# Inflammatory bowel disease

**BACKGROUND** Inflammatory bowel disease (IBD) is increasing in frequency in Australia. General practitioners play an important role in early diagnosis and in a multidisciplinary approach to managing such patients. Keeping abreast of evolving concepts, particularly in treatment, is challenging.

**OBJECTIVE** This article aims to address key issues in diagnosis and management to better equip general practitioners for their role in multidisciplinary management of patients with IBD.

**DISCUSSION** Making the diagnosis can be difficult, but is facilitated by appropriate clinical suspicion and sensible judgment as to who undergoes diagnostic tests such as colonoscopy. Treatment of ulcerative colitis has changed little in recent years, except for our improved ability to deliver mesalazine to the large bowel via the recent availability of several oral and rectal preparations. Prevention of relapse using these is an important strategy in the majority of patients. Treatment of Crohn disease is changing due to more realistic concepts of the natural history of the disease and the development of new, powerful anti-inflammatory therapies. Attention to issues other than intestinal inflammation such as nutrition, education and counselling, remain important in achieving optimal management.

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The past 40 years have seen inflammatory bowel disease (IBD) move from a boutique oddity to a relatively common illness.[1] It is estimated that up to 10 000 people are affected in Australia. There is an approximately equal distribution of the two clinically definable entities, ulcerative colitis and Crohn disease (CD); although in 15% of patients with colitis, the distinction is not clear and these patients are classified as having indeterminate colitis. Inflammatory bowel disease is characterised by chronic inflammation in the gastrointestinal tract of unknown aetiology; the distribution being large bowel only in ulcerative colitis, and most commonly ileum and colon in CD. Keeping abreast of the evolving concepts, particularly in treatment is challenging.

## Making the diagnosis

The clinical presentations and symptoms of IBD are well described. It is not uncommon for patients with IBD to describe a long diagnostic process that can take months or years. The key to avoid such an event is to suspect IBD (*Table 1*). Almost all patients with IBD have bowel symptoms, ie. abdominal discomfort or pain and/or change of bowel habits (usually diarrhoea). The vast majority of patients with such symptoms however, will have irritable bowel syndrome (IBS) and require less aggressive investigation. The distinguishing features are 'alarm' symptoms or signs, such as:

- rectal bleeding
- weight loss
- abdominal mass
- fever
- nocturnal symptoms
- pallor, or

**Table 1. How not to miss IBD**

- When diagnosis of IBS is being considered, think 'could this be IBD?'
- Beware of symptoms suggestive of acute gastroenteritis which continue or become worse after 4 days
- Think of possible IBD for a combination of abdominal symptoms and signs of inflammation
- Think possible IBD for unexplained abdominal pain, either intermittent or continuous
- Insist on colonic biopsies and ileal inspection when colonoscopy is sought for investigation of diarrhoea and/or abdominal pain
- Rectal bleeding always requires inspection – but depending on characteristics and age, sigmoidoscopy is often sufficient

- tachycardia

and clues from simple screening blood tests, such as:

- elevated C-reactive protein, white cell and/or platelet count, or erythrocyte sedimentation rate, or
- pus cells on faecal microscopy (when bowel infection is sought but no pathogens detected).

The diagnosis is usually secured by findings at flexible sigmoidoscopy or colonoscopy (*Figure 1*) that should include ileoscopy if possible, together with compatible histopathological features on multiple biopsies. In some patients, small bowel imaging such as by barium follow through, is needed. Two easy ways to avoid missing a diagnosis are to use clinical suspicion wisely, eg. do not be deterred by normal screening blood tests if clinical suspicion is high, and abide by the rule that chronic diarrhoea and rectal bleeding are two symptoms warranting endoscopic examination of the large bowel.

## Treating IBD

Much of the clinical decision making for patients with IBD involves how to reduce the inflammation because of the potentially severe consequences of the inflammation itself, and because effectively dealing with this leads to gratifying improvement in most aspects of the patient's wellbeing and quality of life. Information that dictates choice and dose of medication is:

- disease distribution
- disease severity, and
- the presence and absence of complications.

It is not difficult to appreciate the difference in managing, for example, mild proctitis versus severe ulcerative colitis involving the entire colon, or ileal CD with obstruction versus patchy colonic CD with perianal abscesses. As there are differences in the therapeutic approach to ulcerative colitis and CD, these will be considered separately.

### Ulcerative colitis

Decision making in ulcerative colitis is relatively easy because disease distribution is easily assessed by colonoscopy, activity is readily evaluated on the basis of the frequency and quality of bowel actions, and complications are unusual. The aim of treatment is also straightforward – to achieve and maintain both clinical and histological remission. This is not unrealistic and can be achieved in at least 80% of patients.

Severe colitis, which is readily identified clinically by marked frequency of bloody bowel actions together with systemic symptoms in a sick patient, nearly always requires hospitalisation for intravenous steroid and possibly other therapy and will not be considered further here. The most frequent presentation is with mild to moderate disease, usually involving only the distal colon and rectum.

#### Mesalazine

The key drug in this setting is mesalazine (5-amino-salicylic acid, 5-ASA), which needs to be delivered topically in large amounts to the large bowel mucosa.[2,3] To do this, mesalazine can be:

- bound to a carrier molecule – sulfapyridine for sulphasalazine (Salzopyrin) and another 5-ASA molecule in olsalazine (Dipentum) – to be released within the colon via bacterial action, or
- coated with a pH dependent substance (Mesasal, Salofalk) so that it is released in the terminal ileum and proximal colon.

Alternatively, mesalazine can be delivered directly to the rectum via a suppository (Pentasa), up to the proximal sigmoid colon by a foam (Salofalk), or up to the descending colon by an enema (Salofalk, Pentasa). Rectal preparations are usually used in conjunction with oral mesalazine drugs, as these have additive efficacy in distal disease.[4]

Mesalazine preparations are the mainstay of maintenance therapy. They will reduce the chance of relapse by two-thirds, and should be recommended for long term use in all patients except those with mild proctitis.[2,3] The additional benefit (and one very important in selling maintenance treatment to patients) is that mesalazine protects against the development of colorectal cancer.[5] The maintenance dose needed is the one that prevents relapse in the individual, and is often only 2 g of sulfasalazine, 1.5 g of coated 5-ASA, or 1 g of olsalazine per day.

### Corticosteroids

Corticosteroids are also very effective remission inducing agents, but carry the burden of adverse effects. While the colorectal delivery of rectal steroids (Predsol, Colifoam) is less of a problem, they are less efficacious than rectal mesalazine.[4] Oral steroids (usually prednisolone or prednisone) have the advantages of usually working relatively rapidly (faster than 5-ASA), and are cheap; but effects on body shape, bones and the psyche mean they should be reserved for those in whom 5-ASA has (or has previously had) insufficient efficacy. They are especially indicated when colitis is on the more severe end of the spectrum, or where more rapid efficacy is dictated by extraneous factors. Steroids have no role in maintenance of remission.

### Immunosuppression

Immunosuppressive therapy with azathioprine (or 6-mercaptopurine) or methotrexate is used in two situations:

- in patients with chronically active disease (ie. where remission and healing of the mucosa cannot be achieved), and
- where relapses occur more commonly than is acceptable to the patient and doctor, despite mesalazine therapy at adequate doses.

### Surgery

Surgery for ulcerative colitis comprises removal of the rectum and the entire colon followed by possible ileal pouch formation, and is indicated for:

- severe, unresponsive disease
- chronically active disease where ongoing symptoms are incompatible with quality existence, and
- neoplastic or preneoplastic changes (dysplasia) in the large bowel.

Surgery has minimal mortality (<1%), acceptable morbidity and the chance of a 'cure'. Unfortunately, an average result is 6–8 watery bowel actions per day (but without urgency) and about one in four patients get inflammation in the pouch ('pouchitis') that requires intermittent or chronic antibiotic or probiotic therapy. These results are highly acceptable to patients when they compare their life before the colectomy and pouch.[6]

## Crohn disease

Assessing the activity of CD is more difficult and requires a combination of the clinical signs, blood markers such as haemoglobin, white cell and platelet counts, serum albumin, and C-reactive protein, and, if available, endoscopic appearances. Treatment decisions in CD are considerably more complex as symptoms less accurately predict disease activity and complications such as perianal disease, bowel obstruction, or abscess formation are more common. The majority of patients should be looked upon as having chronically active disease rather than having a disease characterised by relapses and remissions. Healing of lesions is unusual. Furthermore, the attainment of 'clinical remission' is somewhat unreliable as patients chronically under-report symptoms such as tiredness and easy fatigue, mainly because they have re-set their perception of normality.

The therapeutic approach to CD is undergoing considerable change including:

- the diminishing use of mesalazine preparations due largely to the lack of efficacy (they still may be useful in mild disease)
- steroid use is now reserved for crisis situations, eg. while waiting the onset of action of other therapies (azathioprine, for example, can take 3–6 months to achieve optimal efficacy)
- antibiotics (eg. metronidazole and ciprofloxacin) are being used more frequently to gain control of inflammation, where previously steroids were always used (however, high level evidence for this approach is limited[7])
- smoking cessation is now a pivotal goal of medical intervention, as smokers are more likely to have a more severe and less responsive course, and these detrimental effects are reversible[8,9]
- aggressive therapy early in the disease course, particularly with the introduction of

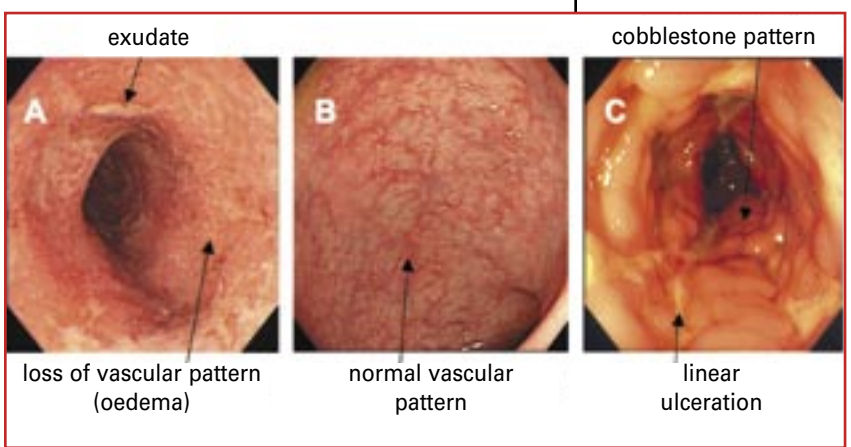


**Figure 1. Typical colonoscopic findings in the rectum in ulcerative colitis (A) compared with normal findings (B), and in Crohn disease (C)**

**Table 2. Essentials on how to manage IBD – the 5 'EEsy' steps**

**E**stablish hierarchy of responsibility
- consider whether primarily GP or specialist (gastroenterologist) care, or whether jointly including a surgeon

**E**valuate patient's level of appreciation of illness
- involve ACCA (or other support organisation) if necessary
- help patient evaluate material from other sources, eg. websites

**E**ncourage patient to accept illness and to respond maturely

**E**ducate patient regarding drugs and side effects and possible role of alternative supports

**E**nsure
- adequate follow up
- nutritional needs and long term complications are being addressed

immunosuppressive therapy such as azathioprine,[10] is often more appropriate than the traditional approach of waiting to see what will be the patient's pattern of disease. This minimises irreversible structural damage which itself might potentiate the disease and/or its symptoms (much like the modern approach in rheumatoid arthritis). However, this aggressive approach is often limited by drug side effects
- our ability to control inflammatory activity has improved markedly with the introduction of 'biological' therapies such as antitumour necrosis factor (infliximab) therapy.[11] These agents have sparked a revolution in the thinking about therapeutic approaches. They are powerful in their efficacy and may lead to healing more often, and are very well tolerated in the majority of patients. However, their use is associated with mortality (up to 1% in some series), mainly from unpredictable, opportunistic infection. This fact alone dampens enthusiasm for their early use unless optimally dosed standard therapies (eg. azathioprine) have failed. Their cost and lack of subsidy by the Pharmaceutical Benefits Schedule in Australia is also a problem
- new and promising therapeutic agents are currently under evaluation and Australian gastroenterologists and patients are experiencing a new phenomenon in IBD – multicentre, international clinical trials.

What has not changed is that surgery remains a key therapeutic tool to treat specific complications such as abscess formation, luminal stenosis or poorly controlled disease. The principle of 'minimal surgery', ie. resect the least that is necessary to get the patient over the current problem, remains the practice.

## Management

Management involves much more than treating the inflammation. Optimal treatment depends as much on the less tangible elements of management of a chronic illness as it does on choice of drug therapy or surgery (*Table 2*). Education and counselling are an important part of the management of a chronic illness. Patients quickly recognise a limited knowledge base in doctors, and this restricts the building of mutual respect. Thus, it is important for the primary clinician to be up-to-date in disease management knowledge. Patient educative material and counselling services are readily available via patient organisations such as The Australian Crohn's and Colitis Association (ACCA).

Many of the concerns of patients with IBD are common to most chronic illnesses in the young. Questions regarding issues relevant to reproduction are frequently asked – will it affect fertility or the outcome of pregnancy, will pregnancy affect the disease course, how safe are the drugs in pregnancy and breastfeeding, and what risk do my children have of getting IBD? While the answers to these questions are beyond the scope of this article, excellent literature is available for patients from ACCA.

Many patients with IBD have an intense interest in diet, but most of their advice generates from outside the medical profession. Three out of 5 Australian patients with IBD take mineral and/or vitamin supplements, yet most of these are probably unnecessary.[12] It is important that we offer dietary advice directed toward ensuring adequacy of nutrition and minimisation of symptoms (eg. avoid seeds, skins, and indigestible fibre when obstructing lesions are found; avoid wheat and onions if bloating and diarrhoea are prominent).

Of the micronutrients, iron deficiency is very common and relates predominantly to the inability to absorb iron when chronic inflammation is present. Oral iron may be poorly tolerated and ineffective in repleting stores.[13] There is a swing toward intravenous iron in such patients as it is safe and well tolerated, and successful iron repletion usually leads to improved energy levels and quality of life.

## IBD and colorectal cancer

The risk of colorectal cancer in patients with IBD involving the colon is increased. Current practices vary as the evidence base for the specifics of a surveillance program is poor. A typical recommendation for a patient with ulcerative colitis involving at least the left colon is to

have a second yearly colonoscopy with multiple biopsies for histopathological assessment for dysplasia after 7–10 years of disease.[14] Surveillance programs have yet to be introduced in CD, although the risk of cancer of both the large and small bowel is probably increased.

## Who should be looking after patients with IBD?

The most important person looking after the patient with IBD is the patient themself. The patient needs to be encouraged to take responsibility, to have a good knowledge of the disease and of the drugs being used, and to be able to work with the attending clinicians. Of the clinicians, management is best directed by someone experienced and knowledgeable about IBD (often, but not always a gastroenterologist) and in whom the patient has confidence and mutual respect. The GP has a key role in early diagnosis, supporting the patient, assisting with smoking cessation, and managing intercurrent issues. The surgeon plays an important role in more specific aspects of the illness. All members of the team should work together and ensure adequate communication.

### Summary of important points

- Early diagnosis depends upon asking the question: 'Could this be IBD?'
- Induction of healing with mesalazine drugs and/or steroids can be achieved in most patients with ulcerative colitis, but must be followed by long term therapy (mesalazine or immune suppressants such as azathioprine) to prevent relapse.
- Healing in CD is more difficult to achieve. Treatment decisions must be made on the basis that many patients have chronically active disease.
- Therapeutic approaches in CD are changing with more aggressive therapy early in the course of the disease, and a shift of emphasis from steroids and mesalazine to immune suppressants such as azathioprine and methotrexate, biological agents such as infliximab, and, to a lesser extent, antibiotics.
- Attention to patient education, nutrition, and issues of living with IBD is an essential part of good management. Enlistment of the help of the ACCA and/or the Gastroenterological Society of Australia is recommended.
- If you or your patients are unhappy with the current status of their IBD, involvement in a clinical trial of a new agent is an option worth considering.

### Resources

Gastroenterological Society of Australia
www.gesa.org.au
Australian Crohn's and Colitis Association
www.acca.net.au
National Association for Colitis and Crohn's disease (UK)
www.nacc.org.uk
Crohn's and Colitis Foundation of America
www.ccfa.org
Crohn's and Colitis Foundation of Canada
www.ccfc.ca
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Conflict of interest: Peter Gibson has acted in an advisory capacity to Schering Plough, Altana, Pfizer, Orphan, and Ferring, and is an investigator in many clinical trials of new agents.

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