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## Reviewing Updated Guidelines and Knowledge Gaps for Pouchitis Management

### Dr. Buch:

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch, and joining us today is Dr. Edward Barnes, who's an Associate Professor of Medicine and Associate Fellowship Program Director at the University of North Carolina School of Medicine. He's also the primary author of "AGA Clinical Practice Guideline on the Management of Pouchitis and Inflammatory Pouch Disorders," which was published in *Gastroenterology* in 2024.

Dr. Barnes, welcome to the program.

### Dr. Barnes:

Thank you so much. I'm really thrilled to be here, and I'm really looking forward to this.

### Dr. Buch:

Looking forward as well. To get us started, Dr. Barnes, what percentage of patients develop pouchitis after ileal pouch-anal anastomosis? And why does this happen?

### Dr. Barnes:

Both great questions. I think the first thing to acknowledge is that pouchitis is common. When we think about a patient undergoing a restorative proctocolectomy with an ileal pouch-anal anastomosis, within the first two years after surgery, approximately 48 percent of patients, so roughly half of patients, are going to develop intermittent pouchitis. If you look at lifetime following patients for 20 or plus years, over 80 percent of patients will go on to develop at least one episode of pouchitis, so this is common.

Now the why patients develop pouchitis, that's a little bit more difficult to answer. We think this is primarily driven by a dysbiosis, not unlike what we think about is driving de novo Crohn's disease or ulcerative colitis. The difference being in pouchitis, this is not only a bacterial phenomenon in a patient that's predisposed to develop inflammation—they have that underlying inflammatory bowel disease—but in this case, it's the bacteria themselves that seem to be causing a problem. And the way I describe it to patients is your small intestine used to be a straight tube and a conduit of stool passing from the upper GI tract down into the colon, and now after you've had a colectomy, we've made it into this new configuration into what we call a J pouch, and it's now serving as a reservoir to hold stool, and that changes some of the interactions between the bacteria in the stool and the bacteria in particular in the lining of the pouch itself. And in some patients, this is predisposed to go on to develop some inflammation in the form of pouchitis.

### Dr. Buch:

So that's going to be a wonderful segue to a couple of questions in the future when we're talking about probiotics. But before we get to them, here's another question, should antibiotics be used to prevent pouchitis?

### Dr. Barnes:

So in terms of prevention of pouchitis, probably not. The data right now would not suggest that antibiotics should be used in the prevention of pouchitis. There has been one randomized controlled trial that looked at this that we evaluated in the process of writing the guidelines looking at the use of tinidazole for the prevention of pouchitis. However, given that there's an unknown of how long patients would have to use an antibiotic therapy for the primary prevention of pouchitis, the risk/benefit of that is yet to be determined, so we would really need more data to make a really strong

recommendation that all patients should be on antibiotics for an unknown period of time for the prevention of pouchitis. It's a really great question though.

**Dr. Buch:**

And let's move on to the preferred antibiotics and the duration to treat pouchitis.

**Dr. Barnes:**

So if you think about that scenario that I laid out at the very beginning, that 48 percent of patients develop intermittent pouchitis in the first year, that initial episode of pouchitis, the most common antibiotics that are going to be utilized are either ciprofloxacin or metronidazole, and for most patients that's going to be a 14-day course, although some providers may choose to use a longer course even for an initial episode of pouchitis. Now those patients, if they have intermittent pouchitis, meaning that you have an episode of pouchitis, you treat the patient with ciprofloxacin or metronidazole, their symptoms get better and the symptoms go totally away, those are going to be great as long as the patients are having normal periods of function in between.

Now there are a portion of patients that will go on to develop what we've termed chronic antibiotic-dependent pouchitis, meaning that as soon as you stop the antibiotics, their symptoms return. And in those patients, the treatment goal becomes somewhat different, and in those patients, you're really looking at chronic antibiotic therapy as a way to maintain that patient in clinical remission. And in those patients, the goal is really not to use intermittent sort of periodic dosing of antibiotics but to use the minimally effective dose of antibiotics to control that patient's symptoms, and it can be really an individualized or tailored regimen and so, for each patient that I see in clinic, we're really trying to figure out if they have chronic antibiotic-dependent pouchitis, what's the smallest or lowest effective dose that we can find and in some cases even cycling different antibiotics to keep their symptoms under control.

**Dr. Buch:**

And when you talked about the two antibiotics, metronidazole and ciprofloxacin, have there been any studies to compare one to the other in terms of effectiveness?

**Dr. Barnes:**

There have. So in the early 2000s, there was a randomized controlled trial that was performed, a relatively small trial, less than 10 patients in each arm, and basically, what that trial showed is that both ciprofloxacin and metronidazole were effective in the treatment of pouchitis. However, the ciprofloxacin was slightly better tolerated than the metronidazole. Roughly, a third of patients with metronidazole had some adverse effects, whereas the ciprofloxacin was tolerated by all of the patients in the initial course of the treatment of pouchitis.

More recently, we actually looked at this in claims data to look at that initial episode of pouchitis treated with ciprofloxacin or metronidazole. I didn't really see a difference. And we followed those patients going forward to see looking at episodes of recurrent pouchitis; although, it's really hard to get that idea of how well the patient tolerates that using claims data compared to a randomized controlled trial like the example that I cited.

**Dr. Buch:**

Thank you for that information. And now here we come to the probiotic question. So what role do probiotics have in the prophylaxis or treatment of pouchitis?

**Dr. Barnes:**

This is a really common question that we get in clinic when we see patients because, as you mentioned from the very top, obviously, probiotics are really an area where we would think they should be effective in both the prevention, and potentially, the treatment of pouchitis given what we think is driving patients to have symptoms of pouchitis. For primary prevention with probiotics, the data is a little bit mixed, and because of this, we didn't make a strong recommendation. And in fact, we really viewed this in the guidelines as a knowledge gap. The reason for this is there were some early randomized controlled trials that would suggest that certain formulations of probiotics—namely, the one that's received the most interest in the lay press certainly is the De Simone Formulation, an eight-strain probiotic where primary prophylaxis was quite successful with only 10 percent of patients developing pouchitis in the first year compared to 40 percent of patients in the placebo arm of this randomized controlled trial. Now if you compare that to secondary prophylaxis or secondary prevention, once the patient has had an episode of pouchitis and you're trying to actually prevent them from having future episodes of pouchitis, here we felt the data was actually stronger in terms of probiotics.

In terms of treatment with probiotics, I think this is also an area where this is really a knowledge gap because there have been some studies that would suggest that probiotics can be effective, but if we really think about using probiotics as a treatment for pouchitis, what we really would like to

see are comparative effectiveness studies, like you mentioned before, comparing probiotics to antibiotics because I think knowing what the downstream effects—if the patient were to develop recurrent pouchitis after being treated with probiotics and knowing what the long-term effects of not having that disease initially under control—those are the outcomes that we need to see rather than just the initial control of symptoms. And so for treatment with probiotics, this was another knowledge gap for us as we did the guideline process.

**Dr. Buch:**

Looking forward to that information in the future.

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 pouchitis.

So given what we talked about so far, Dr. Barnes, let's turn our attention to advanced therapies. When should we consider immunosuppressives to treat pouchitis? And is there data comparing biologics with small-molecule drugs?

**Dr. Barnes:**

So I think the most logical algorithm where we definitely want to think about introducing advanced therapies is in another group of patients with chronic pouchitis where they're no longer responding to antibiotics. And there was a recent randomized control trial that was published in *The New England Journal* last year known as the EARNEST study where vedolizumab was introduced in this scenario. Patients took four weeks of ciprofloxacin, and then were treated with vedolizumab or placebo, and that EARNEST study did show a statistically significant benefit of vedolizumab at week 14 and at week 34.

Now the other scenario where we think about advanced therapies is in the treatment of Crohn's-like disease of the pouch because these patients don't necessarily have to go through that same algorithm of intermittent pouchitis, chronic antibiotic-dependent pouchitis, chronic antibiotic-refractory pouchitis. Patients may develop pre-pouch ileal inflammation, inflammation of the small bowel above the pouch, or inflammation of the pouch itself with deep ulcers or strictures or even development of perianal fistula or other fistulizing complications, and so in those scenarios where a patient has one of those three diagnostic criteria and they have Crohn's-like disease of the pouch, use of an advanced therapy makes sense.

Now we don't have randomized controlled trial data within the Crohn's-like disease of the pouch space, but in both chronic antibiotic-refractory pouchitis and in Crohn's-like disease of the pouch, any advanced therapy that would otherwise be used for ulcerative colitis or Crohn's disease de novo, has essentially been looked at, at least in real world studies or observational studies, and there is some evidence to support that, and so we felt like as a guideline committee that those therapies could logically be utilized or repurposed in the treatment of patients with chronic antibiotic-refractory pouchitis or Crohn's-like diseases in the pouch.

Now we don't have head-to-head comparative effectiveness studies of biologics versus small molecules. And I think that, as we think about future directions, that's a really logical place where we'd like to do more rigorous comparative effectiveness studies to think about how we best position drugs for these chronic inflammatory conditions in the pouch in particular.

**Dr. Buch:**

And, Dr. Barnes, what should we know about mesalamine and budesonide to treat pouchitis?

**Dr. Barnes:**

Well, mesalamine is one where I think the jury is still out. We really did not find a lot of evidence to either support or refute the use of mesalamine in patients with inflammatory conditions of the pouch, specifically pouchitis. There is a very small amount of data evaluating the use of sulfasalazine. The other thing to note about sulfasalazine is, obviously, there's a sulfa component, and some authors have hypothesized that maybe this sulfa component has some antibacterial properties and that's why sulfasalazine may be effective in the treatment of pouch-related disorders.

The other point about mesalamine is that when we have these other therapies that we've been mentioning that we know are effective for the treatment of pouchitis, specifically, if we're thinking about intermittent pouchitis, knowing how well antibiotics work, using a therapy like mesalamine that may actually delay the use of a known effective therapy, this may potentially lead to some harm for patients, and so this is one I think I would be at least considering where the right role of mesalamine is as far as oral mesalamine.

Now if a patient has disease of their rectal cuff, that's a little bit of a different story because this is essentially residual proctitis. This is the small one to two centimeter of rectum that's left. And in that case, topical mesalamine or other topical therapies for ulcerative colitis are fair game, and we found these to be quite effective, and I've seen this in my practice as well.

Now budesonide, we did feel like there was relatively robust evidence for the use of budesonide in both chronic antibiotic-refractory pouchitis and Crohn's-like disease of the pouch for short periods of time, eight to 12 weeks. In that case, if the patient is responding to budesonide, it's logical—just like we would do in ulcerative colitis or specifically in Crohn's disease with the ileal release budesonide that we recommended—you would be thinking about what your maintenance therapy is going to be, and that's where we revert back to those advanced therapies that we talked about earlier.

**Dr. Buch:**

What an excellent discussion on pouchitis. I want to thank my guest, Dr. Edward Barnes, for sharing his knowledge. Dr. Barnes, thank you so much for joining me today.

**Dr. Barnes:**

Thank you for the opportunity, and for the chance to get to talk with you.

**Dr. Buch:**

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit [reachmd.com/Glinsights](https://reachmd.com/Glinsights), where you can Be Part of the Knowledge. Thanks for listening, and looking forward to learning with you next time.