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At a clinical meeting at The London Hospital on October 7, 1966, the following papers were read:

Carpal Tunnel Syndrome in Rheumatoid Arthritis. By C. G. Barnes (London). (see this issue, p. 226)

A Family with Osteo-arthritis of the Hip Joints. By W. M. Zinn and P. Schmied (Bad Ragaz, Switzerland): Osteo-arthritis of the hip joint is sometimes secondary to definite causes such as inflammation or trauma. The cause of the so-called idiopathic or primary cases is unknown but it is occasionally familial. The family studied originated in Herisau in the Canton of Appenzell-Innerrhoden/Switzerland, though in 1907 most members moved to the Canton of Graubünden (Les Grisons). More than 95 per cent. of 157 members distributed over four generations were examined clinically and radiologically. Two x ray films of the pelvis were taken, one in a standard position, the other by the technique of Dun-Rippstein which permitted measurement of the real mechanics of the hip joints.

Different but always bilateral deformities were found in the pre-arthrotic stage: flattening and depression of the femoral head, slight gliding of the epiphysis with subsequent decentralization of the femoral head in relation to the axis of the neck of the femur, slight coxa valga with normal acetabulum, one case of acetabular dysplasia, and one severe case of coxa vara congenita. As the spine was normal and the knees and feet showed only axis variations, these changes could be called multiple epiphyseal dysplasia as described by Rubin (1964). In this systemic skeletal abnormality an hereditary disturbance of ossification of cartilage is postulated and it has a good prognosis. Its clinical manifestation therefore is frequently limited to the hip joints which are subject to the most mechanical stress.

The osteo-arthritis stage starts with cystic degeneration in the femoral head with increasing planification, the joint space sometimes being preserved for many years. Later on there is narrowing of the joint space and typical cystic involvement of the acetabulum leading to a uniform final stage of typical cystic osteo-arthritis with severe pain and marked joint stiffness.

For the genetic evaluation the study was based exclusively on the objective radiological changes. Only the following signs were considered pathological: definite flattening of femoral head, depression of the upper circumference of femoral head, cystic changes, osteo-arthritic changes, severe degree of coxa vara congenita, severe degree of acetabular dysplasia. Slight mechanical abnormalities were not considered because no definite and generally accepted limits of what is normal were available.

The genetic study showed that this was an hereditary form of bilateral osteo-arthritis of the hip joint with incomplete regular dominance. The penetrance was different in the four branches of the family and varied from 0 to 60 per cent.

Discussion.—Prof. E. G. L. Bywaters (Taplow): I am not quite clear from what Dr. Zinn said whether this was in homozygotes. Did you have any heterozygotes marrying each other?

Dr. Zinn: This study of the genetic tree shows that almost 50 per cent. of members of the family over a certain age are affected. This would be compatible with a heterozygous hereditary condition. There is no inbreeding in this family and the spouses of the family members have been very helpful. All have been interviewed as well.

REFERENCE

Pathogenesis of Gout. By Dr. K. T. Rajan (Stoke Mandeville): Human neutrophil polymorphonuclear leucocytes treated with microcrystalline sodium monooctanoate release lysosomal enzymes. The relationship of degranulation to phagocytosis of crystals was studied, the process of degranulation being observed by phase microscopy and checked by Acridine orange staining.

The mode of action of Colchicine on phagocytosis and activation of lysosomes had been examined. Evidence was presented for the mode of mechanism of acute inflammation in gout and possible sites of action of drugs.

Discussion.—Dr. J. H. Glynn (London): Can Dr. Rajan explain to us the probable similarities and differences between the modes of action of colchicine and corticosteroids at the connective tissue level, with particular reference to their effects on lysosomal enzymes and the stabilization of lysosomal membranes?

Dr. Rajan: Both drugs resemble each other in their action on lysosomes in stabilizing the membrane. Colchicine apparently also inhibits phagocytosis.

Dr. F. M. Andrews (Reading): Have you studied the effect of calcium pyrophosphate and other crystals on polymorphs? Do other crystals have the same effect on lysosomes and if so what effect does colchicine have on the lysosomes?

Dr. Rajan: We have not yet studied what effect colchicine has on phagocytosis and lysosomes when polymorphs ingest calcium pyrophosphate crystals. This work is in progress.
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Dr. J. T. Scott (London): A good deal remains to be learnt about the action of colchicine. Dr. R. Penny was recently working with us at Hammersmith and found that it appeared to depress neutrophil adhesiveness at concentrations equal to those produced by doses used for the treatment of acute gout. Phagocytosis of heat-killed yeast cells was not affected (Penny, Galton, Scott, and Eisen, 1966). What kind of subjects were these polymorphs taken from?

Dr. Rajan: Normal human volunteers.

G. Loewi (Taplow): Have you actually demonstrated increased permeability of lysosomes containing crystals? Have you shown a similar phenomenon with polymorphs obtained from peripheral blood?

Dr. Rajan: I think by “lysosomes containing crystals” you mean phagosomes. We have not yet been able to demonstrate any increased permeability of phagosomes. This study is in progress. All the polymorphs obtained for our studies in vitro were from peripheral blood only.

A. G. S. Hill (Stoke Mandeville): It intrigues me that we have evidence of two things which stabilize membranes. The first is hydrocortisone and the second is colchicine. It seems unlikely that only lysosomal membranes in gout are so stabilized although not impossible. One wonders whether colchicine is as specific as is thought.

P. J. L. Holt (London): When Dr. Norman Williamson and I were working on this in Birmingham we found the lysosomes were unstable and the lysosomal enzymes increase in almost all inflammatory arthropathies from Reiter’s syndrome to gout.

REFERENCE

DNA AND RNA Content of Blood Lymphocytes in Normal Individuals and in Rheumatoid Arthritis. By A. C. A. Glen and M. K. Jasani (Glasgow): Pure lymphocyte suspensions were prepared from peripheral blood by a modification of the published method of Coulson and Chalmers. Chemical estimations were carried out on the isolated cells, measuring the DNA and RNA content per million lymphocytes. These two parameters were studied in a series of normal individuals, and in twenty patients with definite rheumatoid arthritis. The DNA content of the cells was the diploid amount in both groups, while increased amounts of RNA were found in the lymphocytes of 50 per cent. of patients with rheumatoid arthritis. The significance of these findings was discussed in relation to morphological studies of lymphocytes, and to present knowledge of their role in the immune response.

Discussion.—Dr. O. Savage (London): When you did your Synacthen test, at what time were these patients taking their Prednisone?

Dr. Hicklin: At 8 or 9 p.m. the previous evening, so that there was at least a 12 hour gap to allow the effect to wear off.

Dr. O. Savage (London): I think most of us have come to the conclusion that the Metapyrone test is unsatisfactory. I am interested to know why you took your low level of normal as 7 µg. Many people working in this field have accepted a lower level.

Dr. Hicklin: We will accept 5 µg./100 ml. as the lower limit of normal at other times of day. However, other workers in the field, particularly Wood, Frankland, James, and Landon (1965) and Grieg, Browning, Boyle, and Maxwell (1966), have taken 8 µg. as their lower limit of.
normal at 9 a.m. We felt that by taking 7 µg, we were making every effort to make people normal rather than trying to create abnormality.

DR. M. K. JASANI (Glasgow): I was most interested in your paper because we are doing similar work in Glasgow. Unquestionably, many factors can determine suppression of the hypothalamo-pituitary-adrenal axis in each patient; it is most valuable that your patients received one dose of corticosteroid at one time of day.

DR. F. E. BRUCKNER (London): The timing of your resting specimen at 9 a.m. is of interest. We did diurnal cortisol rhythms on normal patients and found that the greatest rise in plasma cortisol occurred between 6 and 11 a.m., the time when you performed your Synacthen tests; so you would expect a rise no matter what you gave them. It may be preferable to do ACTH stimulation tests in the afternoon instead of the morning. Were you intending to repeat this test with the same total dose of steroids, but giving Prednisolone twice a week instead of daily? There is evidence that if you give the pituitary a few days’ rest, it will have a chance to recover during this time.

DR. HICKLIN: I hardly think it possible, even accounting for the morning rise in cortisol, to see such sharp rises to so high levels after the injection of anything but an adrenal stimulant. From this and other studies we have only information about the normal behaviour under Synacthen stimulation at 9 a.m. and I am unable to express any opinions about what might happen at 5.30 p.m. As far as the study of the effects of 15 mg, twice a week is concerned we feel that we have enough trouble on our hands already!

DR. A. J. PEPPE (Worcester): Was there any difference in the severity of the rheumatoid arthritis in the patients tested?

DR. HICKLIN: They were all much of a muchness, that is the kind of patient who needs some help over morning stiffness.

PROF. E. G. L. BYWATER (Taplow): Does not the President think the pituitary is the most important part of the axis and if so what does he think is the best combination of tests to use at the present time?

DR. O. SAVAGE (London): The Synacthen test is very satisfactory. It does not upset the patient. The real problem is the test of the pituitary. The Metapyrone test is unsatisfactory. The hypoglycaemic test is about the best at the moment, but it does entail lowering the blood sugar to a level which can produce stress and may need repeating. We need a measurement of ACTH in the blood. Once we can obtain this we shall be in a position to measure both pituitary and adrenal response separately.

DR. ALAN MYLES (London): We have been doing similar studies but our results have been rather different. We have found, in a group of patients who had had corticosteroids for up to 13 years and in a total dose of up to 62 g, that three-quarters had a normal synacthen test. We have used different criteria since we have taken 5 µg, per cent. as being the lower limit of normal for plasma cortisol and 7 µg. per cent. as the minimum rise for a positive synacthen test. We used the method of Spencer-Peet, Daly, and Smith (1965) for the estimation of blood cortisol, because we think this is more accurate at low levels. We have found that all cases having an initial cortisol in the normal range have had a normal synacthen test and we think that a normal cortisol may indicate that the patient does not have pituitary adrenal suppression.

REFERENCES

BOOK REVIEW


The tenth volume of the "Beiträge", under the joint editorship of Prof. Hans Tichy of Dresden and Prof. Kurt Seidel of Jena, is devoted to a review of the efforts made by the various European countries to deal with the rheumatic diseases. It also traces the development of international co-operation in the specialty, first proposed by the late Jan van Breemen in 1913. A good deal of information had obviously to be collected before giving a detailed study of every major institution and organization, country by country. Its accuracy may be gauged by the close description of such rheumatism centres, and the names of those in charge, in the United Kingdom. While certain senior members of the Heberden Society may be surprised to find they have acquired a professorship, it is but a commentary on the paucity of chairs in the specialty and, perhaps, a portent of things to come.

This volume, like its predecessors, is printed on excellent paper and contains numerous excellent illustrations; some of these are architectural drawings of new or proposed centres and should arouse the envy, if not the interest, of many a clinician. There is a table of contents and a comprehensive index. The least attractive feature is the high price.

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