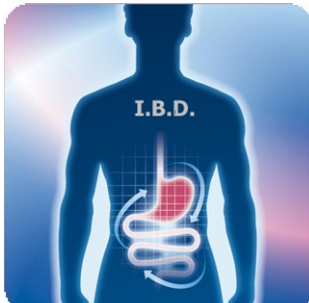


Inflammatory Bowel Disease



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The term inflammatory bowel disease (IBD) covers a group of disorders in which the intestines become inflamed (red and swollen), probably as a result of an immune reaction of the body against its own intestinal tissue.

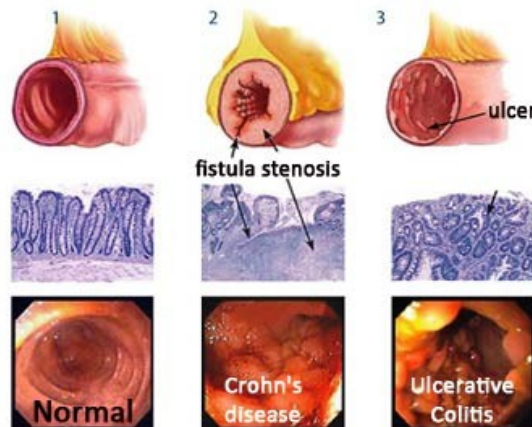
Two major types of IBD are described: ulcerative colitis (UC) and Crohn's disease (CD). As the name suggests, ulcerative colitis is limited to the colon (large intestine). Although Crohn's disease can

involve any part of the gastrointestinal tract from the mouth to the anus, it most commonly affects the small intestine and/or the colon.

Both ulcerative colitis and Crohn's disease usually run a waxing and waning course in the intensity and severity of illness. When there is severe inflammation, the disease is considered to be in an active stage, and the person experiences a flare-up of the

condition. When the degree of inflammation is less (or absent), the person usually is without symptoms, and the disease is considered to be in remission.

produce an inflammatory reaction in the intestinal tract that continues without control. As a result of the inflammatory reaction, the intestinal wall is damaged leading to bloody diarrhea and abdominal pain.



Inflammatory Bowel Disease Causes

Researchers do not yet know what causes inflammatory bowel disease. Therefore, IBD is called an idiopathic disease (disease with an unknown cause).

An unknown factor/agent (or a combination of factors) triggers the body's immune system to produce an inflammatory reaction in the intestinal tract that continues without control. As a result of the inflammatory reaction, the intestinal wall is damaged leading to bloody diarrhea and

abdominal pain. Genetic, infectious, immunologic, and psychological factors have all been implicated in influencing the development of IBD. There is a genetic predisposition (or perhaps susceptibility) to the development of IBD. However, the triggering factor for activation of the body's immune system has yet to be identified. Factors that can turn on the body's immune system include an infectious agent (as yet unidentified), an

immune response to an antigen (eg, protein from cow milk), or an autoimmune process. As the intestines are always exposed to things that can cause immune reactions, more recent thinking is that there is a failure of the body to turn off normal immune .

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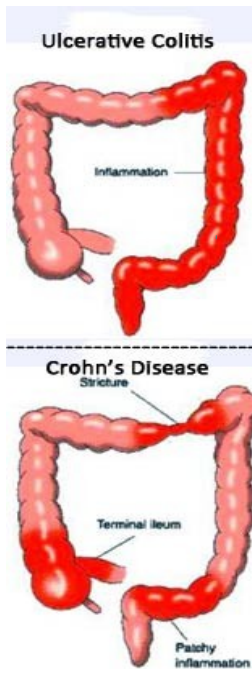
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Inflammatory Bowel Disease Symptoms

Because inflammatory bowel disease is a chronic disease (lasting a long time), you will go through periods in which the disease flares up and causes symptoms. These periods are followed by remission, in which symptoms disappear or decrease and good health returns.

Symptoms may range from mild to severe and generally depend upon the part of the intestinal tract involved.

They include the following:

- Abdominal cramps and pain
- Bloody diarrhea
- Severe urgency to have a bowel movement
- Fever
- Loss of appetite
- Weight loss
- Anemia (due to blood loss)

Intestinal complications of inflammatory bowel disease include the following:

-Profuse bleeding from the ulcers

-Perforation (rupture) of the bowel

-Strictures and obstruction:

In persons with Crohn's disease, strictures often are inflammatory and frequently resolve with medical treatment. Fixed or fibrotic (scarring) strictures may require endoscopic or surgical intervention to relieve the obstruction. In ulcerative colitis, colonic strictures should be presumed to be malignant (cancerous).

-Fistulae (abnormal passage) and perianal disease: These are more common in persons with Crohn's disease. They may not respond to vigorous medical treatment. Surgical intervention often is required, and there is a high risk of recurrence.

-Toxic megacolon (acute nonobstructive dilation of the colon): This is a life-

threatening complication of ulcerative colitis and requires urgent surgical intervention. It is fortunately relatively rare.

-Malignancy: The risk of colon cancer in ulcerative colitis begins to rise significantly above that of the general population after approximately 8-10 years of diagnosis. The risk of cancer in Crohn's disease may equal that of ulcerative colitis if the entire colon is involved. The risk of small intestine malignancy is increased in Crohn's disease.

Extraintestinal complications
Extraintestinal involvement of IBD refers to complications involving organs other than the intestines. These affect only a small percentage of people with IBD. Persons with IBD may have arthritis, skin conditions, inflammation of the eye, liver and kidney disorders, and bone loss. Of all the extraintestinal complications, arthritis is the most common. Joint, eye, and skin complications often occur together.

Exams and Tests

Your health care provider makes the diagnosis of inflammatory bowel disease based on your symptoms and various exams and tests.

Stool examination

A stool examination is done to eliminate the possibility of bacterial, viral, or parasitic causes of diarrhea.

A fecal occult blood test is used to examine stool for traces of blood that cannot be seen with the naked eye.

Complete blood count

An increase in the white blood cell count suggests the presence of inflammation in the body.

If you have severe bleeding, the red blood cell count may decrease and hemoglobin level may fall (anemia).

Both the above tests are not diagnostic of IBD, as they may be abnormal in many other diseases.

Barium x-ray

Upper gastrointestinal (GI) tract: This exam uses x-rays to

find abnormalities in the upper GI tract (esophagus, stomach, duodenum, sometimes the small intestine). For this test, you are required to swallow barium (a chalky white substance). When barium is swallowed, it coats the inside of the intestinal tract, which can be documented on x-rays. If you have Crohn's disease, abnormalities will be seen on barium x-rays.

Lower gastrointestinal (GI) tract: In this exam, barium is given in an enema that is retained in the colon while x-rays are taken. Abnormalities will be noted in the rectum and colon in persons with Crohn's disease and ulcerative colitis.

Sigmoidoscopy:

In this procedure, your health care provider uses a sigmoidoscope (a narrow, flexible tube with a lens and a light source) to visualize the last one-third of the large intestine, which includes the rectum and the sigmoid colon. The sigmoidoscope is inserted

through the anus and the intestinal wall is examined for ulcers, inflammation, and bleeding. During this procedure, your health care provider may take samples (biopsies) of the lining of the intestine.

Colonoscopy:

A colonoscopy is an examination similar to a sigmoidoscopy, but with this procedure, the entire colon can be examined.

Upper endoscopy:

If you have upper GI symptoms (nausea, vomiting), an endoscope (narrow, flexible tube with a light source) is used to examine the esophagus, stomach, and the duodenum. The endoscope is inserted through the mouth, and the stomach and duodenum are examined for ulceration. Ulceration occurs in the stomach and duodenum in 5-10% of persons with Crohn's disease.

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Inflammatory Bowel Disease Treatment

Self-Care at Home

It is important to eat a healthy diet. Depending on your symptoms, your health care provider may ask you to decrease the amount of fiber or dairy products in your diet.

Diet has little or no influence on the inflammatory activity in ulcerative colitis. However, diet may influence symptoms. For this reason, people with inflammatory bowel disease often are placed on a variety of diet interventions, especially low-residue diets. Evidence does not support a low-residue diet as beneficial in treating the inflammation of ulcerative colitis, though it might decrease the frequency of bowel movements.

Unlike ulcerative colitis, diet can influence inflammatory activity in Crohn's disease. Nothing by mouth (NPO status) can hasten reduction of inflammation, as might the use of a liquid diet or a predigested formula. When you become extremely upset, your symptoms may get worse. Therefore, it is important that you learn to manage the stress in your life.

Medical Treatment

The goal of medical treatment is to suppress the abnormal inflammatory response. This allows the intestinal tissue to heal, thereby relieving the symptoms of diarrhea and abdominal pain. Once the symptoms are under control, medical treatment is used to decrease the frequency of flare-ups and to maintain remission.

A stepwise approach to the use of medications for inflammatory bowel disease may be taken. With this approach, the most benign (least harmful) drugs or drugs taken for a short period of time are used first. If they fail to provide relief, drugs from a higher step are used.

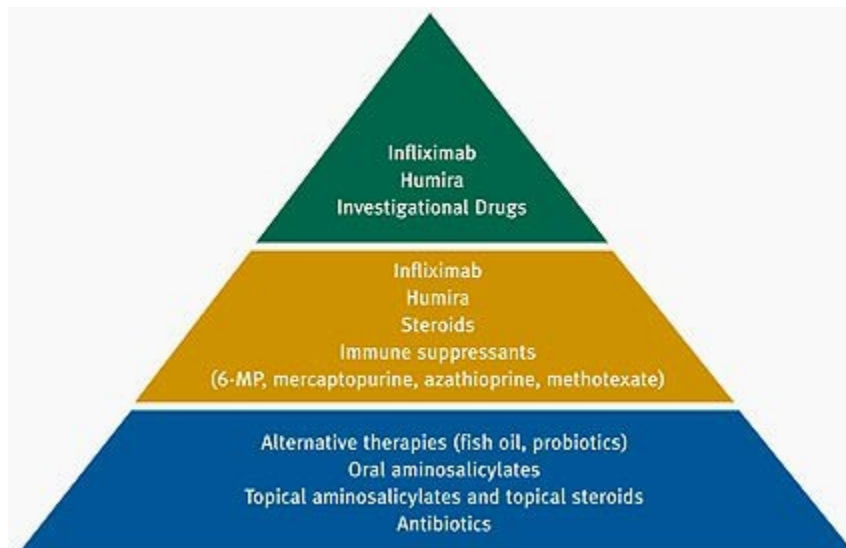
The aminosalicylates and symptomatic agents are step I drugs under this scheme. Antibiotics are a step IA; they are particularly used in persons with Crohn's disease who have perianal disease or an inflammatory mass.

Corticosteroids constitute step II drugs to be used if the step I drugs fail to provide adequate control of the IBD. They tend to provide rapid relief of symptoms as well as a significant decrease in inflammation.

The immune modifying agents are step III drugs to be used if corticosteroids fail or are required for prolonged periods. These agents are not used in acute flare-ups because the time from initiation of treatment to the onset of significant action may be as long as 2-3 months. Infliximab is a step IIIA drug to be used in persons with Crohn's disease. As of this writing, the medications approved by the US FDA for the treatment of Crohn's disease are prednisone, budesonide, and infliximab.

The experimental agents are step IV drugs to be used only after failure of the previous steps and only by health care providers familiar with their use.

Note that drugs from all steps may be used additively; in general, the goal is to wean off the corticosteroids as soon as possible to prevent long-term side effects. There may be different opinions regarding the use of certain agents in this stepwise approach.



Medications

Different groups of drugs are used for the treatment of persons with inflammatory bowel disease. These include aminosalicylates, corticosteroids, immune modifiers, anti-tumor necrosis factor (TNF) agents, and antibiotics.

Aminosalicylates

Aminosalicylates are aspirinlike anti-inflammatory drugs. There are 5 aminosalicylate preparations available for use in the US: sulfasalazine (Azulfidine), mesalamine (Asacol, Pentasa), olsalazine (Dipentum), and balsalazide (Colazal).

These drugs can be given either orally or rectally (enema, suppository formulations). They are useful both for treating flare-ups of the IBD and the maintenance of remission.

Corticosteroids

Corticosteroids are rapid-acting anti-inflammatory agents. The indication for use in IBD is for acute flare-ups of the disease only. There is no role for corticosteroids in the maintenance of remission.

Corticosteroids may be administered by a variety of routes, depending upon the location and severity of disease; they may be administered intravenously (methylprednisolone, hydrocortisone) in the hospital, orally (prednisone, prednisolone, budesonide, dexamethasone), or rectally (enema, suppository, foam preparations).

Corticosteroids tend to provide rapid relief of symptoms as well as a significant decrease in inflammation, but their side effects limit their use (particularly longer-term use). The consensus for treatment with corticosteroids is that they should be tapered as soon as possible.

Immune modifiers

Immune modifiers include 6-mercaptopurine (6-MP, Purinethol) and azathioprine (Imuran). Immune modifiers may work by causing a reduction in the lymphocyte count (a type of white blood cell). Their onset of action is relatively slow (typically 2-3 months).

They are used in selected persons with IBD when aminosalicylates and corticosteroids are either ineffective or only partially effective. They are useful in reducing or eliminating some persons' dependence on corticosteroids.

Immune modifiers may also be helpful in maintaining remission in some persons with refractory ulcerative colitis (persons who do not respond to standard medications).

They are also used as primary treatment of fistulae and the maintenance of remission in persons who cannot tolerate aminosalicylates.

If you are taking immune modifiers, your blood cell count will be monitored on a regular basis [Title] because the immune modifiers can cause a significant reduction in the number of white blood cells, predisposing you to serious infections

Anti-TNF agent

Infliximab (Remicade) is an anti-TNF agent. TNF is produced by white blood cells and is believed to be responsible for promoting the tissue damage noted in persons with Crohn's disease. Infliximab acts by binding to TNF, thereby inhibiting its effects on the tissues.

It is approved by the FDA for the treatment of persons with moderate-to-severe Crohn's disease who have had an inadequate response to standard medications. In such persons, a response rate of 80% and a remission rate of 50% have been reported.

Infliximab is also used for the treatment of fistulae, a complication of Crohn's disease. Closure of fistulae has been reported in 68% of persons treated with infliximab. Infliximab must be given intravenously. It

is very expensive, so insurance coverage may play a factor in the decision to use this drug.

Antibiotics

Metronidazole and ciprofloxacin are the most commonly used antibiotics in persons with IBD.

Antibiotics are used sparingly in persons with ulcerative colitis because they have an increased risk of developing antibiotic-associated pseudomembranous colitis (a type of infectious diarrhea).

In persons with Crohn's disease, antibiotics are used for the treatment of complications (perianal disease, fistulae, inflammatory mass).

Symptomatic treatments: You may be given antidiarrheal agents, antispasmodics, and acid suppressants for symptomatic relief.

Experimental agents

Drugs used in Crohn's disease include methotrexate, thalidomide, and interleukin-11.

Drugs used in ulcerative colitis include cyclosporine A, nicotine patch, butyrate enema, and heparin.

