



Better health through
laboratory medicine.

PEARLS OF LABORATORY MEDICINE

Pearl Title: *Clostridioides (Clostridium) difficile*

Name of Presenter: Margaret E. McCort

Affiliation: University of Chicago Medicine

DOI: 10.15428/CCTC.2019.311670



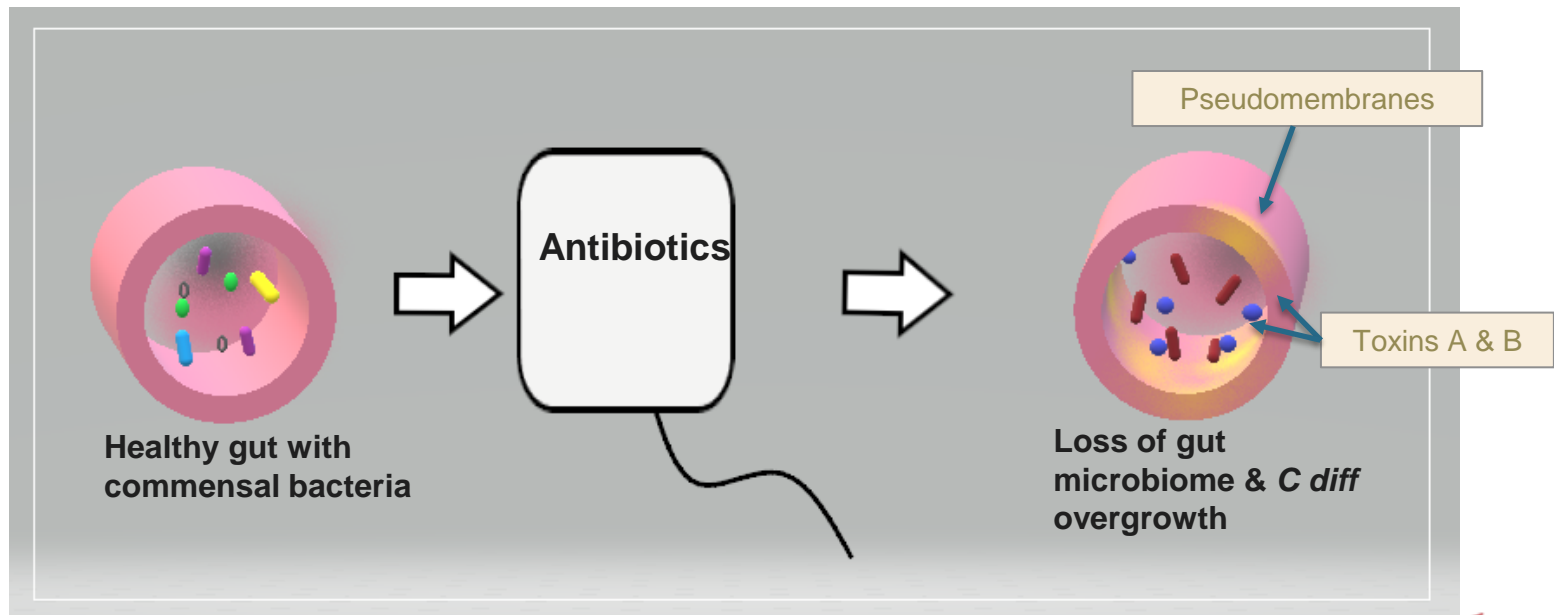
***Clostridioides difficile*: an introduction**

- Formerly known as *Clostridium difficile*
- Spore forming, gram positive rod
- Discovered in 1935, linked to infection in 1977
- Associated with hospitalization and antibiotic use
→ most common nosocomial infection in US
- Importance of infection control



C. difficile: the pathogen

- Ingest endospores
- Effects of antibiotics on gut flora
- Overgrowth of CD bacteria
- Toxins cause epithelial damage
- Inflammation, diarrhea, and pseudomembranes



***C. difficile* Epidemiology**

- 2-5% healthy adults colonized
- 3-26% hospitalized patients are colonized
- <1% hospitalized patients with CDI
 - Incidence is higher in immunocompromised
- Healthcare-Associated vs Community acquired



Clinical Presentation

C. difficile infection (CDI) = diarrhea + positive test

C. difficile (CD) colonization = positive test *without* symptoms

- Diarrhea
 - Spectrum of severity, but typically >3 BMs/day
- Fever
- Abd pain
- Leukocytosis
- Severe: development of ileus, distension, sepsis



Risk Factors for *C. difficile* Infection

- Prolonged healthcare exposure
- Older age
- Antibiotic exposure
 - Fluoroquinolones
 - Clindamycin
 - Cephalosporins
- Proton Pump Inhibitor (PPI) use
- Immunocompromise

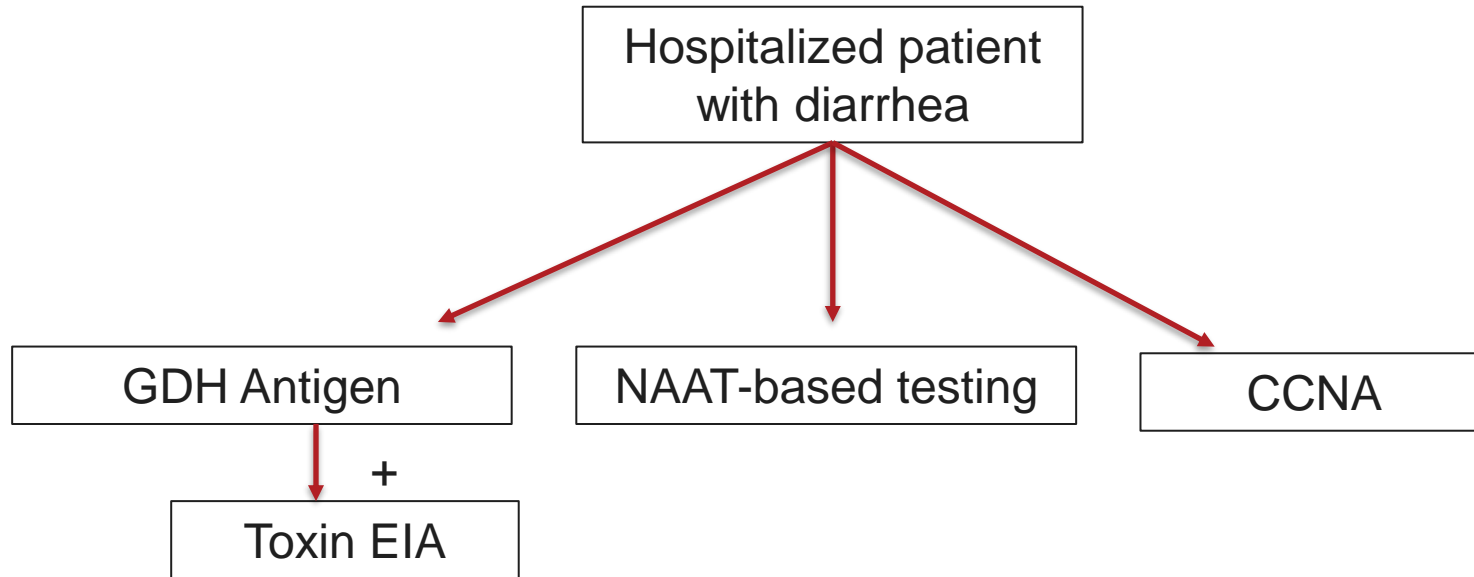


CD Diagnosis

Test Name	Time to diagnosis	Pros	Cons
Anaerobic toxigenic culture	4-5 days	Highly sensitive	Labor intensive Must confirm toxin assay Selective media* Not very specific
Cytotoxic Cell Neutralization Assays (CCNA)	3-4 days	Very sensitive Very specific	Labor intensive Time consuming Lacks standardization
Toxin Immunoassay (EIA)	Rapid	Moderately specific	Not very sensitive Variable performance
GDH EIA + toxin EIA	1-2 days	Very sensitive	Difficult to interpret Expensive Low specificity
NAAT-based test	Rapid	Very sensitive Moderate specificity	False positives in colonized

* *Selective media = cycloserine-cefoxitin-fructose agar*

Controversies in *C. difficile* diagnosis



Potential false negatives

Potential false positives



C. difficile Treatment

Treatment type	Indication
Vancomycin (PO)	First episode mild/moderate CDI; first recurrence CDI; high-dose for severe
Fidaxomicin (PO or IV)	First episode mild/moderate CDI; recurrent CDI
Bezlotoxumab (IV)	Reduce risk of recurrent CDI when used as adjuvant to vancomycin or fidaxomicin course
Metronidazole (IV)	Severe CD infection (or mild/moderate without enteral access)
FMT	Treat recurrent CDI
Surgery	Toxic megacolon, colon perforation



***C. difficile* Treatment: Fecal Microbiota Transplant**

- Indication: Recurrent CD, *when combined with antibiotic discontinuation*
- Administration: enema, pill, or endoscopic
- Proposed method of action: restore gut microbiome
- Risks:
 - No standardized formula
 - Expensive
 - CD may recur if antibiotics given after FMT



CD Complications

- Toxic megacolon
- Colon perforation
- Dehydration
 - Kidney injury
- Sepsis / Shock
- Bacteremia



***C. difficile* Prevention**

Spores are easily spread, not easily killed

- Handwashing with soap & water
- Contact isolation
 - Gown
 - Gloves
 - Private room
- Cleaning the environment
 - Sodium hypochlorite (5000ppm chlorine bleach) solution x 10 min



Future Directions for CD Research

- Gut biodiversity & microbiome
- Bile salt conjugation and toxin production
- Host response to CD

Remember: to prevent CDI, think twice before prescribing antibiotics & always wash your hands!

Remember: only treat CDI if there is a positive test **and** symptoms present!

CDI= positive test + symptoms



References

- Curry SR. Clostridium difficile. Clin Lab Med 2017; 37:341-369.
- Curry SR, Muto CA, Schlackman JL, et al. Use of multilocus variable number of tandem repeats analysis genotyping to determine the role of asymptomatic carriers in Clostridium difficile transmission. Clin Infect Dis 2013; 57(8):1094-102.
- Czepiel J, Drozd M, Pituch H, et al. Clostridium difficile infection: a review. Eur Journ Clin Micro & Infect Dis 2019;
- Dubberke E, Burnham CD. Diagnosis of Clostridium difficile infection: treat the patient, not the test. JAMA Intern Med 2015. 175(11): 1801-2.
- Feher C, Munez Rubio E, Merino Amador P, et al. The efficacy of fidaxomicin in the treatment of Clostridium difficile infection in a real-world clinical setting: a Spanish multi-center retrospective cohort. Eur J Clin Microbiol Infect Dis 2017. 36: 295-303.
- Mamo Y, Woodworth MH, Want T, et al. Durability and Long-term clinical outcomes of fecal microbiota transplant treatment in patients with recurrent Clostridium difficile infection. Clin Infect Dis 2018; 66(11): 1705-11.
- McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for Clostridium difficile infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). CID 2018; 66(7): e1-e48.
- McFarland LV, Mulligan ME, Kwok RY, et al. Nosocomial acquisition of Clostridium difficile infection. NEJM 1989; 320: 204-10Mullane KM, Dubberke ER, AST ID Community of Practice. Management of Clostridioides (formerly Clostridium) difficile infection (CDI) in solid organ transplant recipients: guidelines from the American Society of Transplantation Community of Practice. Clin Transplant 2019. e13564.
- Wilcox MH, Gerding DN, Poxton IR, et al. Bezlotoxumab for Prevention of recurrent Clostridium difficile Infection. NEJM 2017; 376 (4): 305-317.



Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

- **Employment or Leadership:** No disclosures
- **Consultant or Advisory Role:** No disclosures
- **Stock Ownership:** No disclosures
- **Honoraria:** No disclosures
- **Research Funding:** No disclosures
- **Expert Testimony:** No disclosures
- **Patents:** No disclosures



Thank you for participating in this
Clinical Chemistry Trainee Council
Pearl of Laboratory Medicine.

Find our upcoming Pearls and other
Trainee Council information at
www.traineecouncil.org

Download the free *Clinical Chemistry* app
on iTunes today for additional content!

Follow us:

