We agree that not all patients with duodenal ulcer disease secrete more acid than normal. Patients with duodenal ulceration, however, on average produce more acid than normal.^{1,2} As gastric metaplasia is an almost constant finding at the margins of duodenal ulcers, increased acid flux may at least be one contributory factor to the development of gastric metaplasia. This is substantiated by many experimental findings and clinical studies.³⁻⁶ Indeed, the high prevalence of gastric metaplasia in dyspeptic patients in general suggests that other, still unknown factors, may also be involved.

The short term lack of regression of gastric metaplasia after eradication of *H pylori* may also point to the multifactorial nature of gastric metaplasia, including ongoing robust acid secretion during the first year after eradication of *H pylori*.⁷⁻⁹ Evidence emerges that gastrin mediated acid output regresses one year after eradication of *H pylori* in duodenal ulcer disease.¹⁰ Up to now, we cannot exclude that gastric metaplasia may be slowly reversible in the long term as has been seen after vagotomy.¹¹ Again, other factors than acid and *H pylori* infection may be responsible for the persistence of gastric metaplasia in other patients.

We do not agree with Savarino *et al* that the pathogenic relevance of gastric metaplasia for duodenal ulcer patients is diminished by the fact that gastric metaplasia failed to regress in the short term follow up after eradication of *H pylori*. In our opinion, the almost invariable presence of gastric metaplasia at the margins of duodenal ulcers shows that both gastric metaplasia and (ulcerogenic strains of) *H pylori* are required for the development of duodenal ulceration. Longer follow up studies will be necessary to find out if, to what extent, and with what velocity gastric metaplasia regresses in duodenal ulcer and non-duodenal ulcer subjects.

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Risk factors for the development of gall bladder disease

EDITOR,—I enjoyed reading the article by Murray *et al* (*Gut* 1994; 35: 107-11). I am surprised that the authors have published data where there is no confirmatory evidence of gall stones in most of their patients. I agree it is unlikely that the general practitioners in the study changed their diagnoses in patients with upper abdominal pain on the basis of smoking habit. On the other hand it is quite conceivable that smokers experienced more episodes of acute upper abdominal pain because of peptic ulceration or reflux disease.

With 80% of patients not even admitted to hospital and no indication of the percentage of patients who had confirmed gall stone disease this paper cannot fully consider the effect of smoking on gall stone disease. It tells us that smokers experience more upper abdominal pain than non-smokers. Whether or not this results from gall stones is another question, which remains unanswered.

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Ileal and colonic epithelial metabolism in quiescent ulcerative colitis

EDITOR,—The paper by Drs Finnie *et al* (*Gut* 1993; 34: 1552-8) showing that mucosal biopsy specimens from sufferers of quiescent ulcerative colitis possess a normal ability to oxidise butyrate is in direct contradiction to our findings where we showed a reduced capability.¹ We used an almost identical technique, which has been validated and exhibits a similar degree of reproducibility.^{2,3} We would concur with the conclusions of Finnie *et al* on tissue viability, effects of lymphocytes, and of contaminating bacteria (although assaying 100 µl of faecal fluid would not ascertain whether there were different adherent bacteria on the mucosal surface in disease and controls) on the assay. It is difficult to account for the differences in the results but we would like to make a few points to complement those of Professor Roediger (*Gut* 1993; 34: 1646).

The rates of oxidation of glutamine and butyrate found by Finnie *et al* were about a 100-fold greater than ours using biopsy specimens, and other workers using isolated colonocytes.³ Working through the calculations of Finnie *et al* it would seem that the protein content of their specimens was far less than would be expected from the wet weights of the specimens.

This problem may be illustrated by

reference to the data shown in Fig 2 where specimens of about 10 mg wet weight were incubated in 1 ml of medium containing 1 mM [1-¹⁴C] labelled butyrate (1 µmol butyrate in total) for up to three hours. After two hours about 200 nmol of carbon dioxide were produced for each µg of tissue protein present in the incubation. As the complete oxidation of butyrate results in four molecules of carbon dioxide this represents the utilisation of 50 nmol of butyrate per µg tissue protein. At this rate of utilisation all the butyrate in the incubation medium would have been oxidised in two hours by a specimen containing 20 µg of protein. It is difficult to envisage that a 10 mg specimen could yield no more than 20 of µg protein.

This same problem can be considered from another angle, without assuming complete oxidation of the butyrate. One µCi (37 KBq) of labelled butyrate was added to 1 µmol of butyrate, thus the specific activity was 2220 disintegrations per minute (DPM) per nmol. Finnie *et al* quote a range of 24 000-115 000 DPM for butyrate. This represents 11-52 nmol/10 mg wet weight/2 hours and converts to 0.55-2.6 nmol/mg wet weight/hour. From Table 1 and Fig 4 the mean rate of butyrate oxidation is about 75 nmol/µg protein/hour. Thus a specimen weighing 10 mg wet weight would be expected to yield 0.3-0.07 µg of protein. In our experience a colonic biopsy specimen with a wet weight of about 10 mg is equivalent to about 800 µg protein weight, which is much closer to the ratio found by other workers.⁴

It is difficult to comment in detail without seeing the raw data but it is possible that the division of the biopsy sample into very small pieces led to the shedding of a significant amount of material as cell clusters during the incubation period. The use of perchloric acid to terminate the reaction and liberate the carbon dioxide may then also have resulted in the precipitation of protein, which was lost to the assay.

All our experiments, as Finnie *et al* correctly pointed out, were performed in the presence of 5 mM glutamine and 5 mM butyrate. It is known that the presence of 5 mM butyrate suppresses the rate of oxidation of glutamine in the rat colonocyte.⁵ If this holds true for the human it is difficult to draw conclusions from the work of Finnie *et al*, as in vivo both glutamine and butyrate will be present.

While we agree that there is evidence to suggest that butyrate concentrations greater than 2 mM may be toxic to certain cell lines there is no evidence to suggest that concentrations of less than 40 mM are toxic to isolated colonocytes.⁶ Finnie *et al* found that using concentrations of either 1 mM or 5 mM butyrate had no significant effect on the ability of the specimens to oxidise butyrate (Fig 3). In our experiments we used a butyrate concentration of 5 mM.³

The finding that the ratio of butyrate/glutamine oxidation in the distal colon is greater than in the proximal colon in the control group and that this relation is lost in the diseased group suggests that this second group has a lower dependency on butyrate and is more reliant on glutamine as a fuel source. It may be speculated that this is a response to an inability to oxidise butyrate and explains why inflammation is more commonly seen in the distal rather than proximal colitic colon.

The results from the ileal mucosal biopsy specimens are at variance with our previously published results⁷ and we wonder if con-