



# **Ulcerative Colitis**

## Overview

- · What is Ulcerative Colitis?
  - Ulcerative colitis (UC) is when the lining of the large intestine gets inflamed. The large intestine is made up of the colon and the rectum. When this gets inflamed, symptoms of UC start.
  - UC involves the rectum in everyone. But in some people it can affect the whole colon. UC belongs to a group of diseases called inflammatory bowel diseases. The other main one being Crohn's disease (CD). Though it was once thought that UC and CD were different, as many as 10% of patients can have features of both. This is called IBD-U (IBD-Unclassified).
- What are the symptoms of UC?

These depend on how bad the inflammation is and the amount of the colon that is involved.

In mild to moderate inflammation, symptoms can include:

- o blood in the stool,
- o diarrhea,
- o mild abdominal cramping,
- o feeling the urge to go to have a bowel movement, and
- o tenesmus (the feeling that bowels have not emptied even after just going).

When more severe inflammation is present, patients often develop:

- o fever,
- o dehydration,
- o severe abdominal pain,
- weight loss.
- o loss of appetite or
- o stunted growth (in children and adolescents with UC)
- o may lose control of bowels (have accidents)

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 may suspect UC based on your symptoms. However tests will need to be done to make the diagnosis.

- Blood work is often checked to look for markers of inflammation or anemia (low blood counts). But these tests can be normal in patients with mild disease.
- o **Stool samples:** Check for blood, inflammation or infections in the stool.
- Special x-rays and CT scans: are usually not recommended but may be performed.
- What endoscopic tests are used to diagnose UC?

All patients with symptoms of UC should have a **colonoscopy** or **flexible sigmoidoscopy**. This will confirm the diagnosis. During this procedure, your doctor will see the lining of your colon and rectum. This can see signs of irritation and small tissue samples (biopsies) can be taken. The samples are looked at under a microscope to see if it is UC.

### What causes UC?

Why patients get UC is still poorly understood.

Causes may have a variety:

- o the unique genetic makeup of a person,
- environmental factors and
- o a patient's specific immune system
- What is known about risk factors for UC?
  - UC is not an infection that can be passed from person to person.
  - $\circ\hspace{0.1cm}$  Men and women are affected the same
  - UC is more common in people who have a first degree relative (sibling, parent, or child) with it. Up to 10% of patients have a family member with UC. Most patients with UC do not pass the disease to their children. But there is no way to predict those at higher risk.
  - Cases of UC have been seen around the world in certain groups. People who live in northern parts and those of Jewish descent, are at higher risk.
  - People having their appendix removed before the age of 20 appear to be at lower risk.
  - A particular infection has not been linked to UC. Diet, breast feeding, and medications have also been looked at, but none have been found to
    cause it.
  - Some patients develop UC after they quit smoking. It looks like smoking tobacco helps UC, since those who smoke have milder symptoms.

    This is opposite for what we see in Crohn's disease. However, it is not recommended to smoke to try and help UC. This is because smoking causes so many other illness and cancers that it is not worth it. /li>
- What are the possible complications of UC?

The complications of UC can be split into those that affect the colon or other parts of the body.

#### • What are the complications of UC within the colon?

Within the colon, UC can rarely lead to colon cancer or toxic megacolon (a rare but potentially deadly widening of the large intestine).

## • What is the risk of Colon Cancer in UC?

UC is known to increase the risk of colon cancer. Patients with UC symptoms for 8 or more years and those with more of the colon affected are at higher risk. Overall, the risk of colon cancer increases 0.5 percent every year after ten years of disease. Therfore a colonoscopy is needed every one or two years starting 8 years after symptoms begin.

Patients with inflammation of the bile ducts, called primary sclerosing cholangitis (PSC), are at highest risk for colon cancer and need a colonoscopy every year as soon as PSC is found.

• Luckily colon cancer is rare in UC. It may not happen if the inflammation of the colon is kept under control. By doing careful colonoscopy exams, biopsies can look for pre-cancerous changes called dysplasia under the microscope. If these are seen, further things can be done to remove it and prevent cancer from forming.

## What are the risks outside of the colon in UC patients?

Patients with UC are also at risk for extra-intestinal manifestations of UC (complications outside of the colon). These complications often involve the liver, skin, eyes, mouth, and joints.

#### • What are the complications within the liver in UC patients?

In the liver, patients may get <u>primary sclerosing cholangitis</u>. This occurs in about 3% of patients with UC. PSC can progress even if UC is not active. It is often detected by increases in liver blood tests. A special MRI scan such as a Magnetic Resonance Cholangiopancreatography (MRCP) can see it. Other times a procedure called an Endoscopic Retrograde Cholangiopancreatography (ERCP) is done.

#### What rashes can appear UC patients?

Patients with UC can develop sores in the mouth or rashes on the skin. These usually appear when UC symptoms are active. The most common rashes that are seen in UC are erythema nodosum (EN) and pyoderma gangrenosum (PG).

- EN are red, raised, painful areas usually on the legs. If they show up, its usually during flares of UC.
- PG can also look like raised lesions on the skin. Again most commonly on the legs. These are different than EN for a few reasons. One is trauma
  to the skin like a cut can cause them. Also they can grow into ulcers on the skin. Last, they may or may not be seen during flares of UC.
- The eyes can become red and painful (uveitis) and vision problems should be reported to your doctor.

#### How does UC affect the joints in UC patients?

Arthritis is commonly associated with UC. It can involve small joints (such as the fingers/toes) or large joints (often the knee). When smaller joints are hurting, they may be going on at the same time as a UC flare. The joints of the spine can be affected as well, but this is less common than it is in Crohn's disease

#### What are mood problems that may impact UC patients?

Anxiety and depression can be common. This is the same in any chronic condition. UC can be irregular and the need to take daily medicines can be frustrating. Even though these feelings are normal, really bad anxiety or depression should be discussed with your doctor. There are many support groups for trouble coping with UC (see the final section).

## • What is the clinical course of UC?

UC can present in different ways. UC is often a chronic, life-long condition. It is often diagnosed between the ages of 11 and 30. Although it can be diagnosed at any age. Early symptoms can be mild and may be confused with other conditions such as Irritable Bowel Syndrome. Other times they are very severe and require a hospital stay and surgery. Usually symptoms vary over time. There can be times where symptoms are constant. Other times symptoms are fully gone. Rarely though will someone just have a single flare.

People with a severe first attack or those whose entire colon is affected usually have a more aggressive course. This means more frequent flares and shorter periods of being symptom-free. The good news is that patients are still able to function well. Also the life expectancy is the same as anyone else's.

## How is UC treated?

Medical treatment of UC has two separate goals:

- the induction of remission (making a sick person well), and
- the maintenance of remission (keeping them well and preventing flare-ups).

Surgery is also a treatment option for UC and will be discussed separately. Medication choices can be grouped into four general categories:

- o aminosalicylates,
- o steroids,
- o immunomodulators, and
- biologics

Aminosalicylates are a group of anti-inflammatory medications. Examples include sulfasalazine, mesalamine, olsalazine, and balsalazide. These are used to get rid of inflammation and keep it gone. They are used in mild to moderate UC. They come in both pill and rectal forms (suppositories and enemas). They 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 forms of mesalamine are used more often if UC is just the end of their colon.

**Steroids**(prednisone or budesonide) work well to get rid of inflammation. They come in oral, rectal, and intravenous (IV) forms. They can be used in more moderate to severe cases. Some steroids are absorbed into the blood and have a number of side effects. That's why they are not a good option for long-term use. Side effects include cataracts, osteoporosis (thinning of the bones), mood effects, and increased chance of infections. Others are high blood pressure, high blood sugar and weight gain. Some steroids are less absorbed and work mainly in the colon with less side effects.

Immunomodulators include medications such as 6-mercaptopurine and azathioprine (thiopurines). These are taken in pill form and absorbed into the bloodstream. They work to just keep inflammation gone but are slow to work. They can take up to two to three months to really help. Because of this, these are usually combined with other medications (such as steroids). Typically in those with moderate to severe disease. Frequent blood tests are needed though. That is because these can injure the liver or decrease blood cells. If either happen, they go away after stopping the drug. Other side effects include nausea, rash, inflammation of the pancreas, and, rarely, lymphoma.

Biologic agents are medications given by IV or a shot that are used to treat moderate to severe UC. There are several different types.

- First is the class of anti-TNF therapies. These target an inflammatory protein called "TNF". They can work for both the induction and maintenance of remission of UC. These include infliximab (Remicade®, Inflectra® and Renflexis®), adalimumab (Humira®) and golimumab (Simponi®). The side effects of these medicines may include an allergic reaction called a "hypersensitivity reaction." There are also rare risks of serious infections with these. Lymphoma is another rare risk. But more recent scientific studies say that this may not be from these medications, but instead due to the thiopurine immune drugs (see above).
- The second class of biological therapy that treats UC is a medication that **blocks the body's ability to send white blood cells (part of your immune system) to the bowel. By doing this it can decrease inflammation.** There is currently one therapy that is in this class (vedolizumab (Entyvio®), and it has been shown to induce and maintain remission of UC.
- A third biologic is one that **blocks two proteins called interleukins that cause inflammation in the colon.** There is just one therapy in this class (ustekinumab (Stelara ®). Again, it has been shown to induce and maintain remission of UC.

Tofacitinib is a newer oral drug (not a biological therapy). It too can induce and maintain remission of UC. Tofacitinib (Xeljanz®) works by blocking an enzyme that is needed to turn on inflammation. This drug can work quickly. However it may increase cholesterol levels. It also may increase the risk of getting the shingles infection (related to chicken pox). This risk can be decreased by getting the shingles vaccine.

The most recent oral drug that's not a biologic is called ozanimod. Ozanimod (Zeposia ®) works to block the blood cells that cause inflammation from ever leaving the lymph nodes. This has been shown to help in both moderate and severe UC but can decrease the heartrate or cause swelling of the eye. An electrocardiogram (ECG) should be done before starting. Also if you have a history of conditions affecting the eye, such as uveitis, you may not be able to use this drug.

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 drugs are sometimes used in those rare cases of severe UC that don't respond to anything else. Side effects can include infections and kidney problems. These are only offered at a limited number of Tofacitinib is a newer oral drug (not a biological therapy). It too can induce and maintain remission of UC. Tofacitinib (Xeljanz®) works by blocking an enzyme that is needed to turn on inflammation. This drug can work quickly. However it may increase cholesterol levels. It also may increase the risk of getting the shingles infection (related to chicken pox). This risk can be decreased by getting the shingles vaccine. hospitals and are usually used for a short period of time. If used, the goal is to get you better long enough to get onto other drugs for long-term.

**Taking Medication for UC as Prescribed:** No matter which medication you and your doctor decide on, it is very important to take it as directed. No medical therapy can work if it is not taken. Missing doses can lead to treatments that may have been avoided if not mentioned to your doctor. Plus uncontrolled inflammation is what causes many of the complications. So by taking your medicine, the chances of these happening are decreased.

• What is the role of surgery?

Surgery in UC is performed for a number of reasons. It is generally considered to cure UC if the entire large intestine is removed. Some common reasons to need the colon removed are:

- · No response to medications
- Severe side effects of medications
- No longer able to safely take medications
- Develop an enlarged colon called toxic megacolon
- Have many areas of dysplasia (pre-cancerous lesions)
- Develop cancer of the colon
- Children who are not growing due to their UC

Several different surgeries are performed for UC. The choice of surgery depends on what the patient wants and the experience of the surgeon. The most common surgery is **total proctocolectomy with ileal pouch anal anastomosis**. This is when the whole colon and rectum are removed. Then the small intestine is used to make a new area to hold stool. This new area is called a "J pouch." This operation usually requires two separate surgeries to complete although it may require three stages in really sick patients.

Following this surgery, patients can expect five to ten stools a day. This is because they no longer have a colon to store stool. Patients usually feel better because their symptoms are gone and their medications can be stopped.

However, inflammation of the pouch known as pouchitis can still happen afterwards which is usually treated with antibiotics. Women who have this surgery may have a 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 done 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.

• <u>Do complementary and alternative therapies work in UC?</u>

Outside of the standard medical therapies discussed for UC, 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. All that is advised is that people eat a well-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, some vitamin deficiencies can also happen in UC patients. For this reason, a multivitamin and a calcium supplement are may be needed.

**Probiotics** are species of bacteria that are proposed to help the bowel. There are a number of scientific studies which have been done to see how probiotics could help UC, but most of these have not shown to help and so these are usually not recommended in UC.

Other herbal remedies and alternative therapies have been studied for use in patients with IBD such as curcumin (comes from the herb turmeric) 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. Therefore they are currently not used.

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

UC is a chronic disease so having a GI doctor with experience in seeing people with UC is best. Many of the medicines used need regular bloodwork. This is to make sure they are not causing any serious problems. Patients with UC have a higher risk of osteoporosis (thinning of the bones). This can be from the disease itself or from long term or frequent steroid use. Therefore your doctor may recommend checking Vitamin D levels and a bone mineral density test called 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 UC. The ACG Web site has additional information. The Crohn's and Colitis Foundation They also have links to various other social, financial, and medical support groups. Other sources of information include the individual drug company websites, and, most importantly, your doctor.

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