Correspondence

HLA-DR4 does not predispose to higher amounts of rheumatoid factors in healthy persons

SIR, Several authors have reported the possible association between rheumatoid arthritis (RA) and the HLA-DR4 antigen.¹⁻⁷ The most recent report has appeared in your columns.⁷ Some of the studies suggested that RA patients with HLA-DR4 more often had positive latex tests for rheumatoid factor, with higher titres than the other patients.³⁻⁶ HLA-DR4 might thus operate in relation to IgM rheumatoid factor production rather than rheumatoid arthritis. As healthy persons have low amounts of rheumatoid factors in their sera,⁸ we therefore investigated whether those with HLA-DR4 had more rheumatoid factors than the others.

Rheumatoid factors were measured quantitatively in the sera of 77 unrelated, healthy persons who had been tissue typed before (mean age 45 years, range 25-75; 47 were women). We used a recently developed highly sensitive, enzyme linked, solid phase immunoassay measuring IgM rheumatoid factors with human IgG as an antigen. There are 5 dilutions in the normal range and the results obtained with this assay show an excellent correlation with those obtained with the latex test used in our laboratory⁶ (to be published). The overall incidence of HLA-DR4 was 21% in the 77 healthy controls; the 55 persons with 'low normal' titres had rather a higher frequency of HLA-DR4 (24%) than the 22 with 'high normal' titres (14%; NS). Although only small numbers of normals were tested, these results do not suggest that DR4 influences rheumatoid factor titres in healthy persons. Similarly, Rodriguez *et al.*⁹ did not find a relationship between HLA-DR4 and in-vitro IgM rheumatoid factor production in normals. In RA the relationship between DR4 and rheumatoid factors has not always been found; the study by Gran *et al.*⁷ is the latest in this line. The difference might be, as these authors suggest, in the selection of the patients with seronegative RA during the different studies.

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ESR in polymyalgia rheumatica and giant cell arteritis

SIR, The recent report by Ellis and Ralston¹ on the ESR in polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) raises some interesting points. They found a normal ESR in 22.5% of cases at presentation, which is, as they state, a much higher incidence than has been found in other series.²⁻⁵ The value they adopted as elevated was 30 mm/h, and they quote that this was one of the diagnostic criteria which we used in our study of 108 patients with PMR and/or GCA.^{6,7} In fact the full version of our criteria read: 'An ESR of 30 mm/h or greater or a C-reactive protein of greater than 6.4 µg/100 ml.' We did not come across one patient with clinical evidence of PMR and/or GCA with an ESR or CRP which was not raised on at least one occasion. In one case the ESR was normal on the 2 occasions it was measured (20 mm/h and 17 mm/h), but the CRP was elevated at 14.5 µg/100 ml.

In 5 of the 108 patients a raised ESR was found when the investigation was repeated after an initially normal reading, while in another 5 patients a normal result was observed after the initial reading had been elevated. Two examples will illustrate the variation in the results.

Patient 1. Initial ESR 66 mm/h, 16 days later 14 mm/h, 7 days later 90 mm/h.

Patient 2. Initial ESR 9 mm/h, 5 days later 48 mm/h, 7 days later 74 mm/h.

Others have noted this day to day variation^{8,9} and it is recommended that the test is performed several times when a normal result is found. Mallaya *et al.*¹⁰ have shown that the ESR can vary from hour to hour. In one of our patients the ESR was recorded at intervals after the daily dose of 15 mg of prednisolone on the fourth day of treatment. The ESR fell from 48 mm/h at 9.00 am to 35 mm/h at 10.00 am and 11.00 am and rose to 58 mm/h at 12 mid-day. By 2.00 pm it was 64 mm/h. Duplicate samples were set up on each occasion and there was never a difference of more than 2 mm/h between specimens.