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. 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. 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. Evidence emerges that gastrin mediated acid output regresses only in the acid of H pylori in duodenal ulcer disease. Up to now, we cannot exclude that gastric metaplasia may be slowly reversible in the long term as has been seen after vagotomy. Again, other factors than acid 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 prevalence of gastri
cal metaplasia in 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 regressions in duodenal ulcer and non-duodenal ulcer subjects.


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 that 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 could be predisposed to develop gall stones after 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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Inleal and colonic epithelial metabolism in quiescent ulcerative colitis

Editor,—The paper by Drs Finnell 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. We used an almost identical technique, which has been validated and exhibits a similar degree of reproducibility. We would concur with the conclusions of Finnell et al on tissue viability, effects of lymphocytes, and of contaminating bacteria (although assaying 100 μl of faecal fluid would not find the neutrophils there would be very different adherent bacteria on the mucosal surface in disease and controls) on the assay. It is difficult to account for the differences in the two reports unless we 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 Finnell et al were about 100-fold greater than ours using biopsy specimens, and other workers using isolated colonicocytes. Working through the calculations of Finnell 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 butyrate per mg tissue 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 14C labelled 2 mg 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 therefore quite conceivable that the authors could have yielded no more than 20 μg of 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. Finnell et al quote a range of 24000–115000 DPM for butyrate. This represents 11–52 kBq of butyrate. This makes it quite easy to oxidise 0–55–2–6 nmol of butyrate per mg 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 yield 750–3000 μCi of endogenous 14C labelled 2 mg 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.

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 perchorlic 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 Finnell 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 secretion of acid and explains why inflammation is in the colonic 454-8. The finding that the ratio of butyrate/glutamine oxidation in the distal colon is greater than that from the proximal colon 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 colonic colon.

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