Fecal Transfer Cures Relapsing *C. diff* Infection

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — A preparation of fecal bacteria from healthy donors successfully resolved chronic relapsing *Clostridium difficile*–associated diarrhea in 46 of 48 patients, of whom all but one underwent the procedure in their homes.

Few conventional therapeutic options are available for patients with multiply recurrent *C. difficile* diarrhea. Such patients often become trapped in "vancomycin dependence" as antimicrobial suppression of the intestinal microbiome maintains vulnerability to recurrence, with a likelihood of relapse exceeding 65% after the third episode. Treatments that have been tried—including vancomycin tapering or pulse dosing, and probiotic therapy using *Lactobacillus GG* or *Saccharomyces boulardii*—have not been shown effective in arresting recurrences of *C. difficile*, Dr. Thomas J. Louie said at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

"Normal" stool microbes, most of which cannot be cultivated, constitute the "ultimate probiotic" and have been shown to be highly effective in arresting recurrences of *C. difficile* infection. Delivery of the microflora by jejunal tube or during colonic endoscopy would typically require clinic or hospital facilities.

Dr. Louie, professor of medicine, microbiology, and infectious disease at the University of Calgary (Canada), has developed a home-based method for colonic fecal transfer that incurs no hospital or clinic costs and allows the patient to remain in bed to promote inoculum retention.

Over an 11-year period, 35 women and 13 men received a total of 59 fecal transfers. All of the patients had been referred by a gastroenterologist or an infectious disease specialist for recalcitrant recurrent disease involving at least four episodes over a period of 6 months or longer; the episodes would respond to vancomycin but would recur despite the use of vancomycin tapering or pulse dosing and probiotics. All but 1 of the 48 patients were ambulatory. They had a mean age of 62 years (range 30-91 years), with a mean relapse duration of 10 months (range 6-24 months).

Prior to the procedure, patients were treated with vancomycin to control the symptoms and signs of *C. difficile* infection completely, generally for 14 days or more, followed by either a 4-day washout period or oral Fleet enema 12 hours before the procedure, in order to reduce vancomycin concentrations in the stool.

Donors had to be healthy, with no antibiotic exposure in the previous 6 months. All were screened for pathogens using the same guidelines used for blood donors. All but 10 donors were genetic relatives of the patient (siblings, parents, or offspring). This was preferred because some data suggest a "relatedness" of stool is beneficial, Dr. Louie noted.

Donors collected sequential stools for 3 days in plastic-lidded pails, stored at 4-8° C, with the final sample collected on the morning of the procedure. The stools were mixed with phosphate-buffered saline with added cysteine and then sieved through a wire mesh to remove particulates.

Following a normal bowel movement or clearing enema and diazepam sedation, the fecal preparation was inserted via a balloon catheter, with the patient lying in a lateral position. This usually was done on the patient's own bed, atop a plastic sheet and layers of absorptive pads to prevent soiling the mattress.

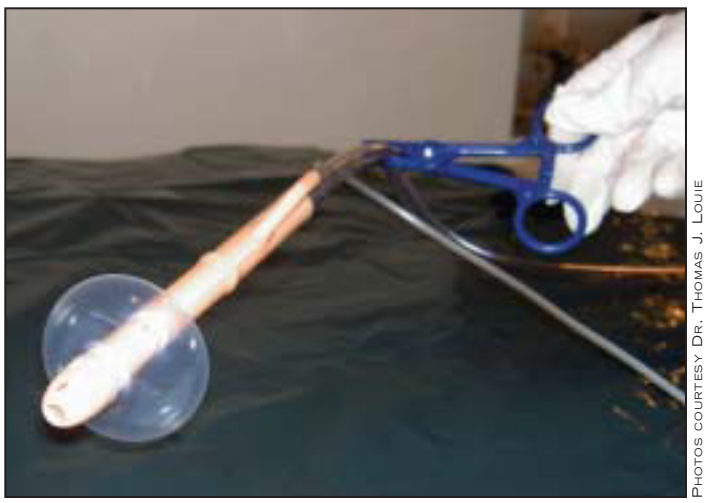
The procedures were carried out over 10-45 minutes, depending on the presence or absence of colonic contractions. During the transfer of 800-1,400 mL of bacterial preparation, the patients were positioned so that the fluid could reach the right side of the colon. They were instructed to eat a very light breakfast and consume only liquids the rest of the day, to avoid triggering a "mass movement." They were also told to rest for 4-6 hours to promote retention of the inoculum.

The *C. difficile* infection was completely resolved with just one fecal transfer in most of the patients, with three required in one patient and two required in four patients. Of the two patients in whom the infection did not resolve, one had a recurrence with initiation of proton pump inhibitor treatment for gastroesophageal reflux, and the other did not respond to a single procedure and was expected to undergo a repeat procedure.

All 10 of the patients whose donors were spouses resolved, but 4 of them had irritable bowel–like symptoms (intestinal cramping and gas) for 3-6 months after the procedure; such symptoms were not noted in those who received stool from genetic relatives. It's not clear if the genetic makeup of the microbiome is the reason, Dr. Louie commented.

A home ceiling fan can be an innovative substitute for an IV pole.

Performing this procedure in patients' homes—or even doing them at all—was something that Dr. Louie "got into by accident." He performed the first one in 1996, when a patient presented with multiply recurrent *C. difficile* for which other treatments had failed. Dr. Louie requested permission from Calgary General Hospital to do the procedure there, but the nurses objected, citing the lack of a precedent and aesthetic issues. "Hence, the idea of a hospital involvement was shelved," he recounted in an interview.



PHOTOS COURTESY DR. THOMAS J. LOUIE

The fecal preparation is inserted via a balloon catheter over 10-45 minutes while the patient lies in their own bed.

Weeks later, that patient asked Dr. Louie if the procedure could be done at home. Such an ambulatory, nonhospital approach was supported by previous U.S. literature dating back to the 1950s, and by more recent reports from Australia, Scandinavia, and the United States.

It became clear that the home-based approach had many advantages. "Patient privacy was difficult to achieve in hospital, especially with shared toilet facilities. Also, because of difficulty admitting patients to a hospital for a procedure when they are otherwise well, it became immensely more practical to do the procedure as a home-based approach," Dr. Louie said in the interview.

He has received research grants from companies that make or are developing products to treat *C. difficile* infection. ■

Antibiotic-Related Diarrhea Not Halted by Probiotic Yogurt

BY DENISE NAPOLI
Associate Editor

WASHINGTON — Probiotic yogurt did not prevent antibiotic-associated diarrhea in a randomized, double-blind trial of about 300 adult patients.

According to the study authors, meta-analyses have suggested that probiotics may be helpful for antibiotic-associated diarrhea, but few large, randomized, controlled trials have been conducted.

A 2007 study did find that probiotics helped prevent antibiotic-associated diarrhea, but the study was fairly small (Can. J. Gastroenterol. 2007;21:732-6).

In the current study, Dr. Alberto Delgado-Iribarren of the microbiology department at the Hospital Universitario Fundación Alcorcón, Madrid, and his colleagues studied more than 300 patients who were admitted to the hospital and started on an antibiotic regimen of either levofloxacin or amoxicillin clavulanate. The mean age of the patients was 76 years; 46% were women.

In all, 122 patients were randomized to receive placebo yogurt (which contained *Streptococcus thermophilus* and *Lactobacillus bulgaricus* but no probiotics), another 125 patients were given a probiotic yogurt mixture specially manufactured for the study (which included both *S. thermophilus* and *L. bulgaricus*, as well as *L. acidophilus, Bifidobacterium lactis, and L. casei*), and 65 patients were randomized to receive no yogurt. The yogurt was given in doses of 150-200 mL. Both yogurts had the same taste, color, smell, and texture.

Patients consumed the yogurt from the beginning of antibiotic treatment to 5 days after discontinuing the antibiotic, and the follow-up period was 1 month.

The patients answered a questionnaire about diarrhea and side effects. Diarrhea was defined as two or more soft stools. Secondary end points included number of days of diarrhea, severity of diarrhea, number of stools per day, and longer hospital stay because of diarrhea.

In his presentation at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America, Dr. Delgado-Iribarren reported that "our data were essentially identical for all three groups," with "a similar proportion of around 20% of patients with diarrhea" and no statistically significant differences among the three groups.

The secondary end points were also mostly similar. Duration of diarrhea was about 3 days, with a maximum of about five stools per day. Controls had a slightly longer average hospital stay than did patients who took the probiotic yogurt."There were no differences in mortality in the three groups," he noted.

"We conclude that probiotic yogurt does not have an effect on … antibiotic-associated diarrhea in adults," Dr. Delgado-Iribarren said. It is, however, safe, he added.

Dr. Delgado-Iribarren did not disclose any conflicts of interest. ■