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- 10 Mowat A G, Hothersall T E. Iron content of synovial tissue in patients with rheumatoid arthritis and in normal individuals. *Ann Rheum Dis* 1968; 27: 345-51.
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SIR, Professor Duthie misunderstands the purpose of our study, which was to examine the *mechanism* of the iron promoted synovial flare and *not* to evaluate the efficacy of this form of treatment of rheumatoid anaemia. As our article and Professor Duthie's letter point out many authors have described the synovial flare. We suggest that the reaction is mediated by iron (rather than dextran) promoted lipid peroxidation.

I have no criticism of Professor Duthie's haematological observations and failed to quote them only because our article did not address this issue. However, I would take the opportunity of describing the results of a study that was omitted from professor Duthie's extensive list of references. Bentley and Williams¹ gave iron dextran (800 mg intramuscularly) to 30 anaemic rheumatoid patients. Twenty six of the 30 patients showed a significant rise in haemoglobin at the two-month mark, but values fell back to the pretreatment level at nine months. The rise in haemoglobin was not related to pretreatment iron levels. They concluded and I quote: 'a therapeutic trial of parenteral iron will produce haematological improvement in the majority of anaemic patients and cannot therefore be taken as an indication that the anaemia was primarily due to iron deficiency. In the majority of anaemic rheumatoid patients, however, therapy should be directed at suppression of the activity of their rheumatoid disease, as this is the only current means by which lasting haematological improvement would be achieved'. Though we did not report the haematological indices in our patients, we found much the same . . . a temporary rise only. I would not choose to describe a treatment that causes the disease to flare, has no significant long-term effect on the haemoglobin, but occasionally causes anaphylaxis as 'very valuable'.

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Reference

- 1 Bentley D P, Williams P. Parenteral iron therapy in the anaemia of rheumatoid arthritis. *Rheumatol Rehabil* 1982; 21: 88-92.

Systemic lupus erythematosus

SIR, The report of Soppi, Eskola, and Lehtonen¹ on identical twins discordant over 20 years for clinically

evident SLE adds to our understanding of the importance of both genetic and environmental factor(s) in the expression of this disease. To date it remains unknown whether the genetic factor(s) is requisite and the environmental factor only stimulatory or whether a certain combined quantity (more or less of one and/or the other) of the two sufficient to reach an expressive threshold is critical.

In the twins described it is of interest that the clinically unaffected sibling had a persistently raised erythrocyte sedimentation rate (ESR), for although the presence of antinuclear antibodies and other protein aberrations, including low complement levels, need not be associated with active disease, a raised ESR, though non-specific, usually suggests the presence of active inflammation or tissue damage. Could something subtle have been missed? Twenty years' observation argues against this notion, but it is not necessarily reassuring for the future. I look forward to a follow-up report 10 years from now.

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Reference

- 1 Soppi E, Eskola J, Lehtonen A. Evidence against HLA and immunological dependence of disease outbreak in SLE. Immunological characterisation of identical twins clinically discordant for SLE. *Ann Rheum Dis* 1985; 44: 45-9.

Detection of anti-dsDNA as a diagnostic tool

SIR, We read with interest the paper by Drs Swaak and Smeenk¹ on the detection of antibodies to double-stranded deoxyribonucleic acid (anti-dsDNA) as a diagnostic tool. Of 441 patients without systemic lupus erythematosus (SLE) but with anti-dsDNA no fewer than 304 (69%) developed SLE within one year as judged by the preliminary classification criteria of the American Rheumatism Association (ARA).² Longer follow up showed a cumulative incidence of SLE of 85%. We have found different results in a group of patients who, in contradistinction to the Dutch study cases, did not have antinuclear antibodies (ANA) on conventional indirect immunofluorescent testing, despite high titres of anti-dsDNA.

By reference to the anti-dsDNA results file in the pathology service laboratory covering the period 1976-83, we have identified 20 patients (12 female, eight male; mean age 51 years) who were followed up for at least a year and who had anti-dsDNA titres in excess of 30 U/ml (anti-DNA kit, Amersham International) on two or more occasions. Tests for ANA with serum diluted 1:16 on a substrate of rat liver slices were negative on every occasion for every patient included in the study. Two patients subsequently developed ANA at 20 and 25 months respectively after the anti-dsDNA were first noted. The other 18 patients remained consistently ANA negative and were tested on three to 12 occasions (mean 5.1).

During the first year after detection of anti-dsDNA there were no cases fulfilling the ARA preliminary classification criteria for SLE. During the second year one patient (of 13 who completed two years' follow up) fulfilled these criteria. At 25 months a second patient fulfilled the revised ARA criteria³ (which allows inclusion of anti-dsDNA as a feature) but had an 'inadequate' three features from the preliminary list. The remaining 18 cases failed to meet either list of ARA classification criteria on follow up of 14–60 months (mean 27 months) from the first detection of anti-dsDNA at high titre. Nine of these patients developed four or more features of SLE from a less restrictive list of disease features which we have previously used,⁴ but none of these would have been counted as SLE cases by Swaak and Smeenk.¹ The cause of the high anti-dsDNA titres in the remaining nine patients is unknown. None has any other connective tissue disease or liver disease (which may be associated with high titres).⁵

Thus when we used the same classification criteria as Swaak and Smeenk we observed a cumulative incidence of SLE of 0% at one year and 8% at two years from the detection of anti-dsDNA. These figures are much lower than found in their ANA positive group and should be borne in mind when viewing the prognostic implications of high anti-dsDNA titres in non-SLE patients who are ANA negative.

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References

- 1 Swaak T, Smeenk R. Detection of anti-dsDNA as a diagnostic tool: a prospective study in 441 non-systemic lupus erythematosus patients with anti-dsDNA anti-body (anti-dsDNA). *Ann Rheum Dis* 1985; **44**: 245–51.
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- 3 Tan E M, Cohen A S, Fries J F, *et al*. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; **25**: 1271–7.
- 4 McHardy K C, Horne C H W, Rennie J A N. Anti-nuclear antibody-negative systemic lupus erythematosus: how common? *J Clin Pathol* 1982; **35**: 1118–21.
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Notes

Lupus: a guide for patients

This 25 page booklet written by Dr G R V Hughes is available free of charge from the author (Dept of Rheumatology, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH) or from the British SLE Aid Group, 25 Linden Crescent, Woodford Green, Essex or from Arthritis Care, 6 Grosvenor Crescent, London SW1X 7ER. Please enclose 7" × 9" stamped addressed envelope.

Workshop on immunogenetics and rheumatoid arthritis

A two-day workshop on this subject will be held at the London Hospital Medical College on 14 and 15 November 1985. The registration fee of £50 includes all catering. Applications and enquiries to the Postgraduate Administrator, London Hospital Medical College, London E1 2AD.