Correspondence

SIR,—Drs Penston and Wormsley might have interpreted more satisfactorily the possible causes and effects of gastric ECL cell hyperplasia in achlorhydric subjects if they had considered the problem from an endocrinological rather than solely a gastroenterological point of view. The endocrine cells of the gut are scattered through the mucosa rather than gathered together in discrete glands, but in all other respects they are similar to the endocrine cells which are found in the pituitary and most other endocrine tissues in the body. Hyperplasia and consequent adenoma formation are extremely common in all endocrine tissue when a feedback inhibitory loop is interrupted. Thus, experimental thyroidectomy[1] or spontaneous longstanding hypothyroidism caused by autoimmune thyroiditis[2] both result in hyperplasia of pituitary TSH-secreting cells and pituitary adenomas. Comparable changes also affect other cells in the pituitary, notably those secreting ACTH or FSH and LH, when there is a deficiency of the secretion of the target organ for these hormones.

In hypocalcaemic states, particularly in patients with renal osteodystrophy, the hyperplasia of the parathyroid glands may be very marked, with considerable glandular enlargement, and in such patients adenomas develop quite commonly.

Thus, hyperplasia of endocrine tissue is very common, as are adenomas of the specialised endocrine cells. Unsuspected and asymptomatic pituitary adenomas occur in over 20% of healthy subjects,[3] and yet malignant change in endocrine tissue on the basis of such hyperplastic changes or adenomas is extremely rare, only a tiny number of cases ever having been reported.

Gastric ECL cell hyperplasia is a consequence of hypochlorhydria, however produced. It is probable that ECL cells play some part in the normal regulation of gastric secretion, and that their hyperplasia in achlorhydric subjects occurs in response to deficient gastric secretion, through the interruption of some feedback loop as yet unknown (and which may well not involve gastrin).

Spontaneous achlorhydria is extremely common in the general population, and ECL cell hyperplasia is therefore presumably also very common. Actual adenomas of ECL cells, however, are relatively infrequent, and malignant tumours of ECL cells are extremely rare. Indeed, when reviewing the literature for our paper on this subject,[4] it was not possible to find a report of even one single documented case of a metastasising gastric ECL cell tumour. ECL cells are totally different from mucus secreting gastric cells, and their malignant potential (if any) in achlorhydric patients is virtually undetectable. The risk of achlorhydric subjects developing malignant tumours of ECL cells is likely to be of the same order of magnitude as the risk to patients with hypothyroidism of developing a TSH-secreting pituitary tumour.

The available evidence indicates that, as far as the malignant potential of hyperplastic gastric endocrine cells in achlorhydric subjects is concerned, Dr Penston and Dr Wormsley are at best incorrect and at worst scaremongering.

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References

1 Furth J, Clifton KH. Experimental pituitary tumours. In: GW Harris, BT Donovan, eds. *The pituitary gland* London: Butterworths, 1966: 460–97.
2 Samaan NA, Osborne BM, Mackay B, Leavens ME, Duello TM, Halmi NS. Endocrine and morphologic studies of pituitary adenomas secondary to primary hypothyroidism. *J Clin Endocrinol Metab* 1977; **45:** 903–11.
3 Costello RT. Subclinical adenomas of the pituitary gland. *Am J Pathol* 1936; **12:** 205–17.
4 Harvey RF, Bradshaw MJ, Davidson CM, Wilkinson SP, Davies PS. Multifocal gastric carcinoid tumours, achlorhydria and hypergastrinaemia. *Lancet* 1985; i: 951–4.

Reply

SIR,—With reference to the letter from Dr Harvey: we made precisely the same points as he about 'feedback loops' and quoted the same examples (although we could have quoted others). Clearly, our message was difficult to read. One of the main points of our critique however, was the absence of proof that ECL cell hyperplasia was the consequence of hypochlorhydria. For Dr Harvey to state dogmatically that hypochlorhydria does cause ECL cell hyperplasia, does not contribute to the resolution of the problem.

Dr Harvey also reflects on the literature relating to carcinoid tumours of the stomach (as did we). Our argument – that the phenotypic manifestation of the carcinogenic process is unpredictable, has not apparently been accepted. If the genetic damage that results in the cancer cells looking like carcinoid cells is associated with reasonable differentiation and slow progression – so be it. That combination occurs in tumours of all tissues. In animals, however, the *same* chemical can produce slow growing carcinoid