

Ulcerative Colitis

Ulcerative colitis (*Colitis ulcerosa*, **UC**) is a form of inflammatory bowel disease (IBD). Ulcerative colitis is a form of colitis, a disease of the intestine, specifically the large intestine or colon, that includes characteristic ulcers, or open sores, in the colon. The main symptom of active disease is usually diarrhea mixed with blood, of gradual onset. Ulcerative colitis is, however, a systemic disease that affects many parts of the body outside the intestine. Because of the name, IBD is often confused with irritable bowel syndrome ("IBS"), a troublesome, but much less serious condition. Ulcerative colitis has similarities to Crohn's disease, another form of IBD. Ulcerative colitis is an intermittent disease, with periods of exacerbated symptoms, and periods that are relatively symptom-free. Although the symptoms of ulcerative colitis can sometimes diminish on their own, the disease usually requires treatment to go into remission.

Ulcerative colitis is a rare disease, with an incidence of about one person per 10,000 in North America. The disease tends to be more common in northern areas. Although ulcerative colitis has no known cause, there is a presumed genetic component to susceptibility. The disease may be triggered in a susceptible person by environmental factors. Although dietary modification may reduce the discomfort of a person with the disease, ulcerative colitis is not thought to be caused by dietary factors. Although ulcerative colitis is treated as though it were an autoimmune disease, there is no consensus that it is such. Treatment is with anti-inflammatory drugs, immunosuppression (suppressing the immune system), and biological therapy targeting specific components of the immune response. Colectomy (partial or total removal of the large bowel through surgery) is occasionally necessary, and is considered to be a cure for the disease.

Ulcerative colitis is a disease that causes inflammation and sores, called ulcers, in the lining of the rectum and colon. Ulcers form

where inflammation has killed the cells that usually line the colon, then bleed and produce pus. Inflammation in the colon also causes the colon to empty frequently, causing diarrhea.

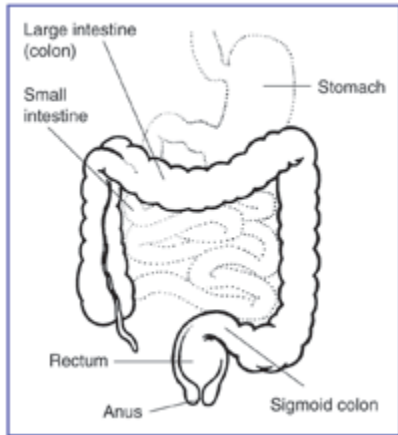
When the inflammation occurs in the rectum and lower part of the colon it is called ulcerative proctitis. If the entire colon is affected it is called pancolitis. If only the left side of the colon is affected it is called limited or distal colitis.

Ulcerative colitis is an inflammatory bowel disease (IBD), the general name for diseases that cause inflammation in the small intestine and colon. It can be difficult to diagnose because its symptoms are similar to other intestinal disorders and to another type of IBD called Crohn's disease. Crohn's disease differs because it causes inflammation deeper within the intestinal wall and can occur in other parts of the digestive system including the small intestine, mouth, esophagus, and stomach.

Ulcerative colitis can occur in people of any age, but it usually starts between the ages of 15 and 30, and less frequently between 50 and 70 years of age. It affects men and women equally and appears to run in families, with reports of up to 20 percent of people with ulcerative colitis having a family member or relative with ulcerative colitis or Crohn's disease. A higher incidence of ulcerative colitis is seen in Whites and people of Jewish descent.

Ulcerative colitis usually affects only the innermost lining of your large intestine (colon) and rectum. It occurs only through continuous stretches of your colon, unlike Crohn's disease, which occurs in patches anywhere in the digestive tract and often spreads deep into the layers of affected tissues.

There's no known cure for ulcerative colitis, but therapies are available that may dramatically reduce the signs and symptoms of ulcerative colitis and even bring about a long-term remission.



What are the symptoms of ulcerative colitis?

The most common symptoms of ulcerative colitis are abdominal pain and bloody diarrhea. Patients also may experience

- anemia
- fatigue
- weight loss
- loss of appetite
- rectal bleeding
- loss of body fluids and nutrients
- skin lesions
- joint pain
- growth failure (specifically in children)

About half of the people diagnosed with ulcerative colitis have mild symptoms. Others suffer frequent fevers, bloody diarrhea, nausea, and severe abdominal cramps. Ulcerative colitis may also cause problems such as arthritis, inflammation of the eye, liver disease, and osteoporosis. It is not known why these problems occur outside the colon. Scientists think these complications may be the result of inflammation triggered by the immune system. Some of these problems go away when the colitis is treated.

- **Age.** Ulcerative colitis can strike at any age, but you are most likely to develop the condition when you are young. Ulcerative

colitis often strikes people in their 30s, although a small number of people may not develop the disease until their 50s or 60s.

- **Ethnicity.** Although whites have the highest risk of the disease, it can strike any ethnic group. If you're Jewish and of European descent, you're four to five times as likely to have ulcerative colitis.
- **Family history.** You're at higher risk if you have a close relative, such as a parent, sibling or child, with the disease.
- **Where you live.** If you live in an urban area or in an industrialized country, you're more likely to develop ulcerative colitis. People living in Northern climates also seem to have a greater risk of ulcerative colitis. Other environmental factors, such as a diet high in fat or refined foods, also may play a role.
- **Inflamed bile ducts.** This condition, called primary sclerosing cholangitis, causes inflammation of the bile ducts of the liver, and is associated with ulcerative colitis. If you have this condition, your doctor may look for ulcerative colitis even if you don't have signs or symptoms.

What causes ulcerative colitis?

While the cause of ulcerative colitis is unknown, several, possibly interrelated, causes have been suggested.

Many theories exist about what causes ulcerative colitis. People with ulcerative colitis have abnormalities of the immune system, but doctors do not know whether these abnormalities are a cause or a result of the disease. The body's immune system is believed to react abnormally to the bacteria in the digestive tract.

Ulcerative colitis is not caused by emotional distress or sensitivity to certain foods or food products, but these factors may trigger symptoms in some people. The stress of living with ulcerative colitis may also contribute to a worsening of symptoms.

How is ulcerative colitis diagnosed?

Many tests are used to diagnose ulcerative colitis. A physical exam and medical history are usually the first step.

Blood tests may be done to check for anemia, which could indicate bleeding in the colon or rectum, or they may uncover a high white blood cell count, which is a sign of inflammation somewhere in the body.

A stool sample can also reveal white blood cells, whose presence indicates ulcerative colitis or inflammatory disease. In addition, a stool sample allows the doctor to detect bleeding or infection in the colon or rectum caused by bacteria, a virus, or parasites.

A colonoscopy or sigmoidoscopy are the most accurate methods for making a diagnosis of ulcerative colitis and ruling-out other possible conditions, such as Crohn's disease, diverticular disease, or cancer. For both tests, the doctor inserts an endoscope—a long, flexible, lighted tube connected to a computer and TV monitor—into the anus to see the inside of the colon and rectum. The doctor will be able to see any inflammation, bleeding, or ulcers on the colon wall. During the exam, the doctor may do a biopsy, which involves taking a sample of tissue from the lining of the colon to view with a microscope.

Sometimes x rays such as a barium enema or CT scans are also used to diagnose ulcerative colitis or its complications.

Your doctor will likely diagnose ulcerative colitis only after ruling out other possible causes for your signs and symptoms, including Crohn's disease, ischemic colitis, infection, irritable bowel syndrome (IBS), diverticulitis and colorectal cancer. To help confirm a diagnosis of ulcerative colitis, you may have one or more of the following tests and procedures:

- **Blood tests.** Your doctor may suggest blood tests to check for anemia or signs of infection. Two tests that look for the presence of certain antibodies can sometimes help diagnose which type of inflammatory bowel disease you have, but not everyone with ulcerative colitis has these antibodies. These tests aren't sensitive enough for routine use, but may be helpful in specific circumstances.
- **Colonoscopy.** This test allows your doctor to view your entire colon using a thin, flexible, lighted tube with an attached camera. During the procedure, your doctor can also take small samples of tissue (biopsy) for laboratory analysis.

Sometimes a tissue sample can help confirm a diagnosis. If there are clusters of inflammatory cells called granulomas, for instance, it's likely you have Crohn's disease, because granulomas don't occur with ulcerative colitis.

Risks of this procedure include perforation of the colon wall and bleeding, especially when a biopsy is taken.

- **Flexible sigmoidoscopy.** In this procedure, your doctor uses a slender, flexible, lighted tube to examine the sigmoid, the last 2 feet of your colon. The test usually takes just a few minutes. It's somewhat uncomfortable, and there's a slight risk of perforating the colon wall. It may also miss problems higher up in your colon.
- **Barium enema.** This diagnostic test allows your doctor to evaluate your entire large intestine with an X-ray. Barium, a contrast dye, is placed into your bowel in an enema form. Sometimes, air is added as well. The barium fills and coats the lining of the bowel, creating a silhouette of your rectum, colon and a portion of your small intestine.

Barium enema isn't as accurate as colonoscopy, it doesn't allow your doctor to take tissue samples, and it's not used in people with moderate to severe disease because of the risk of complications.

Small bowel X-ray. This test looks at the part of the small bowel that can't be seen by colonoscopy. You drink a barium "shake," and then X-rays are taken of your small intestine. This test can help distinguish between ulcerative colitis and Crohn's disease.

Genetic factors

A genetic component to the etiology of ulcerative colitis can be hypothesized based on the following:

- Aggregation of ulcerative colitis in families.
- Identical twin concordance rate of 10% and dizygotic twin concordance rate of 3%
- Ethnic differences in incidence
- Genetic markers and linkages

There are 12 regions of the genome which may be linked to ulcerative colitis. This includes chromosomes 16, 12, 6, 14, 5, 19, 1, 16, and 3 in the order of their discovery. However, none of these loci has been consistently shown to be at fault, suggesting that the disorder arises from the combination of multiple genes. For example, chromosome band 1p36 is one such region thought to be linked to inflammatory bowel disease. Some of the putative regions encode transporter proteins such as OCTN1 and OCTN2. Other potential regions involve cell scaffolding proteins such as the MAGUK family. There are even HLA associations which may be at work. In fact, this linkage on chromosome 6 may be the most convincing and consistent of the genetic candidates.

Multiple autoimmune disorders have been recorded with the neurovisceral and cutaneous genetic porphyrias including ulcerative colitis, Crohn's disease, celiac disease, dermatitis herpetiformis, systemic and discoid lupus, rheumatoid arthritis, ankylosing spondylitis, scleroderma, Sjogren's disease and scleritis. Physicians should be on high alert for porphyrias in families with autoimmune disorders and care must be taken with potential porphyrinogenic drugs, including sulfasalazine.

Environmental factors

Many hypotheses have been raised for environmental contributors to the pathogenesis of ulcerative colitis. They include the following:

- **Diet:** as the colon is exposed to many different dietary substances which may encourage inflammation, dietary factors have been hypothesized to play a role in the pathogenesis of both ulcerative colitis and Crohn's disease. There have been few studies to investigate such an association, but one study showed no association of refined sugar on the prevalence of ulcerative colitis.
- **Diet:** A diet low in fermentable dietary fiber may affect ulcerative colitis incidence.
- **Breastfeeding:** There have been conflicting reports of the protection of breastfeeding in the development of inflammatory bowel disease. One Italian study showed a potential protective effect.
- **Other childhood exposures, or infections**

Autoimmune disease

Some sources list ulcerative colitis as an autoimmune disease, a disease in which the immune system malfunctions, attacking some part of the body. As discussed above, ulcerative colitis is a systemic disease that affects many areas of the body outside the digestive system. Surgical removal of the large intestine often cures the disease, including the manifestations outside the digestive system. This suggests that the cause of the disease is in the colon itself, and not in the immune system or some other part of the body.

Alternative theories

Levels of sulfate-reducing bacteria tend to be higher in persons with ulcerative colitis. This could mean that there are higher levels of hydrogen sulfide in the intestine. An alternative theory suggests that the symptoms of the disease may be caused by toxic effects of the

hydrogen sulfide on the cells lining the intestine. It may be caused occlusions in the capillaries of the subepithelial linings, degenerated fibers beneath the mucosa and infiltration of the lamina propria with plasma cells

Epidemiology

The incidence of ulcerative colitis in North America is 10-12 cases per 100,000, with a peak incidence of ulcerative colitis occurring between the ages of 15 and 25. There is thought to be a bimodal distribution in age of onset, with a second peak in incidence occurring in the 6th decade of life. The disease affects females more than males.

The geographic distribution of ulcerative colitis and Crohn's disease is similar worldwide, with highest incidences in the United States, Canada, the United Kingdom, and Scandinavia. Higher incidences are seen in northern locations compared to southern locations in Europe and the United States.

As with Crohn's disease, ulcerative colitis is thought to occur more commonly among Ashkenazi Jewish people than non-Jewish people.

Clinical presentation

GI symptoms

The clinical presentation of ulcerative colitis depends on the extent of the disease process. Patients usually present with diarrhea mixed with blood and mucus, of gradual onset. They also may have signs of weight loss, and blood on rectal examination. The disease is usually accompanied with different degrees of abdominal pain, from mild discomfort to severely painful cramps.

Ulcerative colitis is a systemic disease that affects many parts of the body. Sometimes the extra-intestinal manifestations of the disease are the initial signs, such as painful, arthritic knees in a teenager. It is,

however, unlikely that the disease will be correctly diagnosed until the onset of the intestinal manifestations.

Extent of involvement

Ulcerative colitis is normally continuous from the rectum up the colon. The disease is classified by the extent of involvement, depending on how far up the colon the disease extends:

- Distal colitis, potentially treatable with enemas:
 - Proctitis: Involvement limited to the rectum.
 - Proctosigmoiditis: Involvement of the rectosigmoid colon, the portion of the colon adjacent to the rectum.
 - Left-sided colitis: Involvement of the descending colon, which runs along the patient's left side, up to the splenic flexure and the beginning of the transverse colon.
- Extensive colitis, inflammation extending beyond the reach of enemas:
 - Pancolitis: Involvement of the entire colon, extending from the rectum to the cecum, beyond which the small intestine begins.

Severity of disease

In addition to the extent of involvement, UC patients may also be characterized by the severity of their disease.

- Mild disease correlates with fewer than four stools daily, with or without blood, no systemic signs of toxicity, and a normal erythrocyte sedimentation rate (ESR). There may be mild abdominal pain or cramping. Patients may believe they are constipated when in fact they are experiencing tenesmus, which is a constant feeling of the need to empty the bowel accompanied by involuntary straining efforts, pain, and cramping with little or no fecal output. Rectal pain is uncommon.



Colonic pseudopolyps of a patient with intractable **ulcerative colitis**. Colectomy specimen.

- *Moderate disease* correlates with more than four stools daily, but with minimal signs of toxicity. Patients may display anemia (not requiring transfusions), moderate abdominal pain, and low grade fever, 38 to 39 °C (99.5 to 102.2 °F).
- *Severe disease*, correlates with more than six bloody stools a day, and evidence of toxicity as demonstrated by fever, tachycardia, anemia or an elevated ESR.
- *Fulminant disease* correlates with more than ten bowel movements daily, continuous bleeding, toxicity, abdominal tenderness and distension, blood transfusion requirement and colonic dilation (expansion). Patients in this category may have inflammation extending beyond just the mucosal layer, causing impaired colonic motility and leading to toxic megacolon. If the serous membrane is involved, colonic perforation may ensue. Unless treated, fulminant disease will soon lead to death.

Extraintestinal features

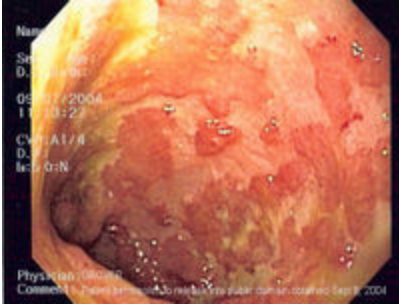
As ulcerative colitis is a systemic disease, patients may present with symptoms and complications outside the colon. These include the following:



Patients with **ulcerative colitis** can occasionally have aphthous ulcers involving the tongue, lips, palate and pharynx

- aphthous ulcers of the mouth
- Ophthalmic (involving the eyes):
 - Iritis or uveitis, which is inflammation of the iris
 - Episcleritis
- Musculoskeletal:
 - Seronegative arthritis, which can be a large-joint oligoarthritis (affecting one or two joints), or may affect many small joints of the hands and feet
 - Ankylosing spondylitis, arthritis of the spine
 - Sacroiliitis, arthritis of the lower spine
- Cutaneous (related to the skin):
 - Erythema nodosum, which is a panniculitis, or inflammation of subcutaneous tissue involving the lower extremities
 - Pyoderma gangrenosum, which is a painful ulcerating lesion involving the skin
- Deep venous thrombosis and pulmonary embolism
- Autoimmune hemolytic anemia
- clubbing, a deformity of the ends of the fingers
- Primary sclerosing cholangitis, or inflammation of the bile ducts.

Similar conditions



Endoscopic image of **ulcerative colitis** affecting the left side of the colon. The image shows confluent superficial ulceration and loss of mucosal architecture. Crohn's disease may be similar in appearance, a fact that can make diagnosing UC a challenge.

The following conditions may present in a similar manner as ulcerative colitis, and should be excluded:

- Crohn's disease
- Infectious colitis, which is typically detected on stool cultures
 - Pseudomembranous colitis, or *Clostridium difficile*-associated colitis, bacterial upsets often seen following administration of antibiotics
- Ischemic colitis, inadequate blood supply to the intestine, which typically affects the elderly
- Radiation colitis in patients with previous pelvic radiotherapy
- Chemical colitis resulting from introduction of harsh chemicals into the colon from an enema or other procedure.

Comparison to Crohn's Disease

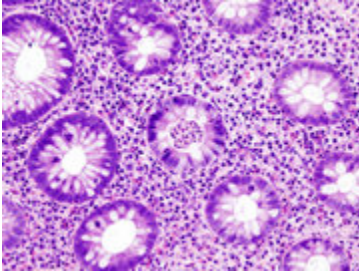
The most common disease that mimics the symptoms of ulcerative colitis is Crohn's disease, as both are inflammatory bowel diseases that can affect the colon with similar symptoms. It is important to differentiate these diseases, since the course of the diseases and treatments may be different. In some cases, however, it may not be possible to tell the difference, in which case the disease is classified as indeterminate colitis.

Comparisons of various factors in Crohn's disease and ulcerative colitis

	Crohn's Disease	Ulcerative Colitis
Involves terminal ileum?	Commonly	Seldom
Involves colon?	Usually	Always
Involves rectum?	Seldom	Usually
Peri-anal involvement?	Commonly	Seldom
Bile duct involvement?	Not associated	Higher rate of Primary sclerosing cholangitis
Distribution of Disease	Patchy areas of inflammation	Continuous area of inflammation
Endoscopy	Linear and serpiginous (snake-like) ulcers	Continuous ulcer
Depth of inflammation	May be transmural, deep into tissues	Shallow, mucosal
Fistulae, abnormal passageways between organs	Commonly	Seldom
Biopsy	Can have granulomata	Crypt abscesses and cryptitis
Surgical cure?	Often returns following removal of affected part	Usually cured by removal of colon, can be followed by pouchitis
Smoking	Higher risk for smokers	Lower risk for smokers
Autoimmune disease?	Generally regarded as an autoimmune disease	No consensus
Cancer risk?	Lower than ulcerative colitis	Higher than Crohn's

Diagnosis and workup

General



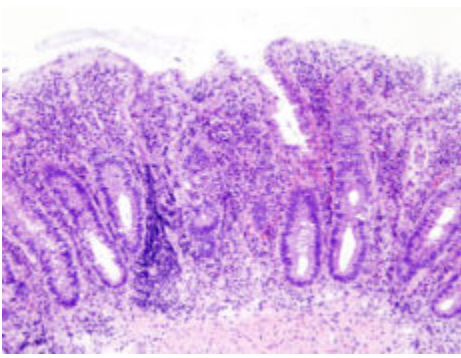
H&E stain of a colonic biopsy showing a crypt abscess, a classic finding in ulcerative colitis

The initial diagnostic workup for ulcerative colitis includes the following:

- A complete blood count is done to check for anemia; thrombocytosis, a high platelet count, is occasionally seen
- Electrolyte studies and renal function tests are done, as chronic diarrhea may be associated with hypokalemia, hypomagnesemia and pre-renal failure.
- Liver function tests are performed to screen for bile duct involvement: primary sclerosing cholangitis.
- X-ray
- Urinalysis
- Stool culture, to rule out parasites and infectious causes.
- Erythrocyte sedimentation rate can be measured, with an elevated sedimentation rate indicating that an inflammatory process is present.
- C-reactive protein can be measured, with an elevated level being another indication of inflammation.

Although ulcerative colitis is a disease of unknown causation, inquiry should be made as to unusual factors believed to trigger the disease. Factors may include: recent cessation of tobacco smoking; recent administration of large doses of iron or vitamin B6; hydrogen peroxide in enemas or other procedures.

Endoscopic



Biopsy sample (H&E stain) that demonstrates marked lymphocytic infiltration (blue/purple) of the intestinal mucosa and architectural distortion of the crypts.

The best test for diagnosis of ulcerative colitis remains endoscopy. Full colonoscopy to the cecum and entry into the terminal ileum is attempted only if diagnosis of UC is unclear. Otherwise, a flexible sigmoidoscopy is sufficient to support the diagnosis. The physician may elect to limit the extent of the exam if severe colitis is encountered to minimize the risk of perforation of the colon. Endoscopic findings in ulcerative colitis include the following:

- Loss of the vascular appearance of the colon
- Erythema (or redness of the mucosa) and friability of the mucosa
- Superficial ulceration, which may be confluent, and
- Pseudopolyps.

Ulcerative colitis is usually continuous from the rectum, with the rectum almost universally being involved. There is rarely peri-anal disease, but cases have been reported. The degree of involvement endoscopically ranges from proctitis or inflammation of the rectum, to left sided colitis, to pancolitis, which is inflammation involving the ascending colon.

Histologic

Biopsies of the mucosa are taken to definitively diagnose UC and differentiate it from Crohn's disease, which is managed differently

clinically. Microbiological samples are typically taken at the time of endoscopy. The pathology in ulcerative colitis typically involves distortion of crypt architecture, inflammation of crypts (cryptitis), frank crypt abscesses, and hemorrhage or inflammatory cells in the lamina propria. In cases where the clinical picture is unclear, the histomorphologic analysis often plays a pivotal role in determining the management.

Course and complications

Progression or remission

Patients with ulcerative colitis usually have an intermittent course, with periods of disease inactivity alternating with "flares" of disease. Patients with proctitis or left-sided colitis usually have a more benign course: only 15% progress proximally with their disease, and up to 20% can have sustained remission in the absence of any therapy. Patients with more extensive disease are less likely to sustain remission, but the rate of remission is independent of the severity of disease.

Ulcerative colitis and colorectal cancer

There is a significantly increased risk of colorectal cancer in patients with ulcerative colitis after 10 years if involvement is beyond the splenic flexure. Those with only proctitis or rectosigmoiditis usually have no increased risk.^[7] It is recommended that patients have screening colonoscopies with random biopsies to look for dysplasia after eight years of disease activity^[15]

Primary sclerosing cholangitis

Ulcerative colitis has a significant association with primary sclerosing cholangitis (PSC), a progressive inflammatory disorder of small and large bile ducts. As many as 5% of patients with ulcerative colitis may progress to develop primary sclerosing cholangitis.^[16]

Mortality

The effect of ulcerative colitis on mortality is unclear, but it is thought that the disease primarily affects quality of life, and not lifespan.

What is the treatment for ulcerative colitis?

Treatment for ulcerative colitis depends on the severity of the disease. Each person experiences ulcerative colitis differently, so treatment is adjusted for each individual. Standard treatment for ulcerative colitis depends on *extent of involvement* and disease *severity*. The goal is to induce remission initially with medications, followed by the administration of maintenance medications to prevent a relapse of the disease. The concept of induction of remission and maintenance of remission is very important. The medications used to induce and maintain a remission somewhat overlap, but the treatments are different. Physicians first direct treatment to inducing a remission which involves relief of symptoms and mucosal healing of the lining of the colon and then longer term treatment to maintain the remission.

The goal of medical treatment is to reduce the inflammation that triggers your signs and symptoms. In the best cases, this may lead not only to symptom relief but also to long-term remission. Ulcerative colitis treatment usually involves either drug therapy or surgery.

Doctors use several categories of drugs that control inflammation in different ways. But drugs that work well for some people may not work for others, so it may take time to find a medication that helps you. In addition, because some drugs have serious side effects, you'll need to weigh the benefits and risks of any treatment.

Anti-inflammatory drugs

Anti-inflammatory drugs are often the first step in the treatment of inflammatory bowel disease. They include:

- **Sulfasalazine** (Azulfidine). Sulfasalazine can be effective in reducing symptoms of ulcerative colitis, but it has a number of side effects, including nausea, vomiting, heartburn and headache. Do not take this medication if you are allergic to sulfa medications.
- **Mesalamine** (Asacol, Rowasa) and olsalazine (Dipentum). These medications tend to have fewer side effects than sulfasalazine has. You take them in tablet form or use them rectally in the form of enemas or suppositories, depending on the area of your colon affected by ulcerative colitis. Mesalamine enemas can relieve signs and symptoms in more than 80 percent of people with ulcerative colitis in the lower left side of their colon and rectum. Olsalazine may cause or worsen existing diarrhea in some people.
- **Balsalazide (Colazal)**. This is another formulation of mesalamine. Colazal delivers anti-inflammatory medication directly to the colon. The drug is similar to sulfasalazine, but uses a less toxic carrier and may produce fewer side effects.
- **Corticosteroids**. Corticosteroids can help reduce inflammation, but they have numerous side effects, including a puffy face, excessive facial hair, night sweats, insomnia and hyperactivity. More serious side effects include high blood pressure, type 2 diabetes, osteoporosis, bone fractures, cataracts and an increased susceptibility to infections. Long-term use of these drugs in children can lead to stunted growth.

Also, corticosteroids don't work for everyone who has ulcerative colitis. Doctors generally use corticosteroids only if you have moderate to severe inflammatory bowel disease that doesn't respond to other treatments. Corticosteroids aren't for long-term use and are generally prescribed for a period of three to four months.

They may also be used in conjunction with other medications as a means to induce remission. For example, corticosteroids may be

used with an immune system suppressor – the corticosteroids can induce remission, while the immune system suppressors can help maintain remission. Occasionally, your doctor may also prescribe steroid enemas to treat disease in your lower colon or rectum. These, too, are only for short-term use.

Immune system suppressors

These drugs also reduce inflammation, but they target your immune system rather than treating inflammation itself. Because immune suppressors can be effective in treating ulcerative colitis, scientists theorize that damage to digestive tissues is caused by your body's immune response to an invading virus or bacterium or even to your own tissue. By suppressing this response, inflammation is also reduced. Immunosuppressant drugs include:

- **Azathioprine** (Imuran) and **mercaptopurine** (Purinethol). These drugs have been used to treat Crohn's disease for years, but their role in ulcerative colitis is only now being studied. Because azathioprine and mercaptopurine act slowly, they're sometimes initially combined with a corticosteroid, but in time, they seem to produce benefits on their own, with less long-term toxicity.

Side effects can include allergic reactions, bone marrow suppression, infections, and inflammation of the liver and pancreas. If you're taking either of these medications, you'll need to follow up closely with your doctor and have your blood checked regularly to look for side effects.

- **Cyclosporine** (Neoral, Sandimmune). This potent drug is normally reserved for people who don't respond well to other medications or who face surgery because of severe ulcerative colitis. In some cases, cyclosporine may be used to delay surgery until you're strong enough to undergo the procedure; in others, it's used to control signs and symptoms until less toxic drugs start working. Cyclosporine begins working in one to two weeks, but because it has the potential for severe side effects, including

kidney and liver damage, fatal infections and an increased risk of lymphoma, you and your doctor will want to talk about the risks and benefits of treatment.

- **Infliximab** (Remicade). This drug is specifically for adults and children with moderate to severe ulcerative colitis who don't respond to or can't tolerate other treatments. It works by neutralizing a protein produced by your immune system known as tumor necrosis factor (TNF). Infliximab finds TNF in your bloodstream and removes it before it causes inflammation in your intestinal tract and contributes to the formation of infected sores called fistulas.

Some people with heart failure, people with multiple sclerosis, and people with cancer or a history of cancer can't take Remicade. If you're currently taking Remicade, talk to your doctor about the potential risks. The drug has been linked to an increased risk of infection, especially tuberculosis, and may increase your risk of blood problems and cancer. You'll need to have a skin test for tuberculosis before taking infliximab and a chest X-ray if you lived or traveled extensively where tuberculosis has been found.

Also, because Remicade contains mouse protein, it can cause serious allergic reactions in some people — reactions that may be delayed for days to weeks after starting treatment. Once started, infliximab is often continued as long-term therapy, although its effectiveness may wear off over time.

Nicotine patches

These skin patches — the same kind smokers use — seem to provide short-term relief from flare-ups of ulcerative colitis for some people, especially people who formerly smoked. How nicotine patches work isn't exactly clear, and the evidence that they provide relief is contested among researchers. Talk to your doctor before trying this treatment.

Don't take up smoking as a treatment for ulcerative colitis. The risks from smoking far outweigh any potential benefit.

Other medications

In addition to controlling inflammation, some medications may help relieve your signs and symptoms. Depending on the severity of your ulcerative colitis, your doctor may recommend one or more of the following:

- **Anti-diarrheal.** A fiber supplement such as psyllium powder (Metamucil) or methylcellulose (Citrucel) can help relieve signs and symptoms of mild to moderate diarrhea by adding bulk to your stool. For more severe diarrhea, loperamide (Imodium) may be effective. Use anti-diarrheal medications with great caution, however, because they increase the risk of toxic megacolon.
- **Laxatives.** In some cases, swelling may cause your intestines to narrow, leading to constipation. Talk to your doctor before taking any laxatives, because even those sold over-the-counter may be too harsh for your system.
- **Pain relievers.** For mild pain, your doctor may recommend acetaminophen (Tylenol, others). Don't use nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen (Advil, Motrin, others) or naproxen (Aleve). These are likely to make your symptoms worse.

Iron supplements. If you have chronic intestinal bleeding, you may develop iron deficiency anemia. Taking iron supplements may help restore your iron levels to normal and reduce this type of anemia once your bleeding has stopped or diminished.

Drug Therapy

The goal of drug therapy is to induce and maintain remission, and to improve the quality of life for people with ulcerative colitis. Several types of drugs are available.

- **Aminosalicylates**, drugs that contain 5-aminosalicylic acid (5-ASA), help control inflammation. Sulfasalazine is a combination of sulfapyridine and 5-ASA. The sulfapyridine component carries the anti-inflammatory 5-ASA to the intestine. However, sulfapyridine may lead to side effects such as nausea, vomiting, heartburn, diarrhea, and headache. Other 5-ASA agents, such as olsalazine, mesalamine, and balsalazide, have a different carrier, fewer side effects, and may be used by people who cannot take sulfasalazine. 5-ASAs are given orally, through an enema, or in a suppository, depending on the location of the inflammation in the colon. Most people with mild or moderate ulcerative colitis are treated with this group of drugs first. This class of drugs is also used in cases of relapse.
- **Corticosteroids** such as prednisone, methylprednisone, and hydrocortisone also reduce inflammation. They may be used by people who have moderate to severe ulcerative colitis or who do not respond to 5-ASA drugs. Corticosteroids, also known as steroids, can be given orally, intravenously, through an enema, or in a suppository, depending on the location of the inflammation. These drugs can cause side effects such as weight gain, acne, facial hair, hypertension, diabetes, mood swings, bone mass loss, and an increased risk of infection. For this reason, they are not recommended for long-term use, although they are considered very effective when prescribed for short-term use.
- **Immunomodulators** such as azathioprine and 6-mercaptopurine (6-MP) reduce inflammation by affecting the immune system. These drugs are used for patients who have not responded to 5-ASAs or corticosteroids or who are dependent on corticosteroids. Immunomodulators are administered orally, however, they are slow-acting and it may take up to 6 months before the full benefit. Patients taking these drugs are monitored for complications including pancreatitis, hepatitis, a reduced white blood cell count, and an increased risk of

infection. Cyclosporine A may be used with 6-MP or azathioprine to treat active, severe ulcerative colitis in people who do not respond to intravenous corticosteroids.

Other drugs may be given to relax the patient or to relieve pain, diarrhea, or infection.

Some people have remissions—periods when the symptoms go away—that last for months or even years. However, most patients' symptoms eventually return.

Hospitalization

Occasionally, symptoms are severe enough that a person must be hospitalized. For example, a person may have severe bleeding or severe diarrhea that causes dehydration. In such cases the doctor will try to stop diarrhea and loss of blood, fluids, and mineral salts. The patient may need a special diet, feeding through a vein, medications, or sometimes surgery.

Surgery

About 25 to 40 percent of ulcerative colitis patients must eventually have their colons removed because of massive bleeding, severe illness, rupture of the colon, or risk of cancer. Sometimes the doctor will recommend removing the colon if medical treatment fails or if the side effects of corticosteroids or other drugs threaten the patient's health.

Unlike Crohn's disease, ulcerative colitis can generally be cured by surgical removal of the large intestine. This procedure is necessary in the event of: exsanguinating hemorrhage, frank perforation or documented or strongly suspected carcinoma. Surgery is also indicated for patients with severe colitis or toxic megacolon. Patients with symptoms that are disabling and do not respond to drugs may wish to consider whether surgery would improve the quality of life.

Ulcerative colitis is a disease that affects many parts of the body outside the intestinal tract. In rare cases the extra-intestinal manifestations of the disease may require removal of the colon.

Alternative treatments

Surgery to remove the colon and rectum, known as proctocolectomy, is followed by one of the following:

If diet and lifestyle changes, drug therapy or other treatments don't relieve your signs and symptoms, your doctor may recommend surgery.

Surgery can often eliminate ulcerative colitis. But that usually means removing your entire colon and rectum (proctocolectomy). In the past, after this surgery you would wear a small bag over an opening in your abdomen (ileostomy) to collect stool. But a procedure called ileoanal anastomosis eliminates the need to wear a bag. Instead, your surgeon constructs a pouch from the end of your small intestine. The pouch is then attached directly to your anus. This allows you to expel waste more normally, although you may have as many as five to seven soft or watery bowel movements a day because you no longer have your colon to absorb water.

If you have surgery, your doctor may discuss whether an ileostomy or an ileoanal pouch is right for you. Between 25 percent and 40 percent of people with ulcerative colitis eventually need surgery.

- **Ileostomy**, in which the surgeon creates a small opening in the abdomen, called a stoma, and attaches the end of the small intestine, called the ileum, to it. Waste will travel through the small intestine and exit the body through the stoma. The stoma is about the size of a quarter and is usually located in the lower right part of the abdomen near the beltline. A pouch is worn over the opening to collect waste, and the patient empties the pouch as needed.

- **Ileoanal anastomosis**, or pull-through operation, which allows the patient to have normal bowel movements because it preserves part of the anus. In this operation, the surgeon removes the colon and the inside of the rectum, leaving the outer muscles of the rectum. The surgeon then attaches the ileum to the inside of the rectum and the anus, creating a pouch. Waste is stored in the pouch and passes through the anus in the usual manner. Bowel movements may be more frequent and watery than before the procedure. Inflammation of the pouch (pouchitis) is a possible complication.

Not every operation is appropriate for every person. Which surgery to have depends on the severity of the disease and the patient's needs, expectations, and lifestyle. People faced with this decision should get as much information as possible by talking to their doctors, to nurses who work with colon surgery patients (enterostomal therapists), and to other colon surgery patients. Patient advocacy organizations can direct people to support groups and other information resources.

Drugs used

Aminosalicylates

Sulfasalazine has been a major agent in the therapy of mild to moderate UC for over 50 years. In 1977 Mastan S.Kalsi et al determined that 5-aminosalicylic acid (5-ASA and mesalazine) was the therapeutically active compound in sulfasalazine. Since then many 5-ASA compounds have been developed with the aim of maintaining efficacy but reducing the common side effects associated with the sulfapyridine moiety in sulfasalazine.^[17]

- Mesalazine, also known as 5-aminosalicylic acid, mesalamine, or 5-ASA. Brand name formulations include Asacol, Pentasa, Mezavant, Lialda, and Salofalk.
- Sulfasalazine, also known as Azulfidine.
- Balsalazide, also known as Colazal.

- Olsalazine, also known as Dipentum.

Corticosteroids

- Cortisone
- Prednisone
- Prednisolone
- Hydrocortisone
- Methylprednisolone
- Beclometasone
- Budesonide - under the brand name of Entocort

Immunosuppressive drugs

- Mercaptopurine, also known as 6-Mercaptopurine, 6-MP and Purinethol.
- Azathioprine, also known as Imuran, Azasan or Azamun, which metabolises to 6-MP.
- Methotrexate, which inhibits folic acid
- Tacrolimus

Biological treatment

- Infliximab
- Visilizumab

Smoking

Unlike Crohn's disease, ulcerative colitis has a lesser prevalence in smokers than non-smokers.

Dietary modification

Dietary modification may reduce the symptoms of the disease.

- Lactose intolerance is noted in many ulcerative colitis patients. Those with suspicious symptoms should get a lactose breath hydrogen test.

- Patients with abdominal cramping or diarrhea may find relief or a reduction in symptoms by avoiding fresh fruits and vegetables, caffeine, carbonated drinks and sorbitol-containing foods.
- Many dietary approaches have purported to treat UC, including the Elaine Gottschall's specific carbohydrate diet and the "anti-fungal diet" (Holland/Kaufmann).
- The use of elemental and semi-elemental formula has been successful in pediatric patients.

Fats and oils

- **Fish oil.** Eicosapentaenoic acid (EPA), derived from fish oil. This is an Eicosanoid that inhibits leukotriene activity. It is effective as an adjunct therapy. There is no recommended dosage for ulcerative colitis. Dosages of EPA of 180 to 1500 mg/day are recommended for other conditions. [1]
- **Short chain fatty acid (butyrate) enema.** The colon utilizes butyrate from the contents of the intestine as an energy source. The amount of butyrate available decreases toward the rectum. Inadequate butyrate levels in the lower intestine have been suggested as a contributing factor for the disease. This might be addressed through butyrate enemas. The results however are not conclusive.

Herbals

- Herbal medications are used by patients with ulcerative colitis. Compounds that contain sulphhydryl may have an effect in ulcerative colitis (under a similar hypothesis that the sulphamoiety of sulfasalazine may have activity in addition to the active 5-ASA component).^[19] One randomized control trial evaluated the over-the-counter medication methionine-methyl sulphonium chloride (abbreviated MMSC, but more commonly referred to as Vitamin U) and found a significant decreased rate

of relapse when the medication was used in conjunction with oral sulfasalazine.^[20]

Bacterial recolonization

- Probiotics may have benefit. One study which looked at a probiotic known as VSL#3 has shown promise for people with ulcerative colitis.
- Fecal bacteriotherapy involves the infusion of human probiotics through fecal enemas. It suggests that the cause of ulcerative colitis may be a previous infection by a still unknown pathogen. This initial infection resolves itself naturally, but somehow causes an imbalance in the colonic bacterial flora, leading to a cycle of inflammation which can be broken by "recolonizing" the colon with bacteria from a healthy bowel. There have been several reported cases of patients who have remained in remission for up to 13 years.

Intestinal parasites

Inflammatory bowel disease is less common in the developing world. Some have suggested that this may be because intestinal parasites are more common in underdeveloped countries. Some parasites are able to reduce the immune response of the intestine, an adaptation that helps the parasite colonize the intestine. The decrease in immune response could reduce or eliminate the inflammatory bowel disease

Helminthic therapy using the whipworm *Trichuris suis* has been shown in a randomized control trial from Iowa to show benefit in patients with ulcerative colitis. The therapy tests the hygiene hypothesis which argues that the absence of helminths in the colons of patients in the developed world may lead to inflammation. Both helminthic therapy and fecal bacteriotherapy induce a characteristic Th2 white cell response in the diseased areas, which is somewhat paradoxical given that ulcerative colitis immunology was thought to classically involve Th2 overproduction.

Nicotine It has been shown that smokers on a dose-based schedule have their ulcerative colitis symptoms effectively reduced by cigarettes. The effect disappears if the user quits.

Is colon cancer a concern?

About 5 percent of people with ulcerative colitis develop colon cancer. The risk of cancer increases with the duration of the disease and how much the colon has been damaged. For example, if only the lower colon and rectum are involved, the risk of cancer is no higher than normal. However, if the entire colon is involved, the risk of cancer may be as much as 32 times the normal rate.

Sometimes precancerous changes occur in the cells lining the colon. These changes are called "dysplasia." People who have dysplasia are more likely to develop cancer than those who do not. Doctors look for signs of dysplasia when doing a colonoscopy or sigmoidoscopy and when examining tissue removed during these tests.

According to the 2002 updated guidelines for colon cancer screening, people who have had IBD throughout their colon for at least 8 years and those who have had IBD in only the left colon for 12 to 15 years should have a colonoscopy with biopsies every 1 to 2 years to check for dysplasia. Such screening has not been proven to reduce the risk of colon cancer, but it may help identify cancer early. These guidelines were produced by an independent expert panel and endorsed by numerous organizations, including the American Cancer Society, the American College of Gastroenterology, the American Society of Colon and Rectal Surgeons, and the Crohn's & Colitis Foundation of America.

Complications

The most serious acute complication of ulcerative colitis is toxic megacolon. This occurs when your colon becomes paralyzed, preventing you from having a bowel movement or passing gas. Signs and symptoms include abdominal pain and swelling, fever and

weakness. You might also become disoriented or groggy. If toxic megacolon isn't treated, your colon may rupture, causing peritonitis, a life-threatening condition requiring emergency surgery.

Other possible complications of ulcerative colitis include:

- Perforated colon
- Severe dehydration
- Liver disease
- Inflammation of your skin, joints and eyes

IBD and colon cancer

Both ulcerative colitis and Crohn's disease increase your risk of colon cancer. Despite this increased risk, however, more than 90 percent of people with inflammatory bowel disease never develop cancer. Your risk is greatest if you've had inflammatory bowel disease for at least eight to 10 years and if it's spread through your entire colon. You're less likely to develop cancer if only a small part of your colon is diseased.

Once you've had ulcerative colitis for eight to 10 years, be sure to have a colonoscopy every one or two years to look for early signs of colon cancer if your disease has spread farther than the rectum.

Pregnancy

If you have ulcerative colitis, talk to your doctor before becoming pregnant or fathering a child. Some medications used to treat IBD have the potential to cause birth defects or can be passed to the baby through breast milk. Active ulcerative colitis increases the risk of fetal death or preterm labor. If you're already pregnant, be sure you're cared for by a doctor who has experience with IBD and pregnancy.

Self-care

Sometimes you may feel helpless when facing ulcerative colitis. But changes in your diet and lifestyle may help control your symptoms and lengthen the time between flare-ups.

Diet

There's no firm evidence that what you eat causes inflammatory bowel disease. But certain foods and beverages can aggravate your symptoms, especially during a flare-up in your condition. It's a good idea to try eliminating from your diet anything that seems to make your signs and symptoms worse. Here are some suggestions that may help:

- **Limit dairy products.** Like many people with inflammatory bowel disease, you may find that problems, such as diarrhea, abdominal pain and gas, improve when you limit or eliminate dairy products. You may be lactose intolerant — that is, your body can't digest the milk sugar (lactose) in dairy foods. If so, try substituting yogurt or low-lactose cheeses, such as Swiss and cheddar, for milk. Or use an enzyme product, such as Lactaid, to help break down lactose. In some cases, you may need to eliminate dairy foods completely. If you need help, a registered dietitian can help you design a healthy diet that's low in lactose. Keep in mind that with limiting your dairy intake, you'll need to find other sources of calcium, such as supplements.
- **Experiment with fiber.** For most people, high-fiber foods, such as fresh fruits and vegetables and whole grains, are the foundation of a healthy diet. But if you have inflammatory bowel disease, fiber may make diarrhea, pain and gas worse. If raw fruits and vegetables bother you, try steaming, baking or stewing them.

You may also find that you can tolerate some fruits and vegetables, but not others. In general, you may have more problems with foods in the cabbage family, such as broccoli and cauliflower, and with very crunchy foods such as raw apples and carrots.

- **Avoid problem foods.** Eliminate any other foods that seem to make your symptoms worse. These may include "gassy" foods such as beans, cabbage and broccoli, raw fruit juices and fruits — especially citrus fruits — spicy food, popcorn, alcohol, caffeine,

and foods and drinks that contain caffeine, such as chocolate and soda.

- **Eat small meals.** You may find you feel better eating five or six small meals rather than two or three larger ones.
- **Drink plenty of liquids.** Try to drink plenty of fluids daily. Water is best. Alcohol and beverages that contain caffeine stimulate your intestines and can make diarrhea worse, while carbonated drinks frequently produce gas.
- **Ask about multivitamins.** Because ulcerative colitis can interfere with your ability to absorb nutrients and because your diet may be limited, vitamin and mineral supplements can play a key role in supplying missing nutrients. They don't provide essential protein and calories, however, and shouldn't be a substitute for meals.
- **Talk to a dietitian.** If you begin to lose weight or your diet has become very limited, talk to a registered dietitian.

Stress

Although stress doesn't cause inflammatory bowel disease, it can make your signs and symptoms much worse and may trigger flare-ups. Stressful events can range from minor annoyances to a move, job loss or the death of a loved one.

When you are stressed, your normal digestive process changes. Your stomach empties more slowly and secretes more acids. Stress can also speed or slow the passage of intestinal contents. It may also cause changes in intestinal tissue itself.

Although it's not always possible to avoid stress, you can learn ways to help manage it. Some of these include:

- **Exercise.** Even mild exercise can help reduce stress, relieve depression and normalize bowel function. Talk to your doctor about an exercise plan that's right for you.

- **Biofeedback.** This stress-reduction technique helps you reduce muscle tension and slow your heart rate with the help of a feedback machine. You're then taught how to produce these changes yourself. The goal is to help you enter a relaxed state so that you can cope more easily with stress. Biofeedback is usually taught in hospitals and medical centers.
- **Regular relaxation and breathing exercises.** An effective way to cope with stress from ulcerative colitis is to regularly relax and exercise. You can take classes in yoga and meditation or practice at home using books or tapes.

You can also practice progressive relaxation exercises. These help relax the muscles in your body, one by one. Start by tightening the muscles in your feet, then concentrate on slowly letting all the tension go. Next, tighten and relax your calves. Continue until the muscles in your body, including those in your eyes and scalp, are completely relaxed.

Deep breathing also can help you relax. Most adults breathe from their chests. But you become calmer when you breathe from your diaphragm — the muscle that separates your chest from your abdomen. When you inhale, allow your belly to expand with air; when you exhale, your abdomen naturally contracts. Deep breathing can also help relax your abdominal muscles, which may lead to more normal bowel activity.

- **Hypnosis.** Hypnosis may reduce abdominal pain and bloating. A trained professional can teach you how to enter a relaxed state and then guide you as you imagine your intestinal muscles becoming smooth and calm.

Other techniques. Set aside at least 20 minutes a day for any activity you find relaxing — listening to music, reading, playing computer games or just soaking in a warm bath.

Coping skills

Ulcerative colitis doesn't just affect you physically it takes an emotional toll as well. If signs and symptoms are severe, your life may revolve around a constant need to run to the toilet. In some cases, you may barely be able to leave the house. When you do, you might worry about an accident, and this anxiety only makes your symptoms worse.

Even if your symptoms are mild, gas and abdominal pain can make it difficult to be out in public. You may also feel hampered by dietary restrictions or embarrassed by the nature of your disease. All of these factors isolation, embarrassment and anxiety can severely alter your life. Sometimes they may lead to depression.

Although support groups are not for everyone, they can provide valuable information about your condition as well as emotional support. Group members frequently know about the latest medical treatments or integrative therapies. You may also find it reassuring to be among people who understand what you are going through.

Counseling

Some people find it helpful to consult a psychologist or psychiatrist who's familiar with inflammatory bowel disease and the emotional difficulties it can cause. Although living with ulcerative colitis can be discouraging, the outlook is brighter than it was even just a few years ago.

Hope through Ongoing research

Recent evidence from the ACT-1 trial suggests that infliximab may have a greater role in inducing and maintaining disease remission.

An increased amount of colonic sulfate-reducing bacteria has been observed in some patients with ulcerative colitis, resulting in higher concentrations of the toxic gas hydrogen sulfide. The role of hydrogen sulfide in pathogenesis is unclear. It has been suggested that the protective benefit of smoking that some patients report is due to hydrogen cyanide from cigarette smoke reacting with

hydrogen sulfide to produce the nontoxic isothiocyanate. Another unrelated study suggested sulphur contained in red meats and alcohol may lead to an increased risk of relapse for patients in remission^[8]

There is much research currently being done to elucidate further genetic markers in ulcerative colitis. Linkage with Human Leukocyte Antigen B-27, associated with other autoimmune diseases, has been proposed.

Low dose naltrexone is under study for treatment of Crohn's disease and ulcerative colitis.

NIDDK, through the Division of Digestive Diseases and Nutrition, conducts and supports research into many kinds of digestive disorders, including ulcerative colitis. Researchers are studying how and why the immune system is activated, how it damages the colon, and the processes involved in healing. Through this increased understanding, new and more specific therapies can be developed. Currently, there are numerous clinical trials being conducted that are investigating ulcerative colitis. A complete listing of research studies on ulcerative colitis may be found at www.ClinicalTrials.gov and www.digestive.niddk.nih.gov