

LETTERS TO THE EDITOR

Audit of upper gastrointestinal endoscopy

EDITOR,—In their audit of 14 149 upper gastrointestinal endoscopies (*Gut* 1995; 36: 462–7), Quine *et al* identified 104 deaths occurring within 30 days. The authors hope their findings will encourage endoscopists to examine their own practices, but we are concerned that the information provided is insufficient to make true comparisons with this 30 day mortality of 0.74%. The audit reports on all upper gastrointestinal endoscopy but without specifying the proportion of inpatients compared with outpatients and the numbers done for bleeding. Such data are important as we have recently found that within our hospital, inpatients accounted for a significant proportion (38%) of new referrals for upper gastrointestinal endoscopy, and that the 30 day 'all cause' mortality in these inpatients was 12%.¹ Inpatients tended to be older and have multiple medical problems. The death rate was even higher in patients who were already in hospital for other reasons and subsequently had upper gastrointestinal bleeding, but even in 251 established inpatients who were endoscoped for reasons other than haemorrhage, mortality was 8%.

Regarding gastrointestinal bleeding, a recent national audit studying a population of 12.5 million found an incidence of 103 upper gastrointestinal haemorrhages/100 000 people/year, of which 75% were endoscoped.² Fourteen per cent died within 30 days and again, established inpatients fared worse (death rate 33%) than acute admissions with gastrointestinal bleeding. Applying these figures to the population (5 533 225) covered by the audit of Quine *et al*, 1420 gastroscopies would have been done for upper gastrointestinal bleeding during the four month period. Assuming a similar death rate (14%) from gastrointestinal haemorrhage, 199 deaths would have been expected. This expected 30 day mortality is almost twice that reported by Quine *et al*, and yet only includes endoscopies done for gastrointestinal bleeding (approximately 10% of the total 14 149 endoscopies). This suggests that in the audit by Quine *et al*, gastrointestinal haemorrhage or its associated mortality was less than expected, or that the 30 day mortality was underestimated.

Thus, without data on numbers of inpatients and numbers of gastrointestinal bleeds, endoscopists may be unable to adequately compare their own figures for morbidity/mortality with those provided by this audit.

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1 Newton M, Hepworth C, Jamieson CP, Smith M, Kamm MA, Burnham WR. A prospective audit of new inpatient referrals for upper gastrointestinal endoscopy to the gastroenterology firm of a district general hospital. *Gut* 1994; 35 (suppl 5): S77.

2 Rockall TA, Logan RFA, Devlin HB, Northfield TC. Incidence and mortality of acute upper gastrointestinal bleeding in the UK. *Gut* 1994; 35 (suppl 5): S47.

Reply

EDITOR,—In our audit inpatients represented 26% of all referrals to the endoscopy unit (65% outpatients, 9% unstated) and likewise these patients were older and had higher comorbidity ratings. The '30 day all cause' death rate for inpatients was only estimated to be 2.6% and this is definitely an underestimation. Similarly the death rate at 30 days for gastrointestinal bleeding was underestimated. A validation process performed on seven per cent of all endoscopies showed that the reporting of deaths for up to 30 days was the only area of possible significant error. There is no argument that an audit such as that performed by Rockall *et al*,¹ which looked specifically at gastrointestinal bleeding, will provide more accurate estimates of mortality associated with gastrointestinal haemorrhage.

Our audit looked at many diverse aspects of endoscopy practice and it is hoped that our results will be of great interest and encourage further study. As regards looking at complications related to endoscopy we feel that the unearthing of seven deaths directly caused by the gastroscopy is the most pertinent discovery especially as it is probable that stricter attention to sedation and monitoring of the patient while on the unit may have prevented some of these deaths.

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Audit of upper gastrointestinal endoscopy

EDITOR,—The risk of gastric perforation following endoscopy, highlighted by Quine *et al* (*Gut* 1995; 36: 462–7), might be greatest when there is coexisting gastric outlet obstruction. Gastric distension resulting from trapped air could, in those circumstances, predispose to perforation at the site of weakness in the stomach wall – that is, at the ulcer site.¹ The ulcer site could be even weaker in gastric ulcers resulting from coprescription of corticosteroid drugs and non-steroidal anti-inflammatory drugs. Because air insufflation can aggravate gas trapping, the duration of the endoscopic procedure should be reduced to a minimum in high risk subjects, and the stomach should be promptly deflated after gastric biopsy.

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1 Pasricha PJ, Fleischer DE, Kalloo AN. Endoscopic perforations of the upper digestive tract: a review of their pathogenesis, prevention, and management. *Gastroenterology* 1994; 106: 787–807.

Local anaesthetic sprays and pneumonia after gastroscopy

EDITOR,—The recent audit of upper gastrointestinal endoscopy by Quine and colleagues (*Gut* 1995; 36: 462–7) was both timely and useful. I am concerned, however, that a conclusion will be drawn that was not intended. It is stated that there was in particular a link

between the use of local anaesthetic sprays and the development of pneumonia after gastroscopy. I suspect that the link was present only in those who had both local anaesthetic sprays and intravenous sedation rather than spray alone. I agree that local anaesthetic spray should not be used if intravenous sedation is also planned. Many endoscopists, like myself, however, do not routinely use intravenous sedation but do use local anaesthetic throat spray routinely in non-sedated patients. I am not aware of data showing a link between local anaesthetic spray and pneumonia in non-sedated patients and yet if the report is taken at face value endoscopists such as myself could be unjustly criticised. It would be helpful if the authors could say how many of the 11 patients with pneumonia after receiving local anaesthesia also had intravenous sedation.

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Reply

EDITOR,—Of the 11 cases of pneumonia occurring shortly after gastroscopy local anaesthesia was used in 10 patients. All of these cases had received both intravenous sedation and pharyngeal anaesthesia. It is regretted that this was not made clear in the paper. We concur that there is no link between postgastroscopy pneumonia and local anaesthesia without prior sedation. We are keen to highlight, however, that local anaesthetic sprays used with sedation may increase the risk of cardiorespiratory complications.

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Gastric metaplasia and *Helicobacter pylori* infection

EDITOR,—In their paper (*Gut* 1995; 36: 193–7), Khulusi *et al* showed that the extent of gastric metaplasia in the duodenum declines 10 months, on average, after eradication of *H pylori*. The close relation of this event with the reduction of duodenal inflammation led the authors to conclude that the bacterium itself rather than the commonly held increase in gastric acid production is, at least in part, responsible for the development of gastric type epithelium in the duodenum. This result is in contrast with that published by Noach *et al*,¹ who excluded any significant change in gastric metaplasia one year after *H pylori* eradication. As the extent of the phenomenon did not differ between patients with eradicated and persisting infection, these authors concluded that the *H pylori* related inflammatory process is less important than gastric acid output in the genesis and persistence of duodenal gastric type epithelium.

These conflicting experimental data achieved in populations of similar sample size and after similar periods of follow up confirm that the pathogenetic link between *H pylori* and formation of duodenal ulcer is still a matter of heated debate. We have already questioned the relevance of gastric acid hypersecretion in inducing gastric type epithelium in duodenum² and Khulusi and

colleagues themselves seem to rule out the hypothesis that gastric metaplasia in duodenal ulcer patients is secondary to the *H pylori* induced augment of gastric acid production with subsequent greater duodenal acidity.³ As it is well known that *H pylori* infection is usually present in all patients bearing duodenal ulcer,⁴ all these patients should be acid hypersecretors, but this is true only in about one third of cases.⁵ Moreover, several studies on the effect of both medical and surgical antisecretory measures have failed to show any reversal of gastric metaplasia in the duodenum.^{6,7} Unfortunately, neither Khulusi *et al* nor Noach *et al* reported data on the acid secretory patterns before and after *H pylori* eradication in the patients in whom they, respectively, showed regressed or unchanged gastric metaplasia in duodenum. The knowledge of this variable would have been of great help in interpreting the role of acid in the reversal or not of duodenal gastric metaplasia in the patients where *H pylori* has been eradicated. We recently studied the circadian pattern of gastric acidity in *H pylori* positive duodenal ulcer patients with (n=24) and without (n=14) gastric metaplasia in duodenum.⁸ Although the acidity of both groups was significantly higher than normal, there was no significant difference between them as regards the 24 hour mean (SD) pH values (1.56 (0.35) *v* 1.44 (0.37)). These findings raise further doubts on the responsibility of hyperacidity in the induction of gastric type epithelium in duodenal mucosa and seem to support the conclusion by Khulusi *et al* that factors other than acid, and possibly also the reduction of duodenal inflammation, are implicated in the partial reversal of gastric metaplasia after eradication of *H pylori*.

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Reply

EDITOR.—We are grateful for the comments of Savarino *et al*. The pathogenesis of gastric metaplasia is indeed a complex issue. Our paper (*Gut* 1995; **36**: 193-7) and other work recently completed in our department¹ suggests that *H pylori* is responsible for extending pre-existing gastric metaplasia, probably as a result of increased duodenal inflammation. The study by Noach *et al*² did show a trend towards reduction in gastric metaplasia with *H pylori* eradication but their small study size had insufficient power to detect a significant reduction. Hence their results cannot be considered to 'contrast' with our own although their interpretation does. We have recently studied the role of acid in the pathogenesis of gastric metaplasia.¹ In a double blind placebo controlled trial we found that profound and prolonged acid suppression with omeprazole does reduce the extent of gastric metaplasia without affecting the severity of duodenitis. Taken together, it seems that *H pylori* extends gastric metaplasia by provoking duodenitis and that acid also extends gastric metaplasia but by a mechanism independent of inflammation.

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- Khulusi S, Patel P, Badve S, Lloyd R, Marrero J, Finlayson C, *et al*. Pathogenesis of gastric metaplasia in duodenal ulcer disease. *Gut* 1995; **36** (suppl 1): A51.
- Noach LA, Rolf TM, Bosma NB, Schwartz MP, Oosting J, Rauws EAJ, *et al*. Gastric metaplasia and Helicobacter pylori infection. *Gut* 1993; **34**: 1510-4.

Helicobacter pylori and gastric metaplasia of the duodenum

EDITOR.—Professor Northfield's group (*Gut* 1995; **36**: 193-7) found a significant decrease in gastric metaplasia in the duodenal bulb after *Helicobacter pylori* eradication. We have three questions.

(1) Duodenal biopsy specimens were examined by two histopathologists. Were they independent, did their results agree, and if not, whose were used?

(2) The extent of gastric metaplasia in the duodenal bulb biopsy specimens was assessed as a percentage of the total duodenal epithelial surface. How was this technique validated? What were the intra- and inter-observer variation of these measurements?

(3) Why were six of 32 (19%) patients with duodenal ulcer without gastric metaplasia or duodenitis in the duodenal bulb?

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Reply

EDITOR.—We thank Dr Baron's group for their questions, in reply:

(1) The assessment of histological sections was carried out by two histopathologists unaware of the treatment status of the subject and working together on the same sections. The grading of gastric metaplasia and duo-

denitis was based on their mutually agreed values.

(2) The extent of gastric metaplasia in the duodenal bulb biopsy specimens was assessed as 'total epithelial surface present' in the biopsy sections themselves. We validated the results on 30 randomly selected sections by a morphometric technique using an interactive image analysis system (OsteoMeasure, Osteometrics, Atlanta, USA). There was a close correlation between the semiquantitative values given in the paper and quantitative measurements ($r_s=0.89$, $p<0.001$).

(3) Duodenitis and gastric metaplasia occur in close proximity to duodenal ulcers. Both have a patchy distribution, however, and can be absent from biopsy specimens,¹ especially if the samples are obtained from specific sites regardless of the endoscopic appearance.

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- 1 Hasan M, Sircus W, Ferguson A. Duodenal mucosal architecture in non-specific and ulcer associated duodenitis. *Gut* 1981; **22**: 637-41.

Cell proliferation and polyposis

EDITOR.—Mills *et al* (*Gut* 1995; **36**: 391-4) describe a small but significant increase in the proportion of Ki-67 labelled cells within the upper crypt and surface epithelium of the colon in polyposis versus control subjects. Conversely there was a small, but non-statistically significant reduction in the number of labelled cells in the crypt base. These small differences were detected by assessing seven perfectly oriented hemicypts in 20 study and 20 control subjects (showing considerable interindividual variation in the labelling index). In both groups, most labelled cells were limited to the lower three fifths of the crypt. The findings are interpreted as confirming the existence of stage II lesions as detected by in vitro studies on mucosal samples obtained from polyposis patients.¹ In fact, the authors are describing stage I lesions, which are characterised by the redistribution of a few cycling cells into the upper third of the crypt with no major shift of the proliferative zone. Stage II lesions are focal and characterised by redistribution of the entire proliferative compartment into the upper two thirds of the crypt.¹ As the authorship includes expertise in the field of histopathology, microadenomas were correctly diagnosed as such. The fact that they do not demonstrate stage II lesions as defined by Deschner¹ suggests that stage II lesions are indeed microadenomas.

Stage I lesions occur in subjects at low risk for colorectal cancer.¹ Minor proliferative deviation may be related to sex, age, anatomical site, dietary supplementation, a variety of colorectal disorders, and surgery.² It is difficult to integrate a putative pre-neoplastic role for minor proliferative changes with current molecular insights into familial adenomatous polyposis.² Is it not more likely that the subtle cell kinetic changes encompassed by stage I lesions are reactive and in the case of polyposis are secondary to adenoma generation? The study negates the existence of the stage II lesion and lends support to the elegant work of Nakamura *et al*.³ I would suggest that