DR. POND Certainly, in the longest surviving dogs, they were always seen together. In the shorter surviving dogs, in which we saw more of the acellular areas and no gross fibrillation, the menisci were sometimes intact and sometimes not. There seemed to be no particular correlation in the early changes.

DR. A. G. S. HILL (*Stoke Mandeville*) I think a fair number of us have been puzzled by the mechanism of osteophyte formation. Did you do any early studies just of the edge of the joint to see what the initial changes were?

DR. POND We looked at a large number of serial sections of the osteophytes as they developed and the findings were very interesting, but these points will have to be investigated further before any conclusion can be made.

Reference

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Use of Radio-active Yttrium-90 in Persistent Synovitis in the Knee.

I. Retention in the knee and spread extra-articularly. By J. M. GUMPEL, D. WILLIAMS, and H. I. GLASS (*Northwick Park and Hammersmith Hospitals*)

II. A comparison of Yttrium-90 resin and citrate. By J. M. GUMPEL, H. E. A. FARRAN, and D. WORTH (*Northwick Park Hospital*)

Part I was published in full in the *Annals* in May, 1973 (vol. 32, No. 3, p. 222)

Complement Metabolism in Rheumatoid Arthritis. By J. M. B. VERSEY, J. R. HOBBS and P. J. L. HOLT (*Departments of Chemical Pathology, Westminster Hospital Medical School, and Rheumatology, Royal Postgraduate Medical School, London*).

To be published in full in the *Annals*.

Measurement of Inflammation.

I. Application of Technetium Clearance to Rheumatoid Arthritis and Animal Models. By H. BERRY, J. P. BROWETT, E. C. HUSKISSON, P. A. BACON, and D. A. WILLOUGBY.

II. Comparison of Technetium Clearance and Thermography with Standard Methods in a Clinical Trial. By E. C. HUSKISSON, H. BERRY, J. P. BROWETT, and H. WYKEHAM BALME (*St. Bartholomew's Hospital, London*).

Published in full in the *Annals* in the March issue (vol. 32, no. 2, pp. 95, 99).

Discussion

DR. J. A. COSH (*Bath*) May I congratulate Dr. Huskisson on his techniques of assessing inflammation by thermography. The president has kindly allowed me to show two slides illustrating similar work. The first shows the quantitation of inflammation and of anti-inflammatory drug action by measuring infra-red radiation from rat paws using radiometry; this work was done in the Department of Pharmacology in the University of Bath (Collins and Ring 1972). A group of five rats had carrageenin

injected into a hind paw and the rise and fall of paw temperature in the ensuing 24 hours was measured with the radiometer and charted. The experiment was repeated with other groups of rats primed with three different dosages of an orally administered anti-inflammatory drug azathioprine. The graph clearly indicates the rise and fall of paw temperatures and the degrees of suppression of inflammation by the drug, the greatest suppression of temperature being shown by the largest dose.

The second slide is based on repeated thermographic measurement of the knee of a patient with rheumatoid arthritis following the temperature week by week of the warmest skin area over the knee joint. The patient was given six injections of a depot preparation of triamcinolone. After each injection the temperature fell for some days and rose again as the anti-inflammatory effect wore off. With repeated depot injections, the absolute temperature fell progressively and the 'escape' after each became less. There was a parallel improvement in hand grip. In clinical measurement by thermography, it is most important to standardize the physical conditions of examination; the patients' legs in this study were exposed for 15 minutes in a room temperature of 18°C. before each measurement was made.

DR. BERRY We tried very hard to measure anti-inflammatory activity using the thermography technique in rats. We found it impossible to get sufficiently accurate results from this because the field of view of the camera was too large.

DR. M. I. V. JAYSON (*Bath*) I am rather concerned about the use of the forearm for correcting the technetium calculations. Forearms are used on the assumption that this reflects the blood flow but both we and Marks, Birkett, and Shuster (1972) have shown that in rheumatoid arthritis there is general increased capillary permeability. Do you not think that this might well invalidate the use of forearms for correcting technetium scans, because there would be an increased outpouring of technetium compounds into the interstitial fluid in rheumatoid arthritis?

DR. HUSKISSON We entirely agree. Our work suggests that the use of any correction of this sort is invalid because of the strange distribution of technetium which is quite different in rheumatoid patients and normal controls. We interpreted the forearm technetium count as representing mainly extravascular fluid, and there was evidence that in rheumatoid arthritis, technetium stayed more within the vascular compartment; increased permeability would have been easier to explain.

PROF. E. G. L. BYWATERS (*London*) These various attempts to define inflammation seem to me to be doomed to failure. You are trying to measure different things; the amount of blood in the part, the blood flow, to some extent the extracellular fluid, the extracellular serum protein, and the extravascular serum protein. Each of these is one of the factors in inflammation, but these different methods vary in themselves according to protein binding or intravascular confinement, etc. Inflammation is a very complicated thing. I am sure your conclusion is probably correct, but equally that our clinical methods are better than these various ones which are looking for something which you are not quite sure how to define.

PROF. C. A. KEELE (*London*) May I ask whether there is any evidence that the technetium is bound to any particular

proteins such as plasma-albumin? The acidic non-steroidal anti-inflammatory drugs displace a number of compounds that are bound to albumin, so this factor might complicate the whole issue. I wonder if you have any evidence in relation to this?

DR. BERRY McCarty, Polcyn, Collins, and Gottschalk (1970) found that it was albumin-bound, but we were unable to prove this ourselves. There was no evidence that drugs displaced technetium from protein binding.

PROF. J. J. R. DUTHIE (*Edinburgh*) It would not be inappropriate to say that many of our young men have devoted a vast amount of energy and expertise to acquire information which might be obtained more readily by asking the patient a simple question, namely 'Do you feel better?'

DR. HUSKISSON It is because of the unreliability of this technique in the past that we are spending so much time and energy to find a better method.

A. SPEAKER We have been studying the metacarpal-phalangeal joints using technetium, and have found in some patients, who have been on large doses of salicylates, that, although there has been a clinical improvement, the technetium count rate has in fact increased. This may reflect displacement of technetium from its binding sites by the salicylates.

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Search for Mycoplasma in Synovial Fluids from Patients with Rheumatoid Arthritis. By G. D. WINDSOR, A. NICHOLLS, R. N. MAINI, R. LEMCKE, D. G. EDWARD, and D. C. DUMONDE (*Kennedy Institute of Rheumatology, Wellcome Research Laboratories, and Lister Institute of Preventive Medicine, London*)

This communication describes attempts to isolate mycoplasmas from the joints of patients with rheumatoid arthritis. Reports of culture isolations have included different strains of mycoplasmas (Bartholomew, 1965; Jansson and Wager, 1967; Williams, 1968) and tiny colonies suspected to be a 'mycoplasma' (Jansson, Mäkisara, Vainio, Vainio, Snellmann, and Tuuri, 1971). One interpretation of the lack of uniformity of observations has been that the organisms were tissue culture contaminants or commensals of doubtful clinical significance. However, the findings of Williams and his colleagues of a particular species, *Mycoplasma fermentans*, in 40 per cent. of synovial fluids from patients with rheumatoid arthritis using sucrose gradient separation techniques, accompanied by an apparent specific *in vitro* cellular immunological reaction to the organism has led to speculation as to its possible aetiological significance (Williams, 1970; Williams, Brostoff, and Roitt, 1970).

73 samples of synovial fluids and nine membranes were obtained from patients with rheumatoid disease (including those with arthritis of recent onset) and with other conditions causing joint effusions. The samples were investigated for the possible presence of mycoplasmas:

(a) By direct culture in solid and liquid media. Some of the specimens were cultured in two independent laboratories.

(b) A sucrose gradient of a similar composition to that described by Williams (1968) was used to separate synovial fluid into visible bands by ultra-centrifugation, and 0.2 ml. volume of material from each band was cultured in liquid and solid medium.

No mycoplasmas were isolated by the direct technique from fourteen synovial fluids and homogenates from nine synovial membranes. The results of examining 69 synovial fluids on sucrose gradients are summarized below:

Fluids	RA	Non-RA
Number synovial fluids	64	5
Visible bands cultured	141	7
Mycoplasma isolations	0	0
Achromobacter isolations	13	0

A colour change to an acid pH was observed in the liquid medium of cultures of sixteen bands which on subculture yielded an organism belonging to the Achromobacter species. This was regarded as a contaminant as further isolation of these bacteria was prevented by suitable precautions. Mycoplasmas were not isolated from any of the samples examined.

Discussion

DR. D. TAYLOR-ROBINSON (*London*) What I have to say confirms what has just been said. I shall briefly summarize about 7 years' work; my colleagues and I have been looking for mycoplasmas in joints since 1965. We started in Salisbury obtaining specimens from a variety of places and after moving to Northwick Park Hospital in 1970 we continued the studies. Synovial membranes and synovial fluids have been examined, and although there were a range of diagnoses, rheumatoid arthritis comprised 109 of 146 cases. Most of these were acute exacerbations of chronic disease, and very few of them early cases. From one case of rheumatoid arthritis, we isolated a glucose-fermenting mycoplasma which was not identified further. In addition, we isolated T-mycoplasmas from the joints of two patients having polyarthritis and psoriasis. This was work done in collaboration with Dr. E. M. C. Dunlop and Prof. Barrie Jones. It is interesting that about 6 months ago Dr. P. Gill (McGill University) told me that he had isolated a T-mycoplasma from the joint of a boy suffering from Still's disease. In collaboration with clinicians at Taplow (Prof. Bywaters, Dr. Ansell, Dr. Gumpel, and Dr. Swannell) specimens have been obtained and divided, a portion being examined by us and a portion by Miss Auriol Hill at the Laboratory Animals Centre, Carshalton. The isolation of a mycoplasma from one patient was of particular interest, because there was a 16-year history of agammaglobulinaemia. Three years before the synovial membrane specimen was taken, a diagnosis of nodular rheumatoid arthritis had been made. At the time of admission to hospital the patient had a respiratory infection and an acute exacerbation of arthritis. The mycoplasma was identified as *Mycoplasma pneumoniae*. In view of the history of respiratory infection, the identification of the mycoplasma and its isolation in two separate laboratories, it is extremely unlikely to be a laboratory contaminant. Finally, my colleague Andrew Campbell has