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Perspective

Clostridium difficile Infection: The Modern-Day Black Plague?

Charles D Shively*

Chief Executive Healthcare Officer, www.AskDrS.org and Founder, The Boca Ciega Research Consortium, Saint Petersburg, FL, USA

***Corresponding Author:** Charles D Shively, Chief Executive Healthcare Officer, www.AskDrS.org and Founder, The Boca Ciega Research Consortium, Saint Petersburg, FL, USA.

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Beware! *Clostridium difficile* infection (CDI) will not go quietly into the night. Can tranquility come on the heels of the infection fire? Also known as *C. diff*, it is a Gram-positive, anaerobic, spore-forming, cytotoxin-producing bacillus causing diarrhea and in more severe cases pseudomembranous colitis. There has been a dramatic increase in the incidence of CDI during the past three decades worldwide. North America has seen CDI incidence increase five-fold in community dwelling populations and in the over 65 age group. Incidence has also increased in Europe, most notably the UK, the Netherlands and France. More disturbing is that the severity has also increased. It has been reported that nearly a ten-fold increase in CDI associated morbidity was observed in Canada alone. The changes appear to be due partly because of new identified hypervirulent epidemic strains of *C. difficile.*

Current medical thinking suggests: Once you have it…you have it…for life! CDI has a high recurrence rate because traditional initial treatments do not kill the *C. diff* spores. Only the active CDI bacteria pathogens are killed. The spores remain. It is similar to how Anthrax exists and is almost impossible to eliminate. Further complicating attempts to reduce even the initial infection in surgery situations is the continued prescribing of calcium for recovery from most surgeries. Recent research at the United States FDA has shown that excess gut calcium awakens the *Clostridium difficile* spores and the hard spore shell breaks and unleases the infections. According to the USA Centers for Disease Control (CDC), 30,000 Americans are killed each year with more than half a million sickened each year. Several factors may play a role in recurrent CDI (rCDI) which presents itself in approximately 20% of the individuals who have an initial episode. These are presented later in this editorial.

Ironically, the current therapy for stopping the bacterial component of CDI is another antibiotic-Vancomycin. Vancomycin is a small intestine specific antibiotic that has no ability to fight systemic infections. It is typically given for mobile patients in non-hospital settings as a four time daily dose of 125 mg for 10 - 14 days. In hospital settings it is often given IV. Published literature suggests those individuals who receive the IV form may be the most targeted for recurrent infection after leaving the hospital. There are variations of oral vancomycin usage for recurrent infections which involve tapering the dosage or giving the vancomycin in an off…then on…again approach.

Several factors may play a role in recurrent CDI (rCDI). This can include conditions influencing germination, the metabolic pathways that influence toxin product of *C. difficile* and the human microbiome composition offering protection against colonization and disease caused by *C. difficile*.

How does CDI occur? Most CDI was initially thought to be related to hospitalization patient fecal exposure following surgeries with antibiotic usage. Today the repeated use of antibiotics (antibiotic-associated diarrhea) in the general population has caused a proliferation shift in outbreaks in *non-surgical* settings. The World Society of Emergency Surgery (WSES) recently issued its 2019 guidelines for management of CDI in surgical settings using a multidisciplinary expert panel of 77 worldwide clinicians. These experts reviewed all existing literature to establish the new guidelines for initial and recurrent CDI infection control. Additionally, important is that these guidelines are also applicable to non-surgical patients. Several factors may play a role in recurrent CDI (rCDI). This can include conditions influencing germination, the metabolic pathways that influence toxin product of *C. difficile* and the individual human microbiome composition offering protection against colonization and disease caused by *C. difficile.*

These learnings beg the question: What lies ahead for non-antibiotic treatment of patients who experience a first time CDI infection, including the possible recurrent infections? The most current research and clinical experiences do suggest that alternative therapies, including dietary supplement and minerals usage, may provide new solutions.

Two of the most promising approaches include adding significant amounts of calcium to the diet to awaken all dormant *C. difficile* spores in a patient's gut at once-and as a result, make the spores vulnerable to antibiotics that will kill the freshly germinated form. When combined with a bile salt produced in the liver (taurocholate), the *C. difficile* spores recognize the extra calcium and bile salt and are triggered to germinate.

A second successful approach, initiated in the UK, was to provide adult inpatients at four acute National Health Service (NHS) hospitals, a unique combination of probiotics. The combination, known as VSL#3, contained *Bifidobacterium breve, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus paracasei, Lactobacillus delbrueckii* subsp. *bulgaricus* and *Streptococcus thermophilus* in a concentration of 450 billion live bacteria per dose. It is recommended to be taken twice daily. The double blind study of 120 patients demonstrated reduction levels to zero presence of the *C. difficile* infection. This probiotic combination, provided to the consumer in a refrigerated package, is available OTC (over the counter) without prescription in the USA.

In summary, the proliferation of indiscriminate use of antibiotics when not needed needs be stopped…worldwide! One example, in the USA, is the demand by most dentists to have 2000 mg of amoxicillin consumed four hours before a routine teeth cleaning. Is this to preclude any possible malpractice challenges against the dentist when a usual problem occurs? Odd. Necessary?

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