REPLY. ERYTHEMA NODOSUM LEPROSUM

Sir,

The points raised by Drs DS Ridley, Marian J Ridley are important, they are not in my view sufficient to disqualify the hypothesis.

Perivasculitis may or may not be conspicuous in ENL lesions, but the argument is centred on the presence of polymorph infiltration in an otherwise chronic inflammation. So far the theories for this have been based on immune complexes and Arthus reaction. Immunologically, however, the ENL syndrome does not seem to be precipitated by an Arthus phenomenon and this is the hypothesis.

The role of antigenic load and antigen–antibody ratios is difficult to assess but must be seen in the context of all the immunological disturbances seen during ENL. Once this is done deposition of complexes or activation of the complement cascade *in situ*, secondary to a delayed type hypersensitivity, becomes a real possibility. The complexes can then regulate the local reaction and thus perpetuate a pathology initiated by a different mechanism. Immune complexes, therefore, have a role to play in ENL, but the argument put forward in the hypothesis is that these complexes are not the initiating factor.

Incidentally, while not offering direct evidence for the hypothesis, we have recently found that together with other immunological disturbances, there is an increased level of Natural Killer (NK) cell activity during ENL (Converse P, Humber DP, Mshana RN, Belehu A, in preparation). These NK cells are known to be stimulated by Interferon (IFN). While the role of these cells in the pathogenesis of ENL is not yet clear, it is of interest to note that IFN has recently been reported to abrogate Suppressor T cell response of delayed type hypersensitivity in animals.[1] If this is true also for human beings it is quite possible that the increase in NK cell activity in ENL is mediated by an increase in IFN which at the same time reduces suppressor cell activity. We are in the process of assaying IFN levels in the evolution of ENL.

Taken as a whole, ENL can only be explained in full by evoking an initiation phase which is most likely to be a cell mediated response, and a secondary perpetuation phase which might involve immune complexes.

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Reference

[1] Knop J, Stremmer R, Neumann C, De Maeyer E, Macher E. Interferon inhibits the suppressor T cell response or delayed type hypersensitivity. *Nature,* 1982; **296**: 757–59.