

- 1 Rijk MCM, van Schaik A, van Tongeren JHM. Deposition of mesalazine from mesalazine-delivering drugs in patients with inflammatory bowel disease, with and without diarrhoea. *Scand J Gastroenterol* 1992; 27: 863-8.
- 2 De Vos M, Verdier H, Schroonjans R, Praet M, Bozeart M, Barbier F. Concentrations of 5-ASA and Ac-5-ASA in human ileocolonic biopsy homogenates after oral 5-ASA preparations. *Gut* 1992; 33: 1338-42.
- 3 Sninsky C, Hanauer S, Powers B, et al. Sensitive markers of renal dysfunction are elevated in chronic ulcerative colitis. 10th World Congress of Gastroenterology 1994; Los Angeles, CA: 1778.
- 4 Calder JC, Funder CC, Green CR, Ham KN, Tange JD. Nephrotoxic lesions from 5-aminosalicylic acid. *BMJ* 1972; 1: 152-4.

### New salicylates as maintenance treatment in ulcerative colitis

EDITOR,—I read with interest the paper by Järnerot (*Gut* 1994; 35: 1155-8) in which he reviewed the oral use of the new aminosalicylates in the maintenance treatment of ulcerative colitis. Firstly, I disagree with the author's suggestion that 5-ASA containing compounds should be relegated to solely maintenance treatment. We, and others, have clearly shown efficacy of 5-ASA preparations in mildly to moderately active ulcerative colitis.<sup>1,2</sup> However, we agree it should not be used as sole treatment for severe disease activity. Secondly, the article attempts to provide a synopsis of available sulpha-free aminosalicylic acid preparations with a guideline for the preferred use of specific 5-ASA preparations. I question the author's statements regarding the comparison of Asacol *v* olsalazine and his conclusions on the risk of renal lesions associated with the use of pH dependent formulations of 5-ASA.

In his review, Järnerot presents the results from a study by Courtney *et al*,<sup>3</sup> which compared the efficacy and tolerability of olsalazine and mesalazine in maintenance treatment of ulcerative colitis. Two separate letters to the editor of *Lancet* have criticised this study and suggested that 'there is good reason to suspect the difference found may be due to chance or some methodologic flaw'.<sup>4-5</sup> Hopefully, well controlled studies in the future will directly tackle this issue.

With respect to renal safety, Järnerot's statements about potential risks of nephrotoxicity associated mainly with pH dependent 5-ASA preparations are at best speculative. The mechanism by which 5-ASA causes nephrotoxicity is still undefined and the mechanism, be it hypersensitivity or dose related toxicity, continues to be investigated. Consequently, the potential of 5-ASA to cause nephrotoxicity should be considered a class effect common to all formulations that release 5-ASA or are converted to 5-ASA, as is the case with olsalazine. This position is reflected in the labelling for all 'new aminosalicylates' available in the US, including Asacol, Dipentum, Pentasa, and Rowasa. In a poster presentation at the 10th Congress of Gastroenterology,<sup>6</sup> we showed that sensitive markers of renal function (alanine aminopeptidase and *N*-acetyl- $\beta$ -D-glucosaminidase) are increased in the absence of clinically significant renal dysfunction in a substantial

subgroup of patients maintained with mesalamine containing formulations (including sulphasalazine) and patients receiving placebo for six months. Further research should clarify whether these changes are: (a) drug effects of mesalamine, (b) clinically relevant, or (c) result from intrinsic renal processes in patients with ulcerative colitis. At present, published works support our recommendation that 5-ASA preparations be used for mildly to moderately active ulcerative colitis and for maintenance of remission. Furthermore, the 5-ASA preparation of choice should be the least expensive, best tolerated preparation with a reported safety profile. We suggest avoiding speculation of toxicity until claims can be substantiated with scientific evidence.

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- 1 Sninsky CA, Cort DH, Shannahan F, Powers FJ, Sessions JT, Pruitt RE, et al. Oral mesalamine (Asacol) for mildly to moderately active ulcerative colitis. *Ann Intern Med* 1991; 115: 350-5.
- 2 Sutherland LR, May GR, Shaffer EA. Sulfasalazine revisited: a meta-analysis of 5-aminosalicylic acid in the treatment of ulcerative colitis. *Ann Intern Med* 1993; 118: 540-9.
- 3 Courtney MG, Nunes DP, Bergin CF, O'Driscoll M, Trimble V, Keeling PWN, et al. Randomized comparison of olsalazine and mesalazine in prevention of relapses in ulcerative colitis. *Lancet* 1992; 339: 1279-81.
- 4 Gait JE, Simerl NA. Comparison of olsalazine and mesalazine in prevention of relapses in ulcerative colitis. *Lancet* 1992; 340: 486-7.
- 5 Record CO, MaCrae K. Mesalazine versus olsalazine for prophylaxis of ulcerative colitis. *Lancet* 1992; 340: 1468.
- 6 Sninsky C, Hanauer S, Powers B, Robinson M, Mayle J, Elson C, et al. Sensitive markers of renal dysfunction are elevated in chronic ulcerative colitis. 10th Congress of Gastroenterology, October 2-7, 1994. Los Angeles, CA: 1778.

### Reply

EDITOR,—My leading article was on new salicylates as maintenance treatment in ulcerative colitis and thus I did not discuss the treatment of mildly to moderately active ulcerative colitis with 5-ASA based formulations. I am aware of the fact that they can be used for that condition. What I pointed out was that they are not as effective as corticosteroids. In my opinion it is important to treat active ulcerative colitis aggressively to reduce the risk of developing a state of chronic continuous or refractory disease.

With regard to the study by Courtney *et al* comparing olsalazine and Asacol, I also remarked that this study was only observer blind. Future studies are needed to discover if the results were caused by chance.

I refer to my reply to Drs Rhodes and Coles with regard to the question of nephrotoxicity.

GUNNAR JÄRNEROT

- 1 Courtney MG, Nunes DP, Bergin CF, O'Driscoll M, Trimble V, Keeling PWN, et al. Randomized comparison of olsalazine and mesalazine in prevention of relapses in ulcerative colitis. *Lancet* 1992; 332: 1279-81.

## NOTES

### Coloproctology

The annual scientific meeting of the Association of Coloproctology of Great Britain and Ireland will take place at University College Cork on 2-4 July 1995. Enquiries to Professor W O Kirwan, Department of Surgery, Cork University Hospital, Cork, Ireland. Tel: 010 353 21546400 ext 2385.

### Liver disease

The XXth International Update on Liver Disease will be held at the Royal Free Hospital School of Medicine, London on 6 to 8 July 1995. Further information from: Professor Neil McIntyre, University Department of Medicine, Royal Free Hospital, Pond Street, London NW3 2QG. Tel: 0171 794 0500 ext 3969; fax: 0171 794 4688.

### Liver studies

The 30th annual meeting of the European Association for the Study of the Liver will be held in Copenhagen, Denmark on 21-23 August 1995. Further information from: Local secretary, Helmer Ring-Larsen, Rigshospitalet, DK-2100 Copenhagen, Denmark. Tel: 45 3545 2451; fax: 45 3545 2913.

### Digestive endoscopy

The European Postgraduate Gastro-Surgical School is organising a course on digestive endoscopy in Amsterdam, the Netherlands on 7/8 September 1995. Further information from: Helma Stockmann, Managing Director European Postgraduate Gastro-Surgical School, Room G4-109.3, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands. Tel: 31 20 5663926; fax: 31 20 6914858.

### Pancreatic Society Travelling Fellowship

The Pancreatic Society awards a fellowship annually to allow a young researcher to travel to obtain experience and visit centres of excellence abroad. The award is made on the basis of applicants' *curricula vitae* and proposed itinerary, and applications are requested in the autumn of each year. An award of £3000 will be made in November 1995, for travel during 1996. Potential applicants should contact the Secretary: Mr C D Johnson, University Surgical Unit, F Level, Centre Block, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD. Tel: 0703 706146; fax: 0703 794020.