scleritis; did you find anything which would suggest any virus disease in any of your patients?

DR. PITKEATHLY As regards the allergy: there were a number of patients with episcleritis who had attacks in the spring or in the summer. As regards the rosacea: we excluded that at the beginning because we were aware that it could produce episcleritis. We did not find any suggestion of virus infection, although it was only looked for if there was some suggestion of this to begin with.

DR. WATSON The point about herpes zoster ophthalmicus is that it can cause both episcleritis and scleritis. It can start an episcleritis which progresses to a scleritis. It is therefore difficult to put it into one group.

Some Aspects of the Radiology of the Shoulder Joint in Rheumatoid Arthritis with a Note on the Findings in Osteoarthritis. By M. M. MCNAIR, J. A. BOYLE, W. W. BUCHANAN, and J. K. DAVIDSON (*Glasgow*)

Antero-posterior radiographs of both shoulder joints were taken in fifty unselected patients with sero-positive rheumatoid arthritis (RA); 46 patients with osteoarthritis (OA) and fifty normal subjects provided control radiographs. The findings of two radiologists without previous knowledge of the diagnosis in any of the subjects, or of each other's opinions, were correlated with the clinical findings.

The radiological appearances of the shoulder joint in RA suggest that:

(i) Radiological abnormalities of the shoulder joint are very common in sero-positive erosive RA and in patients with OA even though these patients may have no complaints referable to the shoulder joint.

(ii) As generalized osteoporosis was found only in the rheumatoid patients, limitation of shoulder joint movement is the clinical feature which correlates best with severe radiographic changes in RA. Of the 47 shoulder joints with this clinical feature, 38 per cent. had radiographic evidence of joint erosions, 50 per cent. had generalized osteoporosis, and 21 per cent. had remodelling of the humeral head.

(iii) Generalized osteoporosis of the shoulder girdle is the radiographic sign which correlates best with the degree of clinical involvement of the shoulder joint in RA: of the 32 shoulder joints with this radiographic finding, 63 per cent. were painful and 75 per cent. had limited movement.

Discussion

DR. A. G. S. HILL (*Stoke Manderville*) I should like to ask Dr. McNair if she attempted any correlation of changes in the shoulder joints with the use of the shoulder as a weight-bearing joint; in other words, does the use of crutches increase the incidence of radiological abnormality in the shoulder?

DR. MCNAIR I am afraid we have not studied this.

Rheumatoid Serum Factors in Families. By J. S. LAWRENCE, J. BALL, and H. A. VALKENBURG (*Manchester*). This article and the discussion thereon is to be published in a future issue of the *Annals*.

Preliminary Results of Azathioprine Therapy in Severe Rheumatic Disease. By A. J. SWANNELL, E. N. COOMES, and J. Q. MATTHIAS (*London*)

Twelve patients on treatment with azathioprine (8 rheumatoid arthritis, 2 psoriatic arthritis, 1 systemic lupus erythematosus), none of whom could be controlled with conventional therapy, including the use of corticosteroids, have been followed.

Azathioprine was used in a dose of 2 mg./kg. body weight; the length of treatment varied from 2 weeks to 1 year.

Three of the patients with rheumatoid arthritis improved, and the skin rash and arthritis disappeared in one psoriatic patient who later developed two episodes of septicaemia, each responding to treatment. Reduction of steroid dose was possible in one patient with SLE.

Six patients had to stop treatment on account of side-effects.

Discussion

DR. B. M. ANSELL (*Taplow*) I should like to report our experience which is not so encouraging. At Taplow we have treated seven patients (age range 30 to 66 years) with rheumatoid arthritis, two because of vasculitis and neuropathy, two because of complicating amyloidosis, and three because of severe uncontrolled disease with side-effects from corticosteroid therapy. A dose of 2 to 2.5 mg. azathioprine per kg. body weight was given for from one week to 7 months. One patient with amyloidosis has shown reduction of the activity of the arthritis, a reduction in the size of nodules, and a fall in proteinuria; he is still receiving therapy. In one other patient there was improvement in the arthritis and reduction of corticosteroid therapy was achieved, but after 2 months' treatment with 100 mg. azathioprine daily she developed a severe anaemia with bone marrow hypoplasia. When the azathioprine was stopped there was an improvement in the haematological state, but an exacerbation of disease activity, and corticosteroid dosage had to be increased again. This patient had not received gold or butazolidin in the past. Therapy had to be stopped in two cases because of side-effects: severe gastrointestinal upset and severe skin infection. In the remaining three patients therapy was stopped after 3 to 6 months because there was little or no improvement with azathioprine.

DR. C. G. BARNES (*London*) We have had some experience with azathioprine at the London Hospital, using it in a dosage of 2.5 mg. /kg. body weight per day. We have treated thirteen patients for from 6 weeks to 27 months on an uncontrolled basis and reviewed their progress. Each of these patients was resistant to normal methods of treatment, including steroid dosage in an unacceptable amount of over 10 mg. prednisolone a day. Six discontinued treatment, four on account of gastrointestinal disturbances; I think that known gastroduodenal ulceration is probably a contraindication to the use of azathioprine. We endeavoured to reduce steroid

dosage in all these patients, and were successful in about half of them. We noted an interesting fall in lymphocyte count, comparing the lymphocyte count with the total white cell count at the beginning of treatment and after one year. Whether or not immunosuppressives have any part to play in treatment of rheumatoid arthritis requires further study; we are at the present engaged in a double-blind controlled trial.*

DR. G. D. KERSLEY (Bath) In my experience in rheumatoid arthritis, the drug has often had to be stopped on account of side-effects. On the other hand we have had very good results in two cases which previously required a large dosage of steroids to control their disease.

DR. T. BITTER (Bad Ragaz) I should like to add one minor comment. The effect on a secondary immune response of a so-called immunosuppressive drug is far from proven. The cytostatic effect is potent and the indications are probably best in highly cellular disease, in which we want to suppress cells. If the cells are sufficiently suppressed, a secondary immune response might appear to be suppressed without actual evidence of an immunosuppression.

*Reference

MASON, M., CURREY, H. L. F., BARNES, C. G., DUNNE, J. F., HAZLEMAN, B. L., AND STRICKLAND, I. D. (1969). *Brit. med. J.*, 1, 420 (Azathioprine in rheumatoid arthritis).

Effect of Rumalon on Embryonic Cartilage in Culture. By K. T. RAJAN (Aylesbury)

Embryonic bones were treated with collagenase which severely depleted the matrix in culture. This effect was reversible and the matrix regenerated when the explants were restored to a normal medium. Paired rudiments treated with the enzymes were subsequently transferred to normal media with and without Rumalon. Preliminary results suggest that in Rumalon treated explants there was:

- (a) Enlargement of the articular cartilage;
- (b) Increased metachromasia;
- (c) Vacuolation of the growth zones.

These changes indicate enhanced function of the chondrocytes; the vacuolation could be due to overstimulation of the cells.

Discussion

DR. G. LOEWI (Taplow) As far as I have understood you, the controls without Rumalon had no similar extract added to them; might not the addition of an extract of some other tissue, not related to cartilage, be another interesting control, because it is just possible that you are adding additional nutrients?

DR. RAJAN Another kind of control would be to inactivate the Rumalon and then put it in and watch the result.

DR. SILBERBERG (St. Louis) As an experimental pathologist, I should like to put in a word for the animal experiment, which is particularly valuable if the animal develops a disease which is an analogue of the human disease. Mice do develop osteoarthritis, and we have

seen that the course of the development of the disease corresponds closely to that in the human. We have in the past months and years treated mice with small doses of Rumalon subcutaneously and have studied the chondrocytes of the hip joint with the electronmicroscope. The articular chondrocytes of adult mice show a hypertrophy of the cell and an overdevelopment of the cytoplasmic organelles which we interpret as a sign of increased function of the cells as a whole.

A Double-blind Controlled Trial of Rumalon in the Treatment of Painful Osteoarthritis of the Hip. By A. ST. J. DIXON, G. D. KERSLEY, R. MERCER (Bath), M. THOMPSON (Newcastle), R. M. MASON, C. BARNES (London), and G. WENLEY (Norwich), with statistical analysis by E. LEWIS-FANING (Rhoose, Glam.)

Rumalon is a bovine bone marrow and cartilage extract which affects the growth and the metabolism of articular cartilage in various experimental animals and procedures. It has been extensively used to treat human osteoarthritis but seldom under the conditions of a controlled clinical trial. A double-blind, four centre, controlled trial of intramuscular injections of Rumalon (R) in osteoarthritis of the hip has been completed. 150 patients entered the trial, of whom 75 were randomly allocated to a control group receiving intramuscular injections of a 1 in 10,000 dilution of Rumalon (P). Aloxiprin or paracetamol tablets were given as needed for pain. Injections of R or P were given three times a week for 12 weeks, followed by 12 weeks of observation. For those who accepted, the treatment and observation schedules were repeated to a total of 48 weeks.

At 24 weeks 132 patients remained in the trial. There was no difference between the R and P groups in the doctor's overall estimate of improvement or deterioration, the patient's overall estimate of improvement or deterioration, or in pain at rest, pain on walking, or several measurements of hip function, or in the reasons for premature withdrawal from the trial. 36 R and 44 P patients considered they were improved.

At 48 weeks 96 patients remained in the trial. Seven of the indices initially studied were considered to be worth further analysis. Five of these showed no difference between R and P groups, but two, namely pain on movement and pain at rest, showed a significant advantage for R at 48 weeks which was confined to patients with lesser radiological grades (grades 2 and 3) osteoarthritis.

X rays taken at weeks 0, 24, and 48 showed no difference in rate of deterioration between R and P groups.

Thus Rumalon, in a dosage of 2 ml. intramuscularly given three times a week for 12 weeks for painful osteoarthritis of the hip was not associated with improvement which was detectable under the conditions of this trial, but when treatment was continued for a total of 24 weeks in patients with lesser radiological grades of osteoarthritis a significantly higher proportion of those treated with R than those with P reported relief of pain.

Discussion

DR. E. B. D. HAMILTON (London) We have carried out a controlled double-blind trial on the knee in 107 patients, at five centres, and over a period of 6 months.