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.¹

Box 6.A Clostridium difficile diarrhea

Causal antibiotics²

Most prevalent Ampicillin Amoxicillin Cephalosporins Ciprofloxacin Clarithromycin Erythromycin *Highest incidence* Clindamycin Lincomycin

Clinical features

Watery diarrhea + mucus ± blood Abdominal pain and tenderness Fever and malaise +/- Dehydration and delirium

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.³
- 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.⁴

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**^{5,6} 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 recommended⁷
- probiotics may reduce the incidence of relapse^{8,9}
- repeated relapses require prolonged treatment with a slowly decreasing dose of vancomycin¹⁰
- 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 WFl to a 500mg vial of powder and give 2.5ml q.i.d. with added flavoring (10-day course = \$110).

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- 3 Bignardi GE (1998) Risk factors for Clostridium difficile infection. *Journal of Hospital Infection.* **40**: 1–15.
- 4 Starr J (2005) Clostridium difficile associated diarrhoea: diagnosis and treatment. *British Medical Journal.* **331**: 498–501.
- 5 Cherry R et al. (1982) Metronidazole: an alternate therapy for antibioticassociated colitis. *Gastroenterology.* **82**: 849–851.
- 6 Teasley D *et al.* (1983) Prospective randomised trial of metronidazole versus vancomycin for Clostridium difficile-associated diarrhoea and colitis. *Lancet.* **2**: 1043–1046.
- 7 Tabaqchali S and Jumaa P (1995) Diagnosis and management of Clostridium difficile infections. *British Medical Journal.* **310**: 1375–1380.
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