Ulcerative Colitis

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 if you experience a significant change in your symptoms.

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. Cases of ulcerative colitis have been identified throughout the world. 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 for 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.

- **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, methylprednisolone and budesonide) 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. Budesonide tends to cause fewer steroid side-effects than prednisone.

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. There are two classes of biologic agents that are approved for use in UC. The first class of medications works on an inflammatory molecule called tumor necrosis factor alpha (TNF-alpha) and is commonly called anti-TNF agents. Anti-TNF drugs approved for the treatment of ulcerative colitis include infliximab, adalimumab, and golimumab. Infliximab is administered by IV infusion generally every eight weeks while adalimumab is a subcutaneous injection every two weeks and golimumab is a subcutaneous injection every four weeks. Side effects of these medications include infusion or injection site reactions and allergic hypersensitivity reactions. There are rare risks of serious infections with these medications. These medications lower one's immune system response so your doctor should perform a skin test or blood test for latent tuberculosis and a blood test for hepatitis B before starting a biologic drug. Lymphoma is a rare risk of these therapies. Combination therapy with azathioprine/6-mercaptopurine and biologics increases the risk of a particularly rare type of lymphoma called hepatosplenic T-cell lymphoma. The second class of biologic medications, called integrin inhibitors, works on receptors called integrins, which control the trafficking of white blood cells to the intestine. The only currently approved integrin inhibitor for ulcerative colitis is called vedolizumab, which is administered as an IV infusion every eight weeks. Side effects include infusion reactions, increased susceptibility to infections, and slightly increased risk of lymphoma or other malignancies. 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 to 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.

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

Many organizations provide support and information for patients with ulcerative colitis. The ACG website (gi.org) has additional information. The Crohn's and Colitis Foundation of America (www.ccfa.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.

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