Clinical management of *Clostridium difficile* infection

Allen Cheng  
Department of Epidemiology and Preventive Medicine,  
Monash University  
Infectious Diseases Unit, Alfred Hospital
C. difficile clinical guidelines

- Recent reports of severe CDI in Melbourne
- ASID CD Working Party established
- Review of literature and current guidelines
- Peer review by ASID members
- Consultation with RACS, TG
- Infection control and laboratory issues addressed separately
Clinical issues

- When to test?
- How to tell if severe?
- How to interpret diagnostic tests?
- How to treat first episode? How to assess response?
- How to treat severe disease? Indications for surgery?
- How to treat recurrences? Role of probiotics?
When to suspect?

- All hospitalized patients with new diarrhoea
- Community-acquired diarrhoea following antibiotics and/or immunosuppression

Risk factors

- Antibiotic use
- Age>65. (Lower rates in children?)
- Chemotherapy
- Gastric acid suppression
Features of severe CDI

- Clinical
  - Fever (T>38.5)
  - Haemodynamic instability
  - Peritonitis or evidence of bowel perforation
  - Ileus or toxic megacolon

- Laboratory
  - WCC>15 x 10^9/L, neutrophils>20%
  - Elevated lactate
  - Rise in creatinine (>50% above baseline)
  - Albumin <25 mg/L

- Other investigations
  - Large intestine distension, colonic wall thickening, fat stranding, unexplained ascites (imaging)
  - Pseudomembranous colitis (colonoscopy)
## Interpretation of tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxigenic culture</td>
<td>Varies</td>
<td>100%</td>
</tr>
<tr>
<td>Cell culture cytotoxicity</td>
<td>Varies</td>
<td>100%</td>
</tr>
<tr>
<td>EIA to GDH</td>
<td>High</td>
<td>Moderate</td>
</tr>
<tr>
<td>EIA to toxin A/B</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>PCR</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>

- Wide diversity of lab practice
  - Varying expertise
  - Optimal strategy varies with volume
- Cost considerations
- Some tests operator dependent
- Screening for hypervirulence with moxi suscept or PCR
Treatment of initial episode

Mild-moderate
- Metronidazole 400 po tds for 10-14 days
- If unable to tolerate oral treatment:
  - metronidazole 500mg iv 8 hourly for 10-14 days

Severe
- Vancomycin 125mg po tds for 10-14 days
- If unable to tolerate oral therapy:
  - metronidazole 500 mg 8 hourly intravenously for 10–14 days plus
  - retention enema of vancomycin 500 mg in 100 mL of normal saline every 4–12 h and/or
  - vancomycin 500 mg qid by nasogastric tube
Why vancomycin?

- Supported by clinical trials (Zar CID 2007)
  - but not in era of 027
- Much higher levels in stool
- Risk of VRE not likely to be impacted on by small numbers of patients with severe CDI
Alternative treatments

- Bacitracin 20,000 units po qid for 7 days
- Fusidic acid 500mg po tds for 10 days
- Tigecycline 100mg IV loading dose, 50mg bd for 14-21 days
- Teicoplanin 100-400mg po bd for 10 days
- Rifampicin 300-600mg po bd (in combination with vancomycin for relapse) for 7-10 days
- Rifaximin 200mg po tds for 10 days
- Nitazoxanide 500mg po bd
- Tolevamer 6g po daily
- Anti-TcdA and TcdB antibodies (10mg/kg, single dose in combination with metronidazole or vancomycin)
- Faecal enema – consider logistical issues, donor screening required
- Intravenous gammaglobulin
Monitoring of response

- Clinical assessment
- 3 days before response
- Re-testing not indicated <30 days

- Indications for surgery
  - Bowel perforation, toxic megacolon
  - Deterioration despite antibiotic treatment
  - Early referral indicated as poor outcome once organ dysfunction established
Treatment of recurrence

- Re-colonisation > relapse
- First recurrence – as for primary episode
- Second recurrence
  - Vancomycin pulsed/tapering course
    - eg 125mg po qid for 14 days
    - then 125mg bd for 7 days,
    - then 125mg every 2^{nd} day for 2-8 weeks
    - (other regimens also described)
  - Other options – fusidic acid, bacitracin
Role of “stool transplant”

- Significant logistical issues
  - Donor screening
  - Processing of the donor specimen
  - Route of administration (NG, PR)
  - Consent
- Difficult to arrange in severe CDI
- “Home blender” protocol (Silverman CGH 2010)
Role of probiotics

- Cochrane review 2008
  - 4 studies of probiotics in treatment
  - Benefit in one study (*Saccharomyces boulardii*) in reducing recurrence rate
- Potential for fungaemia
- Role of probiotics in prevention uncertain
Summary

- Testing required where clinically suspected
- Assess for severity – refer for surgery early
- Different testing strategies
- Metronidazole preferred, vancomycin indicated for severe disease
- Refractory recurrent disease – vancomycin or other alternatives
Areas of uncertainty

- Validity of severity criteria
- Optimal lab testing strategy
- Role of re-testing
- Role of testing in children
- Relative effectiveness of vancomycin vs metronidazole
- Role of alternative treatments (esp tigecycline for severe disease)
ASID CD Working Party

- Allen Cheng, John Ferguson, Mike Richards, Jenny Robson, Lyn Gilbert, Alistair McGregor, Sally Roberts, Tony Korman, Thomas Riley

- Comments from Anton Peleg, Paul Johnson, Chris Lemoh, Kate Cherry, Gerhard Weldhagen, Craig Boutlis, Helen Van Gessel, Raymond Chan, Karen Rowland, David Mitchell, Gillian Wood, Ian Civil, Deirdre Mansell and Michael Grigg