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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.

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SHORT REPORTS

Functions of phagocytic cells in chronic mucocutaneous candidiasis

Chronic mucocutaneous candidiasis (CMC) is a group of uncommon immunodeficiency disorders characterised by chronic infection of the skin, nails, and mucosal surfaces caused by Candida albicans. There are few reports about the functions of phagocytic cells in CMC. This led us to investigate phagocytosis and intracellular killing of Candida by granulocytes and monocytes in CMC with a recently-developed technique.

Patients, methods, and results

Leucocyte functions were tested in five patients (two men (cases 2 and 5) and three women (1, 3, and 4)) with CMC. In four of these patients the candida infection was limited to the skin, nails, and mucosal membranes; the fifth patient (case 1) also suffered from recurrent bacterial infections (affecting the respiratory tract) and had the most severe candidiasis. Case 4 also suffered from hypoallergenism and hypoparathyroidism.

The method for measuring phagocytosis and intracellular killing by C albicans has been reported. To prevent a decrease in the number of the yeast cells caused by clumping of the yeast during the test period C albicans was precultured for at least five days at 30°C. Phagocytosis was assessed from the decrease in the number of extracellular candida determined in a haemacytometer. The rate of intracellular killing was determined microbiologically from the decrease in the number of viable candida after lysis of the phagocytic cells.

In all patients phagocytosis of C albicans by granulocytes was normal in the presence of both normal serum and the patient's serum. Phagocytosis by monocytes of cases 1, 2, 4, and 5 was in a normal range (93.8-98.9 %), whereas the monocytes of case 3 showed slightly diminished phagocytosis (90.9 %). The intracellular killing by granulocytes in the presence of normal serum or patient's serum was normal in all patients.

In the presence of normal serum the intracellular killing by monocytes was normal in four patients (cases 1 and 2), whereas two patients (4 and 5) showed a slight decrease in intracellular killing (50 %, 60 minutes) (see figure). Case 3 showed a slightly diminished killing. When patient's monocytes were used together with patient's serum, however, both cases 1 and 2 showed diminished intracellular killing and the results for cases 3, 4, and 5 were not altered (see figure).

Intracellular killing of Candida albicans by human monocytes.

Intracellular killing of Candida albicans by human monocytes.

(see figure). When normal monocytes were used together with patient's serum, serum of case 2 showed increased intracellular killing, whereas with the serum of case 1 the intracellular killing was still diminished (see figure).

Comment

Concerning the functions of phagocytic cells in CMC Valdimarsson et al reported normal intracellular killing by granulocytes in five patients using the dye exclusion method. This method has the disadvantage of subjective microscopic judgment of candida cells being stained. Phagocytosis and intracellular killing of bacteria by leucocytes was normal in a child with recurrent pyogenic infections, CMC, and defective neutrophil chemotaxis. We found that phagocytosis and intracellular killing by granulocytes were normal in all patients, and that phagocytosis by monocytes
was slightly diminished in one (case 3). Intracellular killing by mono-
cytes 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 infec-
tion. The slightly decreased killing by monocytes in case 3 was prob-
ably 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 con-
tains an inhibitor or lacks a stimulant is under investigation. In two
patients with CMC an inhibitor of intracellular killing of candida
granulocytes has been reported.1

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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%,2 and 60%3 in the first two years. The use of
healer-healing drugs to prevent relapse has received relatively little
attention, though carbexolone has been used, but with little success.4
An acceptable prophylactic drug would be of considerable
value in the management of gastric ulceration, and we undertook a
trial of deglycyrrhizinsed 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 and no previous ulcer history had been shown both radio-
logically and endoscopically within the previous four weeks, were selected
for this study. All were aged under 75, and women of child-bearing age were
excluded.

The trial was a double-blind controlled study, in which participants
received five capsules a day, each containing either 450 mg of DGL (Ulccdal)
and biochemical, or haematological abnormality was detected during treatment and
no evidence of long-term toxicity was found.

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

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Mean age (years)</th>
<th>Mean duration of symptoms (years)</th>
<th>Mean duration of treatment (months)</th>
<th>Recurrent ulcer</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGL</td>
<td>11 (4-74)</td>
<td>1 (1-15)</td>
<td>16 (4-29)</td>
<td>22</td>
<td>59*</td>
</tr>
<tr>
<td>Placebo</td>
<td>12 (7-77)</td>
<td>1.5 (1-20)</td>
<td>15 (5-24)</td>
<td>12</td>
<td>59*</td>
</tr>
</tbody>
</table>

*Difference not significant.

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 ulceration1 (although this has been disputed5) 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.

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