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.

We wish to thank Mr. Radley Smith for referring those cases which we originally saw; Dr. Ernest Fletcher, under whose care they were admitted; and the Board of Governors of the Royal Free Hospital.

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ACUTE DIFFUSE LUPUS ERYTHEMATOSUS

REPORT OF A CASE WITH PREDOMINANT PULMONARY MANIFESTATIONS

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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 costo-phrenic 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.

On September 24, about five months after the onset of his illness, "L.E." cells were found in the peripheral blood. The possibility that these were penicillin-induced (Walsh and Zimmerman, 1953) was seriously considered but rejected on the following grounds: (1) the clinical course of the illness, and (2) re-examination of the stained section of skin biopsy (taken before high-dosage penicillin was given) was considered to show some early characteristics consistent with those found in diffuse lupus erythematosus.

The diagnosis was now evident, and efforts to control the disease with A.C.T.H. were begun on October 10. A prompt fall in temperature ensued, together with clinical improvement. Oedema necessitated the stopping of A.C.T.H. on October 19, and immediate relapse resulted. Resumption of A.C.T.H. was followed by remission.

Since the patient continued to improve, domiciliary maintenance with corticoids was decided on. Accordingly cortisone by mouth was substituted for A.C.T.H. He was discharged on December 24, taking 50 mg. of cortisone acetate daily. Out-patient follow-up showed maintained improvement, but with dyspnoea, tachycardia, and some collapse at the left base. Finger-clubbing persisted, and "L.E." cells were still demonstrable in the peripheral blood.

Discussion

Pulmonary involvement in diffuse lupus erythematosus is more commonly the result of secondary bacterial invasion, as may be seen in many extremely debilitating illnesses. These lesions are usually lobar or lobular in distribution and respond to adequate antibiotic measures. Miliary tuberculosis has been described as an occasional terminal event.

However, specific pulmonary lesions have been reported. Teilum (1946) described a "focal allergic pneumonia" which may be present throughout the lung but is more often subpleural. Microscopically he found a fibrinoid necrosis with histiocytic infiltration of the connective tissue and capillary walls of the alveolar septa. With less pronounced necrosis there is a tendency towards organization and fibrosis. Nevertheless, Foldes (1946) described a case of massive fibrosis with alveolar obliteration which he named "primary atelectasing pneumonitis." Presumably, despite Teilum's contention, the lesions may be either focal or diffuse. Baggenstoss (1952) described a basophilic mucinous oedema of the alveolar wall together with peribronchial and perivascular tissues. He suggested that the alveolar wall oedema was the precursor of the interstitial pneumonitis. Rakov and Taylor (1942), studying post-mortem material in their case, reported a chronic interstitial pneumonitis with atelectasis.

Thorell (1952) claimed that there are specific pulmonary radiological changes. These consist in mottling and streakiness, mainly subpleural and more marked at the bases; there was usually pleural thickening, often with small pleural effusions. However, pulmonary lesions similar to those described above have been reported in a wide variety of conditions. These include protein hypersensitivity, acute glomerulonephritis, rheumatic pneumonitis, dermatomyositis, scleroderma, and rheumatoid arthritis, as well as acute diffuse lupus erythematosus. Sante and Wyatt (1951) grouped these similar pulmonary lesions under the term "antigenic pneumonitis," pointing out that their common denominator is the involvement of connective tissue. Barden and Cooper (1948), discussing the pulmonary radiological findings in this group of diverse but probably related conditions, laid emphasis on increased permeability of vessel walls as a cause for the x-ray signs. They described characteristic radiological patterns resulting from patchy or massive pulmonary oedema. The usual appearance, according to them, is that of massive fluffy shadows extending outwards from each hilus in a symmetrical fashion, the periphery of these shadows blending with the adjacent aerated lung. In less severe cases they described scattered subpleural shadows, again without definite margins. These may rapidly enlarge and merge.

In our case the fluctuating nature of the pulmonary lesions was noticeable, the signs varying first on the left and

then from side to side. In general, the radiological picture accords with Thorell's description except that partial collapse of the left lower lobe was a prominent feature in this instance. Unlike Thorell, we feel some doubt about the specificity of the radiological signs in disseminated lupus, but we agreed that where obscure, diffuse, or fluctuating radiological signs are observed in the course of an otherwise unexplained illness the possibility that these are due to disseminated lupus should be seriously considered.

It is apparent that, although pulmonary involvement in diffuse lupus erythematosus may occur, it is very unusual for it to predominate, more especially so in the early phase of the disease. When it does, as in the case presented, diagnostic difficulties may arise. It is suggested that an examination for "L.E." cells be carried out in cases of pneumonia running an unexpectedly atypical or prolonged course.

Summary

An unusual case of acute diffuse lupus erythematosus is described in which the pulmonary manifestations were the predominating features.

The pulmonary pathology and radiological features of this condition are discussed and their relationship to the other collagenoses is briefly reviewed.

The value of examination for "L.E." cells in unusual pneumonias is mentioned.

We should like to thank Dr. R. L. Mackay for giving us details of the early stage of the illness. To Dr. D. R. Humphreys we are grateful for help and permission to publish.

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DIFFUSE SARCOIDOSIS ASSOCIATED WITH HYPOPIUITARISM AND TERMINAL RENAL FAILURE

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Sarcoidosis is being increasingly recognized as a disease of protean clinical manifestations and widespread distribution in the body. The organs most often attacked are the lungs, lymph nodes, skin, spleen, liver, and eye. As the pituitary is rarely involved, the following record is presented of a patient who, after showing for many years the signs and symptoms of hypopituitarism and dying from renal failure, was found at necropsy to have widespread sarcoidosis.

Case History

A man aged 52, given as retired, but occupation not known, first attended the out-patient department of this hospital on June 13, 1949. He gave a history of ill-health extending over many years. It first began 15 years previously, when he had an attack of vomiting green fluid, lasting about three weeks. This was followed by loss of hair