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

BY

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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

from the axillae, pubes, legs, and eyebrows. In 1939 he suffered a loss of libido, and two years later began to complain of tiredness and listlessness. In 1945 he had one blood examination, and a diagnosis of pernicious anaemia was made, but the diagnosis was not supported by marrow puncture or a test meal. He was treated with liver, iron, and thyroid extract. In 1948 he had an illness described as "pneumonia." Apart from this he had been fairly well until about two months before attending this hospital, when he began to complain of loss of appetite and loss of weight. The past history held only one point, and this was an attack of probable erythema nodosum at the age of 11. The family history gave one brother dead from pulmonary tuberculosis.

On examination the patient's face and hands were pale and puffy, and he had a sandy freckled complexion. The pulse was regular, rate 72 a minute; the mucous membranes were pink; and the blood pressure was 200/115 mm. Hg. The optic fundi, heart, and lungs were normal. The tip of the spleen could be felt and there was slight pitting oedema of the legs. There was no axillary hair, and the pubic hair and eyebrows were very scanty. He was admitted to hospital on July 14, 1949.

Investigations.—Urine showed a cloud of albumin (Esbach consistently 0.25 to 1 g.); deposit and culture were negative except for a growth of streptococci on one occasion. Blood urea, 45 mg. per 100 ml.; plasma proteins, total 7.48 g.% (albumin 4.44 g., globulin 3.04 g.), A/G ratio, 1.4:1; blood cholesterol, 196 mg. per 100 ml.; haemoglobin, 84%; leucocyte count and differential normal; erythrocyte sedimentation rate (Wintrobe) 29 mm. in one hour; Wassermann reaction negative; intravenous pyelogram normal; basal metabolic rate -3%.

He ran a temperature of 101 to 102° F. (38.3 to 38.9° C.) for a few days following admission, but was discharged after a fortnight. He was given injections of testosterone, at first 25 mg. daily and later 100 mg. twice a week. A tentative diagnosis of chronic nephritis with endocrine dysfunction was made.

He attended as an out-patient, and in December, 1949, the spleen was easily palpable. The urine still contained albumin; also scanty red cells and leucocytes, and a moderate number of granular and hyaline casts.

Until April, 1951, he remained very well; it was then noted that the hair in the axillae and pubes had to a certain extent returned, and he stated that he was no longer impotent. The blood urea was 39 mg. per 100 ml.

On June 29 he was readmitted, giving a history of anorexia, vomiting, increasing weakness, and loss of weight of two months' duration. On examination it was found that the blood pressure had fallen to 125/80 mm. Hg, and he was obviously ill. The blood urea had risen to 168 mg. per 100 ml., and the albumin-globulin ratio was reversed, total plasma proteins being 7.1 g.%, albumin 3.25 g.%, globulin 3.85 g.%, ratio 0.85:1. The serum sodium was 309 mg. per 100 ml., potassium 20.4 mg. per 100 ml., and chlorides 641 mg. per 100 ml.

In spite of treatment by intravenous and rectal saline, the output of urine was scanty, and the blood urea continued to rise, reaching 264 mg. on July 22. He gradually deteriorated, the blood pressure continued to fall, and numerous crepitations were heard at the bases of the lungs. Addison's disease was suspected, but he did not respond to injections of deoxycortone acetate, and he died on July 30. For the last nine days of his illness his temperature was subnormal, never rising above 95.2° F. (35.1° C.).

Post-mortem Report

At the post-mortem examination both the pleural and the cut surfaces of the lungs showed numerous grey granules, more numerous in the upper parts of the lungs and resembling miliary tubercles. The heart weighed 11 oz. (310 g.), and, apart from two small petechial haemorrhages on the surface, appeared normal. The liver weighed 64 oz. (2 kg.) and was of a tawny brown colour. The gall-bladder was fibrosed.

The right kidney weighed 3½ oz. (106 g.) and the left 3 oz. (85 g.). Both appeared to be arteriosclerotic, with thin not clearly demarcated cortex. Both suprarenals were very small, only one-quarter the normal size. The spleen weighed 24 oz. (680 g.); the cut surface had a gelatinous look and showed numerous very small nodules; normal Malpighian bodies were not visible. The tracheo-bronchial and tracheal lymph nodes were much enlarged and soft, as were also the nodes around the head of the pancreas. The thyroid was small and the testes were atrophied. The brain showed no abnormality, but on searching for the pituitary it was a surprise to find the pituitary fossa completely empty. Careful examination was made for remnants of pituitary tissue or scar tissue, but none was seen.

On histological examination, sections of the lung, liver, spleen, and tracheo-bronchial and pancreatic lymph nodes all showed the characteristic picture of sarcoidosis—namely, discrete epithelioid-cell follicles containing giant cells. There was no tendency to caseation, but some follicles were in the stage of hyaline fibrosis.

The kidney showed glomerulitis, many glomeruli being enlarged and a few showing fibrosis and hyaline degeneration. The tubules contained granular debris, and an occasional tubule had a deposit of calcium. The condition appeared to be subacute, and there was not the degree of interstitial fibrosis that one would have expected in kidneys of such small size due to chronic nephritis. A very occasional sarcoid lesion was present, but this was obviously insufficient to cause disturbance of function by anatomical destruction of tissue.

In the liver numerous sarcoid follicles were present. The normal architecture of the liver was considerably disorganized, resulting in fibrosis and some nodular reparative hyperplasia of the liver cells. The lungs showed miliary sarcoidosis. The testes showed fibrosis of the walls of the tubules. A layer of spermatogenic cells were present, but there were no spermatocytes. There was a complete absence of interstitial cells. Occasional sarcoid follicles were present in the interstitial tissue. The suprarenals showed marked atrophy of the cortex. A few sarcoid lesions were seen in the myocardium. A section of the infundibular stalk and hypothalamic region was prepared, but no evidence of sarcoidosis was found.

Discussion

This case shows many of the features of hypopituitarism as described by Sheehan and Summers (1949) in their comprehensive review of the syndrome—namely, (1) atrophy of testes, (2) complete loss of sex function, (3) loss of axillary and pubic hair, (4) absence of normal skin pigment, (5) characteristic flabby facies with thinning of the eyebrows and pallor of the skin, and (6) physical weakness. The return of sexual potency which occurred on testosterone treatment is also consistent with a pituitary deficiency. The patient was also at one time diagnosed, and treated, as a case of pernicious anaemia—a not infrequent error.

The history is clearly, therefore, one of hypopituitarism lasting for 17 years. Although it was not possible to demonstrate the actual sarcoid lesion in the pituitary, the finding of an empty sella indicates previous destruction by some pathological process, and, taking into consideration the known long duration of sarcoidosis, it seems probable that this had early affected the pituitary. Among other possible causes the "giant-cell granuloma of the pituitary" described by Oelbaum and Wainwright (1950) and by Doniach and Wright (1951) should perhaps be considered. This seems an extremely unlikely cause, however, as in two of the cases reported by them there was a peculiar granulomatous infiltration of the suprarenals, which was absent in our case; and also an empty sella has not so far been recorded as a result of this condition. Syphilis is another cause of hypopituitarism. Oelbaum (1952a), in a review of hypopituitarism in males, due to syphilis, mentions that in 2 out of 14 subjects the lesion resulted in an "empty sella." There was no question of syphilis in the case here reported.

Sheehan and Summers (1949) mention that sarcoidosis has been reported as a cause of hypopituitarism, and they discuss the empty sella. They state that it is a peculiar type of scarring in which the sella appears quite empty, but histological examination of the floor shows that there is a dense layer of fibrous tissue enclosing a very thin lamina of anterior lobe parenchyma. Tissue was unfortunately not taken from the floor of the sella in this case, but a section from the pituitary stalk and hypothalamic region revealed no evidence of disease. This finding of a normal hypothalamic region is probably to be correlated with the absence of diabetes insipidus.

Of particular interest is the nature of the renal failure and glomerulitis, which was the terminal event. Longcope and Freiman (1952), in their study of sarcoidosis, mention that transient albuminuria and cylindruria are not infrequent accompaniments of active sarcoidosis. In their series of cases at the Massachusetts General Hospital were four cases showing a significant amount of impairment of renal function, but in none was it severe enough to lead to a fatal issue. Klinefelter and Salley (1946) reviewed four cases of renal failure in sarcoidosis, including one of their own, but this case was unsupported by necropsy evidence. Without doubt, renal failure is a very rare complication of sarcoidosis, and it is difficult to state what relationship the nephritis bore to the sarcoidosis. Possibly it was some sort of toxic or allergic reaction.

On the other hand, the renal failure may have been partly due to the suprarenal atrophy secondary to the hypopituitarism. Oelbaum (1952b) reviewed six cases of hypopituitarism due to post-partum necrosis, and remarked that there may be a marked dissociation in the degree of functional impairment of the thyroid, adrenal cortex, and gonads. It has been known for many years that renal failure and a high blood urea occur in suprarenal insufficiency. Lewis (1952) has suggested that the mechanism of this failure may be the low renal blood flow and filtration rate resulting from the reduced blood pressure, blood volume, and cardiac output. A remarkable feature of this case was the fall in blood pressure at the time of the last admission. In view of the glomerular changes, it is suggested that there was probably a combination of the two factors.

Summary

A case of hypopituitarism which appeared to be due to sarcoidosis is reported and a discussion of its relationship to renal failure given.

We wish to express our thanks to Dr. T. Robson for the clinical notes, and to Professor H. L. Sheehan for his advice on the sections.

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At a small reception held at the Royal College of Midwives on October 25, the President and Council of the College were officially presented with a colour film, "The British Midwife," by the chairman of the board of directors of Cow and Gate Ltd. The film outlines the training of the midwife and goes on to illustrate the work of a rural practising midwife and her management of a normal case in all its stages, including close-ups of the delivery. Even if the picture shown is that of the rosier side of a midwife's life—the country scene is gay with blossom and sunshine—and a short film cannot show everything, it leaves one in no doubt that the work of the British midwife calls for standards of professional competence and a sense of vocation of a high order. It should appeal to the best type of recruit to the profession.

SIX CASES OF INFANTILE SCURVY

BY

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"To-day in its grosser manifestations (scurvy) may be said to have ceased to exist."—H. C. CAMERON (1941) in "Fifty Years of Progress in Paediatrics."

Scurvy is one of the classical diseases with a simple, straightforward aetiology, which is easily prevented and cured, and which should be easily diagnosed. The infantile form (Barlow's disease) differs from the adult form in its clinical features only because of differences in anatomy and physiology.

Scurvy has been recognized for centuries, and, though nowadays very rare in this country, persists at the two ends of life. The type occurring in elderly people who live alone and do their own cooking is often termed "bachelor scurvy." Series of this type are recorded by McMillan and Inglis (1944) and by Brown (1951).

It is remarkable that, with the varieties of organization and propaganda brought to bear on the mother, infantile scurvy exists at all. It is, however, difficult even approximately to determine its present incidence. The authors of most standard textbooks confine themselves to variations on the theme that it is "a very rare condition." Garrod *et al.* (1953) record that from 1933 to 1942 only 25 cases of infantile scurvy were admitted to the Hospital for Sick Children, Glasgow. Brailsford (1953) quotes one case seen in 1947. This apart, we can trace no recent specific reference. During the past five years only 10 cases have been seen at the Hospital for Sick Children, Great Ormond Street (figures quoted by permission of the Medical Committee).

Reports from America (Ellenbogen *et al.*, 1951; Silverman, 1953), Canada (Coward, 1950), Australia (Packer, 1947), France (Guerin, 1949), Italy (Camera, 1948), and India (Mukherjee, 1952) all confirm that the disease is now rarely seen.

When infantile scurvy occurs nowadays it is always in artificially fed babies whose feeds have been so treated by heat or commercial process as to destroy the vitamin C and who have had no supplementary feeding with fruit or vegetable juices. The practice of warming orange juice occurs quite commonly in this country. Rarely, but not recently, scurvy has been reported in breast-fed babies when the mother also has a very deficient diet.

Case 1

A girl aged 1 year was admitted to hospital with a complaint of painful paralysed legs. The illness had begun four days earlier with cough, sore mouth, pyrexia, and apparent pain with inability to move the legs. Signs of bronchopneumonia had developed the following day, but, although the chest had improved with sulphamerazine, the other symptoms had grown worse. On admission to hospital, undiagnosed, the child was very pale, but was well developed and nourished. Temperature was 101° F. (38.3° C.) and pulse 140. There were no skin rashes or petechiae. Four incisor teeth were through, and around them the gums were red and swollen. Both legs were oedematous up to the