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See the Difference in *C. difficile*

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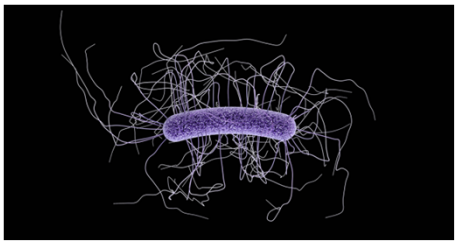
Disclosures

- None

Changing Times … Changing Names

- Updated nomenclature for *C. difficile* in 2016[1]
  - *Clostridium difficile* → ***Clostridioides difficile***
- Disease = *C. difficile* infection (CDI) or *C. difficile* associated disease (CDAD)



https://www.cdc.gov/cdiff/index.html

Burden of *Clostridioides difficile* Disease

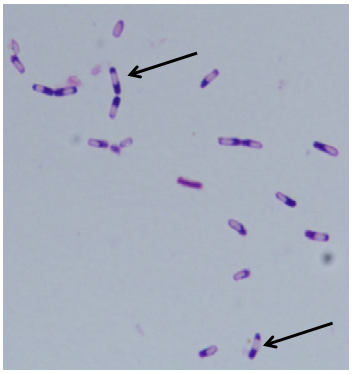
- *Clostridioides difficile* remains the most commonly reported pathogen causing healthcare-associated infections in US hospitals[2]
  - Healthcare-associated CDI cases have been decreasing somewhat since 2015, but community-associated CDI cases have not
  - Mandated reporting of *C. difficile* infections in United States
- Accurate and rapid diagnosis of *C. difficile* infection (CDI) is important!
  - Treat with appropriate antimicrobial agent
  - Discontinue the precipitating antimicrobial agent
  - Institute infection control precautions

Clinical Disease

- Spectrum of clinical findings
  - Diarrhea
  - Pseudomembranous colitis
  - Toxic megacolon
- Antibiotic exposure
  - Clindamycin
  - Broad-spectrum cephalosporins
  - Ampicillin
  - Any antibiotic

Pathophysiology

- Spore-forming Gram-positive rod, obligate anaerobe
- Originally named *Bacillus difficilis*
- Spores are ubiquitous!
  - Spread by fecal-oral route, person to person
  - Present on environmental surfaces and on hands of caregivers
  - Resistant to alcohol gels and many hospital disinfectants
  - Persist on inanimate surfaces for several months



Gram stain of *C. difficile* colony; arrows = spores

Changing Face of *C. difficile*

- Since 2000, rise in severity of disease
- NAP1/BI/027 strain / Hypervirulent strain[3]
  - Compared to non-NAP1 strains:
    - May be associated with increased CDI frequency, more severe disease, and complications
    - Higher rates of fluoroquinolone resistance
    - Produce binary toxin as well as toxins A and B
- Non NAP1 strains have also been associated with severe CDI and production of binary toxin[4]
- Prevalence of various *C. difficile* strains varies according to different geographical regions and patient subsets

C. difficile Toxins

- Toxin A (*tcdA* gene)
  - Enterotoxin causes fluid accumulation in bowel
- Toxin B (*tcdB* gene)
  - Cytopathic to (causes distortion of) cells when cultured in the laboratory
- *tcdC* gene regulates toxin A and B production
- Binary toxin (*cdtA* and *cdtB* genes)

C. difficile Colonization

- Asymptomatic carriage can occur with nontoxigenic or toxigenic strains
  - Carriage is predominantly with toxigenic strains
- 0.4%-15% of healthy adults[5] in general population are colonized
  - Percentage increases with particular risk factors, such as elderly, hospital inpatients, long term care facility residents, and others
- 18%-90% of neonates and infants[5] are colonized with *C. difficile*
- The sole presence of *C. difficile* toxins is insufficient for a diagnosis of CDI
- Test only unformed stools when assessing for CDI

Strategies for *C. difficile* Diagnosis[6]

Assay	Target	Advantages	Disadvantages
Nucleic acid amplification test (NAAT)	*C. difficile* toxin genes	High sensitivity	Concern for detection of colonization state
Toxin enzyme immunoassay (EIA)	Toxins A and B	Rapid; easy to perform	Low sensitivity (50-75%)
Glutamate dehydrogenase (GDH) enzyme immunoassay	Highly conserved enzyme present in all *C. difficile*	High sensitivity	Poor specificity and only a screening step; GDH assay never used alone
Cell cytotoxicity neutralization assay (on stool filtrate)	Toxin B primarily but also toxin A to some extent	High sensitivity and specificity	Long TAT (up to 48 hrs); labor-intensive
Toxigenic stool culture (culture for *C. difficile* then perform an assay to detect toxin)	Toxigenic *C. difficile*	High sensitivity	Long TAT (48-96 hrs); labor-intensive

TAT = turnaround time

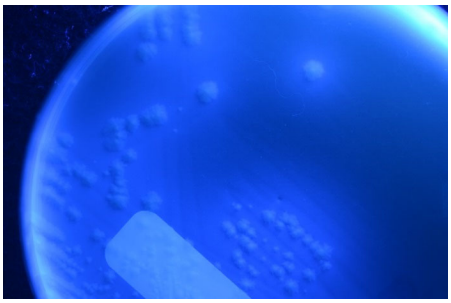
Culture

Advantages

- Highly sensitive
- Allows for molecular typing studies or antimicrobial susceptibility testing

Disadvantages

- Recovery of nontoxigenic strains
- Time to results generally 24-48 hours



CHROMagar™ *C. difficile*

Updated Clinical Practice Guidelines for CDI in Adults and Children[7]

Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

What is the ***most sensitive*** method of diagnosis of CDI in stool specimens from ***patients likely to have CDI based on clinical symptoms***?

Recommendation:

Use a NAAT alone or a multistep algorithm for testing (i.e., GDH plus toxin; GDH plus toxin, arbitrated by NAAT; or NAAT plus toxin) rather than a toxin test alone ***when there are pre-agreed institutional criteria for patient stool submission***.

Updated IDSA/SHEA Clinical Practice Guidelines for CDI in Adults and Children[7]

What is the ***best-performing method*** (ie, in use positive and negative predictive value) for detecting patients at increased risk for clinically significant *C. difficile* infections in ***commonly submitted stool specimens***?

Recommendation:

Use a stool toxin test as part of a multistep algorithm (i.e., GDH plus toxin; GDH plus toxin, arbitrated by NAAT; or NAAT plus toxin) rather than a NAAT alone for all specimens received in the clinical laboratory ***where there are no pre-agreed institutional criteria for patient stool submission***.

Fidaxomicin

- Macrolide antimicrobial agent
- Approved for treatment of CDI
- Bactericidal
- Oral administration leads to high fecal concentrations
- Mayo Clinic offers metronidazole and vancomycin susceptibility testing for *C. difficile* from intestinal sources

Testing Guidelines

- Repeat testing for “test of cure” is not acceptable[8]
- Formed stools should not be tested when used for CDI
- Testing should not be performed on children under 1 year of age
- Laboratories may use more than one testing platform in reflexive or algorithmic approaches

References

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