Correspondence

Synovial amyloid deposits and chronic haemodialysis

SIR, In their recent paper Muñoz-Gómez *et al*¹ suggested that localised synovial amyloidosis might be peculiar to chronic renal failure treated with periodical haemodialysis, and they made the assumption that it was the cause of an arthropathy. In fact localised amyloid deposition in synovium and also in articular cartilage is a common aging phenomenon² apparently associated with osteoarthritis, and it is relevant that four of the seven patients studied were aged 50 years or more. This type of aging deposit was actually referred to in the preceding editorial as 'joint capsule and articular cartilage' deposition.³ The nature and extent of synovial amyloid deposits described in the article did not appear to differ from those associated with aging, and I would suggest that the finding of such deposits may represent no more than an accelerated age change. It is of interest in this context that synovial and articular cartilage amyloid deposits in patients with the so called amyloid arthropathy syndrome of multiple myeloma and primary amyloidosis do not appear to differ qualitatively from aging deposits either.⁴ Such patients may, however, show gross soft tissue amyloid deposition around joints.

The finding of synovial amyloid deposits in chronic haemodialysis patients may be unrelated to any arthropathy present and should not prevent other causes for an arthropathy from being sought.

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SIR, Recently, the biochemical nature of amyloid fibrils in haemodialysis associated amyloidosis has been characterised.¹ Amyloid fibrils isolated from tissue containing amyloid obtained during carpal tunnel decompression from a patient undergoing long term haemodialysis were found to contain as a major component a protein

homologous to the normal plasma protein β_2 -microglobulin. This protein has not previously been shown to be a fibril constituent in amyloid deposits. β_2 -Microglobulin is known to accumulate in the circulation of patients undergoing haemodialysis since this procedure does not remove the protein from the plasma,^{2,3} and Gejyo *et al* postulate that sustained increase of plasma concentrations of β_2 -microglobulin leads to the accumulation of protein in tissues, causing the formation of amyloid fibrils.¹ Interestingly, both AL amyloid fibrils⁴ and β_2 -microglobulin derived fibrils appear to have a relatively high affinity for the carpal tunnel, and in both cases precursor proteins are related to immunoglobulins.

It is likely that the amyloid deposits in the joints of patients undergoing long term haemodialysis also contain β_2 -microglobulin as the fibril precursor, and it may be possible to confirm this relatively easily by immunohistochemical techniques. Similarly, although the biochemical nature of amyloid deposits in osteoarthritic joints has not been characterised, it should be possible to determine whether these or any other age related amyloid deposits contain β_2 -microglobulin.

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Combination chemotherapy in rheumatoid arthritis

SIR, Would that the situation as outlined by Dr Bamji were so simple.¹

Hodgkin's disease is a malignancy and in the majority of patients suffering from it the outcome, untreated, is death. Justification for using such toxic regimens is therefore easy and indeed giant strides have been made in improving survival. Rheumatoid arthritis cannot be considered comparable. Whether we are right in considering it to be a non-malignant B lymphoproliferative disease remains to be

seen, but for the majority of patients the slight reduction in longevity is in no way equivalent to that in the lymphomas. While we may anguish over the ravaging and debilitating aspects of this disease, I do not think this justifies, at the present time, trials with these drugs which have known severe short and long term side effects, especially when we have not even illustrated that we can carry out adequate trials of our current second line agents nor agree on acceptable measures of disease outcome.

One further point is pertinent. If sums of money similar to those poured into cancer research had been made available for research into rheumatic diseases, always unfashionable with both public and media, then I am sure we would be in a better position to answer many of the above questions.

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Sulphasalazine therapy in RA

SIR, Pullar *et al* reported recently the effect of acetylator phenotype on the efficacy of sulphasalazine therapy in rheumatoid arthritis (RA).¹ We would largely agree with their conclusion that there is little practical value in determining acetylator phenotype before therapy² but would like to comment on the incidence of slow and fast acetylator phenotypes in RA and the suggestion that fast acetylators may be subject to more severe disease.

During the course of investigations on the use of sulphasalazine in RA we have phenotyped 108 patients using a modification of Schroder's method.³ Thirty three patients (30.6%) were male and 80 (74.1%) were seropositive. Sixty two (57.4%) of our patients were slow acetylators, a figure which is in agreement with the reported incidence in the general UK population⁴ and other studies of RA patients.^{5, 6}

It is always dangerous to decide what is serious or mild disease at a single point in the evolution of a chronic relapsing disorder, but all of our patients were felt to have disease of sufficient severity to warrant second line therapy, and the mean erythrocyte sedimentation rates (mm/1st h) at the start of treatment with sulphasalazine were 50.2 (SD 29.4) in the slow acetylators and 51.7 (SD 24.5) in the fast. There is no statistical difference between these figures.

We would conclude therefore that the distribution of acetylator phenotype in patients with RA is the same as that in the general population and that acetylator phenotype has no bearing on the severity of RA.

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Retroviruses in rheumatoid arthritis

SIR, Rheumatoid arthritis (RA) is characterised by both in vivo and in vitro depression of cell mediated immunity. The mechanism for this depressed cellular immunity is not known but may be due to deficient interleukin-2 production.¹ Since retroviruses have been associated with deficiencies of immune reactivity we used standard techniques to look for the presence of antibodies to the human T cell retroviruses (HTLV-I, II, and III) in the sera from 60 patients with classical or definite rheumatoid arthritis.^{2, 3} The results were uniformly negative. Since RA is linked to HLA-DR4 these findings indicate that false positivity on this account might be a rare event.⁴ It may be concluded from this work that if retroviruses are involved in the pathogenesis of rheumatoid arthritis then they are not serologically related to the known retroviruses as detected by presently available techniques.

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