GUT INSTINCT
By Mark Harris

For individuals diagnosed with Crohn's disease, uncomfortable, often painful, and even debilitating symptoms can be a part of life. From abdominal cramps and fatigue to constipation and rectal bleeding, Crohn's patients are likely to experience a host of troubling symptoms. For some, surgery is also not uncommon.

Crohn's disease affects as many as 780,000 Americans. While the disease can afflict any age group, the initial diagnosis often occurs among adolescents and young adults up to the age of 35.1

What exactly is Crohn's disease? As a chronic inflammatory condition in the gastrointestinal (GI) tract, Crohn's falls under the category of an inflammatory bowel disease (IBD). Typically, the disease affects the end of the small bowel and the beginning of the colon, but Crohn's can occur anywhere in the GI tract. The inflammation can also penetrate all layers of the bowel wall, not just the superficial lining.1 The cause of Crohn's disease is not definitively known, but genetics and the immune system are believed to play a significant role.1,2 As such, many experts suspect that microorganisms or other factors present in the GI tract are responsible for triggering the inflammatory immune response that characterizes Crohn's disease.2

Overall, some 1.6 million Americans have IBD, diagnosed primarily as Crohn's or ulcerative colitis. The latter can produce similar symptoms to Crohn's but affects only the colon's innermost lining. Significantly, the incidence of IBD overall is on the rise in the United States, with about 70,000 new cases diagnosed every year.3

Crohn's disease derives its name from the pioneering work of Burrill B. Crohn, MD, who wrote—with gastroenterology colleagues Gordon Oppenheimer, MD, and Leon Ginzburg, MD—a seminal paper in 1932 on an inflammatory GI tract condition they termed regional ileitis.4 Until that time, any disease in the small intestine was treated as a type of intestinal tuberculosis. Gradually, thanks to Dr. Crohn's original efforts, the disease came to bear his name.
Two of a kind
Crohn’s disease and ulcerative colitis (UC) are inflammatory bowel diseases (IBDs) that differ in several key ways:

Crohn’s disease
- May develop anywhere in the gastrointestinal tract (from the mouth to the anus)
- Most commonly occurs at the end of the small intestine
- May penetrate all layers of the bowel wall
- May appear in patches
- About 67 percent of patients in remission will have at least one relapse during the following five years

Ulcerative colitis
- Limited to the large intestine (colon and rectum)
- Involves a part of or the entire colon
- Affects the intestine’s innermost lining
- Appears in a continuous pattern
- About 30 percent of people in remission will experience a relapse in the next year

A fine lining
While treatment has advanced considerably over the years, Crohn’s disease by its nature does not lend itself to an easy or straightforward diagnosis. This is largely because symptoms of the disease can mimic those of many other conditions:

- Ulcerative colitis
- Infectious gastroenteritis
- Traveler’s diarrhea
- Celiac sprue (i.e., celiac disease)
- Gallbladder disease
- Pancreatitis
- Stomach ulcers
- Irritable bowel syndrome
- Colorectal cancer
- Abdominal pain
- Fatigue
- Rectal bleeding
- Diarrhea
- Bowel urgency
- Diarrhea without bleeding
- Rashes
- Joint, bone, and eye symptoms
- Kidney and liver issues
- Extraintestinal symptoms
- Melanoma of the small intestine
- Colorectal cancer
- Squamous cell cancer
- Kidney and liver issues
- Irritable bowel syndrome
- Stomach ulcers
- Joint, bone, and eye symptoms
- Kidney and liver issues
- Celiac sprue
- Ulcerative colitis
- Chronic diarrhea
- Diarrhea without bleeding
- Rectal bleeding
- Fatigue
- Abdominal pain
- Bowel urgency
- Rashes
- Joint, bone, and eye symptoms
- Kidney and liver issues

“Every patient needs a history, a physical exam, and appropriate testing with blood and sometimes stool,” says Dr. Kane. “There should also be endoscopy, plus or minus X-rays. We also say that you cannot start to treat Crohn’s without a tissue diagnosis. You can make the patient worse, or certainly not better, if you are treating them with Crohn’s therapy when they do not have Crohn’s.”

Indeed, Dr. Kane, who is the author of IBD Self-Management: The AGA Guide to Crohn’s Disease and Ulcerative Colitis, notes the care needed in establishing the diagnosis. “Over-the-counter or prescription nonsteroidal anti-inflammatories, like ibuprofen and naproxen [Aleve], can cause ulcers of the small intestine that look like Crohn’s. Lymphoma can look like Crohn’s. Melanoma of the small intestine can look like Crohn’s. There are certain infections that can look like Crohn’s. And none of those should be treated with the immune suppression therapies used to treat Crohn’s.”

A key diagnostic tool for detecting Crohn’s disease is the endoscopy procedure, says Dr. Kane. With endoscopy, the physician uses a scope with a tiny camera attached to a slim, flexible tube that shows magnified intestinal images on a screen. The process allows the clinician to assess the severity of any inflammation in the GI tract and intestinal lining, identify where it is, and take biopsy tissue samples.

There are different types of scoping procedures, depending on the area of the GI tract under examination, such as a colonoscopy and sigmoidoscopy. At times, clinicians will also use a video imaging technique in which a patient swallows a tiny capsule-enclosed camera. The camera can transmit images to a receiver as it travels through the GI tract identifying the location of ulcers in the GI tract, says Dr. Kane. “Of course, even a study where we see ulcers doesn’t necessarily mean it’s Crohn’s disease. We then use an appropriate scope to get tissue for biopsy.”

As such, the biopsy can be the key to confirming a diagnosis of Crohn’s disease. “There are certain biopsy findings that definitely indicate you have Crohn’s,” says Scott Snapper, MD, PhD, director of the Inflammatory Bowel Disease Center at Boston Children’s Hospital and professor of medicine at Harvard Medical School. “If somebody looks under a microscope and [sees] something called granuloma [small areas of inflammation in tissue], that means it’s Crohn’s. There are other things that..."
can cause granuloma, like tuberculosis, but it pretty much means you have Crohn’s. Other findings can also mean you have Crohn’s. If you have intestinal inflammation and fistulae, you’ve got Crohn’s.”

A fistula is a kind of hollow tube that connects two different intestinal areas or organs, or leads from an organ to outside the body. In Crohn’s disease, fistulae form as a result of intestinal perforations. Another major disease complication is what is known as stricturing, characterized by obstructions related to swelling and formation of scar tissue. As a result, the bowel wall can thicken, and this leads to a narrowed intestinal passage.\(^8,9\)

Notably, more patients with Crohn’s disease don’t have granuloma than those who do, adds Dr. Snapper. That is why a Crohn’s diagnosis typically must encompass a multiplicity of findings. “For both Crohn’s and ulcerative colitis, the diagnosis is largely a clinical diagnosis,” says Dr. Snapper. “That is, there isn’t a blood test for Crohn’s. There isn’t an exact finding, but a constellation of findings. With Crohn’s, it involves finding strictures, fistulae, granuloma, and [disease] involvement of the small intestine and/or large intestine that doesn’t have to be continuous where everything’s involved. Whereas ulcerative colitis never has fistulae, rarely has strictures, never has granuloma, and is . . . continuous.”

**Mix and match**

The treatment of Crohn’s disease can involve a combination of therapies precisely tailored for each patient. These may include the use of medications, surgery, dietary or nutritional therapy, and other ancillary or supportive treatments.\(^10\)

Several medication choices are currently in use to treat Crohn’s disease. In general, the goal of each is to provide symptom relief while simultaneously reducing the body’s inflammatory response to allow the intestinal tissue time to heal. Once symptoms, such as abdominal pain, diarrhea, and fever, are in remission, continued medical therapy seeks to decrease the frequency of disease flare-ups.\(^11\) Some of the medications in use include aminosalicylates to reduce inflammation in the intestinal lining. Typically, these drugs are used in patients with mild-to-moderate Crohn’s and as maintenance therapy to reduce relapses. Corticosteroids, such as prednisone (Deltasone) and methylprednisolone (Medrol), can also provide temporary symptom relief. However, corticosteroids can cause significant side effects (e.g., diabetes, osteoporosis, increased risk of infection) and are not recommended for long-term use. A group of drugs called immunomodulators is often also used alone or in combination with other drugs.\(^3,10-11\)

A newer category of drugs used to treat Crohn’s disease is tumor necrosis factor (TNF) inhibitors, otherwise known as biologics or anti-TNF agents. These drugs work by targeting the immune system protein from which they derive their name. In this category are such drugs as infliximab (Remicade), adalimumab (Humira), and certolizumab pegol (Cimzia).\(^10\) These are called biologics because they are derived from laboratory-grown antibodies. In recent years, biologics have shown much promise in relieving inflammation in Crohn’s patients and promoting disease remission.\(^11\)

Some of the medications used to treat Crohn’s may lower an individual’s resistance to infection and increase the risk for certain cancers. As such, their long-term use is always closely monitored.\(^10\)

Treatment for most Crohn’s patients does not end at medication. An estimated two-thirds to three-quarters will eventually have one or more surgeries over time.\(^12\) Two of the more common procedures include strictureplasty and small bowel resection. The former is designed to widen narrowed intestinal areas, but without removing parts of the intestine. The procedure is most effective in correcting strictures in lower sections of the small intestine. During a small bowel resection, the surgeon removes a segment of the small intestine and joins two ends of healthy intestine. A bowel resection can potentially offer many years of symptom relief. Still, about 50 percent of adult patients will have a recurrence of symptomatic Crohn’s disease within five years of a resection procedure.\(^11\)

**Gutbusters**

People with Crohn’s disease may develop complications, including the following:\(^3:\)

- **Fistula**—ulcers on the intestinal wall that extend and create a tunnel (fistula) to another part of the intestine, skin, or another organ.
- **Stricture**—a narrowing of a section of the intestine caused by scar tissue. Crohn’s disease can lead to an intestinal obstruction.
- **Abscess**—a collection of pus that can develop in the abdomen, pelvis, or around the anal area.
- **Perforated bowel**—chronic inflammation of the intestine may weaken the wall to such an extent that a hole develops.
- **Malabsorption and malnutrition**—these include deficiency of vitamins and minerals.

**Crohn’s crew**

In caring for a chronic disease such as Crohn’s, providers must go beyond the physical symptoms of the disease to caring for the whole person. In other words, the long-term management of Crohn’s disease requires not only good health care but good health care relationships. As treatment is invariably highly individualized, patients must enjoy good working relationships with their physicians and providers—relationships built on trust, communication, and shared decision making.

Patients should look for physicians who want to work with their patients as collaborators in care and who value their concerns and input as they meet the ongoing, often complex treatment challenges the disease can pose. Advises Keri Flaccomio, from Paramus, New Jersey, speaking as a patient advocate who was diagnosed with Crohn’s disease in 2007 during her first semester of college.\(^14\) Flaccomio is also a development coordinator for Mount Sinai Adolescent Health Center in New York City.
A taste of treatment

A single diet or eating plan will not work for everyone with inflammatory bowel disease (IBD). Dietary recommendations are individualized and tailored for each patient—depending on the disease and what part of the intestine is affected. Additionally, these diseases are not static; they change over time, so eating patterns should reflect those changes. The goal is a well-balanced, healthy diet. Of course, healthy eating habits are desirable for everyone, but people with IBD share an additional incentive to eat right.

Each patient will need to identify if they have trigger foods—those that bring about the onset of symptoms. The process involves a bit of trial and error, but these tend to be common culprits worthy of attention:

- Alcohol
- Butter, mayonnaise, or oils
- Chocolate
- Coffee or tea
- Fatty or fried foods
- Red meat or pork
- Raw fruits or vegetables
- Whole grains and bran

Flaccomio says nearly three years passed after her original diagnosis before she found a treatment approach that offered substantial relief from her acute symptoms. With the decision to pursue a more aggressive treatment approach, Flaccomio was prescribed Remicade, a biologic, as an infusion treatment. Subsequently, the drug has worked well for her, bringing what she describes as all-around relief from pain and discomfort.

Flaccomio’s experience over the last 10 years, which has included surgery, has taught her the value of forging a strong relationship with her physicians and care team. This includes becoming an informed advocate for her own health care needs.

“As a patient, you really do have to be an advocate for yourself,” she says. “I knew at a certain point [that] I was ready to switch from an oral medication to taking Remicade as an infusion, even though my family had concerns about the risks. But I knew my body better than anyone else and knew when I was ready to try it.”

Later, she also recalls inquiring whether her Remicade medication schedule and dosage could be adjusted, based on concerns she had about how she was feeling. It was adjusted, but only after a long interval and after finally switching physicians.

Despite her progress, like many Crohn’s patients, Flaccomio has experienced the ups and downs associated with her condition. Yet as an informed patient, her input has at times made a difference not only in her care but even in her diagnosis. In the fall of 2015, for example, a colonoscopy and capsule endoscopy failed to explain a flare-up of constipation, bloating, and related issues.

“We kind of came up empty,” she recalls. “But I knew something was off. Doing my own research, I found out about a condition called SIBO, or small intestinal bacterial overgrowth. I thought my symptoms seemed to match this, so I asked my doctor if we could test for this. The doctor agreed, we did the test, and it turned out I was positive for SIBO. I took a course of antibiotics and then I was OK. These symptoms might have continued on for many more months if I, as a patient, hadn’t taken the initiative.”

Indeed, many gastroenterologists who treat Crohn’s disease recognize the value of such shared decision making with their patients. Such interaction is a related component of what Dr. Kane refers to as “IBD self-management.” “There needs to be give and take on both sides,” she remarks. “Physicians who are dogmatic are going to get into trouble with their patients, because there is room for negotiation on most things. Certainly, an informed patient who understands their disease can help guide decisions.”

The right tract

Ideally, every Crohn’s patient should be under the care of a gastroenterology practice, advises Dr. Kane. But that may not always be possible, depending on the availability of nearby resources, insurance, and other factors. Where should patients be advised to go if a GI specialist practice is not nearby?

“Every Crohn’s patient should be seen at least once at an IBD center, such as at a major teaching institution in their state, to make sure the diagnosis and management plan from their physician is correct,” says Dr. Kane. “When I say correct, I mean the best plan for that individual. Obviously, some treatments that are appropriate for one Crohn’s patient are not appropriate for another. Just because you have Crohn’s doesn’t mean you necessarily have to be on a special diet, for example. Treating Crohn’s is not ‘cookbook’ or ‘cookie-cutter’ medicine.”

While individually customized, precision medicine defines the clinical management of Crohn’s disease, there is one universal that does apply to all Crohn’s patients—the support they need from the entire health care team. This may be especially true with a disease in which medical tests and procedures are often a regular part of care. This is an insight well understood by Seana Sakai, CMA (AAMA), who has several years’ experience as a certified gastroenterology technical (GI tech) specialist with Seattle-based Pacific Medical Centers.

As a GI tech with certification through the Society of Gastroenterology Nurses and Associates (SGNA), Sakai has assisted physicians directly in colonoscopy and endoscopy procedures. In this position, she has also assisted patients before procedures, calling patients a few days before their scheduled appointments to ensure that they are following proper dietary guidelines in preparation. Working with patients undergoing endoscopy procedures requires equal measures of both technical and relationship skills, she says.

“It’s not unusual for patients to be nervous about the procedure they’re scheduled to have,” says Sakai. “They’re often anxious about being sedated with intravenous medications, for example. . . . I think it helps to let them know I’ve been in the procedure room...
and assisted the doctor, and can tell them firsthand what they will probably experience.”

Under such circumstances, Sakai urges staff to recognize the patient’s perspective. “Remember that patients getting colonoscopy or endoscopy are, in a sense, at their weakest point,” she remarks. “They’re under a lot of duress. They’ve been denied food and are about to be sedated. . . . I’ve learned it really helps for us to be personable, to be there with a kind face, listen and speak with the patient, and try to help them to relax. It can make a difference.”

Silver lining

As research continues, there are many reasons to be hopeful about the future of medical treatment for Crohn’s disease. Earlier this year, the Crohn’s & Colitis Foundation’s RISK Stratification study reported a breakthrough in identifying important biological signatures in newly diagnosed pediatric patients. These markers can be used to predict whether a patient will develop major complications with strictureing or penetrating disease (sustained inflammation that spreads beyond the intestinal wall resulting in the creation of fistulae) that are likely to require surgery within three to five years.9

What is impressive about the RISK study, says Dr. Snapper, is that it represented the first time an extremely large prospective study group, involving over 900 patients, was followed for over four years from the time of diagnosis. “The goal of the study was to be able to tell at the time of diagnosis the chances that a patient will have a pretty benign course of disease, or a much more complicated course,” explains Dr. Snapper. As he notes, this would ideally allow physicians to let patients know the likelihood that they would end up having penetrating or strictureing disease.

In terms of early intervention, Dr. Snapper says the study results could significantly impact future care for newly diagnosed patients. “In this case, we’re talking about the use of antibodies against TNF. If you get biologics early, does it prevent any of these complications?” According to the study results, early use of biologics (i.e., within three months of diagnosis) increased the odds of patients being able to discontinue steroid use and grow physically, while decreasing the odds of penetrating complications—in effect reducing the chance of fistulae.

Today, Crohn’s disease research is also increasingly concerned with how environmental factors may be contributing to the rising incidence of the disease. “This is true for a lot of immune-mediated diseases, but there is no question that the environment matters,” concludes Dr. Snapper. “Crohn’s and ulcerative colitis have increased dramatically over the last five decades, and that’s not because of genetics. The challenge now for the community of doctors and scientists is trying to figure out the environmental factors that work with genes, . . . bacteria that live in our intestines, and our immune response,” he notes. “What are the environmental [factors] that determine why a patient gets the disease?” he continues. “And, how will [patients] respond to a therapy? I would say these are our biggest challenges.”

Dr. Snapper is optimistic that health care will meet and eventually overcome these challenges. “There’s a lot more understanding now of how one would go about trying to figure these issues out,” he says. “From the research perspective, this is an incredibly exciting time because cures and better therapies for inflammatory bowel disease are not only possible, but they will happen.”

Such research advances over the years speak to the steady progress in furthering medical care for individuals with Crohn’s disease. Today, Crohn’s patients can ben-

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**Testing intestines**

An accurate diagnosis of Crohn’s disease relies on a number of interrelated factors, and the tests used to identify its hallmarks are similarly varied. In addition to endoscopy, the following procedures can assist in the diagnostic process:8

- **X-rays.** Patients may undergo standard X-rays of the abdomen or contrast X-rays of the small or large intestine, which track the movement of a small amount of barium through the body.

- **Computerized tomography (CT) scans.** Used primarily to detect disease complications, CT scans can also help rule out other diseases with similar symptom profiles.

- **Leukocyte scintigraphy (white blood cell scan).** White blood cells are attracted to areas of inflammation, and a primary sign of Crohn’s disease is inflammation of the gastrointestinal (GI) tract. This process tags white blood cells with a harmless amount of radiation and injects the blood back into the patient to see where the cells gather.

- **Blood tests.** Multiple blood tests can support an accurate diagnosis, though they cannot identify Crohn’s on their own:
  - Complete blood cell count
  - Inflammation markers (e.g., C-reactive protein or erythrocyte sedimentation rate)
  - Liver function tests
  - Electrolyte panel
  - Vitamin B₁₂

Newer, more sophisticated blood tests analyze two antibodies produced by the immune system to differentiate between Crohn’s disease and ulcerative colitis. The two antibodies the tests focus on—called *biomarkers*—are perinuclear anti-neutrophil antibodies and anti-*Saccharomyces cerevisiae* antibodies. However, the tests are not foolproof: the presence of one or both antibodies does not definitively indicate the presence of one or both diseases.18
Eyes on the insides
Endoscopy serves as a valuable diagnostic tool for diagnosing Crohn’s disease and other conditions that affect the gastrointestinal (GI) tract. Specific types of endoscopy are named for the part of the GI tract they examine:

- **Sigmoidoscopy** examines the rectum and the sigmoid colon—in other words, the lining of the lower third of the large intestine. The procedure can confirm Crohn’s in the lower part of the colon, ulcerative colitis, inflammation, or bleeding.

- **Colonoscopy** looks at the lining of the entire large intestine and can examine the end of the small intestine, as well. This test can analyze the severity of Crohn’s disease or ulcerative colitis and help distinguish between the two.

- **Esophagogastroduodenoscopy (EGD)** checks the stomach, esophagus, and duodenum (the first section of the small intestine), which can be affected by Crohn’s disease.

- **Endoscopic retrograde cholangiopancreatography (ERCP)** examines the pancreatic duct and the bile ducts in the liver. The test can also detect primary sclerosing cholangitis (PSC), a liver disease that affects a small number of people with Crohn’s disease or ulcerative colitis.

References


