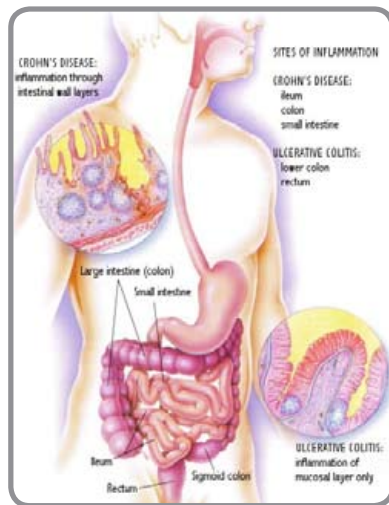


Crohn's Disease

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Crohn's Disease is an inflammatory condition of the digestive tract that affects children and adults. The cause of Crohn's disease is unknown. Common features of Crohn's disease include mouth sores, diarrhea, abdominal pain, weight loss, and fever. Patients can also have problems outside of the digestive tract, including a skin rash, joint pain, eye redness, and, less commonly, liver problems.

Although Crohn's disease is usually chronic, medical and surgical treatment can help control the course of the disease, allowing many patients to experience long periods of symptom-free remission.



*Crohn's Disease
compared to
Ulcerative Colitis*

Most cases of Crohn's disease primarily affect the terminal ileum (a region of the small intestine) and the colon, producing ileitis (inflammation of the ileum) and colitis (inflammation of the colon). Inflammation in these areas can lead to the formation of abnormal passages (fistulas), perforation of the intestinal wall, or narrowing of the digestive tract (stricture) and obstruction. Crohn's disease can also affect the perianal area, producing fissures, ulcers, pockets of pus (abscesses), and fistulas.

Crohn's Disease Medications

Many different drugs are used to treat Crohn's disease. The choice of medications will depend upon the area of the digestive tract affected by the disease and the symptoms. The following is a summary of commonly used medications.

Sulfasalazine — Sulfasalazine was one of the first drugs used to treat Crohn's disease and is still used for treating Crohn's disease that is restricted to the colon. Sulfasalazine usually begins to reduce symptoms within a few days, but its full effect may require up to four weeks of treatment. A problem with sulfasalazine is that it can cause an allergic reaction in a minority of patients and can cause headaches, particularly when given in high doses.

5-aminosalicylates — The 5-aminosalicylate (5-ASA) drugs (such as Asacol® and Pentasa®) are similar to sulfasalazine, but are less likely to cause headaches and allergic reactions. An advantage is that they can be given in relatively high doses compared to sulfasalazine. In addition, they are formulated to be released in the terminal ileum (with Asacol®) and throughout the small intestine (with Pentasa®). This permits the drugs to target the inflamed areas. Their major disadvantage is their relatively high cost.

Crohn's Disease Causes

The exact cause of Crohn's disease is unknown. What is known is that the disease tends to run in families and affects certain groups more than others, suggesting that genetic factors are important.

Course Of Crohn's Disease

Crohn's disease usually follows a pattern of flares (when the condition worsens) and remissions (when it improves). About 10 to 20 percent of patients will enter remission after their first flare of Crohn's disease. The pattern in other patients can be quite variable, ranging from recurrent periods (weeks to months) of symptoms such as mild diarrhea and cramping to, less commonly, severe and disabling symptoms (such as severe abdominal pain and bowel obstruction). Treatment can help drive active disease into remission and then prolong remission.

Antibiotics — Antibiotics can reduce the number of bacteria in the intestines, which can in turn reduce inflammation. The antibiotics most frequently used are metronidazole and ciprofloxacin.

Steroids — Steroids (such as prednisone and budesonide) can induce remission in patients with active, moderate to severe Crohn's disease. However, steroids do not prolong remission and there are many serious side effects of long-term steroid use.

Immunomodulator drugs — Immunomodulator drugs decrease the inflammation associated with Crohn's disease. The most commonly used drugs include azathioprine, 6-mercaptopurine, and methotrexate, although many new drugs continue to be studied and are already used occasionally. These drugs have traditionally been used for patients who have not responded to "first line" therapy with drugs such as antibiotics, sulfasalazine, and 5-aminosalicylates, particularly those who depend upon steroids to control symptoms. These drugs are also very helpful for maintaining remission.

Immunomodulator drugs take a long time (three to six months) to produce a maximal effect and are often prescribed for long-term therapy. The major side effects of these drugs include lowering of the white blood cell count (the cells that help fight off infection in the body), hepatitis (inflammation of the liver), and pancreatitis (inflammation of the pancreas). As a result, blood testing is performed regularly to monitor for these side effects.

Biologic response modifiers

Infliximab — Infliximab (Remicade®) is a medication developed for the treatment of inflammatory conditions. It contains an antibody that neutralizes tumor necrosis factor, which is believed to promote inflammation within the bowels.

Infliximab is generally reserved for patients who do not respond adequately to first line therapy with antibiotics and 5-ASA drugs. It is especially effective in patients with fistulizing Crohn's disease and those with active, moderate to severe nonfistulizing Crohn's disease.

Infliximab must be injected into a vein in a clinician's office. The second dose is given two weeks after the first, and the third dose is given four weeks later. If the initial treatment is successful, a maintenance dose is then given once every eight weeks.

Adalimumab — Adalimumab (Humira®) also uses an antibody to neutralize tumor necrosis factor. Adalimumab is approved to reduce the signs and symptoms of Crohn's disease, and also to induce and maintain remission in adults with moderately to severely active Crohn's disease who have an inadequate response to first line therapy with antibiotics and 5-ASA therapy. Adalimumab may also be used by people who have lost response to or are intolerant to infliximab.

Adalimumab is injected under the skin by the patient or a family member and therefore do not require treatment in a doctor's office. Several doses are given in the first few weeks, with the maintenance dose given every other week beginning in the fourth week.

Certolizumab pegol — Certolizumab pegol (Cimzia®) is a medication that is approved as a second-line treatment for adults with moderate to severe Crohn's disease who have not responded to other therapies. It works by neutralizing tumor necrosis factor. It is given as an injection every two weeks for six weeks, and then a maintenance dose is given every four weeks thereafter. However, there are no data about the long-term safety or efficacy of certolizumab. The most common side effects are headache, upper respiratory infections, abdominal pain, injection site reactions and nausea.

Side effects of biologic response modifiers — Biologic response modifiers interfere with the immune system's ability to fight infection and should not be used in people with serious infections. Careful screening for tuberculosis is necessary prior to starting therapy since the risk of developing active TB infection is increased. If there is evidence of prior infection with tuberculosis, treatment to prevent reactivation is recommended.

These drugs are not recommended for patients who have lymphoma or have been treated for lymphoma in the past because of the increased risk of lymphoma in some studies; more research is needed to define this risk.

Other Crohn's Disease Treatments

Dietary recommendations — It is not clear if a specific diet can improve Crohn's disease. Many such diets have been proposed although there have been few scientific studies.

Other measures

Smoking worsens Crohn's disease and should be avoided. Nonsteroidal anti-inflammatory drugs (such as ibuprofen and naprosyn) should generally be avoided since they can worsen the disease.

Surgery — Medical treatment can help control the symptoms and complications of Crohn's disease and may delay the need for surgery. Surgery is usually used as a last resort since it does not cure the disease, although in some patients it may be the fastest way to restore health. About 80 percent of patients with Crohn's disease will require an operation at some time, usually to stop bleeding, to close fistulas and bypass obstructions, and often to remove the affected areas of the intestine.

It is important to have realistic expectations of surgery. Surgery can improve a person's medical condition and can even be lifesaving. However, surgery does not cure Crohn's disease, and recurrence is likely. Between 85 and 90 percent of

patients are symptom-free during the year following surgery, and up to 20 percent of patients are still symptom-free 15 years after surgery. If Crohn's disease is confined to the colon and the colon is removed, only 10 percent of people will have a recurrence within 10 years. Prompt and long-term use of medications, started at the time of surgery, decreases the risk of recurrence.

Recurrent disease treatment — If Crohn's disease flares after a remission or surgery, it is usually treated according to the same guidelines as the initial episode of Crohn's disease. In some cases, different medications are used to treat a recurrence.

Crohn's Disease Complications

Over time, the intestinal problems of Crohn's disease and the ongoing inflammation can lead to secondary health problems. Fortunately, many of these problems can be anticipated and prevented; if they do occur, most can be successfully treated.

Inflammation of the stomach and upper small intestine — Crohn's disease of the upper part of the digestive tract may respond to drugs used to treat stomach and intestinal ulcers. In severe cases, oral steroids and immunomodulator drugs may be necessary to control inflammation.

Ileitis — Active ileitis is first treated with 5-aminosalicylate drugs. Antibiotics, steroids, and immunomodulator drugs may be required in patients with moderate to severe symptoms. Antidiarrheal drugs can also help relieve diarrhea. Severe ileitis may require close monitoring, bowel rest (avoiding solid food), enteral feeding (feeding by a nasogastric tube) or total parenteral feeding (intravenous feeding), and surgery. Remission can be maintained with 5-aminosalicylate drugs in some patients.

Ileocolitis and colitis — Active Crohn's disease that affects the ileum and colon, or the colon alone, is first treated with sulfasalazine or a 5-ASA drug. In some patients, treatment will also include antibiotics and steroids. Severe ileocolitis or colitis may require hospitalization, bowel rest, enteral feeding or parenteral feeding, and long-term treatment with immunomodulator drugs. The 5-ASA drugs are usually used to maintain remission of ileocolitis and colitis.

Malnutrition — Malnutrition occurs in patients with Crohn's disease as a result of inflammation in the digestive tract. This prevents the body from absorbing the normal amount of calories, nutrients, and fluids from foods that are eaten.

Between 50 and 70 percent of patients with Crohn's disease develop malnutrition or are underweight. There can be many consequences of malnutrition, including delayed growth and puberty in children, osteoporosis, a decreased ability to tolerate surgery, and psychosocial problems.

Malnutrition can often be prevented by regular nutritional assessments. Typically, a doctor or dietitian reviews the patient's diet, performs a physical examination, and orders

laboratory tests to detect deficiencies. In most patients, dietary supplements can reverse malnutrition. Patients with Crohn's disease often have a poor appetite, and they should not restrict their diet unless instructed to do so by a healthcare provider.

Enteral feeding (feeding through a nasogastric or gastric tube) and total parenteral feeding (intravenous feeding) can provide nutrients when the digestive tract cannot tolerate normal food or has been effectively shortened by disease or surgery. In some cases, parenteral feeding can also help achieve remission. However, for the majority of patients with Crohn's disease, neither feeding procedure is a practical option for long-term nutrition.

Bone complications — Up to 30 percent of patients with Crohn's disease develop osteoporosis, which can lead to bone fractures. Patients who take steroids for long periods of time and postmenopausal women are particularly at risk. Regular bone mineral density tests can detect early osteoporosis in patients with Crohn's disease.

Osteoporosis usually results from deficiencies of vitamin D, calcium, and sex hormones (estrogen and testosterone). Regular blood tests can detect these deficiencies, and supplements and drugs can be used to restore the levels to normal. Patients can further strengthen their bones by performing low-impact, weight-bearing exercises at least twice a week.

Liver and gallbladder complications — Crohn's disease can lead to inflammation of the liver, which often responds to the drugs used to treat intestinal Crohn's disease. Crohn's disease can rarely cause inflammation of the bile ducts (a disease called primary sclerosing cholangitis). Crohn's disease can also increase the likelihood of gallstones, which sometimes require treatment.

Colorectal cancer — Overall, patients with Crohn's disease have an increased risk of developing colorectal cancer in areas of active inflammation. However, cancer usually does not arise until a patient has had Crohn's disease for many years. Most experts recommend a regular screening colonoscopy to identify premalignant and malignant changes in the colon.

Skin conditions — Several inflammatory skin conditions can develop in patients with Crohn's disease, including erythema nodosum and pyoderma gangrenosum. This often subsides when the intestinal symptoms are treated, but a course of oral steroids may be required.

- Erythema nodosum occurs in up to 15 percent of patients. This typically appears as raised, tender, red or violet nodules under the skin that are 1 to 5 cm in diameter. Areas commonly affected by erythema nodosum include the front of the lower legs.

- Pyoderma gangrenosum occurs in up to 2 percent of those with Crohn's disease. The lesions initially may appear as single or multiple reddened papules or pustules that are often preceded by trauma to the skin. They occur most commonly on the legs, but can develop in any area of the body.

Eye inflammation — Inflammation of the eyes (uveitis or scleritis) occurs in up to 5 percent of patients with Crohn's disease. Features of uveitis include the appearance of "floaters" in the vision, eye pain, blurred vision, sensitivity to light, and headaches; one or both eyes may be affected. Scleritis can cause burning or itching of the affected eye.

These conditions often respond to the drugs used to treat Crohn's disease, but topical medications (eye drops) may also be necessary. Careful monitoring by an eye specialist is recommended to avoid complications.

Mouth sores — Mouth sores, known as aphthous stomatitis, often occur during flares of Crohn's disease. They are usually found between the gums and lower lip, or along the sides or underside of the tongue. They are often painful, but usually respond to the medications used for treatment of intestinal disease. Medications applied directly to the sore (such as hydrocortisone or sucralfate) may also help with healing.

Perianal complications — The major perianal complications of Crohn's disease include fissures (tears), ulceration, fistulas (an abnormal connection between the intestine and other organs), abscesses, and stenosis (narrowing of the anus). These conditions may occur alone or in combination. Symptoms can vary from anal pain and purulent discharge to bleeding and incontinence.

Up to 45 percent of patients with Crohn's disease will develop perianal complications at some time during their life. Some will spontaneously heal without treatment, but others will require treatment with antibiotics, steroid suppositories, immunomodulator drugs, or surgery. Sitz baths and careful, gentle cleaning of the perianal area can promote healing. Although treatment resolves most perianal complications, recurrence is frustratingly common and may require long-term treatment.

Clinical Trials

For clinical trials in Crohn's disease, please visit www.clinicaltrials.gov.