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*) Englargement 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 nutriments?

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 osteoarthrosis, 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 Osteoarthrosis 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 osteoarthrosis but seldom under the conditions of a controlled clinical trial. A double-blind, four centre, controlled trial of intramuscular injections of Rumalon (R) in osteoarthrosis 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 withdraw 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) osteoarthrosis.

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 osteoarthrosis 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 osteoarthrosis 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.

Effect of Rumalon on embryonic cartilage in culture.

K T Rajan

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Notes