



Crohn's Disease

Crohn's disease is a chronic inflammatory bowel disease (IBD) that can affect any area of the gastrointestinal tract, from the mouth to the anus, either in continuity or as isolated areas. The inflammation can involve the inner mucosal lining, up to the full thickness of the bowel wall, and consists of swelling, dilated blood vessels, and loss of fluid into the tissues. It often occurs at the lower end of the small intestine (terminal ileum), which joins with the large intestine (colon).

Crohn's disease can arise at any age, commonly occurring in young people. About 10% of newly diagnosed cases each year are in children. Although there are various treatments to help ease symptoms and induce remission, there is currently no cure. There is an increased risk of a Crohn's disease diagnosis for some ethnic groups, and for those who have a family member with the condition. Although Crohn's disease is currently the proper name for the condition, sometimes you might hear older terms, such as regional enteritis, terminal ileitis, granulomatous colitis, or ileocolitis, used interchangeably.

Crohn's disease has many similarities to ulcerative colitis, another IBD. The main differences between Crohn's disease and ulcerative colitis are that in Crohn's disease inflammation can affect any part of the digestive tract and extend into the muscle wall, whereas ulcerative colitis occurs only in the surface of the colon lining.

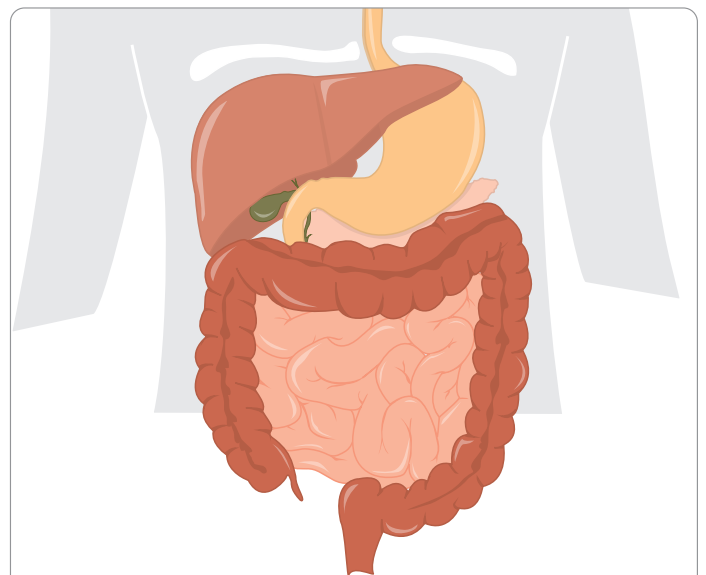
The cause of Crohn's disease is undetermined but there is considerable research evidence suggesting that interactions among environmental factors, intestinal microorganisms, immune dysregulation, and genetic predisposition are responsible.

A diagnosis of Crohn's disease can occur at any point in life, with the highest occurrence of diagnoses in young children and for those around 40-50 years of age. Currently, Canada has among the highest prevalence and incidence reported in the world, with an estimated 161,000 diagnosed individuals.

Symptoms/Complications

Diarrhea, rectal bleeding, pain, and weight loss are common recurring symptoms of Crohn's disease. Inflammation decreases the intestine's absorptive surfaces, triggering watery stools that can lead to fecal urgency and poor control of bowel function. Constipation can also develop, as the body struggles to maintain normal bowel function.

The intestine may narrow and shorten, whereby contents cannot completely pass through the digestive tract (obstruction). Abdominal pain is a frequent symptom, resulting from the muscle spasms of the inflamed intestine, or from a build-up of pressure behind a narrowed section of the bowel. Fever may accompany the inflammation. In children, a delay in growth and



Crohn's disease can affect any area of the digestive tract, from the mouth through to the anus. It even affects other parts of the body.

maturity may result, so close attention to medical and nutritional management of the disease is particularly important.

Low red blood cell count (anemia) can result from blood loss due to ulcerations in the intestine and from general malnutrition due to decreased nutrient absorption and the debilitating effects of the disease. These conditions may also cause depletion of blood proteins.

Fissures may form in the rectum and anus, producing an accumulation of large pus pockets or abscesses, leading to severe pain and fever. An abnormal, tunnel-like connection between the intestine and the skin (fistula) may occur near the opening of the rectum, between loops of intestine within the abdomen, or between the intestine and the abdominal wall, particularly following surgery.

Crohn's disease is a systemic disease, meaning that it affects other parts of the body in addition to the intestinal tract. Some of these extra-intestinal manifestations include arthritis, skin problems, liver disease, kidney stones, and eye inflammation.

You may be at an increased risk for colorectal cancer if you have disease located within the colon for 10-15 years or more. If this is the case for you, regular screening should begin at an earlier age and on a more vigilant schedule than that recommended for the general population.

Diagnosis

Blood tests are helpful in assessing the activity level of the inflammation, the potential of developing anemia from ongoing bleeding, and the nutritional state of an individual.

Stool sample analysis can sometimes be helpful. Your physician will determine which among several procedures are best to assess your intestinal symptoms, based on your medical history.

While used less often, X-rays can be helpful to observe the shape and function of the digestive tract. When needed for the upper GI area, you will have to drink a liquid that coats the walls of the esophagus and stomach. This drink contains barium, which shows up as bright white on X-rays, providing a contrasting picture of the shape and function of the upper GI tract during the X-ray. When requested to provide details of the lower GI tract, you will undergo a barium-containing enema to allow your physician to view the contours of the bowel.

Endoscopy might help to determine the nature and extent of the disease. In these procedures, the physician inserts an instrument into the body via the mouth (gastroscopy) or anus (sigmoidoscopy/colonoscopy) to allow for visualization of various areas within the digestive tract. The scopes are made of a hollow, flexible tube with a tiny light and video camera. An advantage of these procedures over a barium X-ray or virtual colonoscopy using computed tomography (CT) scan is that a physician can biopsy suspicious looking tissue at any time during the examination for subsequent laboratory analysis.

Depending on what part of your digestive tract is affected, magnetic resonance imaging (MRI) may be useful.

Once all this testing is complete and other possible conditions are ruled out, your physician might make a diagnosis of Crohn's disease.

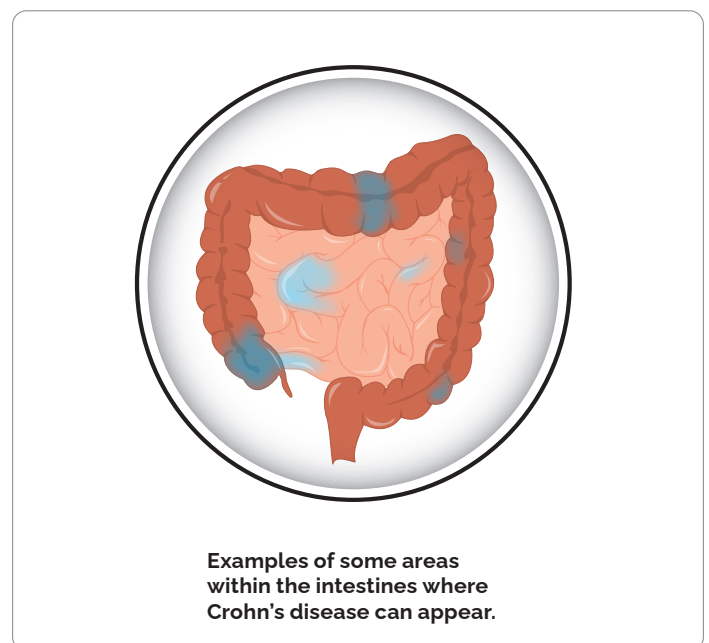
Management

The treatment of Crohn's disease is multi-faceted; it includes managing the symptoms and consequences of the disease along with therapies targeted to reduce the underlying inflammation.

Dietary and Lifestyle Modifications

Nutrition is a primary component of digestive health, and it is important to follow *Canada's Food Guide*. However, even when following these guidelines, Crohn's patients could be falling short of nutrient needs due to the effects of an inflamed intestine. Studies show that poor nutrition is prevalent in Crohn's patients, who should direct extra attention to special diets and supplements. We encourage those who have Crohn's disease to consult a registered dietitian, who can help set up an effective, personalized nutrition plan by addressing disease-specific deficiencies. If bleeding is excessive, problems such as anemia may occur, and modifications to the diet will be necessary to compensate for this.

Some foods may irritate and increase symptoms even though they do not affect the disease course. Specialized diets, easy-to-digest meal substitutes (elemental formulations) and fasting can achieve incremental degrees of bowel rest. During fasting, intravenous feeding (total parenteral nutrition, TPN) may be required to allow for complete bowel rest.



Symptomatic Medication Therapy

Several treatments exist to address diarrhea and pain. Dietary adjustment may be beneficial and antidiarrheal medications have a major role to play. Analgesics can be helpful for managing pain not controlled by drugs that address the underlying inflammation, listed below. Acetaminophen (Tylenol®) is preferred over medications called non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Advil®, Motrin®), aspirin, and naproxen (Aleve®, Naprosyn®), as they can irritate the gut.

There are two types of antidiarrheal medications directed at preventing cramps and controlling defecation. One group alters the muscle activity of the intestine, slowing down content transit. These include: non-narcotic loperamide (Imodium®); narcotic agents diphenoxylate (Lomotil®), codeine, opium tincture and paregoric (camphor/opium); and anti-spasmodic agents dicyclomine HCL and hyoscine butylbromide (Buscopan®).

The other group adjusts stool looseness and frequency by soaking up (binding to) water, regulating stool consistency so it is of a form that is easy to pass. Plant-based products are helpful such as inulin fibre (Benefibre®) and psyllium (ispaghula) husk (Metamucil®). Plant fibres are also useful to manage constipation, due to their stool regulating effects. Cholestyramine resin, a bile salt binder, can also help with stool looseness.

Extra-intestinal symptoms of Crohn's disease, such as arthritis or inflamed eyes, may require targeted medications and referrals to other specialists. If anxiety and stress are major factors, a program addressing this may be valuable. Ask for our pamphlet on *Stress Management*.

Individuals with Crohn's may be anemic from a combination of factors, such as chronic blood loss or malabsorption of certain vitamins and minerals. Iron supplements could help improve this condition, with oral heme iron polypeptide (e.g., Hemaforce I, Hemeboost, OptiFer® Alpha, Proferrin®) being the preferred option, due to quick-acting and low side-effect profiles. Iron isomaltoside 1000 (Monoferric™), iron sucrose (Venofer®), and sodium ferric gluconate (Ferrlecit®) are indicated for intravenous (IV) treatment of iron deficiency anemia in adults who have intolerance or unresponsiveness to oral iron therapy. Occasionally, a blood transfusion may be necessary.

The most widely prescribed antibiotics are ciprofloxacin (Cipro®) and metronidazole (Flagyl®). Broad-spectrum antibiotics are important in treating secondary manifestations of the disease, such as perianal abscess and fistulae.

Anti-Inflammatory Medication Therapy

There are two goals in the treatment of Crohn's disease: to eliminate the symptoms (induce clinical remission) and to prevent future disease flare-ups (remission maintenance). To

accomplish these goals, physicians aim treatment at controlling intestinal tract inflammation, and the natural consequence of reducing and eliminating inflammation is the reduction and elimination of symptoms. This therapy comes in many forms, using various body systems. Your physician may prescribe any of the following medications alone or in combination. It could take some time to find the right mix for you as each case of Crohn's disease is unique.

5-Aminosalicylic Acid (5-ASA)

These medications are used to reduce inflammation in mild to moderate Crohn's disease, including mesalamine (Pentasa® and Salofalk®), which is available orally in the forms of tablets and capsules. Depending on the location of your disease, you may be required to administer mesalamine rectally, in the forms of enemas or suppositories. A combination of 5-ASA and sulfa antibiotic is available orally as sulfasalazine (Salazopyrin®).

Corticosteroids

To reduce inflammation in moderate to severe cases of Crohn's disease, corticosteroids might help. These are prednisone and budesonide (Entocort®), which are taken orally, although prednisone tends to have greater side effects. For topical relief of Crohn's disease in the colon, budesonide (Entocort®), hydrocortisone, and betamethasone are available in rectal formulations (enemas, foams, and suppositories). In hospital, hydrocortisone (Solu-Cortef®) and methylprednisolone (Solu-Medrol®) can be administered intravenously.

Immunosuppressive Agents

SMALL MOLECULE

These drugs are used to treat both ileal and colonic Crohn's and to reduce dependence on steroids; they include azathioprine (Imuran®), cyclosporine, mercaptopurine/6-MP (Purinethol®), and methotrexate sodium (Metoject®). It could take up to 12 weeks or more of therapy to see results.

A newer class of medication, Janus kinase (JAK) inhibitors, typically work faster than biologics, pose no risk for immunogenicity, and are easy and convenient to take since they are in pill form. This includes a selective-JAK-inhibitor upadacitinib (Rinvoq®).

BIOLOGICS (LARGE MOLECULE)

Biologic medications are important treatment options for those who have moderate to severe Crohn's disease. These products are specifically developed proteins that selectively block molecules involved in the inflammatory process. Gastroenterologists routinely prescribe biologics to reduce inflammation and control the symptoms (induce clinical remission) of Crohn's disease.

The first biologic that Health Canada approved to treat Crohn's disease was the anti-TNF agent infliximab (Remicade®) in 2001. Later biologics include an anti-TNF agent, adalimumab (Humira®), an alpha-4/beta-7 integrin inhibitor, vedolizumab (Entyvio®), an IL-12/23 inhibitor, ustekinumab (Stelara®), and an IL-23 inhibitor, risankizumab (Skyrizi®). As the patents expire for these medications, their biosimilars come to market. So far, there are biosimilars of infliximab (Avsola®, Inflectra®, Ixifi®, Omvyence™, Remsima™SC, Renflexis®), adalimumab (Abrilada®, Amgevita®, Hadlima®, Hadlima® PushTouch®, Hulio®, Hyrimoz®, Idacio®, Simlandi™, Yuflyma™), and ustekinumab (Wezlana™). See our website for more information about biosimilars

These medications are proteins, which our bodies might identify as foreign invaders and then develop antibodies to fight them off, which can diminish the drug's effectiveness over time. If you stop taking the drug for some time and then try to resume it, what worked wonderfully for you before might not work the next time you take it because of these antibodies. This means that it is extremely important that you only stop treatment if your physician advises you to do so. Stopping a treatment because you are feeling well might result in that drug not working to make you feel well again.

Currently, Humira® (and its biosimilars), Entyvio®, Stelara® (and its biosimilar), and Skyrizi® are available for self-administration under the skin (subcutaneous). Remicade® (and its biosimilars, except Remsima™SC), Entyvio®, Stelara®IV, and Wezlana™IV are available as intravenous (IV) infusion by a healthcare professional. The dosage of both types can be in various intervals, depending on the medication and the response. In some cases, you might need to start on a biologic medication by receiving it as an IV infusion and then move on to subcutaneous injection for maintenance.

One tool to help physicians be sure that patients are on the right medication at the right dose is Therapeutic Drug Monitoring (TDM), which involves laboratory testing to determine the level of the drug in the system. A second vital test is fecal calprotectin, which measures an inflammatory substance in your stool. A gastroenterologist assesses these results in the context of a person's symptoms at specific periods during the treatment schedule. See our video explaining TDM at www.badgut.org/tdm.

Surgery

Sometimes a surgeon will remove severely diseased portions of the digestive tract, but this is only as a last alternative, usually in cases where medical management fails and complications arise, such as obstruction, strictures, and fistulae, or abscess formation. An unfortunate feature of Crohn's disease is that there is a high recurrence rate, even after surgical removal of

all visible and microscopic disease. Therefore, it is pragmatic to treat Crohn's disease with the most effective therapies to prevent these complications. Even though most physicians are slow to recommend surgery, there are times when it will be required. An emerging surgical therapy is intestinal transplantation, but there are barriers yet to overcome, such as tissue rejection and inflammation in the newly transplanted organ.

What is a Flare?

When you have Crohn's disease, your physician will try to find the right medications to control your symptoms. However, since there is no cure, the systemic disease is always there. When the symptoms aren't present, you are in **remission**. If the symptoms return, especially if they are worse than before, it is a **flare**. This is why it is important to continue taking any medications your doctor prescribes, even if you feel better. If you stop taking your medication, then you can increase your chance of experiencing a flare and progression of the disease. Infections, stress, and taking antibiotics or NSAIDs (including aspirin, ibuprofen, and naproxen) can also make you more susceptible to a flare.

When to Get Treatment

An increase in inflammation causes a flare, and the nature of inflammation means that you should treat it as quickly as you can. Inflammation grows exponentially because inflammation itself causes an increase in inflammation. The longer you leave it untreated, the worse it will get. Pay attention to your symptoms and visit your physician if you notice that they change or increase even a small amount.

Flare Treatment Options

Particularly if you are seeing a gastroenterologist who has a long waiting time to get an appointment, it is important to discuss with your physician in advance exactly what he or she would like you to do if the disease flares. You might be taking medication regularly but still experience a flare. Even if you have a plan in place, you should still call your physician's office to report your symptoms. This is an important conversation to have with your healthcare team, so you can prepare for self-management, when necessary, while keeping them aware of your condition.

Your specific situation and history will determine what your physician recommends.

Is it important to treat a flare early, or is it ok to wait a bit?

Inflammation typically does not resolve without treatment and early intervention has a better outcome than waiting to treat. At an early stage of a flare, a more optimal baseline (5-ASA) treatment might be enough to get the inflammation under

control. If you wait, there is a greater risk that you might need drugs with greater side effects, such as oral steroids. By waiting, you will have to manage longer with your symptoms before getting relief. Living with constant or longer periods of inflammation might increase your risk for future complications, as inflammation might cause damage to the gut wall that accumulates in severity with each flare.

If you are experiencing worsening symptoms, you have probably already had the flare for some time without symptoms. Evidence shows that a stool test for inflammation in the colon, called fecal calprotectin, is often elevated for two to three months before any symptoms appear. Your intestine might also start to show visual (during a scope) evidence of inflammation before you have symptoms, or at least indicate an increased risk for a flare.

Looking into the digestive tract gives a better, more reliable picture of what is truly going on with your disease. For this reason, your specialist might suggest a colonoscopy so he or she can have a closer look inside your colon to determine the best course of action. However, in most instances, a physician might still base a decision to prescribe medication on the severity and the nature of your symptoms. This is particularly the case when the symptoms are still mild.

Action Plans

Want to learn more about managing flares? We have printable Action Plans available for both Crohn's disease and ulcerative colitis. These documents outline which symptoms are normal, which indicate a flare, and which require emergency care. They also contain spaces to write in details about your medications, disease status, and healthcare team contact information. Go to www.badgut.org/ibd-flare-video to download the Action Plans and watch a short video with more information about flares.

Outlook

Crohn's disease is a chronic inflammatory condition manifesting primarily in the digestive tract. Because there is no cure, you will require continuing medical care. Those with Crohn's disease must adhere to a specific nutrition and medication regimen, even when things appear to be going well. Your physician will monitor your disease regularly, even during periods of remission. For more information about living with Crohn's disease, see www.badgut.org/crohns-disease-patient-journey-video.

About the Gastrointestinal Society

The GI (Gastrointestinal) Society is a registered Canadian charity committed to improving the lives of people with gastrointestinal and liver conditions, supporting research, advocating for appropriate patient access to healthcare, and promoting gastrointestinal and liver health.

Want to learn more on this subject? The *Inside Tract*®, the GI Society's quarterly newsletter, provides the latest on digestive and liver research, disease and disorder treatments (e.g., medications, nutrition), and a whole lot more. If you have any kind of digestive problem, then you will want this timely, informative publication. **Subscribe today!**

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