Prognosis of Rheumatoid Arthritis: A Prospective Survey over 11 Years. By R. K. Jacoby, J. A. Cosh, and M. I. V. Jayson (Department of Medicine, University of Bristol, and Royal National Hospital for Rheumatic Diseases, Bath).

A prospective investigation into the course of rheumatoid arthritis is reported. 100 patients presenting within one year of the onset of their disease were documented and re-examined after mean intervals of 3 and 11 years.

By final follow-up, 83 patients still alive were reassessed, and of the seventeen deaths, five could be related to the disease or its treatment.

Although, in the series as a whole, females were more common than males (64 to 36), of the 42 patients presenting within the first 3 months of the illness the sex ratio was nearly equal.

88 patients had positive Waaler-Rose tests at some stage in the disease; of these eighteen converted to positive from negative during an exacerbation of the arthritis, whereas eight reverted to negative during remissions.

After 11 years there was a significant deterioration in functional capacity, but significant improvement occurred in erythrocyte sedimentation rate, haemoglobin, Waaler-Rose titre, and stage of the disease.

The original Waaler-Rose titre correlated with the number of joints involved after 11 years and with the x-ray scores for large joints.

There was no significant differences between men and women and family history, and the site and speed of onset of arthritis did not affect the final outcome. There was no correlation between maximum erythrocyte sedimentation rate in the first year of disease and the final functional capacity, nor between the haemoglobin when first seen and the final outcome.

Although this group of patients was collected at a rheumatology clinic and does not reflect the disease in the population at large, it does show that in the majority, the activity of the disease will remit. The poorer functional capacity may reflect an ageing population, whose average age at the onset was 50-6 years.

Discussion

Prof. J. J. R. Duthie (Edinburgh) In our 307 cases (Duthie, Brown, Truelove, Baragar, and Lawrie, 1964), we found that admission to hospital or being seen at a hospital clinic within the first year of onset meant a much better prognosis. So you have selected here a prognostically excellent group. Did you find any correlation between the ultimate outcome and the type of onset?

Dr. Jacoby Yes, I would agree with that.

Prof. J. J. R. Duthie (Edinburgh) The other thing that I find surprising is that you speak of 'speed' of onset; now I am not quite sure what you mean by speed?

Dr. Jacoby The patients were asked how quickly their disease began when they were seen for the first time. There were three types: 1. Acute—on a given day; 2. Sub-acute—within a given week; 3. Gradual—over a month or more.

Prof. J. J. R. Duthie (Edinburgh) And you found no correlation between the ultimate result and the type of onset?

Dr. Jacoby No.

Prof. J. J. R. Duthie (Edinburgh) We have tried to do the same thing and have compared acute onset with sub-

acute or intermittent onset. There is no question that patients with an acute onset had the best prognosis of all and this nearly always correlated with early admission to hospital. The highest proportion of patients in functional grade I after 10 years' follow-up was the group with an acute onset. I think it is very important to realize this, as otherwise we might be tempted to give corticosteroids to patients with very acute onset. Furthermore, we have not treated any of our patients with the modern immunosuppressive agents, and so any drug on trial which does not produce some improvement in at least 80 per cent. of patients is not influencing the natural progress of the disease. Single estimations of the erythrocyte sedimentation rate and haemoglobin bore no relationship to the end-result, while consistently high erythrocyte sedimentation rate and low haemoglobin values carried a much worse prognosis.

Dr. Jacoby I am sorry that I cannot give you that information for our series.

Prof. E. G. L. Bywaters (London) I am not sure whether it is possible to compare groups from different times and from different places. I presented to the Society in 1960 a study of some 250 patients which started 25 years ago, and this is still going on (Bywaters and Dresner, 1952). The majority are now dead of course. At the last analysis we found this improvement in the early years of the disease was followed by a long period of stabilization, followed in its turn by a gradual deterioration. We also found a great difference between the cases presenting before 3 months of onset and those presenting after one year. This we felt was due to a bias of presentation or selection rather than to the good effort of early treatment.

Dr. D. A. H. Yates (London) Was there any indication that those who contracted the disease later in life fared any better than those who started earlier?

Dr. Jacoby No, not that we noticed.

References


Cell-mediated Mechanisms in Murine Lupus. By A. S. Russell, C. R. Stillier, and J. B. Dossettor (Department of Medicine, University of Alberta, Edmonton, Canada)

N.Z.B. mice spontaneously develop immune-complex nephritis comparable to that of human systemic lupus erythematosus, in which the principal immunological mechanism is thought to be humoral. A prominent histological feature of lupus nephritis is round cell infiltration, suggesting that cell-mediated immunity may also be important. Fibroblast monolayers from N.Z.B. and Balb/c (H-2 identical) embryos were cultured with spleen cells, using 51Cr release and morphological criteria to estimate monolayer damage. Cytotoxicity against autologous fibroblasts was present when the spleen cells were from nephritic animals. Cells from younger N.Z.B. mice, before the development of renal disease, show cytotoxicity of intermediate degree. No significant cytotoxicity was demonstrable against Balb/c monolayers by the N.Z.B. cells. We interpret this as indicating the reactivity is not H-2 related. An interesting possibility is that it is a determinant on the ubiquitous virus particles seen.
Discussion

PROF. D. L. GARDNER (Belfast) There is some indirect evidence which supports Dr. Russell's interesting hypothesis. We have recently examined the kidneys from two cases of infectious mononucleosis nephritis and there is a striking similarity in the microscopical findings and those pictures shown today. A further situation which supports your general hypothesis is Aleutian disease of blue mink. I wonder whether you would like to comment on the possible relationships between N.Z.B. disease, Aleutian disease of blue mink, and the infectious mononucleosis nephritis in terms of virus nephritis.

DR. RUSSELL We are also looking at the Aleutian mink disease, which again shows a marked vascular infiltration of superficially the same type, but in fact the cells are largely plasma cells. Infectious mononucleosis has also depression of T-cell controlling factors and they show depression in the PHA and PPD responses. So again this may be a similar type of mechanism. There is also the possibility that it is an immune complex nephritis which may be generated in the classical way or perhaps again by autoantigens, because patients with infectious mononucleosis develop nuclear antibodies.

DR. W. C. DICK (Glasgow) Do your experimental methods exclude the possibility of complement-mediated killing or of B-cell killing? I am interested by your ratio of lymphocytes to target cells which seem to me very similar to that of the Hellströms. Why do we need so many cells to kill one target cell?

DR. RUSSELL I think these target cells can rapidly resynthesize the lesions in the cell membranes and that is why you have to hit them in several places at once. There is no overt complement in this system; the question is whether complement is synthesized by the cells that are present. I think this is irrelevant, because we know that lymphocytes do contain some complement components, C9 for example, and maybe the lesions are mediated by a C9 but this is nevertheless cell-mediated toxicity. They did not synthesize all the components of complement so it is not conventional cytotoxicity.

DR. L. E. GLYNN (Taplow) The proportion of sensitized cells amongst the number you put into the tube is probably very low. In the in vivo system, the whole body content of the sensitized cells becomes available to make the necessary contacts. So you would need a very much higher proportion of static cells for the right number of sensitized ones to make contact.

Fifteen patients with benign gonococcal arthritis accompanied by cutaneous lesions were seen over a period of 18 months.

The diagnosis was suspected when patients presented with joint pain and swelling usually associated with typical cutaneous lesions and pyrexia. Confirmation required the isolation of Neisseria gonorrhoeae from the genital tract, blood, or synovial fluid.

The age range of the patients was 17 to 43 years; all except three were females, and the series included a married couple.

On clinical examination all fifteen patients had an inflammatory arthropathy that was asymmetrical, sometimes migrating, predominantly of the larger joints, and in thirteen accompanied by pyrexia.

Typical cutaneous lesions appeared in thirteen patients a few days after the arthralgia. These were initially erythematous macules which became maculopapular, vesiculopustular, and usually haemorrhagic. They were distributed over the limbs and were found on the trunk in only two patients. Skin biopsy in three patients showed no evidence of focal sepsis.

None of the patients complained of urogenital symptoms and no evidence of salpingitis was found in the females.

All patients responded dramatically to antibiotics within 24 to 48 hours of treatment.

Benign gonococcal arthritis with cutaneous lesions has been found to be less rare than has been previously thought (Boyle and Buchanan, 1971). In fact, nine of these patients were presented within a period of 5 months.

The findings indicate that a diagnosis of benign gonococcal arthritis with cutaneous lesions must be considered in any patient with a combination of fever, polymyalgia, and vesiculopustular or haemorrhagic skin lesions.

Discussion

DR. F. DUDLEY HART (London) This condition is rather more common nowadays. For years I never saw gonococcal arthritis at all and Reiter's syndrome dominated the scene. The problem is not so much one of the individual but of the social group and family.

DR. A. S. RUSSELL (Canada) Did the three men have urethral discharge or was it rectal gonorrhoea that they contracted? For the joint fluid cultures, did you use regular media or the hyperosmolar media to try to culture the L forms?

DR. SEIFERT The three men denied having urogenital symptoms, though they did have urethral discharge on examination; they did not have rectal gonorrhoea. I am not aware of the cultural techniques used by the bacteriology department.

DR. R. GRAHAME (London) Does the gonococcal complement-fixation test help in the diagnosis of this condition?

DR. SEIFERT In eleven cases we performed the gonococcal complement-fixation test and only four of these were positive.

DR. G. V. HUGHES (London) I noticed a marked difference in the prevalence of gonococcal arthritis between America and the United Kingdom and I do not think it is