clear from their data that a genetic interpretation of normopepsinogenenaemic DU could be rejected in other populations. In other populations we have developed considerable evidence that normopepsinogenenaemic I DU may be composed of both genetic and non-genetic forms.

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References


Reply

Sir,—Our studies in an Indian population using a proteolytic assay to determine total serum pepsinogen revealed that healthy first degree relatives of hyperpepsinogenaemic duodenal ulcer (DU) patients have serum values intermediate between the patients and controls. It was also concluded that the segregation of hyperpepsinogenaemia is consistent with an autosomal dominant mode of inheritance in the families of these patients.

From the results obtained by us we concluded that total serum pepsinogen may be a better serum marker of duodenal ulcer. In order to support this speculation in our publication we cited the reference of Mirsky who observed a tendency for higher values of total serum pepsinogen among patients with active lesions using the same proteolytic assay used by us in our study. In fact we are planning to take further studies to test our hypothesis by determining serum pepsinogen by both proteolytic assay as well as radioimmunoassay in the same population. So far as the division of DU cases into a genetic hyperpepsinogenaemic form and a non-genetic normopepsinogenaemic form is concerned, it was based on two observations. Firstly, we found no familial aggregation of DU disease in our cases with normopepsinogenaemia. The second observation that lead us to this conclusion was a high frequency (54.2%) of 'O' blood group among DU patients with hyperpepsinogenaemia compared with a relatively very low frequency (23.5%) of this blood group in normopepsinogenaemic patients. Further, a careful perusal of our paper reveals that our conclusion with regards to a non-genetic basis for DU disease with normopepsinogenaemia was tentative as we admitted that the number of such cases (DU cases with normopepsinogenaemia) was limited (refer page 1383, second paragraph). We hope this clarifies the issue raised.

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Sticking of dosage forms in the gastrointestinal tract

SIR,—In recent months there has been a number of reports or suggestions of sticking of dosage forms in the gastrointestinal tract. The term 'sticking' is an unfortunate choice, as it is not always clear whether an author or reported speaker is referring to obstruction, periods of stagnation, or to actual adherence to the gastrointestinal mucosa. Studies on the gastrointestinal transit of dosage forms in man show clearly that there are periods of stasis especially in the region of the ileocaecal junction and at the hepatic and splenic flexures of the colon. Such periods of delayed transit occur for all types of dosage form (pellets, single units) and it is not unusual to observe a formulation resident in the ileocaecal region for periods in excess of four hours. There is no evidence, however, to suggest that this is because of physical adherence of the dosage form to the mucosa. In vitro tests conducted on isolated oesophagus or even glass beakers have shown that certain single unit dosage forms can adhere, but such tests are hardly relevant to the normal physiological situation. Nevertheless, the hydroxypropylmethylcellulose film coating of an osmotic pump containing indomethacin (Osmosin) was judged to be responsible for reported adverse reactions to this formulation. A recent study showed, however, that the Osmosin formulation was far less adherent than conventional gelatin based capsule systems. Studies of the gastrointestinal transit of placebo Osmosin tablets lend no support to the speculation that these devices stick to the gut.

Various authors have studied the question of oesophageal transit of dosage forms in man. Both tablets and capsules can be retained in the oesophagus in patients and tablets have been reported to have a much greater liability for retention than capsules. It is clear from these clinical studies that capsules and tablets should be administered only after a lubricating bolus of water, followed by a further swallow of water. Posture is another important factor because the occurrence of oesophageal retention is enhanced in supine subjects. Patients, or those responsible for dose administration to patients, should be aware that dosage forms, whether they are tablets or capsules, should be taken with a drink, whilst in an upright posture.

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References