GUIDELINE FOR THE MANAGEMENT OF ANTIBIOTIC- ASSOCIATED DIARRHOEA IN ADULTS

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Evidence Base	<ul> <li>Clarkson, Maureen Milligan and Sarah Pacey.</li> <li>Local microbiological sensitivity surveillance</li> <li>Published evidence from studies.</li> <li>Draft report from the Steering group on Healthcare Associated Infection report on <i>C difficile</i> How to deal with the problem A Board to Ward Approach</li> </ul>
Changes from	New severity criteria
previous Guideline	Oral vancomycin first line for severe disease
Inclusion Criteria	<ul> <li>Adult patients with diarrhoea who have also received antibiotics in the previous 4 weeks.</li> </ul>
Exclusion Criteria	Haematology patients – see local guidance
Audit	Annual Directorate Audit Plans as appropriate
Distribution Local Contacts	<ul> <li>NCH and QMC Antibiotic websites</li> <li>Consultants via trust e-mail.</li> <li>NUH document library</li> <li>Dr Vivienne Weston, Consultant Microbiologist, QMC</li> <li>Ext 64179</li> <li>E-mail vivienne.weston@nuh.nhs.uk</li> </ul>

This guideline has been registered with the Trust. However, clinical guidelines are 'guidelines' only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt consult a senior colleague or expert. Caution is advised when using guidelines after the review date.

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# MANAGEMENT OF ANTIBIOTIC-ASSOCIATED DIARRHOEA IN ADULTS (EXCLUDING HAEMATOLOGY PATIENTS)



# Antibiotic associated diarrhoea and C. difficile infection

Diarrhoea is a common side effect of antibiotic use and can be due to a number of causes. An important cause in hospitalised patients is due to infection with *Clostridium difficile*. Antibiotics disrupt the protective normal bacterial flora of the gut, allowing colonisation by *C. difficile*, following the germination of ingested spores. The diarrhoea and colitis occur as a consequence of toxins secreted by *C. difficile*. The clinical picture in *C. difficile* infection may vary from mild diarrhoea through to a fulminant life-threatening pseudomembranous colitis.

Symptoms may start as early as day one of antibiotic use or even up to four weeks after discontinuation of antibiotics. Most antibiotics have been implicated in the development of *C. difficile*-associated diarrhoea but broad-spectrum penicillins (e.g. amoxicillin, co-amoxiclav), clindamycin and the cephalosporins are common culprits. Previously, oral quinolone antibiotics e.g. levofloxacin, were recommended for use as alternative treatments in units where *C. difficile*-associated disease is endemic as they were active against *C. difficile* and produced lower rates compared to the broad-spectrum penicillin and cephalosporin agents. This advice has now changed as quinolone resistant, highly virulent strains (causing increased mortality), are emerging across the UK. In areas where these strains are established (e.g. Quebec, Canada), quinolone antibiotics were the most common cause of *C. difficile*-associated disease, it is important that antibiotics are used appropriately and that the more narrow-spectrum agents are prescribed where possible.

*C. difficile* infection is usually acquired in hospital and because the elderly are especially susceptible, this infection can be a particular problem in health care of the older person and medical wards, where outbreaks have occurred. Recent studies in Nottingham suggest that 20-30% of patients with *C. difficile* infection are admitted to hospital following the onset of diarrhoea in the community particularly in the elderly population where they have recently had antibiotics e.g. nursing home patients.

Affected patients with diarrhoea secrete large numbers of *C difficile* and its spores, leading to contamination of the environment surrounding the patient. The spores are resistant to most commonly used disinfectants and transmission of infection is generally thought to occur via hands of staff, direct contact with affected patients or contaminated surfaces in the ward (e.g. bathrooms, furniture, bed sheets). Enteric precautions (as per infection control policies on *Clostridium difficile* and isolation) are therefore an important aspect of patient management and the Infection Prevention and Control Team should be consulted for further advice. Ward F22 at the QMC campus is a dedicated Gastroenterology facility with single room accommodation. A patient with *C.difficile* diarrhoea at the QMC campus should be referred and transferred to this facility as per the F22 Admission criteria located on the Infection Prevention and Control Intranet Site.

## Microbiological Examination for C. difficile Toxin

The laboratory test for evidence of *C. difficile* infection involves examination of a diarrhoeal stool sample for the presence of *C difficile* toxin (CDT). The toxin biodegrades at room temperature (increasing the possibility of false negative results), stool samples should therefore be placed in a refrigerator if there is to be any delay in transportation. If the first stool sample is negative for CDT, another sample should be sent for examination before the patient is considered to be CDT negative. Liquid stools from adult patients (Bristol stool chart types 6 or 7) will be examined for CDT routinely; non-diarrhoeal formed stools will not be processed even if CDT is specifically requested. Relevant history and details of the antibiotics the patient has taken should be given on the request card.

## Sigmoidoscopy (excludes haematology and neutropaenic patients)

.Please contact the Gastroenterology Nurse Specialists at City and QMC campus using the NOTIS referral 'Diarrhoea Services' for consideration of flexible sigmoidoscopy if the patient has:

1. Frequent diarrhoea (>7x/day), or features suggesting severe disease, without waiting for stool *C. difficile* toxin result - stool sample can be taken at sigmoidoscopy.

2. Moderately frequent diarrhoea (4 - 7x/day) and one stool sample negative for *C. difficile* toxin

3. Mild diarrhoea (<4x/day) and two stool samples negative for C. difficile cytotoxin.

Recent studies in Nottingham have shown that the first stool *C. difficile* cytotoxin test may be negative in a significant proportion of patients with pseudomembranous colitis.

Sigmoidoscopy (ideally flexible sigmoidoscopy) should therefore be considered early in any patient suspected to have pseudomembranous colitis, especially if the first stool sample is negative for *C. difficile* cytotoxin. Since flexible sigmoidoscopy may also enable other causes of diarrhoea to be determined (e.g. inflammatory bowel disease), early endoscopy may facilitate rapid diagnosis and treatment. For patients with *C. difficile* infection such a strategy may also reduce the risk of transmission to others

#### Management of the affected patient

#### See flow diagram

If the patient is still on other antibiotics consider whether these can be stopped.

Severe disease i.e. pseudomembranous colitis (PMC) needs to be considered and appropriate treatment initiated immediately. If the patient has or has had diarrhoea after antibiotic therapy in the preceding 4 weeks and develops abdominal distension and pain, dilated colon on AXR or other radiological imaging, pseudomembranous colitis on sigmoidoscopy, or 1 or more of the following:- WBC >15x10<sup>9</sup>/L, temperature >38.5 °C, acute rise in serum creatinine e.g. >50% increase above baseline or tachycardia >100 bts/min .The patient will be excreting *C. difficile* Nottingham University Hospitals Antimicrobial Guidelines Committee Updated May 2008 Review May 2010

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therefore they should be nursed with appropriate enteric precautions (as per infection control policies on *C. difficile* and isolation). Contact Infection Prevention and Control Team for advice (Ext. 63866 Queens campus; 55578 or HISS referral CNSIC at City campus).

In Nottingham oral Metronidazole is currently the antibiotic treatment of first choice for non-severe disease due to concerns about the emergence of Vancomycin resistance in enterococci. **Oral** (not IV) vancomycin is reserved for severe or non-responsive disease. Only about 5-10% of IV metronidazole enters the bowel and IV vancomycin does not enter the bowel, therefore treatment should be given orally where possible, if the patient is vomiting the alternative is IV Metronidazole. For these and other cases with severe pseudomembranous colitis, please seek early specialist advice. [Gastroenterology Nurse Specialist NOTIS referral DIRR].

Disease recurrence occurs in 20-30% of patients, and is more common in elderly patients, once the patient has had one recurrence the risk of a further recurrence increases to 40-60%. It is therefore important to consider *C.difficile* disease and to initiate early appropriate treatment and investigation, to avoid unnecessary use of antibiotics and use narrow spectrum agents wherever possible. If the patient was successfully treated with an initial course of oral Metronidazole, a further course of oral Metronidazole would be appropriate (unless they now have severe disease) as normally the recurrence is due to a new infection in an at-risk individual rather than re-activation of unsuccessfully treated disease. Patients who deteriorate clinically, fail to respond after 3 days therapy, or have a further recurrence of disease following two courses of Metronidazole should be treated with **oral** Vancomycin for 10 days. For cases with recurring disease please contact gastroenterology / microbiology as above for consideration of use of other forms of treatment, which are currently being evaluated and therefore their use is restricted.

# Remember:

- 1 Use antibiotics appropriately.
- 2 Follow the hospital formulary and prescribing guidelines available at <u>http://nuhweb/antibiotics</u>.
- 3 Use narrow spectrum antibiotics whenever possible
- 4 Review all antibiotics daily, intravenous antibiotics at 48 hours and oral antibiotics at 5 days. Add durations and indications to antibiotic prescriptions.
- 5 Review empiric treatment with microbiology results. Convert to a narrower spectrum agent if possible.
- 6 Consider the diagnosis of *C. difficile* diarrhoea in patients who develop diarrhoea having had antibiotics in the preceding 4 weeks
- 7 Clearance stools samples are not required.