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Systemic lupus erythematosus without clinical renal abnormalities

SIR, We read with interest the study of O'Dell *et al*¹ showing a high incidence of mesangial changes in renal biopsies from patients with systemic lupus erythematosus (SLE) without clinical renal abnormalities. They found no cases of focal or diffuse proliferative glomerulonephritis. These results are different from those previously reported by other authors^{2 3} and question the relevance of renal biopsy in these patients.

Recently we have performed renal biopsy in 13 patients with SLE (fulfilling the American Rheumatism Association revised criteria⁴) who had no clinical signs of renal involvement (no urinary sediment abnormalities, absence of proteinuria, and serum creatinine below 1.3 mg/dl (115 µmol/l)). All renal biopsy specimens were examined by two pathologists and categorised according to the modified classification proposed by the World Health Organisation.⁵

Five cases (38%) showed no histological or immunofluorescence changes (type I), six (46%) patients had a mesangial nephropathy (three type IIa and three type IIb), and two (15%) had a focal proliferative glomerulonephritis (type III). None of the patients had previous evidence of neurological abnormalities. Patients with normal renal biopsies (type I) only had arthritis, skin lesions, and Raynaud's phenomenon. In contrast, six patients with histological renal involvement had serositis or haemolytic anaemia. All cases with silent nephropathy were treated with steroids and showed a benign clinical course with stable renal function and absence of urinary abnormalities during follow up (one to 76 months, mean 27 months).

On the basis of these results we agree with O'Dell *et al*¹ that, in the absence of clinical renal abnormalities, significant renal involvement is uncommon in SLE. However, as reported by Mahajan *et al*² and Lehey *et al*³

and confirmed in the present study, a few patients may have severe renal lesions requiring steroid therapy. Thus until more information becomes available we believe that a renal biopsy should be performed in those SLE patients presenting with clinical manifestations other than arthritis or cutaneous lesions since this policy may allow detection of silent nephritis lesions.

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SIR, We appreciated the letter of Font *et al* and the opportunity to respond to it. The findings of Font *et al* that none of the 13 lupus patients without clinical evidence of renal disease had diffuse proliferative glomerulonephritis are very similar to our findings but very different from the findings of Mahajan *et al*.¹ We were surprised that five of the 13 lupus patients in their study (Font *et al*) had completely normal renal biopsies. All of our patients, despite the absence of clinical renal abnormalities, had mesangial abnormalities as shown either by light microscopy or by immunofluorescence studies. Our findings are similar to those of most other studies published in the literature, which show that most patients, despite the absence of clinical renal disease, have abnormalities on renal biopsies.¹⁻⁴

We do not agree with the recommendation of Font *et al* that because they found focal proliferative glomerulonephritis in two of their patients they would advocate renal biopsies in lupus patients in the absence of clinical renal abnormalities. As stated in our paper there is no evidence in the literature to suggest that early treatment of histopathological abnormalities found on renal biopsy in the absence of clinical findings will in any way influence prognosis. In fact, all studies in lupus nephritis that have looked at the question have concluded that clinical parameters are a much stronger indication of prognosis than histological classification.

In summary, we agree with the findings of Font *et al* that significant renal pathology in lupus patients without clinical renal abnormalities is rare, but we do not advocate renal biopsy in this group of patients.

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Ankylosing spondylitis, HLA-B27, and klebsiella

SIR, With particular reference to our studies^{1 2} and those of Ebringer and his associates,^{3 4} the article by Singh *et al* (p. 190, this issue), attempts to address the controversial issue of cross reactivity between certain strains of klebsiella and the lymphocytes of HLA-B27 positive patients with ankylosing spondylitis (B27⁺AS⁺). Controversy is a healthy byproduct of scientific interest, and it is essential that our findings and those of other workers in the field be subjected to the closest scrutiny and evaluation. Those entering this debate, however, should do so with a sense of responsibility; presentation of data which are based on questionable or inadequately controlled techniques must be considered scientifically misleading. I refer specifically to the ⁵¹Cr release technique used by Singh *et al* that attempts to reproduce the specific cytotoxicity of anti-klebsiella sera for B27⁺AS⁺ cells. There are several important differences between their technique and ours, and their departure from our published methods passes without comment or justification. Firstly, the ⁵¹Cr labelled cells are incubated *simultaneously* with antiserum and diluted complement for one hour at 37°C. The more conventional method and the one favoured by our group is to incubate the radiolabelled cells with antiserum for 30 min at room temperature (20-24°C) *before* adding neat complement for a further 60 min at the same temperature. Secondly, Singh *et al* complete their assay by adding to each tube 1.5 ml of cold 0.9% NaCl. The significance of this cold saline step is not entirely clear. We have recently tested five B27⁺AS⁺ cells (which were positive with our ⁵¹Cr release technique) according to the Singh method and we were unable to demonstrate cross reactivity between klebsiella K43 BTS1 and other enteric bacteria and the patients' lymphocytes. Furthermore, the failure of the

Singh method in our hands is due largely to the simultaneous, rather than sequential, addition of antiserum and complement. Singh *et al* justify their choice of this unconventional cytotoxicity technique by pointing out that . . . 'high levels of cytotoxicity were obtained against the lymphocytes in control tests with antilymphocytic serum'. However, most antilymphocytic sera are active in the absence of complement and since details on the production and source of this reagent are not given in the paper one assumes that the success of their assay technique rests largely on the activity of an *alloantiserum*, anti-HLA-B27.

We have been concerned by the non-confirmatory reports of this work and in an attempt to identify some of the factors which might contribute to the failure of others to confirm our findings we have recently completed a double blind trial involving B27⁺AS⁺ cells from a New Zealand population.⁵ This successful study, together with two previous confirmatory reports (in preparation),⁶ suggests that the phenomenon of 'cross reactivity' between enteric bacteria and B27⁺AS⁺ cells is not simply an Antipodean curiosity.⁷ Although many aspects of this controversy remain to be resolved, it is worth noting that of the non-confirmatory reports only Beaulieu *et al*⁸ have adhered to our published methods, while other workers found it necessary to modify one or more parameters of the ⁵¹Cr release assay.

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