LETTERS TO THE EDITOR

Towards a better assessment of reflux oesophagitis

SIR,—We read with interest the exhaustive and balanced overview by Dr Colin-Jones on gastro-oesophageal reflux.¹ We were particularly pleased to see that an authoritative reviewer has at last officially suggested an adaptation of the notorious endoscopic classification of oesophagitis by Savary and Miller.² For reasons which are beyond our understanding, the oesophageal mucosa is the only one in the digestive system (or, better, in the whole body), the lesions of which were graded starting from erosions. Thus, in clinical practice, when patients with symptoms of gastro-oesophageal reflux have endoscopic evidence of erythematous areas in the distal oesophagus the term of 'grade 0 oesophagitis' is often used. In our opinion mild (non-erosive) oesophagitis should be graded from longitudinal red streaks to circumferential erythema, but any attempt to include non-erosive lesions within the concept of 'oesophagitis' is welcome.

On the other hand in clinical trials the endoscopic evaluation criteria are often at variance with Savary and Miller's classification and tend to include non-erosive forms as well, in order to obtain a more realistic approach to the problem.³⁻⁵

As for the possibility of improving the results of H₂ receptor blockers in the treatment of reflux oesophagitis, we believe that the time of administration can also play a major role. Contrary to that reported in the past,⁶ daytime reflux has been claimed to be an important factor in the pathogenesis of the disease.⁷ Therefore a single dose of a H₂ blocker at night might not be ideal in some subjects. The results of a recent cooperative study performed in northern Italy⁸ seem to support this view.

A group of 33 healthy controls was initially examined by means of 24 hour ambulatory pH-metry to determine the upper normality limit, on the basis of De Meester's criteria⁹ (mean $\pm$ 2SD) of the percentage of time with pH below 4. Accordingly, 112 consecutive subjects with abnormal pH-metry were detected and could be divided in upright (53%) or supine (11%) refluxers and in patients with reflux in both positions (36%).⁸ These figures differ from De Meester's findings and in particular the number of upright refluxers is substantially higher (53% *v* 9%). The reasons for those discrepancies are unclear. It must be noted, however, that the Italian study was carried out in outpatients and not subjected to dietary restrictions, whereas DeMeester examined only hospitalised patients on a standard diet. At any rate, the high number of upright refluxers in the Italian series makes the habit of indiscriminately treating reflux oesophagitis with a single bedtime dose of a H₂ receptor blocker questionable.

To achieve better results, the choice of administering the drug in the morning and at bedtime or only at night should be based on the results of 24-hour pHmetry. For practical reasons we cannot expect that each and every subject with reflux oesophagitis can have previously been submitted to the test in order to obtain a 'personalised' therapy. On the other hand, at least in patients who fail to respond to treatment, the time of administration of H₂-

blockers should be adjusted to the results of pHmetry. This does not apply to omeprazole, the long lasting action of which makes it irrelevant the time of administration. The superior results observed with omeprazole, including healing of most cases resistant to H₂-blockers, possibly rely not only upon its greater antisecretory effect, but also upon its ability to suppress the acidity of refluxate throughout the whole day.

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- 1 Colin Jones DS. Histamine₂ receptor antagonists in gastro-oesophageal reflux. *Gut* 1989; **30**: 1305-8.
- 2 Savary M, Miller G. The esophagus. *Handbook and atlas of endoscopy*. Soluthern: Gassman, 1978.
- 3 Guslandi M, Testoni PA, Passaretti S, et al. Ranitidine vs metoclopramide in the medical treatment of reflux esophagitis. *Hepato-Gastroenterol* 1983; **30**: 96-8.
- 4 Niemela S, Jaaskelainen T, Lehtola J, et al. Pirenzepine in the treatment of reflux oesophagitis. A placebo-controlled, double-blind study. *Scand J Gastroenterol* 1986; **21**: 1193-9.
- 5 Sandmark S, Carlsson R, Fausa O, Lundell L. Omeprazole or ranitidine in the treatment of reflux esophagitis. Results of a double-blind, randomized, Scandinavian multicenter study. *Scand J Gastroenterol* 1988; **23**: 625-32.
- 6 De Meester TR, Johnson CF, Guy JJ. Pattern of gastroesophageal reflux in health and disease. *Ann Surg* 1976; **184**: 459-70.
- 7 De Caestecker JS, Blackwell JN, Pryde A, Heading RC. Daytime gastro-oesophageal reflux is important in oesophagitis. *Gut* 1987; **28**: 519-26.
- 8 Bortoli A, Prada A, Passaretti S, et al. Distribution of acid gastro-oesophageal reflux in a regional group of healthy people and in refluxers. *Ital J Gastroenterol* 1989; **21**: 365-6.

Macrophage activity in inflammatory bowel disease

SIR,—I read with interest the recent article by Mahida and coworkers.¹ They clearly showed that macrophages isolated from inflamed colonic or ileal mucosa in Crohn's disease show an enhanced respiratory burst compared with those isolated from normal mucosa.

I disagree, however, with their conclusion that the respiratory burst capacity of macrophages isolated from normal colonic and ileal mucosa is downregulated compared with inflamed bowel.

It is well recognised (since the original observation by Metchnikoff that macrophages in infected hosts respond more vigorously to the introduction of phagocytic particles²) that tissue macrophages exist as two distinct populations;^{3,4} (i) Resident/basal (poorly active) state. (ii) Primed/transformed (activated) state. Macrophages in both states can produce free radicals and release lysosomal enzymes. Those macrophages which are in the primed (transformed) state, however, will react much more vigorously.^{4,5} A number of stimuli will provoke this transformation—for example, prostaglandin E₂, lipopolysaccharide, C5a, tumour necrosis factor, gamma interferon and fMLP (N-formylmethionyl-leucyl-phenylalanine), BCG vaccination, corynebacterium parvum inoculation, and low concentrations of A23187 (calcium ionophore).^{4,6}

Thus those macrophages isolated from inflamed mucosa in inflammatory bowel disease have been upregulated (activated) into a primed state as a consequence of the inflammatory process.

The authors were able *in vitro* to show a response with IFN- γ but not lipopolysaccharide upregulating macrophages isolated from normal colonic mucosa, and it may be that

other factors are important *in vivo* in enhancing this response.

Free radical production by activated macrophages may be an important mechanism of tissue injury in inflammatory bowel disease.

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- 1 Mahida YR, Wu KC, Jewell DP. Respiratory burst activity of intestinal macrophages in normal and inflammatory bowel disease. *Gut* 1989; **30**: 1362-70.
- 2 Metchnikoff E. *Immunity in infective diseases*. Binnie FG, trans London: Cambridge University Press, 1905.
- 3 Johnson RB, Godzik CA, Cohn ZA. Increased superoxide anion production by immunologically activated and chemically elicited macrophages. *J Exp Med* 1978; **148**: 115-27.
- 4 Nathan CR, Cohn ZA. Cellular components of inflammation: monocytes and macrophages. In: Kelly WN, Harris DE, Ruddy S, Sledge L, eds. *Textbook of rheumatology*. Vol 1. Philadelphia: Saunders, 1985: 144-69.
- 5 Arthur MJP, Kowalski-Saunders P, Wright R. Corynebacterium parvum elicited hepatic macrophages demonstrate enhanced respiratory burst activity compared with resident Kupffer cells in the rat. *Gastroenterology* 1986; **9**: 174-81.
- 6 Nathan C, Horowitz CR, De la Harpe J, Vadhwan-Ray S, Sherwin SA, Oettgen HF, Krown SE. Administration of recombinant interferon to cancer patients enhances monocyte secretion of hydrogen peroxide. *Proc Natl Acad Sci USA* 1985; **82**: 886-90.

Helicobacter associated gastritis in patients with duodenal ulcer: the influence of various drugs

SIR,—We read with great interest the study reported by Loffeld *et al*¹ on the effects of colloidal bismuth subcitrate (CBS) on Helicobacter associated gastritis in patients with non-ulcer dyspepsia.

We report here our preliminary results of a study, concerning the influences of CBS, sucralfate and ranitidine on Helicobacter associated gastritis in patients with active duodenal ulcer (DU).

Thirty one patients with active duodenal ulcer who fulfilled the following criteria were included in the study: all patients were subjected to upper GI endoscopy and biopsy twice that is, before any therapy started as well as six weeks afterwards; biopsies were taken from the gastric antrum for HLO test (1-2) and histological examination (2-3); thus, the presence of helicobacter associated gastritis was initially confirmed and subsequently followed up in all the patients. Sections for histological detection of helicobacter like organisms (HLO's) were stained with Giemsa stain.

HLO test results were arbitrarily classified into four grades, as follows: grade 3: positive within the first 20 min of inoculation; grade 2: positive within the first two hours; grade 1: positive within the first 24 hours; grade 0: negative.

Antral gastritis was classified histologically into four grades (1, 2, 3, 4) according to Hafter and Siebenmann² by one pathologist (PD); semi-quantitative estimation of HLO's presence on biopsy material was made by the same pathologist 'blindly'—that is, without any information on the HLO test results. There was, however, reasonable correlation between his semiquantitative estimation and the HLO test results. If HLO test was positive and the histology failed to show HLOs, or *vice versa*, the HLO test was considered to be positive, grade 1.

The patients were divided into three groups (a, b, c) according to the medication given: Patients in group a (12) were given CBS, 240 mg/bid, in group b (13) sucralfate, 2 g/bid, and