POLYARTERITIS NODOSA TREATED WITH A.C.T.H.

REPORT OF A CASE, WITH RECOVERY

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For some years it has been suspected that polyarteritis nodosa is by no means uncommon. The disease manifests itself in many forms, and an excellent review of the clinical features is provided by Miller and Daley (1946). As these authors infer, in many cases the condition presents in a manner extremely difficult of diagnosis, and, though suspected, it most frequently remains unproved. They estimate the mortality rate to be well below 50%, but, even so, it must still be accounted a formidable disease. Probably the majority of cases recover spontaneously, and this factor renders hazardous the assessment of any particular form of treatment, particularly as reference to a substantial series of cases is difficult to find. Lovshin and Kernohan (1949) collected only 29 cases in a search through the records of ten consecutive years at the Mayo Clinic.

A.C.T.H. and cortisone have been used in treatment by a number of workers. Mundy *et al.* (1951) give a full account of one case, complicated by asthma, treated at first with a series of short courses of A.C.T.H.; each course lasted a week and was succeeded by improvement which was in part subjective (for example, relief of asthma), but in part objective (for example, recovery of muscle power and subsidence of E.S.R.). Treatment suppressed rather than eradicated the disease, and the patient was subsequently kept on maintenance treatment with intramuscular and oral cortisone. Drury *et al.* (1951) published a single case treated with cortisone. Although their patient was desperately ill, and died six days after treatment was started, there was suggestive histological evidence of retrogression of some of the arterial lesions. This was observed also by Shick *et al.* (1951), who treated 13 cases with A.C.T.H. and cortisone. The dosage of A.C.T.H. was inconstant owing to a temporary shortage. Clinical improvement was marked by early subsidence of fever and more gradual decrease of E.S.R. Two patients died, and in most there was evidence of residual vascular damage. These authors claim no more than remission of the disease process from use of A.C.T.H. and cortisone. They advise early, intensive, and prolonged treatment.

Case History

A 15-year-old schoolboy was admitted to hospital on April 10, 1951. In the previous January he developed a fever accompanied by a purpuric eruption of the legs. The fever subsided, but there followed recurrent crops of purpura on the limbs which lasted a few days and left a brown staining of the skin. Occasional attacks of vomiting with generalized colicky abdominal pain were noted, and on one occasion a

haematemesis followed by melaena was observed. In February there was a short-lived bout of frank haematuria, which was not repeated. Admission was requested on account of recurrent purpura, three weeks' persistent fever, and pain in the muscles of the upper arms, thighs, and calves. His illness had been marked by loss of over one stone (6.35 kg.) in weight.

Examination showed an intelligent, co-operative lad who had evidently lost flesh recently; temperature 100° F. (37.8° C.). There was a purpuric eruption on the thighs and genitalia, and post-purpuric staining of both arms, especially the elbows; no significant adenopathy; no nodules. Pulse, 120 a minute; sinus rhythm; heart sounds normal; B.P. (resting), 160/90; electrocardiogram normal. The abdomen showed no clinical abnormality; liver and spleen were not felt. The C.N.S. was normal, as were the optic fundi. There was no evidence of peripheral neuritis, and the chest was clear.

Investigations.—Haemoglobin, 66%; red blood cells, 4,260,000 per c.mm.; leucocytes, 9,800 per c.mm. (neutrophil polymorphs 78%, lymphocytes 19%, monocytes 3%); stained films showed no abnormal cells; platelets were plentiful; clotting-time, 3 minutes 25 seconds; bleeding-time 5 minutes 45 seconds; blood culture, sterile in three separate specimens; E.S.R. (Westergren), 75 mm. in one hour. The plasma proteins totalled 8.75 g. per 100 ml. (albumin 4.6 g., globulin 3.55 g., fibrinogen 0.6 g.), and serum agglutinations were negative in the enteric group and *Brucella abortus*.

The urine contained a large amount of albumin, and a centrifuged deposit showed 5 leucocytes and 10 red blood cells per high-power field; culture was sterile. Radiographically the lungs were clear. The capillary resistance test was negative.

Treatment.—Within a week of admission a crop of subcutaneous nodules appeared, some of which were tender. Excision of one of these resulted in arterial spurring. The pathological report (Dr. Morgan Hall) was: "Section of the biopsy specimen shows a small artery in which there is hyaline necrosis of the subendothelial tissue and of the inner media and irregular necrosis of the outer media. The lumen is filled with thrombus. There is dense inflammatory infiltration, mostly acute, in the adventitia and perivascular tissue. The histological picture is characteristic of the acute arteritis and periarteritis of polyarteritis nodosa." During this week there were recurrent attacks of abdominal colic, with no localizing signs, and vomiting. The vomitus contained small quantities of blood. There was, in addition, diarrhoea with streaks of bright-red blood. Fever persisted, there was marked generalized muscular tenderness, and the patient was accounted gravely ill. For these reasons treatment was started with A.C.T.H., 15 mg. six-hourly for three weeks, the dose then being reduced to 15 mg. twelve-hourly. This was continued for a further three months, when it was reduced to 15 mg. daily, after one week of which all treatment was stopped. The dosage of A.C.T.H. was regulated on the basis of his response to treatment as judged by the following criteria: (1) subjective improvement; (2) subsidence of fever; (3) disappearance of subcutaneous nodules and purpuric spots; (4) disappearance of blood from urine; (5) gain in weight; (6) lowering of blood pressure and pulse rate to normal; and (7) decrease of E.S.R. to normal.

Progress.—His response, as judged by factors (1), (3), and (5) above, was immediate. Fever subsided within three weeks and the quantity of blood in the urine steadily diminished. The E.S.R. decreased very slowly, but by August 21 it was 14 mm. in one hour. The blood pressure also dropped only slowly, but on July 26 it was 130/90, and thenceforward remained at a normal level. On August 25, the 140th day in hospital, he was transferred to a convalescent home. He had gained 25 lb. (11.34 kg.) in weight while in hospital. There were no untoward effects of treatment, no fluid retention, and no psychic disturbance. He did, however, develop a mild degree of "moon-face."

This boy has been seen and examined at regular intervals as an out-patient. He has had no symptoms since discharge,

and sixteen months have now elapsed from that date. In that time he has gained over 26 lb. (11.8 kg.) in weight. There remains only faint staining of the skin over his elbows and a minute trace of albumin in the urine, the centrifuged deposit containing no abnormality. His blood pressure and E.S.R. are normal. He has completed his schooling, and is an apprentice in a sheet-metal factory.

Discussion

Although the history and clinical findings were characteristic of polyarteritis nodosa, we were fortunate in obtaining early histological proof of the diagnosis. The absence of polymorphonuclear leucocytosis and eosinophilia does not confound the diagnosis, for Miller and Daley (1946) state that the former finding occurs in 70% of cases, whilst eosinophilia is relatively unusual, being found in approximately 20%. Our patient gave no antecedent history of a specific infection or of upper respiratory tract infection, and he had taken no drugs before his illness.

It cannot be stated categorically that he would not have recovered spontaneously, though the clinical course certainly suggested otherwise. There is no doubt that improvement dated from the beginning of treatment with A.C.T.H. and, furthermore, that from that time a prolonged remission was established. The plan of treatment differed from that set out by Mundy *et al.* (1951) in that a prolonged consecutive course of A.C.T.H. was given, and was continued until all clinical and laboratory signs of activity had subsided. Whether the patient can be regarded as cured can be determined only by prolonged surveillance.

Summary

A case of polyarteritis nodosa in an acute phase is presented, with clinical and pathological findings. Treatment was provided with intramuscular A.C.T.H., which was continued until no clinical or laboratory evidence of activity was forthcoming.

Complete remission of the disease process for over one year to date has been achieved.

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Rabies is still an acute problem in many parts of the world where dogs are often in contact with wild animals. The World Health Organization's Expert Committee on Rabies has been meeting in Rome this week to examine new developments resulting from large-scale experiments in rabies control sponsored by W.H.O. in Spain, Greece, Yugoslavia, Mexico, and other countries. In this second session in three years the Committee has discussed various improvements in types of vaccines for human and veterinary use. The success of canine vaccination in many countries, including the United States, has been reviewed, and the Committee has received reports on systematic treatment with hyperimmune serum in Iran among people bitten by rabid wolves, and on the local treatment of wounds in laboratory animals in Spain. Another task of the Committee was the final approval of the text of the W.H.O. *Manual of Laboratory Techniques in Rabies*, which is designed to standardize laboratory procedures and facilitate comparison of international experiments. Training courses and meetings are organized by W.H.O. to spread information on new and effective techniques of rabies control throughout the many countries which, unlike England, Switzerland, and the Scandinavian countries, have been unable to achieve complete control of the disease.

COMPOSITION OF ARTICULAR CARTILAGE IN OSTEOARTHRITIS CHANGES IN COLLAGEN/CHONDROITIN- SULPHATE RATIO

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The bluish-white hyaline cartilage of healthy articular surfaces is a smooth, glistening, and resilient tissue, and it is here that the earliest morphological changes characterizing osteoarthritis or degenerative joint disease appear. Opacity and yellow discoloration accompanied by progressive loss of elasticity are evidence of senescent change preceding the appearance in the surface layer of small blisters, grooves, and pits. Later, as larger circumscribed erosions approach the underlying bone, the articular surface assumes a velvety appearance and spongy texture resulting from loss of intercellular substance and exposure of collagen fibres. Histologically, the affected cartilage is cleft along its fibrillary planes, and, since the superficial fibres are tangentially arranged, the earliest lesion is horizontal flaking of the surface cartilage. Ultimately, as extension along the path of radially disposed collagen bundles occurs, splitting and the concomitant loss of tissue result in exposure of subchondral bone. Fibrillation, as this process is known, is the hall-mark of osteoarthritis.

These changes occur first and foremost in weight-bearing joints. In the knee, fibrillation of articular cartilage occurs principally in those areas in which weight-bearing is concentrated, and which are most subjected to shearing stress (patella, exposed portions of the tibial condyles, patellar surface of the femur, and the anterior and middle thirds of the medial femoral condyle) (Bennett *et al.*, 1942).

Little work has been devoted to chemical aspects of fibrillation. Preliminary data (Matthews, 1952), dealing with the proportions of the two main organic components of healthy articular cartilage, indicated the importance of mechanical function in determining the ratio of collagen to chondroitin sulphate. Using similar chemical methods, we have investigated this ratio in fibrillar articular cartilage compared with that of healthy cartilage within the same joint.

Materials and Methods

The material was taken at necropsy. A knee-joint was opened, and, after flexing the joint fully, the articular surface of the lower end of the femur was inspected for fibrillar lesions. Knee-joints showing frank degenerative change more than fibrillation were not used, since they yielded insufficient material for analysis.

The areas selected for this investigation, therefore, were moderately advanced circumscribed lesions, about 2-3 cm. in diameter, showing fibrillation with loss of superficial cartilage, and affecting the medial condyle and the patellar surface of the femur, or the medial condyle alone. The whole of the fibrillar material constituting the lesion was excised with a sharp scalpel, care being taken to exclude the healthy adjacent and underlying articular cartilage. For control material, a piece of healthy cartilage of similar area and thickness was pared from a corresponding site on the