CLOSTRIDIUM DIFFICILE DIARRHEA

*Clostridium difficile* diarrhea is a complication of antibiotic therapy. A pseudomembranous colitis is present in severe cases (Box 6.A), with sloughing of the inflamed colonic epithelium, manifesting as foul-smelling diarrhea mingled with mucus and blood. *C. difficile* diarrhea has a mortality of up to 25% in elderly frail patients.

<table>
<thead>
<tr>
<th>Causal antibiotics</th>
<th>Most prevalent</th>
<th>Highest incidence</th>
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<tbody>
<tr>
<td>Ampicillin</td>
<td>Clindamycin</td>
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<tr>
<td>Amoxicillin</td>
<td>Lincomycin</td>
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<tr>
<td>Cephalosporins</td>
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<td>Ciprofloxacin</td>
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<td>Clarithromycin</td>
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<td>Erythromycin</td>
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<table>
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<tr>
<th>Clinical features</th>
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<tr>
<td>Watery diarrhea + mucus ± blood</td>
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<tr>
<td>Abdominal pain and tenderness</td>
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<tr>
<td>Fever and malaise</td>
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<td>+/- Dehydration and delirium</td>
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Symptoms generally begin within 1 week of starting antibiotic therapy or shortly after stopping, but may occur up to 1 month later. It is caused by colonization of the bowel by *C. difficile* and the production of toxins A and B which cause the mucosal damage. A failure to mount an immune response is associated with colonization and toxin production. Risk factors include:

- increasing age
- severe underlying disease
- immunosuppression
- treatment in an intensive care unit
- long inpatient stay in hospital
- long duration of causal antibiotic treatment
- multiple antibiotics
- non-surgical gastro-intestinal procedures
- nasogastric tube
- anti-ulcer medication

*C. difficile* is spread indirectly by the fecal-oral route, by spores left on surfaces:

- asymptomatic colonization in the general population is about 5%
- asymptomatic colonization in a hospital population may be >20%
- in about 1/3 of those colonized, *C. difficile* produces diarrhea-producing toxins.

**Diagnosis**

- a high level of suspicion in high-risk patients who develop diarrhea (>300ml of liquid feces in 24h)
• *C. difficile* is strongly anaerobic and difficult to culture; most laboratories no longer attempt to culture it.
• Diagnosis is confirmed by the detection in the feces of toxins produced by *C. difficile*.
• If in doubt, endoscopy and rectal biopsy are of value, although a trial of therapy is more practical.

**Management strategy**

**Preventive measures**
Spread of *C. difficile* is by the ingestion of spores from the environment around symptomatic patients. Environmental controls (‘universal precautions’) will generally prevent the spread of outbreaks:
• Patients should be isolated while they have diarrhea.
• Carers should use gloves and gowns, and thoroughly wash their hands after patient contact using either soap or alcohol-based products.

**Drug treatment**
• Metronidazole is the treatment of choice; it is as effective as vancomycin and much cheaper.
• Vancomycin is generally reserved for patients with an ileus or those who are severely ill.
• About 20% of patients relapse, most within 3 weeks. This may be caused by germination of residual spores within the colon, re-infection with *C. difficile* or further antibiotic treatment.
• Mild relapses often resolve spontaneously; repeat treatment with metronidazole is still recommended.
• Probiotics may reduce the incidence of relapse.
• Repeated relapses require prolonged treatment with a slowly decreasing dose of vancomycin.
• Relapse due to resistance of *C. difficile* to antibiotic treatment is rare.

**Dose and use**
• Metronidazole 500mg PO t.i.d. for 10 days.
• Vancomycin 125mg PO q.i.d. for 10 days.

**Supply**
See metronidazole, p.282.

**Vancomycin (generic)**
*Injection (powder for reconstitution)* 500mg, 1g vial = $11 and $21 respectively (AWP).

Vancocin® (Lilly)
*Capsules* 125mg, 250mg, 10 days @ 125mg q.i.d. = $256.
*Oral suspension* 250mg/5ml, 10 days @ 125mg q.i.d. = $186 (AWP).
*Injection* 500mg/100ml, 100ml bag and 200ml bag = $18 and $35 respectively (AWP).
Vancomycin injection can be used to prepare an oral solution as a cheaper alternative to the capsules and suspension; add 10ml WFI to a 500mg vial of powder and give 2.5ml q.i.d. with added flavoring (10-day course = $110).

9 Surawicz CM et al. (2000) The search for a better treatment for recurrent Clostridium difficile disease: use of high-dose vancomycin combined with Saccharomyces boulardii. Clinical Infectious Diseases. 31: 1012–1017.