Methylprednisolone pulse therapy in rheumatoid arthritis

Sir. The paper entitled 'Combination of methylprednisolone pulse therapy and remission inducing drugs in rheumatoid arthritis' published in the Annals1 concludes that pulse therapy is of little or no value in the long term treatment of rheumatoid arthritis.

We believe that there are several deficiencies in this study and that the conclusions are not justified. To justify such a conclusion the authors must ensure that a type I error has not occurred. There is no estimate of the power of their study, but it is possible to calculate it.2 We estimated that their study would not be able to detect a 30% difference between the two treatment groups because of the small numbers in each group. In fact there is a trend in all their results which favours the active pulse group. This is further compounded by the fact that three different remission inducing drugs were used in each treatment group, which removes homogeneity of the treatment groups and adds another variable to the treatment protocol. Also, although this is claimed to be a double blind study, the fact that the first assessment was performed only two weeks after treatment when the patients receiving active pulse therapy showed significant disease suppression, means that the observer could not possibly have been blinded to the treatment the patient had received. As most patients have disease duration of at least two years, during which time most of the erosive changes are known to occur, it is hardly surprising that x-rays taken only eight months after treatment failed to show any difference between the two treatment groups. The authors decided to delete error bars on their figures and not include any results from immune complex estimations, which makes it difficult for the reader to assess the results independently. Finally, no assessment was made at any stage, as to whether the two treatment groups were identical at the start of treatment. As a result of these deficiencies we believe that this paper has not justified the conclusions that the authors have drawn.

The question of whether initiation of pulse methylprednisolone therapy at the start of treatment with remission inducing agent alters the efficacy or side effects of such an agent remains unanswered.

References

Sir. Doctor Smith and his colleagues incorrectly quoted from the abstract of our paper that pulse therapy is of little...
or no value in the long term treatment of rheumatoid arthritis. In the abstract we state that a single pulse of methylprednisolone can give a short lasting anti-inflammatory effect but is of little or no value in the long term treatment of rheumatoid arthritis. Furthermore, in the discussion we emphasise that the question as to whether repeated pulses can affect the long term prognosis is still unanswered.

The power of the tests varies for each variable with the standard deviation and the estimated smallest medically relevant difference. For the detection of a 15% difference in the haemoglobin concentration the power of the test was about 80% in the present study. The power was of course less when the standard deviation was greater. This was the case for most of the clinical variables. In the study, however, it was of interest that for most variables there was a statistically significant effect of pulse therapy during the first days or weeks; whereafter the effect seemed to disappear.

The similarity between the two treatment groups appears from Table 1 in the article and from the fact that there was no statistically significant difference in any measured variable between the two groups at day 0.

We do not understand the postulation that the detection of a clinical effect should imply that the observer cannot be blinded.

We do not agree that it is uninteresting that the progression in erosions seen in x rays in nine patients was not reduced in the pulse treated group.

We shall be very happy to send details about the individual measurements on request. Owing to the large number of variables, however, we decided to omit the details of variables in the article when no effect of pulse therapy was observed.

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Book reviews


I welcome the 4th edition of this standard text which is highly appropriate for keen medical students, the MRCP candidate, and the general practitioner. Experienced rheumatologists will also find some chapters valuable. Until recently Mason and Currey was the single, obvious book that one would recommend to medical students, but there are now many rivals in the critical market of rheumatology primers. Such books may mould the attitude of young doctors towards the subject for the rest of their professional lives. I well recall being almost seduced by endocrinology through the excellence of Hall, Anderson, and Smart. Mason and Currey is usually fuller on most subjects than its rivals and must appeal mainly to that coelacanth-like breed of medical students who prefers to write essay answers to the examiner rather than telesex or mindless ticks. Some pithy alternatives might provide a better preparation for the latter.

The 4th edition is written by 15 authors and has many strengths. We value Professor Vernon-Roberts's anatomical and histological accounts of the joint as scene-setting, and many immunologists who dabble in the occult would be well advised to return to Vernon-Roberts at regular intervals to keep their feet on the ground. Even the mast cell gets a mention in despatches. Professor Brewerton has written an excellent short chapter on immunogenetics without recourse to references which are necessary in this book so that one can make the first steps back into the literature. In contrast, Dr Denman's superb account of immunoregulation and autoimmunity, which really stretches the reader, is followed by four pages of references up to 1985. Many chapters lack an up to date reference list and give the impression that research retired with the hippies. The clinical chapters are solid and comprehensive, perhaps lacking sufficient illustrations in parts. Professor Currey's emphasis on mechanisms of joint destruction in osteoarthritis steers the student away from the concept of a 'wear and tear' disease, a phrase which he will hear rheumatologists use when giving explanations to their patients. I also recommend the appendix on clinical examination of joints, which does not figure adequately in shorter rivals. Full accounts of the physical medicine of rheumatology are given by Drs Yates and Mathews and are compulsory reading for those students who have chosen a shorter rheumatology text. Experienced rheumatologists need know no more about gout than Dr Scott has described in a most full chapter. Dr Seifert's account of infectious arthritis is also valuable, though obviously completed too soon to share with us the experience of St Mary's Hospital of human immunodeficiency virus and joints.

In a multiauthor book a consistent treatment of the subject is difficult, but Dr Seifert writes about the same amount on Lyme disease as Professor Cohen offers on Paget's disease in a chapter on metabolic bone that requires expansion. Dr Barnes' peripatetic journey through 'less common rheumatic conditions' covers much ground in remarkable detail. Mr Freeman does not settle for a bland account of orthopaedic interventions but provokes us with