Discussion

DR. K. WHALEY (*Glasgow*) The low percentage of 'T' cells using your rosette test is extremely interesting; this is far lower than most people report. I wonder whether there are technical variations between your technique and that of other workers. Two things spring to mind; one, how do you define the rosette, perhaps you have more stringent criteria than most other people, and secondly at what temperature do you perform the assay?

DR. HOLT The rosette has to have 5 red cells on it to be a positive and the assay is performed at 4°C, but the preliminary incubation with sera is at 37°C.

DR. K. WHALEY (*Glasgow*) Quite. One of the problems at 37°C is that rosettes are very unstable and tend to breakdown very quickly. Therefore, most people, including yourself, perform the test at 4°C. The other point of 5 red cells being necessary before one can definitely say a rosette is present is more than most people accept. This variation could account for your low results.

DR. HOLT We are aware of this point. Our interest was to find a level at which we could show the change. Because by using one method you can push the results for 'B' and 'T' cells up to 100%, it does not necessarily mean it is the ideal way of doing the test, nor that it represents normality.

DR. K. WHALEY (*Glasgow*) Yes, I agree; most people push it upto 60% but it may in fact improve your results. There may be bigger differences.

DR. HOLT If you push it like that, I think you would probably improve the ability of the rosettes to stick together and you do not get this variability coming out quite so easily.

DR. W. C. DICK (*Glasgow*) Have you completely excluded by studies both *in vitro* and *in vivo* that these as yet undefined factors which are albumin bound and of small molecular weight could not be drugs that the patients are receiving?

DR. HOLT I did not say they were albumin bound, I said they were of similar size. I think we can exclude the effect of drugs. We find similar effects in, say, pregnancy where there are no drugs being given, and we have dialysed the serum and after dialysis it is still the same. Further, it is rapidly reversible, which is a little against drug effect. I would say we have gone a reasonable way towards exluding this possibility.

DR. P. A. BACON (*Bath*) A couple of years ago I presented some evidence that in both RA and SLE there were large lymphocytes in the blood which in autoradiography were shown to be spontaneously transformed cells (Bacon, Crowther, and Sewell, 1971). Do these cells in fact rosette or do they contribute to your low number of peripheral 'T' cells?

DR. HOLT The labelled cells do not form rosettes.

References

Bacon, P. A., Crowther, D., and Sewell, R. (1971) *Proc. VII European Rheumatology Congress*, Brighton, 1971.

Comparison of ultrasound and positive contrast arthrography in the diagnosis of popliteal and calf swellings. By H. MEIRE, D. J. LINDSAY, D. R. SWINSON, and E. B. D. HAMILTON (*King's College Hospital, London*)
Published in full in the *Annals* 1974, **33**, 221.

Discussion

DR. J. M. GUMPEL (*Northwick Park*) At Northwick Park I have had the privilege of working with radiologists who are very interested in soft tissue shadows and have been surprised how often on a plain lateral radiograph of the knee they have predicted that I will have found or should have found a Baker's cyst. Have you compared your findings with plain *x*-rays of the knees, to assess whether you could have seen a Baker's cyst?

DR. SWINSON We have not compared it with soft tissue *x*-rays. We have used it in patients with suspected rupture of the cyst and have found it useful, though these patients were not in the results.

DR. M. I. V. JAYSON (*Bristol and Bath*) I think that one should point out that when we (Genovese, Jayson, and Dixon, 1972) examined a series of rheumatoid knees routinely by arthrography we found that over 90% of them had popliteal cysts, so that I think that you are quite likely to find them in any series in which you are looking for them. I just wonder how much this technique depends upon the actual pressure within the cyst? With a low pressure cyst which is difficult to detect clinically, might you find it difficult to detect it by ultrasonic scan because you do not have a nice tense surface under pressure to reflect the ultrasonic beam?

DR. SWINSON I think it depends principally on the size of the cyst. As long as it has fluid in it you have an area of different density to the structure around it and therefore it should show up if it is a reasonable size, say 2 cm.

Reference

Genovese, G. R., Jayson, M. I. V., and Dixon, A. St. J. (1972) *Ann. rheum. Dis.*, **31**, 179

Atlanto-axial Subluxation—a 5-year Follow-up Study in Rheumatoid Arthritis. By J. A. MATHEWS (St. Thomas's Hospital, London) To be published in full in the *Annals*.

Rheumatoid Discitis in the Thoracic Region due to Spread from Costovertebral Joints. By E. G. L. BYWATERS (*M.R.C. Rheumatism Unit, Taplow and Royal Postgraduate Medical School, London*)

A detailed dissection of the rheumatoid spine shows lesions in thoracic discs due to spread from adjacent costovertebral (diarthrodial) joints. This has not hitherto been recorded clinically, radiologically, or pathologically. The process is essentially similar to that shown by Ball (1964) for the cervical discs where there is spread from the oncovertebral joints. Lesions in the lumbar spine previously described radiologically (Lawrence and Sharp, 1964) can be seen to be due to rheumatoid invasion of a degenerate disc.

Discussion

DR. J. BALL (*Manchester*) I would like to congratulate Prof. Bywaters on an excellent illustration of the thoracic lesions. I can certainly confirm that arthritis of costo-

vertebral joints is readily found. I have a macerated specimen of a rhematoid spine in which every costovertebral joint shows naked eye erosive change. Indeed the costovertebral joints, that is to say the facets on the vertebral body, are more severely involved than the corresponding posterior zygapophyseal joints, and I wonder whether this kind of differential has been found by Prof. Bywaters? However, in the thoracic spine all the lesions I have encountered have been restricted in terms of their erosion of the vertebral bodies, that is, the erosion does not spread around as it does in the cervical spine. Now, just to comment about the lumbar lesions. In the original cases reported by us which were subject to histological study, I found no evidence that any of the lesions in the lumbar spine could be attributed to what I would recognize as a rheumatoid process: all of them were explicable in terms of disc and end-plate failure, porotic collapse, or pyrogenic inflammation. The first slides shown by Prof. Bywaters of the lumbar spine show lesions which one can find quite readily in nonrheumatoid lumbar spines and I think we should be very careful about interpreting tissue damage in the rheumatoid as always being of rheumatoid origin.

PROF. BYWATERS Involvement of apophyseal joints, I agree, may be slightly less frequent. The thoracic costovertebral lesion does not involve the whole of the disc as I have already shown in a number of areas: I think this is possibly because of the more restricted movement there is in the thoracic spine as compared with the cervical spine or even the lumbar spine. In the cervical spine there can be complete loss of disc substance and complete loss of all cartilage on the apophyseal joints. The lumbar spine lesions are always very difficult to interpret. I raised with the Society some years ago when was a pile a rheumatoid pile, and I think the same question may be being raised in relation to the lumbar disc lesion. I thought they were rheumatoid because they showed inflammatory characteristics and reactive sclerosis. These spinal lesions do not show the characteristic plasma cell and lymphocyte deposits which you see in peripheral joints and they are always more difficult to interpret, but I thought they were rheumatoid lesions. One does not see uncomplicated disc degeneration with collapse, and this bony sclerosis which is a characteristic sign of an inflammatory response.

DR. J. BALL (*Manchester*) It is important to recognize that a little inflammatory infiltration associated with loss of haemopoetic tissue will occur in the vicinity of traumatic lesions in vertebral bone. It is just because this can happen in a clearly nonrheumatoid state that you have to be really careful about putting too much emphasis on a few lymphocytes and plasma cells.

DR. R. J. FRANCOIS (*Brussels and Louvain*) I congratulate Prof. Bywaters for his very interesting data. About the patient, whose microscopical sections were shown, I would like to know for how long he had been suffering from the thoracic spine, and if the involved discs showed any development of syndesmophytes?

PROF. BYWATERS No syndesmophytes! The duration of the clinical lesion was very difficult to determine. The lady who had had rheumatoid arthritis for some 30 years was in a very decrepit state and complained of pain all over for many years.

DR. F. DUDLEY HART (*London*) Did she have restriction of chest and thoracic spinal movement?

PROF. BYWATERS There was general restriction of movement during the last years of her life. I was unable to show any particular thoracic lesions, though the *x*-ray did show these, and I imagine she did have limitation.

References

Ball, J. (1964) 'The articular pathology of rheumatoid arthritis' *in* 'Radiological Aspects of Rheumatoid Arthritis, Proc. ISRA Symposium, Amsterdam, 1963', ed. Mary E. Carter, p. 25. Excerpta Medica, Amsterdam

Lawrence, J. S., and Sharp, J. (1964) 'Lumbar spine', *idem.*

Metabolic Studies of Thiopurinol in Man and Pig. By R. GRAHAME, H. A. SIMMONDS, A. CADENHEAD, and B. M. DEAN (*Departments of Rheumatology and Medicine, Guy's Hospital, and Professional Medical Unit, St. Bartholomew's Hospital, London; Rowett Research Institute Aberdeen*)

Thiopurinol (mercapto-4-pyrazolo (3,4-d) pyrimidine) has been shown in two French studies (Delbarre, Auscher, de Gery, Brouilhet, and Olivier, 1968; Serre, Simon, and Claustre, 1970) to effectively reduce plasma and urine uric acid levels and to be a clinically effective drug in the treatment of gout. But, despite this fact, it has never been introduced into the United Kingdom. The mode of action of thiopurinol is not fully understood, but previous studies suggest that significant inhibition of xanthine oxidase does not occur *in vivo*, since the reduction on uric acid levels is not accompanied by increased excretion of xanthine and hypoxanthine as is the case with allopurinol. It has been shown that allopurinol therapy may be associated with:

(1) Deposition of xanthine, hypoxanthine, and oxipurinol in muscle (Watts, Scott, Chalmers, Bitensky, and Chayen, 1971).

(2) Xanthine nepropathy (Ablin, Stephens, Hirata, Wilson, and Williams, 1972).

(3) Disturbance of pyrimidine metabolism with orotic aciduria and orotidinuria (Fox, Royse-Smith, and O'Sullivan, 1970), it follows that thiopurinol could have certain advantages over allopurinol, provided that clinical side effects and tissue incorporation could be ruled out.

In this study thiopurinol was administered to 2 patients with primary gout and to a third suffering from gout associated with a partial deficiency of HG-PRTase. In the former two patients an effective reduction of plasma and urine uric acid levels occurred *without* increasing xanthine and hypoxanthine excretion. In the latter case no effect on uric acid metabolism was observed—a result similar to that obtained by Kaplan (1970).

In duplicate studies in the pig, uric acid levels (normally low), were reduced during thiopurinol therapy, as were levels of allantoin, the principal urinary purine metabolite in this animal. In this laboratory studies with ^{14}C thiopurinol and ^{14}C allopurinol have shown no measurable tissue incorporation with either drug (Simmonds *et al.*, 1974); almost total recovery of radioactivity was obtained in urine and faeces alone. The finding that 36·5% of the radioactivity from orally administered thiopurinol was recovered in the faeces, compared with only 7% in the case of allopurinol, suggests that thiopurinol is less well absorbed from the gastrointestinal tract.