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Reply

SIR,—We should like to thank Professor Marks for his kind and interesting remarks which focus on the two questions of tachyphylaxis and rebound hypersecretion which may or may not be related. Neither of these questions formed the primary objective of our study.

Professor Marks concludes that the study by Prichard *et al*[1] and the brief abstract by Hyman *et al*[2] show tachyphylaxis to continued H_2-receptor antagonist administration. In these studies the gastric secretory response to pentagastrin or a peptone meal was altered by a course of ranitidine showing reduced effectiveness on the peak and maximal acid output. This could have resulted from several possible mechanisms other than tachyphylaxis, which could not be determined by the methodologies used in these studies. The possibilities include a change in the parietal cell mass or the secretory drive, and/or an increase or decrease in the density or affinity of any of the four recognised receptors for the gastric parietal cell.

Our study showed an enhanced effect of ranitidine on the H_2-receptor but whether there were changes in any other modalities was never addressed. The response of the gastrin and/or cholinergic receptors might for example have been paradoxical? The accentuated effect of an intravenous bolus of ranitidine at the end of the study, as Professor Marks concedes, cannot be reconciled with tachyphylaxis.

Prichard*et al* and Hyman *et al* used pentagastrin as their secretagogue which raises two immediate problems with interpretation. H_2-receptor antagonist inhibition of pentagastrin stimulated acid secretion is non-competitive[3,4] and the secretagogue action of pentagastrin is indirect *via* ECL and other cells.

The Prichard study[1] should have been able to detect an increase in BAO and MAO if the parietal cell mass increased with treatment and an accompanying decreased response to ranitidine. Even if this had been present, however, it could have been masked by the lack of a ranitidine pretreatment at the beginning of the study. This was corrected in our study and although Professor Marks asks whether the effect of ranitidine '. . . three days pretreatment could have been greater than after three months

treatment?' this would have no adverse bearing on our converse findings with impromidine.

A receptor is a protein or glycoprotein moiety which must be linked to a physiological response.[5] The H_2-receptor is virtually confined to the gastric mucosa and is linked specifically to gastric acid secretion providing us with a unique opportunity in man to study stimulation and blockade by highly specific ligands – impromidine as agonist and ranitidine as antagonist. Thus our study shows that for any agonist antagonist ligand receptor event ranitidine taken for three months resulted in an exaggerated response. This was not simply due to more or less parietal cells or a change in receptor density or affinity, which could not be determined in man, but represents true up-regulation.

The place of H_2-receptor up-regulation in relation to rebound hypersecretion or ulcer relapse is unclear and the implication by Professor Marks reflects his extension rather than any made in our paper, and a recent review suggests that although an alteration in acid secretion does occur after treatment with H_2 receptor antagonist treatment no clear mechanisms can yet be defined.[6] Studies to evaluate this in the future will need close attention to study design. Nevertheless his suggestion that one or more of our subjects might have experienced asymptomatic ulcer recurrence at the time of the second study is intriguing, especially in view of the recent findings from carefully designed studies[7] by his own Cape Town group, and making further studies in this area most important.

We thank Professor Marks for noting the inconsistency regarding the p values between the Table and Figure. The values in the Table are correct, and the p values in the Figure should not have been included.

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News

British Society of Gastroenterology

The 1989 Spring Meeting of the British Society of Gastroenterology was held on 12–14 April at the University of Bradford under the presidency of Dr J H Baron. The scientific sessions were preceded by a Teaching Day on 'Molecular biology'; the theme was continued with a lecture by Dr John Walsh on the use of monoclonal antibodies to study gastric secretion. Continuing clinical education was provided by three 'State-of-the-Art' lectures, and Dr J M Rhodes gave the Sir Francis Avery Jones BSG Research Medal Lecture on 'Mucus, colitis, and cancer'; it is to be hoped that the Society may devise a shorter title for the award. Receptions were held at the National Museum of Photography, and at Cartwright Hall, and the Conference Dinner took place at Salt's Mill, Saltaire. The BSG tradition (established at the last meeting) of opening the plenary morning with 'Plenary posters' was maintained by the Programme Committee, and much appreciated by those delegates who were slow to recover from the social obligations of the previous evening.