's and my paper in *Gastroenterology*.²³ Most of these are legitimate based on what we believe is true. I'm going to show you a little data later that raises some questions about it.

Treatment Adjustment for Symptomatic but Without Suspicion of Active UC Inflammation

IBD treatments safe to continue

- Aminosalicylates (first line and maintenance treatment)
- Topical rectal treatment
- Dietary management
- Antibiotics
- Budesonide, continue if needed for ongoing control of IBD

5-ASAs, 5-aminosalicylates.

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Rubin DT, Cohen RC, et al. *Gastroenterology*. 2020;50(4):505-514.e1-5. doi:10.1053/j.gastro.2020.04.012

Overall Treatment Modification for UC Patients With Severe COVID Symptoms but Stable UC

- Discontinue thiopurines, methotrexate, tofacitinib
- Discontinue anti-TNF, ustekinumab, unless updated clinical data suggest benefit
- Discontinue vedolizumab?
- Re-start therapies after complete symptom resolution, plus follow-up viral or serologic tests to confirm recovery

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Rubin DT, Cohen RC, et al. *Gastroenterology*. 2020;50(4):505-514.e1-5.

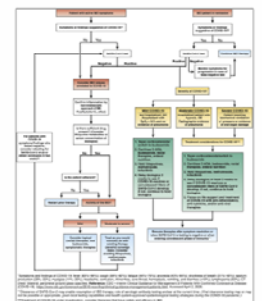
As I mentioned earlier, so this is again a patient who has COVID *and* is symptomatic with COVID, we would certainly stop the thiopurines, azathioprine, 6-MP, methotrexate. Right now we're saying tofacitinib. It may be a role for the JAK inhibitors in treating COVID, but we'll get back to that. And right now, if someone has COVID with symptoms, we're holding their anti-TNF, their ustekinumab. We are holding vedolizumab. It probably doesn't matter. I mean, vedolizumab is typically only given every 2 months. And the every 2-month data is similar to every 3-month data in stable patients, so it's probably fine just to hold off on that, too. We don't think that is going to increase your infection risk. But it's important that once patients are better, and they are recovered, ideally, if they have proof that they don't have the virus—although, we don't necessarily rely on them entirely—you'd want to restart the biologics. Probably still hold off on the immunosuppressants in those cases.²³

So, first line therapies we believe should be safe: 5-ASA (aminosalicylates), sulfasalazine, topical therapies... Although, remember that hydrocortisone enemas, up to 40% of the 100 mg of hydrocortisone is systemic, which is about 10 mg of prednisone systemically, so perhaps use something different than that. Try dietary adjustment. Antibiotics, probably is more of a Crohn's thing than an ulcerative colitis thing. And budesonide.²³ There's oral budesonide, there's different formulations. There's a controlled ileal release, which releases in the small bowel, right colon, which is usually used more for Crohn's. And there is the multi-matrix release, the 9-mg once-a-day pill that is colonic release. And there's a budesonide foam. Other countries may have other formulations for budesonide as well, too.

AGA Decision Tool—Algorithm

AGA Clinical Practice Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic: Expert Commentary.
 David T. Rubin, Joseph D. Feuerstein, Andrew Y. Wang, Russell D. Cohen
Gastroenterology. DOI: 10.1053/j.gastro.2020.04.012

- Algorithm Guide to assist with complex clinical decisions when your patient is symptomatic or with active UC inflammation
- Flowchart provides management of patients with IBD during the COVID-19 pandemic



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Rubin DT, Cohen RC, et al. *Gastroenterology*. 2020;50(4):505-514.e1-5.


Remember earlier on, I said, "Make sure you download the slides." You definitely want to download this slide because I'm not going to read this whole thing to you. It's a long one. Dave and I, Dave Ruben, along with Joe

Meeting the Medical Needs of Patients with **Ulcerative Colitis**

During the **COVID-19** Pandemic

Feuerstein and Andrew Wang, published this in *Gastroenterology*.²³ It's an algorithm, and it gives you different scenarios. What do you do (on the left-hand side of the top) if someone has IBD symptoms, vs (on the right-hand side of the top) if they are in remission. And then you go down, well, what if they have symptoms of COVID-19, yes or no? And then once they get tested, if it's positive, where do you go? If it's negative, where do you go? A lot of this I'm covering in the presentation, and I'm not going to read you this entire slide. It is somewhat what I already said, but it is helpful. And if you print it out, you can have it for your reference, as well. I believe if you go to the AGA website, gastrojournal.org, it's a PDF, so I believe you can download that, as well.

SECURE-IBD Registry Protocol




- IBD clinicians worldwide are encouraged to report all cases of confirmed COVID-19 in individuals with IBD in a secure electronic database using a secure web-based platform
- Report a case <https://covidibd.org>
- Report after ≥7 days with sufficient time to observe disease course through resolution of acute illness and/or death
- The case report form includes items relating to the patient's:
 - Demographics (eg, age, gender, race)
 - Country/state of residence
 - Diagnosis
 - Year of COVID-19 diagnosis
 - Immunosuppressive medication at time of diagnosis
 - COVID-19-related death
 - COVID-19 treatments prescribed
 - Hospitalization (includes name of hospital, length of stay, if need of a ventilator)

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covidibd.org, Accessed June 10, 2020.

You can get all this information. I'm going to go through some of the data in a few minutes, and it's really giving us terrific information about what happens to IBD patients who test positive for the SARS-CoV-2. It does not tell us what's the risk of getting SARS-CoV-2 and what happens to IBD patients who don't have SARS-CoV-2. That's not included. And you can see the case-form information here, which I am not going to read to you.

Corona and Its Prevalence Specific to IBD

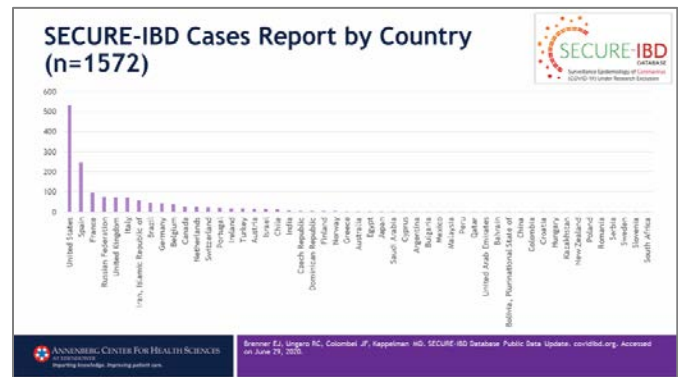


Surveillance Epidemiology of Coronavirus Under Research Exclusion (SECURE)-IBD database

- An international collaboration between experts in epidemiology and IBD created a voluntary registry for professionals to report patients who test positive for SARS-CoV-2
- Tracks impact and clinical outcomes with dynamic data
- Publicly accessible and updated every day
- International database monitors and reports outcomes of COVID-19 occurring in pediatric and adult patients with IBD
- Tracks epidemiology of COVID-19 among individuals with IBD
- Evaluates for potential associations between COVID-19 prevalence and severity and demographic and medical factors

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covidibd.org, Accessed June 10, 2020.



So, one of the exciting things that was done is, very soon after things started with COVID-19, a bunch of IBD specialists from around the country, and even some international colleagues, created this Surveillance Epidemiology of Coronavirus Under Research Exclusion, or SECURE-IBD Database.²⁸ We call it the **SECURE-IBD Database** for obvious reasons. And what this is, and if you are a provider, please do this: If you have a patient with IBD who tests positive for the COVID-19, for the SARS-CoV-2, so for the virus, *please* report the case in this database.²⁸ It's free. Anybody can access it. You can access it right now, except you're paying attention to what I'm saying, and you will be contributing to the data. But it's only if they have IBD *and* they test positive for the virus. It's very easy. It's covidibd.org. It's updated daily.

So, what do we know so far? This recent update, this was assessed yesterday. No, 2 days ago, June 29th, 2020. You can see that most of the cases reported are from the United States and then Spain, France, and going down. This is not a reflection of where IBD cases who have COVID are located. It's just where they have been reported.²⁹

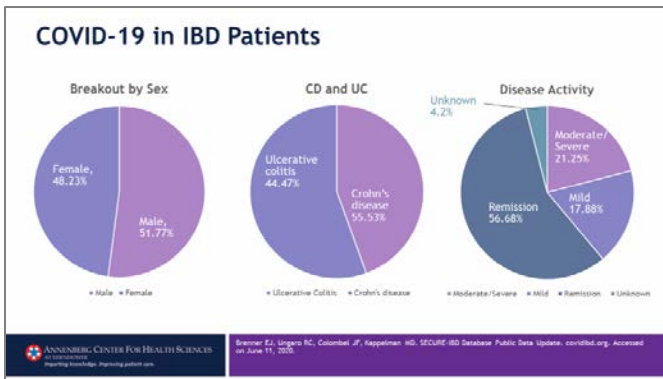
Look at this beautiful map they have showing you... And you can even change the date on the bottom to show the change in color in time. And I believe many, if not most of the people on today's program are living in the United States, and you can see it doesn't look very good for us. Spain, in particular doesn't look good, too. It's actually a

Meeting the Medical Needs of Patients with **Ulcerative Colitis**

During the **COVID-19** Pandemic

nice geography test for your kids, too, or maybe your spouse... and gives you the dates, the cases, the hospitalizations, the deaths, whatever may be.²⁹

hospitalized numbers: 25% of Crohn's, 34% ulcerative colitis.²⁹



Initial Published Analysis of SECURE-IBD Registry

Brenner et al.

- n=525 from 33 countries (data collection as of May 8, 2020)
- 37 patients had severe COVID-19 infection
- 161 were hospitalized
- 16 died

Monotherapy with anti-TNF and anti-IL12/23 agents appear to have a lower association for IBD patients with severe COVID who require hospitalizations, ICU, intubation, death.

Risk factors for severe COVID-19 infection included increasing age and use of systemic corticosteroids, sulfasalazine, or 5-aminosalicylate. Anti-TNF treatment was not correlated with severe illness.

Risk factors in patients with IBD for severe COVID-19 (similar general population): age or increasing number of comorbidities ≥2, in addition to IBD.

Strongest risk factor in patients with IBD for severe COVID-19 was systemic corticosteroid use. Patients had at least a 6-fold higher risk for developing severe COVID-19. Findings reiterate importance of limiting and tapering use of steroids in IBD patients during era of COVID-19.

anti-TNF, anti-tumor necrosis factor.

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Brenner EJ, et al. *Gastroenterology*. 2020;16:1053.

So, what's some of the data? Well, COVID-19, or the virus at least, does not discriminate by gender. You can see of the cases that are reported, they are equal gender and about equal in Crohn's and ulcerative colitis. And most of the patients are in remission or just mild disease. So, 57, right? And 18, right? It's like 75%.²⁹ So, three quarters of the patients are in remission or mild disease, which is good. It means that we're doing a good job, if patients are in remission or mild disease. And especially going into the pandemic with patients on immune suppressants, it's nice that they're already well, and hopefully well off of steroids.

An initial publication came out summarizing some of the data.³⁰ These were actually kind of surprising. We would suspect, "Well, you're in trouble if you're on a biologic." Not true. People on monotherapy with an anti-TNF or an anti-12/23, so the anti-12/23 right now for IBD is ustekinumab. The anti-TNFs are infliximab, adalimumab, golimumab, and certolizumab. They have a lower association for patients with severe COVID who require hospitalization, ICU, intubation, or death. Lower. I'm going to show you the numbers in a minute.

But what is the risk factors for patients who have the COVID-19 infection getting bad, being bad and being hospitalized or worse? It's increasing age and the use of steroids. It also showed up for sulfasalazine or 5-ASA. I mentioned that a little earlier. I think that that's probably an issue with the patients and the data, but we can look into that more. And what was the risk factor for having severe disease? Increased age or a number of comorbidities. And the strongest risk factor was systemic steroid use. Patients had a 6-fold increase of getting severe COVID if they were on steroids. So, we really don't want our patients on steroids.

IBD Patients With COVID-19 Recent Hospitalization

- Patients with severe IBD and COVID-19 are more likely to be hospitalized than patients with mild to moderate symptoms of COVID.
- SECURE-IBD (as of June 29, 2020)
 - n=1572
 - 455 (29%) hospitalized, of those:
 - 220 (25%) Crohn's disease
 - 234 (34%) Ulcerative colitis

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Brenner EJ, Ungaro RC, Colombel JF, Heppner HD. SECURE-IBD Database Public Data Update. *crohnlibd.org*. Accessed on June 29, 2020.

So, patients with COVID-19 recent hospitalization. It turns out that, and this is important, patients who have active IBD are more likely to be hospitalized, especially severe IBD, are more likely to be hospitalized than those with mild-to-moderate symptoms. And you can see the numbers, I think we just showed, and here's the

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During the COVID-19 Pandemic

IBD Medications Used in Patients With Severe COVID-19 Steroid, Immunosuppressive Agents

Source: <https://covidibd.org/current-data/>
Date last updated: 06/29/2020

IBD Medication	Total N	Outpatient only n (%)	Hospitalized n (%)	ICU n (%)	Ventilator n (%)	Death n (%)	ICU/Ventilator/Death n (%)
	1572	1097 (70%)	455 (29%)	85 (5%)	69 (4%)	51 (3%)	118 (8%)
Sulfasalazine/mesalamine	481	284 (59%)	193 (40%)	41 (9%)	38 (8%)	27 (6%)	60 (12%)
Budesonide	41	25 (61%)	15 (37%)	4 (10%)	3 (7%)	2 (5%)	4 (10%)
Oral/parenteral steroids	126	52 (41%)	71 (56%)	20 (16%)	15 (12%)	11 (9%)	25 (20%)
6MP/azathioprine monotherapy	156	104 (67%)	52 (33%)	13 (8%)	10 (6%)	3 (2%)	15 (10%)
Methotrexate monotherapy	11	6 (55%)	5 (45%)	0 (0%)	0 (0%)	1 (9%)	1 (9%)

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Brenner EJ, Ungaro RC, Colombet JF, Neppleman HD. SECURE-IBD Database Public Data Update. <https://covidibd.org/current-data/>. Accessed on June 29, 2020.

IBD Medications Used in Patients With Severe COVID-19 Biologics

Source: <https://covidibd.org/current-data/>

IBD Medication	Total N	Outpatient only n (%)	Hospitalized n (%)	ICU n (%)	Ventilator n (%)	Death n (%)	ICU/Ventilator/Death n (%)
	1572	1097 (70%)	455 (29%)	85 (5%)	69 (4%)	51 (3%)	118 (8%)
Anti-TNF without 6MP/AZA/MTX	454	377 (83%)	72 (16%)	9 (2%)	5 (1%)	3 (1%)	10 (2%)
Anti-TNF + 6MP/AZA/MTX	150	101 (67%)	49 (33%)	10 (7%)	5 (4%)	3 (2%)	12 (8%)
Anti-integrin	153	108 (71%)	40 (26%)	7 (5%)	7 (5%)	5 (3%)	11 (7%)
IL-12/23 inhibitor	139	116 (83%)	19 (14%)	5 (4%)	4 (3%)	1 (1%)	5 (4%)
JAK inhibitor	22	17 (77%)	5 (23%)	2 (9%)	1 (5%)	1 (5%)	2 (9%)
Other IBD Medication	60	35 (58%)	24 (40%)	5 (8%)	3 (5%)	2 (3%)	5 (8%)

6-MP, 6-mercaptopurine; AZA, azathioprine; MTX, methotrexate.

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Brenner EJ, Ungaro RC, Colombet JF, Neppleman HD. SECURE-IBD Database Public Data Update. <https://covidibd.org/current-data/>. Accessed on June 29, 2020.

Here's some of the data. And the next 2 slides show this. On the left is the medicine. And these are the mesalamines and the steroids and the immunosuppressants. And then it shows you the total number. So again, everybody has IBD, and they all tested positive for SARS CoV-2 and were reported by their provider. You can see the percentage that are outpatient, the percentage that are hospitalized, the percentage—I'm going across—ICU, ventilator, death, or combined.

Look in the middle row: oral/parenteral steroids. Hospitalized, so the fourth column down, half of them, 56% of them are hospitalized; 16% in the ICU, 12% on a ventilator, 9% death, 20% combined ventilator death.²⁹ It's much higher than the other rows.

What's even more impressive is when you go to the more "serious medicines" (the top row here), anti-TNF monotherapy: hospitalized was only 16%, 2% in ICU, 1% in ventilation, 1% death, 2% ventilator or death. I mean, I'm actually just going to go back if I can. So, compared to 56% hospitalized if they're on steroids, you have 16%. That's a 40% decrease. And virtually nobody is going on a ventilator or dying on the anti-TNFs. The rates, if you're on anti-TNF combined immunosuppression, are a little higher. You go down next, anti-integrin, you're again very low rates of hospitalization. The anti-IL-12/23, very low rates, the same as the anti-TNF.²⁹ Virtually nobody got very sick. The JAK inhibitors, there were only 22 patients. It's hard to make conclusions on that. We think that they may be somewhere protective based on some other data, perhaps with other JAK inhibitors that we don't use right now.

So, these are numbers you can access right now or anytime you want. And you can tell your patients who are on ... most of your patients who are on biologics and don't want to be taking them. You would say, "No, actually you do want to be taking them, because if you're not going to take them, you're going to get sick and end up on steroids. And then you're going to have bad outcomes."

Module 5: Medication management of UC patients with symptomatic COVID-19 with symptoms of active inflammation

- Confirm active inflammation
- Mildly active UC
- Moderate to severely active UC
- Managing UC patients hospitalized for COVID-19
- Post-pandemic considerations

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The last module of the group are the people who not only do they have COVID-19 and are sick with it, but they also have *active* IBD. And that can be tough.

Outpatient Clinics—Confirm Active Inflammation

- Confirm active inflammation with non-endoscopic tests
- Limit endoscopy
- Clinical scenarios that may prompt endoscopy include need to
 - Obtain biopsies to diagnose new severe IBD,
 - Exclude cytomegalovirus (CMV) if noninvasive tests are equivocal,
 - Note: CMV testing may be done as a serum polymerase chain reaction to avoid need for colonoscopic procedures
 - or in patients with severe disease or suspected cancer where mucosal inspection might direct surgical intervention

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Rubin DT, Cohen RC, et al. Gastroenterology. 2020;50(16):5683-62.e4.

Meeting the Medical Needs of Patients with Ulcerative Colitis

During the COVID-19 Pandemic

We already told you that we don't want to give steroids, but you might have to. And it may not be as bad if they have active COVID, as we'll talk about in a minute. You may still have to do endoscopy, but probably not. Probably try to, if you think someone has CMV [cytomegalovirus], you may even do a flex sig [flexible sigmoidoscopy]. You can check sim serum CMV. Obviously, a cancer patient, you may have to do that. You can do imaging, but you might have to do scopes.²³

We tried to limit in the IV steroids to 3 days. However, all what I'm telling you right now may be changed... since remember, these are patients who are sick with COVID in the hospital and have IBD that is active. But the infectious disease people may say, "No, we actually want you to continue the steroids based on this newer data with the dexamethasone." So, you're going to certainly have to work with them in that case. And as we mentioned, bad things happen to people with active COVID if they go to surgery. I certainly would prefer giving someone steroids or biologics than sending them to surgery and having very poor outcomes and expose the entire OR and the staff to COVID.³¹⁻³³

Mild or Moderate to Severely Active UC

<p>Mildly active UC Use safer therapies</p> <ul style="list-style-type: none"> 5-ASA (UC) Budesonide (CD and UC) Partial or full enteral nutrition (CD, mostly pediatric) 	<p>Moderate to severely active UC usual treatments if COVID symptoms are mild</p> <ul style="list-style-type: none"> Avoid steroids if possible (even for induction) Treat with the same therapies you would choose in the pre-COVID-19 era
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5-ASA, 5-aminosalicylates; CD, Crohn's disease; UC, ulcerative colitis.

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Rubin DT, Cohen RC, et al. Gastroenterology. 2020;501(6):5083-542-6.

Post-Pandemic Considerations

Pertinent questions for gastroenterologists and those treating patients with UC:

- Address lapses in monitoring and follow-up
- Assess patient adherence to therapy
- Consider reintroduction to therapy
- Uncover symptom exacerbation
- Revisit HCP-patient communication

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As we mentioned, it's probably okay to be on the first-line therapies for IBD. But if someone's really sick, then you might be in a bind. We're leaning more towards giving those patients biologics, but now given the data with the dexamethasone—and unfortunately, I don't believe we've seen the full data yet, we just had the press release, although I might be incorrect. They may have released that. We're now saying, "Well, if the patients really need IV steroids, then perhaps they should get it." Give them topical therapies, and watching with the surgeons as well, too. And again, you can download these slides.

So, now all of a sudden, you're going to see patients, or you're going to have virtual video visits or telephone visits with your patients, and guess what? They stopped their medicines months ago. Right? They saw the news, they turned off the television, they ran into the bathroom, and they throw them out. They threw their injectables into a dartboard. Who knows what they did? And now they're saying, "Well, what do I do?" Well, you try to get people back on therapy, even if they're feeling well, because you want to prevent relapses. It's usually very easy to restart therapies in patients and emphasize to them the data that the **IBD medicines are good, and that not being on them is bad**. You want to assess their adherence and reinforce that they need to stay on their medicines, and certainly [encourage them] to contact you if they have concerns with symptoms of COVID. You can review with them what those are as well, too, as well as what resources are available for them.

Hospital Admission Requirements:

Criteria
≥6 bowel movements along with ≥1 of:

- Medical resistance +/- systemic toxicity
- Tachycardia
- Fever
- Hemoglobin <10.5g/dL
- CRP elevated

<p>Initial Workup</p> <ul style="list-style-type: none"> Test for COVID-19 Rule out CDI and CMV VTE prophylaxis Assess for toxic megacolon Endoscopy only if it changes management 	<p>IBD Management</p> <ul style="list-style-type: none"> IV corticosteroids (max 60mg/day of methylprednisolone) for 3-5 days Topical hydrocortisone enemas/budesonide foam Surgical consultation Serial KUB if dilated colon seen on imaging Assess symptoms and CRP daily NO narcotics/anticholinergics/antimotility therapies 	<p>Clinical Response Assessment</p> <p>NO</p> <ul style="list-style-type: none"> Initiate therapy with either infliximab or tacrolimus Consider tofacitinib in select patients Surgery <p>YES</p> <ul style="list-style-type: none"> Transition to oral prednisone Treat as outpatient
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Adapted from Naur R, et al. Clin Gastroenterol Hepatol. 2020;18:1346-1355.
Reprinted from Rubin DT, Cohen RC, et al. Ann J Gastroenterol. 2020;114:308-413.

As I mentioned, as your states and your localities are opening up, particularly people with symptoms, you got to bring them in for scopes. I mean, we just had a recent

patient, this person was failing, failing their IBD therapy, miserable, they had to come in the hospital, whatever it may be. I actually didn't do the scope, because I'm talking to you, but my fellow, my partner just texted me while I was talking to you. But nevertheless, they contacted me, and they said that her colon was virtually normal, that the IBD was not active. So, look and see. Goodness, we would have been giving this patient high-dose steroids and all this and that, too. If you don't want to look and see, check the faecal calprotectin, especially if you know people make faecal calprotectin. Take a CRP, especially if they make CRP. Not everyone does. With this patient, this individual, I'm kind of cheating a little bit because we got her CRP, and she makes CRP when she has inflammation, and it was normal. But she was already on the endoscopy schedule and we wanted to see what's going on anyway.

Try to use noninvasive methods, like I said, too. But at the same time, especially if the rates are low, all the patients now, or at least in Illinois, are tested COVID negative. And ulcerative colitis, just do a flex sig. You just stick a scope in and see what's going on.

You may have had patients who you were supposed to do follow up for dysplasia. Okay? So, things kind of shut down in March. So, now we're in July. That's right, July 4th this weekend. You were holding off their annual dysplasia, or maybe every 6 months dysplasia screening, and that was supposed to be 4 months ago. You're going to be kind of behind the 8 ball. So, maybe bring those patients in, maybe not the patients who are just routine surveillance, if you're not ready for that, yet. But certainly, and in being gastroenterologists, consider that patients who have rectal bleeding, as you know, unfortunately some of them have colon cancers. And we've seen that even in young people, and the ones who were told it's hemorrhoids by the college nurse or whoever, and it turns out that the thin young person never had hemorrhoids. Consider being a gastroenterologist again, getting the patients in, reassuring them about the procedures, about the locations, and as I mentioned in IBD, about their therapies.

Key Takeaways

- IBD medication adherence should be encouraged to prevent disease flare¹
- When possible, high-dose of systemic corticosteroids should be avoided¹
- Patients who test positive for COVID-19 should¹
 - Stop use of corticosteroids
 - Withhold immune-suppressing medications until infection resolves
- Anti-TNF not associated with an increased risk for COVID-19 infection
- Therapeutic approach needs to be personalized and based on balance between risk of viral infection and the risk of disease recurrence²
 - Effective disease control carries less risk than poorly considered withdrawal of therapy³
- If your patient with IBD has had COVID-19, report the case in SECURE-IBD registry: <https://covidibd.org>⁴

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As we're finishing up the formal presentation, and before we open up for questions, I really want to encourage you to be active in these patients' care. They're terrified of SARS and COVID. You probably know that from your patient calls and your staff, as well, too. Knowing what you do either before my presentation or afterwards, that **steroids are bad, that IBD medicines are generally good** other than steroids. Try to get your patients off of steroids, but also really encourage them to **go back on their therapies to stay well**. We don't want a bunch of sick IBD patients running into our hospital in the middle of a COVID flare or whatever, this and that too. We don't want them to go into surgery. We don't want to have to do an endoscopy in those situations. **Don't stop their anti-TNFs or their other biologics unless they're diagnosed with active SARS COV-2, and then you'd hold off for 2 weeks**, as I mentioned. And if they're sick, maybe longer.

Don't tell them to avoid the infusion centers, and get them back in. Like I said, you can verify these centers are taking the steps they need to be. I'd be shocked if they weren't considering the patients that go there are mostly chemotherapy patients. And another issue I brought up, I didn't bring up, but I want to, is that some of our patients on combination therapy who have been doing well... we're stopping the azathioprine, 6-MP, or methotrexate in this setting, because those patients from that database I showed you—the covidibd.org database—didn't seem to do as well as the monotherapies. We're not doing that if patients really need to be on combo therapy. People have made antibodies against their previous anti-TNF; patients who had tough perianal disease or failed multiple biologics. But I am someone who routinely was giving combo therapy to my anti-TNF patients. It's probably less

necessary with the other therapies, but this may be a time to get them off the combo and onto monotherapy if they've been well, documented well, endoscopic remission when the last time you saw [them], clinically in remission, as well too. It may help the patient with their stress and anxiety, as well too.^{17, 28, 34, 35}

Do report your cases to the database. You can become one of the valiant caregivers to help us find out more information about what happens to IBD patients who

test positive with COVID. It's not a dog of a questionnaire for you to fill out. Because some of them are ridiculous. I mean, they ask you the name of your grandmother's pet cat or something. This is pretty straightforward. They just [ask for] the information that you need. It is allowed through the database. Well, it did get approval through the University of North Carolina, through their IRB, so that it can be done without concerns for HIPAA. They don't get the patient's name and things. They don't reach out to the patient and contact them either.

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