Heberden Society

Annual General Meeting, November, 1970

The following papers were presented at the annual general meeting on November 20 and 21, 1970.

Crystal Deposition in Hyperparathyroidism. By R. GRAHAME, M. B. MITCHNER, and D. JUNE SUTOR (*Guy's Hospital and University College Hospital, London*). Articular calcification is well known to occur in hyperparathyroidism and an association has been reported between hyperparathyroidism and hyperuricaemia and gout. Yet the literature concerning the pathology of the joints with special reference to articular crystal deposition in this condition is scanty.

This clinicopathological case report concerns a 64-year-old man who in life suffered from attacks of both urate and calcium pyrophosphate synovitis. Hyperparathyroidism was diagnosed but he succumbed to the effects of a calcific mitral valvulitis before operative treatment could be undertaken. At autopsy a large parathyroid adenoma was found measuring $3 \times 1.5 \times 1$ cm. All joints examined showed a chalky encrustation of the cartilage which was demonstrated by x-ray diffraction to contain both sodium acid urate and a mixture of the triclinic and monoclinic forms of calcium pyrophosphate dihydrate. A tophaceous deposit adjacent to one big toe joint showed calcium pyrophosphate dihydrate in addition to sodium acid urate. The calcific material in the heart valve was identified as carbonated apatite.

Discussion

DR. J. T. SCOTT (*London*) The relationship between calcification and hyperuricaemia requires further investigation. When we looked at the records of twelve patients with hyperparathyroidism some years ago we found that eleven had hyperuricaemia but there were three unsatisfactory features to this study:

- (1) The exact nature of the acute synovitis which occurred in five patients was never clarified; these patients were either studied in retrospect or were seen before we knew the significance of crystals in joint fluid.
- (2) Some of these patients were in severe renal failure.
- (3) Even those patients without obvious azotaemia were not studied in detail with regard to glomerular filtration and urate clearance.

This was largely a retrospective study and sometimes the situations were relatively acute.

It is surprising that there has been no further definitive study of this matter. I have seen only two or three patients with hyperparathyroidism since then and these have had normal uric acid levels. The time is ripe for those studying patients with hyperparathyroidism or hypercalcaemia from other causes to clear up this problem.

PROF. E. G. L. BYWATERS (*Hammersmith*) First, since I understand there was no difference in distribution of the urate and the pyrophosphate within articular cartilage, did they appear in the same sites? Secondly, the distribution shown by x-raying articular cartilage appeared to be a series of 'nets', whereas that in the meniscus seems to be a series of dots. I should very much like to know what this corresponded to histologically. Thirdly, it appears that the deposition of pyrophosphate depends very largely on a synovial milieu. We have recently seen two cases of seropositive rheumatoid arthritis, when reviewing routine biopsy sections at Taplow, which showed positively birefringent crystals in the rheumatoid synovial membrane, in one case surrounded by giant cells and in the other in association with ischaemic villi and a good deal of hydroxyapatite. These have been studied only under the polarizing microscope; we have not carried out any x-ray diffraction studies. I suppose they might be something else, but I should not have thought so because histologically they look exactly like our sections from hyperparathyroid cases at Hammersmith showing pyrophosphate in the discs and in the articular cartilage.

DR. GRAHAME We always found the two crystals together wherever we looked in cartilage or in ligament. In some areas one type predominated over the other, but we never found pockets of either one or the other in isolation. I am afraid we cannot answer your second question.

Substrate Stabilization: Genetically-controlled Reciprocal Relationship of Two Enzymes. By J. A. BOYLE, M. L. GREEN, and J. E. SEEGMILLER (*University of California and The Centre for Rheumatic Diseases and University Department of Medicine, Glasgow*).

An increased activity of adenine phosphoribosyltransferase (A-PRT) of erythrocytes has been one of the puzzling accompaniments of the deficiency of hypoxanthineguanine phosphoribosyltransferase (H-PRT) found in the Lesch-Nyhan syndrome (X-linked uric aciduria). The present study investigates the mechanism responsible for the elevated A-PRT activity in these patients. Purification of A-PRT from normal human erythrocytes yielded a protein, 6,700-fold purified, homogeneous on gel electrophoresis and in the ultracentrifuge. 5-phosphoribosyl-1-pyrophosphate (PRPP), a shared substrate for both H-PRT and A-PRT, protects purified A-PRT against heat inactivation, whereas other