

COLON AND RECTAL SURGICAL ASSOCIATES

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Fecal Microbial Transplantation It Works!

NO GOOD DEED GOES UNPUNISHED.

Everything comes at a cost. Not uncommonly, patients who have been treated with antibiotics for one type of infection, develop a second, opportunistic infection. When a majority of normal or pathogenic bacteria are removed by antibiotics used to treat an active infection, there may be an overgrowth of previously dormant and harmless bacteria, which now have the "opportunity" to wreak their own brand of havoc. This first unintended consequence has led to a second unintended consequence, the emergence of resistant strains of new opportunistic bacteria such as the commensal *Clostridium difficile* (*C. diff*).



Clostridium difficile.
A bacillus and a spore.

In the gastrointestinal tract, the opportunistic *Clostridium difficile*, an anaerobic, spore-forming, Gram-positive bacillus, is the potential culprit which may produce toxins that cause abdominal discomfort and diarrhea. *C. diff* is the most common cause of pseudomembranous colitis, a term which refers to the membranes seen in an infected, inflamed colon. The membranes are thick collections of inflammatory cells, fibrin and necrotic debris. Pseudomembranous colitis can progress to toxic megacolon, which is a life threatening, acute colonic distention.

Each year, fifteen thousand hospitalized patients die as a result of toxic megacolon, an unintended result of antibiotic usage.

Pseudomembranous colitis may affect outpatients or inpatients. The infection rate in inpatients increases with the length of hospitalization. The most common symptoms are abdominal pain and bloating and a profuse watery diarrhea in an individual who has been treated with antibiotics or chemotherapeutic drugs. Almost any antibiotic can cause a *Clostridium difficile* infection, with the most common offenders being the cephalosporins and the fluoroquinolones. Symptoms are often accompanied by lethargy, fever and an elevated white blood cell count.

ROW, ROW, ROW YOUR BOAT. HAPPY BIRTHDAY TO YOU.

When present outside of the body, the bacteria exist as heat-resistant spores, which are viable for long periods of time and are resistant to the majority of the commercially available alcohol-based disinfectants. The commonly used hand gels, so often found in dispensers throughout hospitals, are likewise ineffective. Soaps and bleach-based products can eradicate the spores. For the average

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person, the most reliable method of killing these spores is good, ole fashioned, thorough hand washing with soap and water. Hand washing while twice, very slowly singing *Row, Row, Row Your Boat*, or *Happy Birthday To You*, should do the job. *C. diff.* does not routinely infect all who come in contact with it. Nevertheless, please continue washing and singing while visiting in the hospital.

If ingested, the acid-resistant spores pass undigested through the stomach and arrive in the colon, where, when exposed to bile acids, they resume bacterial growth and reproduction, and produce disease-causing cytotoxins and enterotoxins. It is these toxins which are responsible for the colonic inflammation and pseudomembranes seen in pseudomembranous colitis.

FIRST, DO NO HARM.

Does all of this vexation and brouhaha revolve around simple diarrhea? Unfortunately, simple diarrhea can rapidly become complicated diarrhea. *C. diff.* diarrhea and pseudomembranous colitis can progress quickly beyond *Row, Row, Row Your Boat*. Most surgeons know of at least one patient who has succumbed to this disease.

Accurate and timely diagnosis is imperative in preventing the spread of the infection and ensuring that the treatment is directed toward the correct disease. As not all diarrhea is caused by *C. diff.*, it is important that treating physicians embark on a protocol which is based on a correct diagnosis.

In the past, toxin identification required the collection of three stool samples. Each sample took unduly long to analyze for the presence of the toxin. This was problematic as antibiotic therapy was delayed pending collection and analysis of multiple diarrheal samples. Today, testing is performed on one fresh, liquid stool and the *C. diff.* toxin can be identified within six hours of collection.

TREATMENT: PRONE TO COSTLY FAILURE.

WOULD VEGAS LIKE THESE ODDS?

The treatment of a mild *C. diff.* infection begins with one of two antibiotics, metronidazole (Flagyl®) or vancomycin. The treating physician chooses the appropriate drug after considering many variables related to the patient's health. A cure is achieved in up to 75% of cases. However, treatment fails in the remaining 25% of patients. Those at risk for failure include the elderly, those with other medical conditions such as diabetes or cardiopulmonary diseases, and those requiring ongoing antibiotic treatment. Recurrence is associated with a 50% to 60% chance of experiencing another recurrence. These are not great odds.

Metronidazole is usually used as the first line antibiotic and vancomycin is used in case of a metronidazole failure, allergy, disease recurrence or other concerns. Metronidazole has the added benefit that it can be delivered orally or by intravenous infusion. Vancomycin is effective only if delivered orally or by enema. Hospitalized patients who respond appropriately to antibiotics may be discharged home and followed on an outpatient basis.

Some patients have resistant disease or develop recurrent disease despite antibiotic treatment. They may develop chronic or refractory *C. diff.* colitis. These patients pose a major dilemma. Prior to the advent of fecal microbial transplantation, the only other management option that could be offered

was an operation to remove the entire colon – a total abdominal colectomy eradicated the disease.

FECAL MICROBIAL TRANSPLANTATION: THE YELLOW BRICK ROAD IS COVERED WITH STOOL. "ICK" AND "GROSS".

Fecal transplantation involves obtaining stool from a healthy donor, and transferring it into the colon of the patient with the stubborn infection. The rationale is that the reintroduced "good" bacteria will replace the "bad" bacteria and allow for a full and complete recovery. And it does just that. It works! However, many respond with an "ick" or a "gross" when FMT is discussed as a treatment option. The desire to overcome a noxious disease eventually triumphs over "ick", and patients readily accept FMT as a life saving alternative.

How is the transplant performed? The recipient undergoes a standard colonoscopy preparation. This is safe in the usual patient with chronic *C. diff.*. The donated stool is converted into a thick liquid solution. Under inpatient or outpatient anesthesia, the solution of "good" stool is placed through the side channel of a colonoscope and into the colon of the recipient.

BETTER ODDS.

While this procedure is still new and more FMT treatment data remains to be collected, there are several hundred patients reported in the medical literature who have shown cure rates of greater than 95%. Rare recurrences usually resolve after a repeat stool transfer.

While there are medical centers that use stool banks to store frozen donor feces for future use, there does not appear to be a shortage of donor stool at this time. Research has shown that using donor stool from an intimate partner of the recipient makes the most sense. The logic is that the recipient has already been exposed to any potential donor infections. There has not been a single case report of a donor-to-recipient infection transmitted by this procedure. However, stool is a bodily fluid, and recipient infection remains a theoretical potential risk. Absent having a related donor, it does not really matter who donates the stool. Importantly, donors should not have taken antibiotics or have been hospitalized within six months prior to the donation, and the donor should not work or have worked in a health care facility which might have the potential for harboring an occult *C. diff.* colonization. It is important that the stool donor be tested for an asymptomatic *Clostridium difficile* infection. The testing protocol for other transmissible diseases is complex and should be undertaken by a physician with diagnostic experience and an established protocol. The final decision as to the extent of donor testing is undertaken after a thorough discussion with the donor and the recipient.

THE END OF THE ROAD.

Symptoms often disappear immediately after the transplant. If patients remain disease-free for at least as long as their prior disease-free period, the treatment is considered to have been curative.

With or without "ick", fecal microbial transplantation, in the hands of an experienced specialist, can cure a "gross" disease.