

examined specimens not only by conventional mycoplasma isolation methods but also by the sucrose density gradient technique. In no case was a mycoplasma isolated. In summary, it seems to me that it is possible very occasionally to isolate a mycoplasma from a joint. This does not seem unreasonable in a patient who has an immunity defect such as agammaglobulinaemia. On the basis of these studies I cannot believe that *Mycoplasma fermentans* is present in a large proportion of joints. I think, however, it is worth remembering that, in mycoplasma-induced arthritis in animals and birds, the organisms disappear although the manifestations of the disease continue. Although my enthusiasm for this sort of study is waning, I firmly believe the continued studies should be directed at looking at very early cases of rheumatoid arthritis where these can be obtained and certainly not at the chronic disease.

DR. K. N. LLOYD (*Cardiff*) I am a clinician and worked with Dr. Williams for some years. I think that there may be a transport problem here. Our specimens came from the patient and were straightaway stored at -70°C . and examined at leisure, can I ask at what temperature your specimens were transported by post?

DR. WINDSOR As the synovial fluid has to be centrifuged for 2 hours at 4°C . we thought it reasonable to transport them on ice. Transport time was about 2 hours. There were some synovial fluids that had been stored at -70°C . but the later ones were cultured direct.

DR. K. N. LLOYD (*Cardiff*) Concerning the band found on the sucrose density gradient, have you looked at it under the electron microscope to see whether there are any mycoplasma-like bodies?

DR. WINDSOR I should think that cultural techniques are more sensitive than electron microscopy; we can put *Mycoplasma fermentans* into synovial fluids and then recover one or two particles per ml. were the isolation techniques good enough.

DR. K. N. LLOYD (*Cardiff*) Dr. Taylor-Robinson and Dr. Mervyn Williams have stressed that the high isolation rate came from the early case. In only ten of your patients was disease duration 1 year or less. Finally, what was the clinical activity of these patients and in particular were they on gold therapy, because we know that gold is mycoplasmacidal?

DR. MAINI All the patients had active rheumatoid arthritis when the synovial fluid specimens were obtained, and they included ten whose arthritis was of very recent onset (a few months to one year). None of the patients was receiving drugs known to suppress mycoplasma growth, such as gold, chloroquine, or antibiotics.

DR. D. TAYLOR-ROBINSON (*London*) Dr. Dourmashkin has looked at some of these specimens by electron microscopy. If you look at the band from a gradient by negatively staining it, then you can see anything you wish to. What you have to do is to examine sectioned material. The best approach is to take a synovial fluid, centrifuge it, and section the deposit. When we isolated *Mycoplasma pneumoniae*, there was not the slightest doubt about it. The difficult problem is looking at specimens when mycoplasma have not isolated. Occasionally you can see things that strongly resemble mycoplasmas but there is no way of knowing whether they are or not.

PROF. D. L. GARDNER (*Belfast*) It is extremely important not to dismiss the controversial work of Mervyn Williams on this one additional piece of evidence. Fraser, Shirodaria, Haire, and Middleton (1971) presented extensive evidence using immunofluorescent and serological techniques that eleven mycoplasma strains of two species could be cultured from joint specimens. They concluded, on the basis of their immunofluorescence studies, that immunoglobulins against the mycoplasmas were not present.

DR. D. TAYLOR-ROBINSON (*London*) I had the opportunity of looking at Prof. Fraser's isolates, some of which turned out to be *Mycoplasma hyorhinis*. This, as you know, is a mycoplasma usually isolated from pigs but also from mycoplasma-contaminated tissue cultures.

PROF. D. L. GARDNER (*Belfast*) No-one has mentioned diphtheroids. Before dismissing the *Achromobacter* species as contaminants it should be remembered that they can occasionally act as human pathogens and, if you dismiss *Achromobacter*, presumably you dismiss diphtheroids.

DR. MAINI Bacteria of the *Achromobacter* species that were isolated generally occurred before rigid precautions were undertaken to prevent contamination of the vials either during transport on ice or during centrifugation in series III. The data we showed you provides circumstantial evidence that these were contaminants.

PROF. J. J. R. DUTHIE (*Edinburgh*) We were well aware of the danger of contamination in our own work on diphtheroids. On the advice of the Professor of Bacteriology, we set up a further twenty cultures of synovial membrane or fluid, taking all possible precautions to avoid contamination, and in the end we found the same rate of isolation as in our previous work, namely 30 per cent. The diphtheroid isolates are very interesting in that they are potent adjuvants, can abrogate tolerance, and in mice can induce autoreactive antibodies against red cells. I am not claiming that diphtheroid organisms are the primary basic cause of rheumatoid arthritis because I do not believe that, but in view of their interesting properties they may have some role in the pathogenesis of this disease.

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Familial Occurrence of Psoriatic Arthritis. By J. M. H. MOLL and V. WRIGHT (*Rheumatism Research Unit, University of Leeds*).

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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.

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Cell-mediated Mechanisms in Murine Lupus. By A. S. RUSSELL, C. R. STILLER, and J. B. DOSSETOR (*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.