

*Ministry of Defence*

## **Synopsis of Causation**

# **Inflammatory Bowel Disease (Ulcerative Colitis and Crohn's Disease)**

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## **Disclaimer**

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This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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# 1. Definition

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- 1.1. **Inflammatory bowel disease (IBD)** can usually be defined as one of 2 separate bowel conditions.
  - 1.1.1. **Ulcerative colitis** is a relapsing and remitting inflammatory condition that only involves the mucosal lining of the large bowel (i.e. the colon and rectum). The rectum is usually involved and the disease can extend in a continuous fashion to affect the whole colon.<sup>1</sup>
  - 1.1.2. **Crohn's disease** is a condition which causes inflammation in all the layers of the bowel wall. It can arise in any location along the gastrointestinal (GI) tract, from the lips and mouth to the area around the anus (perianal disease). Unlike ulcerative colitis, Crohn's disease can occur in patches along the GI tract. The most commonly affected areas are the last part of the small bowel (ileum) and the colon (Crohn's colitis).<sup>2</sup>
- 1.2. Ulcerative colitis and Crohn's disease are distinct conditions at either end of the spectrum of IBD. They can be treated in similar ways, and it can sometimes be difficult to distinguish between them as a cause of colitis.

## 2. Clinical Features

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- 2.1. The clinical features of IBD often depend on the severity of the disease and the part of the GI tract that is involved.
- 2.2. Ulcerative colitis involving only the rectum may present with intermittent bleeding from the rectum, or mild diarrhoea. If the whole colon is involved, patients may have bloody diarrhoea more than 10 times a day, which can commonly wake them from sleep. They may also complain of generalised or cramping abdominal pains. Severe or fulminant colitis can cause severe pains, fever and rectal bleeding which may require blood transfusion. In this situation, patients have often lost a significant amount of weight. With fulminant colitis, patients are at risk of developing a dilated colon (toxic megacolon) and perforating the bowel.<sup>1,3</sup>
  - 2.2.1 Most patients who develop ulcerative colitis have gradual onset of symptoms which they may dismiss at first. Less than 10% are seen for the first time with fulminant colitis and only a small proportion of these are at significant risk of perforating their bowel.<sup>1</sup>
- 2.3. The symptoms of Crohn's disease are much more variable and less specific than those of ulcerative colitis. For this reason it can take much longer to diagnose than ulcerative colitis. Patients often complain of longstanding diarrhoea, fatigue and cramping abdominal pains, but rectal bleeding is much less common than in ulcerative colitis. Fever and weight loss may be evident by the time of diagnosis.<sup>2,3</sup>
  - 2.3.1 Crohn's disease can also cause the formation of abscesses and fistulae or tracts between the bowel and other parts of bowel or other organs, such as the bladder, vagina, or skin. This is most obvious in the perianal area where discharge of pus may be evident or swelling and pain from an abscess may be felt.<sup>2,3</sup>
  - 2.3.2. Less commonly Crohn's disease can affect the upper GI tract causing severe mouth ulcers, pain on swallowing due to inflammation in the oesophagus (gullet) or pain in the upper abdomen and vomiting from involvement of the stomach.<sup>2,3</sup>
- 2.4. Both ulcerative colitis and Crohn's disease can affect parts of the body other than the GI tract. A relatively small proportion of patients may have eye problems, arthritis predominantly affecting the large joints, or specific skin disorders such as erythema nodosum or pyoderma gangrenosum. It is also possible to develop an associated liver condition called sclerosing cholangitis.<sup>1-3</sup>

### 3. Aetiology

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- 3.1. Aetiology is not yet fully understood. It is thought that patients are likely to have been born with a **genetic predisposition** to develop IBD as these conditions often affect more than one member of a family. A large number of different genes have been shown to be linked to ulcerative colitis or Crohn's disease, but these differ between populations and no one or two genes have been found to be common to all people with the condition. Having inherited this predisposition, further interaction between a person's immune system and environmental factors is required before IBD can develop. The exact nature of these trigger factors is still being actively debated and may differ for ulcerative colitis and Crohn's disease.<sup>4</sup>
- 3.2. **Smoking** will worsen Crohn's disease but does not have the same effect on ulcerative colitis. The role of **diet** in the development of IBD is still being actively debated.<sup>3-5</sup>
- 3.3. **Drugs.** The use of non-steroidal anti-inflammatory drugs (NSAIDs) may increase the frequency of exacerbations of IBD although not all studies are in agreement about this. However, it does appear clear that use of the oral contraceptive pill can lead to an increased risk of IBD.<sup>6</sup>
- 3.4. **Infections.** For some time a number of infectious agents (bacteria, viruses, and fungi) have been suggested as possible triggers for IBD. However, no specific infections have been linked to the condition and current thinking suggests that components of normal gut flora are more likely to have a role.<sup>4,5</sup> In tropical populations, IBD is much less common than in the developed world. Studies have been carried out in people living either permanently or temporarily in the tropics to look for a link between IBD and infections such as amoebiasis, but these have failed to show a connection between the two.<sup>7</sup>
- 3.5. **Stress.** The role of stress in triggering exacerbations of IBD is not clear. Although patients often suspect a link between the two, this has proven difficult to illustrate in scientific studies. In recent years however, it has become increasingly recognised that psychological stress can play a role in relapses of IBD.<sup>8</sup>
- 3.6. **Physical exercise** is not thought to be harmful to people with IBD and may in fact be beneficial.<sup>9</sup>

## 4. Prognosis

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- 4.1. Prognosis in IBD is exceedingly variable and depends on the type and, more importantly, the extent of disease. Both diseases naturally run a relapsing and remitting course. The aim of management is to treat the relapse and then try to reduce their incidence in the future. Around 50% of patients with ulcerative colitis will have a relapse in any one year. A minority will have frequently relapsing or continuous disease.<sup>3</sup>
- 4.2. Typically, a patient may present when symptoms have been present for some time and it may be necessary to use steroids intravenously, in tablet, or in topical forms (enemas, foams and suppository preparations) to bring symptoms under control. They usually do so rapidly and can be effective in bringing severe and even fulminant colitis into successful remission. Steroids can also be very effective in the treatment of exacerbations of small bowel Crohn's disease. They have side-effects such as hypertension, diabetes and osteoporosis, and therefore, are usually only used in the short-term for flares of disease. Usually, patients will start on higher doses, which are then weaned down over approximately 2 months.<sup>3</sup>
- 4.3. For almost all patients with ulcerative colitis and some with Crohn's disease, 5-aminosalicylates (5-ASAs) such as mesalazine (including Asacol, Pentasa), balsalazide and olsalazine are used in tablet or suppository form, to keep the disease in remission once the steroids have been stopped.<sup>3</sup>
- 4.4. Some patients with Crohn's disease are treated with immunosuppressants to keep their disease in remission. Most commonly, this is with azathioprine, a drug which controls the IBD well but has some side-effects. This means that patients require regular blood tests to ensure they are on the correct dose of the drug for them. Some patients with ulcerative colitis also require to take azathioprine to keep their colitis under control. Alternative immunosuppressants that may be used include 6-mercaptopurine, ciclosporin, mycophenylate and methotrexate.<sup>3</sup> New biological agents such as infliximab are likely to find a role in the treatment of severe resistant Crohn's disease and ulcerative colitis.
- 4.5. Surgery for IBD is usually used only when medical therapy fails. In the case of ulcerative colitis this is most often in patients with fulminant colitis who do not go into remission with high dose intravenous steroids. A colectomy will eventually be necessary for 20-30% of patients with colitis affecting the whole colon. Following colectomy, these patients will have either an ileostomy or an ileo-anal pouch, which may develop an inflammatory pouchitis. In Crohn's disease, surgery may be considered in patients with troublesome perianal abscesses or if fistulae have developed and require drainage, as well as for troublesome small bowel disease or colitis. Around 50% of patients with Crohn's disease will require surgery of some description in the first 10 years of disease. This increases to 70-80% within their lifetime.<sup>3</sup>
  - 4.5.1. If colectomy is required in ulcerative colitis, this effectively results in cure of the condition as this is the only part of the bowel that ulcerative colitis can affect. In Crohn's disease however the disease may recur in other parts of the GI tract such as the small bowel, and this may need further medical or surgical treatment. Patients with intestinal resections

for Crohn's disease can develop malabsorption, typically of vitamin B12, bile salt diarrhoea, and short bowel syndrome.

- 4.6. Patients who have had colitis (ulcerative colitis or Crohn's colitis) for more than 10 years, have an increased risk of developing colorectal adenocarcinoma. This risk is greatest if the whole colon is, or has been, affected by the colitis. For this reason, patients with colitis are recommended to undergo regular colonoscopy every 1-3 years, the frequency of screening depending upon how long they have had colitis and how much of the colon is affected.<sup>10</sup>
- 4.7. A large amount of research is being carried out examining genes linked to IBD. In years to come it may be common for genetics to be used to screen family members for the potential to develop IBD, to give an indication of prognosis once the condition develops, and to provide specific targets for gene therapy.
- 4.8. More data may become available regarding the role of gut flora in the development of IBD and any benefits to be derived from changing this flora using probiotics and prebiotics.
- 4.9. Work is ongoing in the development of more specific therapy for IBD, which is difficult to treat, particularly for Crohn's disease.

## 5. Summary

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- 5.1. Inflammatory bowel disease is a combined term for ulcerative colitis and Crohn's disease. Both are relapsing and remitting conditions, with unclear aetiology. It is thought they require a combination of genetic and environmental factors to develop.
- 5.2. Ulcerative colitis affects only the large bowel and inflammation is only in the mucosa.
- 5.3. Crohn's disease can affect any part of the gastrointestinal tract and is often patchy. Inflammation involves the whole thickness of the bowel wall.
- 5.4. Symptoms vary markedly depending on the severity of disease and the part of the bowel that is affected.
- 5.5. Treatment is usually with drugs. These aim to keep the IBD in remission but do not often get rid of it completely. Often, patients can have occasional exacerbations or "flares" of disease despite their treatment, but these usually settle with steroids.
- 5.6. Surgery is reserved for severe colitis not responding to maximum drug therapy and to special situations in Crohn's disease.

## **6. Related Synopses**

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Irritable Bowel Syndrome

Colorectal Cancer

## 7. Glossary

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5-aminosalicylates (5-ASAs)	Group of drugs most commonly used in the treatment of IBD.
amoebiasis	A cause of diarrhoea among travellers to developing countries. It is caused by the parasite <i>Entamoeba histolytica</i> .
azathioprine	A drug used to suppress the immune system and reduce inflammation.
colectomy	Surgical removal of the colon.
colitis	Inflammation of the colon.
fistula	Abnormal communication between two hollow organs, or one hollow organ and the skin.
fulminant colitis	The most severe manifestation of colitis.
gut flora	The bacteria that are found in a normal intestine.
ileo-anal pouch	An internal reservoir formed after colectomy to store faeces.
ileostomy	A stoma (surgically created opening) where the ileum drains into a bag attached to the abdominal wall.
immunosuppressant	Type of drug developed to diminish the immune response in order to reduce inflammation caused inappropriately, for example, in IBD.
non-steroidal anti-inflammatory drugs (NSAIDs)	A group of drugs that inhibit inflammation but are not steroids. Examples include ibuprofen and diclofenac.
mucosa	A membrane that lines a body cavity and is covered in mucous, a smooth, slimy fluid composed of secretions, white blood cells, desquamated cells, and various salts. Hence: <i>mucosal</i> .
osteoporosis	Thinning of the bones, which increases the risk of fractures.
perforation (bowel)	The creation of a hole in the bowel. In IBD, this is a result of the inflammation present.
perianal	Area around the anus.

## 8. References

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