Correspondence

Sensitisation model still satisfactorily explains parietal cell activity

Sir,

In the recent paper by Boulos, Faber, Whitfield, Parkin, and Hobsley (*Gut* 1983; **24**: 549–56), they propose a new hypothesis that there are two types of parietal cell categorised by their responses to histamine and vagal stimulation. Seventy per cent of the stimulatory effect of histamine on gastric secretion is argued to be mediated *via* acetylcholine. One of the main observations upon which this hypothesis is based is the reduction in histamine-stimulated secretion after vagotomy. Vagotomy, however, does not decrease the capacity of the stomach to secrete acid; the decrease in secretion observed after vagotomy is caused by reduced sensitivity.¹ Although the dose of histamine used by Boulos *et al.* (40 µg/kg/h) would appear to cause maximal secretion before vagotomy, it is sub-maximal after vagotomy, and increasing the dose of histamine will increase acid output,² a finding inconsistent with the new hypothesis. Vagotomy similarly reduces the sensitivity to pentagastrin.²

Boulos *et al.* further suggest that their hypothesis explains the smaller secretory response to insulin compared with that to histamine. Insulin is a complex stimulant and the notion that stimulation of gastric secretion by insulin is mediated solely *via* vagal cholinergic fibres is an unproven assumption.¹ Similarly, the multiple actions of insulin may contribute to its failure to produce maximal secretion. Insulin induces hypokalaemia, and prevention of this increases acid output, although not to the maximum observed with histamine.³ Insulin-induced hypoglycaemia, as well as stimulating gastric secretion, may be a further restraint on parietal cell activity.^{4–6} Insulin and the associated hypoglycaemia also have other actions which may limit acid secretion including release of glucagon⁷ and catecholamines,⁸ and hypotension.⁹ Consideration of these, and other, varied and widespread inhibitory mechanisms make it unnecessary to discard the sensitisation hypothesis.¹⁰

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Reply

Sir,

We are grateful for the opportunity to reply to the above letter.

The basic problem is whether the reduction in histamine-stimulated secretion resulting from vagotomy can be restored by increasing the dose of histamine to the preoperative level in man. There is no question that it can be in dogs,¹ but the evidence in man is unconvincing. Konturek reported that a four-fold increase in histamine raised the post-vagotomy secretion rate from 70% to 85% – that is, not to 100%. This was a marginal increase, especially as no measurements of pyloric losses or duodenogastric reflux had been made. Such errors could well account for the reported increase. Moreover, completeness of vagotomy had been adjudged only by Hollander's criteria which are grossly inaccurate^{2,3} and the fact that the post-vagotomy histamine test at conventional dosage produces 70% of the preoperative response indicates that several of the subjects had had an