POLYMYOSITIS SYNDROMES

I. Classification of Polymyositis Syndromes. Although electron microscopic (1) and light microscopic (14) evaluation of muscle changes have failed to show consistent differences in the different clinical varieties of polymyositis, the clinical classification (2,3) of these syndromes is useful in predicting response to treatment and ultimate prognosis.

A. Group I. Classical Polymyositis with minimal skin changes and few features of the other collagen diseases. About 75% of this group responds to steroid therapy. It has a low incidence of associated malignancy and includes most children with the disease.

		Barwick & Walton (2)	Ziff et al
Acute with myoglobinuria		0	0
Subacute or chronic	in childhood	3	7
	in early adult life	3	5
	in middle or late life	11 [3]*	12

*malignancy

Case 1. [redacted] This 35 CM was admitted on [redacted]-65 with a 6 month history of insidious increase in proximal muscle weakness and atrophy. No muscle tenderness was noted, but he showed diffuse erythema of the skin of the face. ESR = 8, WBC = 18,000, SGOT = 221, CPK = 6.7, Aldolase = 25, EMG = "positive for polymyositis," muscle biopsy = "consistent with polymyositis or dystrophy." He was begun on 60 mg prednisolone with decrease in serum enzymes toward normal and significant improvement in muscle strength. However, he developed diabetes and repeated attempts were made to reduce his steroid dosage. This led to a course characterized by repeated flare-ups of muscle weakness and abnormal rises of SGOT. Enlarged heart, gallop, PAC's and pericardial effusion appeared. EKG was consistent with myocardial infarction. Cardiac symptoms subsided on 60 mg prednisolone/day. In mid-1967 following an exacerbation, restitution of steroids to 40 mg/day failed to depress disease activity, so 6-MP (1.5 mg/kg) was begun. Within 10 days marked improvement in strength and return to normal of SGOT occurred. However, bacterial pneumonia forced withdrawal of 6-MP and he has done well on prednisone alone since (now 12.5 mg/day). He has residual atrophy of about 50% of the shoulder girdle musculature, but now manages to climb the stairs at the Cotton Bowl to observe, vicariously, others flex their muscles.

Case 2. [redacted] This 44 CF was admitted on [redacted]-68 with a one-month history of dysphagia and respiratory muscle weakness. A breast nodule and early pneumonia were found on admission with profound proximal muscle weakness of all extremities. Erythematous scaling was noted over the knuckles and sl. swelling of the cuticles was present. SGOT = 1,006 and EMG compatible with polymyositis. It was assumed that she had carcinoma of the breast, but biopsy was benign adenoma. Respiratory paralysis, bilateral pneumonia and wound dehiscence delayed onset of high dosage steroids until she had been in the hospital two weeks and had become critically ill. Then 80 mg prednisolone/day was begun with rapid improvement. Within 4 weeks, SGOT and CPK were within normal limits and she could raise her arms above her head. Continued muscle improvement has occurred with reduction of prednisolone to 30 mg/day and physical therapy.

B. Group II. Polymyositis With Significant Skin Changes or Features of Another Associated Rheumatic Disorder (major problem still the muscle disease).

Barwick & Walton (2)	Ziff et al
16 [2]*	1

Case 3. [redacted]. This 53 CF was admitted on [redacted]-68 with a 15-month history of severe weakness of the proximal muscles of upper and lower extremities. A butterfly rash was present. No previous steroid therapy had been given. The severe weakness had been accompanied by mild polyarthritis. Laboratory evaluation showed VDRL +, ANF = 3+, Latex fixation = 1+, ESR = 100, L.E. prep = one positive, one negative, A/G = 3.0/6.1 gm%, SGOT = 134, CPK = 5.2, Aldolase = 8.1. She was begun on 60 mg prednisolone/day with drop in SGOT to 76, but without further drop on continued therapy. Some subjective increase in muscle strength has been reported by the patient, but this is minimal at best. Renal work-up normal thus far.

C. Group III. Florid Dermatomyositis or Severe Associated Rheumatic Disease With *Less* Striking Muscle Disease.

Barwick & Walton (2)	Ziff et al
14 [1]*	10

Case 4. [redacted] This 17 CF developed severe proximal muscle weakness after having had well-documented SLE for 1.5 years. Renal disease, seizures, psychosis, fever, polyarthritis, skin rash, infections and steroid induced diabetes mellitus were present before the abrupt onset of progressive proximal muscle weakness and pain in the thigh muscles. Dysphagia and inability to lift her head from the pillow were present at the time of hospitalization on [redacted]-67, when SGOT = 108, CPK = 2.2, Aldolase = 2.7. EMG was positive for polymyositis. ANF = 2+, ESR = 47, WBC = 2100, stool guaiac = 4+, urine protein 300 mg%. Muscle biopsy in an area of tenderness, however, was normal.

After therapy with 30 mg of prednisolone and 2 mg/kg of cyclophosphamide/day the WBC dropped to 1200/mm^3 and cyclophosphamide was stopped. On 60 mg prednisolone/day she had rapid return of muscle strength and serum enzymes to normal. Continued improvement has persisted although steroids have been tapered to 15 mg/day.

D. Group IV. Carcinomatous Myopathy.

Barwick & Walton (2)	Ziff et al
[6]*	[1]*

Case 5. [redacted]. This 60 WM was admitted on [redacted]-60 with a 3-year history of atrophy and muscle tenderness of the proximal, spinal and cervico-facial muscles. He had a chronic erythematous rash on the fingers attributed by the patient to "metal allergy."

Deltoid muscle biopsy was normal as was the SGOT determination. EMG showed myopathy and neuropathy and ankle jerks were considered hyperactive. Laryngoscopy showed a carcinoma of the larynx which was removed at laryngectomy. Past history included intermittent heavy alcohol intake. He was seen one year later without evidence of metastasis and with no complaints of muscle tenderness. No comment was made regarding muscle strength or atrophy, and he has since been lost to follow-up.

II. Clinical Findings in Acute Polymyositis.

A. Table I. Analysis of Some Clinical Signs and Symptoms in 100 Cases of Poly- and Dermatomyositis (4) and Our 36 Patients

	Eaton (41 cases)	Walton & Adams (40 cases)	Pearson & Rose (19 cases)	Total affected of 100 cases	Ziff (et al) %
Cutaneous features	22	23	16	61	58
Raynaud's phenomenon	10	10	2	22	19
Arthritic or rheumatic features	10	10	10	30	42
Muscular pain or tenderness	18	16	14	48	20
Muscular atrophy	19	?	15	34	36
Muscular contractures	11	8	14	33	--
Muscular weakness:					
Proximal muscles	38	40	19	97	97
Distal "	24	14	6	44	11
Neck "	14	33	15	62	--
Dysphagia	22	21	14	57	31
Facial "	5	5	1	11	3

B. Urinary and Serum Enzyme Changes

Table II. Urinary Creatine and Creatinine (22)

Urinary Creatine	Patients		
	Pediatric (17)	Adult (35)	Total (52)
mg/24 hr		No.	
0-100	2	1	3
100-303	9	4	13
301-500	1	8	9
501-1000	2	11	13
Over 1000	3	11	14
mg/kg/24 hr			
0-2.2	2	1	3
2.2-13	7	20	27
13.2-24	7	9	16
24.2-33	1	3	4
Over 33	0	2	2

Urinary Creatinine	Men	Women
	g/24 hr	
Normal adult mean value	1.90	1.20
Our patients (21 men, 12 women)--mean value	0.86	0.61
Range:	0.56-1.44	0.24-1.02

Table III. SGOT Values in 25 Patients During Hospitalization (22)

SGOT, units	37	41-100	101-200	201-500	501-700
Number of patients	2	7	10	4	2

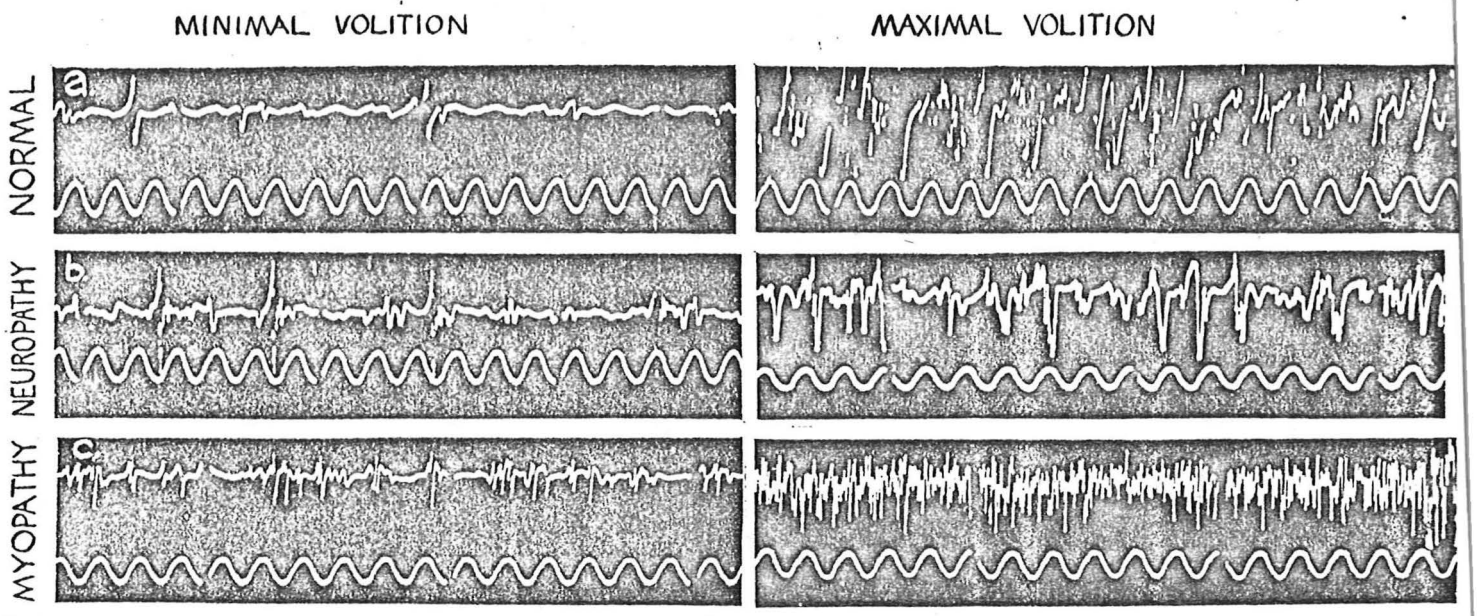
Serum aldolase and creatine phosphokinase (CPK) are also consistently elevated above their normal values of 2.5 and 1.0 units, respectively (6, 8, 9). Earlier belief that the CPK reflected muscle disease exclusively while other enzymes were derived from many tissues has been shown to be false by Perkoff (10) who demonstrated significant CPK in lung tissues and in serum after pneumonia or pulmonary infarction.

C. Electromyographic changes. An electromyogram should be done in all suspected patients.

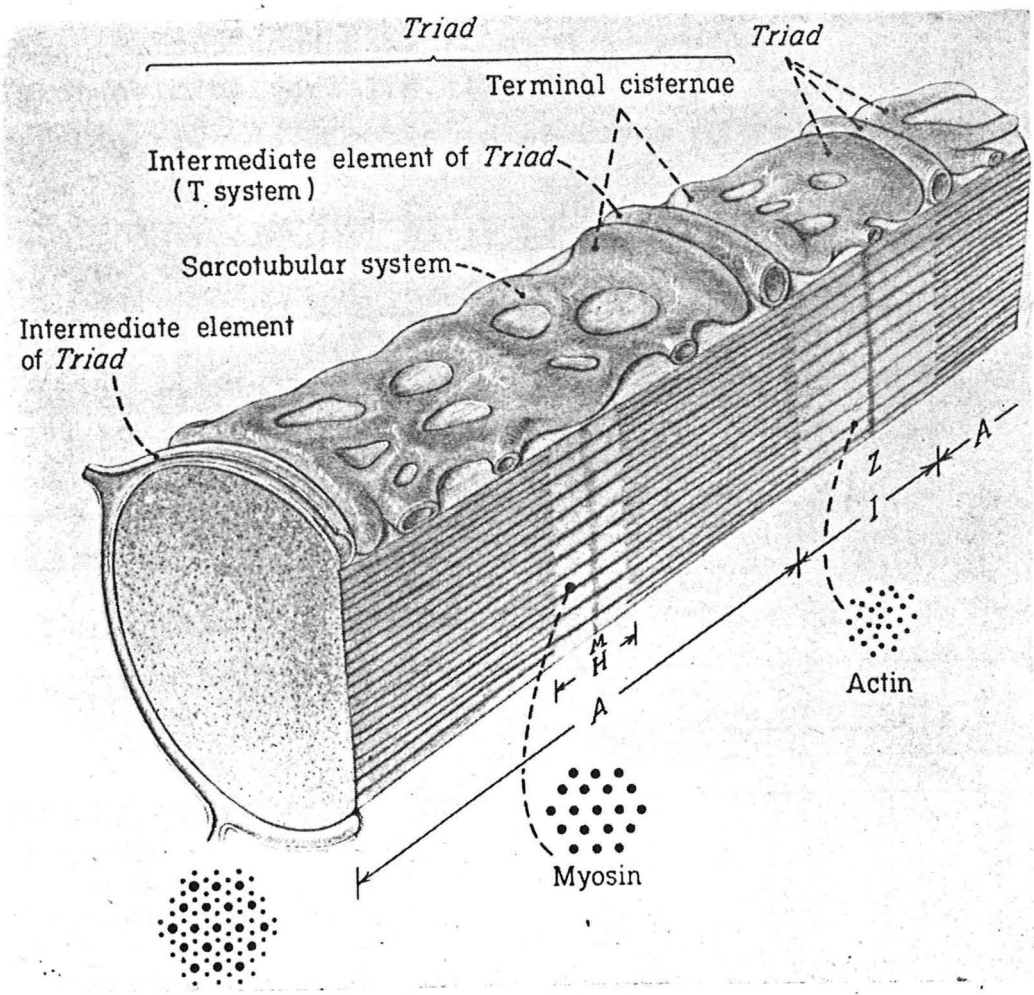
Table IV. Differential Findings of EMG in Normal and Diseased Muscle (Courtesy of Dr. A.D. Raptou)

Muscles	Insertional Activity (Pos.waves)	Fibrillation	Fasciculation	Motor Unit Action Potentials
Normal	Normal	None	None	Normal no. (50/sec), amplitude (2-4 m volts), and duration (9 m-sec).
Neuropathic				
Periph. Neuropath.	2+	2+	0	Decreased no. Increased amplitude
ALS	1-4+	1-4+	+	Increased duration
Myopathic				
Musc. Dystrophy	1-2+	1-2+	0	Increased no. Decreased amplitude Decreased duration
Polymyositis	3-4+	3-4+	0	Same as Musc. Dystrophy but greater no. firing and smaller amplitude

EMG Patterns in Normal and Diseased Muscle (Richardson Ref. 11)



Minimal and maximal volition in a. normal muscle; b. neuropathy; c. myopathy. Calibration 50 cycles at 300μV.



Schematic illustration of a muscle myofibril (From Peter [23]).

D. Muscle Biopsy. Findings diagnostic of polymyositis were found in 34 of 54 patients studied by Walton (46) but were minimal or non-specific in the remaining 20 patients.

Table V. Variability of Findings on Muscle Biopsy (22) in 60 Patients

Findings	Number of Patients
Perivascular infiltration	33
Infiltration in or around muscle fibers	21
Degeneration of muscle fibers	30
Necrosis of muscle fibers	17
Atrophy of muscle fibers	19
Proliferation of muscle nuclei	17
Calcification	4

E. Unusual complications of polymyositis
1. Myocarditis, pericarditis and arrhythmias (15)
2. Amyloidosis (16)
3. Pulmonary fibrosis (17, 18)

III. Late Developments and Prognosis

A. Calcinosis universalis (19, 20)

Table VI. Calcinosis in 15 Cases of Polymyositis (6)

Age at Onset of Polymyositis, Yr	Patients Having Calcinosis		
		Sex	
	No.	Male	Female
0 to 9	5	2	3
10 to 19	3	1	2
20 to 29	2	0	2
30 to 39	1	0	1
40 to 49	2	0	2
>50	2	0	2

B. Muscle and skin residua

Table VII. Physical Findings on Follow-up of 37 Surviving Patients (22)

Physical Findings	Age of Onset, Yr				Total Number of Cases
	1-14	15-30	31-40	Over 41	
	No.				
Subcutaneous calcifications	8	0	0	3	11
Skin atrophy	7	1	4	2	14
Skin scarring	5	1	2	2	10
Skin pigment changes	3	1	2	2	8
Skin itching	0	2	1	2	5
Skin sun-sensitivity	0	1	1	0	2
Muscle atrophy	8	3	5	4	20
Contractures	6	2	1	2	11
Ankylosis	2	0	0	1	3
Raynaud's phenomenon	2	2	0	3	7

C. Prognosis. In the 36 patients seen by the SWMS Rheumatic Diseases Unit from 1959-1968, 10 are known to have died. However insufficient duration of disease and loss to follow-up may contribute to a worse prognosis than this would suggest. In the series of Logan et al (22) of 63 patients there were 26 deaths, 9 within one year of onset of the initial muscle weakness and the remainder within 4 years.

Table VIII. Survival by Age of Onset (22)

Patients	Age of Onset, Yr		
	0-20	21-40	41+
Total number	25	14	24
Number surviving	20	9	8
Percentage surviving	80	62.3	33.3

Table IX. Status of 37 Surviving Patients (22)

Patient Status	Age of Onset, Yr.				Total Number of Patients
	1-14	15-30	31-40	Over 41	
	No.				
Recovered (functionally)	11	3	2	3	19
Active disease	1	2	3	2	8
Disabled	5	0	2	3	10
Total patients surviving	17	5	7	8	37

Table X. Cases of Polymyositis Terminating Fatally (2)

Case No.	Age at Death (yr.)	Sex	Immediate Cause of Death	Duration of Muscle Disease Prior to Death (yr.)	Other Significant Postmortem Findings
2	50	M	Bronchopneumonia	4-1/2	Bronchogenic carcinoma
3	60	M	Bronchopneumonia	8/12	No evidence of malignancy
4	55	M	Staphylococcal pneumonia	1	No evidence of malignancy
6	57	M	Bronchopneumonia	3	Bronchogenic carcinoma
25	51	F	Bronchopneumonia	6/12	Carcinoma of pancreas
29	61	M	Bronchopneumonia, respiratory paralysis	1-9/12	Carcinoma of esophagus
32	41	F	Pulmonary embolism	2	No evidence of malignancy
35	46	F	Bronchopneumonia, chronic urinary infection	2-1/2	No evidence of malignancy
37	68	F	Bronchopneumonia	6/12	No evidence of malignancy

IV. Differential Diagnosis

A. Table XI. Classification of Myopathies (23)

I. Dystrophic Myopathies

A. Duchenne's (24)
B. Limb-girdle (25)
C. Facioscapulohumeral (26)
D. Distal (27)
E. Ocular

II. Myotonic Syndrome

A. Myotonic muscular dystrophy (28)
B. Congenital myotonia
C. Paramyotonia
D. Drug-induced myotonia
E. "Pseudomyotonia"
   Hypothyroidism (29)
   Polymyositis
   Chronic denervation

III. Inflammatory Myopathies

A. Known etiology
 1. Bacterial (30)
 2. Fungal
 3. Parasitic (31)
 4. Viral
B. Unknown etiology
 1. Polymyositis syndrome
  a. With skin manifestations (dermatomyositis)
  b. With connective tissue disorders (32)
  c. With neoplasm (33)
  d. With Sjögren's syndrome
 2. Sarcoidosis (34)

IV. The Periodic Paralyses

A. Primary
 1. Hyperkalemic (35)
 2. Hypokalemic
 3. Normokalemic
B. Secondary
 1. With hyperthyroidism
 2. With renal disease
 3. With hyperaldosteronism

V. Myoglobinuric Myopathies

A. Idiopathic
B. Stress-induced
C. With polymyositis
D. With McArdle's disease
E. With alcoholism
F. With trauma
G. With vascular insufficiency

VI. Endocrine Myopathies

A. Thyroid (36)
B. Parathyroid (37)
C. Adrenal
D. Pituitary

VII. Congenital Myopathies

A. Z-band (nemaline)
B. Central-core disease
C. Mitochondrial myopathies
D. "Myotubular" myopathy (38)
E. Dystrophic (arthrogryposis multiplex)
F. Unclassified

VIII. Defects in Carbohydrate Metabolism

A. Myophosphorylase deficiency (McArdle's disease)
B. Acid alpha-1, 4-glucosidase deficiency
C. Branching enzyme deficiency (amylo-1, 4-1, 6-transglucosidase)
D. Debranching enzyme deficiency (amylo-1, 6-glucosidase)
E. Phosphohexoisomerase deficiency
F. Phosphofructokinase deficiency
G. Phosphoglucomutase deficiency

IX. "Toxic" Myopathies

A. Deficiency states
 1. Tocopherol
 2. Postgastrectomy
B. Exogenous toxins
 1. Steroids (39)
 2. Chloroquine (40)
 3. Alcohol (41)

X. Miscellaneous

A. Amyloid (16)
B. Myositis ossificans (42)
C. Myasthenic myopathy (43)
D. Neuromyositis (44)

B. Summary of ultimate diagnoses in 9 patients seen at Parkland with muscle pain or weakness who did not have polymyositis 1959-1968.

1. Toxic alcoholic myopathy - 4 patients
2. Trichinosis } one
3. Steroid-induced } patient
4. Primary amyloidosis } each
5. Amyotrophic lateral sclerosis
6. Undiagnosed

V. Treatment of Polymyositis Syndromes

A. Steroids (45, 46) in doses of 60-80 mg of prednisolone equivalent/day produce improvement in 75% or more patients.

Table XII. A comparison of the outcome in adequately treated patients in Groups I and II of the present series with the results in a group of patients with dermatomyositis not treated with steroids (46)

	Total No. of Cases Followed	Patients Virtually Recovered	Patients With Residual Static Disability	Continued Deterioration at Time of Study	Died	Too Recent To Assess
O'Leary and Waisman, 1940	38	10%	18%	16%	50%	5%
Rose and Walton, 1965: Adequately treated cases in Groups I and II	51	58%	22%	0	14%	6%

Table XIII. The incidence of relapses after reduction or withdrawal of steroid therapy in patients who improved after its reinstitution (46)

Group	Total Number of Patients	Total Number Adequately Treated	Total Number of Relapses	Duration of Steroid Therapy Before Relapse				Mean Duration of Steroid Therapy in Survivors
				2-6 mos.	7-12 mos.	13-24 mos.	25-36 mos.	
I	33	32	15	4	6	1	1*	3 years
II	25	18	6	3	0	2		2.8 years
III	17	17	5	1	2	1	1*	3.2 years
IV	14	8	1		1			6 months
Total	89	75	27	8	9	4	2	

*Deteriorated despite adequate maintenance therapy

B. Antimetabolites and Immunosuppressants

The experience with methotrexate was encouraging in three patients in whom steroids had failed to produce clinical remission of polyarteritis (48). However, total experience with the antimetabolic agents is very limited in these syndromes. Antilymphocyte serum (49) has produced remission in two patients with the disease.

VI. Consideration of Etiologic Factors

A. Autoimmunity

Table XIV. Serum Antibodies to Muscle Components in Polymyositis Compared to Other Muscle Diseases and Normal Controls (50)

Group	Antimyosin Antibody*		Antinuclear Factor†	
	No. Tested	No. Positive	No. Tested	No. Positive
Polymyositis	25	12	23	9
Muscular dystrophies	27	12	23	3
Neurogenic muscular atrophy	24	13	24	7
Controls	76	36	41	0

*Tanned Rbc method
†Fluorescent antibody method

Association of thymoma, circulating muscle antibodies and polymyositis has been noted occasionally (51).

In addition, cross-reactivity of an antigen in voluntary muscle, saliva, andsmooth muscle with an antigen in β-hemolytic streptococci has recently been observed (52).

B. Infectious Aspects. The recent observation by Chou (54) of myxovirus-like structures in muscle from a patient with chronic polymyositis has stimulated other electromicroscopic studies of muscle from patients with polymyositis.

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