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.

SAMUEL MEYERS

Mt Sinai School of Medicine,
Mt Sinai Hospital,
One Gustave L Levy Place,
New York, NY 10029, USA.

References

1 Rao SSC, Read NW, Holdsworth CD. Influence of olsalazine on gastrointestinal transit in ulcerative colitis. *Gut* 1987; **28:** 1474–7.
2 Sandberg-Gertzen H, Hanerot G, Kraaz W. Azodisal sodium in the treatment of ulcerative colitis. A study of tolerance and relapse-prevention properties. *Gastroenterology* 1986; **90:** 1024–30.
3 Gabel L, Turkin D, Moore M, Lepski N. Open study of azodisalicylate (Dipentum) in sulfasalazine-intolerant ulcerative colitis patients [Abstract]. *Am J Gastroenterol* 1985; **80:** 127.
4 Meyers S, Sachar DB, Present DH, Janowitz HD. Olsalazine sodium in the treatment of ulcerative colitis among patients intolerant of sulfasalazine. A prospective, randomized, placebo-controlled, double-blind, dose-ranging clinical trial. *Gastroenterology* 1987; **93:** 1255–62.
5 Hetzel DJ, Bochner F, Imhoff DM, *et al.* Azodisalylate (ADS) in the treatment of ulcerative colitis (UC) [Abstract]. *Gastroenterology* 1985; **88:** 1418.
6 Selby WS, Barr GD, Ireland A, Mason CH, Jewell DP. Olsalazine in active ulcerative colitis. *Br Med J* 1985; **291:** 1373–5.

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 effect[1] 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.

C D HOLDSWORTH, S S C RAO, AND N W READ

Royal Hallamshire Hospital,
Glossop Road,
Sheffield S10 2JF.

References

1 Rao SSC, Cann PA, Holdsworth CD. Clinical experience of the tolerance of Mesalazine and Olsalazine in patients intolerant of sulphasalazine. *Scand J Gastroenterol* 1987; **22:** 332–6.
2 Rao SSC, Holdsworth CD, Palmer KR, Dundas SA, Cann PA, Corbett CL. Olsalazine versus sulphasalazine (SASP) in first attacks of ulcerative colitis (UC): a double blind study [Abstract]. *Gut* 1988 (In press).
3 Rao SSC, Holdsworth CD, Read NW. Symptoms and stool patterns in patients with ulcerative colitis. *Gut* 1988; **29:** 342–5.

Changes in gastric alkaline secretion by ulcer healing drugs

SIR,—Professor Konturek's findings that pirenzepine does not influence gastric bicarbonate production in man[1] 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 HCO_3 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