'Throw Everything' at Refractory *C. difficile* Disease

BY BETSY BATES
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LAS VEGAS — When confronted with severe or refractory *Clostridium difficile*–associated disease, act fast, act aggressively, and don't be afraid to try unorthodox methods if standard therapies don't work, Dr. Christina Surawicz stressed during a symposium at the annual meeting of the American College of Gastroenterology.

Virulent strains are emerging, so look for a rapid response to standard therapy and then be prepared to move on, said Dr. Surawicz, professor of medicine at the University of Washington, Seattle.

"Basically, my philosophy is to throw everything at [it] because it's such a serious disease that there is no harm in maximizing treatment right away," she said.

Metronidazole, given in a dosage of 250 mg four times daily for 10 days, is still considered first-line treatment for *C. difficile* disease, and it shows efficacy equal to vancomycin in patients with mild disease. However, patients with severe disease or risk factors for progression might be better off with vancomycin from the start.

"We've all been indoctrinated to use metronidazole first line," she said. But "Metronidazole response rates are not the 90% or 95% we were used to seeing 5 or 6 years ago." Recent data show metronidazole response rates in the 70%-78% range, or even lower, in severe *C. difficile* disease. Relapses are increasingly common.

Don't wait more than 3 days to make the switch in patients with mild to moderate disease, and consider vancomycin first line in those with severe disease, which is typically marked by pseudomembranous colitis, severe pain and abdominal distension, presence of colon wall thickening and/or ascites on CT, hemodynamic instability, declining mental status, elevated white blood cell count, elevated serum creatinine, and low albumin levels, Dr. Surawicz advised. The standard oral vancomycin dosage for *C. difficile* is 125-250 mg four times daily, but Dr. Surawicz advised quickly increasing the dosage to 2 g/day if necessary.

Small trials have convinced Dr. Surawicz to try 500 mg of intravenous metronidazole every 6-8 hours in patients with refractory disease, and to give vancomycin enemas using 500 mg of the intravenous form of the drug in 100 mL of normal saline 3-4 times daily.

"We should be consulting our surgical colleagues earlier rather than later," said Dr. Surawicz, who disclosed that she is a consultant to or on the speakers' bureau for ViroPharma Inc., manufacturer of vancomycin. ■

Crohn's Perianal Fistulas Respond To Therapy

ORLANDO — About 25% of children newly diagnosed with Crohn's disease will develop perianal fistulas within 2 years, but the majority of these fistulas will resolve in response to medical management alone, Dr. David J. Keljo reported at a poster session at the annual meeting of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

Using data from a prospective, observational registry that enrolled pediatric patients with irritable bowel disease (IBD), investigators assessed outcomes for 263 children under age 16 years newly diagnosed with Crohn's disease. All participants had at least 24 months of follow-up.

Dr. Keljo and his associates from the Pediatric IBD Collaborative Research Group in Hartford, Conn., studied the frequency and clinical course of perianal fistulas in these children. Roughly 25% had fistulas within the first 2 years, and three-quarters of the latter children had them within the first 30 days.

Fistulizing patients were more likely than nonfistulizing patients to be treated with infliximab, 6MP/AZA6 [mercaptopurine (6MP) and its prodrug azathioprine (AZA)], methotrexate, and antibiotics.

A total of 47 children (18%) had fistulas by day 30 after diagnosis. Of these, fistulas resolved in 35 (75%) patients, including 7 whose fistulas resolved after infliximab therapy. None required surgery, said Dr. Keljo, who is on the pediatric gastroenterology staff at Children's Hospital of Pittsburgh. Another 18 patients (7%) developed lesions after 30 days but before 2 years.

—Damian McNamara