

RECENT HEADLINES

KEEP UP WITH THE LATEST RESEARCH

THE LINK BETWEEN GUT BACTERIA AND P-GP

New research may explain the role that gut bacteria play in inflammatory bowel disease. Researchers found that people with a healthy balance of gut bacteria also have healthy levels of a protein called P-gp. But people who have inflammatory bowel diseases have lower levels of this important protein. That matters because P-gp cuts inflammation in the gut and protects the walls of the intestines. Without enough P-gp, gut inflammation can get out of control. Understanding the connection between gut bacteria and this important protein can lead to new treatments for IBD or dietary recommendations to improve the makeup of the gut bacteria.

SOURCE: Microbiome

6.8 MILLION

Estimated number of IBD cases worldwide.

SOURCE: The Lancet

Smokers' risk of developing Crohn's disease compared with nonsmokers' risk.

SOURCE: Crohn's & Colitis Foundation of America

COULD A NEW PILL PREVENT INFLAMMATION?

Researchers at Harvard's Brigham and Women's Hospital have souped up a healthy microbe in the hope that it will treat inflammatory bowel disease. They took the same type of yeast that's in beer and genetically reengineered it to detect inflammation in the gut. Aptly named a "Yeast Bot," the idea is that when the pill reaches the gut, it will find inflammation, and emit an anti-inflammatory substance to stop the process and repair the damage. But before you can get a prescription for this newfangled drug, the researchers must put it through clinical trials. Stay tuned.

SOURCE: Nature Medicine

GET STRESS IN CHECK

Does stress trigger your Crohn's disease flares? Researchers may have discovered why. In a small laboratory study, they found that hormones the body releases when under stress weakened the part of the immune system whose job is to protect the gut from harmful bacteria. This can make the gut more prone to infection with *Enterobacteriaceae*, a group of bacteria that include *E. coli* and has links to Crohn's flares. If unchecked stress is causing you frequent flares, talk to your doctor about how to manage it. Exercise, proper sleep, meditation, and "me" time may help.

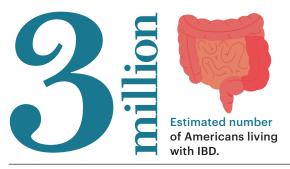
SOURCE: Nature Communications

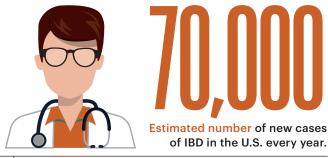


STATS & FACTS

By Sonya Collins

Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor







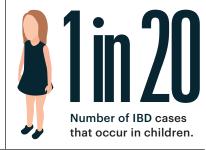






How much more often Crohn's disease appears in children compared with ulcerative colitis.

Ages at which most people with IBD get a diagnosis.



Number of people with IBD who have a next of kin with the condition.



Important Safety Information for ENTYVIO® (vedolizumab)

- Do not receive ENTYVIO if you have had an allergic reaction to ENTYVIO or any of its ingredients.
- ENTYVIO may cause serious side effects, including:
- o Infusion-related and serious allergic reactions can happen while you are receiving ENTYVIO or several hours after treatment. You may need treatment if you have an allergic reaction. Tell your healthcare provider or get immediate medical help if you get any of these symptoms during or after an infusion of ENTYVIO: rash, itching, swelling of your lips, tongue, throat or face, shortness of breath or trouble breathing, wheezing, dizziness, feeling hot, or palpitations (feel like your heart is racing).
- ENTYVIO may increase your risk of getting a serious infection. Before receiving and during treatment with ENTYVIO, tell your healthcare provider if you think you have an infection or symptoms of an infection, such as fever, chills.

- muscle aches, cough, shortness of breath, runny nose, sore throat, red or painful skin or sores on your body, tiredness, or pain during urination.
- o People with weakened immune systems can get progressive multifocal leukoencephalopathy (PML) (a rare, serious brain infection caused by a virus). Although unlikely while receiving ENTYVIO, a risk of PML cannot be ruled out. PML can result in death or severe disability. There is no known treatment, prevention, or cure for PML. Tell your healthcare provider right away if you have any of the following symptoms: confusion or problems thinking, loss of balance, change in the way you walk or talk, decreased strength or weakness on one side of the body, blurred vision, or loss of vision.
- Liver problems can happen in people who receive ENTYVIO. Tell your healthcare provider right away if you have any of the following symptoms: tiredness, loss of appetite, pain on the right side of your abdomen, dark urine, or yellowing of the skin and eyes (jaundice).

- The most common side effects of ENTYVIO include common cold, headache, joint pain, nausea, fever, infections of the nose and throat, tiredness, cough, bronchitis, flu, back pain, rash, itching, sinus infection, throat pain, and pain in extremities. These are not all the possible side effects of ENTYVIO. Call your healthcare provider for medical advice about side effects.
- Before receiving ENTYVIO, tell your healthcare provider about all of your medical conditions, including if you: have or think you may have an infection or have infections that keep coming back; have liver problems; have tuberculosis (TB) or have been in close contact with someone with TB; have recently received or are scheduled to receive a vaccine; or if you are pregnant, breastfeeding, plan to become pregnant, or plan to breastfeed.

Please see the Important Facts for ENTYVIO on the following page and talk with your healthcare provider.

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Uses of ENTYVIO® (vedolizumab)

ENTYVIO is a prescription medicine used in adults for the treatment of:

- moderately to severely active ulcerative colitis
- moderately to severely active Crohn's disease



ENTYVIO is a trademark of Millennium Pharmaceuticals, Inc., registered with the U.S. Patent and Trademark Office and is used under license by Takeda Pharmaceuticals U.S.A., Inc.

IMPORTANT FACTS

ENTYVIO (en ti' vee oh) (vedolizumab) for injection, for intravenous use

What is the most important information I should know about ENTYVIO?

ENTYVIO may cause serious side effects, including:

- Infusion-related and serious allergic reactions. These reactions can happen while you are receiving ENTYVIO or several hours after treatment. You may need treatment if you have an allergic reaction. Tell your healthcare provider or get medical help right away if you get any of these symptoms during or after an infusion of ENTYVIO: rash, itching, swelling of your lips, tongue, throat or face, shortness of breath or trouble breathing, wheezing, dizziness, feeling hot, or palpitations (feel like your heart is racing).
- Infections. ENTYVIO may increase your risk of getting a serious infection. Before receiving ENTYVIO and during treatment with ENTYVIO, tell your healthcare provider if you think you have an infection or have symptoms of an infection such as fever, chills, muscle aches, cough, shortness of breath, runny nose, sore throat, red or painful skin or sores on your body, tiredness, or pain during urination.
- Progressive Multifocal Leukoencephalopathy (PML). People with weakened immune systems can get progressive multifocal leukoencephalopathy (PML) (a rare, serious brain infection caused by a virus). Although unlikely while receiving ENTYVIO, a risk of PML cannot be ruled out. PML can result in death or severe disability. There is no known treatment, prevention, or cure for PML. Tell your healthcare provider right away if you have any of the following symptoms: confusion or problems thinking, loss of balance, change in the way you walk or talk, decreased strength or weakness on one side of the body, blurred vision, or loss of vision.
- Liver Problems. Liver problems can happen in people who receive ENTYVIO. Tell your healthcare provider right away if you have any of the following symptoms: tiredness, loss of appetite, pain on the right side of your stomach (abdomen), dark urine, or yellowing of the skin and eyes (jaundice).

See "What are the possible side effects of ENTYVIO?" for more information about side effects.

What is ENTYVIO?

ENTYVIO is a prescription medicine used in adults for the treatment of:

- · moderately to severely active ulcerative colitis.
- moderately to severely active Crohn's disease.

It is not known if ENTYVIO is safe and effective in children under 18 years of age.

Who should not receive ENTYVIO?

Do not receive ENTYVIO if you have had an allergic reaction to ENTYVIO or any of the ingredients in ENTYVIO. See the end of this Medication Guide for a complete list of ingredients in ENTYVIO.

Before receiving ENTYVIO, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection, think you may have an infection or have infections that keep coming back (see "What is the most important information I should know about ENTYVIO?").
- have liver problems.

- have tuberculosis (TB) or have been in close contact with someone with TB.
- have recently received or are scheduled to receive a vaccine.
 Talk to your healthcare provider about bringing your vaccines up-to-date before starting treatment with ENTYVIO.
- are pregnant or plan to become pregnant. It is not known if ENTYVIO will harm your unborn baby. Tell your healthcare provider right away if you become pregnant while receiving ENTYVIO.
 - Pregnancy Registry: There is a pregnancy registry for women who use ENTYVIO during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk with your healthcare provider about how you can take part in this registry or you may contact the registry at 1-877-825-3327 to enroll.
- are breastfeeding or plan to breastfeed. ENTYVIO passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take ENTYVIO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Especially tell your healthcare provider if you take or have recently taken Tysabri (natalizumab), a Tumor Necrosis Factor (TNF) blocker medicine, a medicine that weakens your immune system (immunosuppressant), or corticosteroid medicine.

How will I receive ENTYVIO?

- ENTYVIO is given through a needle placed in a vein (intravenous infusion) in your arm.
- ENTYVIO is given to you over a period of about 30 minutes.
- Your healthcare provider will monitor you during and after the ENTYVIO infusion for side effects to see if you have a reaction to the treatment.

What are the possible side effects of ENTYVIO?

ENTYVIO may cause serious side effects, see "What is the most important information I should know about ENTYVIO?".

The most common side effects of ENTYVIO include: common cold, headache, joint pain, nausea, fever, infections of the nose and throat, tiredness, cough, bronchitis, flu, back pain, rash, itching, sinus infection, throat pain, and pain in extremities.

These are not all of the possible side effects of ENTYVIO.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about ENTYVIO

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about ENTYVIO that is written for health professionals.

Manufactured by: **Takeda Pharmaceuticals U.S.A.**, **Inc.** Lexington, MA 02421

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For more information, go to www.ENTYVIO.com or call 1-877-TAKEDA-7 (1-877-825-3327).

YOUR MENTAL HEALTH

A CLOSER LOOK AT THE IMPACT OF THIS CHRONIC DISEASE

By Kendall K. Morgan Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor

When you have inflammatory bowel disease (IBD), it's natural to struggle with mental health and tough emotions. Fatigue, pain, and frequent trips to the bathroom can get in the way of doing what you love. But, there's more to the link between IBD and mental health than this, according to Charles Bernstein, MD, a gastroenterologist and director of the IBD Clinical and Research Centre

at the University of Manitoba in Winnipeg, Canada.

"People with IBD are more likely to have mood disorders or depression or generalized anxiety disorders for years prior to the IBD," Bernstein says.

In addition, the symptoms of IBD and daily challenges of having any chronic disease add stress to one's life.

You also may take steroids to help with the inflammation that comes with IBD. "Steroids are one medication we know can have an adverse affect on emotional state," Bernstein says.

MANAGE YOUR MENTAL HEALTH

Bernstein says it's not clear that stress actually makes your gut inflamed. But he has noticed that people feeling under stress more often do have symptoms flare up. Mental health challenges may make it harder for you to stick to your medications, too.

He says that your IBD doctor should ask you not just about IBD symptoms, but about how you are feeling in other ways, too. Whether your doctor asks you or not, let them know if you are having trouble, even if you don't think it's related to your IBD. Ask if they have ways to help or can refer you to someone who can.

Online resources might help you, too. In fact, Bernstein is studying whether an online program that teaches how to manage stress can help in dealing with IBD symptoms.

TRY SOME ALTERNATIVES

"There are many things people can do," Bernstein says. "In general, mindfulness techniques, yoga, meditation, physical exercise—these are all things I would encourage."

You might not feel up to boot camp or some other intensive exercise regimen and that's OK. Try long walks, cycling, or tai chi—anything that works for you to relieve stress and get active, Bernstein says. Think about what your stressors are and who can help. Those stressors "may be work or financial or may be related to other health problems," he adds.

Bernstein says he has at times referred his IBD patients to a social worker. To manage your IBD, it's important to take an open and holistic approach. Find a doctor who is willing to consider everything that's going on in your life. The first step for you, Bernstein says, is having some awareness that your "mental health may affect how you feel from a GI perspective."





ULCERATIVE COLITIS CHANGED ME FOR THE BETTER

By John Hardisky

Reviewed by Brunilda Nazario, MD, WebMD Chief Physician Editor, Medical Affairs

I was 37 when I started having digestive pain that just kept getting worse. I was having mucus in my stool, and lost so much blood that I developed anemia. For a cyclist, anemia isn't a good thing; you want your blood count to be high so your body has the oxygen it needs. But I was constantly fatigued.

Still, I avoided the doctor because I dreaded procedures like colonoscopies. I'm also a little stubborn and tend to wait until things are really bad before addressing them. Finally, when I couldn't ignore things anymore, I told my wife, who's a medical student, what was going on. She immediately told me to get my butt to the doctor. (No pun intended.)

THE WINDING ROAD TO DIAGNOSIS AND TREATMENT

But even once I was under medical care, it took a while to get a diagnosis. My general practitioner ran tests, but couldn't pinpoint what was going on. I just thought this was part of getting older. My best guess was that I had

hemorrhoids. Finally, I saw a gastroenterologist, and a year after my symptoms began, I got my ulcerative colitis diagnosis, and a whole new chapter of my life started.

The doctors tried steroids and other first-line treatments, but ultimately, biologics are what I needed to get my UC under control. It took about 6 months, but we found a biologic that got me into remission, which is incredible. I still have symptoms from time to time, so I try to stay aware of what might trigger a flare. Usually for me it's stress.

DAILY LIFE WITH UC

Even through my worst symptoms, I tried to keep training and racing and parenting just like I always had. I didn't want to let UC disrupt the enjoyment of my life. But there were times I had to stop—literally—and deal with the reality of my disease. Road trips required a lot more bathroom breaks, for example. It's kind of a joke in the IBD community that we know where all the bathrooms are.

As an athlete, "pushing through" is

- + **Be open to help.** Never be afraid to ask for support when you need it.
- + Find joy. When my symptoms were at their worst, making time for things I enjoyed helped me keep hope alive.
- + Connect. Organizations specific to IBD, such as the Crohn's and Colitis Foundation, can offer community and information as you navigate life with UC.

what I know to do, but the physical toll of UC was really wearing me down and making that tactic unsustainable.

Mentally, I was suffering, too. I rely on the physicality of training as an outlet for my mental health. So to lose that was really hard. I was fortunate to find a lifeline in Ride4IBD—a movement that combines my love of cycling and a passion for IBD awareness.

Being diagnosed with UC brought out the fighter spirit in me and gave me a deeper appreciation of life and health. I no longer take these things for granted. In that respect, it really has changed me for the better.



HOW STRESS CAN AFFECT YOUR IBD

WHY SOOTHING YOUR STRESS CAN HELP YOUR SYMPTOMS

By Rachel Reiff Ellis

Reviewed by Melinda Ratini, DO, WebMD Medical Reviewer

Everyone deals with stress, but when you have a chronic condition like IBD, you may feel it more often-and in more ways than one. Stress can often bring on flares of your disease, causing even more stress. Managing these outbreaks requires breaking the stress-flare cycle.

"When there is a large amount of stress we can see an increase in inflammatory type symptoms," says J. Casey Chapman, MD, chief medical officer at GI Alliance in Baton Rouge, LA.

STRESS AND INFLAMMATION

Stress has a physical effect on your body. It causes muscle tension, rapid breathing, increased heart rate, a rise in cortisol (the stress hormone), and higher blood pressure. It also has an impact on your brain-gut connection.

Here's how it works: Stress can bring on changes in your gut bacteria, which in turn can shift mood. So your gut's nerves and bacteria strongly influence your brain and vice versa.

"While it is not clear that stress directly causes inflammation, we do know that stress can indirectly increase the likelihood [you'll have] symptoms that can mimic inflammation," Chapman says.

Some studies show stress may even mess with your body's ability to shut down its own immune response (inflammation) after it gets started.

IMPACT OF STRESS ON **DISEASE MANAGEMENT**

Chapman says that when it comes to living well with IBD, the effect of stress on your mind is just as important as its effect on your body. "Stress can affect your motivation to seek self-care, maintain medication adherence, [practice] stress avoidance, and pursue exercise," he says.

In other words, even if you're not directly flaring during stressful times, you may not have the mental bandwidth to care for your condition the way you should, which can lead to an increase in your symptoms.

It's also common for people with IBD to have anxiety and depression,

which can increase disease activity, too. Chapman says it's important to ask your doctor about screening for these mental health disorders to be sure vou're not overlooking a key part of your disease management.

"Without correct diagnosis and treatment, things may be labeled as normal stress when it may actually be something very impactful to [your] outcome," he says.

TIPS FOR TAMING STRESS

Try these methods to calm your mind and body.

- + Do breathing exercises.
- + Meditate or practice mindfulness techniques.
- + Listen to soothing music or calming sounds.
- + Take a gentle yoga class or a tai chi lesson in person or online.



BEYOND THE GI SYSTEM

SYMPTOMS OF IBD THAT AFFECT OTHER PARTS OF THE BODY

By Kendall K. Morgan

Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor

The inflammation caused by IBD comes with plenty of gastrointestinal (GI) trouble. But at least 1 in 4 people with IBD have signs in other parts of the body. Doctors sometimes call these "extraintestinal manifestations" of IBD.

ARTHRITIS

"The predominant one is joint pain," says Charles Bernstein, MD, gastroenterologist at the University of Manitoba in Canada. "About a quarter of people with IBD also have redness and other signs of arthritis."

People with IBD may have arthritis symptoms at a young age in large joints of the arms and legs. They also may have symptoms in various parts of the spine, although this is less common. Often, the joint pain gets better as GI symptoms improve with treatment.

SKIN CONDITIONS

About 1 in 5 people with IBD have skin conditions,

either related to the IBD or its treatment. Some common ones include erythema nodosum, in which tender red bumps appear on the shins, and pyoderma gangrenosum, in which lesions or ulcers form often where there's an injury.

Bernstein says that the red bumps typically show up when IBD is most active. The lesions of pyoderma gangrenosum can arise separately from IBD flares. They're often related to ostomy surgery, which allows waste to leave your body through a pouch, or other trauma. IBD also can come with painful tears around the anus and small ulcers called canker sores in your mouth.

EYES, BONES, AND LIVER

Approximately 1 in 10 people with IBD have problems with their eyes. These may involve redness and pain in different parts of the eye. While it can change your vision, these eye problems in IBD are treatable with eye drops or other medicines.

Up to 60% of people with IBD have thin and weakened bones, too. As a result, Bernstein says they are more at risk for

- have be linked to my IBD?
- + Are there other medicines to take for them?
- + What can I do to prevent bone loss?
- + I feel tired a lot. Could it be low iron (anemia)?

osteoporosis. This can happen from using steroids for a long time or from the inflammation itself. While relatively rare, about 5% of people with IBD have serious liver disease.

WHICH COMES FIRST?

Bernstein says that these other conditions may come up before, after, or around the same time as a diagnosis of IBD. While it's good to know these can happen, he says he doesn't want folks with IBD to worry about every minor discomfort.

"Aches and pains can be normal," he says, and all people feel them. "It's good to be aware of it, but just because you have red eyes one day doesn't mean you've got iritis [inflammation of the eye's iris]. I try not to make my patients too vigilant about short-lived symptoms."

OPTIONS TO TREAT CROHN'S DISEASE

TALK TO YOUR DOCTOR ABOUT WHICH ONE IS BEST FOR YOU

By Kendall K. Morgan Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor

There's no cure for Crohn's, but there are ways to control it. The goal is to get your Crohn's disease into remission and keep it there.

You and your doctor will have many medicines to choose from. They fall into different categories based on how they work to control the disease and its symptoms. Najwa El-Nachef, MD, a gastroenterologist at the University of California at San Francisco, says that the best place for you and your doctor to start will depend on how severe your disease and inflammation is.

AMINOSALICYLATES

Aminosalicylates, which lower inflammation, can be an early step in treating Crohn's disease. There are several to choose from. They can be applied to the surface of your intestine with an enema or suppository or you can take them by mouth.

"If someone has very mild disease, you may start with these more topical therapies," El-Nachef says. But, she adds, they less often work well for Crohn's compared with other types of inflammatory bowel disease. Doctors used them more in the past.

STEROIDS

Corticosteroids can fight inflammation in your gut. But steroids aren't a long-term solution. That's both because they aren't the best way to keep Crohn's in remission and they have side effects if taken too long.

"Steroids help with flares," El-Nachef says.

"They're not considered good long-term agents."

IMMUNE SUPPRESSORS

You might also hear these drugs, which are taken by mouth, called "immune modulators." There are several of them, all of which work to lower the activity in your immune system that's causing the problems in your gut. But, El-Nachef says, these treatments also are falling out of favor for treating Crohn's as safer and more effective treatment options have grown.

"There's an idea out there that a pill is safer than an infusion or injection, but that's not always the case," El-Nachef says.

BIOLOGICS

You'll get biologic therapies as an infusion or injection once every several weeks. They're antibodies that target the immune system in one of a few different ways. Your doctor will help you decide which to try first.

El-Nachef says any of today's biologics "are reasonable first-line treatments" for Crohn's. They work better than earlier medicines and come with fewer side effects.

DIET AND SURGERY

In addition to biologics or other medicines, your doctor may suggest changes to your diet or letting your bowel rest. Sometimes people with Crohn's also need surgery, but this is becoming less common thanks to treatment advances.

"[Biologic] medications have changed the whole landscape of what it means to have Crohn's," El-Nachef says. "People have less surgery now and, if they do, they are less likely to have another surgery [later]."





Over 66,000 veterans in the United States live with inflammatory bowel disease (IBD).

Are you one of them? The Crohn's & Colitis Foundation is here for you.

Whether you were diagnosed while in service or after you were discharged, you may have questions about your disease, need resources to navigate your healthcare options, or want to connect with others who understand what you are experiencing.

Visit www.crohnscolitisfoundation.org/veterans to find resources just for you or contact our IBD Help Center at info@crohnscolitisfoundation.org or 888-MY-GUT-PAIN to get answers to your questions.

