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NIH starts clinical trial for FMT

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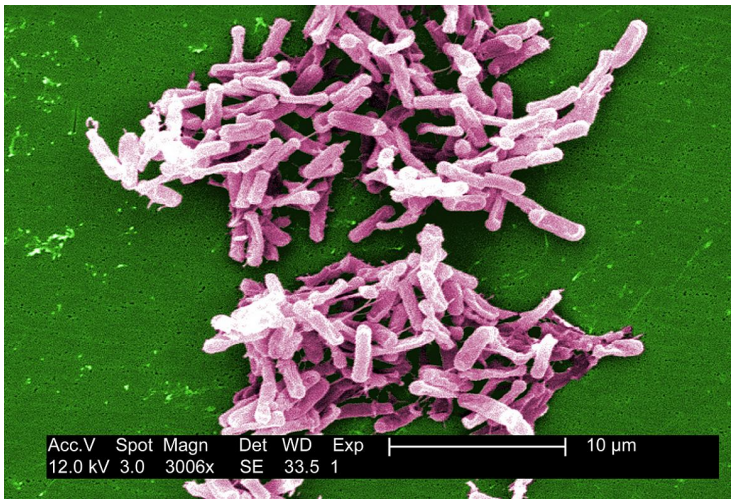
Study enrollment is expected to be completed in three years



A research consortium of NIH recently began enrolling patients in a clinical trial examining whether fecal microbiota transplantation (FMT) by enema—putting stool from a healthy donor in the colon of a recipient is safe and can prevent recurrent Clostridium difficile-associated disease (CDAD), a potentially life-threatening diarrheal illness.

Investigators aim to enroll 162 volunteer participants 18 years or older who have had two or more episodes of CDAD within the previous six months.

Trial sites include Emory University in Atlanta, Duke University Medical Center in Durham, North Carolina, and Vanderbilt University Medical Center in Nashville, Tennessee. Each location is a Vaccine and Treatment Evaluation Unit (VTEU), clinical research sites joined in a network funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

Anthony S. Fauci, director, NIAID said, “Clostridium difficile-associated disease, a significant problem in healthcare facilities, causes an estimated 15,000 deaths in the United States each year. This randomized, controlled trial aims to provide critical data on the efficacy and long-term safety of using fecal microbiota transplants by enema to cure C. diff infections.”

Clostridium difficile, commonly referred to as C. diff, is a bacterium that infects the colon and can cause diarrhea, fever, and abdominal pain. CDAD most commonly occurs in hospitalized older adults who have recently taken antibiotics. However, cases of CDAD can occur outside of healthcare settings as well. Although antibiotics often cure the infection, C. diff can cause potentially life-threatening colon inflammation.

People with CDAD usually are treated with a course of antibiotics, such as oral vancomycin or fidaxomicin. However, CDAD returns in approximately 20 percent of people who receive such treatment, according to the Centers for Disease Control and Prevention (CDC).

Multiple research studies have indicated that FMT is an effective method for curing patients with repeat C. diff infections. However, the long-term safety of FMT has not been established. Although more research is needed to determine precisely

how FMT effectively cures recurrent CDAD, the treatment appears to rapidly restore a healthy and diverse gut microbiome in recipients.

Physicians perform FMT using various routes of administration, including oral pills, upper gastrointestinal endoscopy, colonoscopy, and enema. The new NIAID-supported trial aims to investigate the safety and efficacy of FMT delivered by enema to patients with recurrent CDAD. The trial is part of an effort to gather data on how best to standardize the FMT process.

Nadine Rouphael, associate professor, Division of Infectious Diseases at Emory University, is the principal investigator for the trial. Volunteers will be enrolled in the trial after completing a standard course of antibiotics for a recurrent CDAD episode, presuming their diarrhea symptoms cease on treatment.

They will be randomly assigned to one of two groups. The first group (108 people) will take an anti-diarrheal medication and receive a stool transplant (FMT) delivered by retention enema. The second group (54 people) will take an anti-diarrheal medication and receive a placebo solution delivered by retention enema. The placebo is saline that has been colored so that it appears identical to the active stool transplant product. The trial is partially blinded so that the participant and the investigators involved in the study will not know who is assigned to which group.

Participants in either group who have diarrhea with stools that test positive for C. diff shortly after the enema will receive an active stool transplant for a maximum of two FMTs. If participants in either group have another C. diff infection after receiving two FMTs, they will be referred to other locally available treatment options.

All participants will provide stool samples and blood samples at designated time points for one year from the date of their effective treatment for CDAD or from the date of their last treatment if it was unsuccessful. Investigators will evaluate the stool specimens for changes in gut microbial diversity and infectious pathogens and will examine the blood samples for metabolic syndrome markers.

To learn more about the long-term outcomes of FMT, all participants will be monitored for adverse side effects for three years after completing treatment for recurrent CDAD. Investigators also will collect information on any new onset of CDAD, related chronic medical conditions or any other serious health issues they may have.

NIAID obtained an Investigational New Drug (IND) Application from the Food and Drug Administration to evaluate FMT as part of this clinical research study. The trial investigators will obtain stool for FMTs from OpenBiome, a nonprofit stool bank based in Cambridge, Massachusetts.

OpenBiome follows standardized clinical and laboratory protocols to screen donors and evaluate stool samples for infectious organisms. Samples are then filtered, processed, frozen, and delivered in a sterilized and controlled method. OpenBiome previously submitted information regarding these processes to the FDA and has a material tracking program to monitor the safety and efficacy of stool product.

A Data and Safety Monitoring Board comprising an independent group of non-NIAID experts will periodically review the study data for safety and make recommendations regarding trial modifications or termination. Study enrollment is expected to be completed in three years.