Heberden Society

Clinical Meeting, February, 1970

At a meeting held at the Oxford Regional Rheumatic Diseases Research Centre, Stoke Mandeville Hospital, Aylesbury, on February 27, 1970, the following papers were presented:

Ulcerative Colitis and Sacroiliitis: A Family Study. By I. F. MACRAE and V. WRIGHT (*Rheumatism Research Unit, University Department of Medicine, Leeds*).

A survey was made of 91 unselected probands with ulcerative colitis, 236 blood relatives, and 56 spouses. The overall completion rate was 75 per cent. The subjects answered a questionnaire and were examined clinically. The motion of the lumbar spine was measured by the method discussed at a previous meeting of the Society, and the sacroiliac joints were x-rayed. The technique and reproducibility of grading of films for sacroiliitis has been discussed at the International Congress of Rheumatology at Prague. Intravenous pyelography films matched for age and sex were used as controls. The data were transferred to punch cards and analysed mechanically.

On application of the New York Diagnostic Criteria for ankylosing spondylitis, the prevalence of definite ankylosing spondylitis in both probands and relatives was significantly in excess of that expected in a normal population. No case occurred among the spouses. The prevalence of definite ankylosing spondylitis in probands was 20 per cent. for males and 7.7 per cent. for females. In blood relatives it was 5.1 per cent. for males and 2.6 per cent. for females.

The prevalence of bilateral Grade 3 (moderate) and Grade 4 (severe) sacroiliitis in the survey population was compared with that in the control series. In males, 22.9 per cent. of the probands, 6.2 per cent. of the blood relatives, none of the spouses, and none of the controls showed these changes. In females, 7.8 per cent. of the probands, 2.2 per cent. of the blood relatives, none of the spouses, and 0.7 per cent. of the controls had the same changes.

This study has demonstrated undoubted aggregation of ankylosing spondylitis and sacroiliitis in the families of probands with ulcerative colitis. It is suggested that genetic factors may explain the coincidence of these diseases.

Discussion

DR. J. S. LAWRENCE (*Manchester*) I was interested to note that the amount of Grade 3 to 4 sacroiliitis found in the first degree relatives was similar to that which we found in relatives of spondylitic patients. This might have very important implications, but before we can assume that it is correct, the x rays of both surveys would have to be read by the same persons. Did you separate the relatives of the patients with spondylitis from the other relatives and look at their families separately with regard to sacroiliitis?

DR. MACRAE This particular point has not yet been analysed, but it would appear that there is no correlation since with many of the relatives who did have spondylitis, the probands did not. I am pretty sure it would turn out like that.

DR. M. I. V. JAYSON (*Bath*) In a survey which we performed on the incidence of inflammatory bowel disease in ankylosing spondylitis, which is the other way round, we also took a family history from our patients, and we did find that there were several first and second degree relatives with a family history of established ulcerative colitis, although they had no spinal disorder. We did not actually see these relatives, but it appeared that there was a distinct association of this type which was almost certainly on a hereditary basis.

DR. MACRAE We asked the relatives about bowel symptoms in an attempt to discover whether there was an increased prevalence of ulcerative colitis and we found that there seemed to be none. It was difficult to know whether the bowel symptoms which they mentioned were in fact those of ulcerative colitis. There was a group of males aged about 50 years who had served in the North African campaign during the second world war and who had had bloody diarrhoea at that time, but not subsequently. Now I presume that these men had in fact had dysentery and not ulcerative colitis, and I think it is very difficult from a history alone to be sure whether a patient has had ulcerative colitis or some other disease of the bowel.

PROF. E. G. L. BYWATERS (*Taplow*) I gather that your cases of bilateral Grade 3 and 4 sacroiliitis included those with spondylitis?

DR. MACRAE Yes.

PROF. E. G. L. BYWATERS (*Taplow*) So that only

two out of 91 probands showed bilateral sacroiliitis alone without spondylitis?

DR. MACRAE Yes.

PROF. E. G. L. BYWATERS (*Taplow*) Isn't this rather low? Or perhaps I should ask Dr. Lawrence?

DR. LAWRENCE I wonder whether your method of assessing the ankylosing spondylitis criteria may have played a part? Taking flexion only as the criterion for limitation would include many people with disc disorders.

DR. MACRAE I think this can be explained on the basis of our epidemiological technique. To my knowledge this is the first time that the New York Diagnostic Criteria have been used in an epidemiological survey. It may be that these criteria are too sensitive. We shall find out when more surveys have been done.

Some Observations on Culturing Human Cartilage and Joints. By K. T. RAJAN, ANNE HOPKINS, and ALAN HILL (*Oxford Regional Rheumatic Diseases Research Centre, Stoke Mandeville Hospital, Aylesbury*)

The technique of culturing limb bone rudiments has for the first time been extended to human tissue. Digits obtained from abortions were maintained in BGJ 5 medium supplemented with fetal calf serum for 12 days. Photomicrographs indicate that articular and epiphyseal cartilage survived for the maximum culture period. Preliminary observations on the development of joints have been made. The system offers potentialities for future studies of human disease.

Discussion

DR. K. M. BACKHOUSE (*London*) You mentioned a cartilaginous bar and you showed the beginnings of the joint. Did you in fact take these fingers before the joint formed or afterwards? Thinking back to Sokoloff, he showed an inter-relationship between muscle activity and joint formation. Does this come into your investigation?

DR. RAJAN In the earliest fetuses—about 10 weeks—you could just see where the future joint cavity was going to form. But in all the older fetuses the joints had already formed. The role of muscle activity in the formation of joints has been suggested by Murray in Australia and by Sokoloff. This is disproved by my experiments because there was no movement at all and we found that especially in the later fetuses which we allowed to grow for 12 days there was no evidence of ankylosis or disappearance of the joint cavity.

DR. J. H. GLYN (*London*) Would Dr. Rajan consider that he has a possible experimental model which could be employed to throw light on the alleged clinical risks of repeated intra-articular corticosteroid injection, in relation to destruction of the joint cartilage? Such an objective method of evaluating the effect of steroids on mucopolysaccharides would seem to be particularly desirable in view of Salter's experimental work on rabbit knee joints.

DR. RAJAN Preliminary work has shown that high doses of steroids in culture can produce osteoporosis. This can also be produced by using high doses of vitamin

A, and we hope by using this carefully controlled condition to be able to develop a dose titration, from which you could say that from such and such a dose you get osteoporosis.

PROF. E. G. L. BYWATERS (*Taplow*) This is a very nice technique with obviously a great future. I was rather surprised that you said cartilage was so pernickety in its growth requirements. Some 30 odd years ago we were able to culture rabbit cartilage in glucose bicarbonate Ringer's solution for 10 days; the metabolic curve showed that there was some falling off but there was good glycolysis right up to the end of the 10 days. Is this difference between animal and human cartilage one of vitamin C requirement?

DR. RAJAN I started growing mouse cartilage, which is comparable to rabbit cartilage, and I subsequently changed to human cartilage. Regarding the question whether human tissue responds differently to biological substances, such as vitamins A and C and hydrocortisone, I have found that adding 10 i.u./ml. vitamin A to post-fetal mouse bones produced loss of metachromasia, diminution of the growth zone, and other effects that have been described by Fell and Mellanby. Adding the same dose to human rudiments, there was complete necrosis. When I added 3 i.u./ml. (one third of the dose necessary to produce the hypervitaminotic effect on mouse cartilage), I was able to obtain a comparable result. Thus one-third of the dose necessary to produce hypervitaminosis on mouse cartilage was sufficient for the human tissue. Our experiments in screening drugs in animals may in the long run not be suitable when we try to extrapolate to human tissue.

Do Oral Corticosteroids cause Osteoporosis in Rheumatoid Arthritis? By W. W. BUCHANAN, B. M. SAMUELS, M. K. JASANI, J. A. ANDERSON, W. M. O'BRIEN, J. A. BOYLE, G. NUKI, and I. T. BOYLE (*The Centre for Rheumatic Diseases and the University Department of Medicine, Royal Infirmary, Glasgow, and the Department of Preventive Medicine, University of Virginia School of Medicine, Charlottesville, Virginia, U.S.A.*)

A technique of multiple regression and covariance analysis has been performed to correct for differences in the many factors, such as age, duration and severity of disease, years since the menopause, and oral corticosteroid therapy, which could influence the development of osteoporosis in rheumatoid arthritis. The analysis showed that oral corticosteroids do cause osteoporosis when given in low doses to rheumatoid patients; a year of therapy causes as much osteoporosis as 5 years of ageing, and 2 years of therapy does as much damage as an increase of one in x-ray class.

Discussion

DR. D. A. BREWERTON (*London*) It seems to be suggested that local factors did not make the metacarpal index unreliable, and I must admit that this surprises me. I should have thought that the severity of local disease activity, local deformities, tendon disease, and so on would have had an enormous effect on local osteoporosis. This might not be well reflected in the radio-