Correspondence

Life events and gastrointestinal symptom

Sir,—The comments on our study of major life events in patients with chronic unexplained dyspepsia published in this issue of *Gut* were appreciated.\(^1\)\(^2\) We believe, however, the criticisms levelled at the methodology are largely inappropriate in view of the findings, and deserve further comment.

Major life event stress was measured by a self-rating scale in our study.\(^1\) We would point out that self-administered rating scales have been widely used, and despite their shortcomings\(^2\)\(^3\) are still considered to have acceptable reliability and validity.\(^4\)-\(^10\) Such instruments do tend to have a bias, however, towards finding a positive association of life events and illness. This is largely because of the ‘effort after meaning’ phenomenon discussed in the leading article.\(^2\) We believe, however, that such a criticism of our study does not apply because no association between life events and essential dyspepsia was detected.

One of the advantages of using a rating scale is that it avoids the problem of the investigator colluding with the patient. With the Brown approach,\(^3\) the meaning of an event for an individual can be determined, but this is rather subjective.\(^11\) Also, although the person who is rating the results is ‘blind’, the initial interviewer who relates the life events and circumstances may consciously or subconsciously alter the presentation to achieve a higher or lower stress score.\(^8\) This approach also requires highly trained investigators and is costlier.\(^9\)\(^1\)\(^2\) For these reasons we used a self-rating scale.

Self-rating scales may be somewhat less sensitive than the LEDS schedule; Bebbington and coworkers found for example that 5% of severe events were missed by the Tennant and Andrews inventory using the Brown method as the ‘gold standard’.\(^9\) The lack of a more definitive ‘gold standard’, however, makes firm conclusions difficult.\(^13\)

In view of the above, we believe the instrument used by us was not flawed. This is particularly the case because no association between major life events and illness was apparent in our study (if any result emerged, bereavements were reported more commonly by the controls).

Exact dating of the illness is important. As it is logistically difficult to gather symptom free subjects and follow them prospectively until some develop chronic unexplained dyspepsia, a retrospective approach was used. As poor memory recall can be a major source of bias, only the 12 month period before endoscopic diagnosis was studied. Patients who had developed their symptoms during this period were compared with those who had a long history by stepwise regression analysis. The number of events, and the distress and life change scores, were similar. As pointed out in the leading article,\(^2\) our approach may have led to a spurious positive finding as some events may have postdated the illness onset, but negative findings were reported. The reviewer commented that these findings were unusual, but no previous studies have assessed such a ‘pure’ group of non-ulcer dyspepsia patients.

It has been postulated that major life events alone may not be important, but in the presence of other factors such as lack of social support and the patients’ personality, they may play a role in causing or precipitating illness.\(^5\)\(^6\) This is clearly acknowledged in our article.\(^1\) In one study it is impossible to take all such variables into account, particularly as there are probably still further factors as yet unrecognised. We have recently studied personality in 76 patients with essential dyspepsia and matched community controls; although it was found patients were slightly more neurotic, anxious, and depressed than controls, the absolute differences and the correlation coefficients were so small that it was concluded these factors were not of clinical importance.\(^14\) The next step is to examine the inter-relationship between personality factors and major life events, and the role of other social factors. Preliminary results suggest these are not significant, and in a recent prospective study we have found life events did not predict a change in symptoms in patients with essential dyspepsia (unpublished observations).

It is stated in the leading article\(^2\) that there is evidence psychosocial factors are of importance in all illness, but we know of no data to support this very broad belief. Furthermore, it is impossible using any valid scientific method to determine the importance of a life event to a particular individual. Only groups or subgroups of patients and controls can be compared and general conclusions drawn.

In summary, despite the limitations of our study which were acknowledged in our paper, there is now evidence that acute stress as measured by major life events may not be important in chronic unexplained dyspepsia.\(^1\) The findings if positive could have been the result of bias, but the negative results indicate the absence of such bias. Although such a result does not concur with general beliefs, only further scientific assessment will determine the truth of the matter. The use of many approaches, including the
one reported in this issue of Gut, may yield the most fruitful information.  

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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 hyperpepsinogaemic DU patients have serum pepsinogen values intermediate between the patients and controls, and that the segregation of hyperpepsinogaemia is consistent with autosomal dominant inheritance in many families.  

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.  

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. Our earlier studies have shown that antral G-cell hyperplasia characterised by DU, hypergastrinaemia and hyperchlorhydria, has a familial basis. We have found that rapid gastric emptying may be another inherited physiologic defect in DU associated with normal concentrations of serum pepsinogen I. 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, has been observed in some DU and gastric ulcer families.

It is likely that both hyperpepsinogaenic I and normopepsinogaenic 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 normopepsinogaenic form of DU has only a non-genetic aetiology. This may be valid for the Indian population; however, it was not valid for the European population.  

SIR.—The study of serum pepsinogen (PG) by Talley and Piper (Gut 1984; 25: 1380–3) is of interest, but there are some reservations. They have found PG I to be a better marker of duodenal ulcer (DU) disease than PG II. This is not in agreement with our earlier findings. We (J Gastroenterol 1984; 19: 261–4) have found that PG II is a better marker than PG I, and have attributed this to the possibility of cross-reacting antibodies in DU patients. We believe that this conclusion is consistent with the findings of others.  

In the study by Talley and Piper, they report a different measurement of PG I, as well as a different method for the separation of the I and II forms. We have not used the radioimmunoassay technique for the latter determination. However, our results are similar to those of the previous studies, and suggest that PG II is a better marker of DU disease than PG I.
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