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Managing Pouchitis: A Review of the Updated AGA Guidelines

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm Dr. Peter Buch. And here to update us on the latest recommendations for pouchitis is Dr. Edward Barnes. He's an Assistant Professor of Medicine and an Associate Program Director for the Gastroenterology and Hepatology Fellowship at the University of North Carolina School of Medicine at Chapel Hill. On top of that, he's also the lead author of the AGA guidelines on pouchitis and inflammatory pouch disorders that were published in *Gastroenterology* in 2024.

Dr. Barnes, I'm looking forward to speaking with you today.

Dr. Barnes:
Thank you so much for the opportunity. This is really a timely discussion. We've had a lot of great advancements in the last couple of years in the management of pouchitis, and we were really happy to summarize these in the most recent guidelines, as you mentioned.

Dr. Buch:
Perfect. Let's get started. Dr. Barnes, could you start us off by giving a brief overview of the different classifications of pouchitis?

Dr. Barnes:
This is something that we really wanted to focus on—thinking about pragmatic definitions of what pouchitis really entails—and one of our real goals is to think about defining pouchitis for research, but more importantly, for clinical practice, so I'll walk you through those. The first is, we've thought for a long time about this definition of acute pouchitis. We sort of flipped that. We actually talked about a definition of intermittent pouchitis because really, when we think about that, that patient that presents with symptoms of frequency, urgency, sometimes incontinence, abdominal pain or pelvic pressure, nocturnal stools. That's the patient who we think about with that classic appearance of pouchitis: that patient where they present, you treat them with antibiotics, they get better, and they have a long period of asymptomatic or normal pouch function. That's the patient we're really thinking about that used to be defined as acute pouchitis. We think about that being intermittent pouchitis because they have these long episodes of normal pouch function with intermittent episodes of pouchitis or increased disease activity. The second category that we think about, though, is really defined into two forms of chronic pouchitis, the first one being chronic antibiotic-dependent pouchitis, in which, as the name would suggest, the patient's symptoms are well controlled when they're on antibiotics, and usually, by the time the antibiotics are stopped, the symptoms will come back.

Now, in a traditional sense, similar to the idea that we're going away from the idea of acute pouchitis, we're going away from a numeric definition where you might have seen in the past more than four episodes of pouchitis in a year. Chronic antibiotic-dependent pouchitis is really defined by the fact that patient symptoms come back when they're not on antibiotics. So really think about a treatment goal where you're trying to find a minimally effective dose of antibiotics and you're just trying to control that patient's symptoms. If you contrast that with the other form of chronic pouchitis where the patient's symptoms are no longer responsive to antibiotics, they're refractory to antibiotics, that patient is most likely going to need some other advanced therapy, some other form of changing their immune system. So usually, that's a biologic or a small molecule.

Now, there's another inflammatory condition in the pouch that doesn't fall in that pouchitis realm necessarily, which is Crohn's-like disease of the pouch, and that's really defined by the disease presentation: the presence of strictures in the pouch body or the pre-pouch ileum, the presence of a fistula—either a perianal fistula, a pouch vaginal fistula, or a fistula to another organ—or the presence of inflammation above the level of the pouch body into the afferent limb or the pre-pouch ileum. Those are the three defining diagnostic criteria when we think about Crohn's-like disease of the pouch. So those are the four inflammatory conditions of the pouch we focused on with those pragmatic definitions.

Dr. Buch:
Perfect. And as a further guideline to our listeners, this is all well-outlined in the article published in *Gastroenterology* in 2024. Now, turning to the AGA clinical practice guidelines on the management of pouchitis and inflammatory pouch disorders, why was this important to update?

Dr. Barnes:
Well, it was important in large part because this is the first society-backed or society-sponsored guideline that had been put forth. We had had several consensus statements that different individual groups or different consortia had put out, but this was the first time that we'd had a society-backed guideline, and that's important for a couple of different reasons. For one, as our readership and as our larger body within gastroenterology looks for those society-backed guidelines for informing clinical practice, and other third-party groups do as well; but the bigger reason too is, our goal here was to standardize clinical practice, both for what we're doing currently but also to push the field forward. That's why it was time to really try to think about standardizing our approach, what we're doing clinically now, and how can we improve outcomes in the future.

Dr. Buch:
Great. And moving on to recommendations, Dr. Barnes, should we be using probiotics or antibiotics prophylactically to prevent pouchitis?

Dr. Barnes:
This is a question where there's been a lot of heterogeneity in the literature, specifically with probiotics, but it's an area where we really need to learn more, because if we think about, potentially, the incidence of pouchitis increasing over time, the ideal way to stop that or to decrease that trend would be to actually prevent pouchitis and to use some of these therapies prophylactically, as you mentioned The problem is, at least in terms of primary prevention, the data on this is a little bit mixed. There were some initial studies from the early 2000s that would have suggested that specific probiotic therapy, such as the eight-strain probiotic, which has been marketed under a couple of different names, may be quite beneficial in terms of decreasing the incidence of pouchitis within the first year after surgery. But when this has been looked at in other real-world studies and in clinical practice, this is not quite borne out, so the data is a little bit mixed. And one of the problems when you think about primary prophylaxis—there are actually two major problems—is we don't know how long you would have to do primary prevention strategy to prevent pouchitis. Is this lifelong? Does the patient have to take prophylaxis for the duration of having a pouch? And the second thing is, and the reason this is important when you think about the duration, is these can be costly therapies because they're often not covered by insurance.

Now, when you think about secondary prevention with pouchitis, the data is actually a little bit stronger there, so we did make a recommendation to consider probiotic therapy when you think about secondary prevention. And when we talk about secondary prevention, what we're talking about is the patient's had an episode of pouchitis that's been treated with antibiotics and then used that probiotic as a secondary prevention to prevent the recurrence of pouchitis.

When you're thinking about antibiotics for the primary prevention, we did not recommend that at this time because the literature just doesn't support it. And there's also questions about, again, would you take lifelong antibiotics from the time that you had the ileostomy takedown or the final stage of the pouch surgery? I think we just don't have the data to support that, especially if you were to consider the sort of risk-benefit of lifelong antibiotics and what that would do. Would a patient be willing to take that? There's a lot of questions we probably need to define better in the literature before we make that recommendation.

Dr. Buch:
That's very helpful. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Edward Barnes about the updated AGA guidelines for managing pouchitis.

So moving on to more technical details, how long should antibiotics be used when treating pouchitis? And when should we also add probiotics under those circumstances?

Dr. Barnes:
So if you think about the duration of an initial episode of pouchitis—so going back to that definition of intermittent pouchitis, a patient has surgery the first time they present— most commonly, we're going to be using antibiotics for the first 14 days. That's the typical course, a 14-day course. Now, some providers may choose to do a longer course, 21 or even 28 days, for that first episode, but the most commonly studied and recommended course is 14 days.

Now, if a patient's starting to have recurrent episodes, then you're going to do one of two things. If a patient has developed into that chronic antibiotic-dependent pouchitis realm, then you're going to try to find a minimally effective dose. And for some patients that I treat, that may be ciprofloxacin, as an example, twice a day, 500 mg. For some patients it may be 500 mg one day a week, and that's

enough to keep their symptoms at bay.

If you want to add in the probiotic, then this is where we're thinking about that secondary prevention strategy that I mentioned earlier. Maybe the patient takes antibiotics for a period of time, 14 to 28 days, and then as soon as they stop the antibiotics, then you start that probiotic. The one that's been studied the best is that eight-strain probiotic that I mentioned before, and maybe that becomes the strategy that you implement. You do the 14 to 28 days of antibiotics, control the patient's symptoms, and get them into remission, and then you start the probiotic immediately after that, and you continue that as your maintenance therapy.

Dr. Buch:
Dr. Barnes, you just reminded me of something. Is there a tachyphylaxis when we're talking about using antibiotics for pouchitis?

Dr. Barnes:
So that is an excellent question and one that is almost individualized to each patient. I don't know that we can make a blanket statement that tachyphylaxis itself exists. What I do see over time is that there are patients that benefit from the idea of cycling antibiotics. And so you take one antibiotic for two weeks, and then you switch to another antibiotic for two weeks, and maybe even some patients take a break of antibiotics for the third part of that cycle for the next two weeks, and then they go back to the original antibiotic. That may be a strategy that's beneficial.

There have been studies, and probably the one that gets quoted the most is a paper that was published in *Gastroenterology* in 2020 from a group in Israel looking at antibiotic resistance patterns that develop after exposure to antibiotics for the treatment of pouchitis, with the suggestion that maybe that's what drives, over time, this chronic antibiotic-dependent pouchitis profile and that minimally effective dosing and even considering cycling of antibiotics would be the strategy to employ. But I think there's a lot we need to learn about that over time as far as how that affects clinical practice.

Dr. Buch:
So let's move on to this. Dr. Barnes, when should we consider immunosuppressives? And which immunosuppressives seem to be most effective?

Dr. Barnes:
So definitely, if a patient's not responding to antibiotics and they're refractory to antibiotics with chronic pouchitis, that's a patient that would benefit from immunosuppressive therapy. There is a question about introducing earlier immunosuppressive therapy, and we did include that within the guideline. For a patient that doesn't want to take chronic antibiotic therapy, that's a consideration to introduce immunosuppressive therapy earlier. And there's a question of whether or not earlier introduction of immunosuppressive therapy with intermittent antibiotics may be beneficial, and the reason I bring that up is the second part of your question: which therapy has been best studied?

There was a randomized controlled trial published last year known as the EARNEST study, which compared vedolizumab versus placebo, and in that study, for the first four weeks of the study, all patients, both placebo and vedolizumab arm, were treated with ciprofloxacin, and then no patients were taken off antibiotics through week 14. After week 14, patients could go back on antibiotics per the discretion of their treating physician. And at the end of that week 34 point, which was their maintenance and evaluation time point, 21 percent of the patients that were treated with vedolizumab were also being treated with antibiotic therapy. So then maybe this group of patients needs both an immunosuppressive therapy and an antibiotic, and they have this mixed population. So vedolizumab is the one that's been studied the best in terms of a randomized controlled trial, but we do have prospective data that's emerging for other therapies as well.

There was a large prospective study evaluating ustekinumab that was published over the summer in *Clinical Gastroenterology and Hepatology* within a prospective registry that we run. We published data on risankizumab earlier this year, and multiple different therapies have been looked at in retrospective studies as well, including anti-TNF therapies and JAK inhibitors. Essentially, all the therapies that we have evaluated for ulcerative colitis and Crohn's disease pre-colectomy have been looked at for the treatment of chronic inflammatory uses of the pouch as well.

Dr. Buch:
Thank you. And in last few moments of today's discussion, Dr Barnes, is there anything else you'd like to share?

Dr. Barnes:
Yeah. One of the things that we haven't talked about, which is really important when we think about these guidelines is what's the abnormal when we think about these inflammatory conditions of the pouch. We also want to think about what's normal and what the patient should expect and how these differ, and that sets the groundwork for what's a normal pouch function. And we think about that

being about 4 to 8 or 4 to 10 bowel movements a day, one bowel movement at night. But also, once we know what's normal, we know what's abnormal—we talked about those definitions—that standardization, that approach, really allows us to look then at the gaps and where the field needs to go.

I think this guideline was not the end-all be-all for the care of patients with inflammatory conditions of the pouch. In fact, it sets the stage for us to take off in terms of our care of patients with pouch-related disorders and improve our research efforts as well. We need to think about what we're doing in terms of, yes, standardization, but more importantly, clinical trial design and what the risk factors are in terms of why people develop these pouch-related disorders, and if can we get at some of those issues that you asked about with probiotics. Can we do prevention studies? I think all this will launch us forward in the next 5 to 10 years and really improve the care of patients and outcomes after patients have this surgery.

Dr. Buch:
With those impacts in mind, I want to thank my guest, Dr. Edward Barnes, for sharing his insights and updates on the AGA guidelines for pouchitis.

Dr Barnes, it was great having you on the program.

Dr. Barnes:
Thank you so much. I really appreciate the opportunity.

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 see you next time.