The haemoglobin was 60% or below in 6 out of 10 cases in which it was recorded, and the colour index was usually high. The platelets were recorded as being markedly diminished in three cases. Sternal puncture revealed a depression of the granulocytes in two cases, aplasia of the bone marrow in a third case, and a normal marrow in a fourth. Thus it appears that a depression of one or all of the blood-forming elements usually occurs.

Although severe leucopenia has been a striking feature of all the present cases, it is a complication rather than an essential feature of the disease, since it is, in our opinion, caused by the action of the tubercle bacillus on the bone marrow. In only one of the above cases (No. 6) was there evidence of a drug playing a part in the development of the leucopenia. In some of the cases the initial leucocyte count was normal or only slightly depressed, the severe leucopenia developing later. Nevertheless, its importance is stressed because it should prove one of the few helpful diagnostic features in a disease in which a correct diagnosis has apparently never been made during life.

Since the disease runs a rapid downhill course, an early diagnosis would have to be made if chemotherapy were to be given a chance of success. The most important factor in making the diagnosis would be to consider the possibility of acute tuberculous septicaemia in cases of high fever associated with leucopenia. The clinical picture often suggests typhoid fever or miliary tuberculosis. Splenic enlargement, abnormal chest signs, skin eruptions, and jaundice may also be present. A certain diagnosis could be made only by finding the tubercle bacillus. Since large numbers of tubercle bacilli can be found in the bone marrow post mortem, von Wyss has suggested that sternal puncture should be performed in an attempt to find the causal organism. Horowitz and Gorelick (1951) have described a method by which tubercle bacilli were demonstrated in the bone marrow in 14 out of 20 patients with advanced tuberculosis. This would seem to be the most likely way of confirming the diagnosis. Aspiration biopsy of the liver might also prove diagnostic.

It is possible that streptomycin might result in a cure if it were administered before irreversible changes had occurred. A trial of the drug would be fully justifiable in what is otherwise a hopeless condition.

Summary

Three cases of acute tuberculous septicaemia with leucopenia are described, and are compared with eight cases which have previously been recorded in the literature.

Rigors, anorexia, and malaise were common symptoms. A high fever was always present and an enlarged spleen was often felt.

A severe leucopenia without a striking relative neutropenia was the commonest finding in the blood. An aplastic anaemia and a thrombocytopenia were also seen.

A rapid downhill course invariably occurred, with death between three and twelve weeks from the first symptom.

Acute tuberculous septicaemia followed a fresh primary infection or a genuine reinfection in each of the three cases.

At necropsy, multiple necrotic foci were seen in the liver and spleen in Case 1, but in Cases 2 and 3 no characteristic naked-eye changes were visible in any organ.

In all cases histological examination revealed numerous necrotic foci containing acid-fast bacilli in many organs.

It is considered that the occurrence of these organisms in the bone marrow accounts for the leucopenia and anaemia.

The difficulty in diagnosis lies in the absence of characteristic features in this disease. Examination of the bone marrow for tubercle bacilli is recommended. Streptomycin should be given a trial in a suspected case.

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ACROSCLEROSIS

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Scleroderma is a condition which may present in several ways. In its commonest form it appears as localized areas in the skin which show thickening, adhesion to the subcutaneous tissues, a smooth waxy surface, and progression to atrophy. This form—localized scleroderma or morphoea—is a disease of little consequence. The generalized form is a serious disease. The skin changes are similar, but large areas of the body are affected and the disease is steadily progressive. It is usually insidious in onset and runs a chronic course, but rarely may occur in acute form with rapid development of the typical changes. Among patients with generalized scleroderma it is possible to separate a group in whom the skin changes are confined to the hands, forearms, face, and upper chest, and are commonly preceded by Raynaud's phenomena in the hands. There is some dispute whether this form, which has been given the name of acrosclerosis, is a disease *sui generis* or is merely one way in which generalized progressive scleroderma may present.

Hutchinson (1893, 1895, 1896) seems to have been the first to recognize the association of Raynaud's phenomena with sclerodermatous changes. He separated such sclerodermatous changes from those of "diffuse scleriosis," not only because of their intimate association with Raynaud's phenomena but also because the skin changes were confined to the digits and, less often, to the face. He used the terms "acrosclerodermia," "acroteric morphoea," and "acroteric scleriosis" to cover the condition. Sellei (1931, 1934) likewise separated acrosclerosis from chronic progressive scleroderma and strongly supported the view that it is a disease in its own right. O'Leary and Waisman (1943), in an admirable account of the condition, also regarded it as

an entity. The main differences between acrosclerosis and generalized scleroderma are shown in the Table.

Main Differences Between Acrosclerosis and Generalized Progressive Scleroderma (Condensed from O'Leary and Waisman's Data)

	Acrosclerosis	Generalized Progressive Scleroderma
Sex	Mainly women	Men and women equally
Onset	In fingers, usually preceded by Raynaud's phenomena	Most commonly on trunk. Raynaud's phenomena rare and do not occur at onset
Distribution ..	Hands, forearms, face, and upper chest	Trunk, limbs, and face
Visceral lesions ..	Frequent (particularly oesophagus)	Rare
Prognosis ..	Favourable so far as life is concerned. Local changes may be arrested	Bad. Most of body involved after 2 years. Arrest rare

The frequency of visceral lesions in acrosclerosis is an important distinguishing feature and has been emphasized by Olsen, O'Leary, and Kirklin (1945). Among 350 patients seen at the Mayo Clinic with scleroderma or acrosclerosis, 36 had dysphagia or lesions of the oesophagus. Of these, no fewer than 33 had acrosclerosis. (Unfortunately the authors do not state how many of their total series were diagnosed as acrosclerosis, so the frequency of oesophageal lesions in this condition is not apparent.) Eighteen of these cases with positive radiological or oesophagoscopy evidence of oesophageal lesions are discussed in detail, and it is of interest that all these patients had Raynaud's phenomena preceding or coincident with the development of cutaneous lesions. In this country, Bourne (1947, 1948, 1949) has reported four cases of acrosclerosis with oesophageal lesions. Although the oesophagus is the most commonly involved of the viscera, lesions have also been recognized in other parts of the gastrointestinal tract, the heart, and the lungs (Weiss *et al.*, 1943; Bevans, 1945; East and Oram, 1947; Mathisen and Palmer, 1947; Dostrovsky, 1947). We present below the case reports of four patients with acrosclerosis who illustrate various aspects of the condition.

Case 1

This patient was an unmarried female clerical worker aged 29. At the age of 18 she developed "arthritis" of the hands and also of other joints. At 22 she had attacks of Raynaud's phenomena which have persisted until the present. At 23 the little finger was amputated because of trouble resulting from the local injection of some agent intended to dissolve restricting fibrous tissue attributed to the "arthritis." A right cervical sympathectomy was performed when she was 26; this was complicated by an arterial thrombosis in the right arm, and left her with Horner's syndrome in the right eye. The sympathectomy did not relieve her Raynaud's phenomena. At the age of 23 she developed mild indigestion; this grew steadily worse and became her most troublesome symptom by the time she was 27. It took the form of a retrosternal pain, which was exacerbated by swallowing food. She had for a considerable time also noticed some difficulty in opening the mouth fully. At this stage she was admitted to the Radcliffe Infirmary.

On examination her face was rounded and smooth, with a notable absence of normal furrows, so that she wore a doll-like expression. The skin had a waxy texture and was not easily moved over the forehead. The mouth was conspicuously small. The hands showed contractions of the fingers without any obvious deformity of bones or joints. The skin was smooth, shiny, thin, and fixed to the underlying tissues. Similar skin changes, though less severe, were present over the lower forearms and on the neck, where

slight pigmentation was present in a reticular pattern. The right radial pulse was absent. Other systems were normal.

A barium swallow revealed very feeble peristalsis, stricture of the lower end of the oesophagus above the cardia, and a short oesophagus with a gastric pouch above the diaphragm; these appearances resemble a congenitally short oesophagus. Oesophagoscopy showed a stricture at the lower end of the oesophagus with oesophagitis and ulceration proximal to it.

It was found impossible to dilate the oesophageal stricture, mainly because the oesophagus bled freely with instrumentation. In consequence she was treated conservatively on the lines of a peptic ulcer of the oesophagus, but she failed to respond to this, both symptomatically and as seen at oesophagoscopy. Gastrostomy was performed in November, 1948, but she tolerated this poorly and continued to have retrosternal pain, so that in January, 1949, trans-thoracic partial oesophagectomy was carried out. Histological changes typical of scleroderma were found in the operation specimen. Persistent discharging sinuses followed the operation and she developed a severe anaemia, which required treatment by transfusion. Retrosternal pain continued and occult blood was still present in her stools. A barium swallow on March 29, 1950, showed a deformity suggestive of an ulcer crater at the junction of the oesophagus and stomach.

Comment.—This patient shows a typical distribution of skin changes, the usual early limitation of joint movement, the early occurrence of Raynaud's phenomena, and oesophageal involvement. She thus appears to be a classical example of acrosclerosis as described by O'Leary and Waisman (1943). It is questionable whether partial oesophagectomy was advisable. Olsen *et al.* (1945) recommended treatment by dilatation alone, but in this patient attempts at dilatation were unsuccessful. However, as it is difficult to excise all diseased tissue, it seems wise to resort to surgery only when all other methods of treatment have failed.

Case 2

A housewife aged 40 had suffered from attacks of Raynaud's phenomena from the age of 14. In cold weather her fingers would become white and numb. Her toes were slightly affected in the same way. At the age of 38 the picture changed: her fingers became swollen, blue, and mottled, and attacks of whiteness and numbness were superimposed. Her fingers were swollen and congested all the time, so that she could not hold things properly. She felt "run down" but had no specific complaints.

On examination her fingers were blue, mottled, and swollen, with limitation of movement. Other systems normal. The haemoglobin was 14.1 g. per 100 ml., and the E.S.R. was 23 mm. in one hour (Westergren).

Raynaud's disease was originally diagnosed. A sympathetic block with procaine hydrochloride caused the ipsilateral hand to become warm and flushed, and the skin temperature rose 10° C. Pre-ganglionic cervical sympathectomy was therefore carried out on the right and, later, on the left sides. After the operation her fingers still went blue in cold weather, but they were no longer painful. The stiffness steadily increased. She now had difficulty in moving her joints, not only those of the fingers but also her wrists, elbows, feet, knees, and hips. Later she noticed subcutaneous nodules in the region of the wrists, elbows, and knees, and that her tongue was becoming difficult to move. Her fingers showed typical sclerodermatous changes, and the skin of her face showed changes similar to, though less severe than, those of Case 1. The face changes were not recognized when she was first seen, and her whole history suggested that the condition was in a stage of progression. She has also developed patchy pigmentation of the arms and abdomen. Her joints were clinically normal, but there was marked tendon crepitus over the dorsum of the hands.

Dysphagia was not present, but a barium swallow showed involvement of the oesophagus.

Comment.—In this case Raynaud's phenomena preceded sclerodermatous lesions by many years. In this connexion it is interesting that O'Leary and Waisman (1943) and Olsen *et al.* (1945) often found this time relationship, and were led to believe that the sclerodermatous changes of acrosclerosis were a direct consequence of vasomotor disturbances. The favourable response to sympathetic blockage with procaine suggests that vasomotor changes were responsible for some of her symptoms (pain and coldness of the fingers), and that these were ameliorated by sympathectomy, whereas those which can be attributed to sclerodermatous changes have progressed since operation. The subcutaneous nodules in this case are similar to those found in many patients with rheumatoid arthritis. Radiological examination did not reveal any calcification.

Case 3

A housewife aged 61 developed indigestion at the age of 16 which has continued in periodic attacks ever since, the symptoms being like those of a peptic ulcer; over the past few years these symptoms have improved. There had never been dysphagia until recently, when she noticed that solid particles sometimes stick in her chest, causing choking fits. All her life she has suffered from chilblains. At the age of 31 pigmentation developed in the hands and arms, which progressed and involved the chest, neck, and abdomen. In 1943, at the age of 54, she developed swelling of the ankles, breathlessness on exertion, and attacks of Raynaud's phenomena of the hands. The attacks were precipitated by cold and were typical, but it was noticed that swelling of the fingers persisted during warm weather. Her feet have been slightly affected, chiefly in that they easily become cold. The oedema of the ankles subsides completely if she rests.

Since 1943 these symptoms have all become more severe, and in addition she has developed sores on her finger-tips and mild "arthritis" of shoulders, hips, and knees. She has lost weight and has not felt well. In 1948 a right cervical sympathectomy was attempted through an anterior approach, but had to be abandoned because of a large substernal goitre which impeded access; the brachial artery was stripped in place of sympathectomy, but with no effect on the symptoms. In 1949 left cervical sympathectomy was performed, also without effect. At various times she has been treated with thyroid extract, vitamin E, and vitamin K, but with no benefit. There was no clinical evidence of thyrotoxicosis and the B.M.R. was normal.

When seen by us in 1950 she exhibited the features of acrosclerosis in their most florid form. Her fingers were swollen, and the waxy inelastic skin could not be moved over the phalanges. The tips of the fingers showed necrotic areas, which were scabbed and scarred. Her fingers were stiff and incapable of full movement. The skin of the dorsum of the hands and the forearms was thickened and inelastic. There was patchy brown pigmentation of the whole body, with a few areas of vitiligo. The skin of the face was typically affected, being smooth and waxy with a notable absence of wrinkles and furrows except for deep creases converging on the mouth, which could not be opened widely (see illustration). It is interesting that in 1949, before the diagnosis was made, the case notes record that she "looks 20 years younger than her age." She also had numerous small red spots (telangiectases) over the upper part of her body. The abdomen and feet showed a few areas of morphea. There was oedema of the ankles and feet. The chest moved well, and the lungs were clinically normal, apart from crepitations over both bases. The heart was enlarged clinically, but the heart sounds were normal and the rhythm was regular and slow. Her blood pressure was 125/75.

The blood W.R. and Kahn test were negative. The haemoglobin was 13.9 g.%; E.S.R., 17 mm. in one hour (Westergren). An E.C.G. showed normal rate and rhythm, negative T₂ and T₃, and R₃ varied from one ventricular complex to another, sometimes being well marked, at others non-existent.

A barium swallow did not reveal any hold-up to the passage of the barium cream; the oesophagus was tortuous, dilated, and showed very feeble irregular contractions.

A radiograph of the left hand showed erosion of the tips of the terminal phalanges of the thumb and second, third, and fifth fingers, and calcified deposits in the soft tissue of the tip of the thumb. A radiograph of the right hand showed erosion of the tips of the terminal phalanges of the thumb, first, second, and third fingers, and calcified deposits in the tips of the thumb and first finger. X-ray examination of the chest revealed partial collapse of both bases, substernal thyroid with displacement of trachea to left, and old resection of the fourth left rib posteriorly. On screening, the cardiac pulsations were of conspicuously small amplitude.

Photograph of Case 3, showing typical facial appearance in acrosclerosis.

Comment.—This patient shows the coincidence of Raynaud's phenomena and well-marked changes of acrosclerosis. The distribution of skin changes is typical, but in addition she has a few areas of morphea on the trunk. The oesophagus shows dilatation with diminished peristalsis, and it is therefore likely to be affected. It is probable that the heart is also involved, because the cardiac symptoms—breathlessness and oedema of ankles—accompanied the development of acrosclerosis; there is no other obvious cause for cardiac failure, and the poor movements of the heart observed on screening are compatible with this diagnosis. These details are similar to those shown by some patients described by Weiss *et al.* (1943) in whom the diagnosis was clinched at necropsy. Our patient also shows calcinosis of the finger-tips. This rare condition is not infrequently found in association with acrosclerosis (Sellei, 1931; Brody and Bellin, 1937) and the combination has earned the eponymous title of Thibierge-Weissenbach syndrome.

Case 4

An unmarried female Red Cross worker aged 58 had had attacks of whiteness of all fingers in cold weather for several years. In the winter of 1947-8 her right forefinger became differently affected, the attacks of whiteness becoming more severe and occurring in all climatic conditions, while the finger felt sore and as though there was a constriction around it. Her general health was good and her past history was clear. Her father's fingers used to go dead in his later years.

When we first saw the patient (August, 1948) slight cyanosis was present in all fingers, which were warm. The right forefinger was slightly but definitely swollen, the skin over the middle phalanx was thickened, and it was less mobile than the other fingers. The radial pulses were normal.

The blood pressure was 140/95 in both arms. Nothing abnormal was noted in the skin elsewhere or in other systems. A provisional diagnosis of acrosclerosis was made and she was kept under observation.

During the following winter (1948-9), when the symptoms were more severe, she was given a course of "priscol" (2-benzyl-4,5-imidazoline hydrochloride) without much effect. In May, 1949, she complained of stiffness and swelling of the knees. On examination these exhibited crepitus but no other abnormality. In August further joints became affected—namely, the shoulders and feet—with no abnormality except pain on movement, which was full. In October it was noted that the "arthritis" flitted from joint to joint fairly rapidly, the shoulders often being affected. At this time it was also noted that the right middle finger showed sclerodermatous changes, with swelling of the skin and limitation of movement. The other fingers were less affected but were all swollen and not very mobile. At this stage she was treated with massive salicylate therapy for two months, with some relief of joint pains but without improvement of the fingers.

Her E.S.R. has varied. At the onset of "arthritis" in August, 1949, it was 28 mm. in one hour (Westergren). In September it was 14 mm., and in October (while on salicylates) it was 35 mm. By the end of 1949 she was complaining of vague ill-health, with lassitude as the prominent symptom. She had difficulty in getting on and off buses, could not write or use a typewriter, and had difficulty in feeding herself. There was no dysphagia.

When last seen (September, 1950) there had been progression of the skin changes. All fingers were now affected, being swollen, with typical sclerodermatous skin, so that mobility was impaired. The skin changes also extended over the hands and wrists, stopping fairly abruptly at the lower ends of the forearms. The skin was not affected elsewhere; in particular she differed from the other patients in showing no changes in the face. There was no abnormal pigmentation. Her joint pains continued to flit from joint to joint, but there was no objective evidence, clinical or radiological, of joint involvement. The E.S.R. remained high, being 35 mm. in one hour (Westergren). Some of her tendons showed gross nodularity, best observed in the flexor tendons at the wrists. The nodules were not calcified as judged by radiological appearances. She had no dysphagia or other symptoms of visceral disturbance. A barium swallow showed a normal oesophagus. Screening the chest showed the heart to be slightly enlarged but pulsating normally.

Comment.—The main interest of this case is that the evolution of the disease has been watched from a very early stage, when objective changes were confined to the skin of one finger. There is no indication that the process is becoming inactive. The prior occurrence of Raynaud's phenomena and the nature and distribution of the skin changes are typical of acrosclerosis.

Discussion

This small series of cases supports the view that acrosclerosis is a disease *sui generis*, and that it differs in a number of respects from diffuse scleroderma. All four patients had Raynaud's phenomena preceding or accompanying acrosclerotic changes. Three of them had evidence of visceral involvement, the oesophagus being affected in all three and possibly the heart also in one of them.

In view of the fact that cervical sympathectomy does not relieve the symptoms of acrosclerosis or prevent its evolution, it seems important that every patient with Raynaud's phenomena should be studied with care for evidence of acrosclerosis. With respect to this, it would seem that persistence of swelling of the fingers between

attacks or after sympathetic blockage with local analgesics is a sign suggestive of acrosclerosis. Changes in the face are definite confirmatory evidence, but are easily missed unless specifically looked for; for example, our Case 2 was shown as a case of Raynaud's disease at a clinical meeting and no comments were made about her face, nor was the diagnosis questioned. Pigmentation of the skin is another sign to look for, as it is a common manifestation and one which occurs early in the course of the illness.

Joint symptoms are common, so that the disease may be confused with rheumatoid arthritis. The symptoms are of pain and stiffness, which may involve many joints. At the same time the E.S.R. is often raised and the patient suffers from vague ill-health and possibly loss of weight. On the other hand, the joints do not display any objective evidence of rheumatoid arthritis other than limitation of movement, and the radiological appearances are normal.

Summary

Acrosclerosis is a form of scleroderma in which Raynaud's phenomena are common and the skin changes are most evident in the fingers and face. Visceral involvement is also common, the oesophagus being affected most frequently.

Four cases of acrosclerosis are described. All had Raynaud's phenomena. The oesophagus was involved in three.

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At a session devoted to the discussion of inter-university relations during the first congress of the universities of the British Commonwealth to be held after the war a resolution was passed inviting official bodies such as the British Council and the various Governments to provide funds to enable members of teaching staffs on leave to travel within the Commonwealth and to encourage distinguished scholars to visit different parts of the Commonwealth. Travel grants amounting to £5,000 were made by the Council during the first year of the scheme (1949-50), and £7,000 was used in this way the following year. There are three types of award: (a) for university teachers on recognized study leave; (b) for distinguished scholars and scientists invited by universities for short visits; (c) for postgraduate research students holding research grants. Most of those awarded grants under category (a) choose to spend most of their time at one or two universities working on a specific piece of research. The second class of grants are mainly to enable experts to meet and talk with younger workers in their own field of studies. About a fortnight is generally spent at each university visited. Fifty-four universities in the Commonwealth have taken part in the scheme by sending or receiving visitors, and the demand for grants is increasing.