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Clostridioides difficile

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Abstract

Clostridioides difficile is a spore-forming, anaerobic, intestinal pathogen that causes severe diarrhea that can lead to death. In 2011, *C. difficile* infected ~500,000 people in the US and killed ~29,000 people. *C. difficile* infection (CDI) is the most common health care related infection in the US, leading to increased health care costs of \$4.8 billion dollars. This pathogen transmits via the oral-fecal route as a highly contagious and resilient spore. Upon exposure to primary bile acids in the intestine, *C. difficile* germinates, and in the absence of colonization resistance from the normal microbiota, the bacterium colonizes the colon and produces toxins. These toxins inhibit actin polymerization in host cells, leading to cell death. *C. difficile* cells can then sporulate in the intestine and exit the body via diarrheal shedding. In culture, sporulation is induced at stationary phase in a nutrient-limiting environment, but the intestinal triggers of sporulation are still unknown.

Key Facts:

- *C. difficile* was first described in 1935, but wasn't linked to antibiotic-associated diarrhea and pseudomembranous colitis until 1978.
- *C. difficile* has a single, circular chromosome comprised of approximately 4.3 Mb.
- *C. difficile* spores are resistant to heat, oxygen, and ethanol-based disinfectants, but can be killed by a 1:10 dilution of sodium hypochlorite (bleach).
- CDI animal models include the hamster, mouse, young hare, infant pig, prairie dog, foal, quail, and, recently, the rat.
- *C. difficile* toxin action has been characterized in the rat, mouse, hamster, rabbit, guinea pig, infant rhesus monkey, and the zebrafish embryo.
- The two major toxins produced by *C. difficile* are TcdA and TcdB, which are glucosyltransferases that inhibit Rho, Rac, and Cdc42. A third toxin, Cdt, is found in the ribotype 027 strain.

Disease Facts:

- People most at risk for CDI are the elderly, people in healthcare settings, and those who have received antibiotic treatment.
- The antibiotics that provide the highest risk of CDI are clindamycin, fluoroquinolones, cephalosporins, monobactams, and carbapenems, with increased risk correlated with greater cumulative dose, number of antibiotics, and duration of exposure.
- The estimated rate of CDI recurrence is 13.5% and death is 1.3%, both within the first 30 days of initial infection.

Taxonomy and classification:

Kingdom: Bacteria

Phylum: Firmicutes

Class: Clostridia

Order: Clostridiales

Family: Clostridiaceae

Genus: *Clostridioides* (formerly *Peptoclostridium* and *Clostridium*)

Species: *difficile*

Gram-positive

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