CASE 3

A 30 year old white man had a four month history of pain and swelling of the wrists, ankles, and knees associated with genital ulcers and sore eyes. A three year history of mouth ulcers, unresponsive to antibiotics and steroid mouth washes, was noted. Tests for syphilis, gonorrhoea, and chlamydial infection yielded negative results. After a 10 month trial of non-steroidal anti-inflammatory agents he was admitted. Results of investigations were normal except that the complement degradation product concentration was raised. With full informed consent he was started on thalidomide 200 mg twice daily for four days and then discharged taking 200 mg at night. The penile and scrotal ulcers healed completely and his oral ulcers improved, although the iritis and arthritis did not.

Comment

Mascaro *et al* reported improvement in six patients with severe recurrent aphthous ulcers when treated with thalidomide,[2] and recently Saylan and Saltik reported good results in 26 patients with Behçet's syndrome, although iritis and arthritis did not improve. We have confirmed these findings and also that ulcers recur when treatment is withdrawn, although they are not as severe or as frequent as before treatment.

It is important that the possible development of neuropathy and teratogenesis is not forgotten and that informed consent is obtained. With this caveat we believe that thalidomide is a valuable adjunct to the treatment of severe orogenital ulcers.

We thank Dr BR Allen, Dr D Bossingham, and Mr K Gibbin for allowing us to study patients under their care and Miss E Allen for her secretarial help.

[1] Saylan T, Saltik I. Thalidomide in the treatment of Behçet's syndrome. *Arch Dermatol* 1982;**118**:536.
[2] Mascaro JM, Lecha M, Torras H. Thalidomide in the treatment of recurrent necrotic and giant mucocutaneous apthae and apthosis. *Arch Dermatol* 1979;**115**:636-7.

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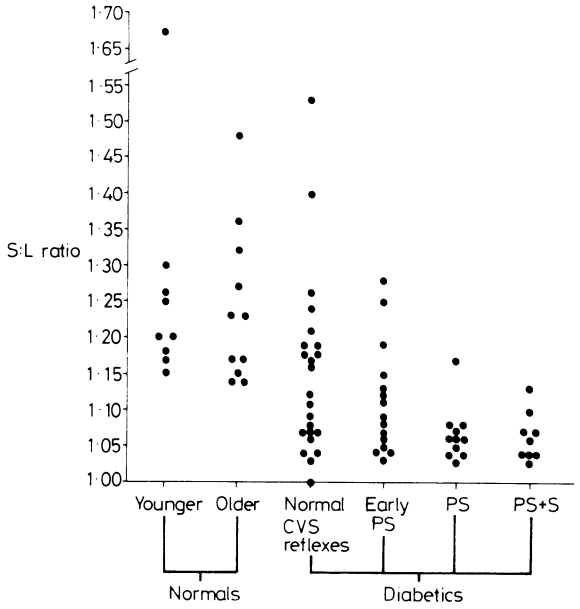
Immediate heart rate response to lying down: simple test for cardiac parasympathetic damage in diabetics

Established simple tests of autonomic function based on cardiovascular reflexes include the heart rate responses to the Valsalva manoeuvre, standing up and deep breathing, and the blood pressure responses to standing and sustained handgrip.[1] We have looked at the possible clinical application of the heart rate response to lying down as a further simple test of cardiac parasympathetic damage. Normally when a subject lies down there is a small but consistent immediate rise in heart rate over three or four beats followed by a fall in heart rate to below the standing level over the next 25-30 beats. This rise is abolished by atropine,[2] thus showing that the early part of the response is mediated by the efferent cardiac vagal pathways.

Subjects, methods, and results

We studied nine younger normal subjects aged 22-32 (mean 26) years and 11 older normal subjects aged 39-65 (mean 50) years. Each of the younger subjects repeated the test five times to assess the reproducibility of the response. In addition, we measured the response in 58 diabetics with a wide range of ages and duration of diabetes: 23 aged 16-60 (mean 36) years with no abnormalities of cardiovascular reflexes (normal CVS); 15 aged 16-59 (mean 42) years with early parasympathetic abnormalities (early PS); 11 aged 19-79 (mean 55) years with definite parasympathetic damage (PS); and nine aged 26-71 (mean 50) years with parasympathetic and additional sympathetic dysfunction (PS+S).[1] We defined subjects with one abnormal heart rate response as early PS, and with abnormalities in at least two of the three heart rate tests as PS. Subjects with additional blood pressure abnormalities were defined as PS+S.



Standing to lying heart rate ratios (S:L ratios) in 20 normal subjects and 58 diabetics with different degrees of autonomic damage (see text for definitions of groups).

Each subject was asked to stand quietly and then lie down without help while a continuous electrocardiogram was made from 20 beats before to 60 beats after lying down. A marker button was used to indicate the point at which the subject started to lie down. The individual R-R intervals were measured with a ruler from the electrocardiogram and the results expressed as a ratio of the longest R-R interval during the five beats before lying down to the shortest R-R interval during the 10 beats after lying down (standing to lying ratio; S:L ratio).

The figure plots the individual results from the different groups of subjects. There was no difference in mean values obtained from the younger (1·25 (SD 0·15)) and older (1·25 (0·09)) normal subjects. All but one of the diabetics with definite parasympathetic damage (mean 1·07 (SD 0·04)) and all those with additional sympathetic damage (mean 1·07 (0·04)) had ratios that were lower than any of the normal subjects. Of the 15 subjects with early parasympathetic damage, 11 also had abnormal S:L ratios. In addition, half of those with otherwise normal cardiovascular reflexes had ratios lower than the normal subjects. The S:L ratio correlated significantly with the 30:15 lying to standing heart rate ratio within the whole diabetic group ($r=0{\cdot}40$; $p<0{\cdot}01$). The test was found to be reproducible in 10 normal subjects, each of whom performed the test five times, coefficients of variation ranging from 3·2% to 10·0% (mean 5·5%).

Comment

We find that as a clinical test the heart rate response to lying down is easy to perform and is repeatable. Older subjects did not have any lower S:L ratios. In diabetics abnormalities were found as expected in those with other evidence of parasympathetic damage, but we also found abnormalities in some diabetics with apparently normal cardiovascular reflexes. This suggests that the standing to lying heart rate response may be a sensitive and useful test of early cardiac parasympathetic disease in diabetics and might be used in conjunction with currently established simple cardiovascular reflex tests.

[1] Ewing DJ, Clarke BF. Diagnosis and management of diabetic autonomic neuropathy. *Br Med J* 1982;**285**:916-8.
[2] Bellavere F, Ewing DJ. Autonomic control of the immediate heart rate response to lying down. *Clin Sci* 1982;**62**:57-64.

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