one year double blind comparative trial. *Br Med J* 1987; **294**: 932-4.

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Reply

SIR,—We appreciate the comments of Dr Antonin and Professor Bieck. As pointed out in the introduction to our manuscript, we agree that our observations differ from those of other investigators. Our experiments were, however, carried out under randomised, double blinded controlled conditions, not always the case in other studies.¹ We evaluated for the first time the effect of TDS on total 24 hour acid secretion and measured acid secretion under basal conditions, in response to food, between meals and during the night. We evaluated the effect of TDS on gastric acid secretion when the drug was used alone and when it was used in combination with cimetidine. We could not show an effect of the medication on acid secretion in either case.

While we did not measure urine levels of scopolamine, as suggested, we assume that the drug used by our patients was similar to that used in other studies as it was sent to us as coded medication directly from the manufacturer, Ciba-Geigy Corp, Summit, NJ, USA. It is possible that the bioavailability of TDS varies from batch to batch and that we received a preparation with relatively low bioavailability.

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Reference

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Vagal control of gastric alkaline secretion

SIR,—The paper of Professor Konturek and co-workers on the vagal control of gastric alkaline secretion (*Gut* 1987; **28**: 739-44) was very informative. Most of the findings are well in agreement with those of Feldman *et al.*¹ and Forsell *et al.*² A comparison between the non-selective anti-muscarinic atropine and the M1-selective anti-muscarinic pirenzepine with respect to gastric alkaline secretion has, however, not been reported before.

Unfortunately, this comparison has not been carried out in an appropriate way, and the results do therefore not support the authors' conclusions, that M2-receptors rather than M1-receptors are involved in the regulation of gastric alkaline secretion. It is well known that the dose/effect relation between atropine and pirenzepine is 1:5 to 1:10 in weight units concerning the inhibition of exocrine glands using parenteral application.³

It would have been logical, therefore, to compare considerably higher doses of pirenzepine than the maximum 20 µg/kg chosen for atropine. It should be remembered that 10 mg is the smallest dose of pirenzepine available for parenteral application in clinical use, and that the highest dose given in the study of Konturek and coworkers to a volunteer of 70 kg body weight was 1.4 mg.

In conclusion, I feel that the question of whether gastric alkaline secretion is an M1- or M2-receptor dependent process is not yet clarified.

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References

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- 2 Forsell H, Stenquist B, Olbe L. Vagal stimulation of human gastric bicarbonate secretion. *Gastroenterology* 1985; **89**: 581-6.
- 3 Jaup BH. Studies on the mode of action of pirenzepine in man with special reference to its anticholinergic muscarinic properties. *Scand J Gastroenterol* 1981; **16**: suppl 68: 1-26.

Reply

SIR,—We greatly appreciate Dr Stockbrügger's comments concerning our recent paper.¹ He raised an interesting theoretical point that our suggestion concerning the involvement of M2 rather than M1 subtypes of muscarinic receptors in the stimulation of gastric alkaline secretion may not be properly documented, because doses of pirenzepine used were too low.

The existence of at least two types of muscarinic receptors (M1 and M2) is based entirely on the comparison of the pharmacological effects of classical antimuscarinic drugs such as atropine, which is believed to be a non selective antagonist and to block M1 and M2 receptors. It is also based on actions of newer agents such as pirenzepine,² or telenzepine,³ which are considered to be more selective by blocking M1 receptors. Hirschowitz and