The inflammatory myopathies[1]

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The inflammatory myopathies are the commonest acquired myopathies presenting in adult life and may also occur in infancy and childhood. They are a group of conditions characterized by the presence of inflammatory infiltrates in skeletal muscle, usually in association with muscle fibre destruction. For practical purposes (Table 1) they can be subdivided into conditions due to viral, bacterial, protozoal or other microbial agents on the one hand, and those in which no such agent can be identified and in which the mechanisms of muscle damage and inflammation have yet to be defined completely.

Inflammatory myopathies due to microbial agents and parasites

Viral myositis

Influenza: While diffuse myalgia commonly precedes or accompanies the other manifestations of influenza, a postinfluenzal variety of myositis is well documented (Lundberg 1957, Middleton *et al.* 1970). This syndrome is seen in the week after an attack of influenza and is characterized by severe pain, tenderness and sometimes swelling, usually of calf muscles but sometimes involving also those of the thigh; it usually resolves spontaneously over the course of about a week. The serum creatine kinase (CK) activity is usually increased. Pathological evidence of a necrotizing inflammatory myopathy is found in some cases (Mejlszenkier *et al.* 1973), and the condition has been observed particularly in children with influenza B, A2 Hong Kong virus (Dietzman *et al.* 1976) and influenza A virus, but can also occur in adults (Congy *et al.* 1980). Influenza virus has been isolated from muscle in a case of acute polymyositis with myoglobinuria (Gamboa *et al.* 1979).

Enteroviruses: The Coxsackie B virus, and particularly B5, is typically associated with epidemic pleurodynia (Bornholm disease), a self-limiting disorder occurring usually in childhood and characterized by acute and severe pain with tenderness of the chest, back, shoulders or abdomen. A fulminant acute form of polymyositis with myoglobinuria has

Table 1. Classification of inflammatory myopathies (from Mastaglia & Walton 1982)

Due to identified infective agent		Idiopathic inflammatory myopathies
Viral:	Influenza Coxsackie A and B	Polymyositis Dermatomyositis Inclusion-body myositis Granulomatous myositis Polymyalgia rheumatica Angiopathic inflammatory myopathies (collagen-vascular disease) Nodular interstitial myositis
Bacterial:	Pyomyositis (*Staph. aureus*; *Strep. pyogenes*) Clostridial myositis	
Parasitic:	Trichinosis Cysticercosis Toxoplasmosis Sarcosporidiosis Echinococcosis Trypanosomiasis Actinomycosis	

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been linked with Coxsackie B6 virus infection (Fukuyama *et al.* 1977). Cases of acute myositis (Jehn & Fink 1980) and acute rhabdomyolysis (Josselson *et al.* 1980) associated with Echo 9 virus infection have also been reported in man. There is also a good deal of evidence to suggest that Coxsackie and Echo viruses may on occasions precipitate the autoimmune process presumed to account for polymyositis and/or dermatomyositis (*see* Mastaglia & Hudgson 1981).

Other viruses: There have also been reports of human inflammatory myopathy in patients harbouring hepatitis B virus (Mihas *et al.* 1978) and viruses of the herpes group (Norris *et al.* 1969, Schlesinger *et al.* 1978), as well as rubella virus (Hanissian *et al.* 1973) and respiratory syncytial virus (Herzberg *et al.* 1980). However, the evidence that the virus in question was the cause of the myositis in each of these circumstances is somewhat indefinite.

Bacterial myositis

Acute suppurative myositis: While suppurative myositis may complicate penetrating or crush injuries or pressure sores and has occasionally been observed in patients with pyococcal arthritis, suppurative myositis is uncommon in developed countries. In tropical and subtropical countries, however, pyomyositis with suppurative staphylococcal inflammation involving the skeletal muscles is not uncommon and is seen more often in men than in women, usually without any specific antecedent illness (Chiedozi 1979). The muscles most often affected are the glutei and quadriceps. Single or multiple muscle abscesses may occur and treatment consists of high doses of penicillin with surgical drainage. Functional recovery is usually good in such cases (*Lancet* 1978).

Clostridial myositis: Clostridium welchii produces a toxin and enzymes including collagenase and hyaluronidase which cause necrosis of muscle fibres and interstitial tissues, with vascular congestion, fibrin exudation, intense polymorphonuclear leukocytic infiltration and haemorrhage. There is evidence that clostridial toxin (Strunk *et al.* 1967) may cause discrete defects in the muscle fibre plasma membrane leading to fibre necrosis. This condition (gas gangrene) usually follows septic wounds involving extensive areas of skeletal muscle; if the infection can be controlled by antibiotics and necrotic muscle tissue is removed in its entirety, regeneration may be effective, but marked fibrosis and muscular atrophy usually result.

Other forms of bacterial myositis: Tuberculous and syphilitic myositis are now virtually unknown, though very occasionally tuberculous granulomas still occur in skeletal muscle in tropical countries. Leprous inflammation of muscle is also occasionally seen and must be considered when there is associated evidence of denervation atrophy with granulomatous lesions in intramuscular nerves (Sebille & Gray 1979).

Parasitic myositis

Trichinosis: This is the most frequent and commonest parasitic infection of muscle. The causative agent, *Trichinella spiralis*, is a nematode usually acquired by man as the result of eating incompletely cooked pork, bear meat or horse meat (Bourée *et al.* 1979). The larvae penetrate the mucosa of the small intestine, enter the lymphatics and the blood-stream and are then disseminated widely. Muscles are invaded at about the end of the first week and there is severe myalgia and tenderness of muscle, often associated with weakness, which may be generalized or limited to certain muscle groups such as the ocular muscles. Periorbital and conjunctival oedema is common and a skin eruption often occurs. There is frequently eosinophilia, and muscle biopsy (Figure 1) may demonstrate the parasites in various stages of development and encystment. An interstitial infiltrate of inflammatory cells is frequently found around muscle fibres and blood vessels (Gross & Ochoa 1979).

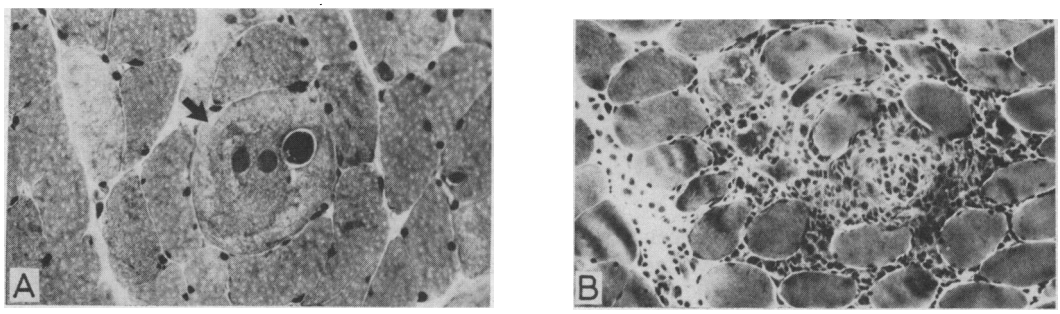

Figure 1. Trichinosis of muscle in a 35-year-old woman. A: Several parasites at different stages of development are present in a large swollen muscle fibre in the centre of the field (arrow). Gomori trichrome × 500. B: Interstitial inflammatory infiltrate consisting largely of histiocytes, lymphocytes and other mononuclear cells. Gomori trichrome ×400. (Reproduced with kind permission from Mastaglia & Walton 1982, by courtesy of Dr J Ochoa)

Cysticercosis: This condition is common in India and Eastern Europe, being less frequent in other parts of the world, and results from infestation with the encysted larval stage of the pork tapeworm *Taenia solium*. The larval parasites invade the intestine and are disseminated by the blood to all parts of the body, particularly muscle and brain. In the acute stage there is often muscle tenderness, fever and eosinophilia, but frequently there is no such illness and evidence of involvement of the muscle and of the central nervous system is only found many years later when the patient presents with a hypertrophic myopathy (Sawhney *et al.* 1976) or with epilepsy (Adams *et al.* 1965, Mastaglia & Walton 1982). Nodules are sometimes palpated in the tongue and other muscles, but in the hypertrophic form gross enlargement of multiple limb muscles may occur. Spindle-shaped cysts may be found in the interstitial connective tissue in muscle biopsy specimens.

Echinococcosis: This is very rare, even in countries in which hydatid disease is common. The cysts forming in muscle are usually solitary, large and surrounded by granulomatous infiltration with eosinophilic infiltration (Adams *et al.* 1965), but on occasions individual cysts may rupture leading to the formation of daughter cysts. When muscles are involved, those most commonly affected are the posterior trunk, inner thigh, neck and upper arm muscles.

Toxoplasmosis: Toxoplasma gondii can give a multifocal disseminated myositis and the organism may be revealed by muscle biopsy (Adams *et al.* 1965). In the foci of myositis, the necrotic fibres are surrounded and infiltrated by neutrophil leukocytes, lymphocytes and plasma cells. Pseudocysts, which are round or oval and often about 20–60 μm in diameter, containing multiple parasites, are occasionally found in otherwise healthy muscle fibres. The fact that some patients with polymyositis show serological evidence of toxoplasmosis (Hendrickx *et al.* 1979) has suggested a possible relationship between toxoplasma infection and idiopathic polymyositis. The question as to whether this is a genuine relationship remains unresolved.

Sarcosporidiosis: Sarcocystis lindemanni rarely invades skeletal muscles in man; when it does so, the condition is usually asymptomatic and the parasite may be found unexpectedly in a muscle biopsy (Adams *et al.* 1965). Rarely, the parasitic cysts, which are filled with many sporozoites and which may be 1–5 mm in length, are associated with muscle aching, slight weakness and loss of tendon reflexes.

Trypanosomiasis cruzi (Chagas' disease): This condition, indigenous to South America, is characterized by disseminated focal polymyositis, myocarditis and encephalomyelitis (Adams *et al.* 1965). In muscle, parasites are localized within individual fibres and form

small thin-walled cysts loaded with trypanosomes which may be difficult to distinguish from toxoplasma pseudocysts.

Fungal myositis

Actinomycosis may involve skeletal muscle through direct extension from a neighbouring infective focus in pleura or skin, when abscesses and fistulae discharging purulent material and containing the characteristic yellow granules composed of colonies of the fungus are often seen (Adams *et al.* 1965).

Idiopathic inflammatory myopathies

In those parts of the world in which bacterial and parasitic forms of myositis are rare, most inflammatory disorders of skeletal muscle fall into this category of illness which embraces the various syndromes of polymyositis and dermatomyositis which occur in childhood and adult life, as well as several other forms of inflammatory myopathy thought to be autoimmune in aetiology.

Polymyositis and dermatomyositis

The classification of these conditions has recently been reviewed by Mastaglia & Walton (1982), and Table 2 lists the classifications previously suggested which they considered. That of Walton & Adams (1958) and that of Barwick & Walton (1963) were largely clinical, while that of the World Federation of Neurology (1968) attempted to identify pure or uncomplicated polymyositis (Type α) which was presumed to be an organ-specific autoimmune disease, while Type β was a non-organ-specific autoimmune disease involving not only muscle but also other tissues and organs including skin; Type γ was considered separately as either an organ-specific or non-organ-specific autoimmune disease conditioned by the presence of a malignant process. The classification of Bohan & Peter (1975) was also largely clinical but implied what the authors saw as being certain pathogenetic differences between the various groups. This view was extended by Carpenter & Karpati (1981) in their recent classification which was based upon new information relating to pathogenetic mechanisms.

Table 2. Classifications of polymyositis and dermatomyositis (from Mastaglia & Walton 1982)

Walton & Adams (1958)

Group I:	Polymyositis – Acute with myoglobinuria – Subacute or chronic (childhood, early adult life, middle or late life)
Group II:	Polymyositis with dominant muscular weakness but with some evidence of an associated collagen-vascular disease; or dermatomyositis with severe muscular disability and often minor skin changes
Group III:	Polymyositis complicating severe collagen-vascular disease (e.g. rheumatoid arthritis), or dermatomyositis with florid skin changes and minor muscle weakness
Group IV:	Polymyositis or dermatomyositis complicating malignant disease

Bohan & Peter (1975)

Group I:	Isolated polymyositis
Group II:	Isolated dermatomyositis
Group III:	Myositis associated with malignancy
Group IV:	Juvenile dermatomyositis
Group V:	Polymyositis or dermatomyositis with systemic features (overlap syndromes)

World Federation of Neurology (1968)

Type α:	Uncomplicated polymyositis
Type β:	Dermatomyositis and polymyositis associated with connective tissue disorders
Type γ:	Polymyositis associated with malignancy

Carpenter & Karpati (1981)

Juvenile dermatomyositis
Adult dermatomyositis
Adult polymyositis
Inclusion-body myositis
Infantile myositis

Clinical features and diagnosis: These conditions may occur at any age from infancy to late adult life but are particularly common during the fifth and sixth decades. Women are more often affected than men (DeVere & Bradley 1975) and approximately 4–5 cases occur per million population each year (Rose & Walton 1966).

In acute cases, profound generalized muscular weakness, pain and tenderness may develop over a period of a few days with a striking increase in serum CK activity and sometimes with myoglobinuria which may occasionally be sufficiently acute to cause fatal renal failure. These patients are acutely ill with high fever, malaise, dysphagia and sometimes with associated oedema of the limbs and face, particularly in the periorbital regions, upper arms and thighs. Occasionally acute respiratory failure may occur, requiring assisted ventilation. The condition may be fatal when as acute as this, but if the patient survives the acute period, the outlook may be reasonably good except in cases associated with malignant disease (Urich & Wilkinson 1970).

In subacute polymyositis or dermatomyositis, which may occur at any age, either in association with malignancy (particularly over the age of 55) or in combination with connective tissue disease such as systemic lupus, progressive systemic sclerosis, rheumatoid arthritis or mixed connective tissue disease (particularly in early and middle adult life), the condition usually evolves over a period of weeks or months. The commonest presentation is that of non-selective muscular weakness involving pelvic and shoulder girdle musculature out of proportion to the severity of the muscular atrophy. The anterior and/or posterior neck muscles are frequently affected, but the facial and ocular muscles are involved only rarely (Arnett & Michels 1973). Occasionally the distal muscles are predominantly involved (Van Kasteren 1979). Muscle tenderness is not common and the deep tendon reflexes are often remarkably preserved (Walton 1965). The skin changes in typical cases include an erythematous rash in butterfly distribution on the face, heliotrope discolouration of the eyelids, a scaling erythematous rash over the dorsal aspect of the metacarpophalangeal and interphalangeal joints, and often tight, shiny and inelastic skin of the hands and fingers (acrosclerosis). In childhood, calcinosis is common over the heels, elbows and knuckles and is occasionally more diffuse; it can sometimes lead to focal ulceration, particularly over the knuckles.

Dysphagia, a Raynaud phenomenon and joint involvement are not uncommon in patients with subacute polymyositis, especially when associated with systemic connective tissue disease, but this is not invariably the case. A mild non-erosive inflammatory arthritis involving hands, wrists and knees occurs in some cases (Schumacher *et al.* 1979) and myocarditis and congestive cardiac failure have been described (Denbow *et al.* 1979).

The association with malignant disease is particularly common over the age of 50 and in patients with dermatomyositis. The commonest sites of cancer are the breast, ovary, uterus and colon in women, and in men the lung, prostate and colon (Barnes 1976). Other forms of carcinoma and reticulosis are also seen but are less common. The dermatomyositis which occurs in childhood is not usually associated with malignancy, but there is often an associated systemic angiopathy leading to ischaemic lesions of the gastrointestinal tract, sometimes with ulceration and perforation (Banker & Victor 1966).

In chronic polymyositis, which may not be associated with skin change, malignancy or other evidence of systemic disease, the onset may be insidious and the clinical course can extend over many years, with slowly progressive weakness and atrophy developing in distal as well as in proximal limb muscles. The response of such cases to treatment with corticosteroids or other immunosuppressive agents is often unsatisfactory and it is thought that some such cases are suffering from inclusion-body myositis (see below). There are other atypical cases occurring from time to time; thus some patients present with a facioscapulohumeral syndrome (Rothstein *et al.* 1971, Bates *et al.* 1973) and these patients must be distinguished from those cases of facioscapulohumeral muscular dystrophy of dominant inheritance in which inflammatory cell infiltration is not infrequently seen in muscle biopsy specimens (Munsat *et al.* 1972). Another unusual presentation is that of patients who present with severe localized muscle pain, swelling and tenderness, often in one

muscle group of a single limb or even in the muscles of the head and neck. These cases have been called localized nodular myositis (Cumming *et al.* 1977, Heffner *et al.* 1977). In some such cases the initial localized onset is followed by a more diffuse involvement of the musculature developing some months or years later.

Confirmation of the diagnosis of polymyositis depends not only upon the typical clinical picture but also upon the finding of a raised activity of CK in the serum (Vignos & Goldwyn 1972), an increased concentration of circulating myoglobin (Kagen 1977), the typical electromyographic changes, including short-duration myopathic potentials, positive sharp waves and fibrillation potentials (Barwick & Walton 1963, DeVere & Bradley 1975), and finally upon the finding of evidence of a necrotizing inflammatory myopathy in a muscle biopsy. It is wise to choose a moderately-affected proximal muscle for biopsy, and $^{99}Tc^{m}$ polyphosphate muscle scanning can be helpful in indicating which muscle is most suitable for biopsy (Brown *et al.* 1976). In general, it is wiser to perform an open biopsy rather than a needle biopsy, since the inflammatory changes in cases of polymyositis are often so patchy that a needle biopsy may miss characteristic and significant changes. In some cases two or even three of the diagnostic criteria listed above may be negative at any one time.

Histopathology: The histological hallmarks of polymyositis and dermatomyositis are those of muscle fibre necrosis and regeneration, along with the presence of interstitial and perivascular infiltrates of inflammatory cells (Figure 2). In cases of active polymyositis or dermatomyositis before treatment, all three of these changes are usually found, but in early, mild or partially treated cases they may not all be present. In very acute cases there may be extensive necrosis and breakdown of a large number of muscle fibres (acute rhabdomyolysis), accompanied or succeeded by profuse regenerative activity with active myoblast and myotube formation at the periphery of the sarcolemmal tubes which survive after complete muscle fibre breakdown (Mastaglia & Walton 1982). In subacute or chronic cases, necrosis may be confined to single muscle fibres which may be hyalinized or may show loss of staining in the early stages but which are later occupied by phagocytes. Necrotic fibres may contain immunoglobulins, fibrinogen, complement and albumin and these changes can be demonstrated by immunofluorescent stains. In some cases of childhood dermatomyositis, portions of a muscle fascicle or even an entire fascicle may undergo necrosis, a finding suggestive of microinfarction (Banker & Victor 1966, Carpenter *et al.* 1976). Similar massive areas of necrosis with cellular infiltration are frequently seen in the focal lesions of localized nodular myositis.

Changes in muscle fibre size and architecture are commonly seen. Perifascicular atrophy, involving both Type 1 and Type 2 fibres, is frequently observed around the periphery of the

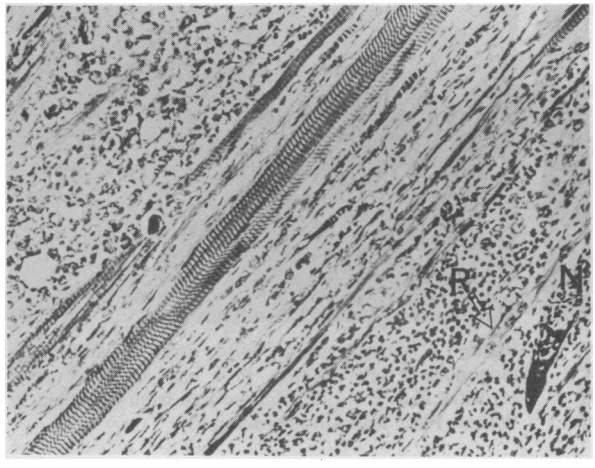

Figure 2. Necrotizing inflammatory myopathy in a 62-year-old woman with an undefined connective tissue disease. There is extensive infiltration with mononuclear cells and marked loss of muscle fibres. A necrotic fibre undergoing phagocytosis (N) and a regenerating myotube (R) are also seen. Phosphotungstic acid haematoxylin × 100. (Reproduced from Mastaglia & Currie 1971, with kind permission)

muscle fibre fasciculi (Figure 3). When small angulated fibres and groups of uniformly atrophic fibres are seen in the muscle biopsy, this may be an indication of neuromyositis or may simply indicate that some of the intramuscular motor nerves are involved in the disease process. Inflammatory cell infiltration is also perifascicular in distribution in many cases (Figure 4). Not infrequently, some muscle fibres show target or targetoid change (Jerusalem *et al.* 1980).

Ultrastructural changes: With the electron microscope, the characteristics of the muscle fibre necrosis and of other focal degenerative change in muscle fibres can be characterized more precisely. Ultrastructural studies have shown a close association between activated lymphoid cells and degenerating muscle fibres (Figure 5) and have given some support to the concept that a cell-mediated immune mechanism is responsible for the fibre damage in many cases (Mastaglia & Currie 1971).

Electron microscopy has also shown virus-like inclusions in muscle fibres in many cases; some of these resemble myxovirus or paramyxovirus nucleocapsids, while some take the form of paracrystalline arrays resembling viruses of the picorna group (Chou & Gutmann 1970, Mastaglia & Hudgson 1981). However, attempts at viral isolation in such cases have rarely been successful (Tang *et al.* 1975).

Changes in intramuscular blood vessels may also be seen, including thickening and reduplication of the basement membrane with swelling of the endothelial cells of capillaries. Sometimes, tubuloreticular inclusions are seen in the vessel walls, particularly in childhood dermatomyositis (Banker 1975, Carpenter *et al.* 1976, Oshima *et al.* 1979). Recent ultrastructural studies have also shown abnormal anastomoses between the transverse tubular system of the muscle fibres and the sarcoplasmic reticulum; these changes may account for the leakage of CK from the damaged muscle fibres (Chou *et al.* 1980).

Pathogenesis: In childhood dermatomyositis and perhaps in certain other cases occurring in adult life, there is evidence to suggest that the muscle damage may be secondary to immunologically-mediated vascular damage caused by immune complex deposition. Whitaker & Engel (1972) found deposits of IgG, IgM and C3 in blood vessel walls, and these findings have been confirmed by Behan & Behan (1977) who also found positive serum anticomplementary activity and low C4 and C1q plasma concentrations in some cases. Immune-complex vasculitis has also been reported in association with polymyositis in an adult with Waldenstrom's macroglobulinaemia (Ringel *et al.* 1979). The available evidence,

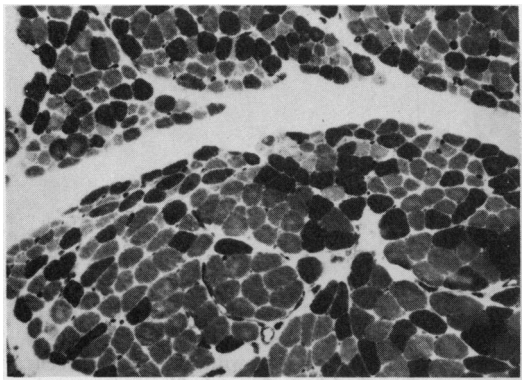

Figure 3. Perifascicular atrophy of muscle fibres (type 1 and type 2) in a case of adult dermatomyositis. Myofibrillar ATPase (pH 9.4) × 120. (Reproduced from Mastaglia & Walton 1982, with kind permission)

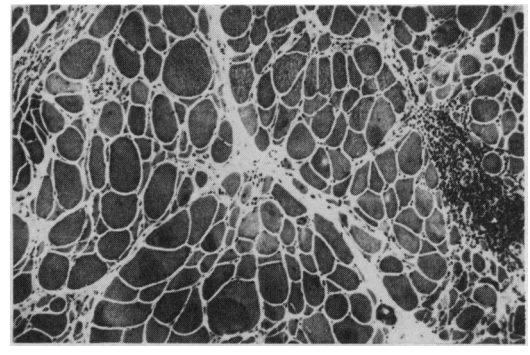

Figure 4. Small group fibre atrophy and focal mononuclear cell infiltrate in a case of adult polymyositis. H & E × 120. (Reproduced from Mastaglia & Walton 1982, with kind permission)

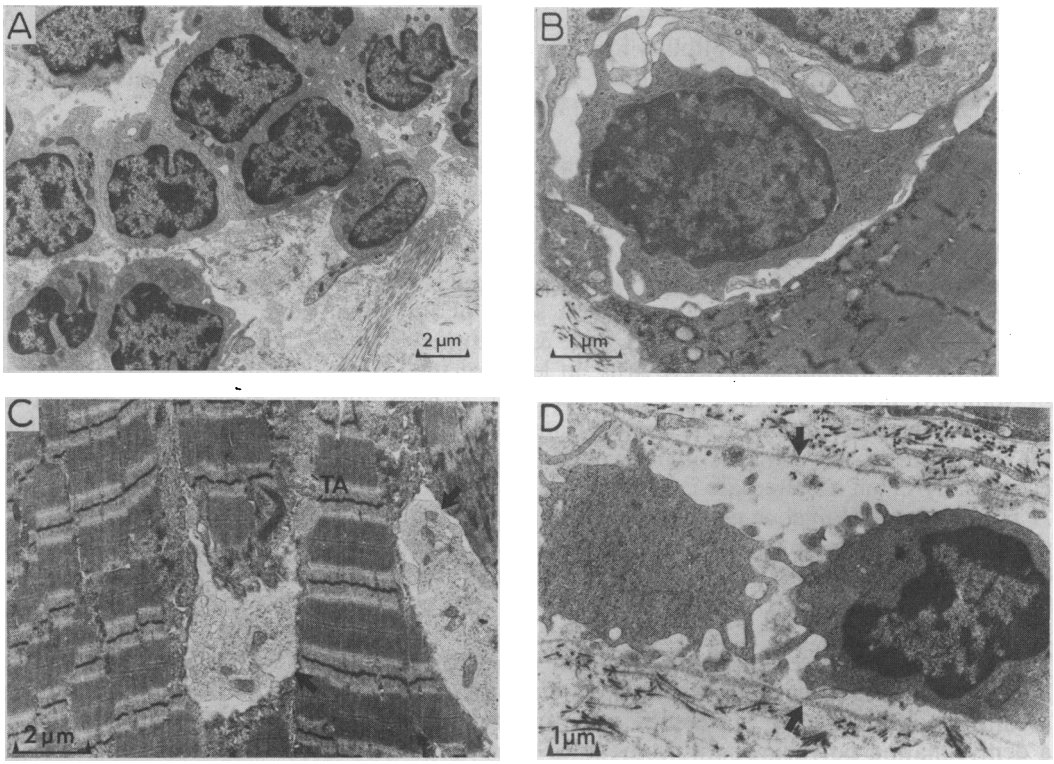

Figure 5. Lymphoid cells in cases of adult polymyositis. A: Aggregate of interstitial cells; × 6300 (courtesy of Mr B Robinson). B: Cells which have penetrated the basement lamina of a muscle fibre to lie in close proximity to its plasma membrane; × 16 200. C: Processes of cells (arrows) which have invaginated the plasma membrane of a muscle fibre to come to lie within it (emperipolesis). Honeycomb-like tubular arrays (of probable T-system origin) are present in the vicinity of one area of invagination (TA); × 9900. D: Two cells in the empty 'sarcolemmal tube' of a muscle fibre which has undergone necrosis and phagocytosis; the basement lamina of the fibre is indicated by arrows; × 12 600 (courtesy of Mr J J Fulthorpe and Dr M J Cullen). (A and B reproduced from Walton 1981, with kind permission)

however, currently suggests that in acute and subacute polymyositis and dermatomyositis occurring in adult life, the process is more likely to be cell-mediated. Thus lymphocytes from patients with polymyositis may be stimulated by muscle antigens (Saunders *et al.* 1969, Esiri *et al.* 1973) and they are also cytotoxic for cultures of human and animal muscle. There is some evidence (Isenberg & Cambridge 1982) that lymphocytes from patients with active polymyositis may elaborate soluble immunological mediators (lymphokines) when cultured with muscle homogenates. Cambridge & Stern (1981) have developed a sensitive assay of specific *in vitro* muscle cell cytotoxicity utilizing a radiolabel, ^{3}H-carnitine, which is only taken up by muscle cells in the culture. Their test for myotoxicity has confirmed that lymphocytes from patients with polymyositis are cytotoxic. Furthermore, Köhler & Milstein (1976) showed that highly specific monoclonal antibodies are produced by fusing antigen-sensitized B lymphocytes with myeloma cells. Subsequently using monoclonal markers for a variety of human lymphocyte antigens, Rowe *et al.* (1981) demonstrated large numbers of T lymphocytes in the cellular infiltrates within muscle biopsy specimens obtained from many polymyositis patients. It has also been possible to show that these T cells carry the HLA-Dr antigen and are in the active state.

All of these observations give considerable support to the importance of cell-mediated mechanisms in the aetiology of this disease. There is also a possibility that a defect of immunoregulatory mechanisms may play a part, since reduced nonspecific suppressor T cell

activity has been observed in occasional cases of polymyositis (Walker *et al.* 1982). A possible role of genetic susceptibility in some such cases has been shown by the finding of an increased incidence of the haptoglobin 2-2, C3 S-F and Rhesus c-c haplotypes in a group of patients studied in the north of England (Walker *et al.* 1982).

Treatment: For many years treatment with prednisone or related steroid drugs has been the mainstay of management of cases of polymyositis and dermatomyositis in all age groups. There is considerable evidence that this form of treatment has greatly modified the prognosis for the better (DeVere & Bradley 1975). It is usual to begin in an adult with 60–100 mg of prednisone daily in the first instance, gradually reducing the dosage according to the clinical response of the patient as measured by a series of functional tests of muscle power and mobility. Since approximately 1970 (Currie & Walton 1971) it has become customary to give in addition an immunosuppressive drug, at least for the first 6–12 months, and azathioprine in standard dosage remains the most popular. Unless there is evidence of associated malignant disease, most patients demonstrate a satisfactory response to treatment, though it may be necessary to continue maintenance therapy with steroids in a relatively small dose, either daily or on an alternate-day basis, for up to 5 years or even for longer in some cases. A recent report (Engel *et al.* 1981) has suggested that in cases resistant to treatment with steroids and immunosuppressive drugs, whole-body radiation may occasionally be dramatically successful. The results of plasmapheresis reported to date are equivocal.

Neuromyositis

This term has been used to identify cases of polymyositis or dermatomyositis in which there is clinical or other evidence suggestive of concomitant involvement of peripheral nerves (Walton & Adams 1958). The combined manifestations of an inflammatory myopathy and of a demyelinating polyneuropathy sometimes occur in patients with connective tissue disease or malignancy. It is not surprising that an autoimmune disorder involving muscle does from time to time also affect peripheral nerve, and there is no benefit in regarding neuromyositis as an independent clinical or pathological entity.

Angiopathic myositis

As already mentioned, the lesions found in skeletal muscle in some cases of childhood dermatomyositis, as well as those seen in polyarteritis nodosa and Wegener's granulomatosis, are consequent upon muscle infarction resulting from granulomatous arteritis. Here again there is little value in identifying a separate form of myositis under this heading; rather it is better to identify the nature of the primary disease responsible for the muscle damage.

Inclusion body myositis

This condition appears to be a distinctive variety of idiopathic inflammatory myopathy (Chou 1968, Ketelsen *et al.* 1977, Carpenter *et al.* 1978). It is a relatively benign and chronic form of myopathy not associated with connective tissue disease or with malignant disease, which occurs particularly in men in their sixties, though there are occasional cases reported in younger patients (Carpenter & Karpati 1981). Slowly-progressive painless weakness involves distal as well as proximal muscle groups and there is often associated dysphagia. The rate of progression is variable and some patients are severely handicapped even within two years; treatment with corticosteroids and other immunosuppressive agents is usually ineffective.

The distinctive features of this condition pathologically are, first, that bluish granular inclusions are found around the edges of slit-like vacuoles within muscle fibres stained with haematoxylin and eosin (Figure 6). These granules are removed by lipid solvents; they often show acid phosphatase activity and ultrastructurally are composed of polymorphic whorls of membrane. There are also interstitial inflammatory cell infiltrates, but the other most distinctive feature of this condition is that under the electron microscope there are masses of

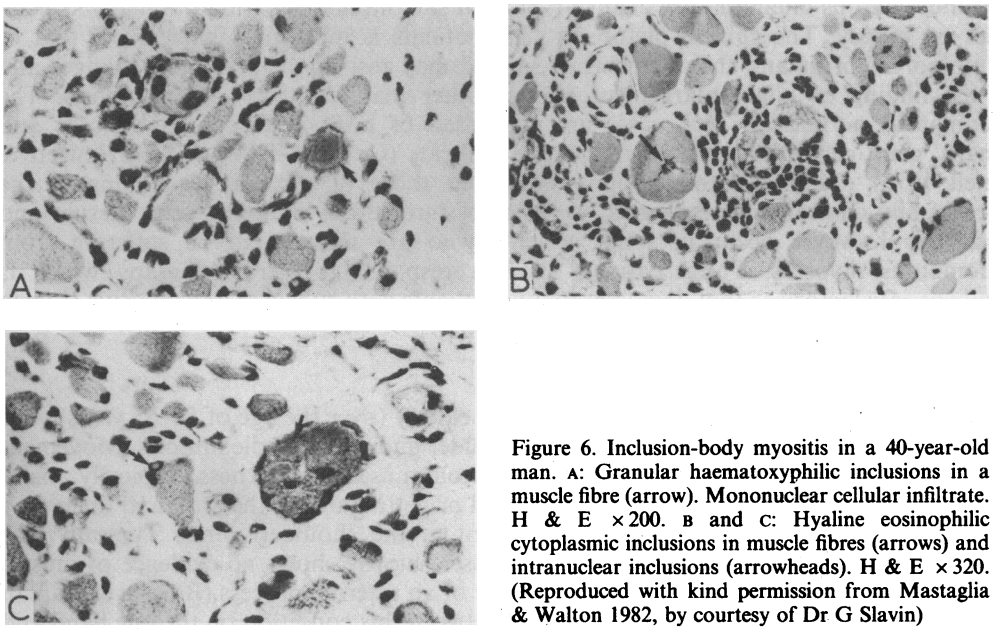

Figure 6. Inclusion-body myositis in a 40-year-old man. A: Granular haematoxyphilic inclusions in a muscle fibre (arrow). Mononuclear cellular infiltrate. H & E ×200. B and C: Hyaline eosinophilic cytoplasmic inclusions in muscle fibres (arrows) and intranuclear inclusions (arrowheads). H & E ×320. (Reproduced with kind permission from Mastaglia & Walton 1982, by courtesy of Dr G Slavin)

filaments or filamentous microtubules, 15–18 nm in diameter, within the nuclei and cytoplasm of muscle fibres. Attempts to isolate a virus from the muscle of such patients have been unsuccessful to date and the nature of the inclusions remains uncertain.

Eosinophilic polymyositis

This rare form of inflammatory myopathy occurs as a part of the systemic hypereosinophilic syndrome characterized by eosinophilia, anaemia, hypergammaglobulinaemia, cardiac and pulmonary involvement, skin changes, peripheral neuropathy and encephalopathy (Layzer *et al.* 1977). The myositis usually presents with a localized tender swelling in a muscle in one calf or thigh. There is an increase in the serum CK and often a more extensive proximal myopathy develops (Stark 1979). The condition must be distinguished from trichinosis and from other parasitic infestations of skeletal muscle. Its relationship to eosinophilic fasciitis (Thornell & Bjelle 1981) is somewhat uncertain, though the fact that in many cases of the latter type the skeletal muscle is also involved makes it probable that the two conditions are closely related. Most such cases show a satisfactory response to steroids.

Interstitial or focal nodular myositis

Focal interstitial accumulations of lymphocytes and of other inflammatory cells are commonly found in muscle biopsy samples otained from patients with a variety of collagen or connective tissue diseases and are also seen in many patients with myasthenia gravis. This finding is also common in drug-induced systemic lupus erythematosus (Mastaglia & Argov 1981). On histological grounds, the lesions of this condition merge with the more typical changes of polymyositis, and may in fact be found in less affected muscles in cases of dermatomyositis. Usually this histological change is asymptomatic and muscle weakness only appears when the infiltrating cells invade and damage muscle, when it is reasonable to regard the patient as suffering from polymyositis.

Granulomatous myositis

Asymptomatic muscle granulomas may be present in acute sarcoidosis (Silverstein & Siltzbach 1969). However, many patients with diffuse sarcoidosis show a subacute myopathy

with granulomatous inflammatory change typical of sarcoid nodules found in many skeletal muscles on biopsy. The clinical picture in such patients is indistinguishable from that of subacute polymyositis and the diagnosis of sarcoid may rest upon the biopsy changes and upon the finding of hilar enlargement and of other manifestations of sarcoidosis. The granulomatous nodules in such cases are composed of histiocytes, epithelioid cells and Langhans' giant cells with a light lymphocytic infiltrate (Gardner-Thorpe 1972, Hewlett & Brownell 1975). Granulomatous lesions similar to those of sarcoid, developing in the absence of any clinical or pathological evidence of sarcoidosis involving other tissues and organs, may however occur in some patients who are thought to be suffering from granulomatous myositis. These patients show a response to steroid therapy which is generally as satisfactory as that demonstrated by patients with subacute polymyositis (Lynch & Bansal 1973).

Polymyalgia rheumatica

This well-defined syndrome usually presents in the elderly (over the age of 50–55 years) with diffuse muscle pain and stiffness involving the shoulder and pelvic girdle muscles. Movement is restricted by pain and stiffness but there is no actual muscular weakness. Typically, many patients complain of difficulty in getting out of bed or getting out of the bath and there may be evidence of pericapsulitis restricting movement at the shoulder joints. Typically, the serum CK is normal, as is the EMG, and the muscle biopsy shows no evidence of muscle fibre destruction. Some cases demonstrate evidence of an arteritic process (Brooke & Kaplan 1972) and there is obviously a close relationship between this condition on the one hand and temporal or cranial arteritis on the other. The ESR is invariably raised and the response to steroid therapy is usually immediate and dramatic (Bird *et al.* 1979).

Conclusions

While some inflammatory myopathies are known to be due to a specific infective agent, others, such as the various forms of polymyositis and dermatomyositis, are still of unknown cause. Nevertheless, there is growing evidence to suggest that the latter conditions are due to an autoimmune process which is sometimes limited to skeletal muscle but which sometimes involves skin and other tissues or organs. While in childhood polymyositis and in some other cases the condition seems to be due to the deposition of immune complexes in the small blood vessels within the muscle, in most cases of polymyositis and dermatomyositis current evidence strongly suggests that the condition is the result of lymphocyte-mediated disordered immunity, a finding which underlines the importance of treating these cases with steroids and other immunosuppressive agents. The role of viral infection in precipitating this autoimmune process is still uncertain.

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