

## ULCERATIVE COLITIS

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### **What is Ulcerative Colitis?**

Ulcerative colitis (UC) is a disease marked by inflammation of the lining of the colon and rectum, together known as the large intestine. This inflammation causes irritation in the lining of the large intestine which leads to the symptoms of UC. Though UC always affects the lowest part of the large intestine (the rectum), in some patients it can be present throughout the entire colon. UC belongs to a group of diseases called inflammatory bowel diseases which also includes Crohn's disease (CD). Though it was once thought that UC and CD were two different diseases, as many as 10% of patients may have features of both diseases and this is called indeterminate colitis. It is important to note that inflammatory bowel disease (IBD) is different from irritable bowel syndrome (IBS).

### **What are the symptoms of UC?**

The symptoms of ulcerative colitis depend on the severity of inflammation and the amount of the colon that is affected by the disease. In patients with mild to moderate inflammation, symptoms can include rectal bleeding, diarrhea, mild abdominal cramping, stool urgency, and tenesmus (discomfort and the feeling that you have not completely emptied your rectum after a bowel movement). When more severe inflammation is present, patients often develop fever, dehydration, severe abdominal pain, weight loss, loss of appetite or growth retardation (in children and adolescents with UC). Individuals with moderate or severe inflammation may also have to wake up at night to have bowel movements and may lose control of bowel movements. Some of the symptoms of UC may be non-specific and could be caused by other diseases such as Crohn's disease, irritable bowel syndrome, or infection. Your doctor can help determine the cause of your symptoms and should be consulted should you experience a significant change in your symptoms.

### **How is UC diagnosed?**

Your doctor will usually suspect the diagnosis of ulcerative colitis based on your symptoms, but confirmation of the diagnosis requires testing. Blood work is often checked to look for markers of inflammation or anemia (low blood counts), though these tests can be normal in patients with mild disease. Tests of your stool to look for evidence of an intestinal infection are often obtained. Radiologic images including x-rays and CT scans are usually not recommended but may be performed. All patients with symptoms consistent with UC should have a colonoscopy or flexible sigmoidoscopy to confirm the diagnosis assuming that they are healthy enough to undergo the procedure. During this procedure, your gastroenterologist will be able to directly examine the lining of your colon and rectum to look for evidence of inflammation and take small biopsies to be examined under a microscope to look for the cause of the inflammation.



## **What causes UC?**

The way in which patients get ulcerative colitis is still poorly understood. There seems to be an interaction between the unique genetic makeup of an individual, environmental factors, and a patient's specific immune system that triggers the disease. UC is not an infection that can be passed from person to person. Men and women are equally affected by UC.

UC is more common in first degree relatives (siblings, parents, and children) of patients affected by UC and up to 20% of patients will have an affected family member. Despite the influence of genetics, the majority of patients with UC do not pass the disease to their children. There is no way to predict those at higher risk. Cases of ulcerative colitis have been identified throughout the world though certain populations, including those living in Northern climates and those of Jewish descent, are at higher risk of developing UC.

Individuals having their appendix removed prior to the age of 20 appear to be at lower risk of developing UC. No specific infectious agent has been linked to UC and diet, breast feeding, and various medications have also been examined but none have been found to cause UC.

It has been observed that smokers have lower rates of UC than non-smokers. Furthermore, those who smoke and have UC tend to have a milder course of UC than those who do not smoke (note that this is the exact opposite effect that smoking has on Crohn's disease). Despite the protective role smoking appears to have on the development and natural history of UC, it is not recommended that patients start smoking to prevent UC due to the fact that there are so many other illnesses and cancers in which smoking is a definite risk factor.

UC is an immune-mediated disease in which there is loss of control of the normal bowel immune activity and the ongoing activity results in damage to the bowel wall.

## **What are the possible complications of UC?**

The complications of ulcerative colitis can be divided into those affecting the colon and those occurring outside of the colon. Within the colon, UC can rarely lead to toxic megacolon or colon cancer.

Toxic megacolon describes a severe disease flare with a high risk of infection and colonic perforation (holes in the colon). Patients may occasionally present with toxic megacolon as their initial presentation of UC and this complication requires hospitalization and may lead to surgery to remove the colon (colectomy).

UC is known to increase the risk of colon cancer. Those patients who have had UC for a long time and those with a longer length of the colon affected are at higher risk of developing colon cancer. In general, patients begin to have an increased risk of colorectal cancer 10 years after the onset of disease symptoms and should have colonoscopy every one or two years starting at this time. Colon cancer is a rare complication and it is thought that it may be preventable based on control of inflammation of the colon and careful colonoscopy examinations that look for any



pre-cancerous changes called dysplasia. Overall, the risk of colon cancer increases 0.5% yearly after 10 years of disease though patients with inflammation throughout their colon may be at higher risk. Those patients with primary sclerosing cholangitis (PSC) are at greatest risk for colon cancer and need to start screening upon diagnosis.

Patients with UC are also at risk for extra-intestinal manifestations of UC (complications outside of the colon). These complications most frequently involve the liver, skin, eyes, mouth, and joints. Within the liver, patients with UC may develop primary sclerosing cholangitis. This occurs in about 3% of patients with UC. PSC can progress even if UC is not active and it is often detected by elevations in liver blood tests and confirmed by the use of MRI scans such as Magnetic Resonance Cholangiopancreatography (MRCP) or endoscopic procedures such as Endoscopic Retrograde Cholangiopancreatography (ERCP).

Patients with UC can develop sores in the mouth or rashes on the skin that generally only appear when UC colon symptoms are active. The most common rashes that are seen in UC are erythema nodosum (EN) and pyoderma gangrenosum (PG). EN usually presents as a red, raised, painful area most commonly on the legs and is most often seen during flares of UC. PG also presents as raised lesions on the skin (most frequently on the legs) that often develops after trauma to the skin and can lead to the formation of ulcers. Unlike in EN, the appearance of skin lesions in PG may or may not mirror the activity of bowel symptoms. The eyes can become red and painful (uveitis) and vision problems should be reported to your doctor.

Arthritis is commonly associated with UC and can affect either small (such as the fingers/toes) or large joints (often the knee), though involvement of the smaller joints may have a course that is not related to activity in the colon. The joints of the spine can be affected as well, though this is less common than it is in Crohn's disease.

As in other chronic medical conditions, anxiety and depression are common in patients with UC. The unpredictability of UC and the need to take medications on a daily basis can lead to feelings of frustration or anger. Though occasional feelings of frustration can be normal, feelings of significant anxiety or depression should be brought to the attention of your physician. There are many support opportunities available for those having trouble coping with UC (see the final section).

### **What is the clinical course of UC?**

Ulcerative colitis can present in a variety of ways. UC is often a chronic, life-long condition. It most often is diagnosed in the 2nd and 3rd decades of life (ages 11-30), although it can be diagnosed at any age. The initial presentation can be mild and is sometimes confused with other conditions such as irritable bowel syndrome or it can be very severe and require hospitalization and surgery. For most patients, UC tends to follow a course marked by periods of disease activity followed by variable periods during which a patient is symptom free. Some patients may have continuous disease activity. Rarely, a patient will have only a single disease flare. In general, those people with a severe first attack of UC and those who have their entire colon



affected by UC tend to have a more aggressive course with more frequent flares and shorter periods of remission. Despite the chronic nature of UC, most patients are able to function well and the life expectancy of a patient with UC is normal.

### **How is UC treated?**

Medical treatment of ulcerative colitis generally focuses on two separate goals: the induction of remission (making a sick person well) and the maintenance of remission (keeping a well person from getting sick again). Surgery is also a treatment option for UC and will be discussed separately. Medication choices can be grouped into four general categories: aminosalicylates, steroids, immunomodulators, and biologics.

Aminosalicylates are a group of anti-inflammatory medications (sulfasalazine, mesalamine, olsalazine, and balsalazide) used for both the induction and maintenance of remission in mild to moderate UC. These medications are available in both oral and rectal formulations and work on the lining of the colon to decrease inflammation. They are generally well tolerated. The most common side effects include nausea and rash. Rectal formulations of mesalamine (enemas and suppositories) are generally used for those patients with disease at the end of their colon.

Steroids (prednisone) are an effective medication for the induction of remission in moderate to severe UC and are available in oral, rectal, and intravenous (IV) forms. Steroids are absorbed into the bloodstream and have a number of severe side effects that make them unsuitable for chronic use to maintain remission. These side effects include cataracts, osteoporosis, mood effects, an increased susceptibility to infection, high blood pressure, weight gain, and an underactive adrenal gland.

Immunomodulators include medications such as 6-mercaptopurine and azathioprine. These are taken in pill form and absorbed into the bloodstream. They are effective for maintenance of remission in moderate to severe ulcerative colitis, but are slow to work and can take up to 2-3 months to reach their peak effect. Because of this, these medications are often combined with other medications (such as steroids) in patients who are very ill. These medications require frequent blood work as they can cause liver test abnormalities and low white blood cell counts, both of which are reversible when the medication is stopped. Adverse reactions can include nausea, rash, liver and bone marrow toxicity, pancreatitis, and rarely lymphoma.

Biologic agents are medications given by injection that are used to treat moderate to severe UC. At the current time, infliximab (Remicade®) is the only biologic agent approved for use in UC, but other biologics used for Crohn's disease under evaluation for the treatment of UC include adalimumab (Humira®), and certolizumab pegol (Cimzia®). Infliximab is effective in both the induction and maintenance of remission in UC. The side effects of this medicine may include an allergic reaction to the medication called an "infusion reaction" or "hypersensitivity reaction". There are also rare risks of serious infections with these medications. Lymphoma is a rare risk of these therapies as well. Combination therapy with azathioprine/6-mercaptopurine and biologics increases the risk of a particularly rare type of lymphoma called hepatosplenic T-cell lymphoma. As with all medications, you should discuss the risks and benefits with your doctor.



Other medications used less frequently for UC include cyclosporine and tacrolimus. These agents are sometimes used in those rare cases of severe UC that are not responsive to steroids. Side effects of these agents include infections and kidney problems. These agents are offered at a limited number of hospitals and are usually used for a short period of time as a bridge to other maintenance therapies such as azathioprine or 6-mercaptopurine.

No matter which medical therapy you and your doctor decide upon, adherence with the prescribed course is essential. No medical therapy can work if it is not taken and failure to take your medications can lead to unnecessary escalation of therapy if it is not brought to the attention of your doctor. Because many of the complications associated with UC are related to ongoing disease activity, good medication adherence may minimize these risks.

### **What is the role of surgery?**

Surgery in ulcerative colitis is performed for a number of reasons and is generally considered to be curative if the entire large intestine removed. Patients who do not respond to medications, are concerned about or have unacceptable side effects from medications, develop toxic megacolon, dysplasia (precancerous lesions) or cancer, or children who are not growing because of UC are often considered for surgery. Several different surgeries are performed for UC and the choice of surgery is dependent on patient preference and the experience of the surgeon. The most common surgery is total proctocolectomy with ileal pouch anal anastomosis (total removal of the colon and rectum with creation of a pseudo-rectum from a portion of the small intestine). This operation usually requires two separate surgeries to complete although it may require three stages in severely ill patients. Following this surgery, patients can expect 5-10 stools daily as they no longer have a colon to store stool. Patients usually feel better because their sense of stool urgency improves, they no longer have bleeding, and their medications can often be stopped. However, these patients are at risk for post-operative inflammation of the pouch known as pouchitis which is usually treated with antibiotics. Women who have this surgery may have decreased ability to get pregnant naturally.

Another common surgical procedure involves a proctocolectomy with ileostomy (removal of the entire colon and rectum and connection of the small intestine to the abdominal wall so that stool empties into a bag). This procedure is often undertaken in elderly patients, obese patients or those with anal dysfunction. Should you need a surgical procedure for UC, your surgeon can help you decide which type of surgery best fits your needs.

### **Do complementary and alternative therapies work in UC?**

Outside of the standard medical therapies discussed for ulcerative colitis, many alternative therapies have been studied. No studies have suggested that diet can either cause or treat UC and there is no specific diet that patients with UC should follow though it is advisable to eat a balanced diet. Likewise, there is no convincing evidence that UC results from food allergies. Though vitamin and mineral deficiencies are more common in Crohn's disease, specific deficiencies can occur in UC patients. For this reason, a multivitamin and a calcium supplement are not unreasonable. Malnutrition can become a concern in severe UC.



Probiotics are species of bacteria that are thought to have beneficial properties for the bowel. There are a number of scientific studies which have been performed to assess the role of probiotics in UC, and most of these have not shown benefit. There is some evidence, however, that a specific probiotic (VSL #3) may be helpful as an additive to other therapies for maintenance of remission.

Various other herbal remedies and alternative therapies have been studied for use in patients with IBD such as curcumin (a derivative of the herb tumeric) and parasitic worms (helminths). Though limited studies have shown promise for a number of alternative therapies, these have not yet been shown to be safe and effective and are not currently recommended. Studies of homeopathic compounds are currently ongoing and will hopefully provide novel treatments for use in UC in the future.

### **What type of follow-up is required?**

As mentioned earlier, ulcerative colitis is a chronic disease and establishing a long term relationship with a gastroenterologist experienced in the treatment of UC is advisable. Many medications used in UC require regular blood work to ensure that they are not causing any serious side effects. Patients with UC have a higher risk of osteoporosis associated with both underlying disease activity and long term or frequent steroid use. Because of this risk, your doctor may recommend measurement of Vitamin D blood levels and a bone mineral density screening with a DEXA scan. Colorectal cancer screening is also important because of the higher risk of cancer in patients with UC as discussed earlier.

### **Where can you get more information?**

Many organizations provide support and information for patients with ulcerative colitis. The ACG website ([www.acg.gi.org](http://www.acg.gi.org)) has additional information. The Crohn's and Colitis Foundation of America ([www.cdfa.org](http://www.cdfa.org)) has extensive patient information along with links to various different social, financial, and medical support groups. Other sources of information include the individual drug company websites, and, most importantly, your personal physician.

