

Diagnosing and managing inflammatory bowel disease

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FIGURE 1

Superficial continuous ulceration with loss of normal vascular pattern in active ulcerative colitis

How do patients present with IBD?

How should disease severity be classified?

What are the treatment approaches?



INFLAMMATORY BOWEL DISEASE (IBD) COMPRISES IDIOPATHIC CHRONIC CONDITIONS OF UNKNOWN

aetiology with an inflammatory intestinal response to unknown triggers. The two major types of IBD are ulcerative colitis and Crohn's disease. Both are characterised by a relapsing and remitting course.

In ulcerative colitis, the mucosal inflammation affects the rectum and to a variable extent the areas proximal

to the rectum in a continuous pattern, see figure 1, above. Although it only affects the colon total colitis can be associated with a 'backwash' ileitis.

Crohn's disease is characterised by discontinuous areas of transmural inflammation that can affect any part of the gastrointestinal tract but most frequently involves the distal small intestine and proximal colon, see figures 2 and 3, p15. Crohn's disease can cause complications such as strictures, abscesses, sinus tracts and

fistulae. These features may also contribute to bowel obstruction.^{1,2}

The revised Montreal classification, see tables 1 and 2, p14, is a practical way of characterising the clinical and endoscopic patterns of IBD.^{3,4}

IBD is most common in Northern Europe and North America with a prevalence of approximately 400 per 100,000 in the UK.^{5,6} There has been an increase in the numbers of Scottish children diagnosed with IBD since the mid 1990s.⁷ Men and women are

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SYMPOSIUM GASTROENTEROLOGY

INFLAMMATORY BOWEL DISEASE

Table 1

Montreal classification of ulcerative colitis⁴

E1	Ulcerative proctitis	Only involves rectum
E2	Left-sided (distal) UC	Extending to the splenic flexure
E3	Extensive colitis (pancolitis)	Extending proximal to the splenic flexure

Table 2

Montreal classification of Crohn's disease⁴

Age at diagnosis (years)	Location	Behaviour
A1 < 16	L1 Ileal	B1 Non-stricturing & non-penetrating
A2 17-40	L2 Colonic	B2 Stricturing
A3 >40	L3 Ileocolonic	B3 Penetrating
	L4 Isolated upper GI disease [†]	+ p if perianal disease

[†] **L4** is a modifier that can be added to **L1-L3** when concomitant upper GI disease is present

Table 3

Truelove and Witts criteria of severity of ulcerative colitis¹⁰

Activity	Mild	Moderate	Severe
No. of stools/day	≤ 4	4-6	≥ 6
Rectal bleeding	Small amounts		Larger amounts
Fever	No	No	>37.5°C
Tachycardia	No	No	Yes
Anaemia	No	No	Yes (Hb < 105 g/L)
ESR	≤ 30 mm/hr	≤ 30 mm/hr	> 30 mm/hr

Table 4

Investigations to confirm the diagnosis of Crohn's disease

Laboratory tests	Raised: CRP, ESR, platelets Reduced: albumin, haemoglobin
Small bowel imaging	Small bowel meal MRI enterography Capsule endoscopy
Colonic imaging	Colonoscopy and biopsy
Imaging for evidence of complications	CT abdomen MRI abdomen Perianal MRI (perianal disease)

similarly affected. There is a bimodal age of presentation with an initial peak in the second and third decades of life followed by another peak in the sixth decade.⁸

PRESENTATION

Ulcerative colitis

Acute ulcerative colitis typically presents with bloody diarrhoea with the passage of mucus, urgency and cramping abdominal pain. There may be a family history of IBD. A history of foreign travel should be sought and infective causes of acute diarrhoea should be excluded. The current British Society of Gastroenterology (BSG) guideline recommends four consecutive stool cultures.⁹

Clinical features are a guide to the

severity of an attack, which can be graded using the criteria of Truelove and Witts, see table 3, above.¹⁰

A severe attack is usually considered to be associated with bloody stools six times a day or more plus one of the features of systemic toxicity. Patients with a severe attack require hospitalisation and intensive inpatient treatment.

Inflammatory markers in the blood (plasma viscosity, ESR, CRP or plasma orosomucoids) are not always raised in ulcerative colitis, particularly when mild or moderate in severity.

At endoscopy the mucosa appears reddened, with loss of the vascular pattern and either bleeds on contact with the endoscope or has evidence of spontaneous bleeding, see figures 2

and 3, p15. Diagnosis is confirmed by typical histological features on biopsy.

Crohn's disease

Crohn's disease presents with a typical combination of abdominal pain, diarrhoea and weight loss. Pain or fever may also signify the development of an abscess and stricture formation will lead to obstructive symptoms.

Physical examination should look for evidence of fever, anaemia or a right iliac fossa mass, which can occur as a manifestation of disease activity due to the presence of inflamed loops of small bowel or an abscess. Perianal disease in the form of abscesses or fistulae may be present in 35-45% of patients during the course of their disease.^{11,12,13}

Further investigation involves blood tests and a combination of endoscopy with biopsy and radiology to image the small and large bowel, see table 4, left.

The clinical course can be very variable in IBD. A more debilitating course in Crohn's disease may occur in those patients who, at presentation, are:

- young
- have extensive proximal small bowel disease, colonic disease, perianal disease or
- require systemic steroids^{14,15}

TREATMENT

For both ulcerative colitis and Crohn's disease, treatment of a flare i.e. induction of remission is followed by treatment to maintain remission.

Ulcerative colitis

Induction: The severity of an acute attack and the extent of disease should be taken into account in deciding on treatment.

Maintenance: Oral aminosalicylates are first-line maintenance therapy in left-sided and extensive colitis, see table 5, p15. Intermittent rectal aminosalicylates are effective maintenance for proctitis and proctosigmoiditis although oral aminosalicylates alone or in combination with topical treatment may be considered,^{16,17} particularly as oral treatment may be better tolerated or more acceptable to patients.

Azathioprine or 6-mercaptopurine should be considered for maintaining remission in the following cases:¹⁶

- Two or more ulcerative colitis flares in the past 12 months requiring steroid therapy
- Following an attack of acute severe colitis

FIGURE 2
Deep colonic
ulceration in active
Crohn's disease

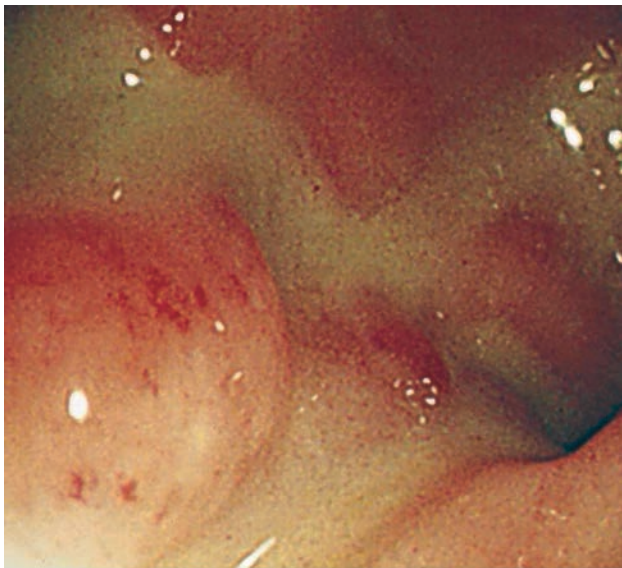
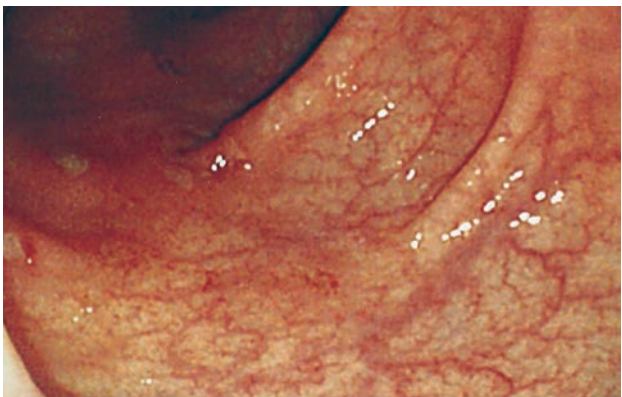


FIGURE 3
Aphthous
ulceration and
discontinuous
colonic
inflammation in
active Crohn's colitis

Surgery: Surgery may be required as an emergency during an acute severe attack of ulcerative colitis for perforation, toxic dilatation, massive haemorrhage or where an attack does not settle with medical treatment – which now usually includes intravenous steroids and ciclosporin or infliximab.

Surgery may also be considered in patients with frequent relapses or less severe chronic symptoms despite medical therapy and where surgery may restore quality of life. Surgical options include colectomy with permanent ileostomy or construction of an ileoanal pouch, which restores intestinal continuity and avoids a stoma. Patients should undergo careful counselling with a specialist colorectal

surgeon and stoma therapist prior to such surgery.

Crohn's disease

Treatment usually follows a sequential step-up approach, in which less aggressive treatments are initiated first, followed by more potent drugs or surgery if the initial medical therapy fails.²

However, there is debate about whether this conventional approach is appropriate and whether more aggressive treatments e.g. anti-TNF agents and thiopurine immunosuppression should be deployed earlier – accelerated step-up or top-down approaches. The role of early surgery for terminal ileal disease is uncertain.

Induction: Options for induction of remission in Crohn's disease, are summarised in table 6, p16.

Maintenance: Aminosalicylates have limited benefit for maintenance of remission in Crohn's disease. Azathioprine/6-mercaptopurine should be considered as the first-line maintenance treatment in the following cases:⁹

- After an acute severe attack
- Two or more relapses in a 12-month period requiring corticosteroid therapy

Methotrexate should be considered for maintenance therapy in patients intolerant of thiopurines. It should also be continued if methotrexate is used for the induction of remission.¹⁸ Conventional glucocorticoids, budesonide or enteral nutrition should not be offered for maintaining remission in Crohn's disease.¹⁸

Infliximab and adalimumab are the only biologic treatments currently approved by NICE for the treatment of severe active Crohn's disease. (Infliximab is also licensed for fistulating Crohn's disease). Both these medications are monoclonal antibodies against TNF-alpha. Infliximab is given as an intravenous infusion whereas adalimumab is administered by subcutaneous injection.

Anti-TNF therapy can be used for both induction and maintenance treatment of severe active Crohn's disease in the following situations:^{9,18,19}

- No response to conventional therapy (corticosteroids and/or immunomodulators)
- Contraindications or intolerance to conventional therapy

Maintenance anti-TNF treatment is more effective than intermittent treatment in terms of reducing the need for surgery or hospitalisation.²⁰

The current NICE guideline recommends annual review of

Table 5
Treatment options for induction of remission in ulcerative colitis based on NICE recommendations¹⁶

	Proctitis or proctosigmoiditis	Left-sided colitis or extensive colitis
Mild to moderate colitis	Topical aminosalicylates alone or: Combined oral and topical aminosalicylates Oral aminosalicylates only (less effective) Topical corticosteroids [†] Consider adding oral corticosteroids to aminosalicylates [‡]	High-dose oral aminosalicylates or Topical aminosalicylates can be added to oral aminosalicylates Consider adding oral beclometasone dipropionate to the above if not effective Oral corticosteroids [†] Consider adding oral corticosteroids to aminosalicylates [‡]
Severe colitis	IV corticosteroids Consider adding IV ciclosporin, infliximab or surgery [§]	

[†] If aminosalicylates are contraindicated, not tolerated or refused by the patient during the first step of inducing remission (stop beclometasone dipropionate if adding oral prednisolone)

[‡] If no improvement within 4 weeks of starting aminosalicylate therapy or if symptoms worsen despite treatment

[§] If little or no improvement within 72 hours of starting intravenous corticosteroids or if symptoms worsen at any time despite corticosteroid treatment (take into account the patient's preferences)

Table 6
Induction of remission for Crohn's disease¹⁸

	Monotherapy	Add-on immunomodulator therapy
First presentation CD or a single inflammatory relapse in a 12-month period	1 Conventional glucocorticoids (PO or IV) 2 Budesonide [¶] 3 Aminosaliculates [¶] (less effective than 1 and 2) 4 Consider enteral nutrition [¶] 5 Surgery (limited terminal ileal disease)	1 Azathioprine/6-mercaptopurine [¶] or 2 Methotrexate [¶]
Severe active CD ^Δ	1 IV corticosteroids ± immunomodulator treatments 2 Infliximab [§] 3 Adalimumab [§] 4 Surgery	
Active fistulating CD	1 Antibiotics 2 Surgical drainage 3 Seton insertion 4 Immunomodulator treatments 5 Infliximab	

[¶] In patients with ileal, ileocaecal or right-sided colonic disease who decline or cannot tolerate conventional steroids as well as those with contraindications for steroid use

[¶] In children or young adults when there are concerns about growth or side effects

[¶] If there are two or more relapses over a 12-month period or if steroids cannot be tapered

[¶] If azathioprine/6-mercaptopurine cannot be tolerated or if TPMT level is deficient

[§] If no response to conventional therapy with steroids ± immunomodulators or intolerance/contraindications to conventional therapy

^Δ Defined as Crohn's Disease Activity Index (CDAI) score of 300 and over or Harvey-Bradshaw score of 8-9 and above

Crohn's disease activity for all patients on maintenance anti-TNF therapy and consideration of withdrawal of treatment in those who are in stable clinical remission.¹⁹ This strategy has been associated with a relapse rate of 44% over the following year.²¹

PRIMARY CARE MONITORING

As many as 32% of IBD patients are managed solely in general practice.²² The overall approach to delivering high quality care for this group of patients has been described in national IBD standards.²³ Hospital services for IBD should provide a multidisciplinary team that includes access to specialised medical and surgical care, supported by specialist IBD nurses, dieticians, stoma therapists, pharmacists and psychologists — though the latter are not widely available. Clear communication between this team and primary care is crucial, with opportunities taken for sharing care where possible.

A number of aspects of the management of patients with IBD can be shared between primary and secondary care. These might include agreed pathways for rapid referral of patients with suspected IBD, treatment of flares using an agreed protocol and monitoring (including blood tests in patients

taking aminosaliculates and immunosuppressive drugs, and bone density).

Particular attention should be paid to the following areas:

Drug monitoring

Aminosaliculates: Monitoring renal function is necessary before and three months after starting aminosaliculates followed by an annual check.²⁴ If there is any suspicion of blood dyscrasia such as unexplained bleeding, bruising or fever, a full blood count (FBC) should be carried out.²⁴

Thiopurines: The level of the enzyme thiopurine methyltransferase (TPMT) should be checked before starting thiopurine therapy (azathioprine/6-mercaptopurine). Enzyme activity is absent in 1:300 of the population and such individuals are at risk of life-threatening myelosuppression if exposed to thiopurines,^{9,18,24} which are therefore contraindicated in this situation.

Myelosuppression is a serious potential side effect of thiopurines. FBC should be monitored throughout the treatment. One common approach is to check the FBC every 2-4 weeks for the first two months followed by 4-8 weekly thereafter⁹ — usually under a shared care scheme agreed locally and with a patient-held record. The

patient should be warned to seek urgent medical help and to stop the thiopurines if fever, sore throat or other evidence of infection develop.

There should be clear local arrangements that define monitoring requirements and specify who is responsible for undertaking this and acting on results.

Thiopurines may also be associated with acute pancreatitis and hepatitis.

Methotrexate: FBC, renal and liver function tests (LFTs) are recommended before starting methotrexate and repeated 1-2 weekly while the dose is stabilised. These tests should then be repeated at 3 monthly intervals.²⁴

Patients should be warned to report urgently any symptoms suggestive of underlying blood dyscrasia (sore throat, bruising, unexplained bleeding), hepatic toxicity or respiratory compromise.²⁴

Anti-TNF alpha: Although anti-TNF alpha therapy (infliximab and adalimumab) in IBD patients is normally closely monitored by secondary care, awareness of the potential side effects is important. Reactivation of latent tuberculosis and hepatitis B reactivation^{9,24} may occur and screening before treatment should include enquiry about possible prior TB exposure, chest X-ray and an interferon gamma release assay (IGRA)

key points

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The two major types of inflammatory bowel disease (IBD)

are ulcerative colitis and Crohn's disease. Both are characterised by a relapsing and remitting course. In ulcerative colitis the mucosal inflammation affects the rectum and to a variable extent the areas proximal to the rectum in a continuous pattern. Crohn's disease is characterised by discontinuous areas of transmural inflammation that can affect any part of the GI tract but most frequently involves the distal small intestine and proximal colon. IBD has a prevalence of around 400 per 100,000 in the UK. There is a bimodal age of presentation with an initial peak in the second and third decades of life followed by another peak in the sixth decade.

Acute ulcerative colitis typically presents with bloody

diarrhoea with the passage of mucus, urgency and cramping abdominal pain. A severe attack is usually considered to be associated with bloody stools six times a day or more plus one of the features of systemic toxicity. Patients with a severe attack require hospitalisation and intensive inpatient treatment. Inflammatory markers in the blood are not always raised in ulcerative colitis. The diagnosis is confirmed by typical histological features on biopsy.

Crohn's disease presents with a typical combination of

abdominal pain, diarrhoea and weight loss. Pain or fever may also signify the development of an abscess and stricture formation will lead to obstructive symptoms. Perianal disease in the form of abscesses or fistulae may be present in 35 to 45% of patients during the course of their disease.

Oral aminosalicylates are first-line maintenance therapy

in left-sided and extensive ulcerative colitis. Azathioprine or 6-mercaptopurine should be considered for maintaining remission. Surgery may be required as an emergency during an acute severe attack of ulcerative colitis for perforation, toxic dilatation, massive haemorrhage or where an attack does not settle with medical treatment. Surgery may also be considered in patients with frequent relapses or less severe chronic symptoms despite medical therapy and where surgery may restore quality of life.

Crohn's disease treatment usually follows a sequential

step-up approach, in which less aggressive treatments are initiated first, followed by more potent drugs or surgery if the initial medical therapy fails. Aminosalicylates have limited benefit for maintenance of remission in Crohn's disease. Azathioprine/6-mercaptopurine should be considered as the first-line maintenance treatment in the following cases: after an acute severe attack or two more relapses in a 12-month period requiring corticosteroid therapy.

for latent TB and serology for hepatitis B, C and HIV.

There is an increased lymphoma risk with both thiopurines and anti-TNF agents. The risk is 4.0 per 10,000 patient-years for thiopurines alone and 6.1 per 10,000 patient-years for combination therapy, compared with a background population risk of 1.9 per 10,000 patient-years.^{25,26} Worsening heart failure and demyelination are among other serious side effects.²⁴

Monitoring bone health

Bone density in IBD may be reduced due to inflammatory activity of the disease itself²⁷ and the effect of corticosteroids. Calcium and vitamin D supplementation should be given and bisphosphonate treatment considered in accordance with national guidelines.^{9,28}

Opportunistic infections and vaccination

Patients with IBD may be at higher risk of infection because of nutritional factors, associated hyposplenism or medication. Corticosteroid therapy with prednisolone > 20 mg daily for longer than two weeks increases the risk of infection.²⁹ Approximately 80% of IBD patients will be treated with steroids, 40% with thiopurines and 20% with anti-TNF agents. The most practical time for checking evidence of previous infection and immune status to a range of viral infections, may therefore be at diagnosis.²⁹ Particular consideration should be given to the following vaccines:

- **Varicella zoster virus (VZV):** consider in IBD patients with negative VZV serology and no previous history of chickenpox, shingles or vaccination against the virus²⁹

- **Human papilloma virus (HPV):** consider in girls aged 11-12, and in cases of delayed or missed immunisation for the 13-18 age group.^{30,31} Regular screening for cervical cancer is strongly advised for women with IBD, especially while on immunomodulator therapy²⁹

- **Influenza:** routine annual immunisation with trivalent inactivated influenza vaccine is recommended for all IBD patients on immunomodulator therapy but the live attenuated vaccine should be avoided^{29,32}

- **Pneumococcal vaccine:** consider in all IBD patients at diagnosis or at least two weeks before immunomodulator therapy with a single revaccination in three to five years' time if ongoing immunosuppression is required^{29,33}

- **Hepatitis B virus:** should be considered for seronegative IBD patients²⁹

IBD patients who are not on any immunomodulator therapies should follow the standard national vaccination guidelines before travelling. Patients on immunomodulator therapy should have a pre-travel consultation with their doctor.²⁹ Non-live vaccines are generally safe but may be less effective in this group; hence vaccination is best given before immunomodulator treatment if possible.²⁹ Live vaccines are contraindicated in IBD patients on immunomodulator therapy.²⁹

CHILDREN AND ADOLESCENTS

Transition to adult care

It is important that young people with IBD, and their families, are part of formal, defined arrangements for transition from paediatric to adult care. This requires careful preparation and co-ordination between paediatric and adult teams. The IBD nurses from both services play a crucial role during this transition. Particular attention needs to be paid to the impact of the condition and treatment on an individual's growth and development, education, relationships and psychosexual issues.

Puberty and growth

Height and weight should be monitored every 12 months in children and young people with IBD and as long as they are in remission, and every six months during the pubertal growth period.¹⁶ This should be intensified to every 3-6 months in those who relapse during puberty, are on corticosteroids or those with chronic active disease.¹⁶

Referral to a paediatrician should be considered in all patients with slow pubertal development.¹⁶

PSYCHOSOCIAL ISSUES

Because of the chronic and, at times, debilitating nature of IBD, special attention to the psychosocial aspects of the disease is very important. There is a clear association between clinical disease activity in this group of patients and depressive disorders and sexual dysfunction.³⁴

Disruption to family life, relationships, education and employment has many implications for IBD patients affecting self-esteem and social function especially among newly diagnosed and young patients.³⁵



CONCLUSION

There have been considerable developments in the management of patients with IBD not only in terms of medical treatment but also in service organisation and standards. Understanding these will help deliver the best care for these, potentially debilitating conditions integrated across primary care and hospital departments.

GPs have a vital role in the management of these patients through rapid recognition of symptoms suggesting IBD leading to earlier diagnosis with a resultant reduction in morbidity, early treatment of exacerbations of symptoms, shared monitoring of drug therapy and bone health, and by providing support and information.

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Useful information

For healthcare professionals

NICE

Guidelines

CG166. Ulcerative colitis

www.nice.org.uk/nicemedia/live/14189/64218/64218.pdf

CG152. Crohn's disease

www.nice.org.uk/nicemedia/live/13936/61001/61001.pdf

British Society of Gastroenterology Guidelines

Inflammatory bowel disease

www.bsg.org.uk/images/stories/docs/clinical/guidelines/ibd/ibd_2011.pdf

Colorectal cancer screening and surveillance

www.bsg.org.uk/images/stories/docs/clinical/guidelines/endoscopy/ccs_10.pdf

National IBD standards

www.bsg.org.uk/attachments/160_IBDstandards.pdf

ECCO guideline-opportunistic infections in IBD

www.epege.gr/assets/GuidelinesFiles/nk_eccoconsensus.pdf

National Osteoporosis Guideline Group

www.shf.ac.uk/NOGG/NOGG_Pocket_Guide_for_Healthcare_Professionals.pdf

For patients

Support groups

Crohn's and Colitis UK

www.crohnsandcolitis.org.uk

The Ileostomy and Internal Pouch Support Group (IA)

www.iasupport.org

CICRA (Children with Crohns and Colitis)

www.cicra.org

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