intact stomach', but this is well known and obvious because duodenogastric reflux is a physiological event, which takes place in all the subjects as well as in all the *H pylori* positive ones. In contrast, in my opinion, because of these *methodological* reasons the statement that 'data suggest that *H pylori* may induce DGR' is apodyctical and needs to be proved by examining wider series and using more adequate methods.

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Reply

EDITOR,—We appreciate the comments raised by Dr P Bechi about our recent publication (*Gut* 1996; **38:** 15–8). We agree that one hour assessment of duodenogastric reflux (DGR) by double labelled scintigraphy may not be the most sensitive method for DGR estimation. However, the use of a nasogastric aspiration tube[1] and perfusion techniques[2] to measure DGR over several hours are unphysiological. The nasogastric tube may induce DGR and the unpopularity of such experiments preclude the investigation of a proper number of patients. The new method of 24 hour portable DGR monitoring (Bilitec 2000, Synectics) is currently the best method to measure DGR quantitatively[3-4] in the fasting and postprandial state, during day and night. This technique was not available when we carried out our study, and it is still under investigation and standardisation.[3 4]

We also agree with the comment that 'normal' subjects have various degrees of DGR, but studies of 'normal' subjects have not discriminated *H pylori* positive and negative persons.[1-4] However, it has recently been shown that patients with type B gastritis have a high incidence of DGR.[5] This study lends support to the results of our experiments, where we have shown that significantly more patients who had DGR were *H pylori* positive (91 *v* 44%, p=0·01) and that DGR is reduced after successful *H pylori* eradication. These evidences justify our statement that '*H pylori* may induce DGR'.

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Calcium and colorectal epithelial cell proliferation

EDITOR,—There is still much debate whether calcium can prevent colorectal cancer in patients with an increased risk of the development of such tumours. Calcium intervention studies, using epithelial cell proliferation as an intermediate end point, have produced inconsistent results. Most studies have focused only on the effect of calcium on the rectal epithelium. Several open uncontrolled studies[1-4] have shown a reduction of rectal epithelial cell proliferation during calcium supplementation, but small placebo controlled studies are not as uniform in their conclusions.[5-8] Recently Weisgerber *et al* (*Gut* 1996; **38:** 396–402) considered this aspect of sample size, as well as the fact that studies were performed with biopsy specimens from the rectum. With respect to the small size of patient populations, two recent studies included much larger numbers of subjects. Bostick *et al*, performed a randomised, double blinded study in sporadic adenoma patients.[9] Patients received placebo (n=66), 1 g calcium/day (n=64) or 2 g calcium/day (n=63) for six months. Rectal biopsy specimens were obtained at baseline, and at one, two, and six months. In this study no difference in proliferation was observed between the three groups. However, calcium normalised the distribution of proliferating cells in the crypts, which is supposedly beneficial with respect to cancer risk. Rothstein *et al*[10] published a preliminary report on a very large study in which adenoma patients were randomised to receive 1·2 g calcium (n=173) or placebo (n=160). Before and after six to nine months supplementation rectal biopsy specimens were taken. Calcium had no effect on proliferation and, in contrast with the previous study, no effect on the distribution of proliferating cells either. With respect to the effect of calcium on proliferation of colonic mucosa, Weisgerber *et al*[11] suggested in their recent paper that, apart from one open uncontrolled trial,[12] this had not been studied before. In another open uncontrolled study we unexpectedly observed an increase of proliferation in the sigmoid of adenoma patients after 12 weeks 1·5 g calcium/day.[13] Weisgerber *et al*[11] performed a randomised, double blinded study and did not find any effect of longterm calcium supplementation on sigmoidal cell proliferation. These results confirm to a great extent our recently reported findings in a randomised, double blinded study in 30 first degree relatives of patients with hereditary non-polyposis colorectal cancer.[14] These subjects are known to have an increased epithelial cell proliferation rate,[1 15] which responded to calcium in two open studies.[1 2] The subjects received 1·5 g calcium/day or placebo. To elucidate the potential site specific effects of calcium in the colorectum, biopsy specimens were obtained from the rectum, sigmoid, and descending colon, before and after three months. In none of the three parts of the colorectum was a significant effect of calcium on proliferation observed compared with placebo. The only noticeable difference between the two groups was a decrease of proliferation rate in the luminal crypt compartment in the rectum during calcium compared with placebo, a finding similar to that of Bostick *et al.*[9]

In summary, from the randomised, double blinded studies reported, the following conclusions can be drawn: (1) in the rectum calcium supplementation may normalise the abnormal distribution of proliferating cells in the crypt without affecting overall proliferation rate; (2) no appreciable effect of calcium supplementation on proliferation in the sigmoid can be observed, and the same seems to be true for the descending colon. Based on these conclusions considerable doubt should arise on the value of calcium supplementation for the prevention of colorectal cancer in people with an increased risk of this disease.

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