one reported in this issue of *Gut*,¹ may yield the most fruitful information.¹ ¹¹

**N J TALLEY AND D W PIPER**

**Department of Medicine, University of Sydney, Sydney, Australia.**

**References**


**Pepsinogen genetics and duodenal ulcer disease**

Sir,—We were pleased to read that our work on the genetics of serum pepsinogen and duodenal ulcer (DU) disease has been essentially confirmed in an Indian population by Habibullah and colleagues (*Gut* 1984; 25: 1380–3). While Habibullah *et al* used a proteolytic assay to determine total serum pepsinogen, and we used a radioimmunoassay for the separate determination of serum pepsinogens I and II, both studies found that healthy first degree relatives of hyperpepsinogaenic DU patients have serum pepsinogen values intermediate between the patients and controls, and that the segregation of hyperpepsinogenaemia is consistent with autosomal dominant inheritance in many families.¹ ³

We take issue, however, with the assertion of Habibullah and colleagues that total serum pepsinogen is a better marker of DU than serum pepsinogen I. There is no published evidence to support this proposal. The testing of this hypothesis would require the determination of serum pepsinogen by both proteolytic assay and radioimmunoassay in the same population. Further, our data do not support the proposal by Habibullah *et al* that DU disease can be divided simply into a genetic hyperpepsinogenemic form and a non-genetic normopepsinogenemic form. In European and North American populations, we have found aggregation of DU and an increased frequency of DU among the relatives of families identified through index cases of DU with normal serum pepsinogen I levels.² ³ We have also found that several pathophysiologic abnormalities characteristic of DU aggregate in some families with DU and normal concentrations of serum pepsinogen I.

Our studies, as well as those of Lam and coworkers, have shown that the genetic heterogeneity of DU disease extends beyond that which can be defined by normal and raised concentrations of serum pepsinogen I.⁴ ⁷ Our earlier studies have shown that antral G-cell hyperplasia,⁸ ⁹ characterised by DU, hypergastrinaemia and hyperchlorhydria, has a familial basis.¹⁰ ¹¹ We have found that rapid gastric emptying may be another inherited physiologic defect in DU associated with normal concentrations of serum pepsinogen I.¹² There is also evidence that in some DU families, gastroduodenal inflammation is a concomitant, and even possibly a precursor of ulcer disease. This can be assessed non-invasively by the pepsinogen I/II ratio. Familial aggregation of low PG I/PG II ratios, a highly sensitive marker of gastritis,¹³ ¹⁴ has been observed in some DU and gastric ulcer families.⁴

It is likely that both hyperpepsinogenaemic I and normopepsinogenaemic I DU disease have multiple underlying causes. Some of these are genetically determined, whether autosomal dominant, autosomal recessive, or polygenic, and some may be primarily environmental. Habibullah and colleagues propose that the normopepsinogenaemic form of DU has only a non-genetic aetiology. This may be valid for the Indian population; however, it was not
Correspondence

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

J I ROTTER, M SAMLOFF, AND GLORIA M PETERSEN
Division of Medical Genetics,
Departments of Medicine and Pediatrics,
Harbor-UCLA Medical Center,
Torrance, California,
and Research Service and Department of Medicine,
Sepulveda VA Medical Center,
Sepulveda, California, USA.

References


Reply

sir.—Our studies1 in an Indian population using a proteolytic assay to determine total serum pepsinogen revealed that healthy first degree relatives of hyperpepsinogenaeic duodenal ulcer (DU) patients have serum values intermediate between the patients and controls. It was also concluded that the segregation of hyperpepsinogenaeism 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 Mirsky2 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.1 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 hyperpepsinogenaeic form and a non-genetic normopepsinogenaeic form is concerned, it was based on two observations. Firstly, we found no familial aggregation of DU disease in our cases with normopepsinogenaeism. The second observation that lead us to this conclusion was a high frequency (54·2%) of ‘O’ blood group among DU patients with hyperpepsinogenaeism compared with a relatively low frequency (23·52%) of this blood group in normopepsinogenaeism patients. Further, a careful perusal of our paper reveals that our conclusion with regards to a non-genetic basis for DU disease with normopepsinogenaeism was tentative as we admitted that the number of such cases (DU cases with normopepsinogenaeism) was limited (refer page 1383, second paragraph). We hope this clarifies the issue raised.

C M HABIBULLAH, M MUIAHID ALI, M ISHAQ, AND YOUSUF SALEEM
Departments of Gastroenterology, Genetics, Osmania General Hospital, Hyderabad, A.P., India
Pepsinogen genetics and duodenal ulcer disease.

J I Rotter, I M Samloff and G M Petersen

Gut 1986 27: 224-226
doi: 10.1136/gut.27.2.224