rates increasing only slightly over the same 30-beat period. These diabetics had other evidence of vagal damage, with abnormal responses to the Valsalva manoeuvre and reduced R-R interval variation. The results of the drug studies on the three controls confirm that the reflex is mediated through the vagus.

In 1895 Hill suggested that changes in posture might provide a "most delicate test of the condition of the vasomotor mechanism," yet surprisingly little attention has been paid to the normal heart-rate response to standing. It is well recognised that there is a transient fall in blood pressure on standing, with stimulation of the carotid baroreceptors and consequent reflex tachycardia and peripheral vasoconstriction. Although it has long been known that in normal people the heart rate increases on standing, the immediate heart-rate response has only recently been briefly documented. As far as we are aware, the characteristic pattern that we describe has not previously been analysed in detail.

Although our results were first obtained from an accurate R-R interval analysis by computer, this study shows that heart-rate changes may also be detected with routine electrocardiography. As loss of a normal response is due to vagal damage, this provides the basis for a simple test of autonomic function that has considerable advantages over those now in use. Measurement of the 30:15 ratio gives a simple numerical value that reflects the presence or absence of the relative bradycardia. When the ratio is 1:00 or less vagal damage is probably present, although a value of less than 1:00 does not necessarily indicate more severe damage, as it will occur when there is a slight increase in heart rate over the 30-beat period. In the most severe cases, in which there is no change in heart rate on standing, the value will be exactly 1:00.

This test is simple to use and requires only a standard electrocardiograph and the ability of the patient to stand up. It is not effort-dependent and, so far as we know, cannot readily be "cheated." It correlates well with other recognised tests of cardiovascular reflex function in diabetes, is objective, requires no special patient co-operation, and is readily applicable as an outpatient procedure.

We thank Dr W G Macfie for allowing us to study subjects from a primary prevention trial of ischaemic heart disease, and Dr P J Watkins for his initial suggestion that we should look at this reflex response.

References

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was slightly diminished in one (case 3). Intracellular killing by monocytes showed a heterogeneous picture: either the monocytes were hyperactive or defective in this respect. The hyperactive killing might be explained as a compensatory mechanism in chronic candida infection. The slightly decreased killing by monocytes in case 3 was probably also due to diminished phagocytosis as our killing assay measures the overall result of phagocytosis and intracellular killing.

In cases 1 and 2 the killing defect was remarkable because this defect is serum-dependent. The conclusion that only the disturbance of intracellular killing is serum-dependent is justified: because the phagocytosis assay showed no difference between normal and patient's serum. The question of whether the serum of these two patients contains an inhibitor or lacks a stimulant is under investigation. In two patients with CMC an inhibitor of intracellular killing of candida by granulocytes has been reported.\(^1\)

We thank Dr C M R Weemaes (Nijmegen), Dr G Hendricks and Dr D B de Geer (Utrecht), and Dr R Schuurman (Rotterdam) for referring their patients. This study was supported by the J A Cohen Institute of Radiopathology and Radiation Protection.

\(^1\) Valdimarsson, H, et al, Cellular Immunology, 1973, 6, 348.

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Prophylaxis with deglycyrrhizinised liquorice in patients with healed gastric ulcer

Recurrence of gastric ulceration after medical treatment is common, with recorded rates of 40 per cent in the first two years. The use of ulcer-healing drugs to prevent relapse has received relatively little attention, though carbenoxolone has been used, but with little success. An acceptable prophylactic drug would be of considerable value in the management of gastric ulceration, and we undertook a trial of deglycyrrhizinised liquorice (DGL) to assess its merit in this respect.

Patients, methods, and results

Forty-one patients (23 men, 18 women) with benign chronic gastric ulceration who had been shown both radiologically and endoscopically to have been healed had been excluded. The trial was a double-blind controlled study, in which participants received five capsules a day, each containing 450 mg of DGL (Ucelad) or an identical placebo. A normal diet was allowed and alcohol and tobacco were permitted in moderation. Antacids were taken as required. We reviewed the patients monthly for recurrence of symptoms, and a full haematological and biochemical profile was taken at each visit. Gastroscopy and barium-meal examinations were performed at six-monthly intervals, or earlier if dyspeptic symptoms arose in the meantime. Patients were followed up for at least two years or until the ulcer recurred.

On completion of the study eight patients had withdrawn, leaving 33 patients for analysis, of whom 22 had received placebo and 11 DGL. The composition of these groups and the ulcer recurrence rate on DGL and placebo is shown in the table. Eighteen patients developed a further gastric ulcer: five were receiving DGL and 13 placebo. This represents a relapse rate during follow-up of 45 per cent for DGL and 59 per cent for placebo. This difference is not significant. Seventy-eight per cent of the total recurrences occurred within the first 10 months of prophylaxis.

Reasons for withdrawal from the trial were defection from follow-up (five patients) and intercurrent illness (three patients). No clinical, biochemical, or haematological abnormality was detected during treatment and no evidence of long-term toxicity was found.

Comment

A compound capable of preventing the recurrence of gastric ulceration would have considerable medical, social, and economic importance. Because the mechanism of gastric ulcer recurrence is unknown the choice of a suitable test compound cannot be entirely rational. We chose DGL because of its reputed effectiveness in healing peptic ulceration and its lack of side effects. It has not previously been used prophylactically in man, but has been shown to protect against gastric ulceration in pylorus-ligated rats. DGL in the dosage used in our study is not an effective prophylactic of chronic gastric ulceration, though the recurrence rate was lower in the treated patients than in the placebo group. Nevertheless, the patients' acceptance of treatment combined with regular endoscopy and barium-meal studies was extremely good, which suggests that prolonged treatment and follow-up could be acceptable to informed patients.

Without precise information on the aetiology of gastric ulceration, the choice of further agents as potential prophylactics must be partly intuitive. Indeed, we cannot be certain that ulcer-healing agents will have any pharmacological activity as prophylactics. Nevertheless, we believe that the search for an effective prophylactic should continue, and suggest that the ideal characteristics of such a drug should be infrequent dosage, low cost, lack of side effects, and absence of long-term ill effects, tolerance, or teratogenicity.

We thank Mrs E M McCrery and Miss T M Hughes for typing the manuscript and Boehringer Ingleheim Ltd for supplying active drug and placebo.

1 Veterans Administration Co-operative Study on Gastric Ulcer, Gastroenterology, 1971, 61, No 4, Part 2, 567.

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Comparative clinical data (ranges given in parentheses) and ulcer recurrence rates in 33 patients with a healed chronic gastric ulcer treated prophylactically with either deglycyrrhizinised liquorice (DGL) or placebo

<table>
<thead>
<tr>
<th></th>
<th>DGL</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>No of patients</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>61 (44-74)</td>
<td>54 (39-74)</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Mean duration of symptoms (months)</td>
<td>7 (1-15)</td>
<td>5 (1-20)</td>
</tr>
<tr>
<td>Mean duration of treatment (months)</td>
<td>16 (4-29)</td>
<td>12 (5-24)</td>
</tr>
<tr>
<td>Recurrent ulcer (%)</td>
<td>45*</td>
<td>59*</td>
</tr>
</tbody>
</table>

*Difference not significant.