Updates in the Objective Diagnosis and Evidence-Based Management of IBD

CME Available Until:
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This activity has been approved for 1.5 AAPA Category 1 CME credits

Contents:

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ACTIVITY OVERVIEW

The important role of PAs in patient care continues to grow. With recent increases in the number of patients entering the healthcare system, the role that PAs play in patient care is most certainly magnified. Inflammatory bowel disease (IBD), an umbrella term comprising Crohn's disease (CD) and ulcerative colitis (UC), is a chronic relapsing-remitting condition characterized by persistent inflammation of the gastrointestinal (GI) tract. Because of its chronicity, the need for increased medical visits, and associated comorbidities, patients with IBD have impaired physical and social/professional wellbeing. PAs caring for patients with IBD require educational programs to evaluate patients and identify differential diagnoses, understand treatment goals and manage IBD flares, and screen for and manage key comorbidities. Through the tactical combination of online and print formats, this program will appeal to various learning styles and allow participants to reinforce their knowledge and acquire new skills that can immediately be applied to clinical practice.

AAPA TAKES RESPONSIBILITY FOR THE CONTENT, QUALITY, AND SCIENTIFIC INTEGRITY OF THIS CME ACTIVITY.

EDUCATIONAL OBJECTIVES

- Accurately assess patients with suspected IBD and provide appropriate referrals to GI specialists.
- Apply knowledge of updated classification and treatment guidelines to support the proper treatment of patients with IBD.
- Monitor and manage IBD patients appropriately for important comorbidities.

ACCREDITATION STATEMENT

This activity has been reviewed by the AAPA Review Panel and is compliant with AAPA CME Criteria. The activity is designated for 1.5 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation. Approval is valid through April 30, 2023.

Estimated time to complete this activity: 90 minutes.

HOW TO RECEIVE CREDIT

There are no fees for participating and receiving CME credit for this activity. Participants must: 1) read the educational objectives and faculty disclosures; 2) study the educational materials; 3) complete the post assessments in Learning Central.

In order to receive credit, participants must complete the post-test and evaluation. You will be able to access your certificate of completion in Learning Central as soon as you complete the post-test with a minimum score of 70%. Your certificate will be available under "Transcript" for your records.

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OFF-LABEL/UNAPPROVED PRODUCT(S) DISCUSSION

This program discusses the off-label use of azathioprine.

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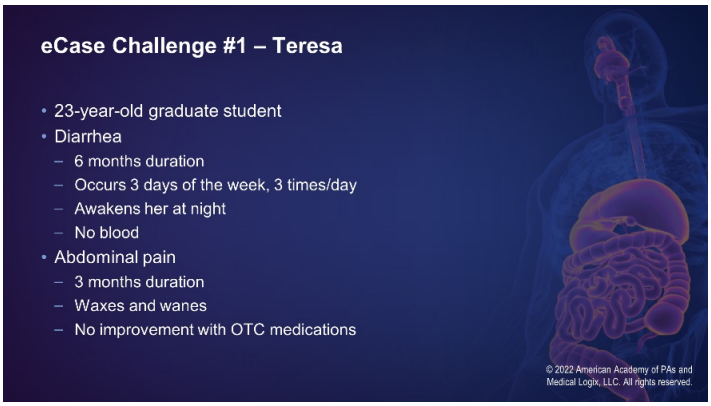
eCASE CHALLENGE #1

Rick Davis, PA-C: Hello, and welcome to this video *eCase Challenge*, "Updates in the Objective Diagnosis and Evidence-Based Management of IBD." I'm Rick Davis, a PA in the Division of Gastroenterology in the College of Medicine at the University of Florida in Gainesville.

Joining me today is Michele Kissous-Hunt, a PA in gastroenterology from Mount Sinai Medical Center in New York City. My thanks to you for your involvement in this important continuing medical education activity, which consists of two video *eCase Challenges*. So let's get started with our first case.

Our first *eCase Challenge* is a patient we'll call Teresa. Teresa is a 23-year-old graduate student who presents to our primary care PA secondary to ongoing diarrhea and abdominal pain. She reports that she was in her usual state of health until about 6 months ago, when she began to have loose stools about 3 days out of the week. She developed associated abdominal pain about 3 months ago.

Of note, her symptoms also began around the time that she moved to a new city to begin her graduate program in engineering. She doesn't recall trying any new foods or medications around the time her symptoms started, and they have remained about the same since onset. Her abdominal pain waxes and wanes, and she has not found any improvement with over-the-counter medications, including NSAIDs, tablet antacids, Pepto-Bismol.



On the days she has loose stools, she reports three episodes of diarrhea a day. She does sometimes awaken at night because of the diarrhea. She has not noted a relationship between any types of foods and the abdominal pain or diarrhea, and she's not noted any blood in her stool or had any nausea or vomiting.

She has not noted any weight loss and reports no fever. She does say that she eats a generally healthy diet with limited alcohol and tries to exercise a few days a week, although this is tough with her rigorous school schedule, which leaves her tired at the end of the day.

Teresa states that her past medical history is pertinent for mild asthma, for which she takes an inhaler PRN. Other than that, she doesn't take any medications except for an occasional multivitamin. She has not had any past surgeries. And regarding family history, her mother has rheumatoid arthritis, and her father has hypercholesterolemia, but that's all. She lives in an apartment with one roommate, and her vaccinations are up to date.

Now, let's pose our first clinical question.

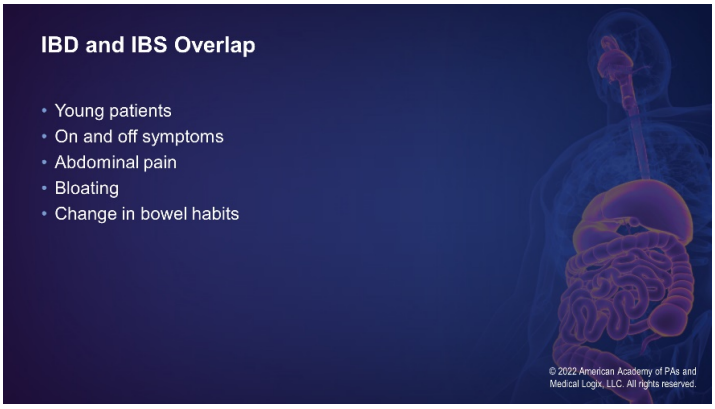
Which of the following elements of Teresa's history is more strongly associated with Crohn's disease than irritable bowel syndrome?

A. Duration of symptoms over 3 months
B. Lack of improvement with OTC medications
C. Maternal history of rheumatoid arthritis
D. Nighttime diarrhea

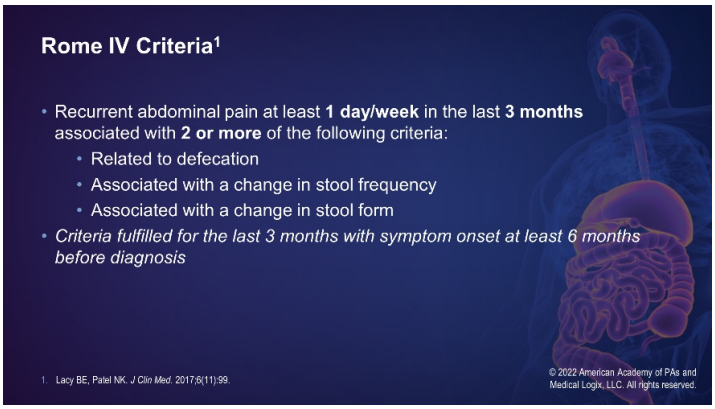
So, remember that IBD and IBS have overlapping symptoms, and it's important to differentiate the two. They can coexist in the same patient, and many times these overlapping symptoms can result in a delayed diagnosis of Crohn's disease, which can present with more nonspecific symptoms.

Michele, have you seen this in your practice, as well?

Michele Kissous-Hunt, PA-C, DFAAPA: So, yes, Rick, absolutely. Since both diseases can occur in young patients and present with symptoms on and off, usually patients will have abdominal pain, change in bowel habits, and this often complicates early diagnosis for these patients.



This is specifically with our IBD patients, specifically harder to make with our Crohn's disease patients. When you look at IBS diagnosis with Rome IV criteria, these patients usually have recurrent abdominal pain at least 1 day per week in the last 3 months that are associated with two or more of the following criteria: related to defecation, associated with a change in frequency of stool, associated with a change in the formation appearance of stool. And these criteria should be fulfilled for the last 3 months with symptoms onset at least 6 months before diagnosis.



So, when we look at our patients with inflammatory bowel disease, or when we're looking for a patient, and we're trying to figure out if they have IBS or IBD, we're really looking for alarm symptoms. We're looking for symptoms such as bright red blood per rectum. Is the patient anemic? Do they have any fever, weight loss, anything like nocturnal symptoms?

So, besides a very careful history, physical exam is key. You have to make sure that these patients have a full head-to-toe physical exam. We really have to make sure that we pick up if these patients have abdominal distention, masses, anything that will clue us in to inflammatory bowel disease rather than irritable bowel syndrome.

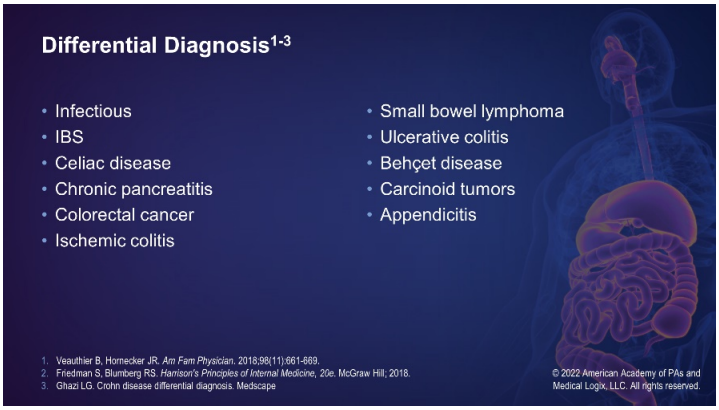
Rick, would you have any other diseases that would mimic Crohn's disease?

Rick Davis: Sure. I think one of the things, too, looking at the history of it being a longer period of time really rules out most of the infectious etiologies, you know, symptoms that have to be for over 3 months or over 6 months. So, these are more chronic symptoms with our patients, not something that's just happened in the past 3 or 4 weeks.

But I think we always need to keep in mind, both for IBD and for IBS, are we missing celiac disease? Chronic pancreatitis, probably more in an older population. Colorectal cancer, of course, probably in an older population. Ischemic colitis, small bowel lymphoma, ulcerative colitis, which tends to be more obvious, with bloody diarrhea.

But there can be other, more rare conditions, including Behçet's disease, carcinoid tumors, that sort of thing. But I think as we get further down on the differential diagnosis list, those tend to be a little bit more on the rare side.

Michele Kissous-Hunt: Okay, so another one that we do see in some patients is appendicitis that can also mimic Crohn's disease. These patients present with right lower-quadrant pain, and it can absolutely mimic chronic disease, as well. So that's another one to look out for.



Rick Davis: So, when we're looking at patients, the diagnostic criteria for Crohn's disease, it's really a constellation of things. Certainly, the clinical presentation, endoscopic evaluation, radiologic, and certainly biopsy, histologic evaluation, as well, in order to make an accurate diagnosis.

Michele Kissous-Hunt: Yes. We should also be looking at inflammatory markers, which we'll be discussing later on in this presentation.

So, let's review the question that is posed, which asks, which of the following elements of Teresa's history is more strongly associated with Crohn's disease than irritable bowel syndrome? So the correct answer here is (D), which was nighttime diarrhea.

Let's take a few moments to review Teresa's history and consider which elements are more consistent with Crohn's disease, which are more consistent with irritable bowel syndrome, and which are overlapping.

The frequency and duration of her abdominal pain and diarrhea can fit with either. The Rome IV criteria for IBS calls for symptoms to have started 6 months prior, and criteria to be fulfilled for 3 months, both of which apply to Teresa. So, she does meet the diagnostic criteria for irritable bowel syndrome.

However, nocturnal diarrhea is unusual in irritable bowel syndrome, and more strongly associated with Crohn's disease. She reported no weight loss or fever, both of which would be more associated with Crohn's disease if present.

Teresa stated that it was hard for her to exercise as much as she would like to because she was tired at night, which she attributed to her school schedule. However, fatigue is often a presenting symptom of Crohn's disease. So, this element of her history needs to be considered more carefully.

The lack of improvement with over-the-counter medications and the remainder of her family and medical and social history do not really help to differentiate between irritable bowel syndrome and Crohn's disease. So, the onset of symptoms upon moving and starting a new school also does not help to identify one condition over the other.

Let's take a few minutes now to review how patient history elements can help us differentiate between irritable bowel syndrome and Crohn's disease. So, Rick, according to the American College of Gastroenterology in 2018 clinical guidelines for the management of Crohn's disease in adults, the hallmark symptoms for Crohn's disease are abdominal pain, diarrhea and fatigue.

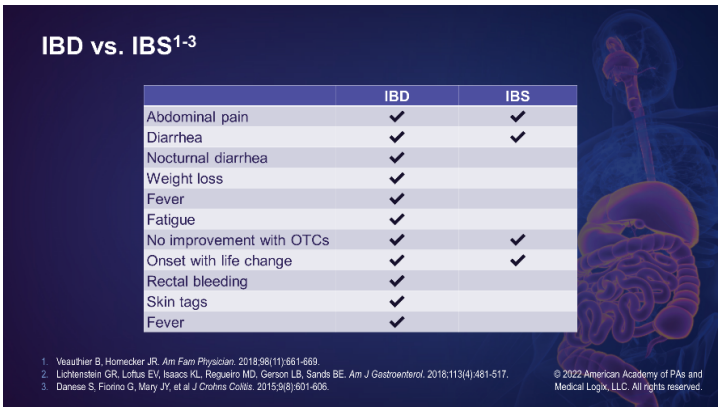
The most common symptom is chronic diarrhea, but not all patients have the symptoms. We know that abdominal pain unfortunately is often seen in the right lower quadrant with these patients, so abdominal pain is often localized to the right lower quadrant and is worse after eating for these patients.

Fatigue is also common and is thought to be multifactorial and related to anemia. This could be due to either iron deficiency anemia or possibly B12 or folate deficiency, inflammation or vitamin and mineral deficiencies, as well.

Rick, anything to add to this?

Rick Davis: Well, I think especially on physical exam, although some patients with irritable bowel syndrome may have rectal bleeding from hemorrhoids and from either constipation or diarrhea, that if patients present with nonhealing or a complex perianal fistula or fissure, which is not in the midline, this might suggest inflammatory bowel disease, or an initial presentation of a perianal abscess and other perianal lesions, may make us think a little bit more of perirectal Crohn's disease.

Michele Kissous-Hunt: Another thing is, if we're doing a physical exam, a rectal exam, and we're seeing skin tags, that should clue us in. A lot of these patients may have skin tags prior to having anything else going on. And we have to make sure that these patients understand that we recognize that these are skin tags and not necessarily hemorrhoids.



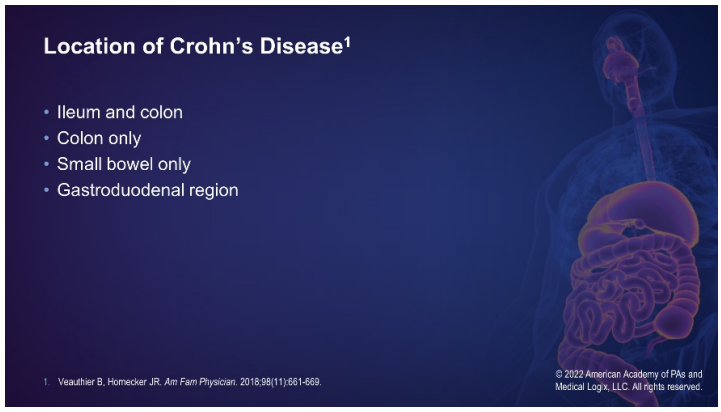
First-degree relatives, also, if they have confirmed inflammatory bowel disease, that should clue us in. Weight loss in these patients should clue us in. Chronic abdominal pain, nocturnal diarrhea, which we already mentioned, as well, and low-grade fever in the last 3 months.

Low-grade fever is extremely important in these patients, and I always say that with Crohn's disease patients, if it's higher-grade fever, like if the patient has spiking fevers, it's an abscess unless proven otherwise, and we should always know about that, right? Always ask our front desk to stop us and let us know if the patient is on the phone calling with high-grade fever. We need to know that immediately. A patient must be seen.

Rick Davis: So, Michele, tell us a little bit about where Crohn's can occur within the GI tract. Where are the most common locations?

Michele Kissous-Hunt: So, Crohn's disease in general can occur anywhere from the mouth down. So patients can have disease, mostly, really the main area is right lower quadrant, that's where we see it most. But many patients can have it in different areas.

They can have in the right lower quadrant, which we'll call ileitis. They can have in the right lower quadrant, as well as some disease in the colon.



Rick Davis: And so generally, if you were evaluating a patient with Crohn's disease, even after the initial diagnosis, you would likely do a complete colonoscopy to assess where disease activity is?

Michele Kissous-Hunt: Yes. So with Crohn's, when we're evaluating these patients, we have to get into the ileum, because we may see some disease in the colon, but we have to get all the way into the ileum, the beginning of the small bowel, see what's going on there, biopsy that area, and that would be our initial colonoscopy.

Okay. So, besides the gastroenterological and constitutional symptoms of Crohn's disease, it's also important to inquire about extraintestinal manifestations when we're considering the diagnosis, as patients with both Crohn's disease and ulcerative colitis can have extraintestinal manifestations at the time of diagnosis.

So before we present more of Teresa's case, we have a new clinical question.

Which of the following is the most common extraintestinal manifestation of inflammatory bowel disease?

- **A.** Arthritis
- **B.** Erythema nodosum
- **C.** Osteoporosis
- **D.** Uveitis

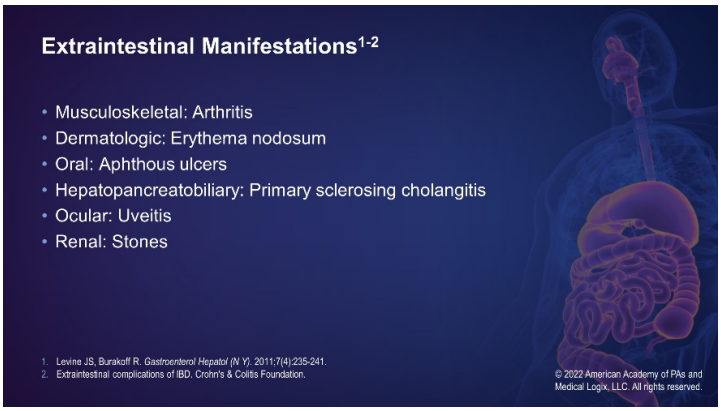
Okay, so up to about half of IBD patients develop at least one extraintestinal manifestation, which can really serve as a diagnostic clue. Joint pain, joint swelling, aphthous ulcers are really one of our major extraintestinal manifestations that we see.

Rick Davis: Some of these can occur even before the diagnosis of inflammatory bowel disease.

Michele Kissous-Hunt: Absolutely, absolutely. So actually, some of the extraintestinal manifestations, about 25% of them, occur before we diagnose, and about 75% of them may occur after diagnosis of inflammatory bowel disease.

So it would be nice, what we'd like ideally to happen is if our dermatology colleagues or our primary care colleagues can even pick up if they're seeing a patient, and they're doing an exam, and they're seeing an erythema nodosum that they might be able to recognize if they can tie that down -- so that they have GI symptoms -- ask these patients more questions and find out maybe this patient has inflammatory bowel disease.

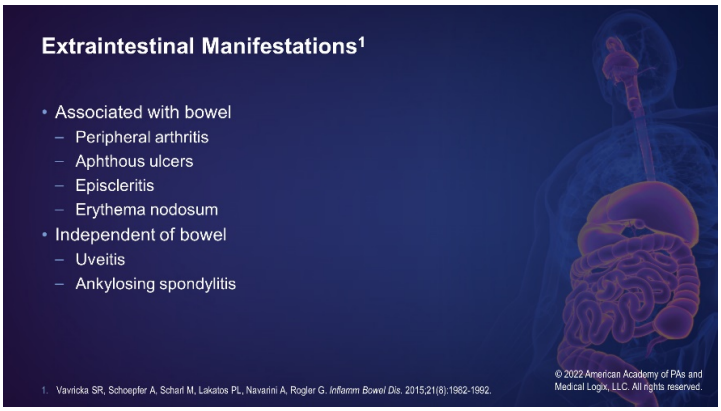
Some of the other key extraintestinal manifestations, and I just want to point out that we really see a lot is the skin, the eyes, the liver and the joints. And we really need to ask every single patient about the mouth, the aphthous ulcers that we're seeing with the eyes, because patients may not know that these are related in any way to their disease.



Arthritis is one of the biggest ones that our patients suffer with. They really suffer a lot with arthritis. Either it's just the joint pain or actual joint swelling. And sometimes when the disease is controlled, then the actual joint pain will be controlled, but not always.

Rick Davis: So, let's say somebody with Crohn's disease, their disease is in remission, but they're still having some extraintestinal manifestations. Can you comment on that a little bit, which ones tend to be more independent of the disease activity in the bowel?

Michele Kissous-Hunt: Yes. So, there are some that are associated, like peripheral arthritis. The oral aphthous ulcers, the episcleritis, erythema nodosum. And then some of the independent ones may be uveitis or the ankylosing spondylitis. Those may be some of the ones that are more independent.



But regardless, if we're treating the patients and treating the disease, a lot of these extraintestinal manifestations actually go away, as well. Rick, do you want to cover any other extraintestinal manifestations?

Rick Davis: Well, I think the dermatologic ones that you mentioned, erythema nodosum, pyoderma gangrenosum, those are not subtle lesions. Usually, they would trigger referral to a dermatologist. We certainly see that in our practice. I think the aphthous ulcers is a great one. A lot of our patients, when they're starting to flare, they may notice more oral ulcers.

Well, I think you mentioned quite a few of them. Certainly, the ocular manifestations, uveitis and scleritis. But the arthritis, the inflammatory arthritides seem to be the most common that we see in our patients, especially when they're having a flare.

Michele Kissous-Hunt: Yes. Those are pretty tough. Patients really suffer a lot with that, and especially when they have the swelling, we tend to sometimes have to use combination therapy on these patients because they could be very sick with the joint swelling. The medication doesn't always work. One medication does not always work for their IBD as well as for their arthritis. So those patients tend to be tough.

Rick Davis: Yes. We often will follow closely with rheumatology.

Michele Kissous-Hunt: Obviously, we're using a multidisciplinary approach on these patients. It's definitely necessary because of all the different organ systems that we mentioned, from ophthalmology. You mentioned rheumatology. And we're really utilizing all our different resources and sending to all our colleagues to work with our patients, as well.

Rick Davis: Yes. Good point. Let's review the last question, which asked, which of the following is the most common extraintestinal manifestation of inflammatory bowel disease? The correct answer is (A) arthritis, which affects about 30% of patients with IBD, as we just discussed.

Now for the next steps in our case. Teresa's physical exam reveals normal vital signs and on the low side BMI of 21. She is well-appearing but mildly pale. On oral exam, she's noted to have aphthous stomatitis. Otherwise, her head and neck exam is normal. Heart and lung, normal. An abdominal exam revealed a soft but nontender abdomen with normal bowel sounds. Her skin exam, no lesions or rashes. And GU exam was normal, as well.

So now, we have the history element of nocturnal diarrhea and a physical exam finding of aphthous stomatitis that are both concerning for Crohn's disease. In addition, her fatigue may be related, and she appears pale, which may point to anemia in association with Crohn's, as well. But we also know that the pattern of her abdominal pain and diarrhea meet the diagnostic criteria for IBS.

So this brings us to our next clinical question.

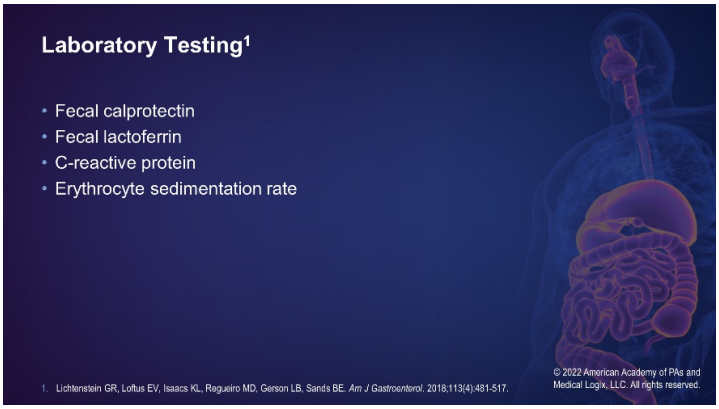
What is the best laboratory test for differentiating between irritable bowel syndrome and inflammatory bowel disease?

- **A.** A complete blood count
- **B.** C-reactive protein
- **C.** Erythrocyte sedimentation rate
- **D.** Fecal calprotectin

So fecal calprotectin is derived from neutrophils and acts to bind calcium. It's involved in the regulation of inflammation and is a surrogate biomarker for intestinal inflammation in IBD and is quantitative. It's stable and resistant to bacterial degradation. Another fecal marker is also lactoferrin. Michele, in your practice, which fecal markers do you use to follow your patients with Crohn's?

Michele Kissous-Hunt: So, we primarily use fecal calprotectin. Really, that's the one that I notice that is mostly used also in clinical trials, in all the new studies. We're always monitoring fecal calprotectin.

Also, besides that marker, we will check for C-reactive protein, like you mentioned, and sed rate, as well. But fecal calprotectin is the one out of those two.



Rick Davis: And in a patient of yours with Crohn's that you are suspecting that they're having a flare, which inflammatory markers do you check? Do you check serology and stool studies, or one or the other?

Michele Kissous-Hunt: So, for these patients, we do check a CBC, a chemistry. We are looking to see to make sure that they're not anemic. We're looking at the sed rate and the C-reactive protein, although many patients do not mount a response. There's about 15 to 20% that do not mount a response to sed rate and CRP, although they may have very active disease, so we can't go by these markers alone.

We will also check a fecal calprotectin. Fecal calprotectin may or may not mount a response, as well, for patients with Crohn's disease, and it depends on where the disease is. So, what we do is we always check all these markers at the beginning when we're evaluating the patients, and we'll see while they're flaring which markers are the ones that are elevated, especially when we're doing the endoscopy, as well. And those are the markers that we're going to continue to follow out.

Rick Davis: That's a good point, and likely making a mention in there, in the chart, so that in the future, not looking at CRP or sed rate in case they might be flaring.

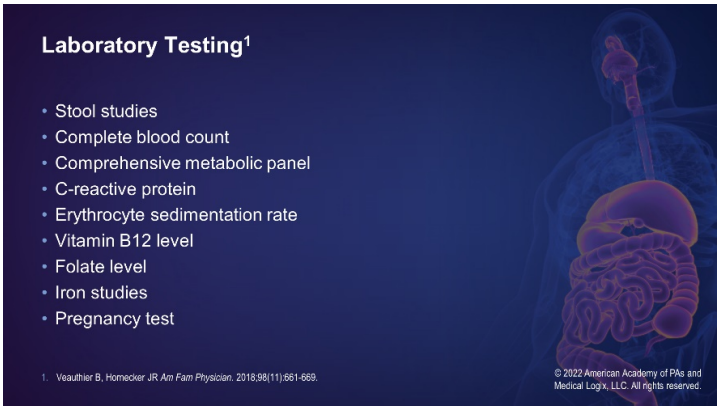
Michele Kissous-Hunt: Absolutely. And you also want to know what numbers you started out with, right? Because fecal calprotectin of 1,000 may be very high for one person, and 200 may be pretty high for another. So, we really have to see what number are we starting out with and to know what's our baseline and where we want to get, especially when we're doing therapeutic drug monitoring and trying to get patients down.

So, before we present more of Teresa's case, let's quickly review the correct answer to the clinical question. Based on the information that was just discussed about the utility of these biomarkers in differentiating IBD and IBS, the correct answer is (D) fecal calprotectin.

Initial laboratory testing should also evaluate for anemia, dehydration and malnutrition. CBC should be obtained, especially because Teresa was noted to be mildly pale on exam, which raised concern for anemia.

Besides the overlap between symptoms of inflammatory bowel disease and irritable bowel syndrome, there is also overlap between the symptoms of IBD and infectious colitis. For this reason, it is reasonable to also obtain stool studies for infection, including *C. diff.*, when considering a diagnosis of IBD.

Therefore, at this time, in addition to the fecal calprotectin, stool for ova and parasites, *C. diff.*, as well as complete comprehensive metabolic panel, a CBC, CRP, sed rate, B12, folate and iron studies, as well as a pregnancy test, should be done.



Now, let's continue the case. Blood and stool studies are completed for Teresa, and she's found to be anemic, with a hemoglobin of 9. And her fecal calprotectin is elevated at 300. She also has an elevated CRP and sed rate.

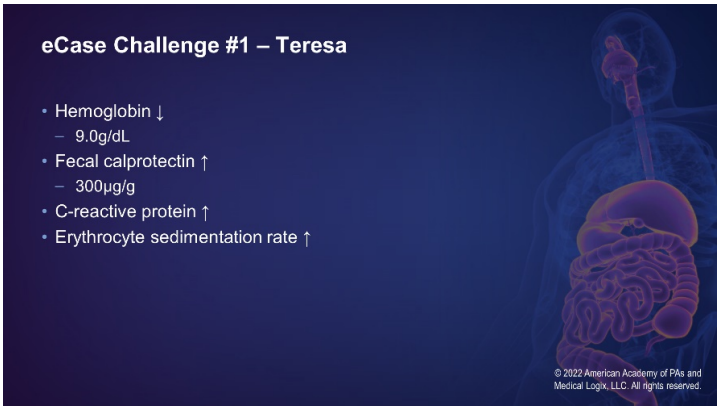
This brings us to our next clinical question.

What is the next best step in Teresa's management at this time?

A. Initiate treatment with sulfasalazine
B. Refer to gastroenterology for ileocolonoscopy
C. Repeat testing of inflammatory markers to monitor disease progression
D. Screen for tuberculosis in anticipation of initiating biologic therapy.

So, Rick, let's talk about this a little.

Rick Davis: Sure. So, Teresa's bloodwork strongly suggests a diagnosis of IBD. She has anemia, elevated fecal calprotectin and elevated inflammatory markers. So, endoscopic procedures allow for direct visualization, but more importantly, the histologic diagnosis to confirm the diagnosis of Crohn's disease.



Talk a little bit more about, you had mentioned previously about some of the endoscopic features that you would see on a colonoscopy. What would be specific for Crohn's disease?

Michele Kissous-Hunt: So, we're looking for cobblestoning. We're looking for ulcerations, edema, nodularity. And really on the histology, usually we'll get something back that may say that there's granulomas, inflammation on histology.

Rick Davis: And the majority of patients with Crohn's disease actually have abnormalities on colonoscopy and biopsy of the terminal ileum, up to 80%. So, interesting, even though Crohn's disease can be anywhere within the GI tract.

Michele Kissous-Hunt: Yes, so there are patients that will have inflammation in their colon, and sometimes the inflammation is really in the ileum is what we're seeing on colonoscopy. So, where the colon might be completely normal, and when we get to the ileum, we intubate the ileum, take biopsies there. And that's where you're seeing the ileitis. So that's really the positive part that we're seeing on the colonoscopy.

Rick Davis: Hm, good point. So, let's review the correct answer to our clinical question, what is the best next step in Teresa's management at this time? The correct answer is (B) Refer to gastroenterology for ileal colonoscopy.

Repeat inflammatory markers would not have much utility at this point, since treatment has not yet been initiated. Screening for TB is likely to be part of Teresa's management, but it's a higher priority at this time to connect her with a gastroenterologist to expedite the diagnosis and treatment of her likely IBD. She should also be screened for iron, folate, vitamin D and B12 deficiencies. And while sulfasalazine may be a part of her treatment, we need further information to confirm her diagnosis before treatment can be initiated.

Teresa follows up with a gastroenterologist, and her ileocolonoscopy reveals edema and ulcerations of the colon and terminal ileum.

This brings us to our last clinical question.

Which imaging study is most appropriate to order for Teresa at this time?

- **A.** Abdominal ultrasound
- **B.** A CT of the abdomen and pelvis with and without contrast
- **C.** A CT enterography
- **D.** Magnetic resonance enterography.

So, Michele, since there are no standardized diagnostic criteria for Crohn's disease other than clinical presentation, endoscopic, radiologic and histologic findings, how often do we see granulomatous disease on the biopsies, and can you still make the diagnosis even if there are no granulomas?

Michele Kissous-Hunt: So, yes, absolutely, the diagnosis can be made even if there's no granulomas on the biopsies. We really go by the clinical presentation as well as the histologic. And the entire presentation, we also go by the radiologic findings. We will have either CT enterography or an MR enterography done on these patients, because with Crohn's disease, this is a transmural disease, so it can affect the full thickness of the bowel.

So, MR enterography is extremely important in these patients and gives us a lot of information on these patients. So, we absolutely can make the diagnosis with all these other modalities, as well.

Rick Davis: Sure. And IBD tends to be more of a young person's disease, although it does have a bimodal distribution. You know, these patients are being scanned frequently throughout the course of their disease, and we're always trying to spare them the radiation exposure. Do you prefer MR enterography in, say, someone Teresa's age?

Michele Kissous-Hunt: Yes. So, since she's young, absolutely. MR enterography would be preferable, also because we know that she's going to have serial imaging throughout her lifetime. So, unless it's an emergency, unless she's presenting with something that we think there's an abscess or an obstruction that needs to be taken care of immediately, we do prefer an MR enterography, since there's no radiation.

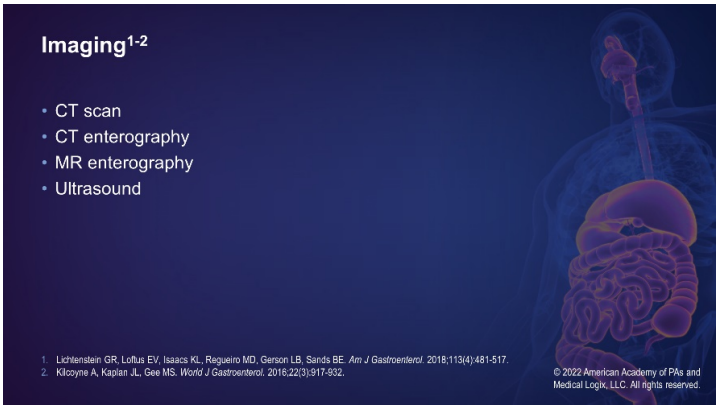
Another thing that I want to point out with MR enterography, another reason to do an MR enterography versus CT enterography is in a patient that is pregnant, you only want to do an MR enterography and not a CT enterography.

And one more quick thing is, ultrasound is becoming very popular now and is being done at the bedside in some clinics, as well.

Rick Davis: So, we've not used that here yet. It's always been conventional wisdom that you don't use ultrasound when evaluating the bowel because of bowel gas interfering with the image.

Michele Kissous-Hunt: Right, that's correct. But now what they've noticed is that ultrasound kind of gives us information in real time. It's basically real-time imaging. It depends really on the operator, and at Mount Sinai, we have gastroenterologists that are doing it at their clinic, at the bedside, and kind of monitoring patients by doing ultrasound while the patient is there and guiding how the patient is doing based on the ultrasound, as well.

Rick Davis: Interesting.



Michele Kissous-Hunt: And this is something that's being taught right now, so it's new and up and coming.

Rick Davis: Okay, good to know.

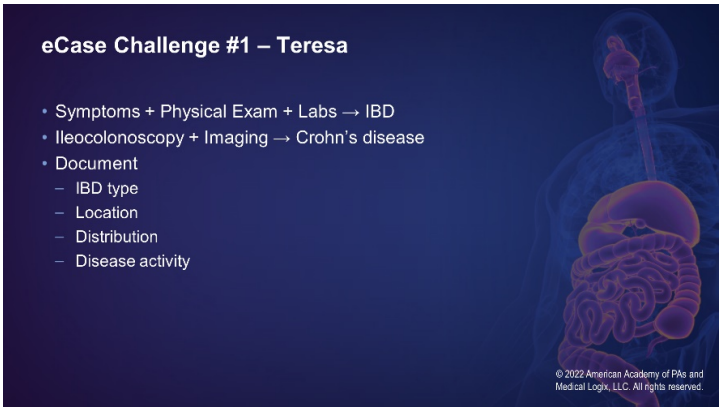
Michele Kissous-Hunt: So, returning to our question, the best imaging modality for Teresa is (D). So MR enterography, and this is because she's young. She's likely to require serial imaging. So, this option with nonionizing radiation is preferred for her.

Our case continues by bringing all elements of Teresa's workup together in order to arrive at a complete and comprehensive diagnosis. Her symptoms, physical exam findings and laboratory

testing results suggested a preliminary diagnosis of inflammatory bowel disease.

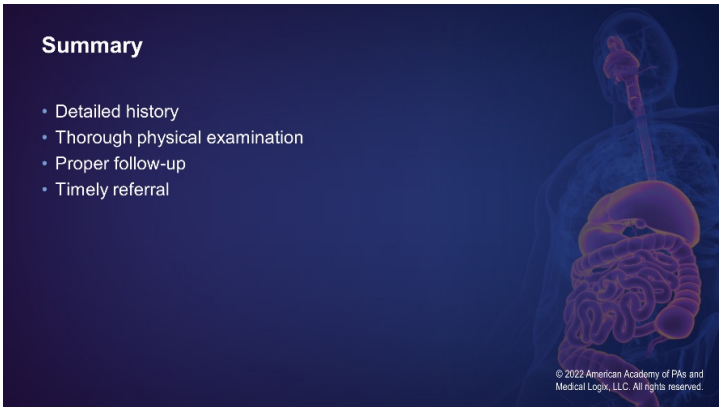
Through further evaluation with ileocolonoscopy, we learned that Teresa's disease involvement extended beyond the colon into the terminal ileum, making Crohn's disease the working diagnosis over ulcerative colitis. Her MR enterography revealed mucosal lesions and wall thickening.

Finally, her complete picture should be documented in her record, including IBD type, location, distribution, and disease activity. This is vital because determination of her treatment course depends on multiple factors, including her age at disease onset, disease distribution, disease activity and disease phenotype.



Disease activity is classified as remission, mild, moderate, or severe based on clinical measures, quality of life, disease complications and therapy complications. Disease phenotype is determined by a combination of age of onset, disease location and disease behavior. With this information, Teresa and her GI clinician can decide on the best course of treatment for her.

Rick Davis: Thanks, Michele. As we bring our case to a close, we should remember that a thorough evaluation is essential for patients with possible inflammatory bowel disease. Importantly, a detailed history and physical exam are vital first steps in differentiating the many possible causes of abdominal pain that may be seen in a primary care office. Proper follow-up and timely referral are also vital components of care in order to prevent diagnosis and treatment delays.



I would like to thank our expert, PA Michele Kissous-Hunt, for your great insights and discussion. And I would like to thank you, our audience, for participating in this *eCase Challenge* on updates in diagnosis of inflammatory bowel disease.

This concludes our video *eCase Challenge*. On behalf of Michele and myself, we hope that you enjoyed it, and thanks for joining us.

CLINICAL PEARL

Crohn's disease is a chronic form of inflammatory bowel disease that often has a delayed diagnosis because its symptoms mimic those of other diseases, including ulcerative colitis and irritable bowel syndrome.

Extraintestinal manifestations are common, with some patients displaying before the diagnosis, making them an important diagnostic clue in some cases. The lack of specific diagnostic criteria is an additional challenge that can contribute to delayed diagnosis.

Because of the multiple challenges to accurate diagnosis of Crohn's disease, PAs should have a high index of suspicion when evaluating patients with chronic diarrhea or other symptoms that could be suggestive of Crohn's disease.

If bloodwork is indicated, this can be initiated by the primary care PA, who can also expedite referral to a gastroenterology clinician for further evaluation, including imaging and colonoscopy.

Initial laboratory workup may include a CBC, inflammatory markers and stool studies, including infectious testing and fecal calprotectin and/or lactoferrin, which are more specific to Crohn's disease diagnosis.

Initial choice of imaging study depends on certain patient-specific factors, including age, a patient's clinical symptoms, physical examination, results of laboratory and imaging studies and findings on endoscopic procedures, must all be considered together in order to make an accurate diagnosis of Crohn's disease.

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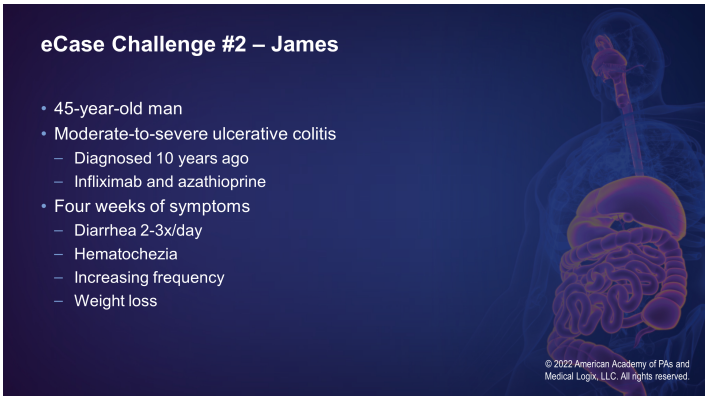
eCASE CHALLENGE #2

Rick Davis, PA-C: Hello, and welcome to this video *eCase Challenge*, "Updates in the Objective Diagnosis and Evidence-Based Management of IBD." I'm Rick Davis, a PA in the Division of Gastroenterology in the College of Medicine at the University of Florida in Gainesville. Joining me today is Michele Kissous-Hunt, a PA in gastroenterology from Mount Sinai Medical Center in New York City.

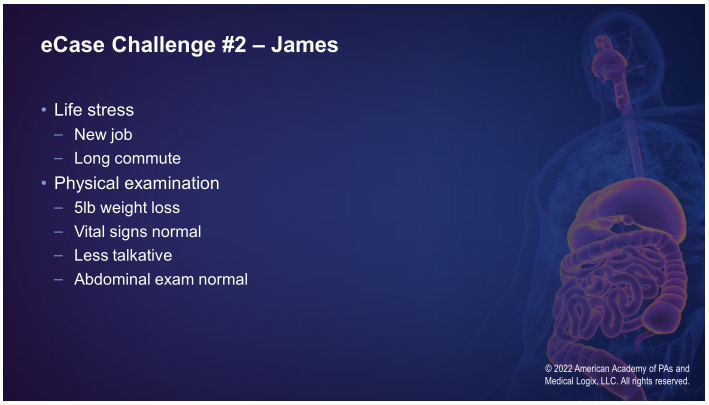
This CME activity consists of two *eCase Challenges*. This is our second *eCase Challenge*, and our patient is James. So, let's get started with our second case.

James is a 45-year-old patient who was diagnosed with ulcerative colitis 10 years ago. He has moderate-to-severe disease and has been asymptomatic on infliximab and azathioprine since his last disease flare 3 years ago.

He presents to his primary care PA's office with concerns that he may be experiencing a disease flare. Over the past 4 weeks, he's been having intermittent diarrhea of 2 to 3 episodes a day, about 2 to 3 days per week, and occasionally with blood. This has been occurring more frequently over the past week, and he has noticed that his pants are fitting more loosely, which makes him concerned that he has lost weight, which he had not intended to do.



James notes that he recently started a new job, which has been stressful for him, especially because he has to commute much further than with his previous job, and his worsening symptoms are making the commute even longer, because he has to stop on the way to and from work. Other than these symptoms, he has been in his usual state of health and eating his normal vegetarian diet. Despite his new job and longer commute, he has not missed any scheduled infliximab infusions and reports rarely missing a dose of azathioprine.



On physical exam, James is noted to have a 5-pound weight loss since his last visit 4 months ago. His vital signs are normal. He's otherwise well-appearing, although not as talkative as he normally is at his visits. The remainder of the physical exam is normal, including his abdominal exam, which reveals a soft and nontender abdomen.

This brings us to our first clinical question.

Given his recent symptoms, which of the following is the best next step in James' management at this time?

A. Increase the dose of infliximab
B. Measure a fecal calprotectin
C. Prescribe nutritional protein shakes
D. Refer to psychology

So, Michele, James seems to be experiencing a flare of his ulcerative colitis, which he's likely familiar with since he's had UC for over 10 years and had a flare about 3 years ago. So the natural course of ulcerative colitis are periods of active disease and periods of remission. So, Michele, how would you go about evaluating the symptoms that James is experiencing currently?

Michele Kissous-Hunt, PA-C, DFAAPA: So, if a patient is coming in with something that sounds like a flare, usually patients know themselves, they know if it feels like a flare to them. But we always have to make sure that this is really truly a flare and that there's nothing else going on.

The first thing that we always have to rule out, that there's no infectious colitis. We have to check that there's no *C. diff.* on top of a flare, even if there is a flare, because our patients, our IBD patients are about 4 to 5 times more likely to get *C. diff.* than patients in the general population, even when they're not on any antibiotics.

So, the first thing we would do is check stools for C&S, O&P, *C. diff.*, as well as a fecal calprotectin. In this case, he's on medication, so we will check labs, as well. We will check levels. We'll check trough levels for the medications that he's on. So, if he's on infliximab, we want to know what is the level, how much of the medication he has in his system at this point. Does he have any antibodies to the medication?

And we'll start doing the workup. We want to get objective findings as well as subjective. So how is he feeling? And also, we want to know some objective findings. So, we want to see labs, we want to see possibly a sigmoidoscopy to see what things look like on the inside, as well. And then we decide how we're going to manage this patient.

Let's review the question posed, which asked, given his recent symptoms, which of the following is the best next step in James' management at this time? The correct answer is (B) measure fecal calprotectin. A stool culture, ova and parasite and *C. diff.* would also be appropriate at this time to rule out other causes of his symptoms.

As we discussed, although his symptoms are concerning for an IBD flare, this should be confirmed with laboratory testing, imaging or endoscopy before determining the course of treatment. He may need an increased dose of infliximab. However, further diagnostic studies are needed before a decision can be made about this.

It would also be a good idea to check a 6-TG level since he's taking azathioprine, as well. 6-TG is a toxic metabolite of thiopurine medication. And while attention to nutrition and mental health are paramount in the care of patients with IBD, it is more pressing, at the moment, to address this possible disease flare.

Especially as you notice that James is less talkative today, it's important to screen him for depression at this visit as well as address the acute concern for an IBD flare. If he has a positive screening test, referral to psychology may be appropriate. Routine screening for depression and anxiety is recommended for patients with IBD, as rates of both for these diseases are higher in patient population, and there is some evidence that psychological stress may play a role in the disease.

Stool studies are negative, and fecal calprotectin and CRP are both elevated compared to his last value 3 months ago, indicating that his recent symptoms are most likely the result of a disease flare.

So this brings us to our next clinical question.

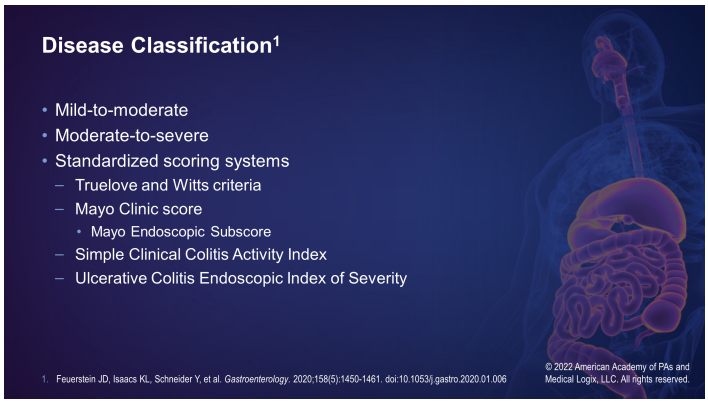
Which of the following is most likely contributing to James' inflammatory bowel disease flare?

- **A.** Location of disease
- **B.** Malnutrition
- **C.** Primary nonresponse
- **D.** Secondary loss of response

Rick Davis: So, Michele, the approach to treatment of ulcerative colitis depends on disease severity, which is classified as mild-to-moderate or moderate-to-severe. These categories are mostly defined kind of in a general sense, although there are some standardized scoring systems that we often use in the IBD clinics.

Some of these include the Truelove and Witt criteria. We usually use the Mayo Clinic Score. There's an ulcerative colitis endoscopic index of severity. Which ones do you use in your practice?

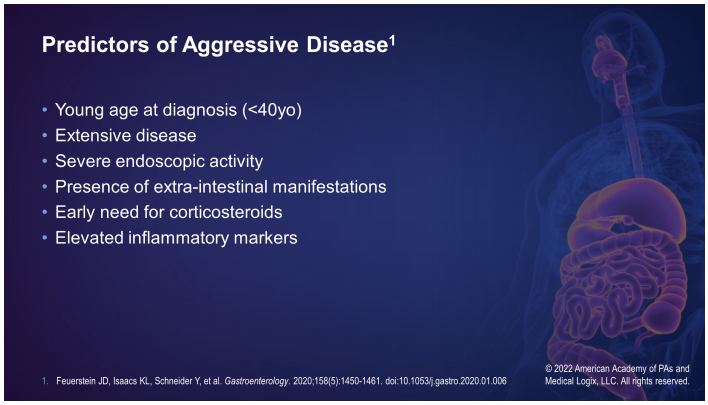
Michele Kissous-Hunt: So, the Mayo score is really the one that we mostly use, and that's the one that is mostly used in clinical trials, as well.



Rick Davis: And since we know that a majority of these patients have mild-to-moderate disease, but about 15% may experience an aggressive course, what might be some of the factors that would predict a worse outcome or more aggressive case of ulcerative colitis?

Michele Kissous-Hunt: So, we usually try to risk-stratify our patients to low risk for colectomy versus high risk for colectomy. Patients that are low risk for colectomy are those that have limited anatomic extent, those that have mild endoscopic disease versus those patients that are at high risk of colectomy have more extensive colitis, deep ulcerations.

So, usually, they're at a younger age, age younger than 40. They'll have a high CRP, sed rate. They may have needed steroids. They may have a history of hospitalization. So, these are our sicker patients. They also may have had already an infection of *C. diff.* or a CMV infection.



So usually, what we do is we really need to risk-stratify those patients to find out who are those patients that are going to be our sickest patients?

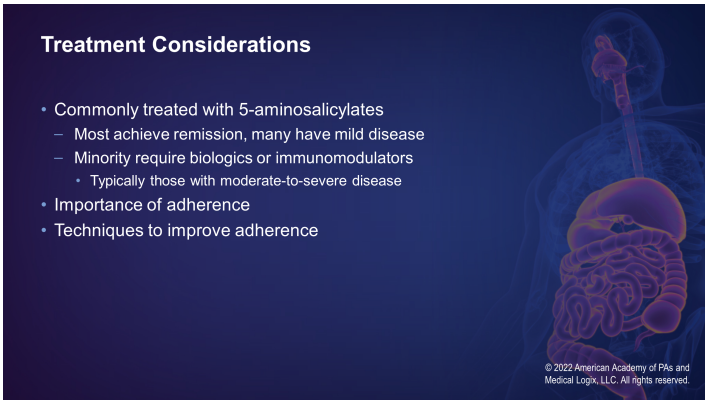
Rick Davis: Okay. That's a good guide. Now, we know that over 90% of ulcerative colitis patients are treated with 5-aminosalicylates, or 5-ASA drugs, following the diagnosis. Most achieve remission with 5-ASAs. But in our practice, adherence seems to fall off, especially in our younger patients, and then we start to see them coming back and having flares.

In your practice, how do you handle that adherence to oral daily medications, and when do you pull the trigger to move on to, say, biologic therapy or other immunomodulators?

Michele Kissous-Hunt: I always have a discussion with the patient reminding them how they feel prior to taking the medication and letting them know that when they start the medication, they're going to feel much better, and they have to remember that it's because they're on their medication that they're doing better, and once they're starting to feel better, not to start

dropping off or down on the number of pills, because they're not going to do as well.

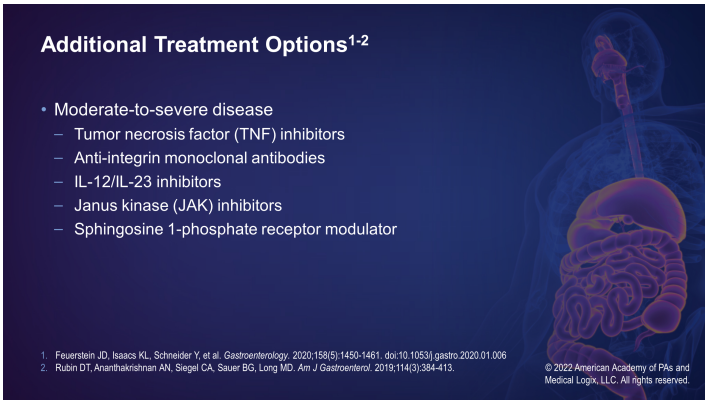
So. we tell them, a lot of these medications, they could take it with or without food. We ask them to keep it by their bed and to make sure that they take it even in the morning or at night, but just take it. The once-dailies, I think, are the easiest to take.



Now, you asked me about biologics. The biologics we really use for moderate-to-severe patients, so those patients that, if they ever need a course of steroids or anything like that, if they're ever sick beyond needing anything more than the 5-ASA, if they're sicker and they need a course of prednisone, right away we're looking for an exit strategy. And our exit strategy would be usually a biologic, something to move up to the next step.

Rick Davis: Okay. And which biologics do you recommend for ulcerative colitis?

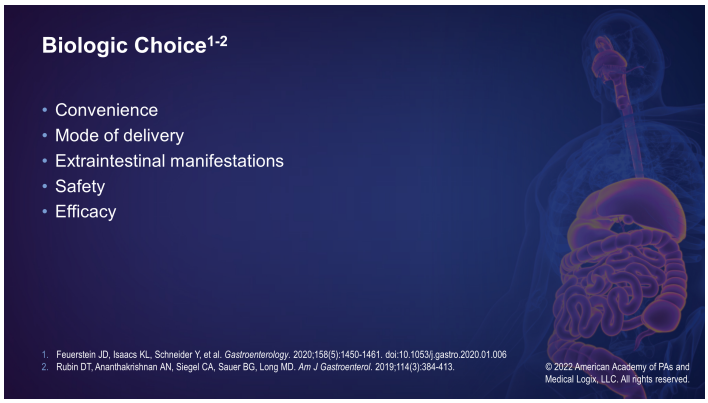
Michele Kissous-Hunt: So we have a lot of biologics now, so this is a great time. I tell our patients, "If you're going to have ulcerative colitis, this is a good time to have it, because we have the anti-TNFs, we have the anti-integrins, we have the small molecules, we have the IL-12/23s, the JAK inhibitors. We really have a good amount of medications out there, and there are more coming down the pipeline, so that's great.



Really, we do it based on convenience for the patient; we may take their extraintestinal manifestations into consideration. We definitely look at safety and efficacy.

Rick Davis: So, you really have to taper the therapy towards the patient?

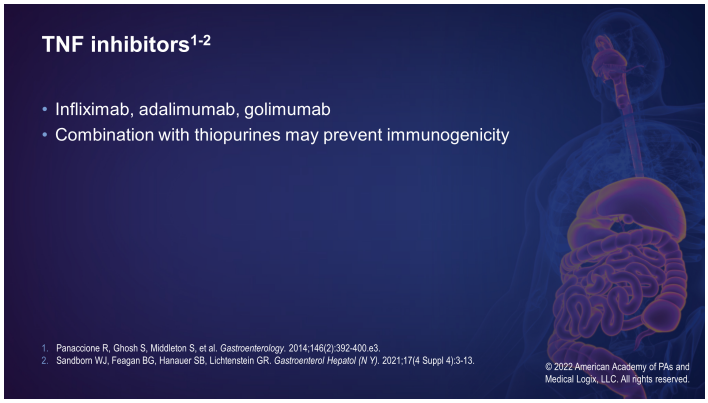
Michele Kissous-Hunt: Yes, absolutely. We really pick the medication based on the patient. It really depends on if they have a specific extraintestinal manifestation, we may tailor the medication even to the patient because of the extraintestinal manifestation, as well.



So not only to the mode of delivery, to the convenience, safety, efficacy, but also to what other extraintestinal manifestations or other comorbidities that they have that we decide to treat, the medications.

Rick Davis: Okay. So, James was already on infliximab and azathioprine. Can you comment a little bit about the use of immune modulators along with an anti-TNF? What's the rationale behind that?

Michele Kissous-Hunt: Absolutely. So, with infliximab, infliximab is an anti-TNF. And with our anti-TNF, patients can build antibodies. So, we need to use immunomodulators, such as 6-MP, azathioprine to try to avoid these, and patients developing these antibodies. So, what we do is we give patients a low dose immunomodulator, and we keep them on combination therapy.



Now, with the other drugs that we have, such as the anti-integrins or the small molecule drugs that we have, we do not necessarily have to use immunomodulators, because those medications, patients do not build antibodies, so --

Rick Davis: Okay.

Michele Kissous-Hunt: -- to the drugs.

When we're not using anti-TNFs, the anti-integrins, the small molecules, the IL-12/23 drugs, we usually do not use immunomodulators because with these medications, we're not worried as much about building antibodies.

Rick Davis: So, let's go back and review the question, which asked, which of the following is most likely contributing to James' inflammatory bowel disease flare? In this case, the correct answer is (D) secondary loss of response. Since he seemed to have a good initial response to therapy over the last 3 years, he would not be classified as a primary non-responder to TNF inhibitor therapy.

And while location of disease and his nutrition status are important considerations in his treatment planning, they're not typically central factors contributing to a disease flare.

In order to further assess whether loss of treatment response is contributing to his flare, infliximab concentration levels are drawn. A trough level is 12 mcg/ml, with normal greater than 3 to 7. And a 6-TG level indicating the azathioprine is at 250.

So, this brings us to our next clinical question.

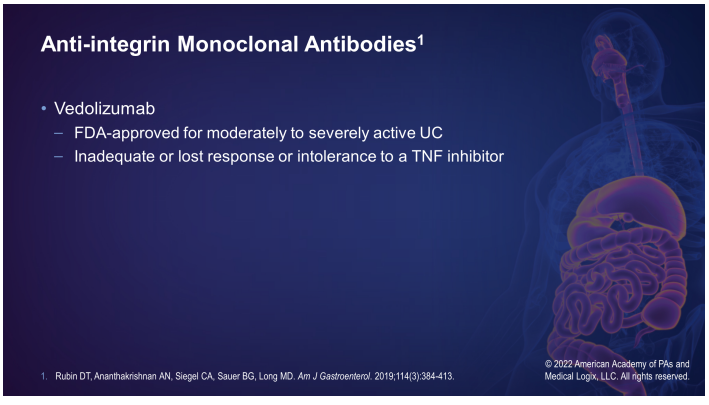
Which of the following is the most appropriate next step in management of James' ulcerative colitis flare?

A. Add tofacitinib to current medication regimen
B. Consult surgery to consider colectomy
C. Discontinue infliximab and initiate vedolizumab
D. Increase dose of infliximab by 20% and recheck infliximab trough levels

Now, discussing the role of anti-TNF antibodies and trough levels in guiding treatment choice, vedolizumab is an anti-integrin monoclonal antibody, FDA approved for moderate-to-severely active ulcerative colitis with an inadequate or a loss of response, or even intolerance to anti-TNF agents.

So, Michele, explain to us why (C) is the best answer, discontinue infliximab and initiate vedolizumab.

Michele Kissous-Hunt: Okay, so in this case, we want to discontinue infliximab and initiate vedolizumab. And the reason is because you want a different mechanism of action here. James has a level we said of 12, so if he has a level of 12, that's already a very good level, and he's not doing well. He's obviously flaring. He had an abnormal sed rate, CRP, fecal calprotectin, and he's still not doing well.



And James had a very good trough level. He was already at a level of 12. He did not have any antibodies. He has a great therapeutic level of 6-TG. It was at 250. And despite all that, he's not doing well, with an abnormal sed rate, abnormal CRP, abnormal fecal calprotectin. So, he's still flaring. So, with a patient like that, we would want to consider switching to a different mechanism of action.

We want to talk about something called treat-to-target approach. And treat-to-target is a proactive therapeutic approach that really requires the predefined specific targets. It requires regular disease activity. So, we look at the disease activity, we assess the patient, and then we make our therapeutic adjustment.

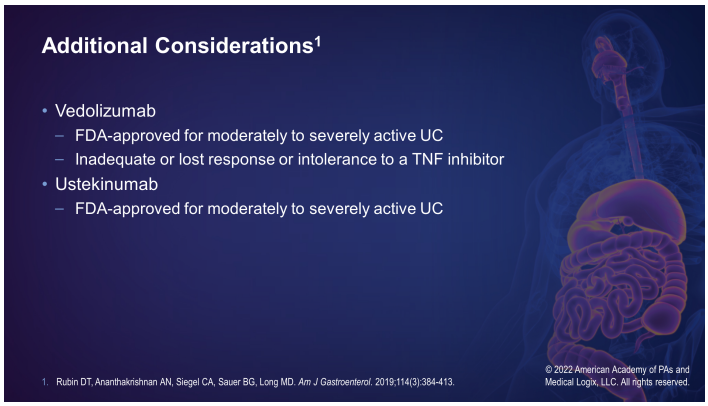
We look for endoscopic healing. We look at clinical response. We're looking for clinical remission. And we're looking at those clinical markers that we mentioned, the CRP, the fecal calpro. As far as how the patients are doing, we're looking for restoration of their quality of life as well as are they disabled, or are they doing better as far as disability goes?

When we're looking at ulcerative colitis specifically, we want to achieve histologic healing, which is a very hard target to achieve, but that's really what we're trying to achieve here.

Now, when we're talking about loss of response, because what happened with James was basically a secondary loss of response, because first, he did very well with the infliximab, and then he started having symptoms. He was doing very well all along.

In this case, James had very good drug levels, so he had enough medication in his system. He did not have antibodies, and despite that, he was not doing well. So that's considered a secondary loss of response.

Rick Davis: In making that decision to go out of class to, say, away from an anti-TNF or immune modulator, vedolizumab, an anti-integrin monoclonal antibody, is FDA approved for moderate-to-severe ulcerative colitis. Ustekinumab has also been recently approved, I think just last year, for moderate, severe ulcerative colitis.



Do you have a preference or a clinical situation when you would use one over the other in someone who may have been failing anti-TNF?

Michele Kissous-Hunt: Again, it goes really based on the patient, based on their insurance. I could tell you that with vedolizumab, a patient gets that medication, it's all IV infusion. So, it's in office,

where the ustekinumab, they originally get the induction doses, one infusion followed by injectables after that.

So, it depends on the patient. If they want to stay home and inject, they may go with ustekinumab. So not always. And then, again, it depends on the extraintestinal manifestations. We may choose ustekinumab because of an extraintestinal manifestation versus someone that's for vedolizumab.

So, again, really, these medications are completely tailored on a case-by-case patient.

And then I just want to get back to if they're subtherapeutic, because we always come back, you may want to know, so what happens with those patients that their levels were not so great, right?

I don't want somebody to say, "Oh, the medication did not work. Let's switch to another class of drug," because if somebody was on infliximab and let's say the level was 5, right, we can still argue and say, "Well, maybe that's not high enough." Or if the patient has fistulizing disease, they may need levels of like 15 or 20, even, if they have fistulizing disease.

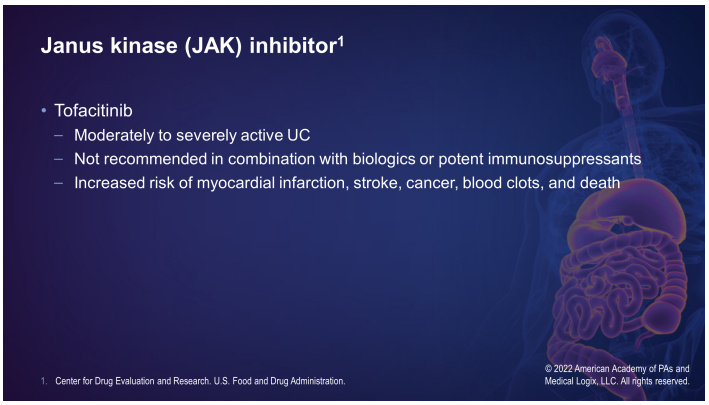
Rick Davis: That begs another question. So, when you have a patient that has low levels on an anti-TNF, do you increase the dose or shorten the frequency or the duration in between infusions? What is your preference and your practice?

Michele Kissous-Hunt: So, great question. And again, that will also depend. So there are some patients, we are able to shorten the frequency up, the shortest that you can go is 4 weeks, okay, if we're talking about infliximab. Though some patients, we're able to shorten it to 7 weeks, 6 weeks or all the way down, the shortest interval we'll ever do for infliximab is 4 weeks. We will not go any shorter than that.

If we get down to 4 weeks, then we will bump up the dose, and we will go from, if it's 5 mg/kg, we'll go up to either 7 and a half or 10 mg/kg, and we'll titrate the dose up. If it's a patient that tells us they cannot come every 4 weeks, or they cannot come every 6 weeks because of their job, then someone like that, we may just increase the dose right away.

Rick Davis: Okay. And what we haven't mentioned is tofacitinib, a JAK inhibitor, Janus kinase inhibitor, that has been approved for moderate to severely active UC. I remember reading that that shouldn't be used in combination with biologics or potent immunosuppressants. Where do you use this medication in your practice?

Michele Kissous-Hunt: So, we actually use it for the ulcerative colitis patients, as well. It works pretty quickly for these patients. There was a black box warning that was issued for this drug. So, they do not allow us to use it as a first line. So, we can only use it as a second line.



So, in order for us to prescribe a JAK inhibitor, first the patient has to fail like an anti-TNF or another drug before we can prescribe a JAK inhibitor.

Rick Davis: Okay. And it would be used as solo therapy, monotherapy?

Michele Kissous-Hunt: Yes, as monotherapy.

Rick Davis: Okay, well, let's return to the clinical question, which asked, which of the following is the most appropriate next step in the management of James' ulcerative colitis flare? The correct answer is (C) discontinue infliximab and initiate vedolizumab. There could be a consideration to switch to tofacitinib, but it would not be appropriate to add this medication without discontinuing infliximab.

And discontinuing infliximab is a very reasonable step to take here, as the presence of a flare despite appropriate trough levels of infliximab indicates resistance to the medication. For this reason, increasing the dose, amount or frequency is unlikely to be helpful.

Ustekinumab may also be a reasonable choice in this case instead of vedolizumab. James may end up needing a surgical consult in the future. However, his medical management should be optimized before that is considered.

James asks what measures he can take in the future to prevent another flare of his ulcerative colitis.

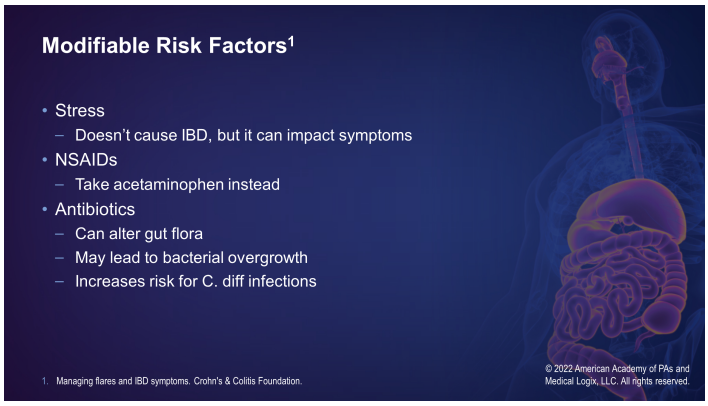
And this brings us to our next clinical question.

Which of the following measures can reduce the risk of disease flare in ulcerative colitis?

A. Begin taking a daily probiotic.
B. Develop coping mechanisms to deal with stress.
C. Initiate weekly prophylactic antibiotics to prevent infection.
D. Participate in moderate exercise five times per week.

Now, there are multiple modifiable factors that contribute to an IBD flare. Michele, in your practice, what are some of the things that you see that contribute more commonly in your patients into their flares?

Michele Kissous-Hunt: So, one of the things that we see is definitely stress. So, stress does not cause inflammatory bowel disease, but stress is a big factor as far as causing increased symptoms for these patients. When they're under a lot of stress, they will sometimes have a flare.



Another thing that we notice is some patients, when they're taking NSAIDs, there are patients that NSAIDs will trigger a flare for them, as well. So, we ask patients to avoid nonsteroidals. And if

they really, really have to take something, then the one medication that we'll ask them to go to is something like celecoxib.

Another medication is antibiotics. You know, many patients will just take antibiotics, will say, "Oh, I have an infection," and be very quick to jump on an antibiotic. We may even put them on a probiotic while they're taking an antibiotic. And we want to know what's the reason they're being placed on an antibiotic, because we know that these patients are more likely to get *C. diff.* already, and we worry about flares due to that.

Rick Davis: Another question that frequently comes up in our practice is, patients always want to know what diet they should follow for their ulcerative colitis. "Is there anything that I should avoid that might trigger a flare? Or is there something I should be eating on a more regular basis that may be more helpful?" What sort of guidance do you give your patients?

Michele Kissous-Hunt: Yes, so patients love talking about the diet. There's one diet that patients swear by. It's called the specific carbohydrates diet. It does definitely make them feel better.

But there was a study that was done recently. It was done by the Crohn's & Colitis Foundation. They compared the specific carbohydrate diet to the Mediterranean diet, and they did not see any improvement as far as improvement of C-reactive protein or anything like that, that they were the same, both the Mediterranean diet and the specific carbohydrate diet.

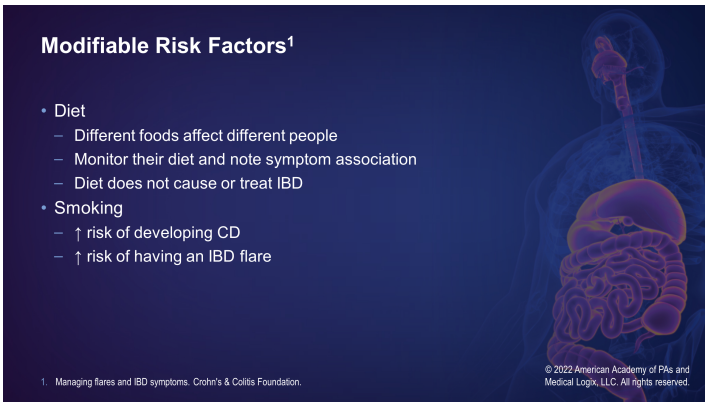
What we ask patients to do is to avoid processed foods. We tell them to have as natural diet as they possibly can. And of course, when they're having diarrhea, back off on the fiber a little bit if they're having discomfort. And also, we ask them to kind of take a look at what they're eating and do kind of an elimination diet and see what triggers them. What are their trigger foods? Because everybody has different trigger foods.

Rick Davis: Mm-hm.

Michele Kissous-Hunt: Smoking is another big one, Rick. I don't know if you want to comment on that or --

Rick Davis: Well, it's interesting. There have been these studies in the past that looked at smoking and ulcerative colitis and Crohn's disease. And in Crohn's disease, it's clearly associated with increasing flares. There may be more advanced disease or more aggressive disease in patients who are smokers. There's a greater chance of recurrence after surgical resection. So, there's a clear association there.

But there were some studies early on that looked at smoking as actually helping patients with ulcerative colitis. And I wanted to know about your thoughts on that.



Michele Kissous-Hunt: Yes, so I agree with everything that you said, and what I always tell patients is, if you were not a smoker, don't start smoking. It's not going to help you. It's really those patients that were smoking, and they stopped smoking for whatever reason. Maybe they went into the hospital for a procedure and they had to stop smoking for a few days, and then they noticed that they developed GI symptoms, and it pointed to a diagnosis of ulcerative colitis. Those are the patients that usually do better when they smoke again.

Even with those patients, because of the high risk of colorectal cancer and the other problems with smoking, we really ask that they do not smoke, and we just treat the disease. We treat the ulcerative colitis and ask them not to smoke. But that's correct.

Rick Davis: Yes, absolutely. We advise the same.

Michele Kissous-Hunt: Okay. So let's go ahead and review the answer to our clinical question, which of the following measures can reduce the risk of disease flare in ulcerative colitis? The correct answer is (B) develop coping mechanism to deal with stress. While exercise is great and it may lead to decreased stress, it does not decrease the risk of disease flare alone.

As we discussed, antibiotics should be avoided unless necessary, since they alter the gut microbiome and increase the risk of *C. diff.* So prophylactic antibiotics would not be advisable. Similarly, no role for probiotics has been identified in IBD.

James sees an improvement in his symptoms with initiation of vedolizumab and his inflammatory markers begin to trend down accordingly. He begins to use a meditation app on his phone that he finds helpful for stress management and reports that the resolution of his IBD flare has also decreased his stress and worry about the long commute to work.

He's now back at his primary care PA's office for a follow-up visit. James reports that he received his annual flu shot last week at the local pharmacy.

This brings us to our final clinical question.

Which of the following vaccines should James receive today if he has not already received it?

A. Measle, mumps and rubella vaccine
B. Meningococcal vaccine
C. Pneumococcal vaccine
D. Varicella vaccine

So, Rick, remaining up to date on vaccination is really critical for our IBD patients, especially those that are on immunosuppressive vaccine therapy. Would you like to comment on that?

Rick Davis: Yes. I think it's really important, especially when a patient is initially diagnosed, and before they start especially any biologic therapy or even immunomodulatory therapy, that they get up to date on their vaccines. There are some, the live attenuated virus vaccines are ones that should be given before any immunosuppressive therapy should be given.

And a lot of times, vaccination, even though we talk about it in a GI practice, it really falls back to the primary care provider as to keeping track of where are they? Have they had their shingles vaccine? Where are they with their pneumococcal vaccine?

Some of the general recommendations are certainly the annual influenza vaccine, and our patient received that. Pneumococcal vaccination. Herpes zoster per current recommendations. Varicella, again, before immunosuppressive therapy. Yellow fever before. Meningococcal vaccine for adolescents. And then, of course, hepatitis A and B.

I wanted to ask you about HPV vaccine. It's usually approved for younger patients. Are you using that in your IBD patients who are, say, over the age of 20?

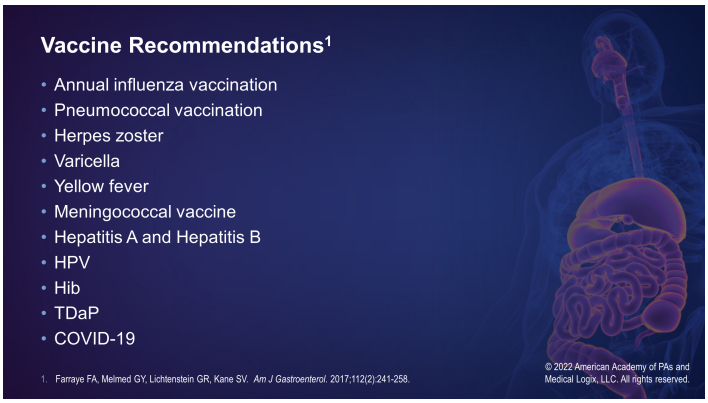
Michele Kissous-Hunt: Yes, so we are using that. We're asking our patients, usually before we'll put them on any biologics, we'll ask them to go to their primary care and to make sure that they're up to date on everything.

And this is usually from their first visit, because we know that, whether they are not on immunomodulators yet, if they have this disease, they may end up on immunomodulators, so we want to make sure that they're up to date, and if they are of that age, they should have this vaccine. And we want to make sure that they have had it. But absolutely, we make sure that they get the HPV vaccine, as well.

The other thing I wanted to mention, since we're talking about vaccine, is the COVID vaccine, which probably is coming up a lot.

Rick Davis: Yes, mm-hm.

Michele Kissous-Hunt: COVID vaccine is safe. We are asking all our patients to get it. Safe as far as IBD. We're asking all our IBD patients to get it. And we want our IBD patients to get it, including booster vaccines if any patients ask you that, or ask us that.



Rick Davis: And then other screening considerations? So, in female population, annual cervical cancer screening in patients that are on immunosuppressive therapy, do you continue that beyond age 40, or do you stop?

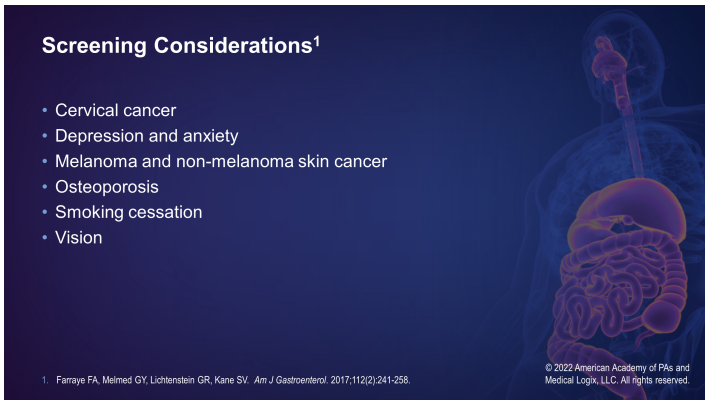
Michele Kissous-Hunt: Yes, so we ask them to continue the pap smear. Especially if they're on immunomodulators or if they're on the biologics, we want them to continue annual pap smears.

We also want them to get annual skin checks, very important, especially if they're on immunomodulators. Especially if they've been on combination therapy, we want that, a full-body skin check. Even if they're just on biologics, we want full-body skin checks on these patients. Anybody that's immunocompromised should be getting this.

Rick Davis: And at what age would you start screening for osteoporosis with DEXA scans?

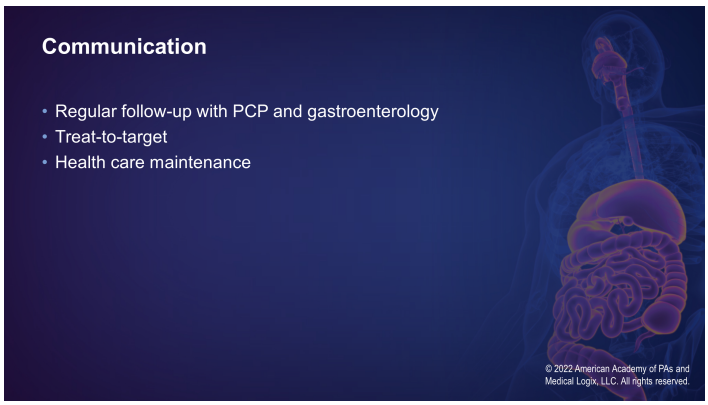
Michele Kissous-Hunt: So really, for our IBD patients, we're starting them right away, because especially with Crohn's patients from nutritional deficiencies, they can be osteoporotic. Especially patients that ended up on prednisone, we want a baseline. We want to see what's going on with their bones and what is their baseline. If they end up on prednisone, for sure, we want a bone DEXA.

And then we take it from there. If they have osteopenia, we'll start treating, and we'll make sure that a rheumatologist is involved in their care, as well.



Rick Davis: Good, good. So, one other thing I wanted to comment are your thoughts on the patient home as far as in IBD world. I know some of our patients, they will only go to their gastroenterologist, but that may be twice a year, maybe once a year, especially our students that are on campus. And we still want them to be involved with their primary care, as well. So how do you handle that?

Michele Kissous-Hunt: So, in general, in our practice, we want to see our patients every 3 months, and that's specifically our IBD patients that are on biologics. Anybody that's moderate to severe is seen in our practice every 3 months because of the medications that they're getting and the follow-up, and that treat-to-target phenomenon that I talked about earlier, that we really need to monitor these patients very closely and make sure that they're being monitored even during maintenance. We want to make sure that they're constantly being watched.



Between that, we also want to make sure that they're seeing their primary care physicians at least once a year. A lot of primary care providers think that the GI provider is taking care of everything. And some GI providers think that the primary care is taking care of everything.

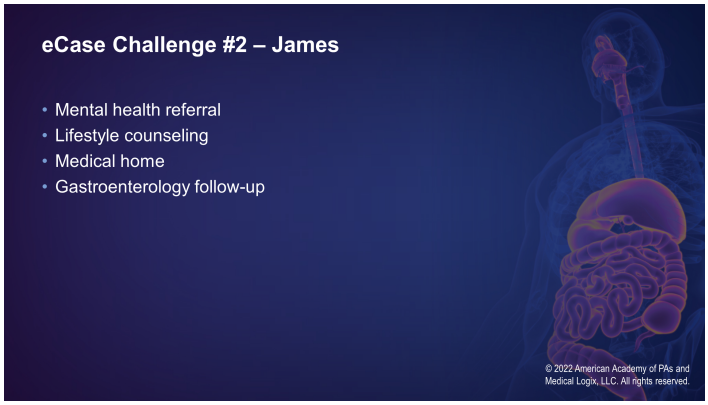
So, we really want to work as a team and make sure that we're communicating and that we're working together and that we're participating, both of us are participating in the patient's care.

Rick Davis: All good points.

Michele Kissous-Hunt: Okay. So now we're returning to our clinical question, and James is then due today for his pneumococcal vaccine. It's making the correct answer, (C). He should not have any live virus vaccine since he's on immunosuppressive medications.

You refer him to a local mental health care clinician who is familiar with the care of patients with chronic diseases based on his screening test for depression. Although he's reluctant to go, he agrees to give it a try. Otherwise, he's doing well with his IBD management.

Rick Davis: As we close this case, you continue to counsel James on the importance of maintaining a healthy lifestyle, including managing his stress in order to better manage his IBD. He expressed understanding that your office remains his medical home for routine treatment despite his regular follow-up visits with his gastroenterologist.



I'd like to thank our expert PA, Michele Kissous-Hunt, for your great insights and discussion. And I'd like to thank you, our audience, for participating in this video *eCase Challenge*.

On behalf of Michele and myself, we hope you enjoyed it and thank you for joining us.

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CLINICAL PEARL

Ulcerative colitis is a chronic disease characterized by waxing and waning symptoms over time. Disease flares do not have specific diagnostic criteria, but rather consist of a return of symptoms such as hematochezia, weight loss, abdominal pain, and fatigue.

However, these symptoms can sometimes indicate an ultimate disease process such as infectious colitis, so a suspected disease flare should be confirmed with objective measures like inflammatory markers, imaging and/or endoscopic evaluation.

Disease flares have multiple etiologies, including loss of response over time to a medication that was previously effective.

Clinical guidelines are available from ACG and AGA that can assist clinicians with progressing pharmacologic treatment in a stepwise fashion based on a patient's symptoms and disease severity. Biologic medications are frequently used in the treatment of ulcerative colitis, and a number of newer agents have recently been approved for this indication.

PAs can play an important role in ongoing management of patients with ulcerative colitis.

They can assist patients with preventing disease flares by counseling about diet, smoking cessation, controlling stress, and providing appropriate referrals for these issues when indicated.

Ensuring that vaccinations are up-to-date is another essential role of the PA, especially for patients taking biologic medications. Importantly, partnership between the primary care PAs and the GI specialists can optimize outcomes for patients with ulcerative colitis.

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CME POST-TEST: Participants must: 1) read the educational objectives and faculty disclosures; 2) study the educational materials; 3) complete the post assessments in Learning Central. See page 2 for further information.

Question #1

Which of the following is the most common location of Crohn's disease in the digestive tract?

A. Colon only
B. Gastroduodenal region
C. Ileum and colon
D. Small bowel only

Question #2

What percent of patients with inflammatory bowel disease (IBD) will have extraintestinal manifestations of the disease prior to diagnosis?

A. 25%
B. 50%
C. 75%
D. 100%

Question #3

Which of the following laboratory tests should be part of the initial workup for patients with suspected IBD?

A. Antinuclear antibody
B. Lipid panel
C. Prothrombin time
D. Stool culture

Question #4

According to the Rome IV criteria, what is the minimum number of days per week that abdominal pain should occur during a 3-month period in order to make a diagnosis of irritable bowel syndrome?

A. 1
B. 2
C. 3
D. 4

Question #5

What finding on colonoscopy would be most consistent with a diagnosis of Crohn's disease?

A. Cobblestoning
B. Continuous lesions
C. Eosinophils
D. Pseudopolyps

Question #6

Which of the following factors can contribute to an inflammatory bowel disease flare?

A. Acetaminophen use
B. Antibiotic use
C. Consumption of lean protein
D. Aerobic exercise

Question #7

Which of the following can be used to assess disease severity in patients with ulcerative colitis?

A. Chronic disease score
B. Mayo Clinic score
C. Polygenic risk score
D. Zimran severity score

Question #8

Which of the following vaccinations should be avoided in patients with inflammatory bowel disease who are taking immunosuppressive therapy?

A. Human papilloma virus
B. Influenza
C. Pneumococcal
D. Varicella

Question #9

Which of the following is a risk factor for developing a more aggressive course of ulcerative colitis?

A. Age >40 years at diagnosis
B. Elevated inflammatory markers
C. Lack of extraintestinal manifestations
D. Presence of comorbid conditions

Question #10

Which category of medications is most commonly prescribed for patients with ulcerative colitis immediately following diagnosis?

A. 5-aminosalicylates
B. Corticosteroids
C. IL-12/IL-23p40 inhibitors
D. Nonsteroidal anti-inflammatories

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