Update on Clostridium difficile infection.

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Introduction

- Gram+anaerobic bacillus responsible for AAC, and 15-25% of cases of nosocomial AAD.

- Wide spectrum of clinical disease: aS, mild to severe diarrhea, PM colitis, toxic megacolon, ileus, sepsis.

- Colonizes up to 5% adults without causing symptom.

- CDI defined as: presence of diarrhea > 3 stools/d, And Stool test+ for CD toxin, Or Colonoscopic or Histologic finding demonstrating PM colitis.
Epidemiology

- Widespread usage of antibio→fluoroquinolone resistance.
- Most common cause of infectious diarrhea in healthcare settings
- Transmission: person to person via fecal-oral route.
- Risk of colonization ↑ linearly with time (40% after 4 wk of hospitalization).
- Changing epidemiology:
Increase in overall incidence

McDonald LC et al, Emerg Infect Dis 2006
Increase in mortality rate

Emergence of hypervirulent strains responsible of outbreaks: NAP1/BI/027

Warny M, Lancet 2005
Pathophysiology

Antibiotics, antibodies and the development of *C. difficile* infection

- **Uncolonised**
  - C. difficile exposure
  - Antibiotic pressure

- **Colonised**
  - No IgG response
  - Antibiotic pressure

- **Asymptomatic**
  - IgG response

- **Diarrhoea**
  - No IgG response
  - Antibiotic pressure + C. difficile exposure

- **Relapse**
  - IgG response
## Risk factors

<table>
<thead>
<tr>
<th>Host factors</th>
<th>Factors that disrupt colonic flora and bowel functioning</th>
<th>Factors that increase exposure to <em>C difficile</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥65 y</td>
<td>Antibiotic use</td>
<td>Antiperistaltic medications</td>
</tr>
<tr>
<td>Comorbidities, IBD</td>
<td>Immunosuppression and chemotherapeutic agents</td>
<td>Contact with spores on hands and objects</td>
</tr>
<tr>
<td>Compromised immune status</td>
<td>Gastric acid-altering medications and PPIs (conflicting evidence)</td>
<td>Contaminated food, water, soil, pets</td>
</tr>
<tr>
<td>Peripartum females</td>
<td>GI surgery and manipulation</td>
<td>Hospitalization</td>
</tr>
<tr>
<td></td>
<td>Obstruction, ileus</td>
<td>Stays in ICU or long-term care facilities</td>
</tr>
</tbody>
</table>
## Risk factors

<table>
<thead>
<tr>
<th>Frequent associated</th>
<th>Occasionally associated</th>
<th>Rarely or No Induction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin or Amoxycillin</td>
<td>Tetracyclines</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Sulphonamides</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Macrolides</td>
<td>Vancomycin</td>
</tr>
<tr>
<td></td>
<td>Trimethoprim</td>
<td>Tetracyclin</td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolones</td>
<td>Chloramphenical</td>
</tr>
</tbody>
</table>


## Diagnosis

- Sigmoido or Colonoscopy with biopsy
- Laboratory tests: ELISA: (most used); PCR (not for routine testing)

<table>
<thead>
<tr>
<th>Test</th>
<th>Detects</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELISA</td>
<td>Assays Toxin A and B</td>
<td>Fast (2-6 hr), easy, high specificity (98.9%)&lt;sup&gt;27&lt;/sup&gt;</td>
<td>Not as sensitive (93.2%)&lt;sup&gt;28&lt;/sup&gt; as cytotoxin assay</td>
</tr>
<tr>
<td>Tissue culture cytotoxin assay</td>
<td>Toxin A and B</td>
<td>Gold standard, high sensitivity (94-100%)&lt;sup&gt;28&lt;/sup&gt; and specificity (85-100%)</td>
<td>Requires tissue culture facility, takes 24-48 hr</td>
</tr>
<tr>
<td>Latex agglutination test</td>
<td>Bacterial enzyme (glutamate dehydrogenase)</td>
<td>Fast, inexpensive, easy to perform</td>
<td>Poor sensitivity &amp; specificity</td>
</tr>
<tr>
<td>Culture</td>
<td>Toxic and nontoxic C. difficile</td>
<td>Sensitive (89 to 100%),&lt;sup&gt;27&lt;/sup&gt; allows strain typing in epidemics</td>
<td>Requires anaerobic culture facility, slow and takes 2-5 days, not specific for toxin producing bacteria</td>
</tr>
<tr>
<td>PCR</td>
<td>Toxin A or B gene in culture isolates or directly in feces</td>
<td>High sensitivity (96.3%) &amp; specificity (100%)&lt;sup&gt;29&lt;/sup&gt;</td>
<td>Costly, requires expertise in molecular diagnostic techniques</td>
</tr>
</tbody>
</table>
Treatment

- Stop Antibiotic if possible.
- Rehydration; Avoid antimotility agents.
- If symptoms improve after a cessation of Antibiotics ➞ no need to treat.
- Asymptomatic patient ➞ no need to treat.
- Treat as: - First episode (mild or moderate, severe),
- Recurrent episode of CDI
Treatment of initial episode of CDI

- First (mild or moderate) episode: Metro 500mg TIDx10-14d, or Vanco 125 mg PO QIDx10-14d which is indicated if no response or intolerance or allergy to metronidazole, or in pregnancy.

- First severe episode: Vanco 125mg PO QIDx10-14d

- First severe complicated episode: Vanco 500mg QID PO/NGT + Metro 500mg TID IV; (Vanco > Metro in severe disease).

A Comparison of Vancomycin and Metronidazole for the Treatment of Clostridium difficile–Associated Diarrhea, Stratified by Disease Severity Clin Infect Dis. 2007
- Adequate replacement of fluid and electrolytes
- Avoid antiperistaltic medications
- Review inciting antibiotic and risk factors for CDI
- Appropriate attention to infection prevention and control

**Mild-to-Moderate CDI:**
- No features of severe CDI
  - Oral metronidazole 500 mg, three times daily for 10–14 days [9**,89**]

**Severe CDI:** (suggested by any of the following)
- Clinical: fever, rigor, abdominal pain
- Laboratory: Leukocytosis of ≥15,000 cells/µl or rise in serum creatinine of ≥50% above baseline [90**]
- Endoscopic findings: pseudomembranous colitis
- Imaging: CT evidence of colitis
  - Oral vancomycin 125 mg, four times daily for 10–14 days [9**,89**]

**Severe, complicated CDI:**
- Suggested by severe disease with:
  - Rising serum lactic acid levels
  - Hypotension
  - Shock
  - Ileus
  - Megacolon
  - Vancomycin 500 mg, oral or nasogastric administration four times daily and
  - Metronidazole 500 mg, intravenous administration three times daily
  - Consider intracolonic vancomycin 500 mg, four to six times daily if ileus present or suspected [89**]
  - Early surgical opinion [91]**
Other antibiotic treatments

<table>
<thead>
<tr>
<th>Reference</th>
<th>Antibiotic</th>
<th>Daily dose*</th>
<th>Duration (days)</th>
<th>No. of patients</th>
<th>Initial cure (%)</th>
<th>Recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wenisch <em>et al.</em> (1996)</td>
<td>Teicoplanin</td>
<td>400 mg b.i.d.</td>
<td>10</td>
<td>28</td>
<td>96</td>
<td>7 NS</td>
</tr>
<tr>
<td></td>
<td>Fusidic acid</td>
<td>500 mg t.i.d.</td>
<td>10</td>
<td>29</td>
<td>93</td>
<td>28 NS</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td>500 mg t.i.d.</td>
<td>10</td>
<td>31</td>
<td>94</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Metronidazole</td>
<td>500 mg t.i.d.</td>
<td>10</td>
<td>31</td>
<td>94</td>
<td>16 NS</td>
</tr>
<tr>
<td>De Lalla <em>et al.</em> (1992)</td>
<td>Teicoplanin</td>
<td>100 mg b.i.d.</td>
<td>10</td>
<td>26</td>
<td>96</td>
<td>8†</td>
</tr>
<tr>
<td>Fekety <em>et al.</em> (1989)</td>
<td>Vancomycin</td>
<td>500 mg q.i.d.</td>
<td>10</td>
<td>20</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td>125 mg q.i.d.</td>
<td>10</td>
<td>24</td>
<td>100</td>
<td>21 NS</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td>500 mg q.i.d.</td>
<td>10</td>
<td>22</td>
<td>100</td>
<td>18</td>
</tr>
<tr>
<td>Dudley <em>et al.</em> (1986)</td>
<td>Bacitracin</td>
<td>25 000 U q.i.d.</td>
<td>10</td>
<td>15</td>
<td>80</td>
<td>33 NS</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td>500 mg q.i.d.</td>
<td>10</td>
<td>15</td>
<td>93</td>
<td>20</td>
</tr>
<tr>
<td>Young <em>et al.</em> (1985)</td>
<td>Bacitracin</td>
<td>20 000 U q.i.d.</td>
<td>10</td>
<td>21</td>
<td>76</td>
<td>24 NS</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td>125 mg q.i.d.</td>
<td>10</td>
<td>21</td>
<td>86</td>
<td>29</td>
</tr>
<tr>
<td>Teasley <em>et al.</em> (1983)</td>
<td>Vancomycin</td>
<td>500 mg q.i.d.</td>
<td>10</td>
<td>52</td>
<td>100</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Metronidazole</td>
<td>250 mg q.i.d.</td>
<td>10</td>
<td>42</td>
<td>95</td>
<td>5 NS</td>
</tr>
<tr>
<td>Mogg <em>et al.</em> (1982)</td>
<td>Colestipol</td>
<td>10 g q.i.d.</td>
<td>5</td>
<td>12</td>
<td>25</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>0</td>
<td>5</td>
<td>14</td>
<td>21</td>
<td>NR</td>
</tr>
<tr>
<td>Keighley <em>et al.</em> (1978)</td>
<td>Vancomycin</td>
<td>125 mg q.i.d.</td>
<td>5</td>
<td>12</td>
<td>92</td>
<td>0†</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>125 mg q.i.d.</td>
<td>5</td>
<td>9</td>
<td>22</td>
<td>44</td>
</tr>
</tbody>
</table>

*Journal of Medical Microbiology, 2005*
Recurrent CDI

- Recurrence rate after a first episode is 20%, and 45% after a second episode, and >60% after 2 or more recurrences.

Recurrent CDI is attributable to:
- Relapse: endogenous persistence of the same strain of CD
- Reinfection: acquisition of a new strain from an exogenous source
- Selection of patients without protective immunity against CD

Mean time to relapse is 14.5 days, whereas mean time to reinfection is 42.5 days

Mechanisms for recurrent CDI are:
- Inadequate immune response to CD toxins.
- Persistent disruption of the normal colonic flora.
Association between antibody response to toxin A and protection against recurrent *Clostridium difficile* infection

Recurrent CDI

Independent predictors of recurrent CDI:

- Age >65 years
- Acquisition of CDI during the hospital stay and a long hospital stay
- Lower quality-of-life score
- Continued use of non-C. difficile-specific antibiotics after diagnosis of CDI
- Concomitant receipt of antacid medication
Recurrent CDI

First recurrence:

Treatment with the same regimen as the initial episode (metronidazole, or vancomycin if severe disease)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of second recurrences/total no. of patients (%)</th>
<th>Unadjusted HR (95% CI)</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment administered for first recurrence of CDAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metronidazole only</td>
<td>42/115 (36.5)</td>
<td>1.00</td>
<td>NS</td>
</tr>
<tr>
<td>Vancomycin only</td>
<td>68/171 (39.8)</td>
<td>0.97 (0.66–1.43)</td>
<td>...</td>
</tr>
<tr>
<td>Metronidazole and vancomycin sequentially</td>
<td>8/20 (40.0)</td>
<td>0.98 (0.46–2.09)</td>
<td>...</td>
</tr>
<tr>
<td>Metronidazole plus vancomycin at once</td>
<td>4/16 (25.0)</td>
<td>0.80 (0.29–2.23)</td>
<td>...</td>
</tr>
</tbody>
</table>

The risk of recurrent CDI is similar with metronidazole and vancomycin

Recurrent CDI

- Second recurrence:
  - Do not treat with metronidazole because of its potential neurotoxicity with prolonged use.
  - Tapered and pulsed regimen of vancomycin is the most widely used: clears *C. difficile* by eradicating cells as spores germinate.
Taper regimen alone has a 31% recurrence rate, and the addition of pulsed doses drops the recurrence to 14.3%
Recurrent CDI

**Multiple recurrent CDI:**

- Probiotics
- Rifaximin
- Nitazoxanide
- Fidaxomicin
- Toxin binders
- Donor fecal transplant
- Immunotherapy
Probiotics (Saccharomyces boulardii)

Potential mechanisms of action:

- **Luminal action**
  - 1. Anti-toxin effect against:
     - (a) *C. difficile* toxins A and B (54 kDa protease)
     - (b) Cholera toxin (120 kDa protein)
     - (c) *E. coli* LPS (63 kDa protein phosphatase)
  - 2. Antimicrobial activity:
    - (a) Preservation of tight junctions
    - (b) Bacteria adhere to Sb, Sb decreases invasion
  - 3. Modulation of intestinal flora
  - 4. Metabolic activity: Sb increases short chain fatty acids, favors normal colonic function

- **Trophic action**
  - 5. Enzymatic activity:
    - (a) Polyamines favor enterocyte maturation
    - (b) Increased disaccharidase levels—beneficial in viral diarrhea
  - 6. Increased sIgA levels increases immune defense in the gut

- **Mucosal action—anti-inflammatory effect**
  - 7. Acts on the cellular signals and decreases synthesis of inflammatory cytokines
Probiotics (Saccharomyces boulardii)

- Probiotics in combination with antibiotics significantly help in preventing recurrences of CDI.

- Risk of fungemia in immunocompromised patients.

- Reduction in the incidence of AAD and CDI associated with a probiotic formula.
Randomized controlled trials for the treatment of C. difficile using *S. boulardii*

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Treatment groups</th>
<th>Study population</th>
<th><em>C. difficile</em> recurrence in probiotic group</th>
<th><em>C. difficile</em> recurrence in placebo group</th>
</tr>
</thead>
<tbody>
<tr>
<td>McFarland et al [52]</td>
<td><em>S. boulardii</em> vs placebo</td>
<td>124 adult patients on varied doses of vancomycin or metronidazole; recurrent and initial CDAD cases; 3 referral sites, US</td>
<td>15/57 (26.3%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>30/67 (44.8%)</td>
</tr>
<tr>
<td>Surawicz et al [60]</td>
<td><em>S. boulardii</em> vs placebo</td>
<td>168 adult patients recurrent CDAD; on vancomycin (2 g/d, n = 32) or V (500 mg/d, n = 83) or M (1 g/d, n = 53); 4 referral sites, US</td>
<td>V (2 g/d) 3/18 (17%)&lt;sup&gt;a&lt;/sup&gt;; V (500 mg/d) 23/45 (51%); M (1 g/d) 13/27 (48.1%)</td>
<td>V (2 g/d) 7/14 (50%); V (500 mg/d) 17/38 (44.7%); M (1 g/d) 13/26 (50%)</td>
</tr>
</tbody>
</table>
Rifaximin

- Poorly absorbed rifamycin derivative
- In cases of multiples recurrences CDI.
- Given with success rate for post-vancomycin treatment with 400mg q 12 h for 14 days.
- But CD may develop resistance to rifaximin which may limit its future utility, particularly against the virulent B1/NAP1/027 strain.
Rifaximin reduced recurrences CDI in vancomycin group.
Therap Adv Gastroenterol. 2010
Nitazoxanide

- Thiazolide compound for treatment of intestinal parasitic infection; interferes with the anaerobic metabolism of protozoa and bacteria, but is expensive.
- As effective as metronidazole and vancomycin, may have role as salvage therapy for refractory-recurrent CDI.

Fidaxomicin

- Macro cyclic antibiotic, active against especially CD, rapidly kills CD (bactericidal) whereas vanco is bacteriostatic.
- Poor activity against gram-negative anaerobes → preserves the normal colonic flora
- Minimal systemic absorption → well tolerated, high fecal concentrations
- Highly active, more selective therapy for CD
Table 3. Rates of Recurrence of *C. difficile* Infection, According to Subgroups, in the Modified Intention-to-Treat and Per-Protocol Populations.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Modified Intention-to-Treat Population</th>
<th>Per-Protocol Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fidaxomicin</td>
<td>Vancomycin</td>
</tr>
<tr>
<td></td>
<td>no./total no. (%)</td>
<td>no./total no. (%)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>19/150 (12.7)</td>
<td>27/134 (20.1)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>20/103 (19.4)</td>
<td>40/131 (30.5)</td>
</tr>
<tr>
<td>Hospital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>24/136 (17.6)</td>
<td>40/146 (27.4)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>15/117 (12.8)</td>
<td>27/119 (22.7)</td>
</tr>
<tr>
<td>Previous episode of <em>C. difficile</em> infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>30/211 (14.2)</td>
<td>52/217 (24.0)</td>
</tr>
<tr>
<td>Yes</td>
<td>9/42 (21.4)</td>
<td>15/48 (31.2)</td>
</tr>
<tr>
<td>Treatment for current episode of <em>C. difficile</em> infection in previous 24 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16/88 (18.2)</td>
<td>25/97 (25.8)</td>
</tr>
<tr>
<td>No</td>
<td>23/165 (13.9)</td>
<td>42/168 (25.0)</td>
</tr>
<tr>
<td>Severity of disease at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>7/59 (11.9)</td>
<td>20/68 (29.4)</td>
</tr>
<tr>
<td>Moderate</td>
<td>20/102 (19.6)</td>
<td>18/88 (20.5)</td>
</tr>
<tr>
<td>Severe</td>
<td>12/92 (13.0)</td>
<td>29/109 (26.6)</td>
</tr>
<tr>
<td>Strain type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NAP1/BI/027</td>
<td>16/59 (27.1)</td>
<td>14/67 (20.9)</td>
</tr>
<tr>
<td>Non–NAP1/BI/027</td>
<td>12/117 (10.3)</td>
<td>34/121 (28.1)</td>
</tr>
<tr>
<td>Concomitant systemic antimicrobial therapy</td>
<td>14/81 (17.3)</td>
<td>25/90 (27.8)</td>
</tr>
</tbody>
</table>
Fidaxomicin/Tigecycline

- Promising drug for treating C. difficile infection because of its efficacy in preventing relapses, the low induction of antibiotic resistance, and the minimal effect on fecal microbiota.

- Fidaxomicin 200mgx2/d at least as effective as Vancomycin125x4/d for treatment of initial or first recurrence of CDI.

- Recurrence rates with fidaxomicin were lower(13%) compared to vancomycin(25%).

- Tigecycline: analogue of minocycline used iv as adjunctive therapy for severe and refractory CDI.
Toxin binders

- Efficacy of these agents in toxin binding has not been clearly established.

- Treatment with ion-exchange resins (cholestyramine) is not recommended when vancomycin is given, due to their antibiotic-binding property.

- Polymer (Tlevamer): inferior to vancomycin and metronidazole for treatment of CDI, but the recurrence rate is lower in those who respond.
Donor fecal transplant

- Efficacy of fecal transplant in restoring the colonic microflora of recurrent CDI patients and preventing additional CDI episodes in patients with multiple recurrences

- Barriers to the use of bacteriotherapy includes: acceptability of fecal transplantation, minimal risk of horizontal transmission of pathogens from the donor, theoretically risk of small intestinal bacterial overgrowth after duodenal instillations of feces.

Aliment Pharmacol Therapy 2011
Passive immunisation:

- A recent study reported a high mortality rate (57%) in 21 patients treated with IVIG for severe CDI.

- IVIG may have a role in recurrent or severe CDI confined to the colon, but may be less beneficial once extracolonic organ dysfunction and systemic inflammatory response syndrome develop.

- Definitive recommendations are not possible with the currently available literature.

Abouergi MS et al. J Hosp Med 2010
Immunotherapy

Monoclonal antibodies to toxins A and B:

Treatment with monoclonal antibodies against C difficile toxins, NEJM 2010
Surgery

- Urgent for patient $> 65$ y with: toxic megacolon, perforation, necrotizing colitis, or refractory disease with multiorgan system failure.

- Two surgical approaches for management of complicated CDI: subtotal colectomy, and diverting loop ileostomy.
Suggested approach to recurrent CDI

Primary CDI
- Discontinue the inciting antibiotic if possible (occasionally this is the only intervention necessary)
- Metronidazole (500 mg Q8H x 10–14 d) OR
- Vancomycin (125 mg Q8H x 10–14 d)$^a$

First CDI Recurrence
- Metronidazole or vancomycin$^a$

Second CDI Recurrence
- Vancomycin taper, followed by pulse (125 mg Q6H x 10–14 d → 125 mg Q12H x 7 d → 125 mg Q24H x 7 d → 125 mg every 2–3 d x 2–8 wks)$^b$

Third and Subsequent Recurrence$^c$
- Vancomycin 500 mg, Q6H x 10 d + S. boulardii (1 g Q24H) x 28$^{45}$
- Vancomycin 125 mg Q6H x 10 to 14 d, stop vanco, then start rifaximin 400 mg Q12H x 2 wk$^{35}$
- Vancomycin 125 mg Q6H + rifampin 600 mg BID x 7 d$^{44}$
- Fecal transplantation$^{53}$
- Nitazoxanide 500 mg Q12H x 10 d$^{43}$
- IVIG 400 mg/kg$^{29}$
# Prevention: infection control measures

<table>
<thead>
<tr>
<th>Variable</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand hygiene</td>
<td>A-II</td>
</tr>
<tr>
<td>Contact precautions</td>
<td></td>
</tr>
<tr>
<td>Glove use</td>
<td>A-I</td>
</tr>
<tr>
<td>Gowns</td>
<td>B-III</td>
</tr>
<tr>
<td>Use of private rooms or cohorting</td>
<td>C-III</td>
</tr>
<tr>
<td>Environmental cleaning, disinfection, or use of disposables</td>
<td></td>
</tr>
<tr>
<td>Disinfection of patient rooms and environmental surfaces</td>
<td>B-II</td>
</tr>
<tr>
<td>Disinfection of equipment between uses for patients</td>
<td>C-III</td>
</tr>
<tr>
<td>Elimination of use of rectal thermometers</td>
<td>B-II</td>
</tr>
<tr>
<td>Use of hypochlorite (1,000 ppm available chlorine) for disinfection</td>
<td>B-II</td>
</tr>
</tbody>
</table>

_SHEA-IDSA Guideline, 2010_
Prevention: prudent use of antibiotics

Valiquette L, CID 2007
- CDI emerged as serious public health threat, with more virulent strains causing severe disease, and increased rate of incidence and prevalence.

- Hypervirulent CD strains causes worldwide epidemics; CDI is primarily a preventable disease.

- Preventing and controlling disease is a huge challenge. Diagnosis; CDI remains problematic, as no single test is sensitive or specific enough.

- Diagnosis is confirmed by culture or the presence of CD toxins in stool, and by colonoscopy and histology.

- First step in treatment is to discontinue offending antibiotic.
Metronidazole and vancomycin are the mainstays of treatment for both initial infection and first recurrence.

Vancomycin is recommended for severe or recurrent episode, and if intolerance for metronidazole, or in pregnancy.

For severe complicated CDI → Vancomycin + Metronidazole

For second recurrence, Vancomycin course (tapering and pulsed regimen) is recommended.

For subsequent recurrences, Fidaxomicin appears promising with less relapses compared to vancomycin.
Thank you