THE FAMILIAL OCCURRENCE OF ANKYLOSING SPONDYLITIS

BY

J. H. JACOBS, M.B., M.R.C.P.
Senior Registrar to the Department of Rheumatism

AND

F. CLIFFORD ROSE, M.B., M.R.C.P.
Registrar to the Department of Rheumatism
(From the Royal Free Hospital, London)

This paper reports a family in which three brothers, one sister, and a paternal uncle suffered from ankylosing spondylitis, and discusses the importance of heredity in this condition.

Although von Becterew and Marie described families with multiple cases of spondylitis, many observers since have believed that there was no familial predisposition in this disease. Llewellyn Jones (1909) said that hereditary transmission was extremely rare. Dunham and Kautz (1941) and Stone, as recently as 1947, made no reference to heredity in the aetiology of ankylosing spondylitis. MacWhirter (1945) stated that the disease may sometimes be familial. Simpson and Stevenson (1949), in an analysis of 200 cases, found a positive family history in only two patients—that is, a familial incidence of 1%. Campbell (1947), in reporting 25 cases of ankylosing spondylitis, mentioned four families in which multiple cases of the disease had occurred, and said that "the family history is significant and inadequately emphasized in the English literature." Stecher and Hauser (1946) reported four instances of ankylosing spondylitis affecting brothers, but were "forced to conclude . . . such a coincidence may have resulted from chance alone." In 1952, however, Stecher reported 59 families with more than one person suffering from the disease, and stated that the incidence of ankylosing spondylitis in relatives of patients was 30 times that of controls. Families have also been reported by Ray (1931–2), Stauffer and Moffett (1946), Tegner and Lloyd (1949), Fraser (1950), and Riecker *et al.* (1950); the last-mentioned authors thought that transmission was probably due to an autosomal dominant gene. Hersh *et al.* (1950), in a study of 50 families of ankylosing spondylitis, concluded that "there can no longer be any reasonable doubt that heredity plays a major role in the aetiology of spondylitis."

Case Reports

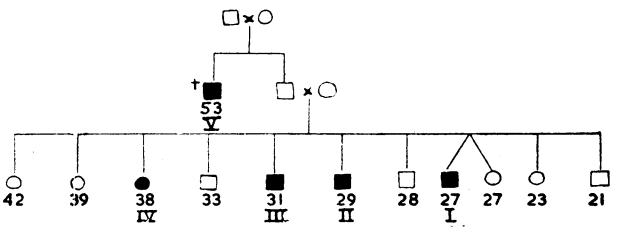
Case I.—A man of 27 had in 1946, when aged 18, suffered from an attack of low back pain which was treated with physiotherapy and went within a few weeks. He remained well until 1953, when he began to develop pain and stiffness in his cervical and dorsal spine, which gradually increased in severity. He had lost 21 lb. (9.5 kg.) in weight over the previous year. Examination revealed a generalized stiffness of his spine, most marked in the cervical region, and he could not reach within 16 in. (40.6 cm.) of his toes. His chest expansion was ¼ in. (6 mm.). His haemoglobin was 13.7 g. per 100 ml.; sedimentation rate (Westergren), 20 mm. at one hour. *X*-ray examination showed: chest normal; early ligamentous calcification of cervical spine; erosions and sclerosis on the left sacro-iliac joint, the right side appearing within normal limits.

Case II.—A male aged 29 was first seen in 1947, when aged 22, complaining of pain at the base of his spine of three months' duration. The pain was worse in bed at night and was relieved by getting up and walking. On examination he was tender over the sacro-coccygeal junction; the diagnosis at first was "coccydynia." *X*-ray examination of the sacro-iliac joints showed some obliteration of the joint space and surrounding bone sclerosis.

Case III.—A male aged 31 suffered in 1944, when aged 20, from pain in his ankles which was thought to be due to rheumatoid arthritis. This pain disappeared after four months, and he remained well until 1952, when he complained of low backache, which persisted. He later developed pain between his scapulae, and his cervical spine became stiff. He had not noticed any loss of weight. Examination in December, 1953, showed limitation of all movements of the cervical spine, kyphosis of the dorsal spine, and limitation of flexion of the lumbar spine. He was not able to reach within 12 in. (30 cm.) of his toes. His chest expansion was ½ in. (1.3 cm.). His haemoglobin was 8.9 g. per 100 ml.; sedimentation rate (Westergren), 20 mm. at one hour. *X*-ray examination: chest normal; dorsal spine showed marked kyphosis, squaring of the bodies, and calcification of the ligaments in the D 11 area; sacro-iliac joints showed marked erosions with partial obliteration of the left joint space.

Case IV.—A woman aged 38 developed psoriasis in 1929, when aged 11. At the age of 25 she complained of vague backache following the birth of her first child. For the past three years the pain in the lower lumbar area had become more severe, with increasing limitation of movement. More recently her right hip and shoulder had become painful. Examination revealed dorsal kyphosis, lumbar lordosis, and limitation of movement of the lumbar spine, and she could not reach within 4 in. (10 cm.) of her toes. Her chest expansion was 2 in. (5 cm.). Her haemoglobin was 13.9 g. per 100 ml.; sedimentation rate (Westergren), 31 mm. at one hour. *X*-ray examination: spine showed squaring of mid-dorsal vertebrae; sacro-iliac joints revealed irregularity and sclerosis.

Case V.—A male aged 53 was diagnosed elsewhere in 1940 as a case of ankylosing spondylitis. He died in 1951 from carcinoma of the pancreas and was not seen by us.



Pedigree of the family. □=Normal male. ○=Normal female. ■=Male with ankylosing spondylitis. ●=Female with ankylosing spondylitis. †=deceased. Arabic numerals give ages in years; Roman numerals indicate cases referred to in the text.

Discussion

West (1948), in a study at Bristol, found a familial incidence in ankylosing spondylitis of approximately 11%. In the same year Rogoff and Freyberg read a paper at the Annual Congress of the American Rheumatism Association and reported a series of 114 patients suffering from ankylosing spondylitis, and in 10 of these cases one or more relatives had the disease; they concluded that the familial incidence was 9–13%. Talkov (1948), in the discussion that followed, said that the familial incidence was less in those patients in whom the peripheral joints were involved. Polley, at the same meeting, reported a family of three brothers and a sister all affected with the disease, but he found a family history in only 0.4% of his cases, and thought that factors other than heredity were more significant in the aetiology. Rosenberg (1948) stated that he now urged radiographic examination of all male siblings of spondylitis patients, and by this means he had discovered five cases in a year. From a survey of case notes of 100 patients with ankylosing spondylitis who attended the Royal Free Hospital, six were found in whom one or more relatives were affected with the same disease. The familial incidence, therefore, is at least 6%.

Since the onset of ankylosing spondylitis is extremely variable, and as the average interval between the first symptoms and diagnosis is three to four years, it is advisable to *x*-ray the sacro-iliac joints in siblings of patients with this disease, and imperative in any relative who complains of pain referable to the locomotor system.

Summary

A family in which five members had ankylosing spondylitis is reported.

The familial incidence is discussed and its importance emphasized.

Radiography of sacro-iliac joints is advised in relatives of patients with ankylosing spondylitis who complain of symptoms referable to the locomotor system.

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REFERENCES

Campbell, A. M. G. (1947). *Lancet*, **1**, 406.
Dunham, C. L., and Kautz, F. G. (1941). *Amer. J. med. Sci.*, **201**, 232.
Fraser, T. N. (1950). *Ann. rheum. Dis.*, **9**, 231.
Hersh, A. H., *et al.* (1950). *Amer. J. hum. Gen.*, **2**, 391.
Jones, R. L. (1909). *Arthritis Deformans*. Wright, Bristol.
MacWhirter, R. (1945). *Brit. J. Radiol.*, **18**, 302.
Polley, H. F. (1948). *Ann. rheum. Dis.*, **7**, 40.
Ray, M. B. (1931-2). *Proc. roy. Soc. Med.*, **25**, 325.
Riecker, H. H., Neel, J. V., and Test, A. (1950). *Ann. intern. Med.*, **33**, 1254.
Rogoff, B., and Freyberg, R. H. (1948). *Ann. rheum. Dis.*, **7**, 40 (Abstract).
Rosenberg, E. F. (1948). Ibid., **7**, 41.
Simpson, N. R. W., and Stevenson, C. J. (1949). *British Medical Journal*, **1**, 214.
Stauffer, J., and Moffett, T. J. (1946). *J. Hered.*, **37**, 287.
Stecher, R. M. (1952). *Acta physiother. rheum. belg.*, **7**, 108.
—— and Hauser, H. (1946). *Amer. J. Roentgenol.*, **56**, 601.
Stone, K. (1947). *Diseases of Joints and Rheumatism*. Heinemann, London.
Talkov, R. H. (1948). *Ann. rheum. Dis.*, **7**, 40.
Tegner, W., and Lloyd, K. (1949). *Lancet*, **2**, 196.
West, H. F. (1948). "A Study of Ankylosing Spondylitis." Bristol (England). Thesis.

ACUTE DIFFUSE LUPUS ERYTHEMATOSUS

REPORT OF A CASE WITH PREDOMINANT PULMONARY MANIFESTATIONS

BY

H. L. MATTHEWS, M.B., M.R.C.P.
Medical Registrar

AND

M. J. MEYNELL, M.D., M.R.C.P.
Clinical Pathologist

(From the General Hospital, Birmingham)

The demonstration of "L.E." cells by Hargraves *et al.* (1948) has considerably broadened the clinical concept of acute disseminated lupus erythematosus. Pulmonary involvement in the collagenoses is by no means uncommon, but it is not widely recognized that in the condition under discussion the pulmonary manifestations may overshadow the more classical features—namely, rash, polyarthritis, polyserositis, adenopathy, splenomegaly, and nephritis. Rakov and Taylor (1942) first described such a case. Israel (1953), recording 22 cases of diffuse lupus, found pulmonary involvement the predominant feature in two. Rapaport *et al.* (1953) described two cases with pulmonary lesions. Their Case 1 is strikingly similar to that cited below, and is another example in which the pulmonary manifestations were the presenting feature. Diagnostic difficulties were experienced until "L.E." cells were demonstrated in the peripheral blood.

Case History

A 39-year-old tool-fitter returning home from work in mid-June, 1953, became extremely fatigued and noticed retrosternal soreness. Fever, dyspnoea, and a productive cough rapidly developed. His doctor treated him with penicillin and sulphonamides with no improvement, and on July 2 he was admitted to hospital. On admission, fever, tachycardia, finger-clubbing, signs of consolidation over the left lower lobe and a systolic murmur at the cardiac apex were present. His blood pressure was 115/70. Examination of other systems revealed no abnormalities.

Investigations.—Radiology: Chest *x*-ray examination (July 2) showed radiological changes of left lower lobe consolidation; barium swallow was normal; bronchography (July 31) revealed minimal dilatation of left posterior basal bronchi. Sputum: microscopy showed pus cells with no predominant organism or acid-fast bacilli; cultures were without significant result. Urine: trace of albumin, no sugar; microscopy showed no casts or red blood cells; cultures were sterile. Blood count (July 28): Hb, 11.6 g.% Haldane; white cells, 12,000 per c.mm. (neutrophils 87%, eosinophils 2%, basophils nil, lymphocytes 10%, monocytes 1%). Widal reactions were negative. E.C.G.: regular sinus tachycardia (120 per minute), with RST depression and inverted T waves in left precordial leads.

Progress.—Parenteral penicillin was given with an initial fall in temperature, but within a week, while he was still on this treatment, fever recurred. Chloramphenicol, 2 g. daily, and later intramuscular streptomycin, 1 g. daily, were in turn substituted for penicillin. These produced the same pattern of response. Meanwhile the patient's condition deteriorated. He lost weight, the retrosternal soreness increased, and the finger-clubbing was more pronounced. Paradoxically the abnormal pulmonary physical signs disappeared. A further chest *x*-ray examination (July 9) showed considerable clearing of the left base, with pleural thickening in both costophrenic angles. Bronchoscopy on August 14 showed a small quantity of pus in the left main bronchus; there was no evidence of neoplasm. On August 22 he was transferred to this hospital. By now he was thin, sallow, and dyspnoeic, and complained bitterly of retrosternal pain. Fever persisted, finger-clubbing was still present, splinter nail haemorrhages and subconjunctival petechiae had appeared. There was no splenomegaly, lymphadenopathy, oedema, or cyanosis. The signs in the lungs were now those of partial collapse of the left lower lobe with some fluid. The heart was as previously described.

Further Investigations.—Blood count: Hb, 10.1 g.% (Haldane); white cells 9,000 per c.mm., the differential count showed a few metamyelocytes; platelets, 300,000 per c.mm.; M.C.V., 84 μ^3; M.C.H.C., 30%. E.S.R. (Westergren): 90 mm./hour. Virus studies for influenza A+B, Q fever, psittacosis–L.G.V., and *Streptococcus M.G.* were all negative. Urine: a few hyalo-epithelial and granular casts with an occasional red blood cell; cultures produced no significant pathogens. Blood urea and plasma proteins were normal. The sternal marrow showed increased cellularity with myeloid hyperplasia; it was sterile on culture. The pleural fluid was clear and straw-coloured; it contained polymorphs 50%, lymphocytes 42%, and monocytes 8%; no malignant cells were seen; cultures, including those for tubercle, were sterile.

By September 14 his condition was critical. In addition to the petechial haemorrhages previously recorded, a scaly papular haemorrhagic rash was noted over the trunk. A skin biopsy showed changes which were not thought to be diagnostic. (These changes are discussed below.) At this stage the possibility of subacute bacterial endocarditis was seriously considered despite negative blood cultures. Accordingly penicillin, 12,000,000 units daily, was given. As before, there was an initial decrease in pyrexia but with a subsequent rise. Three weeks later oxytetracycline 2 g. daily was substituted for penicillin and continued for six weeks, again without obvious result.