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 department[1] 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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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 duodenitis 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 hemicrypts 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 Deschner[1] 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