



## An Update on Inflammatory Bowel Disease



**Charles N. Bernstein, MD**

Presented at the University of Manitoba's College of Family Physicians of Manitoba Annual Update on Gastroenterology Lecture, May, 2008.

Inflammatory bowel disease (IBD) includes Crohn's disease, a chronic inflammatory disease affecting the GI tract from the mouth to the anus but most typically occurs in the distal ileum and/or the colon. This disease is transmural and often focal. It can be associated with granulomas histologically in approximately 50% of cases and can be associated with intestinal stricture and fistula development. Fistulas occur in up to 25% of patients and are often among the most disabling of intestinal complications. Perianal fistula development is an important and sometimes difficult to manage complication of Crohn's disease. The peak age of presentation is the third decade of life but it can present at any age.

Ulcerative colitis (UC) is a chronic inflammatory disease confined to the superficial layer (the mucosa) of the colon. It can also present at any age with no single peak decade of onset. These diseases tend to present with similar symptoms and signs. They may be associated with similar extraintestinal complications (such as inflammatory diseases of the joints, eye and liver) and may be treated with similar pharmacological approaches. Both diseases are associated with an increased risk for colon cancer. Canada has among the highest incidence rates for both Crohn's disease and UC in the world. Approximately 0.6% or about one in every 160 Canadians has a form of IBD.

### ► *How do we diagnose IBD?*


The history is important because the typical GI complaints of diarrhea (including bloody diarrhea), abdominal pain, weight loss, nausea and occasionally vomiting may be associated with either disease. These types of complaints lead to a series of blood tests, stool tests and ultimately imaging tests.

In pediatrics, it is important to consider that patients may present primarily with growth failure or even arthritis. Rarely, adults may present with obscure blood loss. In the setting of ulcerative proctitis, patients may present with constipation rather than diarrhea. However, the majority of patients present with typical overt GI symptoms and for Crohn's disease, abdominal pain is usually a primary symptom whereas in UC it is bloody diarrhea.

### *Other important diagnoses to consider*

While IBD affects approximately one in every 160 to 200 Canadians, irritable bowel syndrome (IBS) may affect one in every seven Canadians. Diarrhea-predominant IBS is a condition where often clinicians consider ruling out IBD.

Generally, patients present with IBS at a young age, much like in IBD, but more often by the time they present to a physician they have had symptoms (often intermittent) for years. Furthermore, these



patients are typically robust without weight loss or anemia and it is unusual for them to have symptoms that awaken them from sleep. Sleep disorders, anxiety and depression are all conditions that may coexist with either IBD or IBS so their presence does not provide diagnostic clues. Celiac disease more typically presents these days as iron deficiency anemia than with overt malabsorption. The serological antibody test for celiac disease has got such high positive and negative predictive value to make it one of the best diagnostic blood tests in medicine. Physicians should have a low threshold to order a celiac antibody screen (a tissue transglutaminase antibody in most labs) on patients who present with GI symptoms.

*While IBD affects approximately one in every 160 to 200 Canadians, IBS may affect one in every seven Canadians.*

Finally, for patients with blood in their stool, colorectal cancer is an important consideration in patients > 40-years-old. In fact, whether or not patients have typical IBD symptoms, if they are > 40-years-old and have blood in their stool, a colonoscopy is indicated.

### *Diagnostic testing*

All patients who present with new onset diarrhea should undergo stool testing for bacterial culture and for *Clostridium difficile* toxin (even if there is no antecedent history of antibiotic use as the presence of this infection in the absence of antibiotics is increasing). If living in an endemic area or if having travelled to one, ova and parasite testing should be undertaken. Routine blood testing should include a complete blood count, serum albumin, serum ferritin and a C-reactive protein (CRP). A

normal CRP does not rule out IBD but an elevated CRP should encourage the physician to investigate further if other bloodwork is normal or negative.

Furthermore, if a patient has borderline indications for imaging investigations, a serum anti-*Saccharomyces cerevisiae* antibodies (ASCA) could be measured as this test has a high specificity for Crohn's disease and a positive result should encourage further pursuit of this diagnosis. Once it is decided that further imaging is required, the hallmark and most important baseline test will be a colonoscopy. This will assess the whole colon and facilitate biopsies so that UC or Crohn's disease (affecting the colon) can be determined and if the colonoscopy is normal, biopsies can be taken to assess for microscopic colitis, a condition associated with abdominal cramps and diarrhea (but not bleeding). Furthermore, the terminal ileum can be intubated to determine if ileal Crohn's disease is present.

In the past, FPs have often ordered small bowel barium x-rays (either follow through tests or small bowel enemas), or barium enemas. While these tests are still accessible to FPs they lack sensitivity (particularly the small bowel barium studies) and combined with associated radiation, a preferred approach to small bowel imaging would be MRI. Since ionizing radiation has increased cumulative effects in those < 35-years-of-age than in older patients MRI is preferable since it is a technique that can be safely repeated.

CT also provides excellent cross-sectional imaging and helps assess for abscesses and fistulas, but it is associated with higher doses of radiation than conventional barium imaging. Transabdominal ultrasound is a safe, less expensive, non-invasive imaging technique widely used to assess the small bowel in Europe but much less used in IBD diagnostics in North America. Video capsule endoscopy has provided an excellent opportunity to image the small bowel and diagnose Crohn's disease in selected cases where ileo-colonoscopy and other conventional imaging techniques have failed to clinch the diagnosis.

### ► *What are the treatments?*

For patients with a diagnosis of colitis that is highly suspected but not yet clinched, it is safe to prescribe 5-aminosalicylate (5-ASA) therapy. These agents are safe and not harmful in the setting of infectious colitis and beneficial in UC and also likely in Crohn's colitis. Typically, 2 gm to 2.4 gm q.d. can be prescribed with similar efficacy as higher doses and the pills can be given as once a day therapy to enhance adherence. There are several choices of oral 5-ASA available in Canada and they are all similarly effective.

If a patient has known small bowel disease or colitis (that is imaging studies have been reported as being suggestive for Crohn's disease or UC) and infection has been ruled out and patients are moderately to severely unwell (considerable abdominal pain or diarrhea, waking from sleep, missing work or school, or marked changes in blood work), then a limited course of corticosteroids can be prescribed. Typically, prednisone at 40 mg p.o. q.d. for two weeks is prescribed with tapering thereafter by 5 mg every week. Patients who start on prednisone should be encouraged to use calcium 1,000 mg and vitamin D 1,000 IU q.d. while on prednisone and if they have low intake of dairy in their diet even if not on corticosteroids. When a segmental enterocolitis is evident in First Nations or immigrant populations, where IBD is uncommon and TB is a risk, this latter diagnosis needs to be ruled out before steroids are prescribed.

If patients start on corticosteroids then a secondary plan needs to be considered for those patients who do not respond, become corticosteroid resistant or dependent, or who flare soon after having completed their corticosteroid withdrawal. Furthermore, for both Crohn's disease and UC, therapy to maintain remission needs to be considered as well. If the patient has had mild colonic disease 5-ASA may suffice, however, if Crohn's disease is present proximal to the colon or if in UC the patient has declared himself as having failed 5-ASA maintenance therapy, then an

immunosuppressive agent needs to be considered. Typically, for either disease, azathioprine or its metabolite 6-mercaptopurine is used. In Crohn's disease, there is evidence that methotrexate can also be successful as a disease remittive agent.

In the past decade anti-TNF- $\alpha$  therapy has become available to treat both Crohn's disease and UC. As a rough rule of thumb two-thirds of patients will respond to these agents and approximately half of responders will achieve a remission. For all patients who start anti-TNF- $\alpha$  therapy, approximately 60% remain on these agents at one year so there still remains a sizable population who either do not respond or who lose response or become intolerant to the drugs.

*Whether or not patients have typical IBD symptoms, if they are > 40-years-old and have blood in their stool, a colonoscopy is indicated.*

Currently, IV infliximab is available in Canada to treat both Crohn's disease and UC (administered as 5 mg/kg at zero, two and six weeks and then every eight weeks thereafter) and adalimumab is available to treat Crohn's disease which is used subcutaneously (administered at 160 mg at baseline, 80 mg at two weeks and 40 mg every two weeks thereafter).

All corticosteroids, immunosuppressive therapy and anti-TNF- $\alpha$  agents carry important side-effect profiles. With all, there are concerns for infections and with anti-TNF- $\alpha$  agents there have been heightened concerns about cancer risk (particularly lymphoma). However, cancer risk seems to be low even for these agents and in the majority, the benefit seems to far outweigh the risks. In the past few years, there has been a heightened interest in

recommending immunosuppressive and anti-TNF- $\alpha$  therapy much earlier into disease course to limit corticosteroid related complications as well as disease complications such as development of strictures and fistulas in Crohn's disease and the need for surgery in either disease. For both diseases, when patients are sufficiently ill or have failed to achieve remission with medical therapy, surgical therapy is an option. Some patients with Crohn's disease get prolonged remissions after bowel resections. In UC, many patients do very well after total procto-colectomies with ileoanal pouch anastomosis.

### *Important tips to remember*

All patients with IBD should take a multivitamin. Serum ferritin should be checked regularly and iron replaced when indicated. As oral iron is often not well tolerated, physicians should have a low threshold to administer parenteral iron. Ensuring patients are remaining nutritionally replete is important and if patients are malnourished or have an active disease they should be encouraged to use nutritional supplements. Vitamin D should be routinely advised as many Canadians, even in the absence of intestinal disease, are deficient simply on the basis of low dietary intake and limited sun exposure.

IBD patients are at risk for osteoporosis and if they have recurrently used corticosteroids or are post-menopausal (or amenorrheic young women) this needs to be considered, including timing of dual energy x-ray absorptiometry. Once patients have a known diagnosis and in particular if it is UC, they often become adept at altering the dose of oral 5-ASA and rectal 5-ASA (enema or suppositories) on their own.



**Dr. Bernstein** is a Professor of Medicine; Head, Section of Gastroenterology; Director, IBD Clinical and Research Centre, University of Manitoba; and Bingham Chair, Gastroenterology, Winnipeg, Manitoba.

## Take-home message

1. Bloody diarrhea is a hallmark of Ulcerative colitis and patients who present with this complaint will require a colonoscopy as an important early diagnostic approach
2. Patients with Crohn's disease present primarily with abdominal pain and diarrhea. Colonoscopy with ileal intubation is an important diagnostic approach but when Crohn's disease is considered, small bowel imaging, particularly with MRI, which is not associated with radiation, is also indicated
3. 5-ASA therapy is a mainstay of mild to moderate UC and can be used in Crohn's colitis. It will have no effect on small bowel or fistulizing Crohn's disease. Steroids are rapid acting therapy in moderate to severely active UC or Crohn's disease. When they are started the clinician needs to be considering what the plan will be to implement disease remittive therapy. Often for either UC or Crohn's disease azathioprine or 6-mercaptopurine is chosen. For patients who become steroid dependent or resistant or fail purine analogs anti-TNF- $\alpha$  therapy can be effective
4. Surgery can be very effective short-term therapy and for many provide long-term relief in Crohn's disease. In UC a total proctocolectomy with ileoanal pouch anastomosis can facilitate drug withdrawal and a very good quality of life

However, they should be discouraged from initiating high dose prednisone on their own and if patients are requiring repeat prednisone courses then they are requiring some other immunomodulatory maintenance therapy. When patients are started on immunosuppressive or anti-TNF- $\alpha$  therapy it is for the long-term in most instances. Patients often ask if it is forever and at present the best approach is to consider it indefinite (until empiric evidence shows the way for a better approach).

**cme**

For references, please contact [cme@sta.ca](mailto:cme@sta.ca)