

# Inflammatory Bowel Disease

## *New treatments for Crohn's disease and ulcerative colitis*

Novel approaches may provide potential breakthroughs to treat the more than 1 million Americans—more than half of them women—with *inflammatory bowel disease (IBD)*. These strategies include less-frequent drug dosing, experimental therapies to attack some of the processes involved in IBD, and bone-sparing medications.

IBD, which includes *Crohn's Disease* and *Ulcerative Colitis (UC)*, “stems from a bacterial trigger which sets up an uncontrolled immune response in susceptible people, which in turn leads to chronic inflammation that eventually breaks down the lining of the intestines,” explains gastroenterologist Ellen Scherl, MD, an assistant professor of medicine at the Weill Medical College of Cornell University. Key symptoms include bloody diarrhea, weight loss, abdominal pain, cramps, bloating, and constipation. “Women with abdominal

pains are frequently told they have ovarian cysts and undergo unnecessary procedures, when they really have Crohn's,” says Dr. Scherl. Women are more likely than men to report more severe symptoms and sexual problems, including painful intercourse.

Postmenopausal women with IBD also have a higher than normal risk for osteoporosis because their disease hinders absorption of bone-enriching calcium and vitamin D, and drugs used to control symptoms can thin bones.

### Easier to take

As with many gastrointestinal (GI) problems, the first step in controlling symptoms is to make simple lifestyle changes (see *What You Can Do*, pg 5). When that's not enough, most IBD patients are helped by drugs. Trouble is, half of them don't take their medicine, mostly because of too-frequent

dosing, says Sunanda Kane, MD, assistant professor of medicine at the University of Chicago. Once-a-day dosing may help change that.

A once-daily dose of the IBD drug *mesalamine (Asacol)* was found to be comparable to conventional twice- or three-times daily dosing for ulcerative colitis patients in remission, Dr. Kane reported to the American College of Gastroenterology annual meeting in October 2002. In a small pilot study of 22 ulcerative colitis patients who had no symptoms for at least six months, nearly 90 percent of those given once-daily doses for six months kept taking their medicine as prescribed, compared to only 76 percent of those taking several daily doses. Dr. Kane has begun a large, randomized trial to further test once-daily mesalamine. “Ultimately, more patients may be able to take more medication in a more convenient way,” says Dr. Kane, who is also president of “We Care in IBD,” a professional organization of specialists in treating Crohn's and ulcerative colitis.

### New treatments ahead

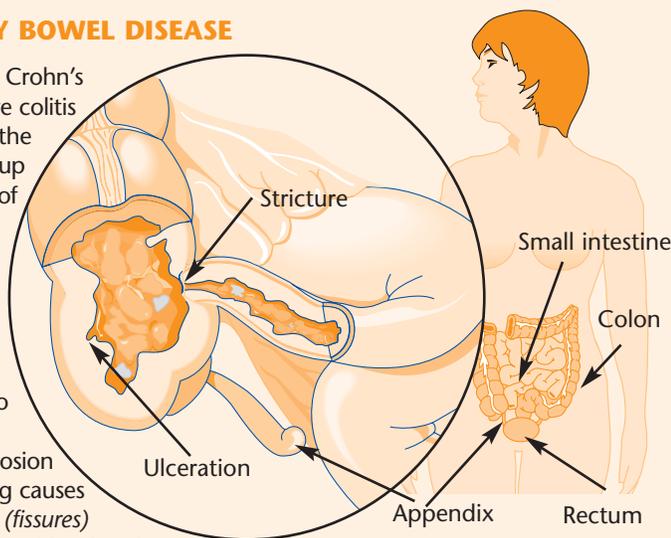
The IBD Center at Cornell headed by Dr. Scherl is taking part in several major clinical trials. One trial compares the efficacy of Asacol and *balsalazide (Colazal)*, a newer version of mesalamine that works quickly and helps hard-to-treat cases of ulcerative colitis. The drug *infliximab (Remicade)* is also being tested in UC. For patients with Crohn's disease, the IBD center is also studying high-dose regimens of Asacol, antibiotics, and a new version of a drug to block the inflammatory cytokine *tumor necrosis factor alpha (TNF- $\alpha$ )*.

Other new treatments now in development show promise, investigators told the gastroenterology meeting. A small randomized trial of 23 ulcerative colitis patients found that 45 percent of those who took a highly concentrated soybean byproduct went into remission, compared to 8 percent in the placebo group, reported Gary Lichtenstein, MD, associate professor of medicine at the University of Pennsylvania. The drug, a *protease*

### INFLAMMATORY BOWEL DISEASE

The inflammation of Crohn's disease and ulcerative colitis attacks the lining of the intestines, speeding up the normal passage of food, causing diarrhea. Malabsorption can cause weight loss and deficiencies in protein, vitamin B12, calcium and vitamin D (leading to osteoporosis).

Inflammation and erosion of the intestinal lining causes ulcerations or cracks (*fissures*) that can bleed, causing blood in the stool (in severe cases it can lead to anemia). The wall of the intestines also becomes thickened and narrowed; in some cases, this can block food passage (*strictures*). Inflammation can also spread outside the bowel wall, penetrating adjacent areas and causing sections of bowel to stick together (*adhesions*). In some cases, a tunnel-like opening called a *fistula* can form between adjacent areas of bowel (or even between the rectal and vaginal areas). Crohn's disease typically affects the lower part of the small intestine (*ileum*), but can produce inflammation and ulcerations in any part of the colon and digestive system, from the mouth to the anus. Ulcerative colitis can affect any part of the large intestine.



## GETTING A PROPER DIAGNOSIS

### Warning Signs of IBD:

- Bloody diarrhea
- Diarrhea that awakens you at night
- Weight loss
- Nausea and vomiting
- Abdominal pain
- Fever, fatigue
- Night sweats
- Mouth ulcers
- Ulcers in the rectal area (Crohn's)
- Joint pain

If you have symptoms like those above, then you may have IBD or infectious gastroenteritis, but you probably don't have *irritable bowel syndrome (IBS)*. IBD can be difficult to diagnose and treatment may be delayed because symptoms frequently overlap with other disorders like IBS, says Christine Frissora, MD, an assistant professor of medicine at the Weill Medical College. "IBD often mimics IBS, which is a disorder that affects muscle contractions in the colon," says Dr. Frissora. Other conditions that have similar symptoms include *celiac disease* or *sprue* (an intolerance to *gluten*, a protein found in wheat, rye, and barley), ovarian cysts, endometriosis, pelvic inflammatory disease, pelvic infections, and food poisoning.

The first goal is to differentiate ulcerative colitis, which affects only superficial layers of the colon, from Crohn's disease, which causes inflammation throughout all layers of the entire GI tract. The basic work-up includes a physical exam, a stool specimen and blood sample, and either *flexible sigmoidoscopy* or *colonoscopy* (examinations of the colon with fiberoptic tubes). A biopsy of the colon and a special x-ray of the GI tract, called a *barium x-ray*, may also help distinguish between the two diseases.

*inhibitor* similar to those used to treat HIV, interferes with the ability of proteins to latch onto cell membranes. Larger trials are planned.

A corticosteroid-like compound called *CBP-1011* is being investigated for use in both ulcerative colitis and Crohn's disease in double-blind, placebo-controlled trials. The experimental drug does not appear to have the side effects of conventional corticosteroids. In one small pilot study of 15 ulcerative colitis patients, the diabetes drug *rosiglitazone (Avandia)* saved patients from surgery and allowed a substantial number to withdraw from corticosteroids.

Preliminary studies show that a compound isolated from animal pituitary glands, dubbed *coherin*, can effectively maintain Crohn's disease remissions, and is being investigated in large, randomized trials for Crohn's disease, says Dr. Lichtenstein.

### Protecting bones

Between 30 to 60 percent of women with Crohn's disease may already have bone loss when first diagnosed, due to malabsorption. Drugs such as corticosteroids used to treat IBD can make this worse. However, studies show two newer drugs may not cause as much

bone-thinning. A large, randomized prospective trial found that modified-release *budesonide (Entocort EC)*, a long-acting corticosteroid, offers a significant advantage in preserving bone mass over the corticosteroid *prednisolone (Prelone)*, Dutch investigators reported. And, a study at UCLA found treatment with infliximab increased bone synthesis without an increase in bone resorption in Crohn's patients who were also receiving corticosteroids.

### Treating IBD now

Currently, the first line of treatment for Crohn's are *aminosalicylates*, aspirin-like drugs that contain *5-aminosalicylic acid (5-ASA)* such as *Asacol* or *Colazal*, and *sulfasalazine (Azulfidine)*. They are effective in treating mild to moderate symptoms. Corticosteroids are used for moderate to severe disease. Immune modifiers including *azathioprine (Imuran)*, *6-mercaptopurine (6-MP)*, *cyclosporine* and *infliximab* are reserved for ulcerative colitis patients who have not responded to aminosalicylates and corticosteroids and, for Crohn's disease, to help decrease the dose of corticosteroids and possibly to maintain remissions.

"Because Crohn's disease involves bacterial infection, we are now using

## WHAT YOU CAN DO

### If you suffer from IBD:

- Eat a heart-healthy diet, drink more fluids, exercise
- Avoid high-soluble fiber foods, such as the skins of eggplant, cucumber, tomato, and potato; seeds and nuts; raw, cruciferous vegetables (e.g., broccoli)
- Avoid artificially sweetened candy/soda, which can trigger symptoms
- If you have Crohn's disease, stop smoking
- Take 1,200 to 1,500 mg of calcium a day, and 400 to 600 IU of vitamin D
- Have your bone density checked regularly

antibiotics as part of the treatment. *Probiotics* may also be a useful adjunct to therapy," remarks Dr. Scherl. Probiotics are actually supplements of live bacteria such as *lactobacillus* commonly found in the gut. "There are a select group of probiotics, including *Culturelle*, which may be very helpful."

When medication no longer controls symptoms, surgery may become necessary. Removing the colon cures UC, but usually requires the creation of an opening in the abdomen to empty wastes into a pouch. For Crohn's disease, surgery may allow many symptom-free years, but the disease can recur, so it's important to be followed by a gastroenterologist. 🦋

### WEBWATCH

For more information on IBD, log into:

[www.wecareinIBD.com](http://www.wecareinIBD.com)

Crohn's & Colitis Foundation of America: [www.ccfa.org](http://www.ccfa.org)

American College of Gastroenterology

[www.acg.gi.org/acg-dev/patientinfo/ct\\_giproblems.html](http://www.acg.gi.org/acg-dev/patientinfo/ct_giproblems.html)