

# The changing spectrum of *Clostridium difficile*-associated disease

## Implications for dentistry

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**C***lostridium difficile* is a gram-positive, spore-forming, toxin-producing, anaerobic bacillus that causes diseases of the gastrointestinal tract ranging from asymptomatic colonization to a life-threatening condition known as “toxic megacolon.” Antimicrobial agent exposure is an important risk factor for *Clostridium difficile*-associated disease (CDAD).

Because antimicrobial agents frequently are used to treat or prevent dental infections, dentists should be aware of this disease. We highlight the clinical presentation of CDAD by describing two previously published case examples<sup>1</sup> followed by an in-depth review of the literature.

### CASE EXAMPLES

**Case 1.** A healthy 48-year-old woman underwent endodontic therapy and was prescribed a 10-day course of the antimicrobial agent oral clindamycin. Approximately eight days after she finished her course of this medication, she began having liquid brown diarrhea with some mucus and a small amount of blood. She called her primary care physician who advised her to take bismuth subsalicylate

## ABSTRACT

**Background.** *Clostridium difficile* is an anaerobic, spore-forming bacterium that causes a wide range of diseases of the gastrointestinal tract. It is best known for its association with uncomplicated antimicrobial-agent-associated diarrhea.

**Case Description.** The authors describe two previously published cases of *Clostridium difficile*-associated disease (CDAD) to highlight its varied clinical manifestations. A 48-year-old woman had mild CDAD after receiving antibiotics after undergoing endodontic surgery. She took metronidazole, and her *C. difficile* infection resolved. A 31-year-old pregnant woman developed severe CDAD after receiving antibiotics for a urinary tract infection. She underwent surgery to remove part of her colon, but her condition worsened, and she died.

**Clinical Implications.** Dentists often prescribe antimicrobial agents to treat infections. Until recently, these agents also were recommended as prophylaxis for infective endocarditis during invasive oral procedures. An important risk factor for CDAD and recurrent CDAD is antimicrobial agent exposure. Dentists should be aware of CDAD to help prevent its spread and facilitate early recognition and treatment to minimize severe outcomes.

**Key Words.** *Clostridium difficile*; antimicrobial agents; emerging disease; diarrhea.

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(Pepto-Bismol, Procter & Gamble, Cincinnati) and loperamide (Imodium, McNeil Consumer Healthcare, Fort Washington, Pa.). She continued to have eight to 10 bowel movements per day while taking these medications, so she scheduled a clinic appointment with her physician. At this visit, she provided a stool sample, which tested positive for *C. difficile* toxin. She was given a prescription for metronidazole, and her symptoms resolved slowly over the next 10 days.

**Case 2.** A 31-year-old woman who was 14 weeks pregnant with twins went to the emergency department with a complaint of having had intermittent diarrhea for three weeks followed by abdominal cramping and watery black stools for three days. Her most recent antimicrobial agent exposure had been to trimethoprim-sulfamethoxazole, which she was prescribed for a urinary tract infection approximately two months before the onset of her diarrhea. Her stool samples tested positive for *C. difficile* toxin, and she was admitted to the hospital. She was treated with metronidazole, cholestyramine and oral vancomycin. She improved while taking the oral vancomycin and was discharged after an 18-day hospital stay. Four days later, however, she was readmitted to the intensive care unit with diarrhea, hypotension and spontaneous abortion of the fetuses. A subtotal colectomy was performed, and histopathology of the colon showed pseudomembranous colitis and toxic megacolon. She died on the third day of her hospitalization.

## DISCUSSION

The patient in the first case developed CDAD after taking a short course of antimicrobial agents after undergoing endodontic surgery. Although the term CDAD encompasses a spectrum of gastrointestinal diseases that vary in severity, the most common manifestation has been uncomplicated antimicrobial-agent-associated diarrhea. The patient initially took over-the-counter (OTC) medications, which provided no benefit. One of these OTC medications, loperamide, slows gastrointestinal motility, and its use has been identified as a risk factor for development of severe CDAD. The patient experienced no adverse effects from the loperamide. Once her physician determined that she had CDAD and treated it with metronidazole, she responded well and her symptoms resolved.

Her story is of particular interest because she received the antimicrobial agents from her den-

tist but called her primary care physician when she developed diarrhea. This situation highlights the fact that dentists may not always be aware of the complications resulting from the antimicrobial agents they prescribe.

The second case is an example of the changing epidemiology of CDAD. There is growing evidence of more frequent and severe occurrences of the disease, not only among hospitalized patients but also among otherwise healthy people in the community.<sup>1</sup> This patient was a young woman with no significant medical comorbidities who was having a normal twin pregnancy until she developed CDAD. She had been experiencing symptoms for more than three weeks before she sought medical care.

Because young, healthy people often see their dentists more frequently than they do their physicians, awareness of CDAD among members of the dental community may increase the likelihood that dentists will identify patients who have CDAD and arrange for them to receive appropriate treatment as soon as possible.

**Pathogenesis.** *C. difficile* is spread by the fecal-oral route and can be ingested in a vegetative or spore form. The spore form of the bacterium is extremely durable, allowing it to survive not only harsh conditions outside of the human body but also the acidic environment of the stomach. After ingestion, spores germinate into the vegetative form in the small intestines. These bacteria then colonize the mucosal crypts of the large intestines and proliferate when the normal flora of the large intestines is disrupted. One of the most common ways that the normal gastrointestinal flora is disrupted is through the use of antimicrobial agents, especially broad-spectrum agents with antianaerobic activity.

The pathogenicity of *C. difficile* is due to the various toxins that it produces, and only toxin-producing strains cause disease.<sup>2</sup> The primary virulence factors are the large clostridial cytotoxins toxins A and B that cause inflammation and mucosal damage and lead to diarrhea or colitis.<sup>3</sup> Colitis that is caused by *C. difficile* characteristically is pseudomembranous with raised white and yellowish plaques.

**Clinical presentation.** The incubation period

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**ABBREVIATION KEY.** **AHA:** American Heart Association. **CDAD:** *Clostridium difficile*-associated disease. **OTC:** Over-the-counter.

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