CLOSTRIDIUM DIFFICILE-ASSOCIATED DIARRHEA

Authored by Dr. Michael Mulvey

Clostridium difficile is the most common cause of hospital-associated diarrhea. Although this bacterium has been known since the 1930's, it was only recognized as a human disease-causing organism in 1978. The bacteria produces toxins which can cause symptoms ranging from mild diarrhea to severe life threatening disease which may lead to rupture of the intestine.

C. difficile is a specialized bacteria that can form spores. Spores are resistant to heat, alcohol, and many disinfectants that kill many other common bacteria. Also, the spores can exist on surfaces for a very long time. One study demonstrated that spores could be found in a patient's room up to 40 days after the patient was discharged from hospital. These factors make *C. difficile* difficult to remove from the environment and this is the main reason it spreads in hospitals. Patients infected with *C. difficile* are isolated from other patients, thus limiting the spread of the spores to other patients. The best way prevent the spread of this bacterium is to thoroughly wash your hands with soap and water.

The most common risk factors for becoming infected with *C. difficile* are exposure to antibiotics, advanced age, and hospitalization. We have discussed why hospitalization can be problematic above, but why are antibiotics a risk factor? Although antibiotics are used successfully to fight infections caused by bacteria, antibiotics can also disrupt the normal beneficial bacteria in your intestines. This allows the *C. difficile* bacteria, that are normally suppressed by the normal beneficial bacteria, to grow and produce toxins which lead to diarrhea and more severe disease. Treatment for *C. difficile* diarrhea is first to take the patient off of the antibiotics that disrupt the normal bacteria, and alter the treatment to specialized antibiotics that kill *C. difficile*, namely metronidazole or vancomycin. After initial treatment, about 20% of patients have a relapse of the disease, usually within one week after terminating treatment, but can be up to 6 to 8 weeks after the initial symptoms have ceased. Most respond well to retreatment, but a small number do not respond or undergo multiple relapses. In these difficult cases, alternative therapies to treat these difficult cases have been described and include other antibiotics, probiotics, which is the ingestion of "good" microorganisms such as *Saccharomyces boulardii* or *Lactobacillus rhamnosus GG*, ion exchange resins to bind the toxin, immunotherapy and normal flora transplants. All of these alternative therapies require further investigations before they are accepted as mainstream therapies for *C. difficile* infections.

How common is *C. difficile* in Canadian hospitals? In a national study conducted in 1997, Canada had similar rates of infection to those reported in many other countries. However, things began to change with the turn of the century. Regions in Quebec were reporting *C. difficile* infection rates in 2003 in hospitals at five times the national average. In addition, the severity of the disease was increasing, with over 1,000 deaths reported due to *C. difficile* at the Quebec hospitals between 2003-2004. At around the same time the Centers for Disease Control and Prevention, Atlanta, USA had observed an increase in the frequency and severity of disease associated with *C. difficile* in a number of states. Both studies showed that a particular strain, called NAP1, was the cause of the problem. The Public Health Agency of Canada conducted a six-month national surveillance study which began in November, 2004 at 41 hospitals across Canada to investigate *C. difficile*. Quebec was found to have the highest rates of *C. difficile* infection but the NAP1 strain was identified in every province. These reports have prompted the European Union to take a closer look at infections caused by *C. difficile*. In 2006, Belgium, the Netherlands, and northern France have had *C. difficile* outbreaks with increased mortality which appear to be the same strain as reported in North America.

Clearly this evidence demonstrates the spread of a particular strain globally. What is different about this strain? Firstly, it contains an additional toxin, called binary toxin, which is not seen in classical hospital strains of *C. difficile*. However, there has been no evidence reported to date that demonstrates the involvement of this toxin in human disease, although the correlation is interesting. Secondly, a mutation has been observed in a gene that normally keeps toxin production at low levels during active growth. This mutation has been shown to increase the toxin production up to 20 times higher than normal. The increased toxin production may be related to the severity of disease but additional studies are required to confirm this.

In conclusion, a strain of *C. difficile* has emerged over the last several years that is associated with more severe disease in humans. It has caused a dramatic increase in the number of cases in Quebec and has been observed in all provinces in Canada. Continued surveillance is necessary to monitor the spread of this strain and additional research is required to develop improved therapies to combat infections caused by this organism.

Selected Reading

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