Antibiotic Cover.—This is of the utmost importance for the patient with congenital or rheumatic heart disease. The method of administration for out-patients must be as simple as possible to avoid default by the patient. From the results recorded here a single combined injection of soluble and procaine penicillin appears adequate to prevent subacute bacterial endocarditis. Of the 11 patients with subacute bacterial endocarditis who received dental treatment, only two appeared to have become apyrexial as a result of the removal of dental sepsis. Nevertheless, it is very important that these patients should be examined dentally, and any teeth which are the seat of apical or parodontal infection should be removed. In subacute bacterial endocarditis adequate dental treatment should always be undertaken while the patient is still on full penicillin treatment. To leave infected teeth after recovery from subacute bacterial endocarditis invites a recurrence of the infection.

Summary

A simple technique for dealing with dental sepsis in the cardiac patient is described. It has been used, with few complications, in the treatment of 313 cases at the Manchester Royal Infirmary. Emphasis is laid on the simplicity of the procedure in order to encourage the cardiac patient to have dental treatment and to avoid disorganizing the routine in a busy dental clinic.

Many patients with advanced caries were treated. This was thought to be due to the patients' fear of the consequences of dental treatment on the heart lesion, or in some cases the medical adviser did not think the patient was fit to undergo dental extractions.

A simple technique is outlined. (1) Antibiotic cover is essential. One single pre-operative injection of soluble penicillin 0.5 mega unit plus procaine 0.3 mega unit is sufficient protection against the risk of subacute bacterial endocarditis. (2) 2% lignocaine with 1/80,000 adrenaline is an effective anaesthetic. The use of adrenaline is not contraindicated. General anaesthesia is necessary in some cases and should be administered by a specialist anaesthetist under hospital conditions. (3) There is no limit to the number of extractions that can be done at any one treatment. In the series of 313 patients treated, no deterioration of the cardiac condition attributable to dental treatment occurred. This justifies the adoption of such a technique as outlined in dealing with dental sepsis in the cardiac patient.

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PERIPHERAL NEUROPATHY IN THE "COLLAGEN DISEASES"

A CASE OF SCLERODERMA NEUROPATHY

BY

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Peripheral neuropathy is well recognized as a frequent complication of polyarteritis nodosa. Lovshin and Kernohan (1948) found "clinically significant" neuropathy in 15 of the 29 cases verified at necropsy, an incidence of 52%. The incidence among the other "collagen diseases," however, is much less.

Though Harvey *et al.* (1954) did not describe a single instance of peripheral neuropathy in their 138 cases of disseminated lupus erythematosus (D.L.E.), it is probably not as rare a complication as this would suggest. Heptinstall and Sowry (1952) and Scheinberg (1956) have each reported a case of D.L.E. verified at necropsy in which a symmetrical polyneuropathy was an early and significant feature of the disease. A clinically similar case was included in the report of Hart *et al.* (1957, Case 11). In a review of the neurological complications of 100 cases of D.L.E., Clark and Bailey (1954) stated that a polyneuropathy was a complication in three. Bailey *et al.* (1956) gave their experience in more detail. Five cases were reported, two with post-mortem examinations, in which either a symmetrical polyneuropathy (four cases) and/or a monoradiculitis multiplex (two cases) was a prominent manifestation. Scheinberg's estimate, therefore, of a 1 to 2% incidence of neuropathy in D.L.E. would not seem to be unreasonably high.

Characteristic perineural inflammatory nodules occur in a high proportion of patients with rheumatoid arthritis (Morrison *et al.*, 1947), but peripheral neuropathy has been regarded as a rare manifestation. In recent years an increasing number of papers have appeared on the development of vascular lesions typical of polyarteritis nodosa in patients with rheumatoid arthritis; and though corticosteroid therapy may be responsible for this apparent increase (Smyth *et al.*, 1959) such cases may occur quite independently of therapy (Ball, 1954). In many of these cases peripheral neuropathy has been an early and prominent manifestation of the arteritis (Ball, 1954; Sokoloff and Bunim, 1957; Kemper *et al.*, 1957). Since the vascular lesion may differ from that seen in polyarteritis nodosa (Robinson *et al.*, 1953; Rose, 1960), it remains controversial whether the arteritis is a feature of rheumatoid arthritis (Sokoloff and Bunim, 1957) or signifies polyarteritis nodosa complicating rheumatoid arthritis (Ball, 1954), so that the concept of a specific rheumatoid neuropathy remains in doubt. Hart *et al.* (1957) have considered the various aspects of this problem in their report of peripheral neuropathy in 10 cases of rheumatoid arthritis.

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The paucity in the literature of accounts of peripheral neuropathy in dermatomyositis and in scleroderma suggests that these associations are rarer than any of those already described above. Kinney and Maher (1940) found at necropsy a moderate degree of demyelination of the peripheral nerves in two cases of dermatomyositis, but neither of these patients showed signs or symptoms of a peripheral neuropathy. Walton and Adams (1958) did not have a single example of a peripheral neuropathy in their series of 40 cases of polymyositis, though at necropsy one case did disclose a small area of inflammatory cells in the perineurium of a peripheral nerve. They concluded from their review of the literature that "clinical evidence of peripheral nerve involvement is lacking in the great majority of cases of polymyositis and dermatomyositis."

In a review of the visceral manifestations of scleroderma, Beerman (1955) stated that, though a number of cases of involvement of the peripheral nervous system have been reported in the older literature, these are uncommon. Leinwand *et al.* (1954), in a study of 150 cases, and Rodnan (1959), in a personally observed series of 75 cases, have not reported peripheral neuropathy in a single instance. There is, however, the unusual case of Richter (1954) in which the signs were almost exclusively those of a severe, rapidly progressive polyneuropathy. Necropsy in this case disclosed a widespread increase in the bulk of connective tissue, particularly in the retroperitoneal tissues and peripheral nerves. Richter considered this a case of scleroderma.

In view of the extreme rarity of peripheral neuropathy in scleroderma and in dermatomyositis as compared with the other members of the "collagen diseases," we considered it important to record the following case.

Case History

A housewife aged 55 was last admitted to the National Hospital on October 20, 1958, under the care of Dr. William Gooddy. There was no relevant family history. The past history showed that from the age of 23 to 26 she had been under treatment for right apical pulmonary tuberculosis. She was then well until January, 1949, when, at the age of 46, she noticed over a few days the symptoms of aching, stiffness, and swelling of the fingers of the left hand. Ten days later she had a mild rash with cervical lymphadenopathy. A diagnosis of rubella was made. This condition subsided at the end of a week, but was followed a fortnight later by an erythematous "burning" rash which affected the skin of the entire body. Generalized exfoliation occurred after 10 days and the illness subsided within three weeks. She then noticed slight weakness of the right leg with a tendency for the right ankle to turn inwards when walking. This difficulty progressed slightly over the next two months, during which time she also had intermittent mild recurrences of the rash and lost a stone (6.4 kg.) in weight.

She was admitted to a general hospital in April, 1949. On examination there was a "seborrhoeic dermatitis" of the forehead, cheeks, and chin. The fingers of the left hand were spindle-shaped, with pain and limitation of movement on flexion, and the skin was tight and shiny. There was weakness of extension of the right knee and eversion of the right ankle. The right knee- and ankle-jerks were absent. The trachea was slightly deviated to the right and there was diminished expansion of both lungs. No other abnormal physical signs were present.

The haemoglobin, total and differential white blood counts, and routine urine examinations were all within normal limits. Serum uric acid was 3.4 and 4.2 mg./100 ml. on separate occasions. *X*-ray films of the chest showed scarring and small areas of consolidation at the right apex. *X*-ray films of the hands showed a considerable degree of decalcification of the bones of the left hand.

Physiotherapy was given and the patient was discharged from hospital after one month. The strength in the leg gradually returned, but one year after discharge she developed a sensation of pins-and-needles in the distal parts of all four limbs. Soon afterwards she noticed difficulty in identifying objects by touch, and her gait became unsteady, especially in the dark. By 1952, at the time of her second admission, she was no longer able to walk unassisted. During the interval of three years she had also experienced occasional difficulty in swallowing solid food. The rash over the upper chest and cheeks had often recurred, but there had been no further joint symptoms.

Examination in 1952 revealed a thin woman with a patchy, erythematous, scaly dermatitis over the chest. The skin over the fingers of both hands was now thin and tight. The limbs were generally wasted, but power was reduced only distally. All deep tendon reflexes were greatly reduced. Moderate impairment of pain and touch sensibility was present over the hands and below the knees. Vibration and position sense were absent in the fingers and toes and moderately reduced at the wrists and knees. The pulmonary changes were as noted previously. There were no other abnormal physical signs. The patient was discharged at the end of two months on a moderate dose of cortisone, but this treatment was without benefit and was stopped three months later.

The patient was admitted to hospital on four further occasions, the last time to the National Hospital in 1958. During the interval her disease seemed to progress less rapidly than before 1952. Constant paraesthesiae in her arms and legs were present until 1956, while the recurrent skin rash and intermittent dysphagia persisted throughout. In 1956 she noticed for the first time that when her hands were exposed to the cold the fingers became stiff and numb, with a blanched or mottled blue discoloration of the skin. On warming her hands the skin became red and she had a sensation of pins-and-needles in the fingers. During the winter of 1957 this condition was so severe that she avoided, so far as possible, the out of doors and cold rooms. At no time did she have any symptoms suggestive of cardiac, pulmonary, or renal involvement.

Last Admission

On admission in October, 1958, she was very thin and wasted. There was a generalized mild increase in skin pigmentation and well-marked palmar erythema. The skin over the fingers was tight, shiny, and atrophic, while that over the forearms, abdomen, and calves was thick and doughy, with slight pitting on pressure. The skin of the left cheek was indurated and less mobile that that on the right. There was a scaly erythematous patch of dermatitis over the upper chest. The muscle tone was diminished in all four limbs, and moderate wasting and weakness were present distally. There was gross ataxia without tremor of the limbs, especially with the eyes closed. All deep tendon reflexes were absent except for very sluggish biceps jerks. Upper abdominal reflexes were present and the plantar responses were flexor. Appreciation of pain and touch gradually diminished below the elbows and knees and was absent over the hands and feet. The sense of passive movement was moderately reduced at the hip- and shoulder-joints and absent more distally. The peripheral nerves were of normal thickness. The only abnormality of the joints was slight enlargement of the proximal interphalangeal joints of both hands. The pulmonary findings had not changed and the remainder of the general examination was negative.

The total and differential blood counts, haemoglobin, and urine examinations were normal on each of her admissions.

The E.S.R. was 30 mm./hr. in 1955, but was always below 24 mm./hr. thereafter. No L.E. cells were present on examination of the peripheral blood in 1955, 1956, and 1958. In 1958 the differential agglutination test was 1 : 8 and the latex fixation and antinuclear factor tests on the blood were negative. The serum electrophoretic pattern was normal in 1956 and 1958. Liver-function tests, E.C.G., and E.E.G. were all normal in 1958. Chest *x*-ray films were unchanged when compared with those taken in 1949. Films of the hands showed only mild generalized decalcification of the bones.

In 1955 and again in 1958 a barium swallow in the supine position revealed a slightly dilated oesophagus with greatly diminished peristaltic activity in its lower half. Barium did not pass into the stomach until the patient assumed the sitting position. There was a small hiatus hernia but no area of constriction and no gastro-oesophageal reflux. The stomach and small intestines appeared normal.

In 1955 a skin and muscle biopsy from the side of the right calf showed no abnormality of the muscle, but the epidermis was thin and showed hardly any papillary bodies. There was considerable oedema of the cutis. Nerve biopsy was refused by the patient.

Electromyography of the left deltoid and quadriceps muscles in 1958 showed normal insertion activity with a decrease in the number of motor units, which were of normal shape. These findings were thought to be in favour of chronic partial denervation without evidence of muscle disease.

The patient seemed to derive very little benefit from repeated courses of physiotherapy. A second three-months course of cortisone in 1956 was without subjective or objective improvement. At the time of her final discharge from hospital in November, 1958, she had to use a wheel-chair and was in need of a great deal of assistance from others.

Comment

The distribution of sensory loss, the distal muscle weakness and wasting, and the absent tendon reflexes all indicate that the patient had a mixed sensorimotor peripheral neuropathy. That the neuropathy was an integral part of her "collagen disorder" is apparent, since its onset coincided with the beginning of her illness and its steady progression over the next 10 years was accompanied by continued activity of the disease in the skin and elsewhere.

The classification of the "collagen disorder" in this case presents certain difficulties, particularly in deciding between dermatomyositis and scleroderma. In view of the changes in the lower oesophagus (Dornhorst *et al.*, 1954) and the absence of any evidence of a primary muscle disorder we have regarded this case as one of scleroderma. All the other features, and in particular Raynaud's phenomenon, are consistent with this diagnosis with the possible exception of the recurrent, scaly, erythematous rash.

Though D.L.E. could be responsible for the skin changes, Raynaud's phenomenon, and the early joint symptoms, there is very little else to suggest this diagnosis. At no time during the entire nine years of illness was there any evidence of cardiac, renal, or serosal involvement, nor were there any changes in the formed elements of the blood or serum proteins. Repeated tests for the L.E. phenomenon were negative. Dysphagia occurs in D.L.E. but has been accounted for either by oesophagitis and ulceration (Harvey *et al.*, 1954) or possibly mediastinitis (Baehr and Pollack, 1947).

The rash, the doughy oedema of the skin of the abdomen, the sclerodermatous changes in the hands, Raynaud's phenomenon, and the abnormalities in the skin biopsy are all compatible with a diagnosis of dermatomyositis (Domzalski and Morgan, 1955). Though dysphagia is a common complaint in dermatomyositis, the changes on barium swallow are maximal in the upper rather than the lower oesophagus, as one would deduce from the distribution of striated muscle. Everett and Curtis (1957) have described "hypopharyngeal paralysis and regurgitation of barium" in six cases of dermatomyositis, while Walton and Adams (1958) have recorded "pooling of barium in the hypopharynx" in three cases of polymyositis. Though Talbott and Moleres Ferrandis (1956) state that the oesophageal changes in dermatomyositis may be indistinguishable from those of scleroderma, Orabona and Albano (1958) consider the "presence of typical visceral changes of scleroderma (particularly oesophageal) an important datum for making an exact diagnosis." In the case described there was no support from muscle biopsy of a primary muscle disorder. So, despite the unusual rash, we feel that the evidence is more in favour of scleroderma. In either disease, however, peripheral neuropathy is of such rarity as to make this case of exceptional interest.

Discussion

Neuropathy was an early manifestation in the case presented. Limited to one extremity at first, it later regressed and then developed as a symmetrical mixed sensorimotor polyneuropathy. In the 15 cases of polyarteritis nodosa with neuropathy reported by Lovshin and Kernohan (1948), the neuropathy was present initially in seven, eight took the form of a mononeuritis multiplex, seven were symmetrical polyneuropathies, and a clear-cut regression of signs and symptoms occurred in four cases. Similar clinical features of the neuropathy have been found in cases of D.L.E. The most distinctive of these features is the involvement of single or multiple nerves in an asymmetrical fashion. Nevertheless, it is only by virtue of the association of the neuropathy with the other manifestations of the "collagen disorder" that the aetiology of the neuropathy can be determined clinically.

Since the collagenous elements of the peripheral nerves are the blood-vessels and the connective-tissue sheaths around the nerve fibres and bundles, it is not surprising that the primary pathological changes have been found in relationship to these structures. Lovshin and Kernohan found the typical lesions of polyarteritis nodosa in the arteriae nervorum of all the 15 patients who had had peripheral neuropathy clinically. Infarct necrosis of nerve bundles was commonly observed in relation to the vascular damage, with diffuse degeneration of the nerves below these lesions. The authors concluded that the neuropathy was ischaemic in origin.

Involvement of the small arteries of the nerves was also present in the case of D.L.E. described by Heptinstall and Sowry (1952) and in the first of the two cases reported by Bailey *et al.* (1956). Unfortunately, no mention of infarct necrosis of the nerves was made in either of these cases. Changes in the vessels of the nerves were not present, however, in the second case

reported by Bailey *et al.* or in the case recorded by Scheinberg, (1956), though vascular lesions were present elsewhere in the necropsy material. Scheinberg concluded that in his case a bluish staining material, perhaps related to haematoxylin bodies, which lay beneath the endoneurium and perineurium was responsible for the diffuse degenerative changes in the peripheral nerves.

The only pathological report of scleroderma neuropathy is that by Richter (1954), in which there was an increased thickness of the connective-tissue sheaths of the nerves and a heavy deposition of mucoid material between them and the nerve fibres. Though the walls of the arteriae nervorum were greatly thickened, almost to the point of occlusion, no infarct necrosis of the nerves could be found. Richter proposed that the deposition of mucoid material had led to the degenerative changes in the nerves.

The pathogenesis, then, is clearly established only for the neuropathy of polyarteritis nodosa. Further necropsy studies are needed before any generalizations can be made concerning the other "collagen diseases." Regardless of the pathogenesis of the neuropathy in these other forms, however, the incidence of neuropathy among the different types of "collagen diseases" does parallel to some extent the degree of vascular involvement found in other tissues. Though vascular lesions similar to those in polyarteritis nodosa occur in D.L.E., they are usually less severe, thrombosis is rare, and smaller arteries tend to be affected (Klemperer *et al.*, 1941). Vascular changes are least severe in scleroderma and dermatomyositis. An increase occurs in connective tissue about the vessels and there is hyalinization of the media and intima with thickening of the latter and occasional obliteration of the lumen. Fibrinoid necrosis of the vessels has also been described, but as discussed by Rodnan *et al.* (1957) this change may be a result of the systemic hypertension occurring in some patients with scleroderma who have renal involvement. Moore and Sheehan (1952) have described "mucoid intimal thickening" of the intralobular arteries of the kidney, which they think may cause acute ischaemic changes in the related cortex. In general, however, changes in blood-vessels have not been considered important in the genesis of extravascular lesions in either scleroderma or dermatomyositis.

In reviewing cases in the literature of neuropathy in "collagen diseases" it was apparent that appropriate consideration was not always given to the possibility of muscle weakness, even distal, being due to a polymyositis; of changes in the hands, particularly in rheumatoid arthritis being due to the carpal-tunnel syndrome; or of the possible role of pressure neuropathies in patients confined to bed. On the other hand, it is possible that, in scleroderma, minor sensory loss and muscle-wasting due to neuropathy may be attributed to the atrophy of the skin and soft tissues.

Summary

The case of a 55-year-old woman with ten years' history of arthritis and skin lesions followed by the development of peripheral neuropathy, dysphagia, and Raynaud's phenomenon is described. It was considered that the peripheral neuropathy was secondary to collagen vascular disease, probably scleroderma.

The differential diagnosis in this patient between scleroderma and polymyositis is discussed, and the difficulties of separating the individual "collagen diseases" are indicated.

The rarity of peripheral neuropathy in scleroderma and polymyositis is emphasized in contrast to the high frequency of this complication in polyarteritis nodosa. The literature relating to the association of peripheral neuropathy and the "collagen diseases" is reviewed and the pathogenesis of the neurological lesions discussed.

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With the proportion of older workers in industry increasing it is vitally important for our economic progress that their skill and abilities are used to the utmost advantage. This is one of the main points made in *The Older Worker and his Job*, a popular and brief account of recent research in this field, and in particular of the studies reported in *Ageing and Human Skill*, by A. T. Welford. The review summarizes the advantages that come with age, such as increased experience, accuracy, loyalty, reliability. It also describes the changes, both mental and physical, which decrease individual efficiency. Suggestions for coping with the problems of ageing workers include modifying the job or a complete change of occupation. But the author emphasizes that research is far from complete and that full co-operation is necessary between those studying the subject and people in industry. (*The Older Worker and his Job*, by Hilary M. Clay. "Problems of Progress in Industry," Series No. 7. Published for the Department of Scientific and Industrial Research by H.M.S.O., price 1s. 3d., by post 1s. 5d.)