These I have not analysed and therefore cannot tell you whether they are significantly different, but the second trial suggests that it is reproducible.

DR. P. H. N. WOOD (*Manchester*) I am very dubious of the power of statistics to answer that particular problem. Reproducibility, for instance, is a function of one patient; you can establish reproducibility only by the fact that it is individually reproducible in individual patients and I do not think your method is revealing this at the moment.

DR. A. ST. J. DIXON (*Bath*) The paper has put forward a claim that this is a simple method, using the out-patient material we have, for screening drugs without too much elaboration, and I think, Dr. Wood, that neither you, nor the authors, have claimed that the statistics are at fault here, or that this could be substituted for a full-dress double-blind trial.

DR. LEE I agree, we do not cite this as the be-all and end-all of all clinical trials. I stated in the discussion that this may be a useful adjunct in the trial of the therapeutic effectiveness of anti-rheumatic drugs; it is not designed to replace the present standard methods.

DR. I. HASLOCK (*Leeds*) It has been suggested that relief of symptoms in rheumatoid arthritis is related not only to analgesia but also to anti-inflammatory activity. As your assessment appears to rely heavily on pain relief; when you used paracetamol, which has no anti-inflammatory action, in your second trial, did you in fact find that this was different from the anti-inflammatory agents?

DR. LEE We did not. Looking at the raw data, the results with paracetamol are not very impressive; the figures are not much higher than those we obtained with the placebo.

DNA-binding in Rheumatoid Arthritis. By P. G. ROCHMIS, H. PALEFSKY, H. ROTH, M. BECKER, and N. J. ZVAIFLER (*Georgetown University Medical School, U.S.A.*)

With the introduction of the Farr ammonium sulphate technique, a more sensitive procedure for the detection of antibodies to deoxyribonucleic acid (DNA) has become available. Published data indicate the usefulness of this technique in the diagnosis of systemic lupus erythematosus (SLE), and also in following the course of this disease. It has been suggested recently that this test is helpful in differentiating SLE from other rheumatic diseases, especially rheumatoid arthritis (Hughes, 1971).

This study presents data on the presence of DNA antibodies in the sera of 62 patients selected by a group of rheumatologists as having unequivocal rheumatoid arthritis. All met the American Rheumatism Association criteria for definite or classical rheumatoid arthritis.

The presence of antibodies to native DNA (nDNA) using the Farr technique was determined, and in addition a titred rheumatoid factor test (Bentonite flocculation test), fluorescent antinuclear antibody (FANA), levels of immunoglobulins A, G, and M, and complement (C3) were also determined. Clinical data were correlated with the laboratory values using a 14×14 matrix and computer-assisted statistical techniques.

The group of 62 patients corresponded well in all

parameters to previously-published series of 'typical' patients with rheumatoid arthritis; 59 of the 62 had DNA-binding values between 0 and 10 per cent, which is considered negative in this laboratory. One patient had 13 per cent binding and two others had values of 19 and 23 per cent respectively. Interestingly, the latter two had negative tests for rheumatoid factor.

These data indicate that antibodies to nDNA are not usually found in patients with 'typical' rheumatoid arthritis, and when found are present in low concentrations only. This is the first presentation of data on the use of this technique in a large group of well-characterized patients with rheumatoid arthritis.

Discussion

DR. D. N. GLASS (*London*) If one standard deviation of the error in your assay for DNA antibodies is 5 per cent, then with a base line of 5 per cent, surely one in 99 sera, i.e. three standard deviations from the mean, could be above 20 per cent binding, assuming a normal distribution of your errors. As you have examined 62 sera, is it possible that your results could be explained by chance? What precautions have you taken to ensure that your 'positive' results represent circulating immunoglobulins specific for DNA?

DR. ROCHMIS Let me preface my answer by saying that much of the vital work on the serum was done in California, and we actually started out using different techniques for detecting DNA antibodies, but discarded them because we felt the Farr technique to be superior. Although in this series of experiments we did not prove the reactant to be immunoglobulin, Farr in his original publications has shown this. In addition, the sera were heat-inactivated, thus eliminating the binding activity of Clq, the other known reactant with DNA. Caesium gradient studies which we performed have shown that 96 per cent of the binding was associated with the native DNA or double-stranded DNA. The error of measurement of the assay in our hands has been calculated to approximate ± 3 per cent of the actual measurement (i.e. not 3 per cent DNA-binding) over the entire range of binding, and it may be even less in the lower ranges. The three elevated values were re-done and fell well within this range.

DR. G. R. V. HUGHES (*Hammersmith*) In our original study of DNA-binding we did find two children with Still's disease who had a very high DNA-binding. Both children subsequently developed florid lupus (Hughes, Cohen, and Christian, 1971). We found no rheumatoid patients with elevated DNA-binding; however, we have recently done a combined study with Dr. Whaley and colleagues in Glasgow on patients with Sjögren's syndrome as part of a study of patients with positive antinuclear factor tests; one or two of these had a slightly abnormal DNA-binding and the rest were normal (Hughes, 1973).

References

- Hughes, G. R. V. (1971) *Lancet*, 2, 861
- (1973) 'Immunological Factors in S.L.E.', in 9th Symposium of Advanced Medicine, ed. J. G. Walker. Pitman, London
- , Cohen, S. A., and Christian, C. L. (1971) *Ann. rheum. Dis.*, 30, 259