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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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

tumours OR *fast growing, metastasising tumours of different phenotype* – that is, different morphological appearance. That is the problem, which, we think needs to be addressed with some urgency.

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^{14}C triolein breath test

SIR,—It was interesting to read the manuscript by Mylvaganam *et al.* (*Gut* 1986; **27:** 1347–52). Our laboratory has been performing ^{14}C breath tests of various types for over a decade both as a research tool and as an aid to patient management. I noted that they used the eight hour cumulative data as their index. This makes the test rather long and contributes to an increase in reagent use and counting time. In 1981 we reported (*Clin Chem Acta* 1981; **112:** 371–4) a simplified method based on assessing the two to four hour rate. This correlates well with peak $^{14}CO_2$ excretion and eight hour cumulative data. More recently (unpublished observations) we have shown that a single estimation at four hours post label ingestion is as discriminant as any of the other collection times. This greatly reduces the cost and complexity of the test.

It is surprising that this breath test and several others have not received more widespread acceptance in gastroenterology. The future I am sure will see a burgeoning of these simple (usually screening) tests in other fields as well as the gut. Perhaps the major roadblock has been the radioactivity (and the long $t_{1/2}$ of ^{14}C) involved with these tests. The risk is minimal at the dosage levels used and even multiple tests result in little exposure, calculated in some cases to be less than the radiation dose from one abdominal radiograph. ^{13}C labelled substrates have been much vaunted as a solution to this perceived problem. As a research tool this is fine but for a practical screening test the label is very expensive and the detector (mass spectrometer) less readily accessible than a liquid scintillation counter.

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Assessment of biliary tract pathology in familial adenomatous coli

SIR,—Sarre *et al* (*Gut* 1987; **28:** 303–14) have again confirmed the common occurrence of upper gastrointestinal polyps in familial adenomatous polyposis although there may be a geographical variation.[1] There is also an increased incidence of periampullary carcinoma in these patients[2] and the occurrence of biliary and pancreatic lesions has also been documented.[3,4]

The necessity to assess the biliary system in these patients has not yet been addressed but if the combined incidence of periampullary, pancreatic and bile ducts lesions is approximately 5%[5] endoscopic retrograde cholangiopancreatography is not only reasonable but necessary in those patients in whom adenomas of the stomach or duodenum have been demonstrated. At present, the incidence of biliary and pancreatic pathology in these patients remains anecdotal but their presence may be of some importance.

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Reply

SIR,—In response to Doctor Aitken's letter regarding our article, Sarre *et al* (*Gut* 1987; **28:** 303–14), I would like to make the following comments: In our communication we presented the prevalence of upper gastrointestinal polyps in a consecutive series of 100 patients with familial adenomatous polyposis undergoing upper endoscopy as a routine screening test. It was obvious in reviewing these results that the patients with adenomas of the duodenum had varying numbers of adenomas present, and some of them had adenomatous change in and around the ampulla. The dilemma that has been created by these observations relates to whether therapy of these lesions should be undertaken and if so by what means. We still do not truly know the incidence of duodenal, bile duct, or periampullary cancer in general in these individuals. We are not aware of any particular subsets that might be more likely to undergo malignant degeneration