

Division of Gastroenterology and Hepatology

UNC Multidisciplinary Center for IBD Research and Treatment

Treatment of Ulcerative Colitis

Medical and surgical therapy- pouch procedure

The primary goal of treatment is to improve patients' symptoms (diarrhea, pain, blood loss) and, once this is successful, to prevent recurrence. The usual first step is the use of drugs. The choice of therapy depends on the severity of patients' symptoms. In cases with mild to moderately severe inflammation, 5-aminosalicylic acid is often prescribed. In patients in whom the joints are also affected, sulfasalazine can be tried. This drug, discovered in 1942 by the Swedish physician Nanna Svartz, was the standard treatment for ulcerative colitis prior to the introduction of 5-aminosalicylic acid. 5-aminosalicylic acid, also known as mesalazine or mesalamine, is a specially manufactured agent designed to be released in the lower third of the small bowel and in the upper two-thirds of the colon. In those cases in which ulcerative colitis affects only the rectum or left side of the colon (up to 80% of patients), the disease may respond to suppositories, enemas or rectal foams that contain either 5-aminosalicylic acid or cortisone preparations. In severe cases, the administration of cortisone preparations either as pills or injections is usually effective.

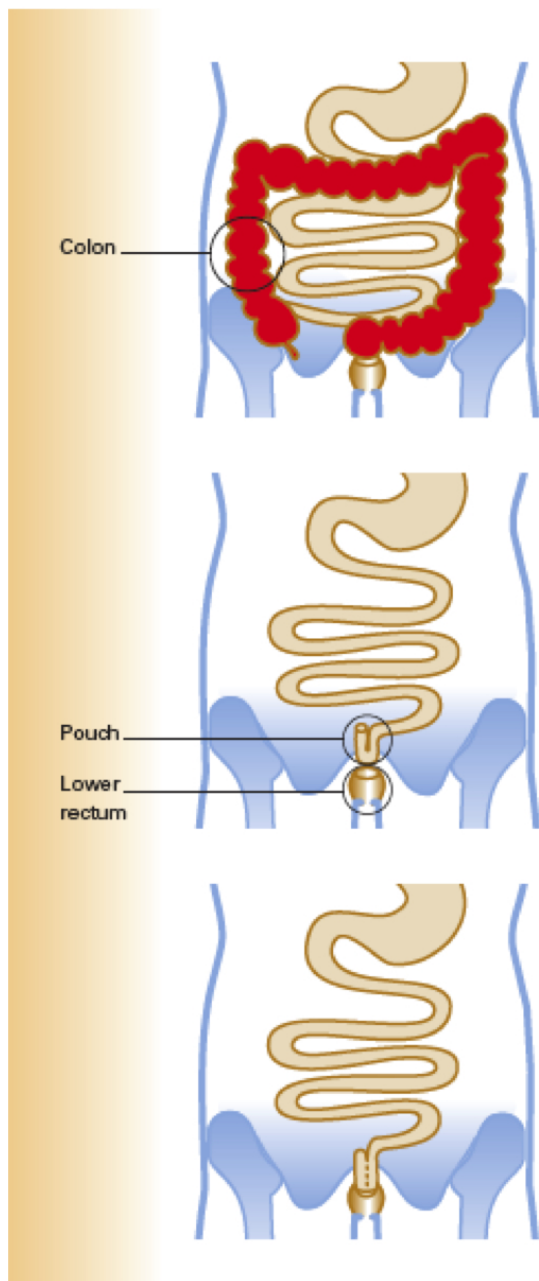
If cortisone in the form of tablets or enemas does not lead to an improvement in a patient's symptoms, the physician may recommend medications that reduce the body's immune reactions. These drugs are frequently effective because, as we noted above, chronic inflammatory bowel diseases represent a disorder in which the body's immune system has been misdirected against its own tissues. If this type of treatment is selected, the first drugs tried are usually Imuran or 6-Mercaptopurin ([IMURAN 6MP.pdf](#)). Their maximum effect, however, becomes apparent only after 10–12 weeks of therapy. Unfortunately, not all patients respond to these drugs and about 10 in 100 patients experience significant side effects, including acute hepatitis, acute pancreatitis or a disorder of blood cell formation. Hence, patients must undergo regular (weekly, then biweekly) laboratory tests of liver and pancreatic function and complete blood counts. If these tests remain normal for three months, the test frequency can be reduced to every 2–3 months.

If azathioprine or 6-mercaptopurine successfully prevent disease recurrence, they should be taken for at least four years. Within this time period, patients must practice a secure form of contraception. If an ulcerative colitis flare is very severe and cortisone therapy does not result in any improvement, patients should be hospitalized. In such cases, cyclosporine or infliximab can be administered intravenously. Cyclosporine was originally developed for use in patients with kidney transplants to suppress the body's rejection of the transplanted organ. Infliximab is a protein, which inhibits an inflammatory mediator

called tumor necrosis factor (TNF), which is elevated in patients with active inflammatory bowel disease. If cyclosporine or infliximab proves ineffective, the last option is the surgical removal of the colon (colectomy). Patients in whom therapy results in resolution of complaints (remission) are usually started on 5-aminosalicylic acid in order to maintain their status of disease remission.

A very important point in the therapy of ulcerative colitis is that the choice between the various preparations and the method of administration depends on the extent and activity of the disease. This fact explains the importance of a complete examination before treatment and in cases in which the pattern of symptoms has changed. In determining the best treatment strategy, the physician will take into consideration the severity of the flare-up and the extent of inflammation. In any case, the drugs must be taken long-term, that is, even after symptoms have resolved. Long-term administration of 5-aminosalicylic acid preparations has been shown to effectively prevent a new flare-up of the disease. As with all medications, undesired side effects may occur. These include headache, stomach complaints, nausea, anemia and hair loss. These side effects, however, are rare and resolve once administration of the drug has been stopped. The detailed description of these side effects on the package insert should not cause you to stop taking the drug out of fear. Instead, you should always consult your physician who will use appropriate methods to determine whether, in your case, the administration of the drug should be stopped or the dosage changed. Complications are more frequently due to patients' discontinuing their medication without consulting their physician than to side effects of the drug themselves. This is also true for patients who are, for the moment, free of complaints.

Recent studies have shown that disease recurrence in ulcerative colitis can be effectively blocked by the administration of a so-called probiotic, which contains *Escherichia coli* Nissle. Probiotics influence the bowel's bacterial flora and include such agents as *Escherichia coli* Nissle and various lactobacilli. *Escherichia coli* Nissle appeared to be as effective as 5-aminosalicylic acid. This method is particularly attractive in patients who do not tolerate 5-aminosalicylic acid, but *Escherichia coli* Nissle is currently only available in Europe. Other probiotics might as well have the same efficacy as *Escherichia coli* Nissle in patients with ulcerative colitis (e.g. VSL#3), but this is not yet clinically proven. The efficacy of probiotics, however, has not been substantiated in the treatment of Crohn's disease or of the acute disease phase of ulcerative colitis.



Beside the testing of new drugs, several new and interesting therapy concepts exist that are currently being investigated in clinical studies, which includes the inhibition of various, recently discovered mediators of inflammation. As with all new therapeutic methods, studies must comprehensively investigate both their effects (here, the success of therapy) and possible side effects.

Because of the success associated with drug treatment, surgery is rarely necessary. Life-threatening complications, severe complaints persisting despite adequate drug treatment and serious drug-induced side effects are indications for surgery. The surgical removal of the entire colon cures ulcerative colitis. In many cases, it may be possible to remove the colon without the need for a permanent "ileostomy" or artificial bowel outlet in the abdominal wall. This usually involves surgical creation of a "pouch" out of loops of small bowel that acts as a reservoir and substitute for the rectum (see figure "Pouch"). In most cases, this results in almost normal stool consistency and a bowel movement frequency of about five to eight times per day [IPAA.pdf].

Patients with ulcerative colitis do not require a special diet. It is advisable, however, to avoid foods such as cabbage, onions or high-fat items that may cause complaints even in healthy persons. In our experience, it is usually best for each patient to test his or her own individual tolerance to different foods. Nutritional deficiencies occur very rarely in patients with ulcerative colitis. These may manifest themselves as edema (swelling due to accumulation of water in various tissues caused by protein deficiency) or anemia (due to blood loss or iron deficiency) occurring most often in instances of prolonged disease flare-ups. They respond to substitution of the appropriate substances.

Disease manifestations outside of the bowel (joints, skin, eyes) can also be successfully treated with medication, usually with preparations containing cortisone. Surgical or dietary measures are usually less effective. Changes occurring in the biliary tract are often treated with ursodeoxycholic acid (UDCA), a bile acid. UDCA does not "cure" these conditions but may significantly slow their progression. Every case of abnormal "liver enzymes" requires

careful study and appropriate treatment.