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# Successful control of *Clostridium difficile* infection in an elderly care unit through use of a restrictive antibiotic policy

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**Toxin-producing *Clostridium difficile* is the commonest bacterial cause of nosocomial diarrhoea and is a well recognized cause of hospital outbreaks in elderly care units. High *C. difficile* disease rates have been associated with the use of broad-spectrum antibiotics, especially cephalosporins. An outbreak of *C. difficile* infection in the elderly care unit at Gloucestershire Royal NHS Trust continued despite increased ward cleaning and strict implementation of infection control measures. A restrictive antibiotic policy that would maintain colonization resistance in the gastrointestinal tract was introduced throughout this unit. Patients admitted with suspected infection were prescribed intravenous (iv) benzylpenicillin 1.2–1.8 g every 6 h to cover streptococcal infections and iv trimethoprim 200 mg twice daily to cover urinary tract pathogens and *Haemophilus influenzae*. If the patient had septic shock a single iv dose of gentamicin was given (120–180 mg) to cover more resistant Gram-negative bacilli. The following were monitored before and after the policy change. The number of cases of *C. difficile* toxin-positive diarrhoea; cefuroxime and total antibiotic use on the elderly care wards; patient mortality rates; and length of hospital stay: two hundred and fifty-two and 234 patients respectively with a discharge diagnosis of infection were admitted before and after the antibiotic policy change. Mortality rates and length of hospital stay were unchanged. Cefuroxime prescribing and total antibiotic prescribing costs fell by £5150 and £8622 respectively in the 7 month period after the change. Thirty-seven cases of *C. difficile* diarrhoea occurred in the period before and 16 in the period after the policy change. The incidence of *C. difficile diarrhoea* and of cefuroxime use has remained low since then. The use of narrow-spectrum antibiotics for hospital treatment of community-acquired infections in the elderly should be encouraged. Outbreaks of *C. difficile* diarrhoea should be managed with the combined approach of infection control and strict antibiotic policies.**

## Introduction

Toxin-producing *Clostridium difficile* is the commonest bacterial cause of nosocomial diarrhoea.[1] There has been a six-fold increase in the number of reports of *C. difficile* diarrhoea in the 1990s.[2] The spectrum of disease is wide-ranging from a symptomatic carriage through mild diarrhoea to pseudomembranous colitis.[3] *C. difficile* is a well recognized cause of large hospital outbreaks of diarrhoea in elderly care units and prolongs hospital stay.[4]

Spread of *C. difficile* is greatly facilitated by asymptomatic carriage and by the formation of spores which are resistant to many disinfectants and which survive in the environment for months.[5,6] High *C. difficile* disease rates have been particularly marked in the elderly, associated with the use of broad-spectrum antibiotics, especially cephalosporins.[7] Management strategies in hospital outbreaks have included stringent infection control procedures and restriction of staff and patient movement.[8] In a recently reported outbreak, infection control measures alone were not sufficient to interrupt transmission and restrictions in antibiotic usage were necessary to control the outbreak.[7]

The management and antimicrobial treatment of the elderly patient with suspected infection are often made

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more difficult by the lack of definitive signs to indicate the exact focus of infection. The British Thoracic Society guidelines[9,10] for the treatment of community-acquired lower respiratory tract infection, promoting the use of cephalosporins in severe infections, have also contributed to increased cephalosporin use.[11]

In January 1994 the background level of two or three cases per month of proven *C. difficile* diarrhoea on the elderly care unit of Gloucestershire Royal Hospital increased to four or five cases per month. Through the first half of 1994 this rose steadily, culminating in a monthly maximum of ten cases of symptomatic *C. difficile* toxin positive infection, in June 1994. Despite measures such as increased ward cleaning, more stringent control of patient isolation and nurse cross-cover, the outbreak continued. This precipitated a meeting of an outbreak infection control team to consider further control measures. The introduction of a restrictive antibiotic policy that would maintain colonization resistance in the gastrointestinal tract but that would still be active against the most likely bacterial pathogens encountered in acute admissions to the elderly care unit was agreed.

The new antibiotic policy came into force during August 1994. Antibiotic use was measured and surveillance of diarrhoea and *C. difficile* infections continued. Length of hospital stay and mortality rates were monitored to determine if these were affected by the change in policy.

## Patients and methods

### *Antibiotic policy*

Before August 1994 clinicians were free to use antimicrobials within hospital formulae and guidelines. For many years the hospital antibiotic policy had encouraged the use of narrow-spectrum antimicrobials targeted to the site of infection, with avoidance where possible of the use of broad-spectrum agents. However, intravenous cefuroxime was frequently prescribed in the elderly care unit for pyrexial patients on admission, to provide cover against urinary, gastrointestinal and respiratory pathogens. Oral cefuroxime axetil was not stocked within the hospital.

After 28 July 1994 a restrictive policy was introduced in the elderly care unit. Patients admitted with suspected infection were prescribed iv benzylpenicillin 1.2–1.8 g every 6 h to cover streptococcal infections, including those caused by *Streptococcus pneumoniae*, and iv trimethoprim 200 mg twice daily to cover urinary tract pathogens and *Haemophilus influenzae*. If the patient had septic shock or was very unwell a single intravenous dose of gentamicin was given (20–180 mg) to cover against more resistant Gram-negative bacilli. The decision to add gentamicin was left to the discretion of the admitting senior house officer (SHO). These agents were chosen as aminoglycosides, trimethoprim and benzylpenicillin are less likely to promote *C. difficile* infection.[2,12,13] Subsequent antimicrobial treatment was modified, if necessary, by the consultant at the post-admission ward round and once-daily gentamicin was continued if appropriate.

The ward pharmacist checked antimicrobial prescribing on her routine daily ward visit. If other antimicrobials were prescribed indication for use was checked and changed if deemed inappropriate. The hospital pharmacy kept computerized records of antimicrobials issued to each ward. The use of cefuroxime, benzylpenicillin, trimethoprim and gentamicin and total antibiotic costs were analysed by month from January 1994 to September 1995.

### *Patient location*

All patients over 75 years admitted to the Gloucestershire Royal Hospital are admitted under the care of an elderly care consultant. The majority of elderly care patients are nursed on four wards with four six-bedded bays and shared toilet facilities. Team nursing is in operation. Each ward has five single rooms. One ward takes acute medical admissions, one takes elderly post-operative patients and two are rehabilitation wards where less acutely ill patients are admitted, or patients are transferred who are awaiting discharge into the community.

### *Infection control*

Hospital policy is to isolate all cases of diarrhoea in single rooms with *en suite* toilet and washing facilities where possible, using enteric precautions, until an infective cause has been excluded by stool examination and culture at the Public Health Laboratory, or patients are asymptomatic for 48 h. The working definition of diarrhoea in the elderly care unit was more than one liquid stool in 24 h in the absence of stimulant laxatives. Patients with *C. difficile* diarrhoea were nursed in isolation, as above; gloves and aprons were worn when handling the patient and ward transfer was avoided until they were asymptomatic. In May dry static mopping of wards was replaced by damp mopping, using detergents, and ward cleaning was increased from once to twice daily. Extra hand-washing posters were placed above sinks at the nurses' station on all wards. As the outbreak progressed, isolation in single rooms was not always possible during June and July, because of pressures from other clinical situations requiring side room care, and symptomatic patients at times had to be accommodated together in bays.

### *Microbiology*

The laboratory has a standard operational procedure for handling stool specimens, which has remained unchanged since January 1994. Stool specimens from all patients are cultured for the usual bacterial pathogens (*Salmonella, Campylobacter, Shigella*). All stool specimens from elderly

care patients, and other patients receiving antibiotic treatment therapy, or those with liquid of bloody diarrhoea are cultured for *C. difficile* using semi-selective medium containing cefoxitin and cycloserine.[14] A *C. difficile* toxin test is performed on all specimens from patients receiving antibiotics, in-patients with liquid or bloody diarrhoea, or if *C. difficile* culture is positive. *C. difficile* toxin B is detected by cytotoxic activity on a fibroblast cell line, with specific neutralization by *C. sordellii* antiserum.[14] During the first month of the outbreak, and at its peak in June 1994, electron microscopy was used to exclude viral enteric infections. Patients were regarded as having *C. difficile* diarrhoea if they had diarrhoea and a stool sample was toxin B positive. Cases of *C. difficile* toxin-positive diarrhoea were recorded by the laboratory at the bench. Such cases were also reported to the infection control nurse who maintained a separate cumulative record of patients. All cases in the figure are distinct patient episodes. We did not attempt strain typing as this would not have altered our management of the incident.

### *Hospital stay and mortality*

Details of admissions under the care of the elderly care consultants in Gloucestershire Royal Hospital were collected for two periods of 7 months before (1 January to 31 July 1994) and after (1 September 1994 to 31 March 1995) the change in antibiotic policy. The data were obtained from the computerized discharge summary database held on the Medical Data Index software (SWIFT), which has been used by the department for 4 years. All admissions with infection as a primary or secondary diagnosis were identified; infections were then grouped as respiratory, urinary or 'other'. Statistical comparisons of the data between the two time periods were performed using the Mann–Witney *U*-test for length of hospital stay and chi-squared test for all other data on SPSS for Windows v.6.1.2. The sample size was large enough to detect a difference of mortality of 5% between the two groups.

## Results

During the periods studied before and after the change in policy there were totals of 1520 and 1612 admissions in the elderly care unit, with 252 and 234 admissions respectively where an infection diagnosis was recorded on the discharge summary. Of these, the proportion that were female (60% and 65% respectively) and the mean age in years for both sexes (85.5 female, 84.1 male before; and 85.5 female, 82.8 male after) were not significantly different for the two periods. The mortality rates and length of stay for the three diagnostic groups—respiratory, urinary and other infections—showed no significant change after the introduction of the revised antibiotic policy (Table). For all infections, the mortality rates were 26% and 21% ($P=0.14$) respectively before and after the change.

An antibiotic audit performed by the ward pharmacist in February 1993 had shown that 50% of patients remained on iv cefuroxime for more than 5 days and 25% for more than 7 days. SHO education led to a reduction in duration of antibiotic prescribing but cefuroxime use was still high in late 1993 and 1994 with expenditure £1000 (266 g) in July 1994 (Figure). After the antibiotic policy change on 28 July 1994 the use of cefuroxime fell rapidly (by >90%) to 18 g in October 1994. 1678 g of cefuroxime were prescribed in the 7 months before the policy change and 279 g in the 7 months after. This equates to 746 days of cefuroxime before the change to 124 days of cefuroxime after the change. The associated cefuroxime prescribing costs fell from £6093 to £943. Total antibiotic prescribing costs also fell from £21,481 to £12,859 between the two 7 month periods. This £8622 decrease also included other savings: parenteral erythromycin (£900), broad-spectrum antimicrobials (£500) and oral vancomycin (£450). Gentamicin use was low throughout 1994–1995 (£40 per annum). There was a drop in gentamicin assay costs as a single trough concentration was determined 12–18 h after the first dose. The projected annual savings on antibiotic prescribing in the elderly care unit amounted to £14,780. Since completion of

**Table.** Length of patient hospital stay and mortality before (1 January to 31 July 1994) and after (1 September 1994 to 31 March 1995) antibiotic policy change, according to site of infection

| | | | Infective diagnosis | | | | | |
|---|---|---|---|---|---|---|---|---|
| | All admissions | | respiratory | | urinary tract | | other | |
| | before | after | before | after | before | after | before | after |
| Number of patients | 1520 | 1612 | 128 | 113 | 75 | 78 | 49 | 43 |
| Length of stay (days) | 17.2 | 18.9 | 18.3 | 18.7 | 23.7 | 18.7 | 14.3 | 20.0 |
| *P* values | | | 0.43 | | 0.96 | | 0.14 | |
| % Mortality | 20.4 | 21.3 | 39.1 | 30.1 | 9.3 | 10.3 | 18.4 | 13.9 |
| *P* values | 0.54 | | 0.14 | | 0.85 | | 0.57 | |

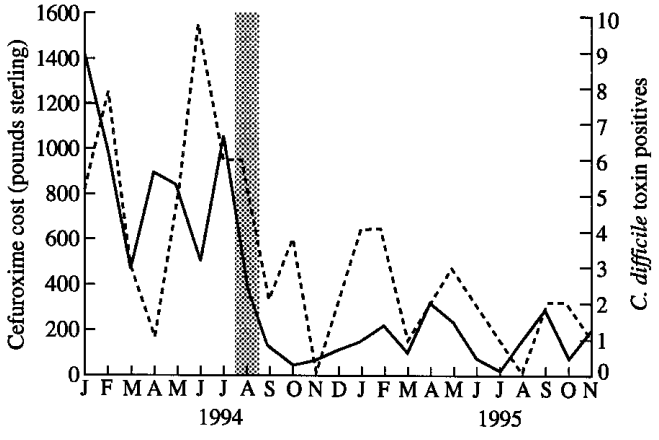


**Figure.** Cefuroxime use in £ sterling (solid line) and cases of *C. difficile* toxin-positive diarrhoea (dashed line) on the elderly care unit from January 1994 to November 1995.

the study, the use of cefuroxime has remained at a low level (Figure).

Thirty-seven cases of *C. difficile* toxin-positive diarrhoea occurred in the 7 months before the change and 16 in the 7 months after the policy change ($P = 0.002$). The incidence of *C. difficile* toxin-positive diarrhoea has remained at three or fewer cases per month since (Figure).

The antibiotic policy was accepted willingly by all the consultants in elderly care and their junior staff and has required minimal policing.

## Discussion

Strict infection control policies and increased ward cleaning did not bring this outbreak of *C. difficile* diarrhoea under adequate control. We felt that cefuroxime use on the elderly care unit was excessive and a major contributing factor. Therefore, a new antibiotic policy was introduced. During August 1994 and by the autumn of that year, monthly cefuroxime use had diminished by 90% compared with July 1994. The number of cases of proven *C. difficile* toxin positive diarrhoea had halved. Our concern that the new antibiotic policy may increase morbidity or mortality by not providing adequate cover against resistant pathogens was unfounded.

This study is uncontrolled because of the nature of the outbreak and relies on the relative timing of a reduction in case incidence and the intervention in order to ascribe a cause and effect relationship. Although the incidence of infection was falling from its peak before the intervention and the outbreak may have ended, the temporal association between the introduction of the new antibiotic policy and the reduction in incidence of *C. difficile* infections make a causal relationship more likely. We did not perform environmental surveillance for *C. difficile*, but previous studies in the hospital environment have shown there is heavy spore contamination with *C. difficile*; this is greatest around colonized patients but is spread throughout the ward.[15] Despite the 90% drop in cefuroxime use, cases of *C.difficile* diarrhoea continued, but only at a low level; this may be due to continued survival of the spores on contaminated wards that are known to remain viable for months.[5,6] For example, caged hamsters placed on a ward that had been closed for 1 month following an outbreak of *C. difficile* diarrhoea became ill with an indistinguishable strain.[15] Cephalosporin use and the numbers of cases of *C. difficile* diarrhoea have remained at a low level in the elderly care wards since. We feel that this is due to the combined approach of restrictive antibiotic prescribing and infection control policies.

*C. difficile* diarrhoea is an increasing problem in the elderly, with over 75% of the 11,352 reports received by the Communicable Diseases Surveillance Centre (CDSC) in 1996 in people over 65 years of age, and 85 reported hospital outbreaks between 1992 and 1996.[16] A recent study[13] linked *C. difficile*-associated diarrhoea in elderly patients with use of broad-spectrum antibacterials and another strongly implicated cefotaxime use.[8]

It may be difficult to establish the presence or source of sepsis in elderly patients. Our antimicrobial combinations attempt to provide empirical cover for the commonest causes of community-acquired pneumonia,[9,17] urinary tract infections and cholecystitis, with narrow-spectrum antimicrobials which are less likely to reduce colonization resistance in the gastrointestinal flora. Consultant review at the post-admission ward round allows modification of antimicrobials if deemed appropriate. Any antibiotic policy incorporates a risk/benefit analysis of each antibiotic chosen. We chose trimethoprim because of its greater activity against Gram-negative pathogens than amoxycillin and narrower spectrum than the cephalosporins and because it is less expensive than the quinolones. However, there is conflicting evidence whether trimethoprim use is associated with *C. difficile* diarrhoea. One small study found that trimethoprim use was relatively commonly associated with *C. difficile* diarrhoea,[18] whereas another found no such association.[11]

In West Gloucestershire 75% of urinary tract pathogens are sensitive to trimethoprim and 96% to gentamicin. Centres will need to review local sensitivity patterns to determine if this regimen is suitable for their population. Our move to once-daily aminoglycoside therapy was prompted by the increasing evidence of sub-therapeutic concentrations achieved with conventional thrice-daily schedules[19] and the relatively low levels of nephrotoxicity observed by Nicolau *et al*.[20] with once-daily gentamicin in treating 800 patients over 61 years of age.

The most frequently isolated pathogen in community acquired pneumonia is *S. pneumoniae* (20–30% of cases),[21] followed by influenza A. *H. influenzae* and *Staphylococcus aureus* are encountered infrequently. In West Gloucestershire 91% of *H. influenzae* isolations from community

sputum samples between January and June 1995 were sensitive to trimethoprim and penicillin-resistant pneumococci are rare. Coliforms and *Pseudomonas* spp. are rarely primary pathogens in community-acquired respiratory infections and would be covered by once-daily aminoglycoside. *Mycoplasma pneumoniae* is an uncommon cause of pneumonia in the elderly. A macrolide is only necessary in this group of patients if atypical pneumonia is suspected, for example during epidemic years, or if there is a poor initial response to empirical therapy.

Our policy was simple to introduce and monitor due to close collaboration between clinicians, microbiologists and pharmacists. In addition to reducing the incidence of *C. difficile* toxin-positive diarrhoea, the new policy was associated with a large reduction in antibiotic costs without increasing mortality or duration of inpatient stay. Furthermore, a restricted antibiotic prescribing policy simplifies education of junior medical and paramedical staff and increases familiarity with the drugs used. We recommend that such a policy should be considered by other units.

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