been unable to show the presence of mast cells in the centrifuged cellular debris of human peritoneal dialysis fluids. It is true that mast cells may be obtained at bronchopulmonary lavage but it seems likely that at most sites mast cells are not desquamated into body cavities.

Freemont and Denton wrongly attribute to me a statement that 'high levels' of histamine occur in the synovial fluid of patients with rheumatoid arthritis. It was Partsch *et al.*² who reported rheumatoid synovial fluid concentrations of 1–23.4 ng/ml (µg/l). I found higher histamine concentrations in the medium of rheumatoid synovial fragments in organ culture.³ However, histamine is rapidly degraded *in vivo* by enzymes not present *in vitro*. Although scanty synovial fluid basophils/mast cells may be a source of histamine production *in vivo*, it is far more likely that mast cell degranulation in the basement membrane-free synovial membrane is the most important mechanism, with simple diffusion into the fluid.

I question the hypothesis that synovial fluid measurements of anything are of much value. It is the close microenvironment of cell-cartilage and cell-bone that should be the focus of our efforts. Histamine receptors are present on cultured human chondrocytes⁴ and human trabecular bone cells,³ and the close apposition of mast cells in pannus to rheumatoid cartilage and bone cells⁵ is probably more relevant.

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SIR, Thank you for giving us the opportunity to reply to Dr Crisp's letter. Perhaps we might answer his points in the order in which he raises them.

We are as certain as we can be that the cells we described were indeed mast cells. In the paper we stated that these cells were 'characterised by their single round nucleus and purple cytoplasmic granules (with Jenner-Giemsa stain) . . . after methanol fixation . . .'. Basophils, on the whole, have bilobate nuclei, and their granules are soluble in methanol. In addition, we have examined a small number of cases for the presence of the enzyme chloracetate esterase and found that the cells we believed to be mast cells were strongly positive. Basophils are not.¹

We apologise for causing any confusion by apparently attributing to Dr Crisp work that was not his own. We were merely quoting from his excellent editorial in the *Journal of the Royal Society of Medicine*² and accept that it would probably have been less confusing to have quoted the source reference rather than Dr Crisp's overview.

It is conceivable that mast cell degranulation occurs in the synovial membrane in rheumatoid disease rather than in the fluid, as we have tentatively suggested. Whether mast cells are undetectable (by our simple method) in the synovial fluid of patients with rheumatoid disease either because they are not there or because they are present in a degranulated form is largely irrelevant to our main argument. The presence of detectable (i.e., non-degranulated) mast cells represents an obvious difference between the synovial fluids of patients with rheumatoid disease and some other inflammatory arthropathies. This must suggest a fundamental difference in mast cell pathophysiology in these disorders and one which may be of more than academic significance. In the case of the disease distribution of synovial fluid mast cells there is the bonus that the observation can be put to diagnostic use.

We cannot accept Dr Crisp's contention that there is little value in measuring anything in synovial fluid. Our experience would suggest that quantitative cytology has considerable diagnostic value, and the fact that we receive more than 500 synovial fluids for cytological analysis every year from our clinical colleagues suggests that they too must, at least in part, share our enthusiasm for this approach to the diagnosis of joint disease.

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Negative anticardiolipin antibodies and vascular complications in Behçet's syndrome

SIR, Recently a striking association has been shown between the vascular complications of arterial and venous thrombosis in patients with systemic lupus erythematosus (SLE) and the presence of anticardiolipin antibodies.¹ This observation followed on related studies showing a correlation with the lupus anticoagulant.² It was also suggested that the lupus anticoagulant may have a pathogenetic role in some patients with Behçet's syndrome (BS),² another

multisystem vasculitic disorder in which thrombosis is a well recognised feature.³ However, unlike the case for patients with SLE, serological markers such as antinuclear and rheumatoid factors are rare in BS.^{3,4}

We therefore studied 25 patients (14 male, 11 female) with BS and thrombophlebitis for evidence of anticardiolipin antibodies. All patients had at least three of the four major criteria for the diagnosis of BS.⁵ The thrombophlebitis involved the leg or arm vessels, or both, and was accompanied by major vessel venous thrombosis (e.g., deep veins of leg or venae cavae) in 15 (60%) of the patients. At least five patients had clinical and arteriographic evidence of pulmonary arterial occlusions, and two of these had pulmonary hypertension confirmed by catheter studies. All but three of the 25 patients were taking corticosteroids or other immunosuppressive drugs, or both. Patients were not known to have autoantibodies, and in particular, none had antinuclear factor, rheumatoid factor, or a false positive reaction for syphilis. Anticardiolipin antibody levels of immunoglobulin classes G and M were determined by a modified radioimmunoassay method,¹ and an abnormal level was taken as being three standard deviations above the mean for normal controls.³

Raised anticardiolipin antibody levels were detected in only two (8%) of the 25 patients, both of whom had IgM antibodies alone. Clinically these two patients were similar to those without raised anticardiolipin antibody levels, and both had orogenital ulceration, uveitis, and arthritis. Neither had evidence of cerebral, pulmonary, or retinal vascular disease, or deep vein thrombosis, features previously associated with the presence of anticardiolipin antibodies in SLE.¹

These results in a group of patients with a high incidence of thrombotic problems and pulmonary vascular disease (admittedly taking corticosteroids and/or other immunosuppressive therapy) suggest that anticardiolipin antibodies do not have a major pathogenetic role in the vascular complications of BS. This contrasts with the results of a recent study of BS from three countries, in which anticardiolipin antibodies were found in 13 of 70 (18.6%) patients, with a particular association being found

with retinal vascular disease.⁶ The cause for this disparity is not clear, particularly as the patients in both studies were apparently diagnosed using the same standard criteria and the anticardiolipin antibody levels measured in the same way.

It is suggested that, as in all studies of this heterogeneous group of patients, a wider and international serological study of BS should be undertaken, with particular emphasis on the vascular complications of the disease and antiphospholipid antibodies.

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Notes

Immunogenetics and rheumatoid arthritis

A two-day workshop on this subject will be held at The London Hospital on Thursday and Friday, 14 and 15 November 1985. Enquiries to: Administrative Officer, Postgraduate Teaching Centre, London Hospital Medical College, 47 Turner Street, London E1 2AD.

VIth Eular workshop on rheumatology research

The VIth Eular workshop will be held in Montpellier, France on 13-14 March 1986. The main topics will be immunopathology of arthritides, immunomodulating drugs, Gougerot-Sjögren's syndrome, bone remodelling and its evaluation, pathology of cartilage, miscellaneous Abstracts should be submitted before 31 December 1985. Correspondence to Professeur J Sany, Secretary of the VIth Eular Workshop on Rheumatology Research, Service d'Immuno-Rhumatologie et Réadaptation Fonctionnelle, Centre Gui-de-Chauliac, 34059 Montpellier Cedex, France.