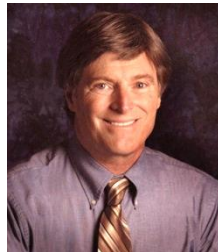
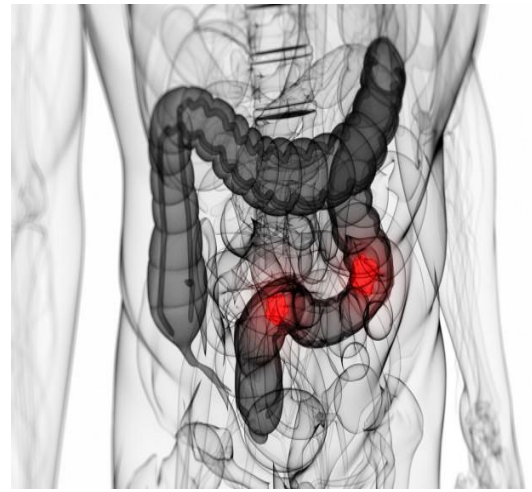


*Increasing incidence of Clostridium difficile infections...*

## Are Fecal Transplants the Answer?



By Jay Hardy, CLS, SM (NRCM)

Jay Hardy is the founder and president of Hardy Diagnostics. He began his career in microbiology as a Medical Technologist in Santa Barbara, California.

In 1980, he began manufacturing culture media for the local hospitals. Today, Hardy Diagnostics is the third largest culture media manufacturer in the United States.

To ensure rapid and reliable turn around time, [Hardy Diagnostics](#) maintains eight distribution centers, and produces over 3,500 products used in clinical and industrial microbiology laboratories throughout the world.

*Clostridium difficile* infections (CDI) have risen in number and severity at an alarming rate recently. It is now estimated that between 500,000 and 700,000 cases of CDI occur annually in US hospitals and long-term care facilities with an estimated hospital excess cost of care of approximately 3.2 billion dollars. The CDC reports that there are about 14,000 deaths due to CDI every year.

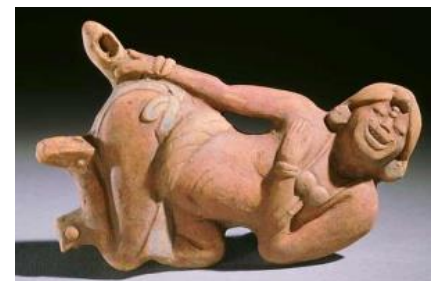
CDI is usually associated with hospitalized patients that have been on antibiotic therapy, usually clindamycin, cephalosporins, or fluoroquinolones. Severe diarrhea follows due to the formation of toxins A and B from resistant *C. difficile*, causing severe mucosal destruction and pseudomembrane formation.

One of the most frustrating features of CDI is its ability to keep coming back with increasing intensity. Patients with CDI will experience multiple recurrences at rates reported as high as 30%. Up to 3% of CDI patients will develop

the more serious toxic megacolon that results in a mortality rate of 38% to 80%.

Patients with recurring CDI make good candidates for stool transplant from a healthy donor, now known as Fecal Microbiome Transplantation (FMT), used to restore the normal microbiota of the bowel and relieve suffering.

The use of human fecal material for therapeutic purposes is not new. The first recorded use dates back to the fourth century in China in which a fecal suspension was ingested by mouth for severe food poisoning and diarrhea. There are other references to the use of stool products used by enema in China in the 16<sup>th</sup> century.



In the 17<sup>th</sup> century, FMT was first used by veterinarians who called the procedure “transfaunation.”

The first modern day use of FMT in humans was reported in 1958 for the treatment of pseudomembranous colitis. There was a resurgence of interest in FMT for the treatment of CDI in the 1980’s.

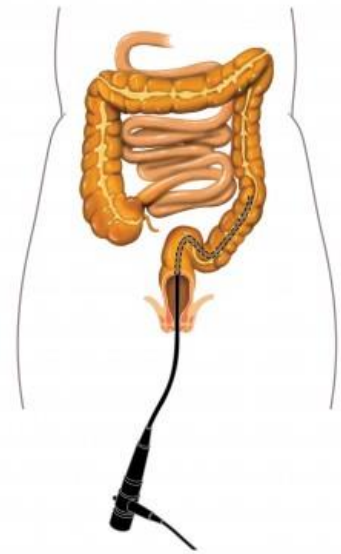
The success rate of FMT is nothing less than astounding. In a recent meta-analysis of eleven studies, Kassam reported that 245 of 273 patients who received FMT experienced clinical resolution of their disease with no reported adverse events (Kassam, et al, *Am J Gastroenterol.* 2013;108(4)). The authors concluded that the 90% success rate make FMT a technique that definitely holds promise and that further randomized-controlled trials are needed. Other studies show an impressive cure rate of up to 98%.

FMT has also been reported as successful in treating Inflammatory Bowel Disease (IBD), Irritable Bowel Syndrome (IBS), and ulcerative colitis. A recent study performed on children with ulcerative colitis in Grand Rapids, Michigan showed that 78% of children with this disease responded favorably within one week. The lead author, Sachin Kunde, MD,

MPH, stated: This study opens the doors for an innovative, inexpensive and natural alternative to improve outcomes of this debilitating disease with billions of dollars in health care cost.

A recent randomized, controlled trial of FMT for patients with recurrent *C. difficile* diarrhea was found to be successful in 94% of patients, the majority requiring only one treatment. The trial was terminated early, because it was felt to be unethical not to offer the treatment to all patients in the trial due to the outstanding success (van Nood et al. *NEJM*, January 31, 2013).

FMT can be carried out by nasogastric intubation, by enema (sometimes self-administered), or by colonoscopy. The nasogastric method has obvious disadvantages due to repulsive sight and smell issues experienced by the patient. In addition, it has proven not to be as effective as other methods. An enema is also not as effective since the higher regions of the colon cannot be reached. Transplantation through colonoscopy appears to be the current method of choice, since the donor bacteria can be placed into the ileum of the small intestine and throughout the entire large intestine.



What follows is a brief description of the method recommended by the American Gastroenterological Association (AGA) as explained by David Johnson, MD, Professor of Medicine and Chief of Gastroenterology at Eastern Virginia Medical School.

### **Patient Selection**

The first step in the FMT procedure is to identify the candidate for the procedure. The AGA recommends selecting patients with three or more recurring episodes or at least two hospitalizations due to CDI. These patients have experienced treatment failures with antibiotics, which is usually metronidazole or vancomycin.

### **Donor Selection**

As for the selection of the transplantation material, the

donor must be healthy and appropriately screened for blood borne pathogens (such as AIDS and hepatitis), parasitic infections (such as *giardia* and *cryptosporidium*), and must be free from all intestinal diseases (such as irritable bowel disease, diarrhea, and constipation). The necessary screening tests can cost about \$500 which may or may not be covered by insurance. The donor must not have taken any antibiotics for at least three months. If the recipient has any food allergies, then the donor must refrain from eating the offending foods for at least five days previous to the procedure. All antibiotic therapy is discontinued for at least three days prior to the transplantation.

### Fecal Preparation



To prepare the specimen, a 50gm stool sample is mixed with bacteriostatic saline, blended under a hood, and filtered through gauze to remove particulate matter.

This solution must be transplanted within 6 to 8 hours. Frozen samples have also been successfully used. The patient's bowel is then prepped to be

made clean for the colonoscopy procedure so that there is no residual stool.

### Transplantation Procedure

During the colonoscopy, from 300 to 500ml of the fecal solution is then flushed starting with the terminal ileum of the small intestine and continued down into the entire colon. The patient is then given Imodium<sup>®</sup> (loperamide) in order to slow down stool transit.



### Results

Molecular techniques show that bacteria in the recipient's stool closely resemble those of the donor about two weeks after FMT and are usually dominated by *Bacteroides* spp.

### Patient Acceptance

Surprisingly, FMT was found to be readily accepted by patients. In the recent multicenter study, 97% of patients with recurring CDI reported a willingness to undergo another FMT if they were to have a repeat CDI

episode. Additionally, 53% stated that they would choose FMT as first-line therapy before taking antibiotics.

To alleviate the psychological reversion to FMT, research is currently being conducted to produce a probiotic soup of about 20 enteric bacteria species as a sort of "artificial feces."

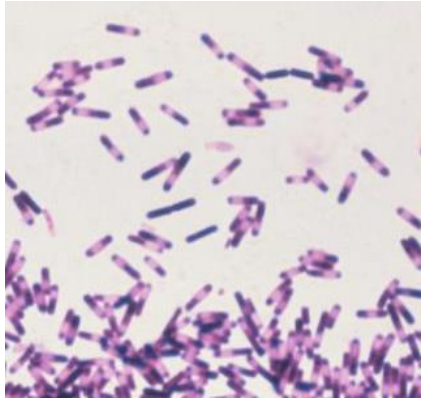
### FMT for Non-GI Disease

Encouraged by the amazing success of FMT in treating GI illness, there is new research being done on treating non-GI diseases as well. Encouraging results have been reported in treating chronic fatigue syndrome, obesity, autism, and autoimmune diseases with FMT.

### Difficulties with Infection Control

Efforts to control CDI with improved hygiene in the hospital setting have been disappointing. According to a recent APIC survey, 70% of infection control specialists say they have implemented additional intervention methods, but only 42% have seen a decline in the number of infections. Bleach is used by 67% of hospitals for room cleaning, and 9% use newer UV light and vaporized hydrogen peroxide methods. 72% say they have stepped up their

promotion of hand washing and the use of alcohol sanitizers. However, *C. difficile* spores are resistant to alcohol exposure.



***Clostridium difficile*, a gram positive rod that grows anaerobically and produces spores, seen here as light sections within the cell.**

Much of these efforts may seem futile for some patients, since a recent study found that 10% of all patients were found to be asymptomatic carriers of *C. difficile* upon admission (Leekha, *American Journal of Infection Control*, May 2013).



Source: Google images

## Conclusion

Due to the failure to control CDI by standard sanitization procedures, it is hoped that more patients can be spared the agony of this devastating disease by implementing the use of fecal transplantation, in spite of the apparent initial hesitancy on the part of patient and physician.

The FMT procedure is slowly gaining in acceptance among clinicians. A new Current Procedural Terminology (CPT) code (44705, "*Preparation of fecal microbiota for instillation, including assessment of donor specimen*") has been assigned to FMT.

Within the hospital, the question often asked is, who will prepare the FMT specimen? The clinical laboratory? The GI lab? The pharmacy? Many issues still need to be resolved before this procedure becomes routine.

As long as antibiotic therapy is used, and sometimes overused, there will be an increasing need for alternative life saving techniques to restore a healthy intestinal microbiome, no matter how revolting it may initially seem.

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The information contained in this article is for educational purposes only and is not intended nor recommended as a substitute for medical advice, diagnosis, or treatment.