Clostridium difficile: Some Routine but Controversial Considerations
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Learning Objectives
1. Compare diagnostic tests for Clostridium difficile detection.
2. Discuss how to determine resolution of Clostridium difficile infection.

Clostridium difficile

- Ubiquitous organism - soil, water, everywhere
- Spore forming - spores resistant to drying, lack of oxygen, temperature extremes, alcohol rub
- Toxinogenic and non-toxinogenic strains
- Glucosyltransferase toxins TcdA and TcdB
- Toxins produced in gastrointestinal lumen

- Responsible for 25% of antibiotic-associated diarrhea
- Disruption of normal GI microbiome leads to colonization and disease from C. difficile
- 20% of asymptomatic patients have colonization with C. difficile in their stools
- High rate of colonization in infants
- NAP1/027 strain virulent, caused outbreaks

Clinical Presentation

- Fever, diarrhea, abdominal pain
- Mild to Severe disease
- Pseudomembranous colitis
- Complications: megacolon, perforation, shock

Mandel, Douglas, and Bennett's Principles and Practice of Infectious Diseases
Gardner, Dale K., Young, Vincent B. Pages 2744-2756 4th @ 2015

Clostridium difficile Epidemiology

- 250,000 cases treated in US hospitals annually
- 5-10 Clostridium difficile infection (CDI) cases per 10,000 patient-days of care
- 14,000 deaths annually
- 25% of cases followed by recurrence
- Attributable mortality 5-10%
**Clostridium difficile Epidemiology**

- Outpatient exposure only
- Inpatient exposure
- High risk health care exposure

![Chart showing percentage of community onset, nursing home onset, hospital onset, and no health care exposure.]

**When to Suspect**

- Presence of risk factors:
  - Prior antibiotic use or course of antibiotic
  - Antibiotic use within 90 days of illness
  - Type of antibiotic
  - Associated sepsis, fever, leukocytosis, neutropenia, and/or diagnosis of sepsis
  - Immunosuppression
diabetes mellitus
  - History of recent travel
  - Age over 65
  - History of recent chemotherapy
  - History of recent radiation therapy
  - History of recent surgical procedure

**Diagnosis**

- Based on:
  - Clinical symptoms (usually defined as more than three watery, loose or formed stools within 48 hours), AND
  - Positive diagnostic test (usually of a stool specimen) that detects the presence of the C. difficile organism or its toxin genes or C. difficile toxin, OR
  - Direct visualization of pseudomembranes in the colon by lower gastrointestinal endoscopy

**5% of patients with severe CDI have obstruction**

- Diagnosis based on radiologic finding of toxic megacolon and confirmed by lower GI endoscopic visualization of pseudomembranes

**Diagnostic Tests**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>EIA</td>
<td>85%</td>
<td>99%</td>
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<tr>
<td>ELISA</td>
<td>85-95%</td>
<td>85-98%</td>
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<tr>
<td>PCR</td>
<td>95-100%</td>
<td>95-97%</td>
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<tr>
<td>cultures</td>
<td>95-100%</td>
<td>95-97%</td>
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**2/3/2015**
Advantages and Disadvantages of Available Diagnostic Tests

Tests performed on liquid stool to ascertain the patient has diarrhea
- EIA: easy to perform, not sensitive enough leading to "C. diff 2.0"
- PCR: highly sensitive, positive for several weeks even after treatment
- Selective anaerobic culture: by itself, does not differentiate toxigenic vs. non-toxigenic strains; can be performed on non-dead specimens (e.g., environmental cultures in an outbreak setting)

Public Reporting

- Hospital-wide C. difficile positive lab tests reported publicly
- Standard Infection Ratio is calculated based on NHSN aggregate data from 2010-2013
- Risk adjustment done for predictors of C. difficile infection, including teaching type, facility bed size, facility prevalence rate, and C. difficile laboratory test type
- Implications for clinical care: Test early to avoid misclassification as hospital-onset case

Epidemiologic Definitions

- Healthcare facility-onset, healthcare facility-associated C. difficile infection (CDI) symptom onset more than 3 days after admission to a healthcare facility, with any of the above cultures
- Healthcare facility-onset, community-onset C. difficile infection (CDI) symptom onset in the community or less than 3 days after admission, provided symptom onset was less than 4 weeks after the last discharge from a healthcare facility
- Community-associated C. difficile infection (CDI) symptom onset in the community or less than 3 days after admission to a healthcare facility, provided that symptom onset was more than 4 weeks after the last discharge from a healthcare facility
- Perineum-onset C. difficile infection (CDI) symptom patient who does not meet any of the above criteria
- Recurrent C. difficile infection (CDI) symptom patient (within 4 weeks of previous episode)
- Non-recurrent C. difficile infection (CDI) symptom patient (within 4 weeks of previous episode)
- Perineum-onset C. difficile infection (CDI) symptom patient (within 4 weeks of previous episode)
- Recurrent C. difficile infection (CDI) symptom patient (within 4 weeks of previous episode)
- Non-recurrent C. difficile infection (CDI) symptom patient (within 4 weeks of previous episode)

Testing During Outbreaks

- Testing Patients vs. Environment
- Testing asymptomatic patients, a.k.a., performing active screening cultures not indicated
- Toxicogenic cultures may be needed to identify transmission
- Environmental cultures identify contamination of hospital environment

Clinical Resolution

- Resolution of diarrhea
- Challenging in critically ill patients because of several other reasons for diarrhea
- Factor in other clinical symptoms and signs – wbc count, stool wbc, abdominal pain

Determination of Clinical Resolution

- Resolution of diarrhea
- Challenging in critically ill patients because of several other reasons for diarrhea
- Factor in other clinical symptoms and signs – wbc count, stool wbc, abdominal pain
Test of Cure?

- No test of cure available
- PCR testing not to be repeated within 1 week of previous test

Risk Factors for Recurrence

- Any prior episodes of C. difficile infection
- Antibiotic use (concomitant and/or post - C. difficile infection treatment)
- Advanced age
- Prolonged or recent stay in health care facility
- High severity of patient's index for underlying illness
- Proton pump inhibitor use
- Infection with NAP1/027 strain type
- Absence of an antitoxin A antibody response

Summary

- CDI a major public health burden
- Diagnostic testing driven by symptoms
- PCR has several advantages, but costly
- No lab 'test of cure' available

Learning Assessment

- Which of the following statements regarding diagnostic methods for Clostridium difficile infections is accurate?
  A. Enzyme immunoassay (EIA) can detect both toxigenic and non-toxigenic strains of C. difficile
  B. Enzyme immunoassay (EIA) is the most sensitive and specific diagnostic method for C. difficile
  C. Polymerase chain reaction detects the presence of toxins A and B and is highly sensitive and specific
  D. Selective anaerobic culture alone can distinguish between toxigenic and non-toxigenic strains of C. difficile

Thank You!