

## LETTERS TO THE EDITOR

### Acute diarrhoea in expatriates in Bangladesh

SIR, — The study by Van Loon *et al* (*Gut* 1989; 30: 492–5) illustrates an important aspect of management of adult acute diarrhoea in expatriates in Bangladesh. We have completed a larger study of loperamide and dioralyte in the treatment of acute adult diarrhoea in servicemen in shore bases and ships visiting foreign ports.

Criteria for diarrhoea were two or more loose stools in the previous 12 hours. Any underlying chronic bowel disease was an exclusion to entering the study. Subjects were randomised to four treatment groups: placebo, placebo + dioralyte, loperamide, loperamide + dioralyte. The study was double blind with respect to loperamide and open with respect to dioralyte. Subjects were instructed to take two capsules (loperamide or placebo) immediately and one capsule after each further loose stool; those in the dioralyte groups took one sachet in water after each loose stool. The occurrence of vomiting, abdominal pain and loose stools were recorded on diary cards, as was their assessment of general well being.

Of 397 subjects randomised in the study only 290 had fully complete diary cards but numbers of uncompleted cards were the same in each treatment group. The 290 cards were analysed for duration of the diarrhoea, severity of the diarrhoea, time of return to normal activity and general assessment of well being. Results were analysed by non-parametric methods using a Kruskal-Wallis test for multiple groups and Wilcoxon's rank-sum test for individual treatment differences.

Duration of diarrhoea was shortest in those taking loperamide and dioralyte (mean 1.5 days) and this was significantly less than those on placebo alone (1.9) or placebo and dioralyte (1.9) (both  $p < 0.01$ ). The loperamide alone group (1.7) was not significantly different from the other groups.

Overall the mean numbers of loose stools showed the same trend; loperamide and dioralyte was the best group (mean 4.9) and next was loperamide alone (mean 5.0). These were significantly less than the placebo and dioralyte group (7.4) although not different from placebo (6.5).

Results of time of return to normal activity and general symptomatic well-being showed a trend towards a benefit from loperamide but these data failed to reach statistical significance.

It is worth noting that Van Loon was studying the effect of loperamide on numbers of stools of patients who were all instructed to take dioralyte in addition. These findings are consistent with ours; the loperamide + dioralyte group was significantly better than the placebo + dioralyte group in terms of duration of diarrhoea and number of loose stools.

There is a continuing tendency to withhold loperamide in the treatment of acute adult diarrhoea on the basis that enteric pathogens may not be excreted. There is no good evidence for this view and it is now clear from our studies and those of Van Loon that the best treatment regime for these patients is loperamide and dioralyte. The patients we were treating had less severe diarrhoea than those treated in

Bangladesh. Van Loon points out that this is the reason the Swedish study<sup>1</sup> failed to show a difference between loperamide and placebo and it is clear that large numbers are needed if less severe symptoms are to be studied.

In summary the results of the study by Van Loon in severe infectious diarrhoea are corroborated by our study in patients with less severe symptoms. The type of infectious diarrhoea we studied is very common in Britain and these data should encourage prescription of loperamide and oral rehydration solutions as an effective treatment combination. Indeed, education of patients may ensure speedier and cheaper treatment for them in view of the findings that both preparations may be obtained at less than the prescription cost as over the counter medicines.<sup>2</sup>

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- 1 Bergstrom T, Alestig K, Thoren K, Trollfors B. Symptomatic treatment of acute infectious diarrhoea: loperamide versus placebo in a double blind trial. *J Infect* 1986; 12: 35–38.
- 2 Medicines that cost less over the counter. *Drug Ther Bull* 1989; 27: 42–3

### Reply

SIR, — Thank you for giving me the opportunity to reply to the letter by Drs JK Ramage, ARO Miller, and PD Clarke.

I am pleased that the study by Ramage, Miller and Clarke fully supports our finding that loperamide and oral rehydration combined constitute a most effective treatment for acute watery diarrhoea in adults, thus refuting the fear of enhanced invasiveness of the pathogens involved. I should stress here again, however, that this conclusion not be extended to infants or children in the developing countries.

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### Peptic ulcer in India

SIR, — We congratulate Professor M S Khuroo and his colleagues on their excellent paper concerning the prevalence of peptic ulcer in Srinagar.<sup>1</sup> Our earlier reviews of the distribution of peptic ulcer in India and Bangladesh preceded the advent of fiberoptic endoscopy.<sup>2,3</sup> Our conclusions depended on the correlation of hospital admission rates, surgical and barium meal reports, and the experience of medical workers in a given area. It is particularly valuable now to have a prospective population survey based on endoscopic findings. It is interesting that their figures confirm that there is a high duodenal: gastric ulcer rates and a marked predominance in men.

Our findings showed a marked difference in the incidence of duodenal ulceration in rural areas between rice and unrefined wheat eating populations. The reports that we received from Kashmir also indicated that the incidence of duodenal ulcer was higher in the rice eating areas around Srinagar than in the unrefined wheat eating areas of Jammu. It would be interesting if this could be confirmed now that endoscopic facilities are available.

In our survey, we were impressed by the high incidence of early pyloric stenosis in

relation to haemorrhage and perforation in rural areas with a high incidence and which were well served by local hospitals. Over the course of time, we noticed a changing pattern in urban areas with an increasing incidence of haemorrhage and perforation, which we attributed to the greater pace and stress of city life. This pattern seems to be present now in Srinagar, although the incidence of stenosis (6.1%) is still a high figure.

We also noted that the incidence of duodenal ulcer tended to be high in the large cities in the unrefined wheat eating regions where the incidence in the surrounding rural areas was low, and again we attributed this to the added stresses of urban life. This may account for the different conclusions reached in other reports about the distribution of peptic ulcer in India because they were largely based on information obtained from urban areas.

Our particular interest was in the relationship between staple diets and the distribution of duodenal ulcer in rural areas. There is increasing evidence of a high incidence of duodenal ulcer in populations of the world where highly milled or polished rice is the staple food and of a low incidence where unrefined wheat is used.

Malhotra, as quoted, attributed this to the greater mastication required in eating unrefined foods such as chappatis as compared with a sloppy rice diet. He attached importance to the buffering effect of saliva and more recently, to its epidermal growth factor content.

Our investigations have shown that unrefined wheat<sup>4</sup> and certain other foods contain a protective factor against ulceration, and that on the other hand, the oil in refined rice on storage gives rise to ketoaldehydes that can be ulcerogenic.<sup>5</sup> We feel that the incidence of duodenal ulcer in a population may depend partly on a balance between dietary protective and ulcerogenic factors<sup>6</sup> and that the refining of rice may be contributing to the high incidence in rice eating populations.

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- 1 Khuroo MS, Mahajan R, Zargar SA *et al*. Prevalence of peptic ulcer in India: an endoscopic and epidemiological study in urban Kashmir. *Gut* 1989; 30: 930–4.
- 2 Tovey F. Peptic ulcer in India and Bangladesh. *Gut* 1979; 20: 329–47.
- 3 Jayaraj AP, Tovey FI, Clark CG. Possible dietary protective factors in relation to the distribution of duodenal ulcer in India and Bangladesh. *Gut* 1980; 21: 1068–76.
- 4 Tovey FI. Duodenal ulcer. In: Trowell H, Burkitt D, Heaton K, eds. *Dietary fibre, fibre-depleted foods and disease*. London: Academic Press: 229–40.
- 5 Tovey FI, Jayaraj AP, Clark CG. Fibre and duodenal ulcers. *Lancet* 1982; ii: 878.
- 6 Jayaraj AP, Rees KR, Tovey FI *et al*. A molecular basis of peptic ulceration due to diet. *Br J Exp Pathol* 1986; 67: 149–55.
- 7 Jayaraj AP, Tovey FI, Clark CG *et al*. The ulcerogenic and protective action of rice and rice fractions in experimental peptic ulceration. *Clin Sci* 1987; 72: 463–6.
- 8 Tovey FI, Jayaraj AP, Lewin MR, Clark CG. Diet: Its role in the genesis of peptic ulceration. *Dig Dis* 1989; 7: 309–23.

### Reply

SIR, — We would like to thank Dr S Tovey and Jayaraj for their encouraging comments on our paper concerning the prevalence of peptic ulcer in Kashmir.<sup>1</sup> The epidemiology of peptic ulcer in India had been extensively studied in the past before the advent of fiberoptic endoscopy.<sup>2,3</sup> The data were collected from hospital