Maintenance Therapy

ABOUT THIS RESOURCE

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The term "maintenance therapy" refers to the various kinds of treatment (usually medical) given to patients to enable them to maintain their health in a disease-free, or limited-disease, state. If you have been diagnosed with Crohn's disease or ulcerative colitis, the first goal of treatment is for you to get better (a stage in the illness known as going into "remission"). The next challenge is to keep you in remission. The treatments used for this second step are referred to as "maintenance therapies."

Why is Maintenance Therapy Needed in IBD?

Both Crohn's disease and ulcerative colitis are chronic inflammatory diseases. Although symptoms may disappear, they tend to recur over time. Many people with IBD respond well to medications when they have a flare-up. Unfortunately, they are at risk for future attacks unless they continue to take certain medications that will keep them in remission. Because these medications are needed over a prolonged period, they must be both effective and safe.

To control inflammation during the acute phase (the initial, active phase of the illness), physicians may prescribe more potent therapies—despite potential side effects—if those therapies will help the patient get better. However, side effects or toxicity from treatment during the maintenance phase are far less acceptable, since IBD can require a lifetime of these medications.

Types of Maintenance Therapies Used in IBD

5-ASA Agents
Sulfasalazine (Azulfidine®) and the newer generation of sulfa-free agents (Asacol,® Dipentum,® Pentasa,® Apriso,™ and Rowasa ® are commonly used to prevent flare-ups of IBD. The benefits of these drugs usually depend on the amount of the dose: The larger the dose, the more likely that patients will improve during the acute phase, and the more likely that they will remain in remission. Sulfasalazine's side effects, however, generally become more intolerable as the dose increases. Headaches, nausea, or fatigue are frequently experienced at these higher doses. In men, long-term sulfasalazine treatment may cause abnormal sperm production, leaving some couples unable to conceive. These effects are reversible once the sulfasalazine is discontinued. Patients taking sulfasalazine should also take a daily 1mg dose of folic acid.

Far fewer side effects are seen with the sulfa-free agents, which contain mesalamine (5-ASA), the same active ingredient as sulfasalazine. Side effects—such as headaches, abdominal cramps, and nausea—are uncommon, and generally are not dose-related. However, if you do notice some side effects, you and your doctor may be able to find a slightly lower dose at which the drug is still effective in maintaining remission yet causes no side effects. These agents are much more expensive than generic sulfasalazine, and may require as many as 12 to 16 pills a day to maintain remission. All of these agents may be continued during pregnancy and nursing.

Doses of these medications are generally higher for patients with Crohn's disease than in those with ulcerative colitis. While most of these drugs are available in capsule or pill form, the sulfa-free agents also are available as enemas and suppositories (Rowasa®) for use in patients with inflammation in the rectum or the lower section (left side) of the colon. The usual dose is one enema nightly or two suppositories daily. Maintaining remission by using an enema or suppository often requires continued use of these agents, either alone or in combination with pills, although some patients may find they only need to use the enema a few times each week.

Antibiotics
Antibiotics are effective as chronic (long-term) therapy in some people with IBD, particularly Crohn's disease patients who have such problems as fistulas (abnormal channels that connect loops of intestine to the skin) or recurrent abscesses (pockets of pus) near their anus. The most commonly prescribed antibiotics are metronidazole (Flagyl®) and ciprofloxacin (Cipro®), although there are many others that may be effective in certain individuals.

Patients whose active disease is successfully treated with antibiotics may be kept on these medications as maintenance therapy if the agents remain effective. Side effects can be particularly troublesome with metronidazole, including tingling of the hands and feet that may persist even after the drug is discontinued. Alcohol intake and exposure to the sun are discouraged, and in most cases these agents are not continued during pregnancy.

Corticosteroids (Steroids)
Steroids (e.g., prednisone, hydrocortisone, Medrol®) are often used in the acute treatment phase when the 5-ASA drugs are not working. Steroids work quickly and effectively in most cases. However, despite their benefit in treating acute illness, steroids are not effective in preventing flare-ups and thus are rarely used as a maintenance medication in either Crohn's disease or ulcerative colitis. Steroids also have many potentially serious side effects—such as elevated blood sugar, high blood pressure, cataracts, osteoporosis (even leading to bone fractures), among others. The risk of adverse effects increases with the duration of the treatment. Thus, steroids should only be used to control the disease. They should then be phased out gradually, while another agent is used to maintain remission.

Strategies to eliminate steroids include increasing the dose of the 5-ASA agents, adding a 5-ASA enema or suppository if the IBD is located in the rectum or distal (lower) colon, or introducing either an antibiotic or one of the newer medications described below. Some patients require surgery if they still cannot effectively reduce or eliminate steroids from their medical regimen.

An exception to steroid elimination rule may be the newer, rapidly metabolized corticosteroids, such as budesonide multiple-release capsule MRC (EntocortREC®). A recent study showed that budesonide MRC is of value as maintenance therapy. Patients on this corticosteroid remained in remission for a markedly longer period than those taking a placebo. The drug was also found to be safe and well tolerated.

6-MP and Azathioprine
6-mercaptopurine (6-MP, Purinethol®) and azathioprine (Imuran®) have been increasingly utilized to take IBD patients off steroids, and to keep them off. They are also beneficial in the treatment of some patients with Crohn's disease who have fistulas. Both of these drugs are effective in treating active IBD and in maintaining remission, and are relatively safe. However, patients taking these drugs must be carefully monitored for signs of a decrease in the number of blood cells, or inflammation of the liver or pancreas. Although it was initially feared that patients given these medications could be at increased risk for infections or certain types of cancers, this has not been conclusively demonstrated.

Although these drugs can be expensive, the required daily dose is low. Patients needing these medications to achieve remission will often suffer a relapse of disease when the medications are stopped; thus, many physicians recommend long-term use as maintenance therapy—in some cases even during pregnancy.

Methotrexate
Methotrexate is recommended in Crohn's disease patients who cannot stop steroid use without a flare of their disease, or in whom other medications have been ineffective. It also may be helpful in improving Crohn's fistulas. This drug has the benefit of once-weekly dosage but must be given as an injection (usually by the patient himself or a family member) for maximum efficacy. Methotrexate is inexpensive, but patients also need to take a daily folic acid pill (1 mg).

If effective, methotrexate should be used on an ongoing basis. Many patients have side effects—most commonly nausea, headache, and fatigue—which may resolve with a lower dose; rarely, liver and lung problems may occur. Careful monitoring by a physician, including periodic blood tests, is essential. Unlike most of the other agents used in IBD, methotrexate is known to cause birth defects. It absolutely must not be taken during pregnancy, or by men or women planning conception.

Infliximab

Infliximab (Remicade®), is effective in treating moderate to severe active Crohn's disease, ulcerative colitis, and fistulas. Studies have demonstrated that infliximab is not only effective for inducing remission but can be used as a long-term therapy to maintain remission.

Infliximab is given as a single-dose intravenous infusion, and many patients may be able to wait a few months (or longer) before requiring another dose. Patients with fistulas often get three doses over an initial six-week period. Many patients respond quickly, usually within one or two weeks, but it is recommended to wait at least for two infusions to see infliximab's effectiveness.

Adalimumab
Adalimumab (Humira®) is effective in treating moderate to severe active Crohn's disease. Adalimumab studies have shown to induce remission and it may help keep symptoms from returning with continued therapy. Patients who are intolerant to infliximab may benefit from adalimumab.

Adalimumab is usually injected once every other week, however some patients may need to inject the medication more often in the begining of their treatment. It can be administered at home by the patient or family member once instructed by a healthcare professional. Patient's response time is usually within four weeks.

Certolizumab pegol(Cimzia ®) is effective in treating moderately to severely active Crohn's disease in adult patients who have not been helped enough by usual treatments. Certolizumab pegol is the first and only PEGylated anti-TNF- alpha. The antibody portion of the drug is combined with a special chemical called polyethelyene glycol (PEG), which delays its excretion from the body.

Certolizumab pegol is dosed subcutaneously every two weeks for the first three injections and every four weeks thereafter.

Natalizumab
Natalizumab (Tysabri®) is effective in treating adult patients with moderate to severe active Crohn's disease. Patients who have had an inadequate

response to, or are unable to tolerate, conventional CD therapies, including inhibitors of TNF-alpha may benefit from natalizumab.

Natalizumab (Tysabri®) is infused into a vein at a certified infusion center and usually given once every 4 weeks.

SPECIAL CONSIDERATIONS

- There have been some reports of serious infections associated with infliximab, adalimumab, and certolizumab use, including tuberculosis (TB) and sepsis, a life-threatening blood infection. You should always have a TB test before you use infliximab, adalimumab or certolizumab because the drugs can increase the risk of re-activating TB for those who have been exposed. It's not that you will "catch" TB when taking infliximab, adalimumab,or certolizumab but if you have latent (inactive) TB, the drug can reactivate the infection.
- Cases of new infection with TB have also been reported. If you have prior exposure to TB, your doctor should begin TB treatment before you start infliximab, adalimumab or certolizumab. The same precaution should be taken before beginning treatment with corticosteroids.

Biologics may reduce the body's ability to fight other infections as well. If you are prone to infections or develop any signs of infection while taking these medications, such as fever, fatigue, cough, or the flu, inform your doctor immediately.

- It may be inadvisable for people with heart failure to take any of these medications, so tell your doctor if you have any heart condition before starting this medication. Inform your doctor at once if you develop new or worsening symptoms of heart failure—namely shortness of breath or swelling of the ankles or feet.
- On rare occasions, blood disorders have been noted with infliximab, adalimumab, and certolizumab. Inform your doctor if you develop possible signs such as persistent fever, bruising, bleeding, or paleness while taking infliximab, adalimumab, and certolizumab. Nervous system disorders also have been reported occasionally. Let your doctor know if you have or have had a disease that affects the nervous system, or if you experience any numbness, weakness, tingling, or visual disturbances while taking infliximab, adalimumab, and certolizumab.
- Although reports of lymphoma (a cancer of the lymphatic system) in patients taking infliximab, adalimumab, certolizumab and other TNF-blockers are rare, they do occur more often than in the general population.
- Progressive multifocal leukoencephalopathy (PML), a rare brain infection, has been reported with natalizumab use. Natalizumab may also cause liver damage and allergic reactions.
- Patients with a medical condition that can weaken their immune system such as HIV infection or AIDS, leukemia or lymphoma, or an organ transplant should not take Natalizumab.
- Your physician will monitor you closely while you are on biologic therapy. It is not advisable to stop and then try to restart infliximab. To achieve and maintain remission, it is advisable to stay on the medication.

Maintenance Therapy after Surgery

Surgery for ulcerative colitis nearly always results in the complete removal of the entire colon and rectum. Patients typically undergo one of two procedures. In the ileal-anal anastomosis, an internal pouch is constructed out of the end of the small bowel (the ileum), which is attached to the anus. In an ileostomy, the surgeon creates an opening from the ileum to the skin. Through this opening, wastes are emptied into a plastic pouch that is attached to the abdomen with adhesive. Ulcerative colitis cannot recur without a colon or rectum; thus, there is no need for maintenance medications. However, these patients may need medication to control diarrhea. In addition, people with an ileal–anal anastomosis may develop inflammation of the internal pouch ("pouchitis") that requires medication to control.

The aftereffects of surgery for Crohn's disease varies, depending upon the location of the inflammation. Patients whose Crohn's is limited to the large intestine (colon and rectum) often do not redevelop the illness (and therefore don't require maintenance medications) if their entire colon and rectum are removed, and they are left with an ileostomy. However, if only part of the colon is removed, then there is a very high likelihood of recurrence of Crohn's disease. At some point, the disease also may recur in patients who have Crohn's of the small intestine, because complete removal of the small intestine is not possible. Patients with Crohn's fistulas often suffer recurrences after surgery, as well.

Until recently, many Crohn's patients were not placed on maintenance medications after surgery. However, drugs such as 6-mercaptopurine and azathioprine, and high doses of the 5-ASA medications and metronidazole have been shown to delay recurrence of Crohn's disease in some patients. Physicians may recommend such therapies to patients who are at high risk for recurrent disease and/or who have already had previous bowel surgeries for Crohn's.

How to Maximize the Chances of Maintaining Remission

Some general guidelines are in order for most patients on maintenance therapies for IBD. They are:

1. The medications won't work if you don't take them.
2. If you have Crohn's disease, stop smoking. Smoking can prevent remissions in Crohn's disease and make it more active. After Crohn's surgery, the illness recurs sooner, and often more severely, in smokers than in non-smokers.
3. Many common over-the-counter and prescription pain relievers have been shown to cause ulcerations in the intestinal tract, and may prompt a relapse. Unless you need these products for a serious health reason (such as heart disease or stroke prevention), you should avoid taking them. Always question your doctor if the following agents are prescribed: aspirin, including enteric coated preparations (Ecotrin®); and non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (Advil,® Motrin,® Aleve,® Anaprox,® Naprosyn,® Daypro® etc.). The new "COX-2" inhibitors (Celebrex,® Vioxx®) may also be "off-limits" for IBD patients.

4. Some patients experience flares of their disease after the use of various antibiotics. Unless an infection is documented by a physician, avoid taking antibiotics. It is a good idea to contact the physician who is managing your IBD before taking any new medications to determine if an alternative should be considered.

Remember, it is often easier to keep IBD under control than to get it under control. Complying with a demanding treatment schedule isn't always easy, but the reward—better health—is definitely worth the effort. As we move forward in our understanding of the causes and genetics of Crohn's disease and ulcerative colitis, new medications will be developed—both to control active disease and to maintain remission.

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For further information, call CCFA at our Information Resource Center: 888.MY.GUT.PAIN (888.694.8872).

Related Resources

- The Intimate Relationship of Sex and IBD (http://www.ccfa.org/resources/sex-and-ibd.html)
- Appeal letter sample: Adalimumab Dosing (http://www.ccfa.org/resources/adalimumab-dosing.html)
- Appeal letter sample: Off Labeling (http://www.ccfa.org/resources/off-labeling.html)
- Appeal letter sample: Pediatric Adalimumab Therapy (http://www.ccfa.org/resources/pediatric-adalimumab-therapy.html)
- Next generation medicine: Individualized treatment (http://www.ccfa.org/resources/next-generation-medicine.html)

View More (http://www.ccfa.org/resources/resources-search-results.html?s=topics&topics=medications)

Questions or Want to Talk?

- Talk to a Specialist (http://www.ccfa.org/living-with-crohns-colitis/talk-to-a-specialist/) by phone at (888) MY-GUT-PAIN by email at info@ccfa.org (mailto:info@ccfa.org;), or live chat. (http://www.answerchat.com/cgi-bin/answerchat.exe?action=js&cPage=http%3A//www.ccfa.org/irc&account=c0100&getInfo=true&cookie=c0100-2129338%3B%20WT_FPC%3Did%3D20079b3eb5d61136a321327335939149%3Alv%3D1339173991581%3Ass%3D1339172424693%3B%20__utma%3D162674862.643486687.1327335939.1339173026.1339176025.40%3B%20__utmz%3D162674862.1338997111.35.3.utmcsr%3Dwww.ccfa.org%7Cutmccn%3D%28referral%29%7Cutmcmd%3Dreferral%7Cutmcct%3D/chapters/wisconsin/events/camp-oasis-august-12-1.html%3B%20__unam%3D79d9b7a-137a4a5dfd1-3081b842-2%3B%20__utmb%3D162674862.5.10.1339176025%3B%20__utmc%3D162674862%3B%20ccfaweb_jsessionid%3D1rt1sm9s2fgm6&browser=Netscape&bVersion=5.0%20%28Windows%29)
- Visit our Community Forums. (http://www.ccfacommunity.org/)