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AUSTRALIAN RHEUMATISM ASSOCIATION

A Meeting of the Australian Rheumatism Association was held at the University of Adelaide in conjunction with the Royal Australasian College of Physicians on May 17, 1966.

Synovial membrane removed at open surgical procedures in five patients with rheumatoid arthritis had been studied with the electron microscope by K. D. Muirden and J. R. E. Fraser (*Melbourne*). An unexpected finding was large numbers of ferritin molecules in synovial cell cytoplasm, concentrated in the lysosomes which were enlarged and more numerous than in normal cells. It was considered that the ferritin probably arises from the red blood cells in the synovial fluid, for synovial cells in culture will take up haemoglobin in low concentration and convert the contained iron to ferritin. It was suggested that the synovial deposits of ferritin may represent iron that is sequestrated and bound in this situation; that, as a ferritin molecule contains 2,000 iron atoms, the innumerable particles shown in such a small area relative to the extensive inflammatory deposits could be significant. If the release of iron from this sizeable store is impeded, anaemia could be the result. It was also suggested that increased fragility of the lysosomal membrane could play a part in the pathogenesis of the disease, and that lysosomes containing phagocytosed material could discharge their enzymes more readily than normal or unaltered lysosomes. The presence of ferritin in the lysosomes may therefore be a significant finding and may provide the connection between minor trauma to the joint and the initiation or exacerbation of joint inflammation in the susceptible person.

Studies of the synovium in rheumatoid arthritis by H. D. Tyer (*Sydney*) revealed the presence of inclusion bodies not present in normal tissue. These have been postulated as diagnostic and also possibly of aetiological significance. A series of rheumatoid synovia revealed wide variation in the frequency and structure of such inclusion bodies. An attempt was made to correlate the appearances with clinical and therapeutic history of the patient. Dr. Tyer also described animal experiments designed in an attempt to determine what role, if any, therapeutic agents may play in the production of these bodies.

A paper entitled "Behaviour of Human Synovial Cells *in vitro*–Reactions with Human Serum" was presented by B. Clarris, G. Harris, and J. R. E. Fraser (*Melbourne*). Preliminary studies of the reaction between synovial cells and rheumatoid serum revealed an unexpected effect of normal serum used as control. This consisted of a marked inhibition of the attachment and spreading of the synovial cells. There were two other less important effects defined on further analysis. The more striking was a heat-labile inhibition of cytoplasmic spreading, but it was also possible to define two factors facilitating spreading, one heat-labile and one heat-stable. It was then shown that the three actions of serum were also detectable in the phase of cellular multiplication, but the cells were much less sensitive to inhibition in this phase of growth. It is therefore clear that the opposing effects found in normal serum present problems in the interpretation of experiments with rheumatoid serum, or lymphoid cells. An inhibitory effect of serum on mucin clot for hyaluronic acid was observed in the course of these studies. It was shown that the mucin clot reaction was quite independent of any effect on the synovial cells. Further analysis implied that fresh serum contains a labile component which inhibits the formation of protein-hyaluronic complexes, but does not depolymerise hyaluronic acid. This interaction may play some part in the physical changes of hyaluronic acid found in inflamed joints where the serum concentration rises well above the normal level.

Necrotizing activity in serum in rheumatoid arthritis was discussed by J. P. Keet and R. R. H. Lovell (*Melbourne*). Blood from a patient with rheumatoid arthritis, injected intradermally in the guinea-pig, caused necrosis. Necrotizing activity proved to be present in a large majority of patients with active polyarthritis. It was also present occasionally in normal people and in patients with a variety of diseases whose common factor seemed to be tissue damage. The salient features of the lesion in the guinea-pig were damage to capillaries and veins, and to the muscle layer of the skin, the panniculus carnosus–lesions in the panniculus carnosus can be produced when necrotizing serum is injected into the skin of a recently killed guinea-pig. The factor is thermolabile, readily lost on dilution, non-dialysable, and lost when serum is decomplemented. It is not lost by adsorption of serum with guinea-pig tissue nor is it due to Forssman antibody. It is associated with the globulin fractions of serum and necrotizing activity is impared at *p*H levels below about 6·5. It can be induced in non-necrotizing serum when this is lyophylized and concentrated and when trypsin inhibitors are added.

Samples of ganglion fluid from seven normal subjects and of Heberden's node fluid from two subjects were examined qualitatively and quantitatively for acid mucopolysaccharide and protein content by M. W. Begg (*Adelaide*). The two fluids were of similar composition. Hyaluronic acid was found to be present in concentrations of 0·25–0·6 per cent. w/w. No other acid mucopolysaccharide was detected. Serum protein was present at 1–2·5 per cent. w/w concentration, showing a preponderance of albumin.

Renal clearance of urate in normal and diabetic subjects was discussed by N. de Coek (*Sydney*). Urate clearance is the net result of the processes of glomerular filtration, tubular reabsorption and tubular secretion.

Stop-flow experiments suggest that the proximal tubules are the site of urate reabsorption and the distal tubules the site of the final excretion. One case of hyperparathyroidism, with calcification of the distal tubules, showed no appreciable excretion of renal urate and the serum level of urate was raised. In diabetic subjects, the serum urate was lower and the urate clearance higher than normal. Thickening of the basement membrane of capillaries, Bowman's capsule, and the tubules is present in all diabetics. Possibly damage to the proximal tubules is the cause of the high urate clearance in a diabetic subject.

Xanthine oxidase inhibition in gout was presented by B. T. Emmerson (*Brisbane*). Allopurinol was studied in patients whose gout was not controlled by currently available therapy, usually because of renal disease. Strict purine control was not maintained after the initial period of study. The nephropathy was due to primary gout in four patients, to secondary gout in two, and was associated with solitary hydronephrotic kidney with previous calculus disease in one, and with advanced chronic renal failure in one. Allopurinol produced a sustained reduction of the serum urate to normal values, a fall in the urinary urate, and a considerable increase in the urinary oxypurine excretion. The serum oxypurine concentrations, though higher than before therapy, remained within the normal range. The combined urinary output of urate and oxypurine during allopurinol therapy was reduced, suggesting an overall suppressive effect on urate synthesis. There was a considerable increase in the clearance of oxypurine indicating more effective clearance relative to urates.

Fourteen virus infections of man which might be complicated by joint inflammation were surveyed by W. Douglas (*Brisbane*). Particular mention was made of eighteen cases studied of epidemic polyarthritis, an illness probably due to a group A arbo virus, characterized by rash, lymphadenopathy, a self-limiting polyarthritis, and a rise in the titre of serum antibody to the Ross river virus. In rubella synovitis, the diagnostic features, particularly the history of contact with rubella, and the presence of plasma cells in the peripheral blood, were stressed. Confusion in diagnosis may arise between epidemic polyarthritis, rheumatic fever, and dengue fever.

Alkaptonuria in two sisters was presented by M. Owen and H. Hinterberger (*Sydney*). A 38-year-old female English migrant had chronic pain and stiffness in the thoracic and lumbar regions of the spine, hips, and knees; pigmentation of the pinnae and sclerae; supraspinatus tendinitis and lateral epicondylitis; homogentisic acid in the urine. *X* rays of the spine revealed widespread progressive calcification and narrowing of the intervertebral discs. Her 26-year-old sister was asymptomatic, but had similarly pigmented urine.

Some consequences to the housewife and wage-earner of developing rheumatoid arthritis were presented by S. Murgo, K. D. Muirden, and R. R. H. Lovell (*Melbourne*). A questionnaire was administered to 76 patients who were attending either the Royal Melbourne Hospital outpatients' department or doctors in general practice. Items covered included work history, home adjustments, cost and type of treatment used, leisure time activities, and the patient's attitude to his illness. The following findings were recorded:

(1) The net cost of treatment to patients was high and there was little difference in the cost from private practitioners or from a public hospital. Evidence suggested long-standing financial strain to the family. This arises from salary loss, transport costs, shopping costs, and reduced hospital benefit rebates, as well as the direct cost of medical and chemist bills.
(2) The cost to the community must also be high, considering the time lost from work from a relatively common disease. The disease has a widespread effect on the male of working age. Forced adjustments to the pattern of work were frequent.
(3) Over half the housewives reported that their disease interfered with home management. Additional home help came mainly from the husband.
(4) The majority of patients sought "cures" and accepted advice from non-medically qualified persons. The use of folk remedies was surprisingly widespread in this community.

Cases of atlanto-axial subluxation treated by surgery were presented by R. G. White (*Adelaide*).

A report on a conference held in Mar del Plata on the training of a clinical rheumatologist was presented by S. G. Nelson (*Sydney*).

A report into the facilities and future requirements of arthritis and rheumatism clinics in Australia was presented by a spokesman of a Subcommittee of the Australian Rheumatism Association.