Pearl Title: *Clostridioides (Clostridium) difficile*

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**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

**Figure 1:** *C. difficile* in the gut. Author’s own.
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

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

*Selective media = cycloserine-cefoxitin-fructose agar*
Controversies in *C. difficile* diagnosis

Hospitalized patient with diarrhea

- GDH Antigen + Toxin EIA
- NAAT-based testing
- CCNA

Potential false negatives
Potential false positives
# C. difficile Treatment

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

Disclosures/Potential Conflicts of Interest

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

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