DR. SCOTT What happens to haemoglobin levels at the time of puberty and menopause? I should think this is a much less likely cause. The changes produced by stilboestrol are very striking, and a hormonal mechanism of this kind could well explain the sex difference in urate levels, though of course this suggestion does not preclude other contributory factors.

References

Acheson, R. M., and O'Brien, W. M. (1966) *Lancet*, **2**, 777
Mikkelssen, W. M., Dodge, H. J., and Valkenburg, H. (1965) *Amer. J. Med.*, **39**, 242
Scott, J. T., and Pollard, A. C. (1970) *Ann. rheum. Dis.*, **29**, 397
Wolfson, W. Q., Hunt, H. D., Levine, R., Guterman, H. S., Cohn, C., Rosenberg, E. F., Huddlestun, B., and Kadota, K. (1949) *J. clin. Endocr.*, **9**, 749

Experimentally-induced Osteoarthritis in the Dog. By M. J. POND (*University of Glasgow Veterinary School*) and G. NUKI (*The Centre for Rheumatic Diseases, Glasgow*)

The development of animal models of arthritis has figured in many investigations into the pathogenesis of connective tissue disease. Some experimentally induced forms of inflammatory arthritis are widely accepted as models for rheumatoid arthritis, but there is at present no adequate animal model of osteoarthritis.

Hind limb lameness in the dog commonly results from rupture of the anterior (cranial) cruciate ligament in the stifle (knee) joint and, if the subsequent instability is not surgically corrected, a high percentage of dogs develop degenerative joint changes.

The anterior cruciate ligament in one stifle joint of each of ten dogs was ruptured using a new closed technique and the opposite joint served as the control. The dogs were killed at various times between 1 and 26 weeks after rupture of the ligament and the radiological and pathological features suggest that this may be a model which closely simulates clinical osteoarthritis.

A large number of investigations were performed at regular intervals before the dogs were killed and a detailed examination was made of all the joint tissues obtained. *post mortem*.

The progression of the experimentally-induced condition follows a very similar course to that of the naturally occurring instability and the final gross pathology is that of an osteoarthritis.

The histological appearance of the articular cartilage varied from normal in the dog killed one week after surgery to gross fibrillation extending into the depth of the tissue in those killed at a longer interval after ligament rupture. In a number of areas that do not show gross fibrillation, an abnormality is seen in the more superficial zones. In these specimens the superficial layers of tangentially arranged cells are absent and so are the chondrocytes in the region immediately beneath the superficial layers. Early fibrillation is seen in some of these 'acellular zones'.

Articular cartilage from areas adjacent to those showing 'acellular zones', when examined under the scanning electron microscope, shows flaking and peeling of the normal surface membrane with exposure of collagein fibre bundles In more severely damaged areas, gross fibrllation is seen on the articular surface and on the fractured specimens.

Discussion

PROF. D. L. GARDNER (*Belfast*) Dr. Pond and his colleagues are not wholely accurate in stating that no other models exist for the reproduction of osteoarthrosis. Division of the sciatic nerve in the dog, the injection of papain into synovial joints, and other techniques have been used in the past. Nevertheless, he has elucidated something of the early changes in one experimental disease. What causes the loss of superficial glycosaminoglycan? What are the changes in the chondrocytes? What relationship do these bear to the human disease?

DR. POND There were few models that satisfied our criteria, though we knew that there had been many attempts. We have planned a more detailed assessment of the biochemical abnormalities in the articular cartilage in these areas and a more detailed investigation of the chondrocytes which we hope will perhaps help to answer your query, but in this pilot study we did not reach those depths.

PROF. V. WRIGHT (*Leeds*) This is a very interesting model. The only thing that worries me about it is that severing the cruciate ligament causes a pretty acute synovitis. That is one reason presumably why the dog cannot walk on its leg for about a fortnight. I wonder therefore how much one can extrapolate from this model.

DR. POND There certainly is a very marked inflammatory response in the synovial membrane for the first 48 hours, which decreases markedly thereafter, and there was very little evidence of an acute synovial inflammation even at one week.

DR. J. H. GLYN (*London*) The nearest clinical analogue of a grossly unstable weightbearing joint is that seen after poliomyelitis. I was very struck in the course of a study carried out a few years ago (Glyn, Sutherland, Walker, and Young, 1966) by how little osteoarthritis these unstable and recurrently traumatized joints developed over the years. I tried to encourage some veterinarian colleagues to carry out nerve-section experiments in dogs, but I was told that they would not work satisfactorily because such quadrupeds would not take any weight on their paretic joints. Therefore, they would not be expected to develop osteoarthritis. Did your dogs distribute their weight normally after you sectioned their anterior cruciate ligaments and do you attribute the changes you found entirely to weight bearing?

DR. POND Most of them will take weight 2 weeks after induction of the disability.

DR. J. H. GLYN (*London*) Would you agree despite this that your experimental model could not be used for nerve-section experiments in order to determine any possible protective effect of such a procedure?

DR. POND Certainly most of our patients when they have had any traumatic injury or experimental induction of nerve trauma just tend to drag their limb around and don't bear weight at all.

MR. A. R. TAYLOR (*Stoke Mandeville*) We often see changes in the femoral condyles at removal of torn menisci. You did not make it clear whether the changes you saw in the femoral condyle occurred irrespective of damage to the menisci?

DR. POND Certainly, in the longest surviving dogs, they were always seen together. In the shorter surviving dogs, in which we saw more of the acellular areas and no gross fibrillation, the menisci were sometimes intact and sometimes not. There seemed to be no particular correlation in the early changes.

DR. A. G. S. HILL (*Stoke Mandeville*) I think a fair number of us have been puzzled by the mechanism of osteophyte formation. Did you do any early studies just of the edge of the joint to see what the initial changes were?

DR. POND We looked at a large number of serial sections of the osteophytes as they developed and the findings were very interesting, but these points will have to be investigated further before any conclusion can be made.

Reference
Glyn, J. H., Sutherland, I., Walker, G. F., and Young, A. C. (1966) *Brit. med. J.*, 2, 739

Use of Radio-active Yttrium-90 in Persistent Synovitis in the Knee.

I. Retention in the knee and spread extra-articularly. By J. M. GUMPEL, D. WILLIAMS, and H. I. GLASS (*Northwick Park and Hammersmith Hospitals*)

II. A comparison of Yttrium-90 resin and citrate. By J. M. GUMPEL, H. E. A. FARRAN, and D. WORTH (*Northwick Park Hospital*)

Part I was published in full in the *Annals* in May, 1973 (vol. 32, No. 3, p. 222)

Complement Metabolism in Rheumatoid Arthritis. By J. M. B. VERSEY, J. R. HOBBS and P. J. L. HOLT (*Departments of Chemical Pathology, Westminster Hospital Medical School, and Rheumatology, Royal Postgraduate Medical School, London*).

To be published in full in the *Annals*.

Measurement of Inflammation.

I. Application of Technetium Clearance to Rheumatoid Arthritis and Animal Models. By H. BERRY, J. P. BROWETT, E. C. HUSKISSON, P. A. BACON, and D. A. WILLOUGBY.

II. Comparison of Technetium Clearance and Thermography with Standard Methods in a Clinical Trial. By E. C. HUSKISSON, H. BERRY, J. P. BROWETT, and H. WYKEHAM BALME (*St. Bartholomew's Hospital, London*).

Published in full in the *Annals* in the March issue (vol. 32, no. 2, pp. 95, 99).

Discussion

DR. J. A. COSH (*Bath*) May I congratulate Dr. Huskisson on his techniques of assessing inflammation by thermography. The president has kindly allowed me to show two slides illustrating similar work. The first shows the quantitation of inflammation and of anti-inflammatory drug action by measuring infra-red radiation from rat paws using radiometry; this work was done in the Department of Pharmacology in the University of Bath (Collins and Ring 1972). A group of five rats had carrageenin injected into a hind paw and the rise and fall of paw temperature in the ensuing 24 hours was measured with the radiometer and charted. The experiment was repeated with other groups of rats primed with three different dosages of an orally administered anti-inflammatory drug azathioprine. The graph clearly indicates the rise and fall of paw temperatures and the degrees of suppression of inflammation by the drug, the greatest suppression of temperature being shown by the largest dose.

The second slide is based on repeated thermographic measurement of the knee of a patient with rheumatoid arthritis following the temperature week by week of the warmest skin area over the knee joint. The patient was given six injections of a depot preparation of triamcinolone. After each injection the temperature fell for some days and rose again as the anti-inflammatory effect wore off. With repeated depot injections, the absolute temperature fell progressively and the 'escape' after each became less. There was a parallel improvement in hand grip. In clinical measurement by thermography, it is most important to standardize the physical conditions of examination; the patients' legs in this study were exposed for 15 minutes in a room temperature of 18°C. before each measurement was made.

DR. BERRY We tried very hard to measure anti-inflammatory activity using the thermography technique in rats. We found it impossible to get sufficiently accurate results from this because the field of view of the camera was too large.

DR. M. I. V. JAYSON (*Bath*) I am rather concerned about the use of the forearm for correcting the technetium calculations. Forearms are used on the assumption that this reflects the blood flow but both we and Marks, Birkett, and Shuster (1972) have shown that in rheumatoid arthritis there is general increased capillary permeability. Do you not think that this might well invalidate the use of forearms for correcting technetium scans, because there would be an increased outpouring of technetium compounds into the interstitial fluid in rheumatoid arthritis?

DR. HUSKISSON We entirely agree. Our work suggests that the use of any correction of this sort is invalid because of the strange distribution of technetium which is quite different in rheumatoid patients and normal controls. We interpreted the forearm technetium count as representing mainly extravascular fluid, and there was evidence that in rheumatoid arthritis, technetium stayed more within the vascular compartment; increased permeability would have been easier to explain.

PROF. E. G. L. BYWATERS (*London*) These various attempts to define inflammation seem to me to be doomed to failure. You are trying to measure different things; the amount of blood in the part, the blood flow, to some extent the extracellular fluid, the extracellular serum protein, and the extravascular serum protein. Each of these is one of the factors in inflammation, but these different methods vary in themselves according to protein binding or intravascular confinement, etc. Inflammation is a very complicated thing. I am sure your conclusion is probably correct, but equally that our clinical methods are better than these various ones which are looking for something which you are not quite sure how to define.

PROF. C. A. KEELE (*London*) May I ask whether there is any evidence that the technetium is bound to any particular