Sir. We were interested to read the comments of Drs Levick and Thompson. Although accepting their observation that as our labelled injections in the synovial fluid of arthritic joints are more dilute the apparent clearance rates are greater, we feel that they may be overinterpreting our data, and wish to make two main points.

Firstly, the experiments measure only the clearance of labelled material and do not take into account the effects of existing proteoglycans in the joint which may compete. Without conducting a detailed analysis of the composition of the synovial fluid, an important study, but one beyond the scope of our original paper, it is very difficult to make reliable predictions of the extent of this effect and to calculate overall clearance rates. We chose to express our results as half lives precisely because this measurement makes no assumptions about the absolute intra-articular concentrations of proteoglycan.

Secondly, the experimental equipment, as described in our paper, measures radioactivity over the whole joint, including the synovium. The data therefore represent clearance from the whole joint area, rather than just the joint cavity. Although one may anticipate that loss from the joint cavity is the rate limiting step, our finding that at 42 hours between a half and three quarters of the residual radioactivity was associated with the synovium suggests that this may not be the case for the whole duration of the experiment. Further detailed experiments are clearly necessary to establish tissue distributions at earlier times, whether or not the radioactivity in the synovium is intracellular or extracellular, and whether it is located predominantly on the surface of the tissue or distributed throughout its volume.

In conclusion, we do not dispute the physical calculations, but question their direct application to competing clearance mechanisms across anatomical structures of complex and variable composition. This is not to denigrate the observations of Dr Levick and his associates, merely to point out that any simple mathematical model of synovial clearance has limitations.

Strangeways Research Laboratory, Worts Causeway, Cambridge CB1 4RN

D Page-Thomas, D Bard, B King, J T Dingle

Anticardiolipin antibodies, livedo reticularis, and cerebrovascular accidents in SLE

Sir. We read with interest the recent article by McHugh et al concerning the incidence of major cerebrovascular events and livedo reticularis in three patients with systemic lupus erythematosus (SLE) and anticardiolipin antibodies. We have encountered a similar association in our patients. Of the 35 patients with cerebrovascular disease and anticardiolipin antibodies seen in our clinic, only one has suffered from subarachnoid haemorrhage, and this resulted from a ruptured aneurysm. A significant number were hypertensive, however, and we therefore question whether hypertension could have been a factor in their single patient with cerebral haemorrhage.

The authors have advocated treatment of the cerebral thromboses with immunosuppressive therapy, and these levels may even be fully suppressed. Furthermore, we have encountered several patients with cerebral thromboses and anticardiolipin antibodies who have had no previous evidence of lupus activity either clinically or serologically. We have advised anticoagulation for prophylaxis and are currently undertaking prospective trials in order to assess its efficacy. It certainly would avoid the hazards of long term immunosuppression, which would otherwise not be indicated for control and treatment of the underlying disease process.

The Lupus Arthritis Research Unit, The Rayne Institute, St Thomas’s Hospital, London SE1 7EH

References


D P Page-Thomas, D R Bard, B King, J T Dingle

Sir. I am grateful for the interest shown in our paper by Drs Baguley and her colleagues, though their letter contains several inaccuracies. We reported four of 98 patients with systemic lupus erythematosus suffering cerebrovascular accidents.

References


events at a young age (range 23–32 years), two having livedo reticularis, and all having raised IgG anticardiolipin antibodies (ACA).1 One of these had cerebral haemorrhage and although she had suffered pre-eclampsia during an earlier pregnancy, was normotensive at the time of the cerebral event. In addition, hypertension would not account for her systemic illness and accompanying severe uterine pain. I assume the patients referred to by Dr Baguley et al3 had cerebral haemorrhage discounted radiologically.

Although we advocated no particular treatment either for the acute cerebral event or for prophylaxis, all four of our patients responded (i.e., systemic illness abated and cerebral status improved) after pulse methylprednisolone and cyclophosphamide. Immunosuppressive treatment is surely not irrational for 'antibody mediated' mechanisms. We have now had the opportunity of studying ACA levels longitudinally in these and other patients. ACA were raised in all four patients before their cerebral events. Falling levels may in fact herald these and other clinical events (e.g., pregnancy loss, renal crisis), though the effects of treatment versus antibody deposition are difficult to distinguish and need resolving.

I entirely support evaluation of the place of anticoagulation or antplatelet agents, or both, in the prophylaxis of arterial and venous thrombosis in association with ACA, although clear guidelines will eventually be needed for when to start, how much to give, and for how long to treat what may be a young population at risk. Consideration should also be given to the risk of cerebral haemorrhage in those patients with prior cerebral events, and the additional benefit of immunosuppression for the acute crisis cannot be dismissed.

Royal National Hospital for Rheumatic Diseases, Bath

N J MCHUGH

References

Adhesion in articular cartilage

SIR. A recent conference report, on the pathogenesis of osteoarthritis,1 includes a discussion of 'the nature of the adhesion or glue' necessary to maintain the structural integrity of the network of collagen fibrils in articular cartilage. The implication of the report is that there must be some bridging molecules (or ions) which bind to specific sites on the surfaces of collagen fibrils if this tissue is to be mechanically stable. Calculations based on the theory of fibre reinforced composite materials, however, of which articular cartilage is a biological example, indicate that the viscosity of the proteoglycan gel and the shear strength of its interface with collagen are adequate to transfer tensile stress to the collagen fibrils without the need for any further linkage.2 3 The fibrils are oriented such that the swelling pressure of the tissue, which enables it to withstand applied compression, then places them under tension so that they provide the necessary reinforcement.3 4

Department of Medical Biophysics.
D W L HUKINS
University of Manchester.
Stopford Building.
Manchester M13 9PT

References

SIR. Dr Hukins' comments are most welcome and underline the importance of contributions from many disciplines in the attempt to elaborate hypotheses about joints. It would, however, be doing less than justice to colleagues at the meeting if we did not add that physicochemical aspects of the matrix were remarked upon by some: comments so diluted and deflected by a preponderance of biological and biochemical arguments that they did not register in a compressed report. We are compiling a dossier of propositions on which to draw in the formulation of extended hypotheses. It is our hope that not only will Dr Hukins let us have his, but also that knowledgeable colleagues will respond to his ideas. Meetings are highly stimulating, but continued application is required to generate and to garner ideas, especially the less familiar. We are appreciative of Dr Hukins' initiative in writing.

Department of Experimental Pathology.
ROBERT BROWN
Institute of Orthopaedics.
Paul BYERS
Stanmore, Middlesex HA7 4LP

Pulmonary hypertension in Sjögren’s syndrome

SIR. The case report on pulmonary hypertension (PHT) in primary Sjögren’s syndrome (SS) was of great interest.1 We have previously reported its occurrence in a patient with ‘secondary’ SS.2 Our patient, a woman with a multisystem illness going back several years, initially presented with nephritis, was diagnosed as having systemic lupus erythematosus (SLE), and long term steroid treatment was started. She presented again seven years later with the lupus inactive clinically and serologically. She