NHS
Liverpool University Hospitals
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Patient information

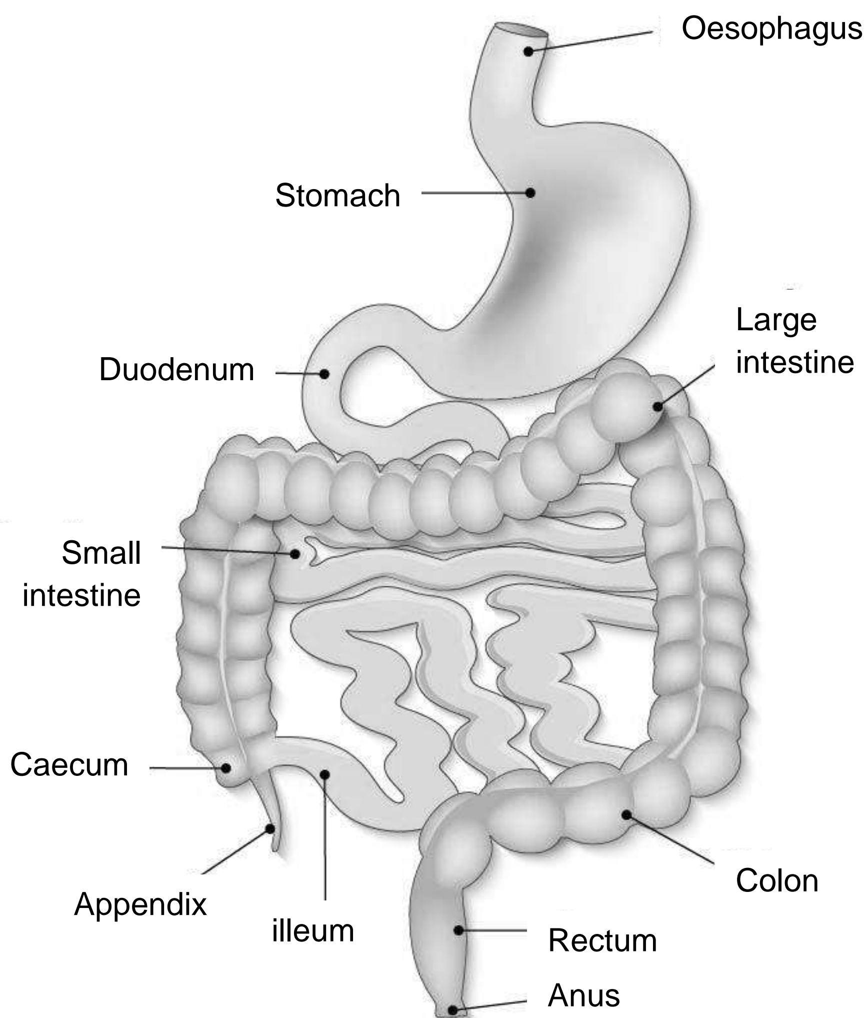
Inflammatory Bowel Disease and Crohn’s Disease

Digestive Diseases Care Group

This fact sheet has deliberately been written in some detail and gives honest information without falsely optimistic “gloss”. It may provide more information than some patients will require and it is important to note it in no way replaces further discussion or queries, in the clinic or with a specialist nurse.

What is Inflammatory Bowel Disease?

This is a term used by doctors to refer to two conditions: ulcerative colitis and Crohn’s disease. They are associated with inflammation of the colon or intestines and are not obviously associated with infections such as Salmonella or Campylobacter. Although there is some overlap between ulcerative colitis and Crohn's disease, for the purposes of this fact sheet we will consider them separately.



Is inflammatory bowel disease a form of cancer?

No. Cancer is caused by a series of changes (mutations) in the DNA of your body's cells. Ulcerative colitis and Crohn's disease are caused by continual inflammation. Statistically, there is an increased risk of cancer, and for this reason you are likely to be offered regular colonoscopic examinations if you have had colonic disease for more than 10 years.

How do the bowel symptoms differ from Irritable Bowel Syndrome (IBS)?

Irritable Bowel Syndrome is a combination of:

- Colicky stomach pain
- Distension (swelling)
- A change in bowel habit
- Alternating constipation and diarrhoea.

Although its cause is not well understood, it tends to be associated with stress and is not associated in most cases with any inflammation of the colon or intestine.

Ulcerative colitis is usually associated with persistent diarrhoea, often with blood, and is fairly easy to distinguish from the diarrhoea of IBS, which is nearly always intermittent and non-bloody.

The symptoms of Crohn's disease do however closely mimic those of patients with IBS. This often results in a delay in diagnosis since IBS affects about one in three of the population at some time or other whereas Crohn's disease only affects about one in one thousand.

Both ulcerative colitis and Crohn's disease are associated with an increased tendency to develop IBS, which can often cause persistent symptoms for a few months after an attack of inflammatory bowel disease has resolved. It is also possible to have both IBD (Ulcerative colitis or Crohn's Disease) and Irritable Bowel Syndrome at the same time.

Crohn's Disease

What is Crohn's disease?

Like ulcerative colitis, it is a relapsing inflammation of the bowel in which no known pathogenic "food poisoning" bacterium can be found and which, unlike ulcerative colitis can affect any part of the intestine from mouth to anus.

Its other name used to be "regional enteritis" but this was such a mouthful (and in some cases inaccurate) so the disease became named after the first author on the first American paper to describe the disease.

A Scot called Dalziel had actually described it earlier but the Americans failed to notice that.!

Symptoms of Crohn's disease:

Abdominal pain present in 85% of patients with active disease

Diarrhoea	62%
Weight loss	50%
Vomiting	48%
Fever	41%
Sweating	14%
Bleeding	13%

Tiredness – this non-specific symptom is very common in anyone with active or inactive Crohn's disease

What is Crohn's disease caused by?

It seems to result from a combination of genetic and environmental factors. If you have an identical twin with Crohn's disease, you have about a one in two risk for developing the disease, and the genetic factors are stronger for this disease than for ulcerative colitis.

One of the genetic factors has recently been identified. It is an alteration in a gene called Nod2, which makes a protein that is found in a type of white blood cell called a macrophage. It is involved in regulating the inflammatory response to bacteria. About 29% of Crohn's disease patients have this altered gene compared with only 7% of the general population.

It is important to note that only one per thousand of the general population gets Crohn's disease, so other environmental or genetic factors must be important in determining whether or not someone with an altered Nod2 gene gets Crohn's disease. There are several other genes which regulate the immune system that are also affected in Crohn's disease (e.g. autophagy)

Crohn's disease has been getting commoner throughout the twentieth century so it is reasonable to assume that the relevant environmental factors are also factors that have been more common during that period. The only environmental factor that has been clearly identified is smoking. About two thirds of Crohn's disease patients smoke, compared with about one third of the general population.

Patients who smoke are 40% more likely to relapse after surgery for the disease and are more likely to get some of the more unpleasant complications such as abscess or fistula formation (see later). If you currently smoke, then it is no exaggeration to say that stopping smoking is likely to be at least as beneficial to your health as any available medication.

What about measles and MMR vaccination?

A group of researchers at the Royal Free hospital in London have suggested that vaccination, particularly with the combined Measles, Mumps, Rubella (MMR) vaccine is associated with an increased risk of subsequent Crohn's disease or autism.

Researchers in many other centres have failed to confirm this either on the basis of finding measles or vaccine virus within Crohn's disease tissue samples or on the basis of follow-up studies of people who have been vaccinated. We think the association is extremely unlikely.

What about Mycobacteria in milk?

This story has a little more support as Crohn’s disease is quite similar to tuberculosis of the intestine and it is possible to find small numbers of a species of mycobacteria called Mycobacterium paratuberculosis in milk.

However, again the positive evidence comes mainly from one centre in London and there is a large amount of negative evidence from many other centres where meticulous studies using the latest DNA technology as well as conventional microbiological techniques have failed to find the bacteria in Crohn's disease tissue. At present, it seems highly unlikely that this bacterium has a major if any part in Crohn's disease.

What about other bacteria?

There is a general acceptance that both Crohn’s disease and ulcerative colitis are related in some way to the "normal" bacteria" which are so plentiful in all our colons. Several studies Liverpool suggest a form of E coli (unrelated to the “hamburger bug” and lacking known pathogenicity ("harmfulness") genes may be contributing to the inflammation.

Will I need surgery?

About 90% of patients with Crohn's disease need surgery at some time. Although surgery does not guarantee cure it can be very effective, particularly if the disease is confined to a short length of the lower small intestine (ileum).

The operation that can then be performed is to remove the lower ileum and the first part of the colon (a right hemicolectomy). This can nearly always be performed without any need even for a temporary bag or stoma. It may be followed by mild diarrhoea but this is usually easily treatable.

Surgery can sometimes by performed by “keyhole surgery” in which case there is a small scar similar to that following appendix removal. Following this operation about 50% of patients have five years without any symptoms even if they have no medication.

Will Crohn’s disease shorten my life?

It is not likely to, but because it can affect any length of the intestine there is a small excess mortality that is mainly associated with very extensive disease. Because of this, there is likely to be some impact on life insurance but different firms vary enormously in their approach to this. We advise you to seek advice from the National Association for Colitis and Crohn's disease (address at end of document) before approaching an insurance company if possible.

Will it stop me working?

Most patients with Crohn's disease are able to work most of the time, but there are likely to be some periods when you will not be fit enough to work particularly if you need surgery.

Because the disease is uncommon (1 in 1000 of the population), employers may have very little knowledge of it. If you have difficulties with an unsympathetic employer please discuss this with the doctor in clinic as we can often help by explaining to the employer the good long term prognosis for health and employment. Published studies show that patients with Crohn’s disease tend to take no more days off work with ill health than “healthy” controls.

Will it stop me from having children?

Fertility is reduced slightly in women with Crohn's disease but most patients have no particular difficulty with conception or pregnancy. It is advisable to avoid conception until the disease is under good control.

Pain during intercourse may be a problem in about 10% of women with Crohn’s disease due to inflammation in bowel. Delivery might have to be by caesarean section if Crohn’s disease has affected the tissues around the anus.

Can other organs be affected apart from the intestines?

It is common for joints to be painful or even swollen if the disease is active. This settles when the underlying Crohn’s disease is brought under control and does not lead to any long-term damage. A rare chronic joint disease called Ankylosing spondylitis in which the spine becomes very stiff is more common in people with Crohn's disease, but the risk for this is nevertheless very low.

Painful red skin lumps "erythema nodosum" are quite common when the disease is active. Again, these settle with effective treatment of the underlying Crohn’s disease. They usually heal without any lasting problems but may cause slight staining of the skin like a bruise.

Eyes may become red and sore in association with activity of the bowel disease but this again is not associated with any long-term eye problems and resolves when the underlying Crohn’s disease is effectively treated.

Will I pass it on to my children?

The risk is very low. About one in fifty children or siblings (brothers or sisters) of Crohn's disease sufferers will have the disease compared with about one per thousand of the general population.

Is Crohn’s disease associated with any cancer risk?

Crohn's disease of the ileum (small intestine) is not associated with any increased risk for colon cancer but extensive Crohn’s disease of the colon is associated with about a five-fold increased risk, which amounts to about a 15% lifetime risk.

It has recently been shown that this can probably be reduced by about three quarters by regular therapy with 5-aminosalicylate preparations such as Asacol and this is a good reason for continuing with these even though they are not very effective at treating the disease.

Can I take the oral contraceptive pill?

Yes, but with reservations. The pill might not be so effective if you have extensive disease and cannot absorb it so well.

There is a slight but definite increased risk for deep vein thrombosis in Crohn’s disease (and ulcerative colitis). There is some rather weak evidence that the pill might make Crohn’s disease worse or perhaps even cause occasional cases of Crohn’s disease, particularly of the colon.

If you are under 30, have no family history of deep vein thrombosis and do not have troublesome colonic disease, the pill will probably be okay but otherwise it may be better to take alternative forms of contraception if possible.

What about hormone replacement therapy (HRT)?

There is little evidence to suggest that HRT is bad for Crohn's disease and osteoporosis is quite common in Crohn's disease. Providing you have no past or family history of thrombosis, HRT may be beneficial.

How do I avoid osteoporosis?

Osteoporosis is thinning of the bones and it increases the risk for fracture, being one of the main causes for fracture of the hip. It can also result in extremely painful collapse of vertebrae in the spine.

There is some increased risk of osteoporosis associated with Crohn's disease if this affects the small intestine (ileum).

The biggest risk factor however is the use of steroids, whatever the underlying disease. Maintenance (long term) steroids are not very helpful in Crohn's disease and are usually avoidable.

Regular prolonged use over many months of more than the equivalent of 7.5 mgs per day of prednisolone is likely to lead to osteoporosis. The degree of osteoporosis is closely related to the total lifetime dose of steroids.

A new steroid preparation, budesonide, is associated with about one half of the risk of steroid side effects and is increasingly used in the treatment of Crohn's disease.

In ulcerative colitis, the risk of osteoporosis is much less and prednisolone is usually used. Post-menopausal women are particularly at risk of developing osteoporosis and in this situation hormone replacement therapy (HRT) is often the best way of preventing further bone thinning. However, the risks and benefits of HRT need to be discussed with your GP.

It is sensible for anyone with small intestinal Crohn's disease or who has had previous small bowel surgery to take regular supplements of calcium and vitamin D. Your doctor can prescribe these.

If osteoporosis is more severe, then the bone thinning can be halted and sometimes reversed by the use of a class of drug called bisphosphonates. These are usually taken orally. The diagnosis and assessment of severity of osteoporosis is made by a low intensity X-ray called a Dexascan.

Crohn's Disease and Drug Therapy

Steroids

Corticosteroids are the most widely used first medication for symptomatic Crohn's disease. They provide good relief of symptoms for an initial three month period in about two thirds of patients. However, they do not achieve healing of ulcerated small intestinal mucosa, and they have been shown to have no effect on the long-term natural history of the disease. Their use is associated with considerable risk of bone thinning (osteoporosis).

The two main types of steroid medications are Prednisolone and Budesonide. Budesonide typically has fewer side effects as most of the medication distributes itself within the gut.

Can I avoid steroids?

Increasingly, yes. The benefits from steroids are much less impressive in Crohn's disease than ulcerative colitis. Although they are a simple way of relieving symptoms in the short term (e.g. for about three months), they have no beneficial effect in the long term and we are increasingly looking towards other forms of therapy. These include antibiotics, dietary therapy, the immunosuppressive drug Azathioprine (which also has some antibiotic effects) or finally biological drugs such as infliximab, adalimumab and vedolizumab.

Azathioprine and 6-mercaptopurine

These related drugs have been shown to be effective at maintaining remission in Crohn’s disease and at inducing healing of ileal ulcers. They are not tolerated in approximately 20% of patients because of side effects, which include:

- Nausea
- Liver toxicity
- Fever
- Pancreatitis
- Bone marrow suppression.

Monthly blood count monitoring is recommended because of the risk of bone marrow suppression. There is some evidence that Azathioprine therapy may allow fistula healing. There is a very slightly increased risk of certain type of cancers such as lymphomas and non-melanoma skin cancers. The risk is exceedingly small.

Methotrexate

Experience with Methotrexate is limited compared with that of Azathioprine but carefully conducted controlled trials have shown that weekly Methotrexate therapy is effective and this is now an acceptable strategy in patients who cannot take azathioprine/6-mercaptopurine. **It must be avoided in pregnancy.**

5-aminosalicylates

There is some evidence that high doses (at least 3g/day) of 5amino-salicylates such as Pentasa may reduce recurrence rates after surgery for Crohn’s disease but this class of drugs otherwise has limited efficacy in Crohn’s disease. Statistical reviews suggest that 5-aminosalicylates taken as maintenance therapy probably only reduce the relapse rate by about 5% compared with placebo (i.e. “dummy” tablets).

Antibiotics

There is evidence from controlled trials that Metronidazole is effective for colonic Crohn’s disease and for preventing post-operative recurrence. Otherwise, there is no controlled evidence for the efficacy of antibiotics in Crohn’s disease.

There is however a rapidly growing amount of uncontrolled evidence (i.e. evidence from series of treated patients but without comparison with placebo) and many physicians are using antibiotics such as Ciprofloxacin or Clarithromycin as first line treatment for patients with or without evidence of sepsis.

Can antibiotics help?

We are now conducting a controlled trial targeting E. coli bacteria using a combination of antibiotics (ciprofloxacin and doxycycline) and an anti-malarial medication called hydroxychloroquine. This combination has been shown to kill E. coli very effectively in the laboratory.

The antibiotic Metronidazole, which is effective against the types of bacteria, which live in environments that lack oxygen, is effective therapy for colonic Crohn's disease and for infections around the anus.

Can these antibiotics be taken long term?

Metronidazole may need to be taken for up to three months to have its best effect on colonic disease and it is sometimes used for a similar period following Crohn's disease surgery.

Longer periods of use are associated with a risk of nerve damage (the first symptom of which is numbness of the fingers). If this occurs, the drug must be stopped. Providing it is stopped promptly recovery of nerve function is usually complete.

Metronidazole must be avoided in pregnancy or if there is any risk of pregnancy.

Antibiotics such as doxycycline and ciprofloxacin cause sensitivity to sunlight.

Anti-TNF (tumour necrosis factor) drugs (Infliximab and adalimumab)

The anti-TNF agents are relatively newer treatments. They are genetically engineered antibody proteins directed against an inflammatory protein called TNFalpha.
They are arguably the most effective therapy for Crohn's disease in terms of its combination of speed of response, percentage response, and ability to heal mucosal ulceration.

It is also unarguably the most expensive! A single infusion of Infliximab (which currently costs about £1500 for an average-sized adult) induces a response that usually lasts for about eight weeks.

However, more recently several manufacturers have started making copies of infliximab (called biosimilar drugs) which are slightly cheaper than infliximab. They are otherwise identical and may be substituted for infliximab. Infliximab is given intravenously while adalimumab can be self-injected under the skin much like insulin injections. There are also some structural differences. Infliximab is made of 25% mouse protein whereas adalimumab is more human-like.

Repeated therapy has been shown to be effective at maintaining this response but it does not provide a permanent cure. If therapy is repeated after a delay, an antibody response occurs against the Infliximab which may cause a febrile reaction (usually not severe) but which also probably negates the therapeutic effect of the antibody. Concomitant prescription of Azathioprine has been shown largely to prevent the development of this antibody response.

Infliximab therapy is associated with fistula healing in about two thirds of patients but this is temporary and most fistulae break down again after the therapy is stopped. The chance of getting antibodies with adalimumab is lower.

Short-term safety seems excellent and is backed up by a large database. The main concerns are re-activation of tuberculosis and a risk of infections such as pneumonia.

It is therefore important to obtain a clear tissue diagnosis of Crohn's disease (and lack of tissue evidence of tuberculosis), plus a normal chest X-ray, before anti-TNF therapy is commenced.

There are several other uncommon side effects such as a lupus like illness and occasionally nerve problems involving the central nervous system (demyelination). Fortunately, these problems are rare.

Which patients should receive anti-TNF therapy?

It is broadly used in patients whose symptoms are not readily treatable by Azathioprine, antibiotics or primary surgical resection of narrowed bowel. Patients who are not suitable include patients who are suspected of having significant sepsis e.g. abscess, patients with significant bowel narrowing e.g. recent or current presentation with sub acute intestinal obstruction. It is estimated that it might be appropriate therapy for about 10-20% of patients with Crohn's disease.

Vedolizumab:

The more recently approved biological drug called vedolizumab works by blocking white cells from entering the gut and causing inflammation. This is an intravenously administered drug which works exclusively in the gut. At present, its use is restricted to patients who have failed anti-TNF therapy. The main side effects with this drug appear to be nasopharyngitis (sore throat) and perhaps an increased risk of gastrointestinal infections.

What about diet?

We know there must be a link between Crohn's disease and diet since the disease often goes into remission if food is avoided and replaced by liquid feed. We still do not understand the mechanism for this.

Research in Liverpool and other centres has shown that the explanation is not due to simple avoidance of foreign protein. Continuing research is investigating the possibility that one or more food additives might be harmful. Suspects include a white pigment called titanium dioxide (E171) and/or exposure to detergents or permitted emulsifiers. There is clear evidence that Crohn's disease has become much more common in the past 50 years and food additives would certainly fit with this.

"Enteral feeding" i.e. feeding with a liquid feed may be effective treatment if you have a relapse of your disease. Although it is not brilliantly palatable and clearly rather inconvenient it is at least without risk of side effects. It is a particularly effective and safe form of therapy for children or adolescents with Crohn's disease where growth failure may be a problem if other therapies are used.

Enteral feeding with liquid diets

There is evidence that about two-thirds of patients with small bowel Crohn's disease can be brought into remission if their normal diet is replaced by a liquid feed. This has to be either an amino-acid based feed or a polymeric (whole protein or peptide-based) feed that has been shown to be effective since some polymeric feeds are strangely ineffective. These have to be prescribed by your doctor. The mechanism for this therapeutic effect is still unclear. Enteral feeding has been shown to induce healing of ileal ulcers and is free from side effects other than lack of palatability.

About two thirds of adult patients are able to tolerate the feed with a flavouring such as Nesquick (children often tolerate it better!).

What is on the horizon?

There are several treatments which have shown preliminary promise and are currently undergoing further trials. These include another biological drug called ustekinumab (which is already used in psoriasis) and Mongersen. Mongersen has shown preliminary promise and is undergoing testing in a much larger group of patients with Crohn’s disease.

General issues

Insurance

Life expectancy is normal in ulcerative colitis. There is an increase in risk of death from bowel cancer, but this is offset by a reduced risk of death from coronary artery disease, which is probably not due simply to the curious association between colitis and non-smoking. Life insurance ought to be fairly easy and straightforward to arrange. However, not all insurance firms are equally enlightened and it is well worth seeking advice on this from NACC (see below) if you are having any difficulty.

There is probably a slight reduction in average life expectancy in Crohn’s disease although this has improved greatly over the past thirty years. This is due to better surgical techniques, and many of the published data is now out of date.

Reduced life expectancy is related mainly to a very small minority of patients who have widespread small bowel disease. The risk therefore varies considerably from one patient to another.

Sex life

Any illness can reduce your sex drive (libido) and treatment should aim to keep the disease in remission so that this does not occur.

Crohn’s disease can cause unpleasant abscess formation and scarring around the anus and fistulae (development of a false passage) from the bowel to the vagina can rarely occur. These problems can usually be reduced, if not completely settled with a combination of medical and surgical treatments.

Fertility

This is usually normal in ulcerative colitis but may be slightly reduced in Crohn’s disease, particularly if surgery has been necessary. This is due to involvement of the fallopian tubes in the inflammation; these are the passages along which the ova (eggs) pass on their way from the ovaries to the uterus (womb)

The drugs used in inflammatory bowel disease do not themselves reduce fertility with the exception of Sulphasalazine, which causes reversible (and unreliable!) male infertility (see earlier).

Colectomy carries a small risk of causing male impotence (less than 3%). Any woman who has had a Colectomy and ileo-anal pouch (Parkes’ pouch) will usually be advised to give birth by Caesarean section because of the need to avoid any risk of damage to the rectal sphincter muscles.

The formation of an ileostomy or colostomy stoma should cause no significant practical problems although it may cause embarrassment and some psychological difficulties. In general though, when a patient is in a long term, stable relationship, any problems are usually manageable.

Pregnancy and breastfeeding

We often get asked about whether or not medications could be safely continued during pregnancy and breastfeeding.

There has been a few high quality studies which have shown that it is safe to use medications such as azathioprine and anti-TNF Treatments. We stop the anti-TNF treatment after 24 weeks and restart it after the baby is born. You could discuss this in detail with the maternal medicine specialist and your IBD specialist.

If you would like to speak to someone confidentially about anything concerning you, please speak to:

- A member of the clinic nursing staff
- The Gastroenterology Specialist Nurse.

Feedback

Your feedback is important to us and helps us influence care in the future.

Following your discharge from hospital or attendance at your outpatient appointment you will receive a text asking if you would recommend our service to others. Please take the time to text back, you will not be charged for the text and can opt out at any point. Your co-operation is greatly appreciated.

Further information

Inflammatory Bowel Specialist Nurses
Tel: 0151 706 2659
Text phone number: 18001 0151 706 2659

Email: IBDnurses@rlbuht.nhs.uk

Website: crohnsandcolitis.org.uk/mersey

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All Trust approved information is available on request in alternative formats, including other languages, easy read, large print, audio, Braille, moon and electronically.

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