# Recurrent *C. difficile* on the Rise, No Silver Bullet

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LAS VEGAS — When *Clostridium difficile* disease recurs, look out.

It's likely to recur again and again in a cycle that can go on for "months or years," Dr. Christina Surawicz said at the annual meeting of the American College of Gastroenterology.

"Are recurrences increasing? The Quebec experience suggests that yes, they are." In the early 1990s, about 15% of patients with *C. difficile* disease experienced a recurrence. That figure climbed to 24%-25% in 1993-1998, and to 47% in 2003-2004, said Dr. Surawicz, professor of medicine at the University of Washington, Seattle.

In the United States, about 20% of patients who initially respond to standard antibiotic regimens for *C. difficile*–associated disease experience a recurrence, usually about 5-8 days after discontinuation of therapy. Subsequent recurrences are seen in 45%-65% of these patients.

Risk factors are thought to include advanced age, fecal incontinence, and disorders that require continuous antibiotic therapy, but Dr. Surawicz said she has also seen cases in young patients whose only initial exposure to antibiotics was for treatment of urinary tract infections or otitis. She has treated two patients who developed recurrent *C. difficile* disease after receiving antibiotics for complications of childbirth.

There is no single treatment strategy that seems to be uniformly efficacious. Some approaches have included repeating courses of metronidazole, or switching to vancomycin (or the reverse if vancomycin was used first), or using elevated doses or pulsed, tapered, or prolonged vancomycin dosing strategies.

Using toxin-binding resins such as cholestyramine or colestipol 3-4 hours after antibiotic administration may improve efficacy, Dr. Surawicz said.

A poster presented at the meeting described using a rifaximin "chaser" (400-800 mg/day in two or three divided doses for 2 weeks) following vancomycin. The strategy halted the recurrence cycle in six of seven patients, reported Dr. Stuart Johnson of Loyola University Medical Center and Hines VA Hospital in Chicago.

It may be useful to try to normalize fecal flora by using probiotic living organisms that are nonpathogenic and nontoxic, such as *Saccharomyces boulardii*, a yeast originally isolated from the lychee fruit. This yeast has been the subject of Dr. Surawicz's research for 14 years.

Several trials have shown efficacy with *S. boulardii* used as an adjunct to antibiotics in recurrent disease, but a prospective, placebo-controlled trial found significant efficacy only when it was used in combination with high-dose vancomycin (2 g/day). Subsequent evaluation suggested that recurrences were much more likely in patients with persistent *C. difficile* in their stools despite therapy with antibiotics and *S. boulardii*.

The value of other probiotics has similarly not held up in randomized, controlled trials; more research is needed to determine how to minimize the risks of using the agents while maximizing benefits, Dr. Surawicz said.

Bacteriotherapy using artificial stool created with anaerobic and aerobic bacteria, and administering nontoxic strains of *C. difficile* have also been reported anecdotally. A toxoid vaccine is in development and looks promising, with three of three treated patients experiencing a resolution of their recurrent disease.

Until such a vaccine is available, fecal enemas using emulsified donor stool is a highly unconventional approach that might actually work, she said.

"For years, I said the whole notion of fecal enemas was just an indication of just how desperate patients and their doctors are, but I changed my mind," Dr. Surawicz said.

She had read about more than a dozen cases in which the technique worked, and she first performed a fecal enema on a patient with multiple recurrences despite repeated courses of vancomycin (tapered, then pulsed) and probiotics over 9 months.

Vancomycin was discontinued 3 days prior to the procedure, and the patient was instructed to use a standard colon cleansing preparation. Donor stool from the patient's husband was then emulsified in nonbacteriostatic saline, filtered, and introduced into the colon using a colonoscope.

The patient recovered fully from her *C. difficile*–associated disease and did not experience any more recurrences, Dr. Surawicz said. ■



Pages 38a—38b