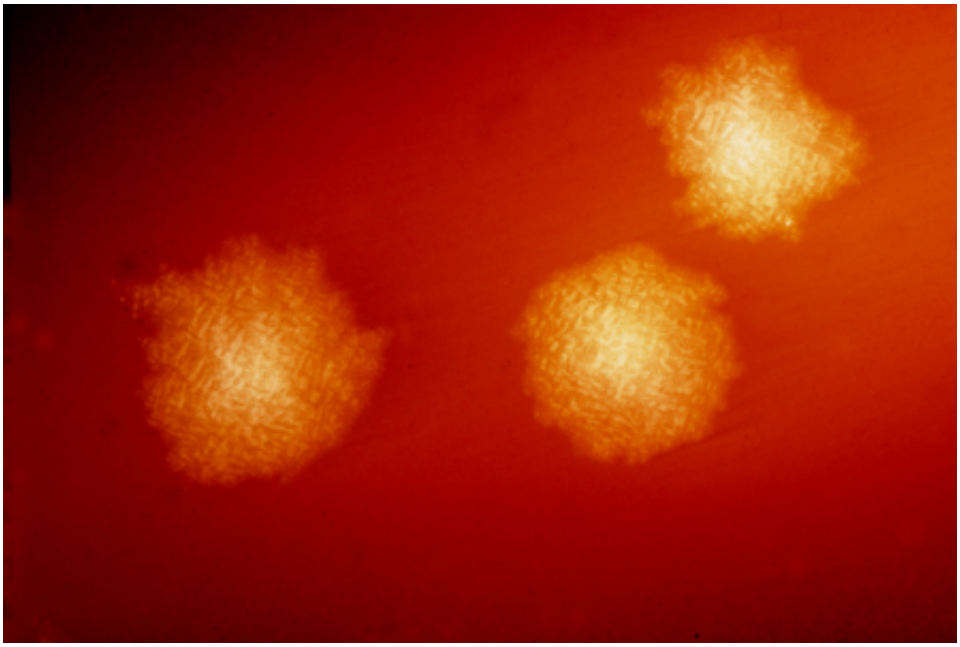
Frozen vs. fresh fecal transplantation for C. diff. infection shows similar effectiveness

January 12 2016



This photograph depicts Clostridium difficile colonies after 48hrs growth on a blood agar plate; Magnified 4.8X. C. difficile, an anaerobic gram-positive rod, is the most frequently identified cause of antibiotic-associated diarrhea (AAD). It accounts for approximately 15–25% of all episodes of AAD. Credit: CDC

Among adults with *Clostridium difficile* infection that is recurrent or not responsive to treatment, the use of frozen compared with fresh fecal microbiota transplantation (FMT) did not result in a significantly lower rate of resolution of diarrhea, indicating that frozen FMT may be a reasonable treatment option for these patients, according to a study in

the January 12 issue of *JAMA*.

Clostridium difficile infection (CDI; a bacterium that is one of the most common causes of infection of the colon) in health care settings and in the community has become a major clinical concern. Increases in failure rates with conventional treatment, and recurrences following initial cure, present significant challenges to health care systems: more than 60 percent of patients experience further episodes after a first recurrence. Treatment options for recurrent CDI are limited.

Restoration of protective colonic microbiota by fecal microbiota transplantation (FMT; i.e., reconstitution of normal flora [gut bacteria] by a stool transplant from a healthy individual) has shown evidence as an effective treatment for recurrent CDI. High cure rates have been achieved with FMT given by enema. However, the usefulness of this approach may be limited by logistic difficulties in preparing fresh material. By contrast, the use of frozen-and-thawed (frozen) FMT offers a number of advantages: less cost with reduction in number and frequency of donor screenings; immediate availability of FMT; and the possibility of delivering FMT at centers that do not have on-site laboratory facilities. Previous studies have supported the use of frozen FMT for management of recurrent CDI but have not directly compared frozen with fresh FMT, according to background information in the article.

Christine H. Lee, M.D., of McMaster University, Hamilton, Ontario, Canada, and colleagues randomly assigned 232 adults with recurrent or refractory CDI to receive frozen (n = 114) or fresh (n = 118) FMT via enema. The study was conducted at 6 academic medical centers in Canada.

A total of 219 patients (n = 108 in the frozen FMT group and n = 111 in the fresh FMT group) were included in the modified intention-to-treat

(mITT) population and 178 (frozen FMT, n = 91; fresh FMT, n = 87) in the per-protocol population. In this group, the proportion of patients with clinical resolution of diarrhea without relapse at 13 weeks was 83.5 percent for the frozen FMT group and 85 percent for the fresh FMT group. In the mITT population the clinical resolution was 75 percent for the frozen FMT group and 70 percent for the fresh FMT group. There were no differences in the proportion of adverse or serious adverse events between the treatment groups.

"In this clinical trial, the use of frozen FMT compared with fresh FMT for the treatment of recurrent or refractory CDI was noninferior [not worse than] in terms of efficacy; findings for frozen FMT and fresh FMT were similar in terms of safety," the authors write. "Given the potential advantages of providing frozen FMT, its use is a reasonable option in this setting."

"The results presented by Lee et al offer the best evidence to date supporting the use of frozen stool, with their finding that use of frozen stool for FMT resulted in a rate of clinical resolution of diarrhea that was no worse than that obtained with fresh stool for FMT and will likely expand the availability of FMT for patients with recurrent CDI," write Preeti N. Malani, M.D., M.S.J., and Krishna Rao, M.D., M.S., of the University of Michigan Health System, Ann Arbor (Dr. Malani is also Associate Editor, *JAMA*), in an accompanying editorial.

"The ability to use frozen stool eliminates many of the logistical burdens inherent to FMT, because stool collection and processing need not be tied to the procedure date and time. This study also provides greater support for the practice of using centralized stool banks, which could further remove barriers to FMT by making available to clinicians safe, screened stool that can be shipped and stored frozen and thawed for use as needed. In theory, procedure costs may also be decreased, since comprehensive donor screening is expensive."

More information: *JAMA*, DOI: 10.1001/jama.2015.18098
JAMA, DOI: 10.1001/jama.2015.18100