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Combination therapy in rheumatoid arthritis

SIR, The case report by Sheldon and Wood¹ is additional evidence of the need to run a full-scale trial of combination chemotherapy in rheumatoid arthritis (RA). The safety of such regimens is well established in Hodgkin's disease and other lymphoproliferative disorders, and it remains 'difficult to accept that, while haematologists obtain ten year "cures" in malignant B-lymphoproliferative disease, only a minority of patients with classical RA . . . a non-malignant B-lymphoproliferative disease—will experience any remission on a single drug chemotherapy.'²

The potential for provoking a cure in RA has enormous implications. However, the selection for chemotherapy trials of only those patients with long-established disease, who have failed on 'conventional' therapy, will produce in all likelihood an equivocal answer. Such patients will already have suffered severe and irreversible joint destruction, and we should be aiming to produce the cure long before this stage. By analogy, in lymphoma the later the treatment is given the less effective it is.

The evidence is pretty clear that patients with seropositive erosive RA who are DR-4 positive are going to do badly. I believe we should be doing our trials on this group of patients within six months to a year of presentation, and I am sure that the well informed patient would let us.

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Recurrent rheumatic fever in adults

SIR, The case report of Murray *et al.* and our own recent experience suggest that rheumatic fever in adults may be more common than has generally been assumed.¹ In our

institution we have seen two such patients in a five-month period. Both patients were Hispanic males, ages 42 and 44, and had past histories of rheumatic fever in childhood. One patient presented with a four-week history of severe polyarthritis, fever, evidence of acute carditis, and an antistreptolysin O (ASO) titre of 250 Todd units. The other patient had a rapidly spreading arthritis over three days, fever, a leucocytosis of 20.3/nl and an ASO titre of 625 Todd units. Both had raised erythrocyte sedimentation rates; but tests for antinuclear antibodies, rheumatoid factor, and multiple blood and throat cultures were negative. These two patients fulfilled the revised Jones criteria for rheumatic fever, and each showed a prompt response to non-steroidal anti-inflammatory drugs within two days.

We were impressed by the sudden onset and severity of the polyarthritis in each of our patients. This clinical pattern of arthritis in adults with rheumatic fever has been well described, as has the rarity of chorea, subcutaneous nodules, and erythema marginatum.²⁻³ This differs from the childhood presentation, where the arthritis may be fleeting and the cutaneous manifestations are somewhat more common.

We agree with Murray *et al.* that the incidence of recurrent rheumatic fever apparently decreases with age. Although a review of the recent literature shows a number of cases of rheumatic fever in adults, the vast majority of patients were in their second or third decade of life.²⁻³ Very few patients in their forties and fifties, as observed by Murray and by us, have been reported. However, there are reasons why rheumatic fever in the adult may go unrecognized. The severe polyarthritis of adult rheumatic fever may present exactly like more common rheumatic disorders, such as rheumatoid arthritis or systemic lupus erythematosus. Physicians may not appreciate the importance of a rheumatic fever history or determine an ASO titre. Throat cultures, when obtained, are often negative in adults. Finally, manifestations are often self-limiting, and a prompt response to self-administered aspirin or other non-steroidal anti-inflammatory drugs may be sufficient so that medical attention is not sought.

These considerations suggest that the true incidence of rheumatic fever in adults over 40 may be underestimated. As in many other situations it may be that a heightened index of suspicion will lead to more frequent recognition and diagnosis of this disease.

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