efficacy and low incidence of side effects from this treatment. Two further papers appeared in the November issue of the *Annals.* The paper by Walters and Cawley showed the value of combining pulse methylprednisolone with sodium aurothiomalate treatment, results similar to our findings in a previous publication, of which the authors appeared not to be aware. The paper by Williams et al again showed the low incidence of adverse effects from this treatment and, more specifically, failed to find an increased incidence of avascular necrosis of the femoral head, which theoretically would be an expected adverse effect in view of the large doses of corticosteroid used in pulse methylprednisolone treatment. This retrospective cohort study needs to be confirmed by a prospective long term study with large patient numbers as well as matched controls, it confirms the favourable risk/benefit ratio of this treatment. It is therefore surprising that our papers on this subject in another journal led to an editorial comment and correspondence describing this treatment as 'ineffective' and 'hardly justifiable' in the treatment of rheumatoid arthritis. Perhaps this simply reflects a conservative attitude of North American clinicians, yet it is surprising that pulse therapy, with its favourable risk/benefit ratio, considerable efficacy in short term control of inflammation, and efficacy as oral treatment, should not be at least as attractive a therapeutic option as the alternatives—namely, non-steroidal anti-inflammatory drugs (low efficacy, high incidence of adverse effects) and disease modifying antirheumatic drugs (slow onset of action, high incidence of adverse effects, high drop out rate). None of the recent publications has advocated pulse therapy as an alternative to remittive agents, but rather as adjunctive treatment to achieve rapid control of inflammation while awaiting control with a remittive agent, or in the event of failed treatment with several disease modifying antirheumatic drugs.

Perhaps it is time for a Viewpoint article in the *Annals* on the place of pulse methylprednisolone therapy in the treatment of rheumatoid arthritis, lest a potentially useful treatment should be neglected as a result of therapeutic conservatism.

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References


Evaluating drugs in rheumatoid arthritis

Sir, In their recent viewpoint Scott et al discussed the problems of assessing rheumatoid arthritis in clinical trials. Some of these prominent workers have apparently changed their minds recently. Some standard variables were not discussed.

The authors did not comment on the use of various analogue scales, McConkey's clinical score, Ritchie index, and patient opinion. Patient opinion is certainly one of the best methods of assessing the value of disease modifying drugs in rheumatoid arthritis. As long as the patient is taking a medicine he or she has accepted it, and the length of the treatment period is a measure of patient opinion of the drug. The time has passed when the doctor's opinion was the deciding factor for the patient. The reasons for withdrawal are often multifactorial, and factors other than those reported may be concealed. If the drug is good for the patient he or she will stick to it and accept a certain degree of inconvenience. Thus in my opinion, treatment survival as a measure of patient opinion is the most important variable in an evaluation of any anti-rheumatic drug.

The authors stated that 'the debate about the true place of x rays using current technology has subsided; there is now a relatively negative view of x rays and less value is placed on them.' This view was not held in recent trials on methotrexate and auranofin, where x ray evaluation was of basic importance. Recently, Symmons and Dawes stated that radiological assessment is useful both in serial studies to assess the severity of disease and as an outcome measure. Presumably, McConkey had stated that his opinion the best way of studying drugs in rheumatoid arthritis is to carry out serial measurements of the acute phase proteins, relating these measurements to changes in function and to changes in the radiographic appearance.

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Sir, Dr Larsen raises several interesting and relevant issues. This is appreciated as the viewpoint article was intended to stimulate discussion. Because it was based on a consensus meeting some individual opinions, often held for a considerable period of time, were influenced by the arguments advanced at the meeting; but it is appropriate that opinions should be modified in the light of further experience. There are undoubtedly occasions for using visual analogue scales, the clinical score, an articular index, radiological assessments, and measures of patients' opinion, but these are not necessarily the most relevant measures to use. For too long rheumatologists have used multiple variables to assess response, and we think the time has come to adopt a more rational approach. This was the basis of our article. Patients' opinions are relevant; no one could use an antirheumatic drug if all their patients held a poor opinion of it. To argue that patients' opinions should form the mainstay of judging the effectiveness of treatment is probably incorrect, however. Effective treatment must be acceptable to patients and, more importantly, should have a demonstrable and clinically valuable influence upon the disease itself. The viewpoint article addressed the question of what we should consider a 'clinically valuable' effect. No matter how many trials use radiographs to evaluate drug treatment it seems common sense that these are not the most important thing to look at.

There was a feeling at the consensus meeting before the viewpoint article that less weight should now be given to radiological assessments. That is not to deny their relevance nor to overlook the valuable work contributed by Dr Larsen in this field. Clearly, rheumatological ideas move on, and this certainly happened with the views expressed in the viewpoint article on the value of x rays. Ten years ago many rheumatologists were convinced that plain radiology provided the gold standard to assess the progression of rheumatoid arthritis. It takes time for such views to become less pronounced, but the moment has now arrived. Clinical trials usually reflect the prevailing opinions when they were set up and so it is hardly surprising that recently published trials of antirheumatic drugs have used x rays, but in future their use may be more restricted. There are no methods of assessing RA which are appropriate in all circumstances, but there is a need for new approaches; this need lay at the heart of the viewpoint article.

Hepatic veno-occlusive disease and herbal remedies

Sir, The recent report by Lemley et al1 of a patient who developed hepatic veno-occlusive disease while taking azathioprine is of interest to us. We have recently seen a patient with veno-occlusive disease and another chronic disease—namely, multiple sclerosis. This patient was taking no drugs but was discovered to be an avid taker of herbal remedies, including comfrey tea.

It has been established that this herbal medicine can result in veno-occlusive disease.2 3 We note the comment of Lemley et al that 'despite years of experience with azathioprine in RA, veno-occlusive disease has never been previously reported in this population'. Although the orthodox drugs taken by this patient are listed, no mention is made of whether he took any herbal remedies or other alternative medicine. Although azathioprine may have caused veno-occlusive disease in the patient described, we feel it is important to remind practitioners treating people with chronic diseases that not all alternative treatments are harmless and also that the side effects of such treatments may be mistakenly assigned to orthodox drugs.

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