**Clostridia Difficile: An Update**

2009

**Clostridia Difficile**
- Gram positive bacillus
- Anaerobic, difficult to grow, thus its name
- Spore forming
- Toxin producing
- Inhabits the colon

**Clostridia Difficile**
- Spores resistant to drying and susceptible to Clorox
- Vegetative form susceptible to drying and pH <5
- Toxins: A=enterotoxin, B=cytotoxin, Binary (new)

**Laboratory Diagnosis of CD**
- Culture: uncommon and requires 48-96 hours
- Toxin A and/or B detection by immunoenzyme assay: common and requires <24 hours
- Cytotoxic assay: gold standard, uncommon, requires 24-48 hours

**Laboratory Testing for CD**
- 1-2 samples sufficient to prove negative
- Do not retest positives
- Do not perform test of cure
Epidemiology in Hospitalized Children

- The incidence increased from 2001-2006, 2.6-4.0/1000 hospitalizations among children 1-11 years of age.
- 67% of children had chronic diseases.
- “Among children less than 1 year of age, the incidence increased from 2.8-5.1/1000 hospitalizations from 2000-2005”.

Risk Factors for CD Associated Disease (AD)
- Antibiotic exposure
- Hospitalization
- Prolonged hospitalization
- Long term care facility
- Increasing age, especially >65 years
- Severe underlying disease
- GI surgery
- Proton pump inhibitors and H₂ blockers

Risk of CDAD by Antibiotic Class
- Fluoroquinolones 3.9
- Cephalosporins 3.8
- Clindamycin 1.6
- Macrolides 1.3

Spectrum of CDAD
- Mild
- Moderate
- Severe

Community Acquired Clostridium difficile (CADC) Infection in Children Undergoing Colonoscopy

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CACD

CD is associated with IBD
CD is associated with gastric acid suppression

Noted CD positive stools in patients
Assessed stool aspirates obtained at colonoscopy for CD

CACD Areas Cultured

<table>
<thead>
<tr>
<th>Areas Cultured</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonoscopes X 10</td>
<td></td>
</tr>
<tr>
<td>Endoscopy Suite</td>
<td>counters and floors</td>
</tr>
<tr>
<td>Outpatient areas</td>
<td>counters, chairs, toilet seats, door knobs, computer key boards, table surfaces, examination tables, floors, sinks, faucet handles</td>
</tr>
<tr>
<td>Inpatient areas</td>
<td>beds, railings, stretchers, showers, bath areas, sinks, faucets</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
</tr>
</tbody>
</table>

CACD

Dr. Faden reviewed procedures for colonoscopy
Cultured 52 sites

CACD

Chart review of all colonoscopies performed between September 1, 2006 and August 31, 2008

322 Total colonoscopies
235 (73%) Colonic aspirates
41 (17%) Positive for CD

CACD

Other infections
1. pin worms (CD +)
2. H pylori (CD -)
3. Y enterocolitica (CD -)
Percent of Colonic Aspirates Positive for C. difficile by Quarter

<table>
<thead>
<tr>
<th>Quarters</th>
<th>% of aspirates positive for C. difficile</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st 2006</td>
<td>20%</td>
</tr>
<tr>
<td>2nd 2006</td>
<td>25%</td>
</tr>
<tr>
<td>3rd 2006</td>
<td>30%</td>
</tr>
<tr>
<td>4th 2006</td>
<td>35%</td>
</tr>
<tr>
<td>1st 2007</td>
<td>40%</td>
</tr>
<tr>
<td>2nd 2007</td>
<td>45%</td>
</tr>
<tr>
<td>3rd 2007</td>
<td>50%</td>
</tr>
<tr>
<td>4th 2007</td>
<td>55%</td>
</tr>
<tr>
<td>1st 2008</td>
<td>60%</td>
</tr>
<tr>
<td>2nd 2008</td>
<td>65%</td>
</tr>
<tr>
<td>3rd 2008</td>
<td>70%</td>
</tr>
<tr>
<td>4th 2008</td>
<td>75%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CD positive</th>
<th>CD negative</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (x̄ + SD, range)</td>
<td>58.5 ( + 14.8, 26-91)</td>
<td>53.1 ( + 14.8, 26-91)</td>
<td>0.37</td>
</tr>
<tr>
<td>Male (%)</td>
<td>57 (38.7)</td>
<td>13 (33.3)</td>
<td>0.47</td>
</tr>
<tr>
<td>Histologic Abnormalities (%)</td>
<td>11 (7.6)</td>
<td>3 (1.3)</td>
<td>0.08</td>
</tr>
<tr>
<td>Endoscopic abnormalities (%)</td>
<td>12 (8.6)</td>
<td>20 (5.3)</td>
<td>0.08</td>
</tr>
<tr>
<td>Normal (%)</td>
<td>2 (1.3)</td>
<td>0 (0.0)</td>
<td>0.37</td>
</tr>
<tr>
<td>Other (%)</td>
<td>12 (8.6)</td>
<td>20 (5.3)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Characteristics of patients Undergoing Colonoscopy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CD positive</th>
<th>CD negative</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final Diagnosis</td>
<td>CD (n=235)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulcerative colitis (%)</td>
<td>40 (%)</td>
<td>140 (%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Crohn's Disease (%)</td>
<td>40 (%)</td>
<td>140 (%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Indeterminate colitis (%)</td>
<td>40 (%)</td>
<td>140 (%)</td>
<td>0.47</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Findings</th>
<th>CD positive</th>
<th>CD negative</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool abnormalities (%)</td>
<td>40 (%)</td>
<td>140 (%)</td>
<td>0.47</td>
</tr>
<tr>
<td>No symptoms (%)</td>
<td>40 (%)</td>
<td>140 (%)</td>
<td>0.47</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>CD positive (%)</th>
<th>CD negative (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>60</td>
<td>30</td>
<td>0.05</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>20</td>
<td>10</td>
<td>0.05</td>
</tr>
<tr>
<td>Perianal abscesses</td>
<td>20</td>
<td>10</td>
<td>0.05</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>20</td>
<td>10</td>
<td>0.05</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10</td>
<td>5</td>
<td>0.05</td>
</tr>
<tr>
<td>Blood</td>
<td>20</td>
<td>10</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Some patients had more than one symptom.
CD = Clostridium difficile

C. difficile Symptoms

No single symptom associated with C. difficile

Multivariate analysis
Only abdominal pain and weight loss (p<0.01) correlated with CD +

C. difficile Outcome

41 CD +
5 lost
33 treated with metronidazole
1 treated with vancomycin
1 treated with rifaximin
1 treated with probiotics
35 symptoms resolved
1 symptoms continued, but follow up CD -

Positive correlation with the use of acid suppression (p<0.01) and CD +
Too few charts to test antibiotic use and CD +, but 33% of CD + had no history of antibiotic use
### CACD Summary

- Community acquired CD exists
- May be increasing in frequency
- Associated with gastric acid suppression
- Symptoms cannot be used to discriminate between CD + and CD -
- 33% had no history of antibiotic use within 3 months of procedure

### CACD What does it mean?

- Consider stool *C. difficile* toxin titers for children with GI complaints in Buffalo area
- Be careful to use acid suppression only when necessary
- Consider screen for CD even if no history of antibiotic use or admission to a health care facility

### Treatment of CD AD

- **Mild:** Stop antibiotics, Metronidazole PO or IV for 10-14 days
- **Moderate:** Stop antibiotics, Vancomycin PO for 10-14 days
- **Severe:** Stop antibiotics, Vancomycin PO for 10-14 days

### Severe CDAD

- Fever
- Hypotension
- Severe abdominal pain and/or distention
- Ascites
- WBC >15,000
- Albumin <2.5
- Pseudomembranous colitis
- Toxic megacolon
- Perforation
- Shock

### Management of Severe CDAD

- Obtain surgical consult
- Add metronidazole
- Consider rectal vancomycin
- Consider IVIG
- Consider colostomy

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**Figure 1.** Response Rates to Vancomycin and Metronidazole Therapy, According to the Severity of *C. difficile* Infection. Kelly and Lamont NEnglJMed 2008 359:1932
Recurrent CDAD

- After first episode = 20%
- After second episode/first recurrence = 45%
- After third episode/2nd recurrence = 65%

Treatment of Recurrent CDAD

1. First recurrence:
   - Mild: repeat metronidazole
   - Moderate/Severe: repeat vancomycin
2. Second recurrence: Tapering Vancomycin
dosing= QID x 14 days → BID x 7 days →
  QD x 7 days → QOD x 8 days (4 doses) → Every 3
days x 19 days (5 doses)
3. Third recurrence: Vancomycin x 14 days
   followed by rifaximin x 14 days

Non Proven Therapies for CDAD

- *Saccharomyces boulardii* x 28 days
- *Lactobacillus GG* (acidophilus)
- Rifampin

New Epidemic Strain of CDAD

- NAP 1 (North American Pulse Field Type 1)/or BI

This organism has a tcd C gene deletion
which allows increase production of toxin.
Also, a new toxin, the Binary toxin is produced.

References

- CP Kelly and JT LaMont. NEJM 2008;359:1932.
- K Bryant and LC McDonald. PIDJ 2009; 28:1
- MD Zilberberg et al. PIDJ 2008; 27:1111