agents and continued fenbufen throughout the time reported. Thrombocytopenia is a recognised complication of other second-line drugs, including gold and penicillamine. It has been reported (as part of pancytopenia) in association with SASP therapy in inflammatory bowel disease\(^6\)\(^7\) but not in RA. It is thought to be due to the sulphapyridine moiety. Hypogammaglobulinaemia has been reported in RA patients treated with chrysotherapy,\(^1\)\(^2\) and selective IgA deficiency has been recorded in RA patients receiving not only gold or penicillamine\(^6\) but also SASP.\(^9\) Although the serum immunoglobulin levels returned to normal in our patient within three months, in some of those treated with gold therapy the immunodeficiency persisted and even required replacement therapy.\(^1\) Since hypogammaglobulinaemia may be associated with infection and thrombocytopenia with haemorrhage, SASP therapy in RA may not be quite as safe as previously thought. Long term monitoring to detect and reverse these adverse reactions is clearly important with SASP treatment as it is with the other slow acting antirheumatic drugs.

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References

**Synovial fluid mast cells**

Sir, The paucity of mast cells in inflammatory synovial fluids reported by Freemont and Denton\(^1\) is not unexpected. The mast cell is primarily a tissue cell, though it is conceivable that its circulatory counterpart, the basophil, may be found in greater numbers in inflammatory synovial fluids. Are the authors certain that these scanty, granular cells were not basophils? Whereas lavage of rodent peritoneal membranes is a rich source of mast cells, I have
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. 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. 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 chondrocytes and human trabecular bone cells, and the close apposition of mast cells in pannus to rheumatoid cartilage and bone cells is probably more relevant.

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References

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 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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References

Negative anticardioliopin antibodies and vascular complications in Behçet’s syndrome

Sr., 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-Giemsua 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

Sr., 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 anticardioliopin antibodies. 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), another
Synovial fluid mast cells.

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