

## Clostridium difficile Associated Disease (CDAD)

*Clostridium difficile* Associated Disease (CDAD) is the most common cause of antibiotic associated diarrhoea. Symptoms present 5-10 days after starting antibiotics. Up to 3% of the population are asymptomatic carriers of *Clostridium difficile* and although they have no symptoms they represent an infection control issue as they can spread the infection.

### Diagnosis of CDAD

- One or more episodes of stool loose enough to take the shape of the container (types 5-7 on the Bristol Stool Chart, see Appendix 2)
  - **PLUS** not attributable to another cause including medicines
  - **PLUS** a positive laboratory test for *Clostridium difficile* toxin
- **OR** evidence of pseudomembranous colitis on endoscopy

### Risk Factors for Severe Disease:

- Age >85 years
- Temperature >38.5°C
- Increasing creatinine
- Signs of colitis
- Colonic dilatation
- Immunosuppressed
- Admission to Intensive Care Unit
- White blood cell count >15 x 10<sup>9</sup>/L **OR** <1.5 x 10<sup>9</sup>/L

### Clinical Features

- Diarrhoea
- Nausea
- Dehydration
- Abdominal pain
- Fever
- Bowel perforation
- Toxic megacolon (>6cm diameter with no obstruction)

### Warning

Certain antibiotics are regarded as high-risk for predisposing to *Clostridium difficile* and should be used with caution. **REMEMBER** the "4Cs":

- **C**ephalosporins
- **C**iprofloxacin (and other quinolones)
- **C**lindamycin
- **C**o-amoxiclav

### Causes

CDAD is caused by toxins produced by the bacterium *Clostridium difficile*.

### Investigations

- Stool (liquid stool only) 2-stage test taking 3-4 hours and performed daily by laboratories
  - All inpatients >2 years old, with a liquid stool sample
  - All outpatients >65 years old, with a liquid stool sample
  - Outpatients under 65 years old, with a liquid stool sample, if specifically requested
- Sampling to test for cure is not required; 50% of successfully treated patients have positive tests up to 6 weeks after infection has cleared.

## Myth

Microbiology laboratories cannot test for *Clostridium difficile* toxin in children under 2 years old. **FALSE** - Laboratories can do this test but the results would be meaningless, as almost all babies are temporarily colonised with *Clostridium difficile* in their guts. This gradually disappears as they get older. Under 2 year olds are not clinically affected by this colonisation because they do not have gastrointestinal receptors for the toxin.

## Treatment

**Stop the offending antibiotic.** If the patient still requires treatment for another infection then discuss the options with a Microbiologist and consider continuing *C. difficile* treatment for 1 week beyond stopping the other antibiotics. Severe and critically ill patients need an urgent surgical review.

Initial Episode of Infection	
Mild/Moderate	PO Metronidazole 500mg TDS
Severe	PO Vancomycin 125mg QDS <b>IF NO RESPONSE</b> PO Vancomycin 500mg QDS
Critically Ill	PO Vancomycin 500mg QDS <b>PLUS</b> IV Metronidazole 500mg TDS

Recurrent Infection	
1 <sup>st</sup> Recurrence	As for Mild/Moderate or Severe above
2 <sup>nd</sup> Recurrence	PO Vancomycin 125mg QDS for 14 days <b>THEN</b> TDS for 3 days, <b>THEN</b> BD for 3 days, <b>THEN</b> OD for 3 days <b>OR</b> PO Fidaxomicin 200mg BD for 10 days
Further recurrences	PO Vancomycin 125mg QDS for 14 days <b>OR</b> PO Fidaxomicin 200mg BD for 10 days <b>THEN</b> PO Rifaximin 400mg TDS for 10 days

Antibiotics that **DO NOT** normally predispose to CDAD:

- IV Piptazobactam
- PO Doxycycline
- IV Benzylpenicillin
- IV Vancomycin
- IV Teicoplanin
- IV Temocillin

## Common Mistake

Some doctors assume that treatment with PO Vancomycin should be converted to IV when treating CDAD in patients who are "nil by mouth". **This is a mistake.** IV Vancomycin does not get into the gut lumen and therefore has no activity in CDAD. If it is not possible to give an oral or nasogastric antibiotic the patient should be discussed with a Microbiologist or Gastroenterologist.

### **Total Duration**

Initial Episode: 14 days

Recurrent Infections: as stated in treatment table

### **Dosing**

See section - Antibiotics, Empirical Antibiotic Guidelines.

### **On the Horizon**

Future treatment of CDAD may include faecal bacteriotherapy, also known as "faecal transplantation", which involves replacement of the colonic content with stool containing normal flora from a related donor. Faecal bacteriotherapy has a 94% cure rate in pseudomembranous colitis caused by *C. difficile*. The lack of widespread adoption in the NHS, even though it is approved by the National Institute for Health and Care Excellence (NICE), is related to the social and medical stigmatisation associated with the concept of deliberately introducing someone else's faeces into another person.

### **Prognosis and Complications**

90% of patients with CDAD respond to treatment. However, 20-30% of these have recurrent infection. These patients should be retreated. The mortality from toxic megacolon is 64%.

### **Prophylaxis and Prevention**

*Clostridium difficile* can exist as both spores and vegetative bacteria and therefore can survive drying. The bacteria can persist in the environment for a long time and hence the need for deep cleaning between patients. Environmental control is the best way to prevent CDAD.

### **Infection Control Precautions**

See section - Infection Control, *Clostridium difficile* Associated Disease.