tutes. We found that all the general practitioners offered counselling about hepatitis, screening, and hepatitis B vaccinations. The audit showed that, of 120 injecting drug users, 30 had been vaccinated against hepatitis B, 30 were immune, and 14 had chosen not to be screened. The hepatitis B status was not known in 42 users, two were carriers, and two had yielded negative results on testing but had not yet been vaccinated.

CHRIS FORD
General practice facilitator, substance misuse

Brent and Harrow Family Health Services Authority,
Harrow,
Middlesex HA1 4BB

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Risk of diarrhoea due to *Clostridium difficile* during cefotaxime treatment

Cefotaxime compares favourably with other third generation cephalosporins

EDITOR,—The retrospective study by M Impallomeni and colleagues shows an increased risk of diarrhoea due to *Clostridium difficile* in elderly patients receiving cefotaxime.[1] The validity of their results is limited by the lack of precise data and by the questionable methodology used.

Firstly, the authors do not specify the number of cases of *C difficile* diarrhoea relating to each antibiotic used. Secondly, they do not state the extent to which all cases were correctly identified. Thirdly, exposure to different antibiotics was estimated from pharmacy expenditure rather than by direct review of patients' records. Fourthly, the absence of precise figures precludes reliable calculation of the frequency of *C difficile* diarrhoea in patients treated with cefotaxime or of the relative risk. Finally, the authors admit that in their univariate analysis they ignored other potential risk factors. Multivariate analysis of risk would have been more appropriate for identifying potential confounding factors, with particular account being taken of single versus combination antibiotic treatment and any use of antibiotics before admission. The fact that the authors calculated the relative risks for different antibiotics implies that not all cases of *C difficile* diarrhoea occurred in association with cefotaxime. The authors' figure, however, relates monthly expenditure on cefotaxime to all cases of *C difficile* diarrhoea. Such observations based on drug use do not show cause and effect, either during the outbreak or after the use of cefotaxime was stopped.

The figure shows that the ward faced an epidemic of *C difficile* diarrhoea from November 1993 onwards. The incidence of superinfection with *C difficile* depends on nosocomial factors[2] and not directly on individual antibiotic regimens. The apparent prevalence associated with any particular antibiotic, however, may be distorted by the policy on use of antibiotics. Oversimplification should be avoided in assessments of the role of any individual or class of antimicrobial agent in *C difficile* disease in a nosocomial epidemic, especially when infection control measures are incomplete and no information on typing of *C difficile* is provided.

The authors' conclusions should be set against extensive experience gained with cefotaxime. With limited influence on normal intestinal flora,[3] cefotaxime compares favourably with other third generation cephalosporins in terms of the rate of acquisition of *C difficile* in healthy volunteers and the occurrence of diarrhoea (1·2%) and *C difficile* disease (pseudomembranous colitis 0·14%) in patients.[4] In terms of risk-benefit analysis, these characteristics have prompted expert panels worldwide to cite cefotaxime as a suitable first line drug for the hospital management of severe community acquired pneumonia.[5]

EUGENE ROTHSCHILD
Head of safety unit for marketed drugs
ALAIN RAUSS
Pharmacoepidemiologist
GABY DANAN
Head of department

Corporate Drug Safety and Epidemiology Department,
Roussel Uclaf,
102 Route de Noisy,
93235 Romainville,
France

1 Impallomeni M, Galletly NP, Wort SJ, Starr JM, Rogers TR. Increased risk of diarrhoea caused by Clostridium difficile in elderly patients receiving cefotaxime. *BMJ* 1995;311:1345-6. (18 November.)
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Mortality due to *C difficile* colitis in elderly people has been underestimated

EDITOR,—M Impallomeni and colleagues report the frequency of diarrhoea due to *Clostridium difficile* in elderly patients receiving cefotaxime.[1] Having seen two cases of fatal toxic megacolon after such infection, we reviewed all the obtainable notes for the 47 patients diagnosed in our hospital during December 1993 as having *C difficile* diarrhoea. Only 30 sets of notes were available for review. The diagnosis was made on the basis of detection of the toxin and the results of stool culture. The patients were all elderly (average age 84 (range 72-98)) and had a variety of diseases, some having multiple diseases. Some had been treated with antibiotics before admission, many having been given them as part of the management of stroke.

Only three had had diarrhoea at home (induced by laxatives in one patient, during treatment with co-trimoxazole in one, and as part of a presumed infectious illness in one). All received more than one antibiotic in the hospital: most received cephalosporins, but erythromycin, co-amoxiclav, and amoxycillin were also given. The diagnosis was made by colonic biopsy in one case and at necropsy in one.

Thirty of the 47 patients with microbiologically diagnosed *C difficile* diarrhoea died, 29 within three weeks of the microbiological diagnosis and one (with persistent colitis) 50 days later. Twelve patients died within one week of the diagnosis, and five died before the microbiological result became available. Pseudomembranous colitis or *C difficile* infection was not mentioned in the death certificates.

To assess the mortality due to *C difficile* colitis in elderly people we looked at the outcome in 57 controls matched for age and sex who had been treated in the hospital at about the same time as the patients. All had received a range of antibiotic treatment. Ten (18%) of the 57 controls compared with 29 (62%) of the 47 patients with *C difficile* diarrhoea died 2-30 days after admission (three of the controls had disseminated malignancies).

We conclude that the mortality from pseudomembranous colitis caused by *C difficile* in elderly patients with multiple diseases has been underestimated. Furthermore, morbidity may be considerably increased in those patients with *C difficile* colitis who survive. Our observation about the association between the cephalosporins, and particularly the mixture of various antibiotics, and pseudomembranous colitis in elderly people is in keeping with Impallomeni and colleagues' conclusions, and a further increase in hospital acquired *C difficile* colitis may be predicted if widespread use of broad spectrum antibiotics continues unabated.

M LESNA
Consultant pathologist
D M PARHAM
Consultant pathologist
Royal Bournemouth Hospital,
Bournemouth BH7 7DW

1 Impallomeni M, Galletly NP, Wort SJ, Starr JM, Rogers TR. Increased risk of diarrhoea caused by Clostridium difficile in elderly patients receiving cefotaxime. *BMJ* 1995;311:1345-6. (18 November.)

Authors' reply

EDITOR,—Eugene Rothschild and colleagues question the validity of our conclusion that the recent outbreak of diarrhoea due to *Clostridium difficile* in our wards was attributable to the 20-fold increase in consumption of cefotaxime. This increase occurred after the British Thoracic Society published guidelines on the treatment of severe community acquired pneumonia. However, all other risk factors in our patients had apparently remained unchanged. Rothschild and colleagues doubt the soundness of using "notional courses" to quantify antibiotic consumption and wonder why we did not state the number of cases of *C difficile* diarrhoea relating to each antibiotic.

The idea of notional courses is widely used in retrospective research.[1] The number of cases of *C difficile* diarrhoea relating to each antibiotic is the basis for the calculation of the risk ratios. We also clearly stated in our paper that one in five patients who received cefotaxime developed *C difficile* diarrhoea. The diagnostic test for the toxin has been well validated.[2] We are surprised by the belief that cefotaxime has limited effect on normal gut flora, as even a study in healthy volunteers has shown that, after a single intravenous injection of 1·5 g cefotaxime, two out of six excreted *C difficile* in their stools and one developed diarrhoea.[3] Antibiotic treatment has been identified as the most important risk factor for *C difficile* diarrhoea, especially in elderly people.[4] The incidence of *C difficile* diarrhoea of 1·2% quoted by Rothschild and colleagues in patients treated with cefotaxime was derived from studies of younger patients, in whom the risk is greatly reduced. Our paper highlights the problems that arise when these data are extrapolated to very old people. The median age of our patients was nearly 84. We trust that expert panels will in future take notice of the issues raised in our paper.

M Lesna and D M Parham produce data derived from geriatric patients of similar age to ours. Although the mortality in our sample was lower than that in theirs (42% *v* 64%), we agree with their observation that *C difficile* diarrhoea is accompanied by increased morbidity. Their conclusion is in keeping with the gist of our paper—that a further increase in hospital acquired *C difficile* colitis may be predicted if widespread use of broad spectrum antibiotics continues unabated.

M IMPALLOMENI
Consultant
J STARR
Senior registrar
Care of the Elderly Unit,
Department of Medicine,
Royal Postgraduate Medical School,
Hammersmith Hospital,
London W12 0NN

T ROGERS
Professor
Department of Infectious Diseases,
Royal Postgraduate Medical School

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