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## Extraintestinal Manifestations of IBD: Evaluation and Management Strategies

### Dr. Buch:

What are the latest strategies in treating the extraintestinal manifestations of inflammatory bowel disease? Welcome to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today we're going to explore this topic with returning guest Dr. David Hudesman. He is a Professor of Medicine at NYU Grossman School of Medicine and Co-Director of NYU Langone's Inflammatory Bowel Disease Center. Welcome back to the program, Dr. Hudesman.

### Dr. Hudesman:

Thank you so much. Happy to be here.

### Dr. Buch:

To begin, Dr. Hudesman, please share some background on the extraintestinal manifestations of inflammatory bowel disease, or IBD.

### Dr. Hudesman:

Sure. So this is something that we don't ask enough about, and I think it's probably underreported. When I see a new patient or an existing patient with Crohn's or ulcerative colitis, I run through my mini EIM review of systems, I like to call it, and pretty much ask about joint pain, skin rashes, mouth sores, and eye pain. But really, you could have pulmonary disease, disease of the liver, cardiac disease, and that's all pretty uncommon. But I think it's important to dive a little bit deeper because if you just look at joint manifestations, any arthralgias, even to some type of arthritis or swelling of the joints, upwards of 35 to 40 percent of our patients with IBD can experience that. So while I take a history, I do ask them about joint pains. I ask them separately about their back pain. Not everybody may think their back is necessarily a joint, so that's pretty common. And then I go into a little more detail about the skin rashes. Eye redness and mouth sores, patients usually bring up on their own.

### Dr. Buch:

Thank you. And if we zero in on some specific manifestations, what treatments can be used for erythema nodosum?

### Dr. Hudesman:

Sure. So for skin manifestations, or dermatologic manifestations of IBD, some classic ones are both erythema nodosum and pyoderma gangrenosum. Now, erythema nodosum doesn't always have to, but classically, goes along with disease activity. If you treat the underlying disease with whatever therapy, whether it's a more targeted therapy like a vedolizumab or more systemic therapy like infliximab, if you heal the bowel inflammation, then that should improve on its own. Saying that, my patients that tend to have erythema nodosum tend to also have some other EIMs, and I lean towards a more systemic therapy, like an anti-TNF therapy.

### Dr. Buch:

And continuing with dermatology, Dr. Hudesman, what is the relationship among medications, IBD and psoriasis?

### Dr. Hudesman:

So it's interesting. There's a genetic overlap. So psoriasis is an immune-mediated condition similar to inflammatory bowel disease, and there are some shared genes. And actually, if you look at some studies looking at the microbiome, there are some similar changes we see both in psoriasis and in IBD. And when you ask patients, if you dive deeper into their history, a lot of times patients may say they have a history of psoriasis or patches of psoriasis. So I think in general, in IBD, we will see psoriasis maybe three percent of the time, give or take. Now, saying that, some of our medications that are used to treat IBD and also used to treat psoriasis could actually cause worsening psoriasis—this psoriasisiform-type reaction. So this, classically, we see with our anti-TNF agents. It doesn't matter which one;

it's across the board from infliximab to adalimumab to certolizumab to golimumab. And when we hear or when I see there's psoriasis on the palms or the soles, that's classically that's psoriasiform reaction. And now that we have so many other therapies, stopping the TNF usually helps, but I would switch to another biologic that's really well suited for psoriasis. Our selective IL-23 inhibitors are some of our better treatments for psoriasis, so that's something I would transition to. Ustekinumab, which is an anti-IL-12/23 inhibitor, is another option to treat psoriasis; there have been reported cases of severe psoriasiform reaction to that, but that's pretty uncommon.

**Dr. Buch:**

And when we're talking about the anti-TNFs causing psoriasis, what's the mechanism involved?

**Dr. Hudesman:**

So it's a good question. I don't think we fully understand what drives that. There's been certain upregulation in certain cytokines when you're blocking TNF. That has been hypothesized. In the past, we used to think maybe it was dose-dependent if we gave too much. But really, in more recent data, and just looking at some of the more recent studies that we do have, it doesn't matter what dose of TNF, it doesn't matter what the TNF is, and the exact mechanism is unknown.

**Dr. Buch:**

Thank you. So now, if we focus on our patient's eye health, how can we assist the ophthalmologist when dealing with the ocular manifestations of IBD?

**Dr. Hudesman:**

So just like with every extraintestinal manifestation—I was mentioning it earlier—I do that initial review. I just ask them if they have eye pain, and usually, patients will then start telling you different manifestations of their eye, and then you have to nail that down. So I had somebody actually just I saw earlier today that was complaining about migraines and their eye hurt. Obviously, that's not an ocular manifestation. So usually, I talk about eye redness, eye pain, and any blurry vision associated with that. So any symptoms like that I'll refer over to ophthalmology, but usually, I have somebody that's a uveitis specialist. That's really what you're looking for: uveitis or scleritis. So I have a team of doctors here that I would send to evaluate specifically for that. But I dive a little bit deeper in my history.

Now, with some of our newer therapies, like our S1P receptor modulators, which include ozanimod or etrasimod, we do want to do an ophthalmological exam on them. It doesn't have to be necessarily before, but before or soon after starting these therapies, and really with this, we're looking to make sure there's no underlying glaucoma. So definitely, if my patient's older, history of steroid use in the past, history of diabetes, or obviously history of glaucoma, I'm having them see the ophthalmologist before. Without that history, I'm still having them screen the patients, but I can get them started on therapy before actually doing that.

**Dr. Buch:**

Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. David Hudesman about the extraintestinal manifestations of inflammatory bowel disease.

So, Dr. Hudesman, when treating arthritis and IBD, are you concerned about bleeding when using NSAIDs?

**Dr. Hudesman:**

Yeah, great question. I think arthritis is one of the more difficult things to treat with our patients with IBD, and also, one of those things we underdiagnose. But I work with a rheumatologist where I really try to minimize NSAIDs, so needing to get them on some other therapy because I'm not worried about bleeding from the lower GI tract—not from the colon or the small bowel, more just sort of the chronic NSAIDs and causing ulcers is more of a concern. And sometimes if you're on those chronic NSAIDs, you could have aphthous ulcers throughout your small bowel or colon, which could sometimes confuse the picture: is your underlying IBD really active or not, or is it from the NSAIDs? So we really try to avoid it. Even the Cox-2 inhibitors I try to avoid as well. And working with my rheumatologist, if they're more peripheral manifestations, we use things like sulfasalazine, probably one of the few instances where I'm still using medication, methotrexate for peripheral arthritis. And when you're talking about more central spondyloarthritis, that's when you're talking about TNFs and JAK inhibitors mostly.

**Dr. Buch:**

So just carrying that to the next level, let's say you have an ulcerative colitis patient who is getting maximum therapy and is doing quite well and you've re-colonoscoped them; not only is the appearance good, but the biopsies are good as well. Would that kind of patient be a candidate for NSAID if they're having arthritic problems?

**Dr. Hudesman:**

Yeah, great question. So first, I would take a step back and see what's causing it. Usually, there's a broad differential for our IBD patients and arthritis or arthralgias. So first, is it driven by active inflammation? Then we would adjust therapy. And in this patient case,

there's no active inflammation. Secondly, some of our therapies can cause joint pain, so if you're having antibodies to a TNF, that could lead to joint pains. I have seen some paradoxical reactions. We talked about psoriasiform reactions, but I have seen paradoxical reactions with vedolizumab with worsening joint pain. So could it be medication related? Could this be more osteoarthritis, wear and tear? Or is this some type of immune-mediated arthropathy or spondyloarthropathy? And if I think that's the case, then maybe if somebody's on a targeted therapy like vedolizumab and there is sacroiliitis or ankylosing spondylitis, maybe that does need to get switched to something more systemic, like an anti-TNF or a JAK inhibitor.

Now, let's say in your specific case, somebody who's in endoscopic remission, doing well, and now they have some peripheral arthritis, should you use NSAIDs? Even in these situations I do try to avoid it. Now, you also have to be practical. I don't think somebody in endoscopic remission taking a few days of an NSAID if they have an acute flare of their joints is necessarily a bad thing and likely to cause a flare. However, again, I wouldn't want that to be a long-term treatment. So, sure, short term, a few days is okay, but then talking to a rheumatologist to have a better long-term plan is key.

**Dr. Buch:**

I really appreciate that answer. So moving on to this one, which hospitalized patients with IBD should be receiving anticoagulation? And how long should it be continued?

**Dr. Hudesman:**

Great question. So in general, somebody with a severe ulcerative colitis flare or Crohn's flare in the hospital, their relative risk of clotting, of developing some type of clot—and it could be a DVT, a PE—is 15 times higher than the relative risk in the general population. The absolute risks in our younger patients are still low, but every one of our patients that are hospitalized for a UC or Crohn's flare, inflammatory flare, I put them on low-molecular-weight heparin during the hospital admission.

Now, there's been some data. One of my colleagues, Dr. Adam Faye, has published looking at this clotting risk both during the hospitalization and within a month or two afterwards, and although there is still that risk after discharge, that risk is very small, and I am not routinely continuing anticoagulation in my patients after discharge as long as the inflammation is well controlled. If the inflammation is not well controlled and we're talking about surgery in the near-term future, that's where I could continue it, but routinely, during the hospitalization, even if their hemoglobin is 5, even if they're bleeding, they're getting anticoagulation with something like low-molecular-weight heparin. There's been nice studies. They're not going to bleed more. You're going to give them blood, or you're going to give them IV iron, and you're going to treat the underlying inflammation. So all patients need that. Venodyne boots are not enough. Again, routinely on discharge I stop it except for those patients that still have pretty significant inflammation.

**Dr. Buch:**

Which brings me to this question: what happens if you have a patient who's not quite severe enough for hospitalization? Would you ever consider anticoagulation at home?

**Dr. Hudesman:**

I think it's a great question, but I do not start anticoagulation in those patients routinely. And I think even though in some studies, that risk might be up, that absolute risk is still very low, so I do not routinely do that in my patients, currently.

**Dr. Buch:**

Thank you. In the last few moments of our discussion, Dr. Hudesman, are there any other insights you'd like to share with our audience?

**Dr. Hudesman:**

I think the most important thing is to take a good history about extraintestinal manifestations. I said this earlier, but I can't tell you how many times I've said, "Do you have joint pains?" the patient says, "No," and then later in the visit he talks about how his back hurts. So asking throughout the visit is what I like to do, and my style is bringing it up, asking it in different ways, and then if they do mention joint pains, having some follow-up questions. If they do mention eye pains, as we mentioned, asking about eye redness, eye pain. And I think, specifically about joints since it's the most common; inflammatory joint pain is usually worse at rest and improves with exercise, whereas something mechanical worsens with exercise, so that's one simple question that could help guide you where to go from there.

**Dr. Buch:**

What a meaningful update on the extraintestinal manifestations of IBD. I want to thank my guest, Dr. David Hudesman, for joining us to share his important insights on inflammatory bowel disease. Dr. Hudesman, it was a pleasure speaking with you today.

**Dr. Hudesman:**

Great speaking with you as well. Thanks so much.

**Dr. Buch:**

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening, and looking forward to learning with you next time.