

Nevertheless, further bacteriological characterisation, including antimicrobial resistance patterns and fermentative reactions in sugars, permitted a clear distinction between six different *Clostridium difficile* species. We would recommend, therefore, that case clustering of PMC, suggestive of nosocomial cross infection, is evaluated prospectively using bacteriological typing methods.

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Reply

SIR,—Dr Tvede and colleagues expand on several of the points made in the discussion in our paper and pose questions regarding the prospective evaluation of case clusters of pseudomembranous colitis (PMC). The cases we described, however, were not studied prospectively because for several reasons their epidemic nature was not initially apparent. The cases occurred in three separate hospitals in patients under the care of many clinicians, the epidemic was of a protracted rather than explosive kind and when clustering was first recognised attention focused not on the possibility of cross infection but on the prominence of exposure to the third generation

cephalosporin, cefotaxime, an association previously little reported. It was only after epidemiologic investigation that the compelling evidence of person to person spread, which is documented in our paper, became clearly evident. As we stated, however, this could not be conclusively proved microbiologically. A typical view of the pathogenesis of PMC is that almost any of the ubiquitous toxin producing strains of *Clostridium difficile* may (because of alteration of flora or other factors) gain a competitive advantage after therapy with certain antibiotics. The ensuing damage to the colonic mucosa by toxin is manifested as PMC. This pattern may have occurred in the six cases described by Tvede *et al.* The relative frequency of isolated cases of PMC compared with cases caused by person to person spread of a particular strain is currently obscure but obviously has important prophylactic and therapeutic implications. The previous description of epidemics of PMC and in particular the latent and protracted nature of the epidemic we describe suggests to us that person to person spread may be more common than previously realised. We feel that wider recognition of the possibility of cross infection together with the use of prospective studies of the type advocated by Tvede *et al.* are necessary to define the relative roles of cross infection and isolated cases in the epidemiology of PMC.

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Olsalazine and GI transit in UC

SIR,—I was most impressed with the report of Rao *et al*¹ who noted an accelerated gastric emptying, mouth to caecum transit time and whole gut transit time caused by olsalazine sodium in ulcerative colitis. Although no change in bowel habits was seen among their patients, they attempted to study the diarrhoea reported to occur with olsalazine therapy in some earlier uncontrolled reports.^{2,3} I would like to emphasise, however, that diarrhoea has not yet been proved to be a definite or common problem with this therapy. In my controlled study of olsalazine sodium, diarrhoea was no more common among patients with ulcerative colitis treated with the active drug than those receiving placebo.⁴ Similarly, in another controlled trial, four patients receiving placebo and only two receiving active drug were withdrawn because of diarrhoea.⁵ In one other controlled trial, however, one patient did have increased diarrhoea thought to be caused by olsalazine sodium.⁶

More rigorous study design may at least partially account for the lower incidence of unwanted effects

reported in the controlled trials. It is very difficult to differentiate the diarrhoea of therapy and that of the colitis without a concurrently studied placebo group. Further research will be necessary to truly determine the incidence of this proposed complication in the general population of ulcerative colitis patients treated with olsalazine sodium.

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Reply

SIR,—We would not disagree with any of the comments in Dr Meyer's letter. Our paper reported a physiological study designed to investigate one of the possible mechanisms for the diarrhoea reported in some clinical studies using olsalazine. We did not attempt to review the rather conflicting evidence on the frequency of diarrhoea in patients taking this drug, and note with interest Dr Meyer's own experience. Our own experience is also that diarrhoea is not a frequent side effect¹ and in a further and controlled study to be published shortly as an abstract we only had one withdrawal because of watery diarrhoea among 20 unselected outpatients with ulcerative colitis given olsalazine; one of the 17 patients on sulphasalazine also withdrew because of diarrhoea exacerbation, in that case bloody.² The patients on olsalazine did, however, have more unformed stools during treatment than those on sulphasalazine. This

is not necessarily undesirable, and could be positively beneficial for the 27% of patients with ulcerative colitis who develop hard stools during exacerbations.³

We agree with Dr Meyer that there is considerable discrepancy in the reported incidence of diarrhoea on olsalazine, and its true frequency is still not clear. In our experience it is infrequent in the typical outpatient with distal ulcerative colitis, responds very rapidly to withdrawal of the drug, and is easily distinguished from the true exacerbation of colitis which can occur with any preparation which relies for its therapeutic effect on the liberation of 5-aminosalicylic acid in the colon.

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Changes in gastric alkaline secretion by ulcer healing drugs

SIR,—Professor Konturek's findings that pirenzepine does not influence gastric bicarbonate production in man¹ has been questioned by Dr Stockbrugger (*Gut* 1987; **28**: 1687) because the dose administered (20 µg/kg) is quite low compared with the normal therapeutic dosage.

Several years ago we performed experiments in 10 healthy subjects in whom HCO₃ secretion was measured by Feldman's method. Either pirenzepine 10 mg or saline were given, in randomised order, by bolus iv injection at 0 and 60 minutes during a 120 minute continuous infusion with pentagastrin (6 µg/kg/h). The results (unpublished) showed, in agreement with Konturek's recent paper, that pirenzepine exerts no direct effects on gastric alkaline secretion in man.

On the other hand, Konturek *et al* have also reported in *Gut*² that intragastric instillation of colloidal bismuth induces a significant increase in alkaline secretion by the human stomach. This remains in apparent disagreement with a recent