# CHAPTER 75
# Inflammatory Bowel Disease

**Hugh W. Grant**
**Atonasio Taela**

## Introduction

Inflammatory bowel disease (IBD) refers to a group of disorders that causes intestinal inflammation. The commonest types of IBD are ulcerative colitis (UC) and Crohn's disease (CD). Other, rare forms of IBD include collagenous colitis, lymphocytic colitis, ischaemic colitis, and diversion colitis. Diagnosis is based on clinical symptoms and signs, upper endoscopy with biopsies, colonoscopy with biopsies (including terminal ileum), and radiological examination (contrast follow-through or enema).

Overall, 25–30% of patients with IBD present in childhood or adolescence. The overall incidence of IBD in children in Africa is unknown, but it is thought to be lower than in Europe and the United States, where it has an incidence of 7 per 100,000 children.[1] In the United Kingdom, approximately 18% of children with IBD are non-Caucasian—mainly Afro-Caribbean or Asian.[2] The literature contains reports of IBD from all over Africa: Tunisia, Egypt, Sudan, Senegal, Côte d'Ivoire, Nigeria, Ethiopia, Zimbabwe, and South Africa. IBD has been reported in all population groups in South Africa—Caucasians, Jews, Africans,[3] and Asians.[4]

Inflammatory bowel disease is thought to be uncommon in Africa—this may be due to underdiagnosis because infectious diseases of the gastrointestinal (GI) tract are very common. Infectious diseases may mimic the signs and symptoms of IBD, so it is highly likely that some cases of chronic diarrhoea in children are misdiagnosed.

## Aetiology and Pathophysiology

Genetics, immunity, environment, and diet all play a part in the aetiology and pathogenesis of IBD. The basic problem in Crohn's disease is a breakdown in the immune tolerance of the gut to intraluminal flora.

### Genetics

The genetics of IBD have not been fully delineated. In Crohn's disease, monozygotic twins have 44–55% disease concordance.[5] The lifetime risk for CD for first-degree relatives is 7% in Caucasians, but 16.8% in Jewish families.[6] Thirty percent of children presenting before 20 years of age have a family history of IBD. A number of IBD-susceptibility genes have been identified (e.g., CARD15 on chromosome 16q).

### Immunity

Patients with IBD demonstrate an abnormal immune response within their own GI tract. There are features of autoimmunity, and the disease can affect other organs outside the gut, such as eyes, skin, and joints. Inflammatory mediators (e.g., Interleukin 23) are overexpressed in IBD, and lymphocyte subsets (CD4) have been implicated in the pathogenesis of the inflammatory response. A recent hypothesis postulates that IBD is caused by an overactive immune system that attacks the digestive tract in the absence of such traditional targets as parasites and worms. This is similar to the hygiene hypothesis of many allergic conditions, and might explain the low incidence of IBD in Africa, where helminthic and parasitic infestations are endemic.

### Environment

Smoking exacerbates CD in adults and children. Diet may be important—serum antibodies to cow's milk protein are elevated in many patients with CD.

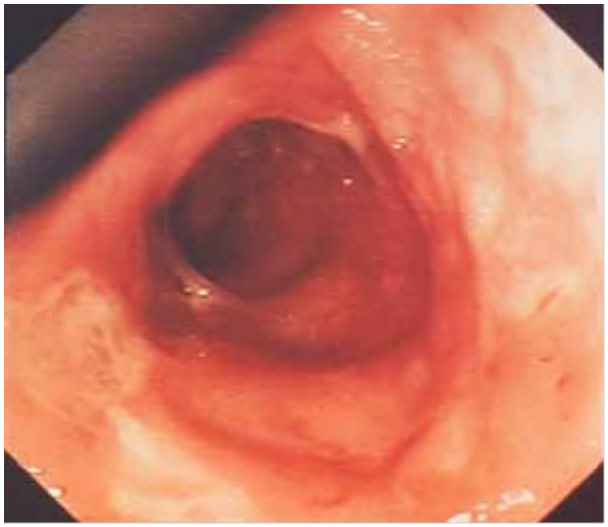
### Infection

The pathological processes seen in CD have similarities to tuberculosis (TB), but no specific organism has ever been identified as an aetiological agent.

## Pathology

### Ulcerative Colitis

UC is a disease that affects the colon. It primarily affects the rectum and a variable extent of more proximal colon. The disease is generally confluent with no skip lesions (unless the patient has undergone treatment). Macroscopically, it can appear as a granular proctitis with superficial ulcers, slough, and contact bleeding (Figure 75.1).



Source: Courtesy of Dr Peter Sullivan, Paediatric Gastroenterologist, John Radcliffe Hospital, Oxford, UK.

*Figure 75.1: Macroscopic appearance of ulcerative colitis at colonoscopy.*

Microscopically, the disease is limited to the mucosa. Inflammation starts at the base of the crypts with acute and chronic inflammatory cell infiltration. Crypt abscesses may be seen well as Goblet cell depletion. There is compensatory cell proliferation. Pseudopolyps are seen when islands of preserved mucosa are surrounded by superficial ulcers (Figure 75.2).

Ulcerative colitis is also associated with extragut manifestations such as arthropathy, uveitis, and skin lesions (pyoderma gangrenosum).

### Crohn's Disease

Crohn's disease can affect any part of the GI tract from mouth to anus. In children, it manifests mainly as terminal ileal disease, colitis, or perianal disease. The lesions can be skip lesions. Macroscopically, CD can appear as patchy or confluent inflamed areas with a cobblestone appearance and apthous ulceration (Figure 75.3). At operation, there may be fat wrapping around the bowel wall.

Microscopically, CD affects all the layers of the bowel wall, with chronic inflammatory cell infiltrate, deep ulceration, granulomas, a thickened mesentery, and lymphadenopathy (Figure 75.4).

The features of CD can mimic tuberculosis. It is also associated with extragut manifestations, such as erythema nodosum, pyoderma gangrenosum, arthropathy, and uveitis.

When the pathologist cannot determine whether the problem is UC or CD, it may be labelled as "indeterminate colitis" or "IBD (not otherwise specified)". It is generally best treated as ulcerative colitis until the clinical picture becomes clear.

## Clinical Presentation

### History

Differences exist in the way IBD presents in children and adults. Abdominal pain is the most frequent symptom in children with IBD,[7] whereas adults tend to present with rectal bleeding in UC and with diarrhoea in CD. Forty percent of children have growth failure at the time of diagnosis[8]—however, this is not an issue with adults.

In ulcerative colitis, the commonest features in children are diarrhoea, abdominal pain, and blood per rectum.[9] UC is predominantly confined to the rectum and left colon in adults, whereas children tend to have pancolitis.[9]

In Crohn's disease, the classic adult triad of abdominal pain, diarrhoea, and weight loss was present in only 25% of children.[7] Many young CD patients present with vague complaints of nausea, vomiting, fever, growth retardation, malnutrition, or extra intestinal manifestations.[1] This clearly makes diagnosis very difficult in Africa, where anaemia, fever, weight loss, malaise, and diarrhoea are very common. For these reasons, the Porto criteria[1] for diagnosis are largely unworkable in Africa.

### Physical Examination

In ulcerative colitis, external physical examination is often unremarkable; there may be some abdominal discomfort. It is important to look for extragut manifestations—pallor, arthropathy, and skin changes.

In Crohn's disease, physical examination may demonstrate identifiable disease. There may be mouth ulcers (Figure 75.5); abdominal tenderness; an inflammatory mass; or perianal tags, fissures, and abscesses (Figure 75.6). Check for extragut manifestations.

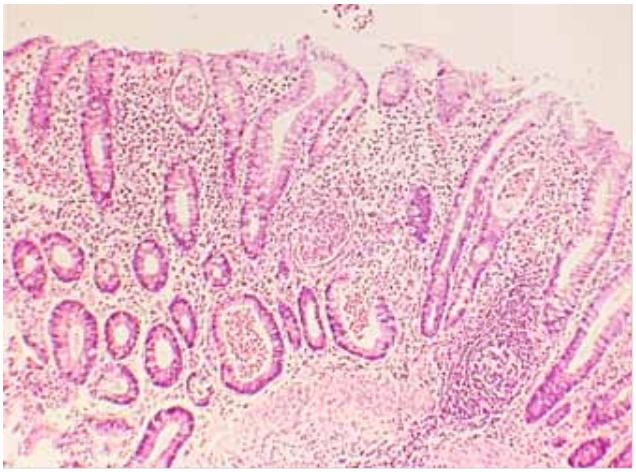
### Investigations

For general testing, send the stool to the lab to exclude infective causes. Perform baseline blood tests: a full blood count (FBC) (looking for anaemia, high white blood count, raised platelets); inflammatory markers (raised erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)); electrolytes (for dehydration); and albumin.

Specific tests depend on their availability.

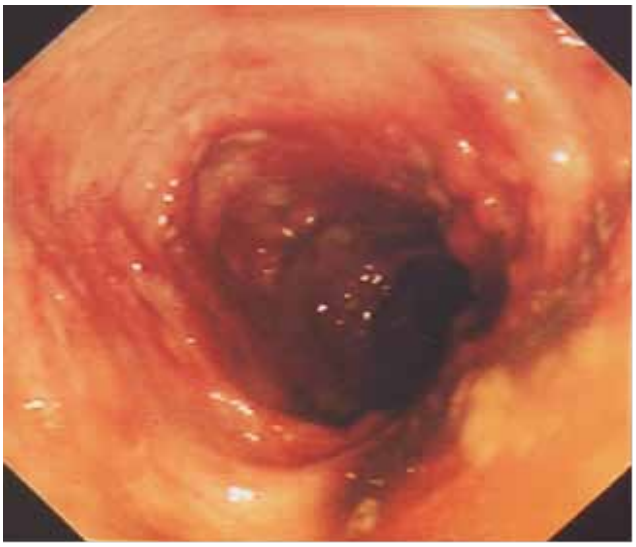
- *Upper endoscopy and colonoscopy* (with ileal intubation) should be performed if possible. Multiple biopsies should be taken along the length of GI tract.
- *Sigmoidoscopy and proctoscopy* can usually be performed if colonoscopy is not available.
- *Double contrast enema* should be performed if the colon is largely affected, and small bowel follow-through (or enema) if Crohn's disease is suspected (Figure 75.7).
- *Ultrasound scan* can be helpful for an inflammatory mass in Crohn's disease.

Differential diagnoses in children presenting with IBD include infective diarrhoea (viral and bacterial, especially *Yersinia enterocolitica* and *Entamoeba histolytica*); enteropathies; malnutrition from dietary deprivation; worm infestations; and tuberculosis. A wise approach is to investigate and treat the common causes of these symptoms but to consider IBD in chronic cases that do not respond to the usual treatments. In CD, tuberculosis must always be excluded before major surgery is undertaken.



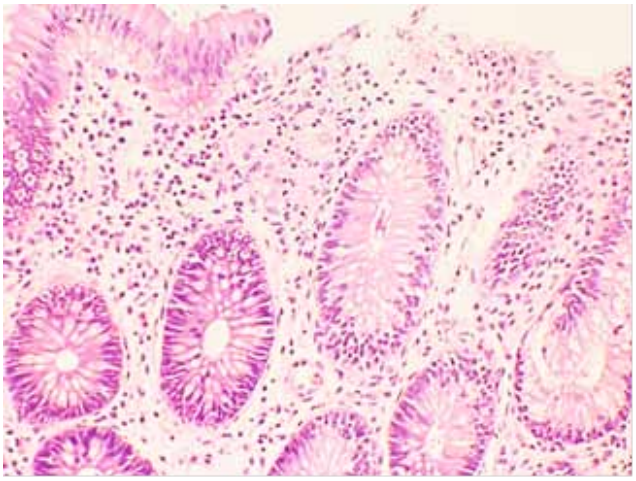
Source: Courtesy of Dr Peter Sullivan, Paediatric Gastroenterologist, John Radcliffe Hospital, Oxford, UK.

*Figure 75.2: Microscopic appearance of ulcerative colitis.*



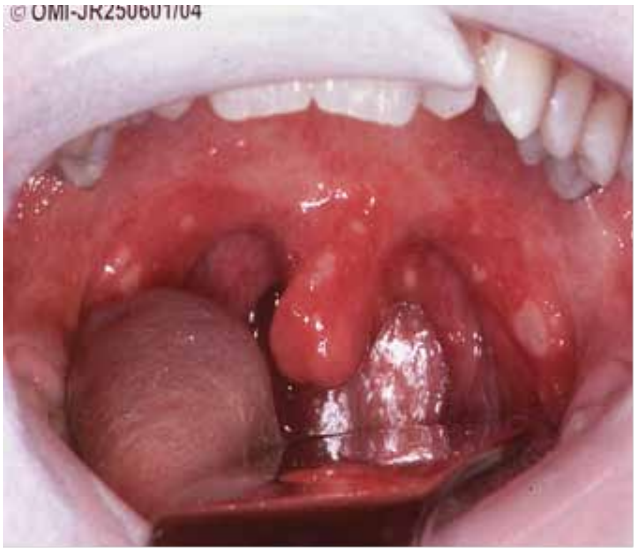
Source: Courtesy of Dr Peter Sullivan, Paediatric Gastroenterologist, John Radcliffe Hospital, Oxford, UK.

*Figure 75.3: Macroscopic appearance of Crohn's disease affecting the terminal ileum.*



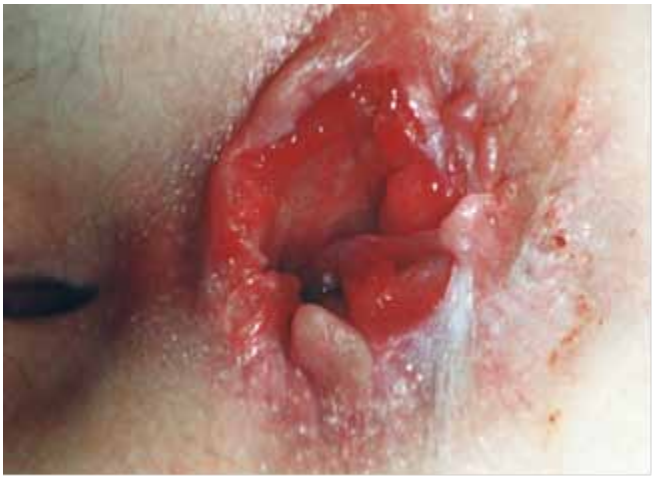
Source: Courtesy of Dr Peter Sullivan, Paediatric Gastroenterologist, John Radcliffe Hospital, Oxford, UK.

*Figure 75.4: Microscopic appearance of Crohn's disease.*



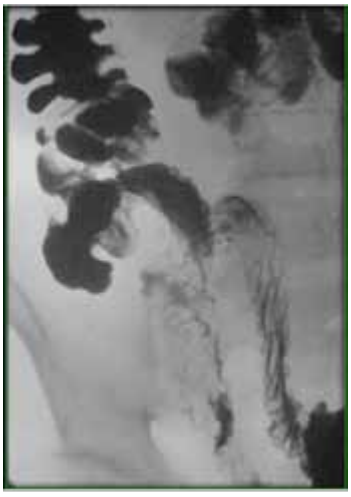

Source: Courtesy of Dr Peter Sullivan, Paediatric Gastroenterologist, John Radcliffe Hospital, Oxford, UK.

*Figure 75.5: Mouth ulcers in Crohn's disease.*



Source: Courtesy of Dr Peter Sullivan, Paediatric Gastroenterologist, John Radcliffe Hospital, Oxford, UK.

*Figure 75.6: Perianal tags and fistula in Crohn's disease.*



Source: Courtesy of Dr Peter Sullivan, Paediatric Gastroenterologist, John Radcliffe Hospital, Oxford, UK.

*Figure 75.7: Contrast follow-through demonstrating stricture in terminal ileum.*

## Management

### Medical Management

In ulcerative colitis, management is primarily medical and depends on the severity and extent of the disease.[2] For mild disease (i.e., fewer than four motions per day), oral aminosalicylates and corticosteroids are prescribed for 2 weeks. Mesalazine enemas are given daily until the bleeding stops, and then on alternate days for one week. For moderate disease (i.e., four to six motions per day, anaemia, slight toxicity), treat as above with oral steroids in a higher dose (2 mg/kg; maximum 40 mg) for 1 month and then reduce slowly over the following weeks. If there is a poor response, treat as for severe disease. For severe disease (i.e., more than six motions per day, toxicity, fever, anaemia), intravenous methylprednisolone or hydrocortisone are given for 3 days, and rectal hydrocortisone or prednisolone enemas are given twice daily. Intravenous fluids, blood transfusion, and total parenteral nutrition may also be required. If a relapse occurs, the patient should go back on rectal corticosteroids and a course of oral corticosteroids. Salicylates are generally lifelong for maintenance. If relapses occur, steroids or azathioprine (in order to limit the dose and complications of steroids) can be given. Other immunomodulating drugs include ciclosporin, methotrexate, and inflixamab.

In Crohn's disease, management is also primarily medical. Relapses can be expected, and many patients will require surgery. An elemental or polymeric diet for 6 weeks can produce remission in small bowel disease, but relapse is frequent. This diet has the advantage of having few side effects, but is poorly tolerated (due to its awful taste). It can be given either orally, through a nasogastric tube, or via a gastrostomy. For acute flare-ups, prednisolone should be given until remission occurs (2 mg/kg; maximum 40 mg) and then slowly reduced (by 5 mg per week). Mesalazine appears to be effective for treatment of small bowel and colonic disease. Azathioprine is effective for long-term maintenance and has steroid-sparing effects. Metronidazole can be helpful in controlling perianal disease with fistulas. Tumour necrosis factor (TNF) antagonists (inflixamab) are increasingly used but are not generally available in Africa.

### Surgical Management

In ulcerative colitis, the indications for surgery are acute toxic megacolon, intractable disease with ongoing symptoms and multiple frequent relapses despite maximum medical therapy, and growth failure. There is a risk of cancer in patients who have had pancolitis for more than 10 years. In ulcerative colitis, the disease affects the colon and can therefore be "cured" by removing the colon. The underlying principle is to remove all the mucosal disease (from the appendix and caecum to the anal margin). Surgery is usually performed in unwell children and it is safest to do this as a staged procedure.

An upper transverse incision should be performed in small children, and a midline for adolescents. A subtotal colectomy (leaving a rectal stump at the pelvic brim) and formation of an ileostomy (spouted) will remove the vast amount of the disease in the affected child. This is increasingly being done laparoscopically. If proctitis is a major problem, the rectal stump can be short. At a later date (usually around 6 months) when the child is off all immunosuppressive medications and when the ileostomy effluent is thicker and of less volume, the standard operative procedure is a restorative proctocolectomy (ileo-anal "J" pouch, with covering loop ileostomy). Six weeks later, a distal loopogram is performed, an examination under anaesthetic is performed (to check on possible stenosis and the condition of the pouch), and—if all is well—the covering ileostomy is closed. In Africa, a simple ileo-anal anastomosis is more appropriate. The eventual endpoint is the same (5-10 stools per day) but takes longer. It avoids any problems relating to the pouch (e.g., pouchitis). When performing an ileo-anal anastomosis, approach from below and start the dissection 1 cm above the dentate line, strip the mucosa for 3–4 cm (keeping very superficial),

and then excise the entire rectal stump (like an endorectal pull-through). Anastomosis is best performed by using interrupted absorbable sutures.

In Crohn's disease, the indications for surgery are intestinal obstruction (due to stricture or inflammatory mass), failure of medical management with relapses, growth failure, fistulas, and perforation. The type of surgery depends on the location and extent of disease: For local small bowel disease, consider stricturoplasty, take out as little bowel as necessary, and avoid stomas if possible. For colonic disease, partial colectomy (preserve unaffected colon) may be required. For perianal disease, drain abscesses, use seton if indicated for fistulas, and avoid sphincter-damaging procedures.

## Postoperative Complications

Complications are common after surgery for IBD.[10,11] The patients are often unwell, malnourished, have depressed immunity (e.g., steroids, failure to thrive), and are generally in poor condition. Specific short-term surgical complications include postoperative bleeding (salicylates), anastomotic leakage (impaired wound healing), fistula formation (part of CD), fluid and electrolyte imbalance, and short-gut syndrome. Medium- to long-term problems include recurrent disease in 10–40% of patients with CD,[12] small bowel obstruction due to adhesions in up to 25%,[10] and reduced fertility in girls following pouch surgery.[13] There is some evidence that continuing immunosuppressive therapy with azathioprine after surgery can reduce the reoperation rate in Crohn's disease.

## Prognosis

Ulcerative colitis can generally be "cured" by colectomy and ileo-anal anastomosis, and patients can come off their medications. In Africa, colectomy carries the hazard of removing the vital absorptive capacity of the colon and may predispose patients to dehydration if they were to pick up infective diarrhoea. Long-term function is generally good, but may take up to 18 months to achieve acceptable bowel control and bowel frequency.

Crohn's disease is not curable; it follows a relapsing and remission pattern.[12] Previously indolent disease can flare up, and previously uninvolved areas can become diseased.

## Evidence-Based Research

Table 75.1 presents a study that is an overview of inflammatory bowel disease.

*Table 75.1: Evidence-based research.*

| | |
|---|---|
| **Title** | Inflammatory bowel disease |
| **Authors** | Baillie RM, Croft NM, Fell JM, Afzal NA, Heuschkel RB |
| **Institution** | Paediatric Medical Unit, Southampton General Hospital, Southampton, UK |
| **Reference** | Arch Dis Child 2006; 91:426–532 |
| **Outcome/ effect** | Twenty-five percent of inflammatory bowel disease presents in childhood. Growth and nutrition are key issues in the management, with the aim of treatment being to induce and then maintain disease remission with minimal side effects. Only 25% of Crohn's disease presents with the classic triad of abdominal pain, weight loss, and diarrhoea. Most children with ulcerative colitis have blood in the stool at presentation. Inflammatory markers are usually, although not invariably, raised at presentation (particularly in Crohn's disease). Full investigation includes upper gastrointestinal endoscopy and ileocolonoscopy. Treatment requires multidisciplinary input as part of a clinical network led by a paediatrician with special expertise in the management of the condition. |

## Key Summary Points

### Ulcerative Colitis

1. Surgery is indicated for complications.
2. Staged procedures should be considered in unwell children.
3. Remove all colon down to anal verge (anal transition zone).
4. Standard operative procedure is ileo-anal anastomosis or ileo-anal J pouch (restorative proctocolectomy).

### Crohn's Disease

5. Surgery will never cure the disease.
6. Keep surgery simple (consider stricturoplasty).
7. Take out as little bowel as necessary.
8. Avoid stomas, if possible.
9. Drain perianal disease (use seton if indicated) and avoid sphincter-damaging procedures.

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