

## IBD LIVE Series—Case 7: The Brain-Gut Connection and the Importance of Integrated Care in IBD

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### LEARNING OBJECTIVES

After completing this IBD LIVE-CME activity, physicians should be better able to:

1. Explain the meaning of the “brain–gut axis” and recognize its important physiologic relationships.
2. Identify the psychological issues that are most prevalent among patients with inflammatory bowel disease (IBD).
3. Explain which types of health care providers are best suited for working with patients with IBD who have mental health needs.
4. Describe treatments that have been shown to be effective for mood disorders in patients with IBD.
5. Describe how pain impacts patients with IBD.
6. Describe the potential emotional impact of surgery on patients with IBD.
7. List common late complications of restorative proctocolectomy and ileal pouch-anal anastomosis (IPAA) surgery.

Presenter: Benjamin H. Click, MD: Gastroenterology Fellow II, University of Pittsburgh School of Medicine.

### PRESENTATION

The patient is a 38-year-old man who was diagnosed with panulcerative colitis in 2000. During the initial years after his diagnosis, he failed medical therapy with azathioprine, 6-mercaptopurine, and methotrexate and also took part in a clinical trial of visilizumab. In August of 2004, the patient underwent a total abdominal colectomy with ileal pouch-anal anastomosis (IPAA) and diverting loop ostomy. In December of the same year, he had an ileostomy takedown and reanastomosis. He has had no other surgeries.

The patient has an extensive psychiatric history. He was first diagnosed with major depressive disorder during adolescence and experienced suicidal ideation after his ostomy was created in 2004. Previously, he has failed multiple antidepressants including the selective serotonin reuptake inhibitors paroxetine and citalopram, the serotonin norepinephrine reuptake inhibitors mirtazapine and duloxetine as well as the norepinephrine-dopamine reuptake inhibitor bupropion. In addition, he carries the diagnosis of generalized anxiety disorder with panic attacks that have been treated with alprazolam as needed and attention-deficit hyperactivity disorder for which he receives amphetamine-dextroamphetamine (Adderall). In the past, the patient’s primary care provider addressed his behavioral health

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care needs but he recently transitioned to seeing both a psychologist and a psychiatrist. The patient has an alcoholic brother with bipolar disorder and his mother has anxiety and depression. There is no family history of inflammatory bowel disease (IBD), but a maternal grandmother was diagnosed with colorectal cancer at age 92. The patient is married and has no children. He has a master's degree in clinical psychology and worked as counselor for at-risk children until 2013, when the stress of his illness interfered with his work and led him to go on disability. He smokes about ½ pack of cigarettes per day, rarely drinks alcohol, and does not use illicit drugs. Over the past decade, he has been prescribed opioid medications on numerous occasions.

The patient's IBD history includes a visit to the emergency department 1 week after his 2004 surgery with complaints of abdominal pain, nausea, and vomiting. He was discharged on oral opiate painkillers. One month postoperatively, he had a similar emergency department visit for abdominal pain, nausea, and vomiting and was again discharged on opiates. Two months after his surgery, he was admitted to the hospital with fever, diarrhea, abdominal pain, nausea, vomiting, and a notable 40-pound weight loss. An esophagogastroduodenoscopy was performed that showed superficial inflammation in the gastric fundus and duodenum with aphthous ulcerations in both the stomach and duodenum. A pouchoscopy at that time demonstrated ileitis and aphthous ulcers extending between 10 and 20 cm proximal to the anastomosis and biopsies showed acute on chronic inflammation with granulomas. Based on these endoscopic and histologic findings, the patient was diagnosed with Crohn's disease. When he was told that he had Crohn's disease rather than ulcerative colitis, he was devastated.

From April of 2005 to April of 2007, the patient did very well on infliximab monotherapy. He had also been tried on immunomodulators but was intolerant of them. Between April of 2007 and early 2009, however, the patient was admitted to the hospital on several occasions because of partial small bowel obstructions. From 2009 to 2012, he was lost to follow-up, and we discovered that he discontinued his infliximab during this time. In 2012, the patient came back into our care after having a small bowel obstruction. He underwent computed tomography (CT) and a pouchoscopy that showed active disease, after which he was restarted on infliximab. Between 2013 and 2015, he had 17 hospital admissions for partial small bowel obstructions although he was on comprehensive therapy that included infliximab 10 mg/kg, methotrexate, budesonide, and IV iron for iron-deficiency anemia. At a 2015 office visit, the patient stated the he felt miserable. Endoscopically, an anal stricture was noted. On imaging, his pouch and distal small bowel were very dilated. Because of the patient's rectal pain, he underwent rectal manometry that demonstrated dyssynergic defecation. Subsequently, he was taught how to use a rectal tube to help with defecation.

The patient's bowel disease has been deeply intertwined with his psychological health, with stress playing a particular role in accentuating his anxiety and depression. As mentioned, he has been on numerous antidepressants in the past and also has used benzodiazepines. He states that he smokes cigarettes to calm his nerves. He began seeing a psychiatrist intermittently in 2009. In 2013, he started cognitive behavioral therapy (CBT) for anxiety, depression,

and pain-coping strategies with a psychologist who specializes in IBD and was able to wean off of narcotics while reporting having better energy. Unfortunately, his pouch symptoms and systemic problems progressed. In 2015, he described having to self-catheterize 3 to 4 times per day to release gas and bowel movements and he stated that he "couldn't live like this anymore."

He had a pouchoscopy in 2012 while on infliximab monotherapy, and there was evidence of several ulcerations as well as inflamed and erythematous mucosa (Fig. 1). The 2012 pouchoscopy seemed to show some improvement compared with previous examinations. His most recent 2015 pouchoscopy is endoscopically normal.

### Dr. Douglas J. Hartman (Pathology, University of Pittsburgh)

I reviewed some pathology slides taken from a 2012 pouchoscopy. Active inflammation is present in all sites, including the ileum above the pouch and the rectal cuff. Active inflammation extends proximally from the cuff to just proximal to the pouch. There is mildly active chronic ileitis without dysplasia, characterized by intraepithelial neutrophils and crypt architectural distortion (Fig. 2). Pathology from his 2015 pouchoscopy shows very minimal architectural distortion but the mucosa looks essentially normal. There is no active inflammation or dysplasia.

### Dr. Peter L. Davis (Radiology, University of Pittsburgh)

Looking at the patient's CT scan from October of 2015 when he had a partial small bowel obstruction, you can see a portion of the ileum tapering into the pouch as you go up from the bottom through the levels on coronal imaging. You may initially note an area of mild enhancement of the distal ileum going into the pouch and there is some mild-to-moderate dilatation of that distal ileum. As you go up further, there is asymmetric enhancement of the J pouch wall with some enhancement of the distal ileum that was dilated before the

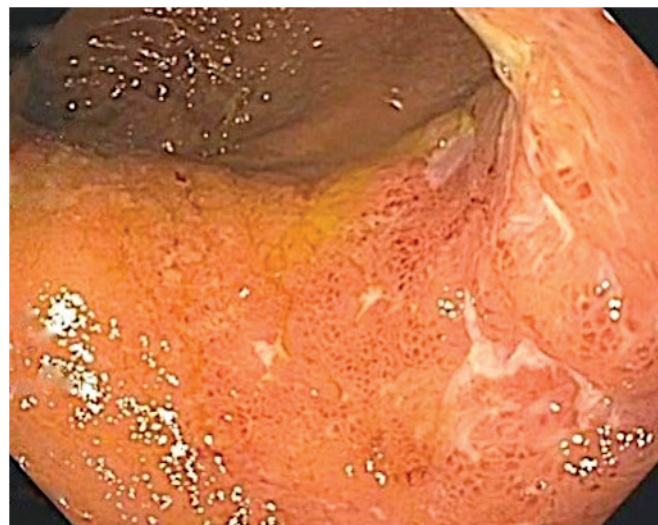


FIGURE 1. A 2012 pouchoscopy image shows evidence of a number of ulcerations as well as erythematous mucosa and active inflammation.

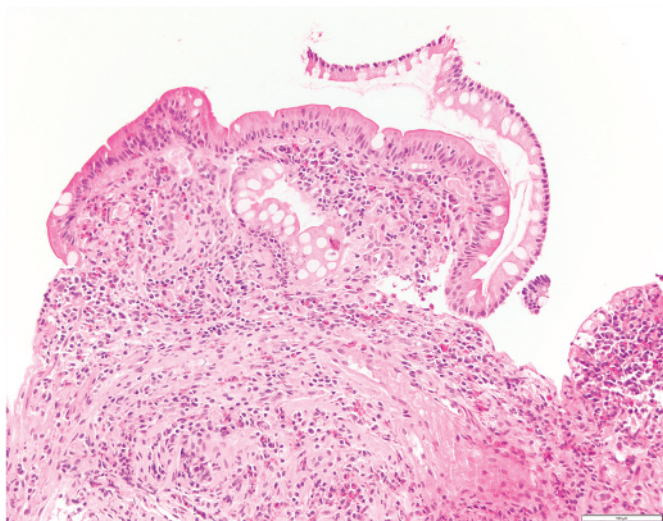


FIGURE 2. The 2012 biopsy from the pouch demonstrates loss of small intestinal architecture, crypt dropout, and intraepithelial active inflammation. These findings are consistent with mild active pouchitis. The biopsies were negative for dysplasia. There is also an increased amount of eosinophils within the inflammatory infiltrate. (Hematoxylin and Eosin,  $\times 200$ ).

pouch itself (Fig. 3). Another coronal CT image shows multiple loops of very dilated small bowel proximal to pouch (Fig. 4). On axial CT imaging, you can see a markedly dilated small bowel immediately proximal to the pouch (Fig. 5). Another slice of the axial CT demonstrates a narrowed proximal pouch and dilated small bowel just proximal to the pouch (Fig. 6). The only other remarkable observation on CT is that the patient has pancreatic divisum. A Gastroview (diatrizoate meglumine and diatrizoate sodium solution) enema that was conducted 5 months previously showed similar problems with the small bowel and pouch (Fig. 7). However, a Gastroview enema that was performed 11 years earlier, before closure of the loop ileostomy, demonstrated a pouch that distends normally and a nondilated small bowel (Fig. 8).

### Dr. Miguel D. Regueiro (Gastroenterology, University of Pittsburgh)

To make a point, I'd like to note that this patient has an exceptionally dilated small bowel. When we scoped him, there was a stricture at the anal anastomosis but his pouch and the area above his pouch were massively dilated. His need to self-catheterize was a result of these issues.

### Dr. Benjamin H. Click (Gastroenterology Fellow, University of Pittsburgh)

The questions we have for the conference members are the following:

1. Does this patient's presentation represent pouch failure?
2. If you were this patient's clinician, what would you do now? Would you offer him a pouch takedown or go straight to end ileostomy?



FIGURE 3. A coronal CT from October 2015 demonstrates very dilated small bowel (arrow) immediately proximal to pouch. It is filled with fecal appearing material.

3. Could surgery remedy this patient's symptoms? If not, how would you treat his symptoms given that there is no active IBD on endoscopy?

### Dr. Miguel D. Regueiro (Gastroenterology, University of Pittsburgh)

I know this gentleman very well and I would like to stress just how anxious he has been over the years although he is showing improvement recently. When I told him that we thought that he had Crohn's disease in his pouch and that his initial diagnosis of ulcerative colitis was incorrect, he came close to having a nervous breakdown in my office.

### Dr. Corey A. Siegel (Gastroenterology, Dartmouth)

I think it's incredibly depressing to tell our patients who we've suddenly realized that they have Crohn's disease when they have carried a diagnosis of ulcerative colitis for many years. Other than in situations in which the diagnosis is absolutely clear-cut, I think that we should get away from that terminology and, instead, use terms such as indeterminate colitis or immune-mediated pouch disease. Otherwise, we create a situation that can be very upsetting for our patients as well as confusing for their medical providers. The only other thing that I think merits consideration in these patients is evaluating for pelvic floor dysfunction. Whether it's a mechanical issue or not, I believe that pelvic floor retraining can be of significant benefit. We had a case that was somewhat similar in that the





FIGURE 4. A second October 2015 coronal CT image demonstrates multiple loops of very dilated small bowel (arrows) proximal to pouch. They are filled with fecal appearing material.

patient had pouch dysfunction and pain and pelvic floor retraining made the problem much, much better. The 2 things that I would advise you to consider are anorectal manometry and pelvic floor retraining.

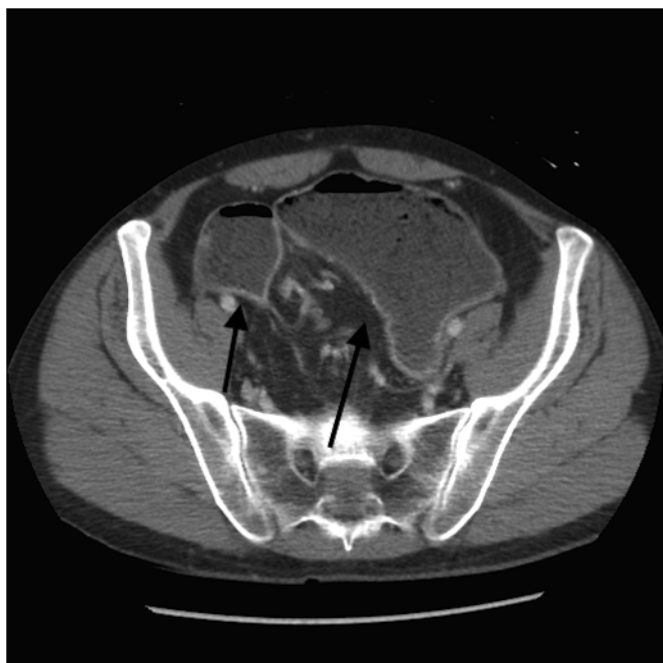


FIGURE 5. An axial CT image from October 2015 demonstrates very dilated small bowel (arrows) immediately proximal to pouch. It is filled with fecal appearing material.



FIGURE 6. Another October 2015 axial CT image demonstrates a narrowed proximal pouch with partially visualized staple lines (short arrow) and dilated small bowel just proximal to pouch (long arrow).

### Dr. Hans H. Herfarth (Gastroenterology, University of North Carolina)

It's a difficult case. I would not think about trying this patient on other medications, given the lack of inflammation or pathology on endoscopy or biopsy with his current regimen. My experience with evacuational pain in the anal area is that physical therapy to treat rectal dyssynergy might help. Also, I have 3 patients who have had their pain completely alleviated by taking alprazolam 3 times daily. Benzodiazepines might help with sphincter relaxation, thus reducing the anal pain. I realize that alprazolam may not be optimal therapy, but it certainly has helped them. However, this young man has been on a number of benzodiazepines and seems to have numerous complicating psychological issues, so I wouldn't expect such a thorough response.

### Dr. Miguel D. Regueiro (Gastroenterology, University of Pittsburgh)

I agree with what Corey is saying about these pouch patients who think they are cured. And to Hans' point, this patient has exhausted a number of IBD medications and has also been on the gamut of antidepressant and anti-anxiety agents. Why don't we get some other opinions? Joel, this is a young man although he is not pediatric age. From an anxiety and depression standpoint with what might be called pouch failure, how would you approach this patient?

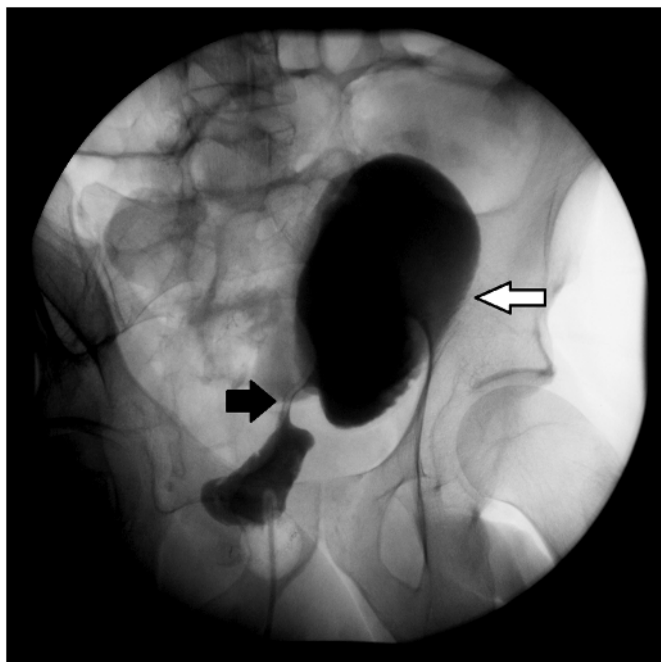


FIGURE 7. Gastroview enema of pouch 5 months earlier in May 2015 demonstrates a stricture at the proximal end of the pouch (solid black arrow) and a very dilated small bowel (white arrow) just proximal to the pouch.

### Dr. Joel R. Rosh (Pediatric Gastroenterology, Atlantic Healthcare)

The medical home advocates are hosting us today and what this young man needs is holistic care. Unlike a patient who has distinct mechanical issues, this patient is in the functional—psychosocial—realm. I don't think that the problem is solely anatomical, save for that stricture. On that point, I'm wondering about the anastomotic stricture and what role it played in those 17 admissions for partial small bowel obstructions versus how much was opioid-induced bowel disorder. You have a little bit of an anatomic issue there with the stricture as well as the chronic opioid use leading to a motility disorder with a massively dilated small bowel. My thoughts are that you have to take care of this patient in a biopsychosocial manner. The biology would be the anatomy and I'd recommend being very aggressive with that stricture. I'm not sure there's much left for him to do because self-catheterization seems to be becoming increasingly frustrating.

However, is there a surgical approach or an endoscopic approach that would be more helpful in dealing with the stricture? To what degree is this pelvic floor dysfunction? We see a lot of what Corey talked about in kids. You can imagine that young kids, especially, who are not very well toilet trained when they go to colectomy, have incredible pelvic floor dysfunction when we put them back together and we work very closely with our physical therapist to retrain them. I would figure the young man in this case could use the same type of retraining. And he needs

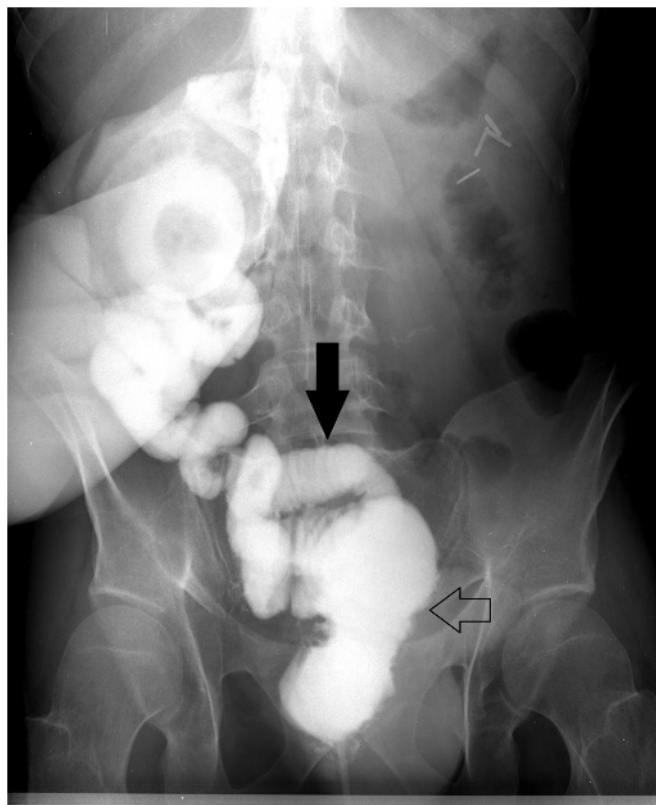


FIGURE 8. The patient underwent a Gastroview enema in 2004, before closure of the loop ileostomy. This image demonstrates a normally distending pouch (black arrow outline) and a nondilated small bowel just proximal to the pouch (solid black arrow).

you—he needs the medical home and he needs Eva to really work on the psychosocial issues. The one last comment that I have about the Crohn's disease was already stated perfectly by Corey. I think that we train our patients to think that ulcerative colitis is better than Crohn's disease, which is probably not always appropriate. So whatever term we use for their bowel disease, it's much less what we call it than how it goes and how we address it. I try to talk with patients in these terms rather than using disease classifications because when we change a patient's disease classification, their world just falls apart.

### Dr. Samir A. Shah (Gastroenterology, Rhode Island)

I agree with Dr. Rosh that this patient merits a biopsychosocial approach. One thing that should be considered, if it hasn't yet, is whether the patient might be taking nonsteroidal anti-inflammatory drugs for his pain since they could be contributing to his symptoms. If you are going to approach this patient from the biological realm, you have to address the stricture because it's certainly contributing to his issues. In the long run, I think that he is likely to do better with a takedown of the pouch and a permanent ileostomy.

**Dr. Miguel D. Regueiro (Gastroenterology, University of Pittsburgh)**

Dr. Walter Koltun at Hershey, from a surgeon's perspective, could you give us your opinion on whether you feel that there is hope of saving this pouch? Given that he is cathing himself 4 or 5 times a day, do you think that he is going to need an ostomy?

**Dr. Walter A. Koltun (Colon and Rectal Surgery, Penn State Hershey)**

From a surgeon's perspective, we would be doing some other studies. We would do a gastrografen enema rather than just a simple CT scan to see exactly where the stricturing issue is. We frequently see dilated loops of small bowel upstream of a pouch. These are not uncommon and patients often evacuate these quite effectively. On the other hand, there are some patients who have diminished peristalsis in that distended bowel and have some problems with evacuation.

I would also remind people that early in the course of the history of the pouch we used to have efferent limbs to the pouch. The reservoir would be about 4 to 6 cm upstream to the efferent component of the small bowel that would then be anastomosed to the anus and patients would self-catheterize in order to defecate. That's what you would do in the old days with the Kock pouch—the continent ileostomy. My personal opinion is that this patient is going to be suicidal if you give him a stoma. By comparison, self-catheterizing is fairly benign. Getting back to the studies, I would also do a defacogram. In a defacogram, you put paste in a patient's pouch or rectum, and they sit on a radiolucent toilet and defecate so that you can see if they have difficulty with dyssynergy of their pelvic floor. It is unclear to me whether this patient has dysmotility, whether he has a mechanical obstruction or whether he has pelvic floor outlet dysfunction—a dyssynergy of the pelvic floor. Those 3 broad categories have not been definitively evaluated so I would do more studies to try to figure out which category he falls into. At the end of the day, inserting a tube in order to defecate isn't all that bad, although you would have to convince him of that.

**Dr. Miguel D. Regueiro (Gastroenterology, University of Pittsburgh)**

To continue with this patient's story, he reached a point where he was so miserable with the pouch that he was actually asking to have it taken down. We did perform a number of the studies that Walter mentioned, and we discovered that the patient could not evacuate. In essence, his pouch had become a "bag" with no motility. On top of that, he had the tight anal stricture. So we got Dr. Szigethy involved because the patient's psychological state had some intense impact on all of these issues.

**Dr. Eva Szigethy (Psychiatry, University of Pittsburgh)**

We started treating this patient with more traditional CBT that can be helpful for pain and motility, focusing on his negative cognitions, such as anxiety and despair, and getting him

behaviorally active. However, his anxiety and his fear of not being near a place to self-catheterize were so great that he began to have life shutdown—avoiding activities and social interactions with increased preoccupation with his gastrointestinal distress. So we introduced him to hypnosis, a technique that takes advantage of the human mind's ability to dissociate to block out painful and anxious signals with diverted attention to pleasant thoughts and behaviors. The trance state allows the brain to be more receptive to healing suggestions. We started with gut-focused hypnosis, an empirically supported intervention shown to be helpful in patients with irritable bowel syndrome. This intervention consisted of teaching him relaxation techniques and weaving in some biofeedback so that more positive emotions and thoughts would be linked to physiological changes in the body. Our goal was to have him develop a different emotional relationship to his somatic symptoms. However, these techniques did not improve his gastrointestinal distress or emotional-cognitive state much. In terms of psychotropic medications, he had failed several different classes of antidepressants with minimal improvement in depression, anxiety, or his chronic pain.

Therefore, I started a course of what we refer to as "trauma-focused" hypnosis, a technique that explores how past traumatic and emotionally painful experiences can influence current psychological and physical distresses. In getting to know him, he discussed a chronic history of being bullied as a child, of not being accepted in his family, and of being fearful of failure. Although we never talked about the specifics of any harrowing events that he had experienced, we had a trusting enough relationship that he allowed us to do age regression work under hypnosis. This technique involves getting to the source of the trauma when the patient is in a deep trance and an altered state of mind, allowing him to disconnect emotional pain and physical pain. We have done many hours of hypnosis at an intensity of 1 hour per week to help him feel competent in obtaining a deep relaxed trance, strengthen his ego, and uncover the early origins of his extreme psychological and physical distress.

What he did with this work, once he remembered that something traumatic had happened when he was 8, was that he was able to recall having a lengthy and pervasive history of abdominal pain that was very tightly linked to the stress that was caused by traumatization. With hypnosis, we also uncovered that the self-catheterization was a way in which he was psychically punishing himself for feelings of chronic failure. Again, there were a lot of indicators that the trauma that he had experienced had caused him to mix up emotional pain and physical pain. During hypnosis, he was taught ways to ameliorate the emotional pain that he encountered during his youth. On the following video, the patient was very happy to talk about what hypnosis had helped him to achieve.

**The Patient**

The hypnosis has been an amazing experience. It has helped me become a better human being, a better person, and a better husband. It has helped my illness to the point where I

have the courage and confidence to do things, when before I didn't. It has definitely been a necessary part of treatment for someone like me with IBD to evolve the mind-body connection. It has allowed me to become who I really am and, for the first time in my life, I am truly free of pain. Medications always stop working, but this is mine and no one can take it away.

### Dr. Miguel D. Regueiro (Gastroenterology, University of Pittsburgh)

I'm sure that this seems like a very nontraditional form of treatment to many of you, but this patient has been helped exponentially by the work that he has done with Dr. Szigethy. In November of 2015, the patient had his pouch taken down. He required ketamine and patient-controlled hydromorphone for pain and was sent home on oxycodone. Currently, he is off of all opioid pain medications and coping with pain and his ostomy extremely well. He continues to receive maintenance therapy from Dr. Szigethy. We plan to do an ileoscopy at 1 year post-surgically to decide on whether or not he has any ileal Crohn's disease that would warrant treatment. It is amazing to see that he is highly functional with a permanent ileostomy. If we did not address the psychosocial aspects of his IBD, we would never have gotten to this point. Dr. Click has an excellent slide showing the timeline from 2000 to 2016 that maps the patient's depression, level of functioning, and the various interventions that were used to help him (Fig. 9).

### Dr. David G. Binion (Gastroenterology, University of Pittsburgh)

I wanted to make a comment about the radiographic studies. We saw a significantly dilated segment of bowel coming

from the pouch up through the distal ileum to the loop ileostomy closure site. We've seen this type of a functional problem in several patients. We actually have a suspicion, based on studies that we've done with animal models, that there is an impaired motility with the typical stapled side-to-side loop ileostomy closure, which has an antiperistaltic orientation. This type of loop ileostomy closure transects circular muscles in addition to its antiperistaltic, side-to-side orientation of bowel, which leads to stasis and the accumulation of bowel contents and gas in this segment. The resulting distention contributes to pain, as the sensory nerves that appreciate stretch are intact in this dilated segment of bowel. In addition to the dilation and stretch related pain, the stasis will contribute to bacterial overgrowth in the segment with diminished motility. If we remember that the J pouch ileoanal reconstruction is deliberately created to interrupt motility and to create a reservoir for stool, functioning as a replacement colon, the loop ileostomy closure site, which uses an identical surgical configuration, can also have stasis. Dilated ileoanal pouches in the absence of stricture are often the result of the surgical reconstruction that has deliberately affected the transmission of peristaltic complexes through the distal bowel. Once these dilated ileoanal pouches and intestinal segments below the loop ileostomy closure form, these patients are likely to require end ileostomy to allow for fecal drainage, preventing recurrent partial small bowel obstruction, and to reduce chronic abdominal pain.

### Dr. Leonard Baidoo (Gastroenterology, Northwestern)

At Northwestern, I've been attempting to address potential psychosocial issues in IBD patients. The first time I see a patient, I

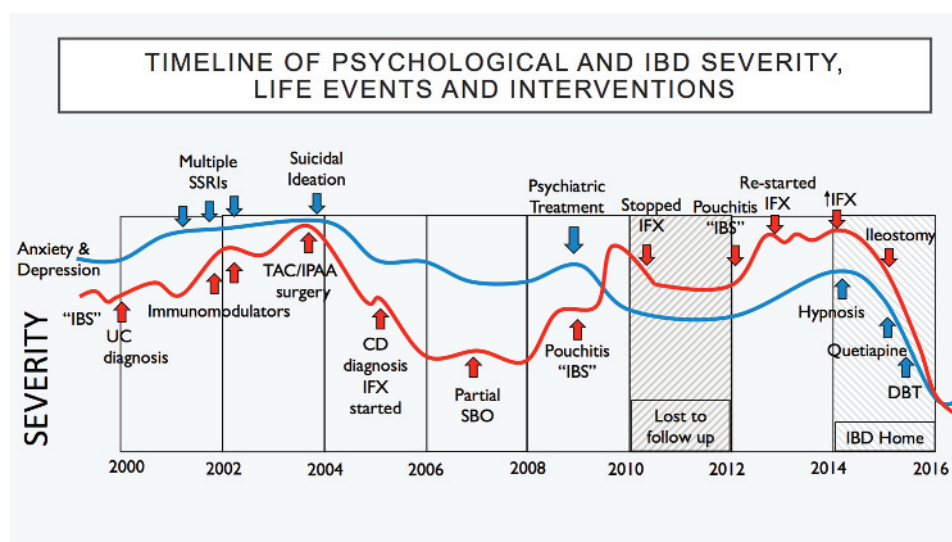


FIGURE 9. A timeline demonstrating the patient's level of psychosomatic depression, overall functioning, and various psychological and IBD-related events and interventions. The x-axis shows chronological progression from 2000 to 2016 while severity is on the y-axis. The blue line demonstrates psychological symptoms and interventions, whereas the red line chronicles bowel-related diagnoses, events, and treatments, including surgery. Abbreviations: IBS, irritable bowel syndrome; UC, ulcerative colitis; SSRIs, selective serotonin reuptake inhibitors; TAC/IPAA, total abdominal colectomy/ileal pouch-anal anastomosis; CD, Crohn's disease; IFX, infliximab; SBO, small bowel obstruction; DBT, dialectical behavioral therapy/core mindfulness.



will meet with the patient with a behavioral specialist so that we can identify higher risk patients earlier in the process. The goal is to make sure that our IBD patients never develop severe psychological issues or reach the stage in which they are suicidal. If the patient does not need to continue to see a behavioral specialist regularly, that is fine. However, from the outset, we're trying to identify patients who may have psychological problems and manage them in a more comprehensive manner. I agree with everything else that is been said about this patient. I believe that this patient has pelvic floor dysfunction.

## DISCUSSION

Psychological conditions such as anxiety, depression, and chronic pain syndromes, are frequent comorbidities among individuals with gastrointestinal disorders. An intricate 2-way system of communication exists between the gut and brain known as the brain–gut axis.<sup>1</sup> The brain–gut axis has been implicated in conditions characterized by chronic abdominal pain, such as irritable bowel syndrome (IBS) and IBD.<sup>2</sup> Chronic psychological stress has been correlated to abdominal pain and alterations in the intestinal barrier function that may be caused by aberrant functioning of the hypothalamic–pituitary–adrenal axis. On a cellular level, the glucocorticoid receptor can activate or suppress gene expression, with regulatory variation being associated with stress-related disorders in both gastroenterology and psychiatry.<sup>3</sup> Childhood trauma and depression also have a biological basis that is associated with the hypothalamic–pituitary–adrenal axis. For example, epigenetic changes in the glucocorticoid receptor gene (NR3C1) in the setting of stress from early life trauma are recognized as being a risk factor for depression that presents later in life.<sup>4</sup>

Pain and other symptoms of functional gastrointestinal disorders are prevalent among patients with IBD and have been associated with mood disorders and increased health care utilization.<sup>5,6</sup> Clinically significant depression and anxiety are mood disorders that are often observed in patients with IBD.<sup>6–13</sup> While pain seems to be more common during active IBD, it may also occur in the absence of signs of inflammation and has been demonstrated among patients of all ages.<sup>14,15</sup>

For example, in a study that included 149 patients with IBD (44 ulcerative colitis and 105 Crohn's disease) who reported inactive IBD during the previous 12 months, 27.3% of the patients with ulcerative colitis and 31.3% of patients with Crohn's disease met the criteria for major depression.<sup>16</sup> When these disorders do occur in patients with quiescent IBD, they may be related to changes in gut motility, visceral hypersensitivity, or psychological dysfunction. Mood disorders can have a significant impact on a patient's overall quality of life.

In a Canadian gender-, age-, and region-matched case–control study that included 388 patients, individuals with IBD were more than 3 times as likely to report poorer health although close to half of the non-IBD group indicated having chronic health conditions.<sup>17</sup> In this study, patients with IBD

who were not in remission demonstrated lower psychological well-being and higher rates of distress than controls. In the results from a recent systematic review of 171 articles that included a total of 158,371 adults with IBD, patients with IBD demonstrated an approximate 20% prevalence rate of anxiety and a 15% prevalence rate of depression.<sup>11</sup> There is a bi-directional relationship between IBD and psychological comorbidity. When they coexist, each may affect the course of the other.<sup>7</sup> Progression of disease and recurrence may be worse in depressed patients.<sup>18</sup> In the Swiss IBD study of 2007 adults with IBD, a significant association was found between depressive symptoms and clinical recurrence of IBD over time.<sup>10</sup> Preexisting psychiatric conditions may also worsen after a diagnosis of IBD.<sup>19</sup>

Severe chronic pain is often treated with opiate painkillers. Approximately 25% of outpatients with IBD are taking opioid medications on a regular basis.<sup>20,21</sup> In addition to pain, narcotic use in patients with IBD has been associated with previous surgeries, anxiety, depression, substance abuse, clinical disease activity, and a history of sexual, emotional, or physical abuse.<sup>20</sup> However, the effectiveness of opiates for IBD has never been substantiated, and they carry myriad health risks, including worsened pain caused by opioid-induced sensitization of the central nervous system (narcotic bowel syndrome) as well as opioid-induced constipation, infections, and even death.<sup>20–22</sup> The patient described in this case had frequent partial small bowel obstructions (SBOs) and typically left the hospital on opiate painkillers, which may have been a major contributor to his symptomatology. Gastrointestinal motor effects of opioids are complex and hinge on whether the particular medication predominantly interrupts excitatory or inhibitory neural pathways, resulting in more prevalent muscle relaxation or spasm, respectively.<sup>23</sup> Treatment with medications such as low-dose tricyclic antidepressants improves pain without the dangers of narcotics.<sup>24,25</sup> Chronic pain in IBD is best addressed using an interdisciplinary team approach that embraces a trusting, extended doctor–patient relationship.<sup>26</sup>

Treatment has been shown to improve patient outcomes in gastrointestinal disorders that can be exacerbated by stress or emotional symptoms.<sup>27</sup> As evidence, functional bowel disorders and chronic pelvic pain are disorders not associated with an organic cause with significant overlap; approximately 35% of patients with chronic pelvic pain have shown significant improvement when treated for functional bowel disorders.<sup>28</sup> Disorders of defecation can be treated effectively with biofeedback.<sup>29,30</sup> Psychological interventions such as hypnosis, CBT, and mindfulness techniques have demonstrated promise for pain management in IBD.<sup>27,31</sup> A recent meta-analysis of 8 randomized controlled trials including 464 patients and a median of 8.5 (7–12) hypnosis sessions demonstrated that hypnosis provided long-term adequate symptom relief in 54% of patients with irritable bowel syndrome refractory to conventional therapy.<sup>32</sup> In general, studies of hypnotherapy in IBD have been smaller but their results show a clear benefit to this treatment. In a study of 15 patients with IBD with severe, medically refractory disease who were on steroids, preanalysis and postanalysis of patient symptoms and well-being were



conducted after 12 sessions of hypnotherapy.<sup>33</sup> Patients were followed for an average period of 5.4 years, with 13 patients demonstrating diminished disease activity (remission in 27% and mild activity in 53%) and 60% of all patients stopping all steroid use. For patients who do not respond to more traditional CBT or hypnosis, approaches focusing on the hypnotic resolution of trauma and associated pain can be helpful.<sup>34,35</sup> The hypnotic technique known as somatic-affective bridge was used for the patient described in our case to increase awareness of bodily sensations to facilitate awareness of unexpressed emotions.<sup>36</sup> These latter approaches are supported by clinical expert opinions and case series but require larger controlled trials for validation.<sup>37,38</sup>

Surgical resection for IBD can incur negative emotions. Surgery may result in distress because of feelings of loss of control, changes in body image, possible need for ostomy, and the potential for complications.<sup>39</sup> Recovery from surgery might also be hampered by psychological factors such as coping with an ostomy or adjusting to drastically altered bowel habits. Late complications of restorative proctocolectomy and IPAA include leaks, strictures, pouchitis, SBO, and fistula formation.<sup>40–42</sup> In a study conducted at Vanderbilt University, close to half of patients undergoing IPAA had recurrent SBO after surgery.<sup>43</sup> A small portion of patients who undergo restorative proctocolectomy will demonstrate Crohn's disease or Crohn's-like changes in the pouch, which has been associated with a greater risk of pouch failure that requires additional surgery.<sup>44</sup> A study of 1965 patients who had proctocolectomy at a single center between 1983 and 2001 noted a rate of pouch failure of 4.1% with independent risk factors including a diagnosis of Crohn's disease, patient comorbidity, diminished anal sphincter manometry measurements, previous anal pathology, anastomotic stricture, anastomotic separation, sepsis, and perineal fistula formation.<sup>45</sup>

## EDITOR'S COMMENT

Addressing psychological concerns in patients with IBD is now recognized as an important step in disease management.<sup>9,46</sup> Some patients will not need ongoing psychological or psychiatric treatment. Others, such as the patient described in this session, may require intensive therapy to achieve emotional wellness to make informed and appropriate medical and surgical decisions regarding his IBD. Although gastroenterologists may be prepared to provide support and encouragement regarding a patient's bowel disease, they lack the time and training necessary to provide comprehensive psychological care. Patients should be referred to social workers, psychologists, or psychiatrists depending on the depth of their needs and the resources available. Patients at higher risk for developing or having progression of psychological problems may include children with multiple first-degree relatives with mood disorders, individuals with a lengthy history of medication-refractory psychiatric illness, people with worsening anxiety and depression in stressful situations, and individuals with a more severe IBD course that requires frequent step-up therapy or

surgery. As we enter a new era of patient-centered health care, treating the "brain" is as important as the "gut" for comprehensive, whole-person IBD management.

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## CME-MOC EXAM—235

## “IBD LIVE Series—Case 7: The Brain-Gut Connection and the Importance of Integrated Care in IBD”

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## LEARNING OBJECTIVES

After completing this IBD LIVE-CME activity, physicians should be better able to

1. Explain the meaning of the “brain-gut axis” and recognize its important physiologic relationships.
  2. Identify the psychological issues that are most prevalent among patients with inflammatory bowel disease (IBD).
  3. Explain which types of health care providers are best suited for working with patients with IBD who have mental health needs.
  4. Describe treatments that have been shown to be effective for mood disorders in patients with IBD.
  5. Describe how pain impacts patients with IBD.
  6. Describe the potential emotional impact of surgery on patients with IBD.
  7. List common late complications of restorative proctocolectomy and ileal pouch-anal anastomosis (IPAA) surgery.
1. Which of the following choices regarding mood disorders among patients with IBD is true?
    - (a) Anxiety and depression are less common conditions among patients with IBD than among the general population.
    - (b) Anxiety, but not depression, is a frequent comorbid psychological problem in patients with IBD.
    - (c) Depression in patients with IBD is typically transient and can be treated by a gastroenterologist.
    - (d) Depression in patients with IBD may influence disease progression and relapse.

**Please see the following references for further study:**

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2. Opiate painkillers are frequently prescribed to treat moderate to severe pain experienced by patients with IBD. Which of the following statements regarding opiate painkiller use in IBD is true?
- (a) A large body of evidence has demonstrated that opiates can provide effective long-term pain relief in patients with IBD.
  - (b) Patients are usually started on a larger dose of opiate painkillers and then titrated to a smaller, standard dose.
  - (c) Long-term use of opiates carries numerous risks with few advantages over other medicines that may be used for pain in IBD.
  - (d) Narcotic bowel syndrome is a term used to describe opioid-induced sensitization of the peripheral nervous system that causes chronic diarrhea.

**Please see the following references for further study:**

- 1. Hanson KA, Loftus EV Jr, Harmsen WS, et al. Clinical features and outcome of patients with inflammatory bowel disease who use narcotics: a case-control study. *Inflamm Bowel Dis*. 2009;15:772–777.
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3. Which of the following tests is the least effective in evaluating disorders of defecation?
- (a) CT
  - (b) Defacography/defacogram
  - (c) Anorectal manometry
  - (d) Gastrografin enema

**Please see the following references for further study:**

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4. Your 22-year-old patient with Crohn's disease has a psychological issue that you feel may be affecting her bowel disease and her overall health. Which of the following treatments is most likely to be used as first-line therapy by a behavioral health specialist for this patient?
- (a) Electroconvulsive therapy
  - (b) Medical therapy with a benzodiazepine and an opiate painkiller
  - (c) CBT
  - (d) Psychoanalysis

**Please see the following references for further study:**

- 1. Palsson OS, Whitehead WE. Psychological treatments in functional gastrointestinal disorders: a primer for the gastroenterologist. *Clin Gastroenterol Hepatol*. 2013;11:208–216; quiz e22–3.
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- 4. Schoultz M, Atherton I, Watson A. Mindfulness-based cognitive therapy for inflammatory bowel disease patients: findings from an exploratory pilot randomized controlled trial. *Trials*. 2015;16:379.

5. Both early and late complications after restorative proctocolectomy and IPAA have been observed. Which of the following is not commonly recognized as a late postsurgical complication?
- (a) Pouchitis
  - (b) Fungal infection

- (c) Small bowel obstruction
- (d) Fistula formation

**Please see the following references for further study:**

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  3. Ryoo SB, Oh HK, Han EC, et al. Complications after ileal pouch-anal anastomosis in Korean patients with ulcerative colitis. *World J Gastroenterol.* 2014;20:7488–7496.
  4. Jacobson T. Stricture and pouchitis after ileal pouch-anal anastomosis. *J Wound Ostomy Continence Nurs.* 1997;24:295–301.
6. In the single-center study of 1965 patients who underwent proctocolectomy, which of the following factors was associated with pouch failure?
- (a) A diagnosis of ulcerative colitis
  - (b) Increased anal sphincter manometry measurement
  - (c) Anastomotic strictures
  - (d) A lack of previous anal pathology

**Please see the following references for further study:**

1. Fazio VW, Tekkis PP, Remzi F, et al. Quantification of risk for pouch failure after ileal pouch-anal anastomosis surgery. *Ann Surg.* 2003;238:605–14; discussion 614–617.
  2. Ryoo SB, Oh HK, Han EC, et al. Complications after ileal pouch-anal anastomosis in Korean patients with ulcerative colitis. *World J Gastroenterol.* 2014;20:7488–7496.
7. Your patient is a 22-year-old man with Crohn's disease and a history of generalized anxiety disorder and panic attacks. You decide to refer him to someone to help with his anxiety. You might refer this patient to any of the following individuals except for:
- (a) A neurologist
  - (b) A psychologist
  - (c) A psychiatrist
  - (d) A social worker

**Please see the following references for further study:**

1. Regueiro MD, McAnallen SE, Greer JB, Perkins SE, Ramalingam S, Szigethy E. The inflammatory bowel disease specialty medical home: a new model of patient-centered care. *Inflamm Bowel Dis.* 2016;22:1971–1980.
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8. Which statement concerning pain in IBD is true?
- (a) Pain occurs almost exclusively during active IBD flares.
  - (b) The brain-gut axis plays a minor role in chronic abdominal pain.
  - (c) Pain among patients with IBD has been associated with decreased health care utilization.
  - (d) Chronic psychological stress has been correlated to abdominal pain and altered intestinal barrier function

**Please see the following references for further study:**

1. Farrokhyar F, Marshall JK, Easterbrook B, et al. Functional gastrointestinal disorders and mood disorders in patients with inactive inflammatory bowel disease: prevalence and impact on health. *Inflamm Bowel Dis.* 2006;12:38–46.
2. Srinath AI, Walter C, Newara MC, et al. Pain management in patients with inflammatory bowel disease: insights for the clinician. *Therap Adv Gastroenterol.* 2012;5:339–357.
3. Mayer EA, Tillisch K. The brain-gut axis in abdominal pain syndromes. *Annu Rev Med.* 2011;62:381–396.

9. Which of the following choices has shown significant symptom improvement following biofeedback?
- (a) Fistula
  - (b) Dyssynergic defecation
  - (c) Bowel stricture
  - (d) Small bowel obstruction

**Please see the following references for further study:**

1. Enck P. Biofeedback training in disordered defecation. A critical review. *Dig Dis Sci*. 1993;38:1953–1960.
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