Letters

Disease assessment in rheumatoid arthritis

SIR, With pleasure we would like to obey the summons of Dr Scott *et al* to take part in the debate about disease assessment in rheumatoid arthritis.¹ We fully agree with the first recommendation of the consensus meeting that we certainly do need a simple validated index to measure disease activity as until now it has been impossible to measure this with one single variable in all patients. The constituent parts of such an index must be chosen and validated on a scientific basis, similar to the way in which the health assessment questionnaires, like the HAQ and AIMS, have been developed and evaluated. In fact already in 1982 Bombardier and Tugwell had provided a methodological framework for developing such an index.²

We do not, however, share the opinion of the meeting about the uselessness of radiological assessments as outcome measures in the evaluation of disease modifying antirheumatic drugs in the treatment of rheumatoid arthritis. One of the reasons that this type of measurement has not been accepted as a useful variable may be owing to its incorrect use in clinical trials. It is probably erroneous to consider patients with comparable disease activity but with a wide range of disease duration as one entity as radiological progression is not linear in time. Besides, influences of treatment on radiological progression are probably best studied on x rays of hands and feet of patients with early rheumatoid arthritis. Taking these thoughts into account we recently were able to show, in a double blind clinical trial in which only patients with early rheumatoid arthritis were included, differences in radiological progression between two disease modifying drugs within one year of treatment.^{3,4}

We strongly believe that radiological assessments are essential in the evaluation of disease modifying drugs in addition to the generally accepted types of measure.

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Phospholipase A₂ and inflammation

SIR, We read with interest the leader entitled 'Synovial fluid phospholipase A₂ in inflammation' by Gonzalez-Buritica *et al* in the *Annals*.¹ Indeed the role of phospholipase A₂ in inflammation is becoming better defined and more obvious, and the above mentioned article was a timely addition to our reviews and editorial.²⁻⁴ We would like to make a few comments that may shed additional light on the role of phospholipase A₂ in inflammation. The synthesis and secretion of soluble phospholipase A₂ seems to be a stereotypic response to several humoral signals in a variety of systemic and localised inflammatory processes. Perhaps the most dramatic is the pathogenetic role of phospholipase A₂ in septic shock, a systemic inflammatory process.^{5,6}

Rheumatoid synovial fluid phospholipase A₂ has recently been completely sequenced by us⁷ and by others. It contains 124 amino acids and has a molecular weight of 13 900. This phospholipase A₂ has recently been cloned. Active transcription of this enzyme was found in both rheumatoid synovial tissue and in peritoneal exudate cells.⁷ We reported that different forms of phospholipase A₂ exist in human serum and synovial fluids.^{7,9-11} Human serum contains at least three forms of extracellular phospholipase A₂, one pancreatic and two non-pancreatic calcium dependent and calcium independent forms. Synovial fluids contain two distinct non-pancreatic forms. These two isotypes are present in different proportions in rheumatoid, psoriatic, and osteoarthritic synovial fluids.¹⁰ Only complete identification of these various activities will open an avenue for the estimation of their biological role(s). Caution should be used when reporting on interaction of phospholipase A₂ with different synthetic substrates¹² and the differences between extracellular and cell related phospholipase A₂ as the results depend markedly on the technical details and may be difficult to interpret.

Out of three forms of phospholipase A₂ in the serum, only the non-pancreatic, calcium dependent form correlates with disease activity in rheumatoid arthritis. Comparison of this form with septic shock serum phospholipase A₂ and peritoneal exudate phospholipase A₂ is necessary to assess whether there is one 'proinflammatory' phospholipase A₂ or whether several forms are produced by various sources. Phospholipase A₂ may yet assume a place amongst the ranks of the broadly recognised autacoids implicated in the genesis and propagation of inflammatory reactions.

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