REVIEW

Pathophysiology, Diagnosis and Treatment of *Clostridium difficile* Infection

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Abstract. ***Clostridium difficile*** **infection has become in recent years an important nosocomial threat. Prevention of the spread of *C. difficile* infection among long term hospitalized patients is a major challenge since *C. difficile* spores can persist indefinitely in the hospital environment. Following antibiotic therapy that disrupts the normal bacterial flora of the colon, *C. difficile* can colonize the large intestine. The bacteria releases two large protein toxins that bind to colonocytes and mediate an acute inflammatory diarrhea characterized by an abundant exudate rich in neutrophils and proteins that in some cases can form the typical "pseudomembrane". *C. difficile* infection shows a spectrum of severity from asymptomatic carrier to fulminant acute pseudomembranous colitis. The gold standard for the laboratory diagnosis of *C. difficile* infection is the stool-cytotoxin test, however recently developed immunoassays represent a good alternative. The treatment of *C. difficile* infection is based on the severity of the clinical picture. In patients with mild diarrhea discontinuation of the causing antibiotic can be an adequate therapeutic approach, whereas patients with more severe symptoms require antibiotic therapy or, in the most severe infections, even colectomy.** (Keio J Med 48 (4): 169–174, December 1999)

Key words: ***Clostridium difficile*****, clolitis, enteric infection, antibiotics, toxins**

Clostridium difficile is the cause of antibiotic-associated diarrhea in humans, now recognized as the commonest enteric infection in US hospitals, with a 10% symptomatic infection rate for hospitalized patients.[1] The organism colonizes the human colon after the normal colonic flora has been altered by antibiotic therapy and then releases two protein exotoxins, toxins A and B. *C. difficile* toxins bind to specific receptor(s) on colonocytes to stimulate a massive fluid secretion (diarrhea) and necrosis of the surface mucosa associated with an acute inflammatory infiltrate. Infection with *C. difficile* produces a spectrum of clinical responses, varying from the asymptomatic carrier state to fulminant pseudomembranous colitis.

Clostridium difficile Bacteriology

C. difficile was first described in 1935 by Hall and O'Toole who were investigating the acquisition of normal bacterial flora in healthy newborns.[2] They decided to name this gram-positive bacillus of the genus Clostridia as the "difficult clostridia" because it was resistant to isolation and culture on conventional media. Although the bacteria was toxigenic and caused rapid death of animals injected with culture filtrate of *C. difficile*, initially it was considered a harmless intestinal commensal since infants colonized by this organism had no signs of illness.[2] Not until 1978 was it discovered that *C. difficile* was the source of the cytotoxin found in the stools of patients with antibiotic-associated pseudomembranous colitis.[3,4] This organism is now recognized as a major nosocomial pathogen with substantial morbidity in elderly hospitalized patients. However, not all strains of *C. difficile* are toxigenic. During outbreaks of *C. difficile* infection in hospitals, some patients may be colonized by non-toxigenic strains. *C. difficile* strains can be categorized as low, medium and high toxin producers, but disease severity does not appear to correlate with the production and concentration of toxins in the stools.[4] *C. difficile* strains have been also classified upon serotype, bacteriophage, electrophoretic profiles of bacterial proteins, however these classifications have

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