

nausea and leukocytosis. Sigmoidoscopy reveals diffuse or patchy, non-specific colitis. Pseudomembranous colitis has a clinical picture similar to *C. difficile* colitis except that local and systemic manifestations are more severe. In addition sigmoidoscopy reveals characteristic adherent yellow plaques or pseudomembranes which may coalesce to form a confluent membrane. In about 10% of cases only the proximal colon is affected; therefore the pseudomembranes can be missed by sigmoidoscopy alone.

Patients with *C. difficile* colitis occasionally present with acute abdomen and fulminant colitis.³³ As a consequence of greatly diminished colonic muscular tone toxic megacolon can result. Plain abdominal radiographs may reveal a dilated colon and ileum or air in the abdominal cavity if perforation has occurred. Massive mucosal edema of the colon may be evident as "thumbprinting" on an abdominal film or as marked thickening of the colonic wall on a computed tomographic scan. Sigmoidoscopy should be avoided to prevent perforation, but a proctoscopy with minimal air insufflation is safe and may be useful for the diagnosis.

Laboratory Diagnosis

The gold standard for the laboratory diagnosis of *C. difficile* infection is the stool-cytotoxin test. This is a tissue culture assay based on the induction of cell rounding by *C. difficile* toxins in stool filtrate. This test is extremely sensitive (94-100%) and specific (99%), since only a few picograms of toxin B are sufficient to induce cell rounding. Neutralization of cell rounding by using specific anti-toxin B sera confers specificity to the assay.³⁴ The test is generally reported as positive or negative, as there is no direct correlation between toxin B levels in the stool and severity of the disease. Stool culture for *C. difficile* is a less specific method for establishing a diagnosis, since non-toxigenic strains of *C. difficile* can also be isolated with this approach.⁵

More recently rapid immunoassays for the detection of *C. difficile* antigens or toxins have been developed and are now commercially available. The latex-agglutination test has been widely used but has poor sensitivity and specificity, since it recognizes a protein present in non-toxigenic strains of *C. difficile*.³⁵ More recently several enzyme immunoassays have been introduced that specifically detect toxin A or toxin B in stool with good sensitivity (69-87%) and specificity (99-100%).³⁴⁻³⁶ These enzyme immunoassays represent a good alternative to the stool-cytotoxin test, since they are quicker and simpler to perform.

Treatment of Acute *C. difficile* Colitis

The first step in managing diarrhea and colitis in

Table 2 Treatment of Antibiotic-associated Colitis

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| 1. Discontinue all antibiotics |
| 2. Correct fluid and electrolyte abnormalities |
| 3. Metronidazole (250 mg po tid a day for 7-10 days) or Vancomycin (125-500 mg tid for 10 days) |
| 4. Avoid antidiarrheal agents |
| 5. Strict contact isolation, stool precautions |

patients with confirmed or suspected *C. difficile* infection is to discontinue antibiotic therapy, if possible (Table 2). In patients with only mild symptoms this measure alone may be sufficient to allow recovery. Specific therapy to eradicate *C. difficile* is required if symptoms are more severe and persistent or the antibiotic therapy that induced the disease cannot be discontinued. Metronidazole (250 mg four times a day) and vancomycin (125 mg four times a day) are equally effective in treating *C. difficile* induced colitis.³⁷ Because of the high cost of vancomycin, metronidazole is the drug of first choice. Symptomatic improvement can be expected within 72 hours, and diarrhea and colitis resolve completely in more than 95% of patients after 10 days of treatment. Patients who cannot tolerate oral medication because of ileus can be treated with intravenous metronidazole. Excretion of the drug into the bile and exudation from the inflamed colonic mucosa will result in bactericidal concentrations in the intestinal lumen.³⁸ The absence of significant improvement after 48 to 72 hours of antibiotic therapy may indicate a more serious infection that requires surgery.

Treatment of Recurrent *C. difficile* Colitis

About 10 to 20% of patients with an acute episode of *C. difficile* colitis will experience a relapse of diarrhea, usually within one week after the antibiotic therapy is discontinued.^{39,40} A possible reason for relapsing disease may be the failure to completely eradicate the organism from the colon during treatment or re-infection of a receptive host from the contaminated environment.⁴¹ The diagnosis of recurrent diarrhea from *C. difficile* infection should be confirmed by a stool-toxin assay.

Relapses characterized by mild diarrhea may be treated conservatively without a new cycle of antibiotics, since they may resolve spontaneously (Table 3). This approach will reduce the risk of new relapses since the normal flora is allowed to reconstitute itself. Patients with more severe symptoms or several relapses may benefit of a new course of metronidazole. There is no clear rationale for using vancomycin as a treatment for relapses after metronidazole therapy, since the development of antibiotic resistance is not usually the