



## What Should You Know About “C. Diff” Infection? (*Clostridioides difficile*)

Antibiotics are medications that kill bacteria. Since their discovery in 1928, antibiotics have been crucial in keeping us healthy. Their ability to fight infection has saved countless lives. But there is a downside as well. As with all powerful medications, side effects may sometimes occur. Often, this will take the form of an allergic reaction, such as a skin rash. Another less well-recognized side effect is diarrhea.

### **The Microbiome: Good Versus Evil**

The problem is one of imbalance. The colon, or large intestine, typically contains trillions of bacteria that multiply happily. This mixed colony of bacteria is called the MICROBIOME. Most of these are considered "healthy bacteria." They do not bother you, and you don't bother them. All is in balance. A small percentage of these bacteria are harmful — but they are kept in check by the healthy bacteria.

A good analogy would be your lawn. If your lawn is healthy, it has few weeds. There may be weed seeds hidden among the blades of grass, but healthy grass suppresses them. In the event of a drought, your grass thins out, and weed seeds may germinate and take control of your lawn. In your colon, the normal healthy bacteria suppress any disease-causing germs. However, when you take antibiotics, the number of beneficial bacteria sometimes decreases, allowing harmful bacteria the opportunity to flourish.



### **Antibiotic-Associated Diarrhea**

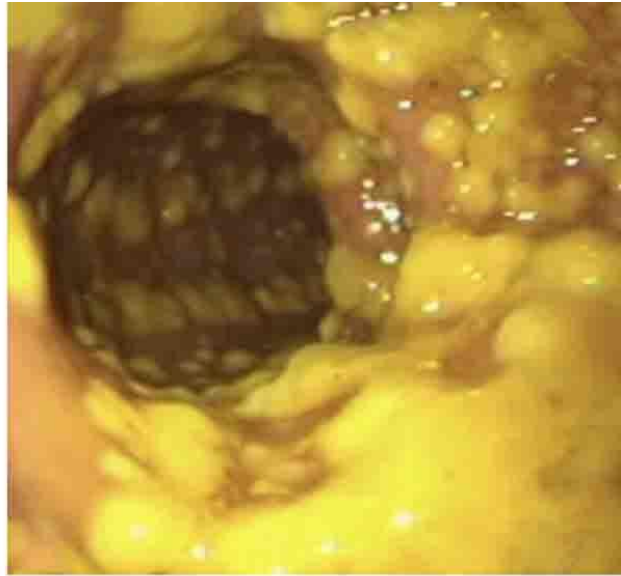
Antibiotics attack disease bacteria like those in an infected tooth and the healthy bacteria in your colon. This disrupts the microbiome and is why many patients experience diarrhea while taking

an antibiotic. This condition is usually mild and resolves quickly when the antibiotic is discontinued. This is called Antibiotic-Associated Diarrhea.

Clostridioides difficile (klos-TRID-e-OY-dees dif-uh-SEEL)



**Normal Colon Lining**



**Active C. difficile Infection**

One form of Antibiotic-Associated Diarrhea is more serious. A certain harmful bacteria called Clostridioides difficile (formerly termed Clostridium difficile) may normally be present in the colon in small numbers. If antibiotics sufficiently suppress the healthy bacteria, this so-called “C. diff” organism can multiply, producing a toxin that inflames the wall of the colon causing diarrhea. This toxin may damage the colon’s wall in high concentrations - sometimes severely. This is called C. difficile colitis.

#### **How Common Is This?**

C. difficile is common. As mentioned, diarrhea is prevalent among people taking antibiotics, with up to one-fourth of all cases caused by C. difficile. We see several new cases in our private Gastroenterology group practice almost weekly - both hospitalized inpatients and less-severe outpatients. C. difficile colitis causes over 500,000 illnesses and up to 30,000 deaths in the U.S. each year.

#### **Who Is At Risk?**

The chance of getting a C. difficile infection is higher while taking an antibiotic or within a month of completing your prescribed treatment. It is also common in patients who have been hospitalized or in a long-term care facility. Significantly higher-risk individuals include people over 65, people with a weakened immune system, and those on immune-suppressive medications, including cancer patients undergoing chemotherapy. Individuals suffering from inflammatory bowel disease (Ulcerative Colitis and Crohn’s disease) can get this infection without any of the previously mentioned risk factors.

A new, more aggressive hypervirulent strain of *C. difficile* emerged around 2003. It produces far more toxin than other strains do. This new strain has shown up in people who haven't been in the hospital or taken antibiotics. The potential for community household contamination in an urban area with *C. difficile* is high. In the past, this was most often a disease of hospitalized inpatients, but now about 40% of patients are infected as outpatients, often with no recent exposure to antibiotics or healthcare facilities.

### **Which Antibiotics Cause This Problem?**

Each antibiotic has a different chemical structure that affects how it works in the body. Some are more powerful than others, but while any antibiotic can suppress the healthy bacteria in your colon, a problem can arise when newer, more powerful antibiotics are prescribed or multiple antibiotics are used for severe infections. Cleocin (clindamycin), often given to treat dental or sinus infections, keeps showing up in patients' histories. The risk of *C. difficile* infection also rises with the antibiotic prescription's dosage, frequency, and duration. However, even the gentlest antibiotics, taken for a short period, can occasionally result in this problem.

### **How Soon Do Symptoms Occur?**

It varies. *C. difficile* infection can occur within two days of completing a course of antibiotics or up to 6 weeks later. Therefore, if you have new symptoms of diarrhea, it is essential that you make your doctor aware of any antibiotics you may have taken over the last few months.

### **What Are The Symptoms?**

This problem is first indicated by a sudden change in bowel habits for most patients. The stools become less formed, loose, and watery. In mild cases, patients may have watery diarrhea three or more times a day with an unusually foul odor, accompanied by abdominal cramping, nausea, and fever.

Severe cases may have more frequent watery diarrhea: as often as 15 times a day. Patients may complain of extreme stool urgency, stool incontinence, and severe abdominal pain. There may also be signs of dehydration, such as increased thirst, weakness, dizziness, and confusion.

### **How Is This Condition Diagnosed?**

**STOOL TESTS:** Since *C. difficile* infection is secondary to the damaging effects of a toxin produced by the *Clostridioides difficile* organism, the diagnosis can usually be made by looking for the presence of this toxin in a fresh stool specimen. Other stool tests can be employed to find the organism itself.

**BLOOD TESTS:** There is no blood test for *C. difficile* infection, but routine bloodwork is performed to check for high white blood cell (WBC) count, a sign of severe infection. Serum electrolytes such as sodium and potassium are tested. Kidney function is evaluated.

**IMAGING:** An Abdominal/Pelvic CT scan may show signs of inflammation in the colon. In severe cases, imaging studies can also detect complications of *C. difficile* infection, such as dilation of the colon (toxic megacolon) or a tear in the colon (perforation).

**SIGMOIDOSCOPY:** A complete colonoscopy is seldom performed in severe cases. However, a limited flexible “short scope” sigmoidoscopy is sometimes performed to directly visualize and assess the damage to the colon's lining.

## **How Is This Condition Treated?**

### **STOP Offending Antibiotics**

The most important aspect of treatment would be to limit the use of powerful antibiotics, mainly when the symptoms of diarrhea occur. Ideally, stopping the offending antibiotics under the supervision of your doctor allows the healthy intestinal bacteria to multiply and repopulate the colon.

### **Do Not Take Antidiarrheals**

It is essential, however, to avoid antidiarrheal medications like Imodium or Kaopectate since diarrhea is nature's way of purging the toxin from the colon. If antidiarrheal medicines are taken, the toxin will remain in the colon for prolonged periods, thus worsening the condition.

### **Rehydration**

Another critical aspect of therapy involves correcting any dehydration caused by bouts of diarrhea. Drinking plenty of fluids is essential. Liquids that contain electrolytes are preferred to plain water. Pedialyte, fruit juices, and salty broths are good choices.

#### **Oral Rehydration Solution**

With fluid loss comes electrolyte loss. You can make a homemade electrolyte drink by mixing the following ingredients:

- 1/4 tsp table salt
- 8 tsp sugar
- 3 TBSP orange juice concentrate
- 4 cups water

Instead of chugging fluids down all at once, take frequent sips or suck on ice chips. A good rule of thumb is to drink 8 oz of liquid every time you have a loose bowel movement.

### Bland diet

It is essential to maintain some nutrition until the diarrhea subsides, but people with diarrhea should eat bland foods. Spicy or more complex foods can irritate the bowels. The following “BRAT” diet is often recommended for the first few days.

- Bananas
- Plain white rice
- Applesauce
- White bread or toast

### Antibiotics against *C. difficile*

It may seem odd, but to treat *C. difficile* infection, one of two special antibiotics is often prescribed – DIFICID (fidaxomicin) or VANCOCIN (vancomycin). Both of these products selectively kill the *Clostridioides difficile* organism allowing the normal bacteria to recover. They can be taken orally, usually 2-4 times a day for ten days. (In the past, a third antibiotic, FLAGYL (metronidazole), was often prescribed, but it has been shown to be even less effective.)

### Recurrent infection is a big problem

As if getting a *C. difficile* infection isn't bad enough, a bigger problem with *C. difficile* infections is the high recurrence rate. About 15% of individuals are reinfected in 2 - 8 weeks. Both DIFICID 200 mg and VANCOCIN 125 mg are about 90% effective in treating the initial infection.

VANCOCIN was the preferred treatment until recent clinical studies have shown that DIFICID is more successful in reducing recurrence. This is because DIFICID has a very narrow targeted spectrum of action and is least disruptive to the normal fecal microbiome.

DIFICID can be given in two different dosing regimens. It is usually given twice a day for 10 days. But, it can also be given twice a day for the first 5 days, then just one pill every other day on days 7-25. Both regimens use 20 pills, but the extended DIFICID version has the lowest recurrence rate, as low as 6.2% vs 19% recurrence with VANCOCIN. Clinical guidelines have been changed to recommend DIFICID as the preferred initial treatment for *C. difficile* infection, and the extended version makes the most sense. VANCOCIN is still often chosen due to the high cost of DIFICID.

### Can You Get *C. difficile* More Than Once?

Unfortunately, yes. Recurrent *C. difficile* infection is one of the most challenging infections to treat. When the symptoms go away and return within eight weeks, that is called recurrent *C. diff*. The chances of recurrence increase with each *C. difficile* episode. The recurrence rate is 15%–35% after the first attack. This increase to 35%–65% after the first recurrent episode.

### Retreatment of recurrent infection

For recurrent infection, tapered-pulsed Vancocin is recommended with a standard vancomycin dose four times daily for 10-14 days, followed by decreasing the dose by 25%-50% every 1-2 weeks with no skipped days and then pulsed at 125 mg dose skipping 1-2 days for 2-4 weeks. Dificid is recommended for recurrent *C. difficile* infection if vancomycin was used initially.

Patients who continue to suffer multiple recurrences are often treated with Zinplava or FMT (see below).

### **Zinplava (Bezlotoxumab) Monoclonal Antibody Infusion**

Zinplava is a human monoclonal antibody that inactivates *C. difficile* toxin B. The main benefit is a reduction in the rate of recurrence. Clinical trials showed that a single intravenous dose of Zinplava had no substantial effect on clinical cure rates - but considerably reduced the risk of recurrence. There have been no significant side effects. It is expensive and usually reserved for patients who have had multiple recurrences. It is also used in patients with a high risk of recurrent disease, such as those with more than one recurrence, those requiring frequent antibiotics for COPD or recurrent bladder infections, immunocompromised individuals, and those over age 65.

### **FMT (Fecal Microbiota Transplant)**

For severe cases and in individuals who experience multiple recurrences of *C. difficile* infection, FMT is available. In this treatment, intestinal bacteria prepared from the stool of a healthy patient is transferred into the affected patient's colon. The FMT mixture can be delivered by enema, colonoscopy, or taken by mouth as capsules. Research has shown extremely high success rates with FMT. One study of 56 patients with severe refractory *C. difficile* infection demonstrated a 75% cure rate with a single infusion and a 100% cure rate with multiple infusions after Vancocin. FMT is currently classified as investigational and only available through specialty centers. As you might expect, stool donors must undergo extensive testing to ensure they have no transmittable disease.

### **REYBOTA - something new December 2022**

For severe cases and in individuals who experience multiple recurrences of *C. difficile* infection, the FDA has approved a prescription-based fecal microbiota transplant called Rebyota (Ferring Pharmaceuticals). Rebyota is prescribed to prevent recurring *Clostridioides difficile* infection (CDI) among patients 18 and older after a failed antibiotic regimen. This novel, first-in-class, microbiota-based live biotherapeutic comes in a pre-packaged, single-dose, 150 mL suspension for rectal administration. Rebyota is sourced from qualified donors and tested for a panel of transmissible pathogens. The FDA approved Rebyota based on findings from a clinical program that included results from the randomized, double-blind, placebo-controlled, phase 3 PUNCH CD3 trial. In the trial, 262 participants were administered blinded treatment with a 70% success, and more than 90% of participants who achieved treatment success remained free of *C. difficile* recurrence through 6 months.

### **VOWST- "poop pill" April 2023**

An even better breakthrough came in April 2023 when the FDA approved the first ORAL CAPSULE for fecal transplant in cases of recurrent *C. difficile* called VOWST. After antibiotic treatment of the second attack, a laxative is taken to purge the colon. Then, you take four capsules of VOWST each morning for the next three days. Clinical scientific studies have shown that this regimen can reduce the risk of a third attack from 40% to 12%. Hooray for science!

## **Surgery**

In extreme cases, complications may occur. Although rare, they can be severe, even life-threatening. Emergency surgery to remove the entire colon may be necessary in such cases. This radical surgery can be lifesaving but usually leaves the individual with a permanent ileostomy “bag” to collect the fecal material.

## **Protecting Your Family**

It is essential to prevent the spread of *C. difficile* infection to others, particularly within your household. It cannot be transmitted through body fluids, but it can be transmitted from person to person by a fecal to oral route. Oxygen kills *C. difficile*, so the active *C. difficile* bacteria cannot survive outside the body for very long. It survives in the environment in the form of inert oxygen-resistant spores – something like a weed seed. Because the spores are metabolically dormant, they are resistant to antibiotics and are not killed by bleach-free disinfectants. These spores can survive extreme environmental conditions and persist for months or years. Touching a contaminated surface may infect other individuals with *C. difficile* spores. To protect others:

1. Alcohol hand sanitizer does not kill *C. difficile* spores
2. Wash your hands often with a full 30-second soap-and-water hand wash, including after you use the bathroom and before you eat
3. Remind friends and family to wash their hands frequently, too.
4. Shower regularly with soap.
5. Use a separate bathroom from other family members when you have diarrhea.
6. Wipe down and clean all surfaces with a bleach-containing spore-killing product like Lysol Multipurpose Sanitizing and Disinfecting Spray with Bleach or Clorox Healthcare Bleach Germicidal Cleaner Spray.
7. Wash bedding, towels, and clothes before anyone else touches them. Use a washer and dryer on the highest temperature setting the items can take.
8. Remove your shoes before entering your home. A 2014 study of environmental surfaces found that shoe bottom swab samples had the highest percentage of positive *C. difficile* spores (40%) followed by bathroom/toilet surfaces, house floor dust, and other surface swabs.

## **Recovery**

No test can guarantee that *C. difficile* is gone. Most patients note improvement in diarrhea episodes within 3-5 days. Older individuals may recover more slowly. You are considered cured if your symptoms resolve and *C. difficile* does not come back during the next eight weeks.

After the infection is treated and symptoms resolve, we do not routinely retest the stool for the *C. difficile* organism, its spores, or the toxin, as they can persist in the stool long after the infection is gone. This is called colonization. After recovery, your stool can still transmit the disease to others. Practice good bathroom hygiene at all times to protect others. Once infected with *C. difficile*, you are at higher risk of infection again following new antibiotic exposure.

## **Post-infectious Irritable Bowel Syndrome (IBS)**

After successful treatment of the infection, as many as 20% of patients still do not have normal bowel movements. This is called “post-infectious Irritable Bowel Syndrome” (IBS). They may experience irregular bowel movements, excessive gas, bloating, nausea, and fecal urgency. This condition may take months to resolve, but treatments are available to lessen the symptoms. If you are having this problem, tell your doctor. While probiotics have not been shown to help treat an active *C. difficile* infection, they may be helpful under these circumstances. We recommend Florastor, which is available over the counter without a prescription.

### **How Can I Prevent This Problem?**

While there is no guaranteed way to prevent *C. difficile* infection, some simple measures are helpful. The most obvious is to avoid unnecessary antibiotics for uncomplicated infections. Have you ever asked your doctor for antibiotics to treat a cold or the flu? These viral infections do not respond to antibiotics, yet antibiotics are often requested. They should not be utilized. You should tell your doctor if you have ever had *Clostridioides difficile* colitis since past episodes increase your risk of future attacks. Other preventative measures, particularly within institutions such as hospitals and nursing homes, include isolating patients who harbor the infection and careful, thorough hand-washing and other hygiene techniques.

Lastly, early diagnosis is essential. Suppose you have recently been prescribed antibiotics and have experienced a significant change in bowel habits. In that case, you should see your doctor as soon as possible since, if untreated, this disease's late stages can be devastating, occasionally requiring the surgical removal of the colon.

### **What About The Future?**

As the prescription and use of antibiotics increase, the incidence of *Clostridioides difficile* infection escalates. Hopefully, a vaccine will become available to immunize high-risk patients. Extensive research is underway on this subject, and new treatments may help to lower the costs associated with *Clostridioides difficile* infections in today's healthcare environment. If you have any additional questions about this condition, you should discuss them with your physician.

### **Remember...**

- Don't insist on a prescription for an antibiotic if you have a viral infection such as a cold or flu.
- Follow your doctor's instructions carefully. Take doses on schedule for the prescribed number of days indicated.
- Tell your doctor if you develop persistent diarrhea symptoms during or within six weeks after a course of antibiotics.
- Never share your antibiotics with anyone. If you have any leftovers, destroy them.



Notes: (Write down any questions you may wish to discuss with your doctor)

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Dr. Robert Fusco  
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**Center For Digestive Health & Nutrition**

725 Cherrington Parkway • Moon Township, PA 15108  
412.262.1000 • [www.gihealth.com](http://www.gihealth.com) • IG: @thedigestivetract

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