Dermatomyositis: observations on the use of immunosuppressive therapy and review of literature

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Summary

Seven young adults, six of whom were male, all suffering from dermatomyositis unassociated with malignancy are described. These patients were not adequately controlled with high doses of corticosteroids but all responded when immunosuppressive therapy was also given.

Introduction

Dermatomyositis (as the name suggests) is a clinical syndrome consisting of polymyositis associated with skin lesions (Pearson, 1966a; Currie and Walton, 1971). The disease is predominantly found in females and is of unknown aetiology, although disordered immunological mechanisms have been suggested (Dawkins and Mastalgia, 1973). A clear association with malignancy has been documented in patients aged 40 years or more (Vanderploeg, 1977; Curtis, Blaylock and Harrell, 1952; Bat-schwarov and Minkov, 1968).

The effects of immunosuppressive drug therapy in a group of patients with dermatomyositis whose disease had proved resistant to corticosteroids are now described and the literature is reviewed.

Patients

The clinical and laboratory data on the seven patients are summarized in Tables 1 and 2.

The response to therapy and the subsequent clinical course are briefly described as follows.

Patient N.D. was treated with corticosteroids. The course of therapy, clinical response and changes in serum muscle enzymes are summarized in Fig. 1. Intravenous dexamethasone was discontinued at the nineteenth week and by the end of the twenty-first week the dose of prednisolone was reduced to 10 mg/day.

The patient was discharged at the end of the twenty-fourth week.

One year later, the patient had a relapse, the subsequent course and response to treatment are summarized in Fig. 2. Methotrexate was discontinued after 14 weeks and the daily dose of prednisolone gradually reduced to 2.5 mg/day at the end of the seventeenth week. At this time the patient was clinically very much improved.

Patient M.B. had a cervical sympathectomy for severe Raynaud's phenomenon of the hands but showed no improvement. One month after surgery, the characteristic skin rash and progressive generalized muscle weakness of dermatomyositis developed. The diagnosis was confirmed by laboratory tests as outlined in Table 2. The course of the disease and the response to treatment are illustrated in Fig. 3.

Two years later, the patient had muscle aches, tired easily and had a recurrence of facial discoloration and fever. Muscle enzyme levels were

TABLE 1. Clinical data for seven patients with dermatomyositis

Patient	Age (years)	Sex	Duration of disease	Skin lesion	Muscle weakness*	Muscle wasting	Myalgia	Approximate weight loss	Other clinical features
N.D.	26	Male	8 weeks	Lilac discoloration of eyelids with peri-orbital oedema. Erythematous rash: neck, chest, and dorsum of hands.	Generalized, predominantly proximal grade 1/5	Generalized, predominantly proximal	Present, with muscle tenderness	20 kg	Dysphagia. Generalized joint pain. Intermittent pyrexia. Tachycardia.
M.B.	25	Male	3 months	Lilac discoloration of face. Widespread blotchy erythematous macular rash.	Generalized, predominantly proximal grade 1/5	Generalized, predominantly proximal	Present, with muscle tenderness	10–12 kg	Raynaud's. Dysphagia. Discharging ulcers of finger tips.
A.M.H.	29	Male	8 months	Lilac discoloration of face with peri-orbital oedema. Erythematous rash over knuckles.	Generalized, predominantly proximal grade 1/5	Generalized	Present, with muscle tenderness	15 kg	Dysphagia. Raynaud's. Pyrexia. Tachycardia. Fixed flexion of both knee joints at 45°. Swelling of both knee and wrist joints. Hair loss.
M.N.S.	28	Male	6 months	Puffy lilac discoloration of face. Macular erythematous rash on the limbs.	Generalized, predominantly proximal grade 2/5	Generalized, predominantly proximal	Present, with muscle tenderness	10–12 kg	Joint pain in the hands, elbows and knees.
E.H.	28	Male	10 weeks	Erythematous macular rash, dorsum of the hands, peri-ungual erythema.	Generalized, predominantly proximal grade 2/5	Generalized, predominantly proximal	Present, with muscle tenderness	18–20 kg	Myocarditis. Hepatomegaly. Dry cough. Intermittent pyrexia. Swelling and pain of small joints of the hands.
M.A.I.	30	Male	9 months	Lilac discoloration of face.	Generalized, predominantly proximal	Generalized, predominantly proximal	Present	12–15 kg	Dysphagia. Paraesthesiae of hands and feet. Polyarthralgia.
M.M.	26	Female	1 year	Erythematous rash over trunk and limbs.	Generalized, grade 2/5	Generalized, predominantly proximal	Present	Some initially.	Was on steroids for 1 year. Dyspnoea on exertion. Generalized arthralgia ulceration over bony prominences at elbows, knees and hips. Generalized osteoporosis.

* Muscle power.

TABLE 2. Laboratory data for seven patients with dermatomyositis

Patient	Muscle		Skin biopsy	Muscle enzymes			WBC (cells/l)	ESR (mm/first hour)	Pulmonary function test
	Biopsy	Electromyography		Creatine kinase ($\mu\text{m/ml}$)	Lactate dehydrogenase ($\mu\text{m/ml}$)	Aspartate transaminase ($\mu\text{m/ml}$)			
N.D.	Positive	Positive	Positive	182	255	67.2	11.4×10^9	30	Restrictive defect
M.B.	Positive	Positive	Positive	390	380	96	12.6	56	
A.M.H.	Positive	Positive	Not done	115.7	255	18.3	12.0	37	
M.N.S.	Positive	Positive	" "	120	240	19.2	5.3	20	
E.H.	Positive	Positive	" "	2000	420	76.8	12.4	64	
M.A.I.	Positive	Positive	" "	97.5	120	48.0	11.6	22	
M.M.	Positive	Positive	" "	65.5	72	5.75	10.2	24

FIG. 1. (Patient N.D.) Changes in the muscle power, pulse rate and serum muscle enzymes during the first course of treatment with oral prednisolone and intravenous dexamethasone. Creatine kinase - - - -; Lactate dehydrogenase —; SGOT aspartate transaminase.....

normal. Prednisolone was increased to 60 mg/day. The patient developed back pain and an X-ray showed collapsed lumbar vertebrae. Prednisolone was stopped and cyclophosphamide in daily doses of 100 mg produced symptomatic relief.

Patient A.M.H. was begun on daily oral doses of 60 mg prednisolone. Serum muscle enzyme had

returned to normal in three weeks and the temperature settled after 5 weeks. Despite high doses of prednisolone over a period of eight weeks, muscle power showed only slight improvement. Because of this, intravenous injections of 50 mg methotrexate were given every 5 days for 12 weeks and subsequent improvement of muscle power enabled the patient

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FIG. 2. (Patient N.D.) Changes in the muscle power, pulse rate and serum muscle enzymes during the second course of treatment with intravenous methotrexate, after relapse. Creatine kinase ----; Lactate dehydrogenase ———; SGOT aspartate transaminase ·····.

FIG. 3. (Patient M.B.) Changes in the muscle power, pulse rate and serum muscle enzymes during the course of treatment with prednisolone and intravenous methotrexate.

FIG. 4. Extensive skin ulceration due to intravenous methotrexate.

to walk. During this time, the patient also received prednisolone which was continued, after methotrexate was stopped, in a maintenance dose of 10 mg/day.

Patient M.N.S. started oral corticosteroid therapy in a daily dose of 80 mg prednisolone. Since there was only slight improvement in the patient's clinical condition, methotrexate was begun after 2 months in gradually increasing doses of 5 to 50 mg/week by intravenous injection. Five weeks after beginning methotrexate, the patient developed necrotic skin ulceration (Fig. 4) which healed when methotrexate was discontinued over a period of 3 weeks, by which time the muscle power had improved considerably. For maintenance immunosuppressive therapy, cyclophosphamide 100 mg orally/day was substituted for intravenous methotrexate which had caused recurrence of the skin ulceration when it was given again to the patient after the ulcers had healed.

One year after admission, the patient was well and continued to take 7.5 mg prednisolone in addition to cyclophosphamide therapy.

Patient E.H. had a severe myocarditis with

cardiomegaly and early heart failure in addition to other features of dermatomyositis. After 8 weeks, there was no significant improvement with 80 mg prednisolone, and cyclophosphamide 400 mg/day was begun. Four weeks later, muscle power had improved and myalgia had disappeared. The heart size had returned to normal and there were no signs of heart failure.

Four months later the patient's condition relapsed. At that time, the patient was receiving 10 mg of prednisolone and 100 mg cyclophosphamide/day. Increasing the dose of the latter to 300 mg/day brought about an immediate improvement. Two years after admission the patient's condition was satisfactory and he continued to take 10 mg prednisolone alone.

Patient M.A.I. was initially thought to have myasthenia gravis until he developed skin lesions typical of dermatomyositis. Laboratory tests confirmed the diagnosis (Table 2).

When the patient failed to respond to 80 mg prednisolone daily after 10 weeks, intravenous injection of methotrexate was begun, beginning with

FIG. 5. Extensive soft tissue calcification in a female with dermatomyositis.

a dose of 5 mg and increasing the weekly dose gradually to a maximum of 50 mg. Six weeks later, the patient showed marked improvement, and he was discharged from hospital on 15 mg prednisolone/day. The patient has remained well on this dose for 3 years.

Patient M.M., female, aged 26 years, had been treated with 20 mg prednisolone for 12 months without effect. On admission to hospital the patient was confined to bed and had severe bed sores. X-rays of her limbs showed extensive calcification of soft tissues (Fig. 5). Laboratory tests confirmed the diagnosis of dermatomyositis (Table 2).

Prednisolone was begun in a daily dose of 60 mg and increased by 20 mg after 2 weeks and 1 month. Muscle power improved only slightly from grade 2/5 to 3/5 (British Medical Research Council, 1943). Intravenous methotrexate was begun in a weekly dose of 5 mg gradually increasing to 50 mg/week. The dose of prednisolone was reduced to 15 mg/day and after 6 weeks the patient was able to climb stairs. The patient has remained well for 2 years.

Comment

The seven patients described all failed to respond adequately to high doses of corticosteroids over a period of 2 months. Most authorities consider that high doses of corticosteroid are effective in the majority of patients with dermatomyositis and especially so when the disease is acute (Winklemann *et al.*, 1968). However, there are a small number of patients who do not respond to such therapy and who improve when immunosuppressive drugs are added to a corticosteroid regimen (Currie and Walton, 1971). The patients described above would appear to fall into this category, but there is no definite proof that the immunosuppressive drugs were responsible. It is very easy to fall into the *post hoc (ergo) propter hoc* fallacy, and it cannot be excluded that the patients might have improved anyway. However, the authors are reasonably confident that if high doses of corticosteroid drugs do not improve the patient's condition after 6–8 weeks of treatment, immunosuppressive drugs should be added. In view of the many possible side effects including late effects such as neoplasm (Burnet, 1967; Editorial, 1972), they believe that immunosuppressive drugs should only be used after an adequate trial of corticosteroid therapy.

Historical review

Dermatomyositis was originally described by Wagner (1887) and by Unvericht (1887). Later, it was thought to be associated with metabolic defects of infection, endocrine dysfunction and allergy (Pick, 1935; Turner, 1937; O'Leary and Waisman, 1940; Holmes, 1948; Wedgwood, Cook and Cohen,

1953), and tuberculosis was thought to be another causative factor (Grunke, 1926); associated malignancy was suggested by Sterz (1916) and Kankeleit (1916) and was present in 12.9% of cases reviewed by Shuermann (1951).

Aetiology and pathogenesis

Evidence is accumulating that cell-mediated immunity plays a central part in the pathogenesis of polymyositis (Haas and Arnason, 1974; Esiri, MacLennan and Hazelman, 1973; Johnson, Fink and Ziff, 1972). Dawkins and Mastalgia (1973) suggested that the cellular immune response was specifically directed at muscle cells. There is also evidence that humoral immune response has an important role in the pathogenesis of dermatomyositis (Wolf, Adelstein and Sharp, 1977; Nishikai and Homma, 1977; Rechlin and Mattioli, 1974). Whitaker and Engel (1972) found IgG, IgM and C3 deposition in the vessel walls of all nine patients with childhood dermatomyositis; Lisk and Zweman (1976) reported increased circulating IgG levels in patients with dermatomyositis. Patients with dermatomyositis and agammaglobulinaemia have been described (Gottorf, Smith and Sugar, 1972; Guillian, 1974). Virus involvement has also been claimed as an aetiological factor (Hashimoto *et al.*, 1971; Sato *et al.*, 1971; Chou and Gutman, 1970; Chou, 1968). Kagen, Limball and Christian (1974) noted serological evidence of toxoplasmosis among patients with polymyositis. Familial incidence of polymyositis–dermatomyositis, has also been described (Lewkonja and Buxton, 1973; Christianson, Brunsting and Perry, 1956). Polymyositis was recently reported following penicillamine therapy (Fernandez, Swinson and Hamilton, 1977) and a case of hereditary complement C2 deficiency and dermatomyositis was reported by Leddy *et al.* (1975).

Incidence

Pearson (1966a) described a female to male predominance of 2:1, but a male to female predominance of 3:1 if malignancy was associated. The disease was commoner in adults than in children, with a peak incidence at the fifth to sixth decade. Pearson saw one patient with polymyositis per million of the population annually. Age-adjusted incidence rate for hospital-diagnosed polymyositis was 5 cases/10⁶ of the population annually over a 22-year period. Incidence was highest in Negro females according to Medsger, Robinson and Masi (1971), and Barnes and Mawr (1976) emphasized the female predominance in dermatomyositis. Polymyositis–dermatomyositis accounted for 22.6% in a group of 186 patients with muscle disease (Fessel, 1973). The group with definite dermatomyositis described in this article and which has a predomi-

nance of male over female ratio, does not conform to the previously described bi-modal distribution of female dominance with a peak incidence in the third to fourth decade.

Clinical features

Muscular weakness and characteristic skin rash are the classical features. The muscle weakness, predominantly proximal and symmetrical with pain and tenderness, progresses during weeks or months. Constitutional symptoms may be severe, leading to death in a few days or weeks (Pearson, 1966b). The rash includes lilac discoloration of the upper eyelids, and peri-orbital oedema; Gottron's sign consists of scale erythema and dusky red patches or linear streaks over the knuckles, elbows, medial maleoli, neck, face, forehead and upper chest and back, with dermal atrophy (Bohan and Peter, 1975). The rash may appear initially with the muscle disease developing later (Krain, 1975). Dysphagia, with the food remaining at the upper part of the oesophagus occurs; there may also be aperistalsis of the whole oesophagus. Arthralgia is common. Raynaud's phenomenon is present in 30% (Pearson, 1966a) or less (Winkleman *et al.*, 1968). De Vere and Bradley (1975) noted that dysphagia occurs in 28%, arthralgia in 32% and Raynaud's phenomenon in 55% of cases of polymyositis. The commonest symptoms in children are muscular weakness, stiffness, fatigability and characteristic skin rash (Hansen and Farnreich, 1967). Development of calcinosis in subcutaneous tissue or muscle may indicate a favourable prognosis in the childhood type. Calcification is more common after a severe episode of acute myositis and in childhood dermatomyositis (Pearson, 1971); it developed in 50% of both treated and untreated children with polymyositis and dermatomyositis in the Rose (1974) series. Calcification occurs with normal levels of inorganic ions of calcium and phosphorus in the extracellular fluids owing to alteration of the tissues or loss of local inhibition of calcification such as tissue protein-polysaccharides or inorganic pyrophosphate in the extracellular fluids (Mills, 1971). Respiratory muscle weakness may occur and lesser skeletal muscles may also become involved including cricopharyngeal, facial, extra-ocular and distal limb muscles (Porubsky, Murry and Pratt, 1973; Bates, Stevens and Hudgson, 1973; Saunders, Huntley and Sharp, 1973; Sanger and Kirby, 1973). Interstitial pneumonia (Degos, Civatte and Belaich, 1971), pulmonary fibrosis, asymptomatic or accompanied by acute febrile pneumonia (Frazier and Miller, 1974; Schwarz *et al.*, 1976). Pulmonary involvement could be fatal (Park and Nyhan, 1975). Myocardial involvement with cardiac failure (Babka and Pepine, 1973) or with arrhythmia and heart block (Schaum-

burg, Nielson and Yurchok, 1971) have been reported. It has been recorded that ophthalmoplegia and retinopathy can occur with dermatomyositis (Susac, Garcia-Mullen and Glaser, 1973; Harrison, Frenkel and Grossman, 1973; Fruman *et al.*, 1976). Erythema of the distal nail fold associated with telangiectasis (Fitzpatrick, Arndt and Clark, 1971). Bluish-red plaques around the base of the nails and diffuse redness and shininess of the nail folds (Rook, Wilkinson and Ebling, 1968) and peri-ungual erythema and linear telangiectasis on the cuticle and the base of the nails (Braverman, 1970) are seen in almost all cases. The nail fold changes are related to the serum enzymes in some patients (Samitz, 1974). The association of amyloidosis with dermatomyositis has been reported (Zilko and Dawkins, 1975).

Classification

Group I: Primary idiopathic polymyositis.

Group II: Primary idiopathic dermatomyositis.

Group III: Dermatomyositis (or polymyositis) associated with malignancy.

Group IV: Childhood dermatomyositis (or polymyositis) associated with vasculitis.

Group V: Polymyositis or dermatomyositis with associated collagen vascular disease.

Diagnostical criteria

Although there are no generally accepted criteria for the diagnosis of dermatomyositis, five criteria could be used (Bohan and Peter, 1975):

1. The symmetrical weakness of limb girdle muscles and anterior neck flexors progressing over weeks or months with or without dysphagia or respiratory muscle involvement.
2. Characteristic muscle biopsy.
3. Raised serum sarcoplasmic enzymes.
4. Electromyography.
5. Characteristic skin lesion.

When the rash is present with three or four criteria the diagnosis is definite, rash with two criteria makes the diagnosis a probable one, and a possibility if the rash accompanies one criterion. The degrees of muscle weakness are classified into six stages (British Medical Research Council, 1943):

0 – no contraction, 1 – flickering or trace of contraction, 2 – active movement with gravity eliminated, 3 – active movement against gravity, 4 – active movement against gravity and resistance, 5 – normal power.

Laboratory findings for the diagnosis of dermatomyositis are summarized in Table 3. The differential diagnosis of dermatomyositis is shown in Table 4.

TABLE 3. Abnormal laboratory tests, with their clinical significance in patients with dermatomyositis

Investigation	Findings	Comment
Serum muscle enzymes	<p>Raised sarcoplasmic enzymes in the serum of the following:</p> <ul style="list-style-type: none"> – Creatine phosphokinase (the most reliable (Vigos, 1972)) – Aldolase. – Lactate dehydrogenase. – Transaminases (aspartate, alanine). 	<p>These enzymes could be found increased also in:</p> <ul style="list-style-type: none"> – Motor neurone disease – Muscle dystrophies – Endocrine myopathies – Toxins – Infection – They may be normal in severe muscle atrophy
Electromyography	<p>Trial of:</p> <ul style="list-style-type: none"> – Polyphasic short small motor unit potentials. – Fibrillation potential. – Bizarre high frequency repetitive discharges (Marinacci, 1965; Lambert <i>et al.</i>, 1954) 	
Muscle biopsy	<ul style="list-style-type: none"> – Muscle neurosis, phagocytosis, large vesicular nuclei and prominent nucleoli. – Type I and II muscle fibre atrophy, especially perivascular with internal migration of nuclei. – Fibre size variation and vacuolization. – Mononuclear inflammatory cell infiltration. – Perifascicular atrophy. – Capillary damage and undulating tubules in muscle, capillary endothelium in all childhood forms but only in some patients with adult type dermatomyositis (Carpenter <i>et al.</i>, 1976). 	<ul style="list-style-type: none"> – True necrotizing vasculitis may be seen in childhood form (Thomson, 1968). – Massive muscle necrosis and absence of inflammation if there is accompanying malignancy (Urich and Wilkinson, 1970).
Skin biopsy	<ul style="list-style-type: none"> – Poikiloderma (epidermal liquefaction of basal cell layer and vascular dilatation (Janis and Winkelman, 1968). – Changes in the involved skin resemble those observed in systemic lupus erythematosus. – Mucin deposits in the form of acid mucopolysaccharides (Alcian blue reaction), in the involved and non-involved skin. 	<p>These changes tend to confirm the diagnosis in the presence of a compatible clinical history.</p>
Capillaroscopy	<p>Dilated irregular tortuous vessels in the nail folds and cuticular thickening and hyperkeratosis with or without erythema (Samitz, 1974).</p>	
^{99m} Tc phosphate	<p>For evaluation of extent and severity of calcinosis (Sarmiento <i>et al.</i>, 1975).</p>	

TABLE 4. Differential diagnosis of a patient with dermatomyositis

Lesion	Muscle disease
Dystrophies	<ul style="list-style-type: none"> – Pseudohypertrophic (Duchenne) – Limb girdle (Erbe)
Granulomatous	<ul style="list-style-type: none"> – Sarcoidosis
Endocrine	<ul style="list-style-type: none"> – Thyrotoxicosis – Myxoedema – Hyperparathyroid – Cushing's disease – Diabetes mellitus
Metabolic	<ul style="list-style-type: none"> – Periodic paralysis
Glycogenesis	<ul style="list-style-type: none"> – McArdle's syndrome (type V)
End-plate lesion	<ul style="list-style-type: none"> – Myasthenia gravis
Infection	<ul style="list-style-type: none"> – Influenza – Rubella – Trichinelliasis – Trypanosomiasis – Schistosomiasis
Vaccination	<ul style="list-style-type: none"> – Rubella vaccination
Neurone lesion	<ul style="list-style-type: none"> – Motor neurone disease – Progressive muscle atrophy of infancy (Werdnig-Hoffman) and early adult spinal muscle atrophy (Kugelberg Wellander)
Drugs	<ul style="list-style-type: none"> – Corticosteroids – Penicillamine – Clofibrate – Alcohol
Rhabdomyolysis	<ul style="list-style-type: none"> – Strenuous exercise – Heat stroke – Crus injury – Malignant hyperpyrexia – Poisoning by certain sea snakes
Unknown	<ul style="list-style-type: none"> – Polymyalgia rheumatica

Malignancy and dermatomyositis

Cases of dermatomyositis complicated by malignancy tend to be reported more often than uncomplicated ones. Malignancy has been reported as occurring in 15–52% of all cases (Rose and Walton, 1966; Barwick and Walton, 1963; Arnudell, Wilkinson and Haserick, 1960) and as much as 71% in men over the age of 50 years (Shy, 1962). Myositis and malignancy follow within a year of each other; the most common malignancy being a tumour of the ovary and stomach; the least common is that of the colon or rectum. Dermatomyositis patients with malignancy tend to be older than those with dermatomyositis alone, and younger than those with cancer alone (Barnes and Mawr, 1976).

The association between malignancy and dermatomyositis has been overestimated. Bohan and Peter (1975) thought that the diagnosis of the one facilitates the diagnosis of the other, increasing the double diagnosis and discrepancy between in-patients and the general population.

Not one of the present seven cases had associated malignancy.

Treatment

To date (1977), there is no report of a controlled study carried out in the treatment of dermatomyositis particularly in acute life-threatening cases (Pearson, 1963) and no differentiation made in the treatment of dermatomyositis and polymyositis. Most investigators feel that corticosteroids are highly effective (Maulder *et al.*, 1963) other than those due to unresectable carcinoma (Pearson, 1969; Winkelman *et al.*, 1968). The treatment of underlying malignancy is claimed to improve the myopathy (Arnudell *et al.*, 1960; Copeman and Alexander, 1967).

In 1940, O'Leary and Waisman reported a 50% mortality rate in untreated cases. Rose and Walton (1966) reported only a 14% mortality rate where steroids were used; whereas Winkelman *et al.*, (1968), reviewing the records of 289 patients, found equal remission and mortality rate in both steroid-treated and untreated groups. This discrepancy could be due to lack of definite criteria in the treated cases. It is claimed that steroids are effective in childhood dermatomyositis (Sullivan *et al.*, 1972). Serious side effects from steroids in polymyositis are claimed to be few (Pearson, 1963b).

Age, sex and race as well as duration of disease did not correlate with steroid resistance (Arnett *et al.*, 1973) which was defined by Metzger *et al.* (1974), as lack of clinical response after a 2–3 months' daily dose of 40–80 mg prednisolone.

To date, various immunosuppressive drugs have been used in the treatment of dermatomyositis, including thioguanine, 6-mercaptopurine, azathioprine and oral methotrexate (Demis, Brown and Crosby, 1964; Schirren, 1966; McFarlin and Griggs, 1968; Haas, 1973; Benson and Aldo, 1973). Bailin *et al.* (1975) and Hurd (1973) claimed that methotrexate is a potent cytotoxic and immunosuppressive drug; Hersch, Wong and Freireich (1966) have emphasized its anti-inflammatory action. Malaviya, Many and Schwartz (1968) successfully treated four patients resistant to prednisolone with intravenous methotrexate. By intermittent intravenous regimen, high portal concentration of methotrexate and hepatotoxicity are minimized (Metzger *et al.*, 1974a; Decker, 1973). Seven patients did not respond to azathioprine, cyclophosphamide and to thoracic duct drainage, subsequently four of them responded

favourably to methotrexate (Metzger *et al.*, 1974a). Methotrexate and azathioprine were recently reported as being effective in acute childhood dermatomyositis (Jacobs, 1977). Prolonged treatment with immunosuppressive drugs may lead to malignancy (Walpolf, 1958; Burnet, 1967). Fifty cases of methotrexate lung disease, including three deaths, have been reported (Filip *et al.*, 1971; Goldman and Marchella, 1971). Testicular and ovarian dysfunction, fetal abnormalities and haemorrhagic cystitis are caused by cyclophosphamide therapy (Warne, Fairly and Hobbs, 1973). Folic acid antagonists are abortifacient (Thiersch, 1952). There is still a possibility of liver cirrhosis and fibrosis developing in patients on an intermittent schedule of methotrexate therapy (Schein and Winokur, 1975). However, promising preliminary results with antilymphocyte globulin have recently been reported (Denman *et al.*, 1976).

Prognosis

Although mortality and morbidity rates were reduced among patients in the acute stages of childhood dermatomyositis receiving high doses of adrenocorticosteroids, late progression appeared to be independent of initial therapy (Miller, 1973). However, there is evidence that over-treatment with corticosteroids may be a factor in the chronicity of the disease with failure of adequate long-term response in children (Dubowitz, 1976). With modern management the mortality rate in childhood dermatomyositis has been reduced from 30% to a maximum of 10% (Jacobs, 1977). Rose (1974) found that in childhood dermatomyositis the patients who were treated with corticosteroids within one to six months after the onset of their disease had a short period of severe disability and that the patients who were not treated had a longer period of severe disability but made a good recovery eventually. Steiner *et al.* (1974) reported regression of calcinosis following the use of disodium etidronate (a diphosphonate), while Metzger *et al.* (1974b) had no success with the same drug.

Studying life table survivorship of 124 patients, Medsger, Robinson and Masi (1971) found no difference in survival between males and females, those with polymyositis and dermatomyositis, or between those treated with or without corticosteroids. They found a significant reduction in survivorship among patients with dysphagia and in those with a greater degree of muscle weakness among Negroes generally and among other adults aged 50 years and over. According to Krain (1975), the prognosis is poor when skin lesions persist in spite of therapy in patients with pulmonary fibrosis.

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