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 synthesis4 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 scleroris2 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
in all the patients who had abnormal autonomic tests. The failure to detect such changes in any of their four cases may have been due to clinical assessment being limited to the lower limbs and to the use of vibration threshold. In addition, nerve conduction studies were performed in only one case, and, moreover, damage to peripheral nerves in systemic sclerosis may be focal. Certainly the disparity cannot be explained by disease duration as this was notably longer in their study than in ours (median 9-5 years compared with 5 years).

Raynaud’s symptoms and dysphagia are both extremely common in systemic sclerosis, and it is therefore not surprising that these complications were present in all the patients with autonomic dysfunction in our study as well as that of Sonnex and colleagues. Although we too found no clear relation between the degree of autonomic dysfunction and the severity of Raynaud symptoms or dysphagia, we consider it would be premature to discount the possibility of some pathophysiological interrelationship.

This is but one intriguing area for future research that has been highlighted by their timely report.

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References
Book reviews


Published two years after the death of Edmund Dubois, this volume on systemic lupus erythematosus (SLE) is a tribute to his understanding of this challenging disease. Dubois’ insight and far reaching perspective are much in evidence despite the book’s multiple authors. When one looks at successive editions his stamp on the language of the book is also obvious. Although it is distinctly North American, it is often somewhat archaic even in discussing recent developments. The book is as up to date as any reference work can be in such a rapidly developing field, and yet one senses a reluctant transition from the era of the LE cell (accorded an entire chapter) to that of antibodies to extractable nuclear antigens and cardiolipin.

Unfortunately, the text seldom invites the reader to go beyond the specific information required. It is often uninspiring and is as difficult to penetrate as earlier editions have been. Tedium is almost inevitable in a medical publication as comprehensive as this, but some freshness in style and presentation would have been most welcome. There are lengthy lists of authors’ names, publication dates, and frequency figures, and often many paragraphs pass without interpretation of this array of information.

Lupus nephritis has long been a controversial subject, and the views of the authors are somewhat unorthodox. This is disturbing considering the authority carried by this text. The author’s preference is, for example, for steroid therapy in fixed dose for fixed periods, and immunosuppressive agents are only recommended for late use in non-responders. The recent work from the National Institute for Health quite convincingly shows the value of immunosuppressive agents over steroids in reducing the slow drift into end stage renal disease. The authors mention this work but do not acknowledge its importance. They have only recently, and apparently with reluctance, given up nitrogen mustard as their drug of choice. They reject azathioprine as having no value in SLE despite evidence to the contrary. They have their idiosyncrasies too in their recommendations for the monitoring of patients with nephritis. Parameters are ranked according to value, and serum creatinine is placed at the top of the list, with creatinine clearance at the bottom. Their conservative views on the indications for renal biopsy are more in line with British than American practice.

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To me no disease is more protean in its manifestations than SLE. It remains clinically one of the great challenges. This book certainly provides ready access to the vast amount of published work on the subject and therefore is invaluable to the clinician. A rheumatology department without it will certainly be the poorer.

Whipps Cross Hospital, London

J LANHAM


For those revising for MB and MRCP examinations this little book of 200 picture tests is excellent value at £6.50. It also provides a quick and entertaining self assessment for those rheumatologists who do not routinely see (or do not diagnose) the broader spectrum of rheumatic diseases. Not quite all the x rays have reproduced adequately; equally, not all my wrong answers could be attributed to this cause. I was interested to note an example (perhaps the first) of the north/south divide in rheumatology, in which the stoical citizens of Leeds must endure five or more attacks of acute gout annually to qualify for allopurinol! How refreshing to find a rheumatology book which can be read from cover to cover with such enjoyment in the course of one evening.

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Bishop’s Stortford

JACQUELINE CURREY


Despite the availability of more non-drug treatments in rheumatology than in most specialties, all clinical rheumatologists need an in depth understanding of therapeutics. This book is devoted entirely to the drug treatment of the rheumatic diseases. The chapters are written mainly by Drs Frank Dudley Hart and Edward C Huskisson. There are, however, contributions by other authors. Particularly noteworthy are the chapters written by Dr Barbara M Ansell on juvenile chronic arthritis and rheumatic fever, which are instructive and well referenced.

The first half of the book deals in depth with the clinical pharmacology of each individual drug used in rheumatology. The balance here is in favour of the many non-steroidal anti-inflammatory drugs available. These are discussed in 56 pages compared with 23 and 11 pages devoted to ‘slow acting drugs’ and analgesics respectively. The detail in this part of the book makes it a useful initial reference book for the clinician with a query in clinical pharmacology in relation to rheumatology.

The second half of the book clearly outlines the drug treatment of the different rheumatic diseases. The limiting factors in this section are the size of the book and the small
More on autonomic neuropathy in systemic sclerosis.

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