Deposition of Urate Crystals in Man. By W. A. KATZ and G. E. EHRLICH (*Albert Einstein Medical Centre, New York*): For more than 60 years the mainstream of investigation into the pathogenesis of gout centred in the mechanism of hyperuricaemia while recently urate crystal-induced arthritis had rekindled interest. Little attention, however, had been drawn to the deposition of these urate crystals in body tissues. It was the purpose of this experimentation to substantiate at a biochemical level heretofore anatomical observations of the predilection of urate crystals to deposit in the connective tissues such as cartilage and synovia. To this end it was demonstrated that an important ground substance component, PPL, a protein-polysaccharide containing chondroitin sulphate, was capable of augmenting urate solubility and inhibiting urate crystallization at 4°C.

A similar substance had been identified in the sera of both normal subjects and those with gout. It travelled electrophoretically with the alpha and beta globulins and was primarily responsible for the ability of serum to hold more urate in solution than buffers of identical molarity and hydrogen ion concentration. Alteration of the urate-bound PPL molecule resulted in precipitation of urate crystals in a manner proposed to occur *in vivo*. Utilizing this material, a schema was evolved which provided a new concept for the development of gout in man.

Discussion.—DR. J. T. SCOTT (*London*) asked if this hypothesis explained the predilection of urates to deposit in the great toe.

DR. KATZ felt that it would be interesting to analyse the nature of the polysaccharide in cartilage from various sites.

Centenary: Charcot's Other Joints. By J. T. SCOTT (*London*): It was exactly 100 year since Charcot had written his original description of neuropathic joints. This account, however, formed only the first part of a double paper dealing with "Arthropathies which appear to depend on a lesion of the brain or spinal cord". The second part described a form of arthropathy complicating cerebral thrombosis and in fact seemed to be a good description of what was now called the "shoulder-hand syndrome". In Steinbrocker's original account of this syndrome in 1947, no mention was made of Charcot's contribution and in the Centennial year it might be thought interesting to bring this to the notice of Heberden members.

Double Charcot's Disease. By F. E. BRUCKNER (*Middlesex Hospital*): Neuroarthropathy was a well-known complication of tabes dorsalis, diabetic neuropathy, syringomyelia, and in children, of meningomyelocoele. Rarer causes were congenital insensitivity to pain, familial dysautonomia, hereditary sensory neuropathy, peripheral nerve injury, the neuropathy of leprosy, and spinal cord injury. A similar radiological picture was described by Alarcon-Segovia and others (1965) after intra-articular corticosteroid injection.

Five cases of Charcot-Marie-Tooth disease were described with arthropathic changes, varying from minor deformity and bony hypertrophy to the full-blown picture of Charcot's arthropathy.

Some Rum and Odd Arthropathies. By DR. DUDLEY HART (*London*): Prof. Bywaters had suggested in the past that at the Annual General Meeting of the Heberden Society, or the Yuletide orgy, there might be one paper a little less serious, while still containing some items of general interest; a break in the academic austerity of the rest of the meeting, a little divertissement between the more serious movements, as it were. This paper described Hart's Retropulsive Arthropathy (H.R.A.), Septic Spinal Polymyalgia (S.S.P.), various arthropathic drug disorders (V.A.D.D.), and some odd bits and pieces (O.B.P.). The whole thing might be called an Arthropathic Hors d'oeuvre (A.H.D.). Avanti!

Effect of Glyvenol (Ciba) on Pain and Capillary Resistance in Rheumatoid Arthritis. By W. C. DICK, G. M. CUNNINGHAM, M. K. JASANI, W. W. DOWNIE, and K. WHALEY (*Glasgow*): This paper was published in the *Annals* (1969), 28, 187.

Azathioprine: a Controlled, Double-blind Trial in Rheumatoid Arthritis. By C. G. BARNES, H. L. F. CURREY, J. F. DUNNE, B. HAZLEMAN, R. M. MASON, I. D. STRICKLAND (*London Hospital*): The ability of azathioprine to lower the corticosteroid requirements of rheumatoid patients was tested under double-blind conditions against placebo.

49 patients (mean age 53 years) had "definite" rheumatoid arthritis with positive serological tests for rheumatoid factor. All had been taking corticosteroids for at least 6 months and the minimum prednisolone requirement of each patient had been established and maintained for at least 2 months. This dose ranged from 5 to 20 mg. prednisolone per day (mean: 11.1 mg.).

Patients then received either azathioprine 2.5 mg./kg. daily or matching placebo tablets. Treatments were allocated randomly; assessments were made under double-blind conditions, and the results were analysed sequentially. The mean steroid requirements after one year of continuous treatment had fallen in the azathioprine group by 4.2 mg./day and in the placebo group by 0.7 mg./day. This difference is significant at the 5 per cent. level.

Of fourteen patients withdrawn from the trial, five were taking azathioprine. In one the white cell count dropped below 3,500 cells/c.mm.; one developed a macrocytic blood picture; another showed both these abnormalities and a fourth developed a rash. These abnormalities reversed rapidly when the drug was withdrawn. The fifth patient had an exacerbation of rheumatoid arthritis two months after starting azathioprine.

Analysis of monthly blood counts among the patients taking azathioprine showed a mean fall in the total white cell count of 2,500 cells/c.mm. (S.D. $\pm$ 2,600) at one year involving both the neutrophil and lymphocyte series.

This contrasted significantly ($P < 0.01$) with a mean rise in the placebo group of 2,000 cells/c.mm. (S.D. $\pm 2,100$). There was no important overall difference in the haemoglobin, the platelets, the E.S.R., the titre of the latex tests, the strength of grip, or the blood pressures between the two groups.

Discussion.—DR. G. D. KERSLEY (*Bath*): reported that he had treated 21 cases of severe rheumatoid arthritis, uncontrolled by a reasonable dose of steroids, with azathioprine. Nine patients improved during the period of treatment, and in four the dose of corticosteroid was lowered. Leucopenia, which was corrected on withdrawal of the drug, occurred in one case. Gastrointestinal symptoms were the most consistent and troublesome side-effects.

DR. J. A. MATTHEWS (*St. Thomas's Hospital*) asked if it were possible from the data to say whether azathioprine was suppressing the disease directly or was potentiating the action of corticosteroids.

DR. DUNNE suggested that on the evidence available azathioprine exerted a direct suppressive effect on the disease.

Natural Antibody to Procainamide and Procainamide-induced Systematic Lupus Erythematosus. By A. S. RUSSELL and M. ZIFF (*Southwestern Medical School, University of Texas, Dallas*): A method was developed for assay of antibodies reactive with procainamide* (PrA) which utilized sheep red blood cells coupled with diazotized PrA. Antibodies of the IgM group were found in 19 to 50 per cent. of populations tested. These included patients with SLE, RA, juvenile RA, miscellaneous diseases, cardiac patients receiving PrA, and normal adults. Only 6 per cent. of patients with PrA-induced SLE had antibody. Antibody was not found in neonatal children nor in rabbits and hamsters but was found in 78 per cent. of normal dogs.

Immunization of rabbits with PrA—bovine serum albumin complex induced anti-PrA antibody in high titre. Antibodies in these rabbits and in man could be removed by adding PrA to the titration system.

74 per cent. of unselected patients receiving PrA for over 2 months were found to have antinuclear antibody in significant titre. It was suggested that the high incidence of antinuclear antibody and SLE-like disease in patients receiving PrA might be related to the wide occurrence of "natural antibody" to PrA.

Discussion.—DR. D. A. PITKEATHLY (*Wigan*) asked why antibody to procainamide should be so common in the population.

DR. RUSSELL suggested that the high incidence of antibody could be explained by cross-reactivity with other substances.

DR. L. E. GLYNN (*Taplow*) asked if procainamide-induced SLE might provide a model for testing drugs.

DR. RUSSELL suggested that this might be so in the

States, but in view of the small numbers taking the drug in Great Britain it might be hard to find suitable patients.

Experiences of Anthroplasty of the Rheumatoid Knee using Macintosh Prostheses. By A. KATES, A. KAY, J. WOJCIK, T. RILEY, E. N. COOMES (*St. Mary Abbots and St. Stephen's Hospitals*): Macintosh arthroplasties have been introduced into the knees of forty patients with rheumatoid arthritis. In six patients the procedure was carried out in both knees.

The period of follow up is from 6 months to 2½ years. The results, so far, suggest that it is a worthwhile procedure.

Selection of patients and problems of management were discussed.

Discussion.—DR. J. D. JESSOP (*London Hospital*) commented that five of thirty patients in whom the Mackintosh operation was performed developed marked flattening of the femoral condyles about 30 months after operation. This phenomenon was noticed whether or not the patients were on corticosteroids.

MR. KATES said that they had not observed this flattening of the condyles. He considered that it might be caused by early manipulation post-operatively. He felt that cementing of the prosthesis greatly improved the results of the operation.

Aggressive Action of Lymphocytes *in vitro*—Investigation of their Property in relation to Inflammatory Joint Disease. By I. C. M. MACLENNAN (*Taplow*): Lymphocytes from the blood of healthy persons had been shown to damage certain homologous and heterologous cells *in vitro*. Quantitative assessment of this phenomenon had shown this aggression to be similar in patients with chronic inflammatory joint disease and healthy controls. Lymphocytes from the synovial fluid of certain patients with arthritis had been found to be quantitatively more cytotoxic to homologous target cells than were equivalent numbers of peripheral blood lymphocytes. Joint lymphocytes from about one-third of patients with seropositive rheumatoid arthritis showed this increased cytotoxicity, and it was seen with joint lymphocytes from a high proportion of patients with psoriatic arthritis and systematic lupus erythematosus. This high level of cytotoxicity of certain joint lymphocytes was not specific to a particular type of human target cell as it had been shown by Hedberg against diploid human foetal cells of both renal and cutaneous origin and by the speakers against polyploid human liver cells.

A factor in joint fluid and serum from certain patients with chronic inflammatory joint disease was described, which increased the cytotoxicity of normal lymphocytes to a polyploid strain of human lymphocytes. Evidence was presented to support the hypothesis that this was an IgG antibody specific for the target cell. This factor had also been found in non-arthritic patients and its significance had still to be worked out.

* Pronestyl.