Phenytoin in rheumatoid arthritis

SIR, We were interested to read the comparative study of phenytoin and gold in rheumatoid arthritis (RA) by Richards *et al*,¹ prompted by the work of Macfarlane *et al*, who had shown improvements in clinical and laboratory tests and suggested that phenytoin may, therefore, have properties of a second line drug.² Richards *et al* found phenytoin to have significant beneficial effects on haemoglobin and the erythrocyte sedimentation rate but on only one of four clinical measurements.

We have also studied phenytoin in RA,³ but without knowledge of other work in progress. Our interest was stimulated by several properties of phenytoin, including inhibition of collagenase and stimulation of collagen synthesis^{4,5}; there appeared to be possible implications with respect to prevention and reversal of rheumatoid bone loss. In an open study with follow up after drug withdrawal we found significant improvements in clinical measurements over 32 weeks; serum C reactive protein, plasma viscosity, and haemoglobin also improved, but changes were not significant.

Three independent studies have, therefore, shown slightly divergent although positive results with phenytoin in RA. Richards *et al* commented that phenytoin may be unique among second line drugs in having a greater effect on laboratory than on clinical tests, though Macfarlane *et al* and we showed significant clinical improvement, albeit in open studies. Confirmation of a positive effect of phenytoin on the erythrocyte sedimentation rate is, however, of particular interest because its control within the normal range may reduce the rate of bone erosion.^{6,7}

The most appropriate assessment of phenytoin in RA may be by its long term effects on bone assessed radiographically and to our knowledge this has not been examined. Although 'phenytoin is unlikely to become a first choice second line agent',¹ it should not now be dismissed.

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More on autonomic neuropathy in systemic sclerosis

SIR, While conducting a study of autonomic function in various connective tissue diseases we became aware of the report by Sonnex and colleagues describing for the first time the occurrence of autonomic neuropathy in systemic sclerosis.¹ Three of their four cases were identified from six patients evaluated systematically, suggesting this complication may not be uncommon. In the circumstances it seemed important to record our findings in the eight cases of systemic sclerosis we have so far evaluated.

These eight cases constituted the total number of patients with systemic sclerosis² under our care during the study period (March to October 1987). Their personal and clinical characteristics are summarised in the Table. Raynaud symptoms and dysphagia were graded according to the intensity of attacks or the degree of disability respectively.

None of the patients was diabetic or in renal failure, or had clinical signs of cardiovascular disease. All were non-smokers and denied alcohol consumption. In no case were drugs being taken in dosages known to affect cardiovascular or peripheral (somatic) nerve function.

Autonomic function was evaluated by the five cardiovascular tests described by Ewing and Clarke.³ Compared with healthy volunteers (control subjects), matched by age, sex, and race, six of the eight patients had abnormal values for one or more of the tests (Table). Classified according to the grading system proposed by these same workers,³ autonomic involvement was 'severe' in patients 3, 5, 6, and 7 and 'early/atypical' in patients 1 and 2.

Six of the patients had electrophysiological evidence of peripheral (somatic) nerve dysfunction (Table). For one patient (No 8), values for all five autonomic tests were within the reference range. Nerve conduction studies also were within the reference range in one of the patients (No 2) with autonomic dysfunction. Distal hypoaesthesia (for pain, light touch, and vibration sense) was present in both upper and lower limbs in this patient, however. In no other case was there a discrepancy between neurological signs and the results of nerve conduction studies (Table).

Our findings affirm the notion implicit in the study of Sonnex and colleagues¹ that autonomic neuropathy may not be uncommon in systemic sclerosis if such patients are evaluated routinely. In contrast with these authors, we found evidence of peripheral (somatic) nerve dysfunction