Fecal Microbiota Transplantation for the Treatment of Recurrent *Clostridium Difficile* Infection

Infectious disease specialists at Penn Medicine are performing fecal microbiota transplantation procedures to treat patients with recurrent *Clostridium difficile* infections. *Clostridium difficile* (or *C. diff*) is the most common cause of nosocomial diarrhea in the United States, and is identified with life-threatening pseudomembranous colitis and toxic megacolon. An endospore-producing Gram-positive bacteria, *C. diff* is characterized by an extraordinary facility for survival (*difficile* means difficult or obstinate). *C. diff* spores are resistant to most oral and parenteral broad-spectrum antibiotics (including the penicillins, quinolones, cephalosporins and lincosamides) as well as chemotherapeutic agents, gastric acid, alcohol and disinfectants. Spores can emerge in the gut after seemingly effective antibiotic treatment and can survive for years on outside surfaces to present an ever-present threat to susceptible hosts. A more virulent and resistant strain of *C. diff* appeared in the U.S. hospitals in 2002.

Once mature *C. diff* appears in the unchallenged environment of the gut following antibiotic treatment, the bacteria spread rapidly, exuding cytoxins as a component of propagation. These toxins bind to and penetrate the gut epithelium and mucosa, destroying cell structure, cleaving the water-tight junctions between cells and contributing to profound colonic mucosal injury and inflammation. The normal balance in the gut then shifts from absorption of fluids and electrolytes to excretion, leading to diarrhea.

**Treatment**

The first line treatment for *C. diff* is metronidazole if the infection is not severe. However, the recurrence rate following an initial infection is 15-30% and there is a 50% chance of a subsequent recurrence if disease reappears once. Metronidazole is not used for recurrent infections. Second and later infections are treated with vancomycin. Both drugs are effective against *C. diff*, but because both alter the gut microbiome to favor their ubiquitous target, some patients will have recurrences despite therapy. Patients who have three or more recurrences may have chronic *C. diff* infection, a course characterized by repeated episodes of treatment followed by disease relapse in which each relapse increases the likelihood of subsequent infections.

At Penn Medicine, infectious disease specialists are successfully treating recurrent *C. diff* infection with an investigational biological alternative to antibiotic therapy. Known as fecal microbiota transplantation (FMT), the therapy involves restoring the normal gut microbiome in patients following repeated recurrences of *C. diff* with antibiotic therapy. In a recent comparative clinical trial, FMT effectively cured 94% of patients in patients with recurrent *C. diff* vs. 31% of patients receiving vancomycin 500 mg 4x daily for five days. [1]

Donors for FMT therapy at Penn Medicine are closely screened to avoid exposing recipients to pathogens, transmissible diseases and inflammatory disorders. The Food and Drug Administration currently considers FMT investigational, and its use is restricted to patients with recurrent *C. diff* infection (R-CDI) not responsive to standard therapies.

**Case Study**

Mr. W, a 63-year-old man, was referred to the Penn Medicine Division of Infectious Diseases for recurrent antibiotic-associated *C. diff* infection. His recent medical history included severe diarrhea with expulsion of blood and mucus following three days of ciprofloxacin therapy for a severe urinary tract infection. Ultimately, the UTI was successfully resolved with a course of quinolone antibiotics.

Several weeks afterward, a second, prolonged bout of diarrhea at his vacation home brought Mr. W back to his physician. A fecal sample at this visit tested positive for *C. diff* toxins. Mr. W was then referred to a local gastroenterologist, who prescribed metronidazole.

Mr. W was counseled at this time about the need for strict hygiene and cleanliness in his personal environment. At the conclusion of therapy, he had no evidence of *C. diff* infection. After a weekend trip to his vacation home, however, Mr. W’s symptoms returned. He was cautioned again about hygiene, and prescribed an extended course of vancomycin.

This time, Mr. W was exceedingly cautious and took great care to avoid infection. Three weeks into his therapy, however, he had another recurrence of diarrhea.

At this point, Mr. W discovered references to FMT therapy at Penn Medicine in an online forum, and was referred to the Division of Infectious Diseases for a consultation, which involved a thorough review of the investigational nature of the therapy and its risks. At the conclusion of this discussion, he provided his informed consent for treatment.

On the day of his treatment, Mr. W stopped taking vancomycin. He received a single infusion of fecal microbiota in saline into his small bowel via a nasoduodenal tube and returned home. His diarrhea resolved the next day and within three days, normal bowel activity had resumed. At his six month follow-up, Mr. W reported no further episodes of diarrheaa. He was cautioned again about hygiene, and prescribed an extended course of vancomycin. Samples taken at this visit demonstrated a robust gut microbiome.

Reference

Faculty Team

Specialists in the Division of Infectious Diseases at Penn Medicine offer consultation regarding infectious disease problems, such as viral infections, diarrhea, tuberculosis, osteomyelitis, parasitology, and HIV. In particular, treatment is available for patients with problems associated with immunosuppression and international travel. Primary care is also available for HIV, hepatitis B, and hepatitis C patients.

Performing FMT Therapy at Penn Medicine

Stephen J. Gluckman, MD
Medical Director, Penn Global Medicine
Professor of Medicine

David L. Holtzman, MD, MSc
Infectious Disease Fellow

Brendan J. Kelly, MD
Attending Physician,
Division of Infectious Diseases

Ebbing Lautenbach, MD, MPH, MSCE
Chief, Division of Infectious Diseases;
Robert Austrian Professor

Pablo Tebas, MD
Professor of Medicine

Access

Hospital of the University of Pennsylvania
3 Silverstein Building, Suite D
3400 Spruce Street
Philadelphia, PA 19104

Penn Presbyterian Medical Center
Infectious Diseases Division
Medical Arts Building, Suite 102
51 N 39th Street
Philadelphia, PA 19104

Pennsylvania Hospital
1 Pine West
800 Spruce Street
Philadelphia, PA 19107