

Investigating IBD



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The chronic bowel diseases, ulcerative colitis and Crohn's disease, are grouped collectively under the term inflammatory bowel disease (IBD). They are both diseases of the gastrointestinal tract, but are quite different in many aspects, including sites of disease, symptomatology, pathophysiology and response to therapy (Table 1).

Treatment goals in both ulcerative colitis and Crohn's disease should include induction of remission, maintenance of remission, improvement of quality of life and minimization of treatment-related side-effects.

How is a patient with suspected IBD evaluated?

If one suspects a diagnosis of IBD, a thorough history can reveal important clues regarding the diagnosis. Both ulcerative colitis and Crohn's disease can present with diarrhea. However, ulcerative colitis usually presents with bloody diarrhea (often with the passage of just blood and mucous due to rectal inflammation) and other hallmarks of rectal inflammation, such as urgency and tenesmus. With colonic involvement the diarrhea is often frequent and of small volumes.

Patients with Crohn's disease often experience right lower quadrant pain because of inflammation of the ileum (present in 70% of patients).

The presence of perianal disease (fissures, fistulas or abscesses) are more common in Crohn's disease.

A family history is found in approximately 10% to 20% of patients with IBD and, therefore, increases suspicion.

Certain epidemiologic risk factors are also important to consider. Smoking has a protective effect in ulcerative colitis. Twenty per cent of newly diagnosed ulcerative colitis patients are recent ex-smokers. On the contrary, smoking appears to be detrimental in Crohn's disease.

Marie's Misery

Marie, 22, presents with a three-month history of:

- intermittent right lower quadrant pain,
- non-bloody diarrhea four to six times per day,
- five-pound weight loss,
- intermittent joint aches in the knees, wrists and hands and
- fatigue.



Her symptoms started shortly after she returned from a vacation in Mexico. She thought she had caught a "bug," but became increasingly concerned when her symptoms became more progressive and she began losing weight.

She was prescribed an empiric course of metronidazole for 10 days, but there has been no improvement.

For more on Marie, see page 71.

Table 1

Differences between ulcerative colitis and Crohn's disease

Significant factors	Ulcerative colitis	Crohn's disease
Anatomical location	Rectum/colon	Any part of gastrointestinal tract
Distribution	Diffuse	Focal with skin lesions
Depth of disease	Mucosal/submucosal	Transmural
Fistulae or abscesses	Rare	Common
Strictures	Rare	Common
Smoking	Protective	Worsens course
Bloody diarrhea	Common	Rare (unless proctitis)
CRC risk	Increased	Increased (with colitis)

CRC: Colorectal cancer

Both ulcerative colitis and Crohn's disease may be associated with a variety of extra-intestinal manifestations, many of which may occur prior to intestinal symptoms (Table 2).

What can trigger a flare in patients with IBD?

Intestinal infections may often precede a flare of IBD.

The use of antibiotics has also been associated with flares of both ulcerative colitis and

Crohn's disease independent of their relationship to the development of *C. difficile* enterocolitis.

Also, it appears the use of non-steroidal anti-inflammatory drugs may flare IBD, although the exact mechanism is not fully known. The newer cyclooxygenase (COX)-2 inhibitors seem to be less frequently associated with causing flares of IBD. Other medications associated with flares of IBD include retinoic acid and chemotherapeutic agents.

What investigations should I order?

All patients should have stool cultures done for *C. difficile*, culture and sensitivity and ova and parasites. *C. difficile* can occur in IBD patients in the absence of antibiotics or known risk factors because of the impaired local immune response.

A complete blood count will reveal anemia (microcytosis if iron deficiency is present, macrocytosis if B12 deficient). A thrombocytosis is often seen in patients with active disease. An elevated white cell count above 16 μ l should alert of the possibility of intra-abdominal abscess. An elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) further heighten suspicions of active inflammation. Serum electrolytes may reveal a decreased potassium with severe diarrhea and, in extreme cases, a metabolic acidosis. A decreased albumin is frequently seen.

If one suspects a diagnosis of Crohn's disease, a small bowel follow-through (SBFT) should be ordered. Seventy per cent of patients with Crohn's will have ileal involvement (Figure 1). A colonoscopy should always be obtained to confirm the diagnosis by endoscopy and histopathology because lymphoid hyperplasia, lymphoma and certain infections can cause an abnormal appearance on a SBFT.

More on Marie

Initial investigations reveal that Marie has a microcytic anemia with evidence of thrombocytosis. Her erythrocyte sedimentation rate and C-reactive protein are both elevated. Her general biochemistry and liver profile are normal. She has stools requested for *C. difficile*, culture and sensitivity and ova and parasites, which return normal.

She is referred to a gastroenterologist who performs a small bowel follow through and a colonoscopy. The small bowel follow through shows a nodular appearance in the last 15 cm of the terminal ileum with evidence of ulceration. The colonoscopy shows punched out and linear ulcers in the terminal ileum consistent with Crohn's disease. The colon is entirely normal. The biopsies confirm granulomata in the ileum. She is started on budesonide, 9 mg, daily.



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A diagnosis of ulcerative colitis usually requires a flexible sigmoidoscopy and, ideally, a colonoscopy to evaluate the true extent of the disease (Figure 2). A small proportion of Crohn's patients have an ulcerative colitis (UC)-like appearance in the left colon seen at flexible sigmoidoscopy, but when a full colonoscopy is performed it is obvious that the diagnosis is Crohn's disease.

What are the treatment options?

The goals of therapy are to induce remission and to maintain remission.

UC is a mucosal-based disease. The first-line treatment is the aminosalicylates (5-ASA). These can be administered either orally or topically in the form of suppositories (which have coverage up to 20 cm) or enemas (which have coverage to 60 cm-splenic flexure). Given that there is a dose response to these agents and the topical mechanism, it makes ideal sense to treat patients with ulcerative proctitis or left-sided disease with suppositories or enemas. Patients with more extensive disease will require oral 5-ASA preparations. Patients who fail 5-ASA therapy after four weeks or have more moderate to severe symptoms often require oral prednisone.

Prednisone dosages begin at 40 mg to 60 mg daily and are typically tapered by 5 mg per week. Patients requiring hospitalization will receive intravenous steroids in the form of methylprednisone or hydrocortisone.

Once in remission patients are maintained on 5-ASA (topically or orally) indefinitely. For oral 5-ASA the minimum dose is in the range of 2 g to 2.4 g per day. Most patients, however, will require higher doses. Patients who are steroid-resistant or steroid-dependent may be started on an immunomodulator, such as azathioprine (AZA) or 6-mercaptopurine (6-MP).

Crohn's disease is a transmural disease. Although often used, the newer 5-ASA agents and antibiotics have never been proven to con-

Table 2

Extra-intestinal manifestations of IBD

Joint manifestations (25%)

- Arthralgia
- Arthritis (axial/peripheral/both)
- Ankylosing spondylitis
- Sacroileitis

Skin manifestations (15%)

- Erythema nodosum
- Pyoderma gangrenosum
- Aphthous ulcers of the month

Ocular (5%)

- Episcleritis
- Uveitis
- Recurrent iritis

Hepatobiliary (5%)

- Primary sclerosing cholangitis
- Gallstones
- Non-alcoholic steatohepatitis

IBD: Irritable bowel syndrome

Role of the family physician in Crohn's disease

- Promote smoking cessation
- Avoid non-steroidal anti-inflammatory drugs
- Rule out infections with flares (stool studies)
- Review medications (*i.e.*, aminosalicylates, budesonide/prednisone)
- Bone densitometry
- Flu vaccine if on immunomodulators
- Review need for surveillance colonoscopy
- Call directly for referral

sistently work in Crohn's disease in the rigors of randomized controlled trials. Sulfasalazine is useful in patients with colonic Crohn's disease. However, most patients who experience a flare will require a course of corticosteroid.

Budesonide is a potent corticosteroid with limited systemic toxicity because of a 90% first pass metabolism. It has become the drug of choice in mild to moderate Crohn's disease of the ileum and/or the right colon. Patients with Crohn's colitis or more severe Crohn's ileocolitis are treated with prednisone similar to patients with UC.

The most important thing in the management of Crohn's disease is maintenance of remission. Corticosteroids are not appropriate as maintenance of remission agents and long-term use should be avoided. However, over half of patients who begin steroids will either not respond or quickly flare after withdrawal. In these instances the introduction of immunosuppressive agents, such as 6-MP, AZA or methotrexate (MTX) is appropriate. The decision to begin these agents is usually left in the hands of the specialist after discussion of the risks and benefits with the patient. However, administration of MTX (which is given via the intramuscular or subcutaneous route) and the monitoring of bloodwork for toxicity is a shared responsibility between the primary-care provider and the specialist.

Unfortunately, a proportion of patients will fail immunosuppressive therapy. In these patients the introduction of infliximab can be particularly beneficial. Infliximab is a murine chimeric monoclonal antibody directed against tumour necrosis factor alpha. It is approved in Canada for the treatment of moderate to severe Crohn's disease failing other therapies and is often the first-line agent for perianal fistulizing Crohn's disease. Patients often feel better within days of receiving infliximab as an intravenous infusion and have substantial improvement in quality of life.

Conclusions...

Management of ulcerative colitis and Crohn's disease has evolved substantially over the last decade with the introduction of new therapeutic strategies, which involve immunosuppressive agents and biological therapy. The key to therapy is to induce remission and to educate patients on the importance of maintenance of that remission with appropriate medication while monitoring for rare treatment-related side-effects.

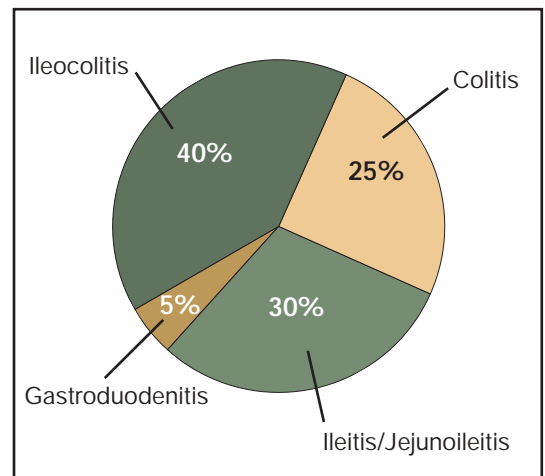


Figure 1. Anatomical distribution of Crohn's disease.

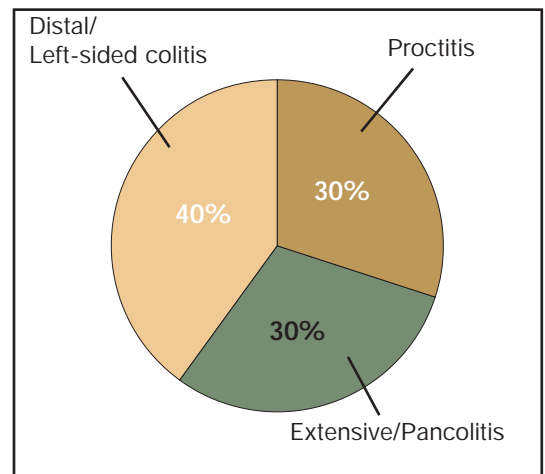


Figure 2. Anatomical distribution of ulcerative colitis.