

Treatment of *Clostridium difficile*

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Introduction and Purpose

Antimicrobial Guidelines are intended to provide clinicians guidance on the management (both treatment and prevention) of common infections. This guideline forms part of a series of antimicrobial guidelines.

The clinical guidelines provide evidence based and best practice on the management of patients with infective episodes. They include empirical antimicrobial therapy including dose, route and duration of therapy and where necessary microbiological investigations.

Objectives

- To improve the quality of antimicrobial prescribing and reduce inappropriate prescribing.
- To maximise the clinically effectiveness of antimicrobial agents used.
- To reduce drug related toxicity and development of antimicrobial resistance.
- To ensure cost effective use of antimicrobial agents.

Scope

This guideline applies to all healthcare professionals involved in the prescription, administration and monitoring of antimicrobial agents.

Development and consultation

The clinical guidelines have been produced by the lead clinician and lead pharmacist for each division in conjunction with microbiology.

Implementation and Monitoring and documentation

Implementation and adherence to the guidelines is the responsibility of the lead clinician and lead pharmacist for each division.

Key aspects of the guidelines will be monitored as part of the annual audit programme.

This document should be used in conjunction with the operational guidance for the control and management of *Clostridium difficile* available at http://www.infectioncontrolservices.co.uk/clostridium_difficile.htm

Background

Clostridium difficile is an important cause of diarrhoea in hospitalised patients. Some will have mild symptoms while others will have severe diarrhoea which may progress to life-threatening pseudomembranous colitis. A virulent strain (type 027) has been responsible for recent outbreaks in many trusts.

Prudent antimicrobial usage is one of the main strategies for control and prevention of *Clostridium difficile* infection (CDI). Some antibiotics appear to have a higher propensity to cause CDI than others. The highest risk antibiotics are:

- 2nd /3rd generation cephalosporins
- Fluoroquinolones
- Clindamycin

Risk factors for *Clostridium difficile* infection (CDI)

The principal risk factors are:

- Recent courses of antibiotics (especially longer courses of broad spectrum antibiotics)
- Patients >65 years and those with underlying co-morbidities
- Patients with a previous history of CDI
- The use of anti-ulcer medications in patients with diarrhoea
- Presence of nasogastric tube
- Prolonged hospital stay

Clostridium difficile toxin (CDT) testing

- Formed stools will not be tested.
- CDT testing is performed from Monday to Saturday.
- Samples should be sent for all hospital patients with diarrhoea and on newly admitted patients with risk factors for CDI.
- Stools will not be tested if CDT has been positive within the last 4 weeks.

- If the result of the CDT test is negative and CDI is still clinically suspected, treatment should continue and a repeat specimen should be sent 7 days after the first negative test.
- If CDI is clinically suspected treatment should be initiated before the result of the test is available.

First episode of CDI (for severe CDI see below)

- Discontinue precipitating antibiotic, if possible, or substitute with antibiotic(s) that have lower propensity to induce CDI. Contact microbiology for advice.
- Correct fluid and electrolytes (orally or intravenously).
- Consider nutritional supplements especially in elderly patients.
- Avoid anti-motility agents (e.g. loperamide, opioids) and any other drugs that may cause diarrhoea.
- Review use of proton pump inhibitors (PPIs) and immunosuppressive agents.

MILD – MODERATE CDI	
1 st line	Metronidazole 400mg PO 8 hourly OR Metronidazole 500mg IV 8 hourly (if unable to tolerate PO medication) for 10 - 14 days Do not exceed 2 weeks of therapy owing to risk of peripheral neuropathy
2 nd line	If poor response to 1 st line agent after 1 week, switch to Vancomycin caps 125mg PO 6 hourly for 10 - 14 days <i>Do NOT administer vancomycin intravenously – it is NOT effective</i>

Response to therapy should be reviewed daily. If there are signs of disease progression, treat as for severe disease.

Severe CDI disease

Severe CDI is indicated by one or more of the following:

- WBC > 20
- Albumin <25
- Dilated, oedematous colon on AXR
- Creatinine > 200
- Temp >38.5⁰ C
- Septic shock

1 st line for severe CDI	Vancomycin caps 125mg PO 6 hourly for 10 – 14 days <i>Do NOT administer vancomycin intravenously – it is NOT effective</i>
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Patients with severe disease MUST be reviewed on a daily basis with input from Microbiology. Contact gastroenterology and/or surgeons for a combined review. ITU may also need to be involved.

Treatment of recurrent or refractory cases of CDI

- Approximately 20-30% of patients infected with *C. difficile* will suffer a recurrence either in hospital or the in the community.
- Confirm diagnosis with toxin test if more than 4 weeks since last positive result.
- Withhold anti-CDI antibiotics if symptoms are mild – this may be adequate treatment.

<p>st 1 line for recurrent/refractory CDI</p>	<p><u>Vancomycin</u> caps 125mg PO 6 hourly for 10 - 14 days <i>Do NOT administer vancomycin intravenously – it is NOT effective</i></p>
<p>nd 2 line if further recurrence</p>	<p>Tapered pulsed oral <u>vancomycin</u> regimen: 125mg PO 6 hourly for 7days 125mg PO 8 hourly for 7 days 125mg PO 12 hourly for 7 days 125mg PO 24 hourly for 7 days 125mg PO alternate days for 7 days 125mg PO every third day for 7 days, then stop</p>

Non-antibiotic treatments for CDI

- Cholestyramine is known to bind C. difficile toxin but is **not** deemed clinically effective and it may in fact bind vancomycin, and therefore it is **not** recommended.
- The evidence for the use of probiotics and prebiotics is equivocal and they are not used either prophylactically or as part of treatment routinely at this hospital but can be considered on an individual patient basis.
- Faecal enemas for relapses have been used in a limited number of patients in Canada and Scandinavia with some success. The decision to proceed with this must be discussed with consultant microbiologist.

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***Clostridium difficile* infection (CDI) treatment algorithm**

