The measurement of the tensile strength of the wounds is done by a Sandberg apparatus. It has prongs on either side and you just pull it apart, the tension being increased at a regular rate until the wound gives. It has quite a sharp endpoint which seems to be reproducible in an animal. In other words, the three duplicate wounds give similar results. If there had been a technical failure it would be expected to give a low result, so we took the two highest readings for tensile strength in both the control and the treated animals.

DR. B. MCCONKEY (Birmingham) What was the histological evidence that the normal skin was affected in the animals treated with Arvin? I am not sure if Dr. Holt mentioned the stain. Would he like to comment on this and the implications of the different staining characteristics?

DR. HOLT The stains were Van Gieson and Martius scarlet blue. I think the significance of the staining reactions is doubtful, and I attach no importance to them. The fibre sizes, I think, are definite. If my photography was good enough, I should have liked to show the polarized light slides which show the fibres very nicely indeed—the quite different size of the collagen fibres in the two groups in the normal skin. The normal skin shows two other characteristics which I have not illustrated: one is that the dermis is about two-thirds as thick in the treated animals as in the controls; the other is an abnormal regrowth of hair. This looks like hair of a newborn rabbit (say in the first 2 months of life), and is more fluffy than that of an older animal.

DR. A. S. RUSSELL (Taplow) From what Dr. Holt was saying about the antibody response to administered Arvin in the course of time, it seems to me that this is an elegant model of complex-induced disease, particularly at the equilibrium point. Did he notice any arteritis in the superficial vessels which might have some relevance, and did he notice whether defibrination had any effect on the development of fibrin deposits in the afferent arterioles of the kidney?

DR. HOLT There is a fibrin deposit, but it is very little and unlikely to cause trouble in the period during which one is able to give Arvin. As to whether these animals had any disease, all I can say is that I produced some hyperimmune animals for another purpose and they have all died. The *post mortem* examinations have shown nothing specific, but we are doing a chronic toxicity study on this basis. It seems unlikely that we shall evolve an immune complex disease because the amount of protein we are using is so small, a microgramme is one unit and to defibrinogenate an animal intravenously we usually use one unit per kg.—a minute amount. For persistent defibrinogenation we use something like 5 units daily intravenously or about 10 units twice daily intramuscularly, but these are still minute amounts of protein. Furthermore, no fall in complement has been shown.

References

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Effect of Arvin on Experimental Immune Arthritis in Rabbits. By P. M. FORD, F. W. S. WEBB, R. H. BLUESTONE, J. M. GUMPFL, AND W. R. BELL (*Department of Medicine, Royal Postgraduate Medical School*)

A component of the inflammatory exudate had been suggested as the significant factor in the production and perpetuation of chronic immune arthritis in rabbits (Phillips, Kaklamanis, and Glynn, 1966). Fibrin has been strongly considered for this role.

Using Arvin (an extract of the venom of the Malayan pit viper) to reduce the amount of fibrin available for deposition in the region of the initial inflammatory reactions, we have sought to determine whether the subsequent arthritis could be modified in either severity or chronicity. Arvin acts by precipitating fibrinogen in the blood in the form of microclots and fibrin split products.

Intravenous Arvin was administered immediately before the introduction of antigen into the knees of previously immunized rabbits. Defibrinogenation was maintained for varying periods up to one month, the animals being killed at the end of the course of treatment.

Frequent measurements of joint diameter and histological examination after death showed essentially no difference between treated and control groups.

It is concluded, therefore, that, in this experimental model of immune arthritis in rabbits, Arvin has no effect on either the severity of the lesion or the establishment of the chronic inflammatory state.

Discussion

DR. P. A. BACON (London) Did the authors skin-test their animals? Suppression or diminution of both Arthus and delayed skin-reactivity has been observed using Heparin and it would be interesting to know whether this occurred with Arvin.

DR. FORD The animals were skin-tested only before intraarticular injection and not at the end of the Arvin treatment.

DR. B. MCCONKEY (Birmingham) Did the fibrinogen response to the injection in the untreated animals show a great variation or was it about the same magnitude for the same sized insult?

DR. FORD In the untreated control animals the mean fibrinogen level rose to 800 mg. per cent. and in fact all four animals showed a large rise to between 700 and 900 mg. per cent.

Reference

- PHILLIPS, J. M., KAKLAMANIS, P., AND GLYNN, L. E. (1966) *Ann. rheum. Dis.*, 25, 165.
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Comparison of a New Latex Slide Test with the Sensitized Sheep Cell Test. By C. J. EASTMOND, D. PHILLIPS, and W. R. M. ALEXANDER (*The Rheumatic Diseases Unit, Northern General Hospital, Edinburgh*)

A new commercial slide test for rheumatoid factor was compared with the standard sheep cell test (SSCT) used in this unit. Two series of tests were made by two individuals: one amateur (CJE) and one professional (DP).

In the first series (CJE), 150 sera from patients with 'suspected' rheumatoid arthritis were tested; 48 per cent. were positive by the slide test and 39 per cent. by the SSCT. 3 per cent. of 83 sera from patients with other inflammatory or non-inflammatory disorders of connective tissue were positive with both tests.

In the second series (DP), 117 sera collected consecutively from all patients with 'classical' or 'definite' rheumatoid arthritis attending the follow-up clinic were tested; 79 per cent. had a positive slide test and 63 per cent. a positive SSCT. 5 per cent. of 140 sera from patients with other diseases had positive slide test; 3 per cent. had a positive SSCT. 107 sera collected from a population sample of persons over the age of 65 were tested; 14 per cent. were positive by the slide test and 4 per cent. by the SSCT. This high incidence of positivity in the slide test in the elderly is in keeping with the observations of Heimer, Levin, and Rudd (1963). The increased sensitivity in the slide test in rheumatoid arthritis was not due to weighting by age. The ratio of positive slide tests to positive sheep cell tests was unchanged by the exclusion of patients aged 65 years or over.

These results suggest that the new slide test is more sensitive than the SSCT as done in this laboratory. In the rheumatoid sera the slide test was found to be 1.20 times more sensitive than the SSCT by CJE and 1.24 times more sensitive by DP. In all but the elderly the specificity of the SSCT was only slightly greater than that of the slide test.

The slide test was easy to read, on either venous or capillary blood, and could be set up quickly. DP managed to set up and read forty tests per hour. It is considered that these advantages are sufficient to justify further work with this test.

Discussion

DR. R. BLUESTONE (*London*) What is the effect on the sensitivity of your new test when you heat inactivate all sera before testing?

DR. EASTMOND We have not attempted to do this at all.

DR. BLUESTONE (*London*) I think you should do this, because there is no doubt that a large number of false positive latex tests using the orthodox technique can be excluded by previous heat inactivation at 55°C. for 30 minutes.

Reference

HEIMER, R., LEVIN, F. M., AND RUDD, E. (1963) *Amer. J. Med.*, 35, 175, 274, 133.

Juvenile Rheumatoid Arthritis: A Serological Survey of 200 Consecutive Patients. By R. H. BLUESTONE, L. S. GOLDBERG, R. KATZ, J. M. MARCHESANO, and J. J. CALABRO (*Department of Medicine and Pediatrics, UCLA Center for the Health Sciences, Los Angeles, California, and Department of Medicine, Jersey City Medical Center, N.J.*)

Rheumatoid factor (RF), antinuclear antibodies (ANA), and aberrations in quantitative immunoglobulins are among the serological abnormalities noted in juvenile

rheumatoid arthritis (JRA). We have studied the immunological features of 200 consecutive unselected patients with JRA, irrespective of disease activity, and have attempted to correlate abnormalities with the clinical features of the disease.

RF was detected in 24 patients (12 per cent.) and ANA in eight (4 per cent.). Elevation of serum IgG was noted in 49 patients (25 per cent.), of IgA in 34 (17 per cent.), and of IgM in twenty (10 per cent.). Low levels of IgG was found in five patients (2.5 per cent.) and of IgM in another five (2.5 per cent.). Complete absence of IgA was found in two patients (1 per cent.) and subnormal levels in two others (1 per cent.).

Children with RF, ANA, or raised immunoglobulin levels tended to differ from the group as a whole, with poorer functional status and an increased incidence of hip involvement, subcutaneous nodules, and generalized lymphadenopathy. There was no correlation with age at onset of disease. Children with low immunoglobulin levels showed no clear clinical correlates. The incidence of selective IgA deficiency is less than that reported by Cassidy and Burt (1967), but greater than the expected incidence in the normal adult population.

The incidence of abnormalities is generally lower than that previously reported. This discrepancy may reflect the fact that almost 60 per cent. of patients are at present in complete remission. Thus, the incidence of serological abnormalities in any group of patients with JRA will largely depend on the selection and clinical status of the patients under study.

Discussion

DR. B. M. ANSELL (*Taplow*) It is interesting that, irrespective of the stage taken (*i.e.* 5-year, 10-year, or 15-year follow-up), our overall incidence of positive rheumatoid factor tests, using DAT and latex tests combined, varies between 10 and 12 per cent., which is very similar to yours. I would disagree with you on one point, because we have found that those patients with a high age at onset tend to have a slightly increased frequency of positive rheumatoid factor tests, particularly the DAT, and also a rather prolonged activity of the disease process. I should like to ask one question on the immunoglobulins: we have found a fairly marked increase in all the immunoglobulins in the majority of cases, and this too correlates fairly closely with the disease activity. Could you comment on the disease activity in relation to your various tests?

DR. BLUESTONE We also found a high incidence of immunoglobulin abnormalities, although I must stress that most of our patients were in clinical remission: it is therefore not surprising that your incidence of immunoglobulin abnormality would be even higher, perhaps in following up a group of more severely affected patients. Is it possible that the reason for our low incidence of rheumatoid factor in the older patients is that in our patients the disease was comparatively inactive?

DR. B. M. ANSELL (*Taplow*) I can not comment without knowing more about your series. The group Dr. John Calabro told me about, which I think is the group you have been studying, does differ slightly from ours. It